# EFC6193 STUDY

## CASE REPORT FORM



# SCREEN FAILURE

A RANDOMIZED, OPEN LABEL MULTI-CENTER STUDY OF XRP6258 AT 25 MG/M<sup>2</sup> IN COMBINATION WITH PREDNISONE EVERY 3 WEEKS COMPARED TO MITOXANTRONE IN COMBINATION WITH PREDNISONE FOR THE TREATMENT OF HORMONE REFRACTORY METASTATIC PROSTATE CANCER PREVIOUSLY TREATED WITH A TAXOTERE®-CONTAINING REGIMEN

Country number:	Centre number:	
SUBJECT NUMBER:	Subject initials:	

XRP6258 EFC6193	Country No.	Centre No	o. Subject No.	NO	<b>1</b> Page
SCREEN FAILU	RE V 00		Date of visit:		month year
	See Page	12			_
DEMOGRA	PHY				DEMOG_1
<ul><li>Date of consent:</li><li>Date of birth:</li></ul>	day month	year year			
• Sex:	Male	V			
• Race:	Caucasian Black Asian, Oriental Other		f Other, specify:		

XRP6258 NO EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	17 Page		
BASELINE	V 00	See Pag			. age		,
INCLUSION CR	ITERIA					CRIT_1	
The Patient must have:						YES	No
1. Diagnosis of histologically refractory to hormone the regimen. Patient must have months after prior hormor Taxotere®-containing there	rapy and previous ve documented per therapy and dis rapies	sly treated rogression sease prog	with a Taxote of disease du ression during	re®-contai ring or with or after	ning nin 6		0
<ol> <li>Patient must have either non-Patient with measurable disease demonstrating at least one visces must measure at least 10 mm in scan or MRI (chest, abdomen, proclearly defined lung lesion surrollesion, and bone lesions will be Patient with non-measurable of lesion. [Rising PSA is defined as reference value (measure 1) take taken at least 7 days after the reterence level) to be greated the 2nd measure. If this is not the measure. The third (or the fourth 3. Received prior castration (LH-RH) agonist with or westramustine, or other hor mandatory. However, if the last antiandrogen withdrawal (LH-RH agonist treatment Chlormadinone acetate or while bicalutamide must be evaluation.) (* The antian stopping an antiandrogen this occurs because the an which is allowing the antian inhibit it)</li></ol>	see must have docume eral or soft tissue meta in the longest diameter pelvis) or 20 mm on counded by aerated lunger considered non-mealisease must have documen at least two consecumen at least two consecumen at least one week afterence value. A third in the second mene case, a fourth PSA in confirmatory PSA is by orchiectomy a without antiandroge monal agents. (A the patient has been administration of syndrome* should continue or flutamide must be a chormace and the confirmatory of	ented progressastatic lesion or (or two times conventional ing. (Previous asurable disecumented risultive rises in apart. The find confirmato easure and it measure is reshould be takend/or Lutengen, antiand a prior treated antiandro dibe confinduring the nave been diat least (all syndroridinone accentioned a restricted anduced a rulate prosti	sion of disease be (including new less the slice thicknown or CT or Chest X-rally irradiated lesionses). Sing PSA levels or PSA to be documented by PSA measure in must be obtained equired to be taken within 4 week inizing Hormodorgen withdrament by antial with antiandrogens, presence med prior to be study treatmented by weeks prior me is a decrea etate, flutamid mutation in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the late cancer grown of the study treatmented in the study treatment	y RECIST critication. This less) on spirally for biopsy prons, primary primary primary prons, primary	lesion I CT proven, prostate of new Ild be Id beyond ys after eater than domizati ng Hor otherap not PSA is ee of ntry).  prior to PSA een upon itamide, recepto than	the 2nd ion] mone by with	
4. Life expectancy > 2 mont	hs						
5. Eastern Cooperative Onco	ology Group (ECC	OG) perfori	nance status (	) - 2			
6. Age ≥ 18 years							
IF THE ANSWER TO ANY	OF THE INCLUSION CR	ITERIA IS NO	, THE SUBJECT IS	NOT ELIGIB	LE FOR TI	HE STUDY.	
NO 17			XRP6258	FF	C6193		
Confidential ■ FINAL	■ 21-Nov-2006	<u> </u>		nofi ave			

XRP6258 EFC6193				NO	18	
BASELINE	V 00	Centre No.	Subject No.	1	Page	
EXCLUSION CF	RITERIA				CRIT_2	
<ol> <li>Previous treatment with m</li> <li>Prior radiotherapy to ≥ 40</li> <li>Prior surgery, radiation, chweeks prior to enrollment</li> <li>Active secondary cancer i disease-free for ≤ 5 years (cancer before 4 weeks priors.</li> <li>Known brain or leptomen</li> <li>History of severe hyperser drugs</li></ol>	% of bone mademotherapy, of in the study in the study including prior However, adeor to entry care ingeal involve astitivity reaction in the study reactio	or other anti-or other anti-or other anti-or malignancy equately treaten be eligible to ment	cancer therapy from which the d superficial be o the study) to polysorbate or intolerance	within 4 e patient ha basal cell ski	s been in	<u>&gt;</u>
<ul> <li>ALT (SGPT) ≥ 1.5 x ULN</li> <li>Creatinine ≥ 1.5 x ULN</li> <li>10. Uncontrolled cardiac arrh</li> </ul>	l ythmias, angir	na pectoris, ai		sion. Histor	y of	
congestive heart failure, o allowed	,				ot 	
<ul> <li>11. Left ventricular ejection from (MUGA) scan or echocard</li> <li>12. Uncontrolled diabetes me</li> <li>13. Active uncontrolled Gastro</li> <li>14. Active infection requiring</li> <li>15. Participation in another claprior to study enrollment</li> <li>16. Concurrent or planned tree (A one-week washout period treatments)</li></ul>	liogram	Reflux Disease Diotic or anti-f h any investig trong inhibitory for patients	e (GERD) fungal medicat gational drug v	vithin 30 da	ys □	
IF THE ANSWER TO ANY OF THE EXC	LUSION CRITERIA IS		ECT IS NOT ELIGI		STUDY.	
NO 18	ı		XRP6258	, EFC	6193	

FC6193	Country No. Centre No. Subject No. Page
CREEN FAILURE	V 99 See Page 474
ND OF STUI	<b>DY</b> 0.ENDST_1
	-
Date of end of study*:	day month year
Main reason for stoppin	ng trial (tick one box only):
Completed follow-u	up period
☐ Death**	
Poor compliance to	o protocol
☐ Subject request, spe	ecify:
☐ Subject lost to follo	w-up
☐ Other reason, speci	fy:
	case of patient lost to follow-up
Date of last contact in In case of Death, comp	·
	·
In case of Death, comp	·
In case of Death, comp "I, the undersigned, cer To the best of my know	tify that I have carefully examined all entries on the CRF for this subject.
In case of Death, comp "I, the undersigned, cer To the best of my know	tify that I have carefully examined all entries on the CRF for this subject. vledge, all information is correct."
In case of Death, comp "I, the undersigned, cer To the best of my know	tify that I have carefully examined all entries on the CRF for this subject. vledge, all information is correct."

XRP6258 EFC6193	Country No. Cen	tre No.   Subje	Ct No.	699 Page	
Visit 99	v 99 🗆		See Page 62		
ADVERSE EVI	ENT FORM			0.1_AE_1	
☐ NONE					
1.	AE form no:	  -	AE fo	ırm no: ШШ-ШL	]
ADVERSE EVENT	AE ref. no:	-L  L	AE ref	. no:       -	
Diagnosis					
2. STATUS OF AE		nonth year	1 Date of start:	day month	JLJLJ year
2= Ongoing from previous period without change	2 (do not complete the remaining	,	2 🔲 (do not com	pplete the remaining items in	
3= Ongoing with change	3 🗖		3 🗖		
3. GRADE (1 - 4)	1 🔲 2 🔲 3	4 🗆	1 🗖 2	3 🗆	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes	□ No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red			nanently discontinued / 2= De 4= Delayed and reduced / 5=	
	0 0 1 0 2 0 3 0	4 🔲 5 🔲	0 🔲 1 🔲	2 🔲 3 🔲 4 🔲	5 🗖
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes	□ No	
7. OUTCOME 1= Recovered	1 <b>□ )</b> Date: └ └ └	ponth war	1 <b>D</b> Date:	LJLJ LJLJ L	
4= Recovered with sequelae	1 Date: LL L day Specify sequelae:		4 🗆 🕽 Specify	y sequelae:	
2= Recovering	2 🗖		2 🗖		
3= Not recovered	3 🗖		3 🗖		
5= Fatal (complete the death report form) 6= Unknown	5  Date of death:	nonth year	5 ☐ Date of de 6 ☐	ath:	year
8. SERIOUSNESS	Yes 🗖	No 🔲		□ No	
CRITERIA	- Date event be	came serious:	[	- Date event became ser	
IF YES, COMPLETE THIS SECTION AND THE <b>SAE</b> COMPLEMENTARY	⇒ IF YES	year	⇒ IF YES {	day month	J L J L J year
FORM	- Tick below al	criteria that apply:	(	- Tick below all criteria	that apply:
	Resulting in death			eath	
	Life-threatening	Life-threatening			
	Persistent/significant disability/i	Persistent/sign	ificant disability/incapacity	🗖	
	Congenital anomaly/birth defection Other medically important eve			omaly/birth defect Ily important event	
Investigator's name, date of repo			L	ne, date of receipt:	<del></del>
* Is there a reasonable	possibility that the AE was caus	ed by study treatmer	nt?		
		VDDear	50	EEC6102	
XT 699		XRP62	) <sub> </sub>	EFC6193	

2			
ADVERSE EVENT FORM  AF form no:		Country No. Centre No. Subje	
AF from no:	VISIT 99	v 99	ee Page 62
ADVERSE EVENT DIAGNOSSIS  AE fort no:	ADVERSE EV	ENT FORM	O.1_AE_1
Seriousness   Carteria   Seriousness   Congenita anomalybinth defect   Seriousness   Serio	Adverse Event		
4. Relationship to Study Treatment*  Yes   No   De None   1= Permanently discontinued   2= Delayed   3= Dose reduced   4= Delayed and reduced   5= Interrupted   3= Dose reduced   4= Delayed and reduced   5= Interrupted   3= Dose reduced   4= Delayed and reduced   5= Interrupted   3= Dose reduced   4= Delayed and reduced   5= Interrupted   3= Dose reduced   4= Delayed and reduced   5= Interrupted   3= Dose reduced   4= Delayed and reduced   5= Interrupted   3= Dose reduced   4= Delayed and reduced   5= Interrupted   3= Dose reduced   4= Delayed and reduced   5= Interrupted   5=	1= New 2= Ongoing from previous period without change	day month year  2   (do not complete the remaining items in the column)	2  (do not complete the remaining items in the column)
5. ACTION TAKEN WITH STUDY TREATMENT  0 = None / 1 = Permanently discontinued / 2 = Delayed 3 = Dose reduced / 4 = Delayed and reduced / 5 = Interrupted 3 = Dose reduced / 4 = Delayed and reduced / 5 = Interrupted 3 = Dose reduced / 4 = Delayed and reduced / 5 = Interrupted 3 = Dose reduced / 4 = Delayed and reduced / 5 = Interrupted 3 = Dose reduced / 4 = Delayed and reduced / 5 = Interrupted 4 = Secovered 4 = Recovered 4 = Recovered 4 = Recovered with sequelae 2 = Recovered 4 = Recovered 5 = Fatal (complete the death report form) 6 = Unknown  8. Seriousness CRITERIA IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM  Yes  No  Ves  No  Date of death:	3. GRADE (1 - 4)	1	1
ACTION TAKEN WITH STUDY TREATMENT    3 = Dose reduced   4 = Delayed and reduced   5 = Interrupted     0	4. RELATIONSHIP TO STUDY TREATMENT*	Yes No No	Yes No 🗆
7. Outcome 1 = Recovered 4 = Recovered 4 = Recovered with sequelae 2 = Recovering 3 = Not recovered 5 = Fatal (complete the death report form) 6 = Unknown 6 = Unknown  8. Seriousness Criteria If Yes, complete this section AND THE SAE COMPLEMENTARY FORM  Possibly in death Life-threatening Requiring/prolonging hospitalization Persistent/significant disability/incapacity Other medically important event    Date: day month year	ACTION TAKEN WITH	3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	3= Dose reduced / 4= Delayed and reduced / 5= Interrupted
Date:   Date	6. CORRECTIVE TREATMENT/THERAPY	Yes  No	Yes  No
CRITERIA   FYES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM   SAE COMPLEMENTARY FORM   Complete the section of the same serious:    FYES   Complete the section of the same serious:   Complete the section of the section	1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered 5= Fatal (complete the death report form)	4  Specify sequelae:	day month year  Specify sequelae:
Life-threatening Life-threatening Life-threatening Life-threatening Life-threatening Requiring/prolonging hospitalization Requiring/prolonging hospitalization Persistent/significant disability/incapacity Persistent/significant disability/incapacity	CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	→ IF YES - Date event became serious:	→ IF YES   - Date event became serious:    □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
		Life-threatening	Life-threatening
			·

XT 699 , XRP6258 , EFC6193

XRP6258 EFC6193			XT	631	0 1
Visit 99	V 99 Centre			Page	
	NOT SUBN	MITTED			
SAE COMPLEM	ENTARY FO	DRM 1/2	O.SAEC	<u>-</u> 1	
AE FORM No.:	1				
1. DEMOGRAPHIC INFORMA	TION	Race:			
Date of birth:	h year	Asian, Oriental	☐ ☐ other, spe	Black Other <i>cify:</i>	
Sex: male ☑	female 🔲	Height: 📖 🗀 cr	n Weig	sht: ШШШ	. Ш kg
<b>4. STUDY TREATMENT</b> First administration of study t					
	t Administration Before SAE	Last dosage Before SAE	Action taken*	New Do	
,	month year	☐☐☐ mg/m²/cycl	е Ц		mg/m²/cvcle
		☐☐☐ mg/m²/cycle			
Prednisone LLL L * 0 = None 1 = Permanently disc	continued 2 = Delayed	mg 3 = Dose reduced 4	= Delayed/	/reduced 5 =	mg Interrupted
5. IN CASE OF HOSPITALIZAT	ION hospital report to be s	sent			
Date of admission:	month year				
6. IN CASE OF DEATH Aut	opsy report:	Yes (copy to be sent	t)	No 🗖	

XRP6258 EFC6193	Country No	. Centr	e No.   Subject No	XT	632 Page	01
VISIT 99	V 99	,	initials	'		
	N(	OT SUBN	MITTED			_
SAE COMP	LEMENTA	RY FO	DRM 2	1 <b>2</b> 0.SA	4 <i>EC_1.1</i>	
7. CORRECTIVE TR	EATMENT/THERAF	Υ				
				(Relevan	t CRF page	can be faxed)
8. PREVIOUS AND	CONCOMITANT A	MEDICATION	ONS:			
9. RELEVANT MEDIC	CAL HISTORY AND	D CONCO	MITANT DISFAS		t CRF page	can be faxed)
OF RELEVANOR MEDI	CAE IIISI CAE ATA	CONCO	WITH BISENS	<b>L</b> 3.		
				(Relevan	t CRF page	can be faxed)
<b>10. STATUS OF TH</b> Is this SAE related to		an cor?	Yes 🔲 No [	7 Unkno	<b>П</b>	
If Yes: Local	Lymph nodes		Peritoneum		Brain	
Liver $\Box$	Bone		Lung			
Other 🗖						
<u> </u>	32		XRP6258	, Е	EFC6193	_
	■ FINIAL ■ 17 OCT	2006		anofi a		

XRP6258 EFC6193	Country No. Ce	entre No. Subject No.	XT	641 0 1
VISIT 99		ect initials		
SAE FOLLOW	NOT SUB I-UP FORM	O.SAEF_1		_
Provide T	HE SPONSOR BY FAX INCLUDING AE	WITH ALL ADDITIO	NAL INFOR	MATION
AE FORM NO.:				
1. SERIOUS ADVERS	SE EVENT (diagnosis):			
2. DATE OF THE EV	ALUATION: Light Light	month year		
3. NEW RELEVANT	NFORMATION ADDE	D TO INITIAL REPO	RT(S):	
Investigator's name, date of	report and signature:	Monitoring represe	entative's nan	ne, date of receipt:
<u> </u>				

641

EFC6193

# EFC6193 STUDY

## CASE REPORT FORM



A RANDOMIZED, OPEN LABEL MULTI-CENTER STUDY OF XRP6258 AT 25 MG/m<sup>2</sup> IN COMBINATION WITH PREDNISONE EVERY 3 WEEKS COMPARED TO MITOXANTRONE IN COMBINATION WITH PREDNISONE FOR THE TREATMENT OF HORMONE REFRACTORY METASTATIC PROSTATE CANCER PREVIOUSLY TREATED WITH A TAXOTERE®-CONTAINING REGIMEN

Country number:	Centre number:	
Subject number:	Subject initials:	

XRP6258 EFC6193	Country No.	Centre	No. Subject N	NO o.	<b>1</b> Page	
BASELINE	V 00		Date of v	isit: day	/ DDD / DD	ear
						_
DEMOGRA	PHY				DEMOG_1	
• Date of consent:		year				
• Date of birth:		⊥  year				
• Sex:	Male	$\checkmark$				
• Race:	Caucasian Black Asian, Oriental Other		If Other, specify:			

XRP6258 NO EFC6193

XRP6258 EFC6193  Country No. Centry	NO 2 Subject No.   Page
BASELINE V 00	
CANCER DIAGNOSIS	O.MALIGN_1
Date of initial diagnosis: LL LL LL LL Lday month	J L J L J year
PRIMARY SITE (TICK ONLY ONE)	
✓ 18 Prostate	
INITIAL PATHOLOGY CELL TYPE	
✓ Adenocarcinoma	
EXTENT AT STUDY ENTRY	
	co regional recurrence
GRADE  ☐ Unknown ☐ Poorly difference ☐ Description	unti ata d
☐ Unknown ☐ Poorly difference ☐ Moderately differentiated ☐ Well difference	
Staging at Diagnosis	Stage at Diagnosis
T	☐ Stage I ☐
	☐ Stage II ☐
N	☐ Stage III ☐
M L	☐ Stage IV ☐

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	3 Page	
BASELINE	V 00					

# PRIOR ANTI-CANCER SURGERIES EXCLUDING O.SURGERY\_1 BIOPSY

☐ NONE

	Date		Describe Procedure
	Day Month	Year	
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

NO	3 ,	XRP6258	EFC6193
		50	nosi aventis

## 1 INTENT:

1 - Neoadjuvant

2 - Adjuvant

3 - Advanced

#### <sup>2</sup> Reason for Discontinuation:

5 - Adverse Event

8 - Subject lost to follow-up

10 - Subject Request

12 - Disease Progression

14 - Completed Treatment

99 - Other

#### <sup>3</sup> BEST RESPONSE:

CR - Complete Response

PR - Partial Response

PD - Progressive Disease

SD - Stable Disease

UNK - Unknown

NA - Not Applicable

NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	<b>4</b> Page	01
BASELINE	V 00					

PRIOR ANTI-CANCER THERAPY						
☐ NONE						
Intent: <sup>1</sup>						
Reason for Discontinuation: <sup>2</sup>						
If other, specify:						
D.						
Relapse / Progression Date:	day month year					
Best Response∙ <sup>3</sup>						

ġ	Drug per Regimen	CUMULATIVE	Unit		START E	Оате		End D	ATE
REGIMEN NO.		Dose		DAY	MONTH	YEAR	DAY	MONTH	YEAR
R									
	1			ШШ			шш		
	2								
1.									
	3								
	4								
	5								

XT	4		XRP6258	EFC6193
Confide	ntial ■ FINIAL ■ 2	1-NOV-2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	<b>4</b> Page	02
BASELINE	v 00	See	Page 16			

PRIOR ANTI-CANCER	RTHERAPY	O.MED_3
Intent: <sup>1</sup>		
Reason for Discontinuation: <sup>2</sup> If other, <i>specify:</i>		
Relapse / Progression Date:	day month year	
Best Response: <sup>3</sup>		

ġ	Drug per Regimen	CUMULATIVE	Unit		Start I	Оате		END D	DATE
Ā		Dose		DAY	MONTH	YEAR	DAY	MONTH	YEAR
REGIMEN NO.									
	1			шш					
	2			ШШ					
2.	3								الالالالالا
	4				1 11 11			1 11 11	1 1 11 11 11 1
	5								

XT	4	, XRP6258	B EFC6193
Confidor	tiol ■ FINIAL ■ 21	76	sanofi aventis

BASELINE	V 00	See F	Page 16			
EFC0193	Country No.	Centre No.	Subject No.	I	Page	
XRP6258 EFC6193				XT	4	03

PRIOR ANTI-CANCER	R THERAPY	O.MED_3
Intent:1		
Reason for Discontinuation: <sup>2</sup> If other, <i>specify:</i>		
Relapse / Progression Date:	day month year	
Best Response: <sup>3</sup>		

ó	Drug per Regimen	CUMULATIVE	Unit		Start D	АТЕ		End	Date
Z Z		Dose		DAY	MONTH	YEAR	DAY	MONTH	YEAR
REGIMEN									
	1			шш			шш		
	2			ШШ					
3.	3						l		
	4								
	5								

XT	4	I	XRP6258	_ EFC6193
Confide	ntial ■ FINAL ■ 21-NOV-2006		sai	nofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	<b>4</b> Page	
BASELINE	V 00	Sag	2age 16			

PRIOR ANTI-CANCEI	R THERAPY	O.MED_3
Intent: <sup>1</sup>		
Reason for Discontinuation: <sup>2</sup> If other, <i>specify:</i>		
Relapse / Progression Date:	day month year	
Best Response <sup>3</sup>		

ġ	Drug per Regimen	CUMULATIVE	Unit	STA	ART DAT	E		End	Date
Z		Dose		DAY MON'	ТН	YEAR	DAY	MONTH	YEAR
REGIMEN NO.									
	1				ا لــالـ			الالالا	
	2				ا لـال		шш	الالالا	
3.									
	3								
	4								
	5							ا الــالــا	

XT	4		XRP6258	_ EFC6193
Confider	tial ■ FINIAL ■ 21-N	Jov-2006	sar	nofi aventis

							_		
		START DATE  Day Month Year	STOP DATE  Day Month Year	TOTAL UNITS DOSE	LOCATION/ORGANS*	TYPE OF THERAPY	D RIO	BASI	XRP6258
Confide	N O	1		☐ Grays		☐ Palliative ☐ Curative	, , , , , , , , , , , , , , , , , , ,	BASELINE	258
ntial ■ FIN	σ	2		☐ Grays		☐ Palliative☐ Curative	RADIATION		
Confidential ■ FINAL ■ 21-NOV-2006	_	3.		☐ Grays		☐ Palliative☐ Curative	TION	<     <     Cor	_
NOV-200		4.		☐ Grays		Palliative Curative		Country No.	
5	_	5		☐ Grays		☐ Palliative☐ Curative	THERAP	Centre No	
	XRP6258	6		☐ Grays		☐ Palliative☐ Curative	<b>*</b>	_	  
sanofi aventis	_	* Indicate location/organs of ra 01 Skin 02 Muscle/Soft Tissue 03 Bone	11.01 Regional Lymph Nodes	18 Prostate	26 Pelvis 27 Periton 28 Testis	eum		Subject No.	NO NO
entis	EFC6193 -	04 Bone Marrow 05 Peripheral Blood Stream 06 Brain/CNS 07 Head/Neck 08 Esophagus 09 Breast	12 Liver 13 Stomach 14 Pancreas 15 Kidneys 16 Ovaries	20.20 Rectum 21 Adrenal 22 Mediastinum 23 Uterus 24 Abdomen 25 Gastrointestinal Tra	29 Thorax 29.01 Ple 30 Other		O.RADTX_8	Page	σı

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	6 Page	01
BASELINE	V 00					

#### PAST MEDICAL AND/OR SURGICAL HISTORY MEDHIS\_1

• Please record relevant past medical or surgical history other than the disease studied. None  $\Box$ 

	DATE OF DIAGNOSIS AND/OR INTERVENTION month year	PAST MEDICAL OR SURGICAL HISTORY	YES	RSISTENCE O TOMS (tick	
	monut yeur		113	 APPLICABLE*	
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					

<sup>\*</sup> In case of surgical history, the "Not Applicable" box for "Persistence of symptoms" must be ticked.

symptoms persist, and disease is not controlled

"yes" means: "no" means: symptoms do not persist "not applicable": use in case of surgical history

condition still persists, but is controlled (by medication for example) "disease controlled" means:

XT	6	XRP6258	EFC6193
Confide	ntial ■ FINAL ■ 21-NOV-2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	6 Page	02
BASELINE	V 00	See P	age 21			

#### PAST MEDICAL AND/OR SURGICAL HISTORY MEDHIS\_1

• Please record relevant past medical or surgical history other than the disease studied. None  $\Box$ 

	_	F DIAGNOSIS NTERVENTION year	Past medical Or surgical history	YES	RSISTENCE ( TOMS (ticl	
1					AFFLICABLE	CONTROLLED
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						

<sup>\*</sup> In case of surgical history, the "Not Applicable" box for "Persistence of symptoms" must be ticked.

symptoms persist, and disease is not controlled

"yes" means: "no" means: symptoms do not persist "not applicable": use in case of surgical history

"disease controlled" means: condition still persists, but is controlled (by medication for example)

XT	6	XRP6258	_ EFC6193
Confider	ntial ■ FINAL ■ 21-NOV-2006	sa	nofi aventis

XRP6258 EFC6193	Country No.	Centre No. Sub	bject No.	XT 6	
BASELINE	V 00	See Page 2	1		

#### PAST MEDICAL AND/OR SURGICAL HISTORY MEDHIS\_1

• Please record relevant past medical or surgical history other than the disease studied. None  $\square$ 

	Date of diagnosis and/or intervention	Past medical or surgical history			RSISTENCE C	- <del>-</del>
	month year		YES	No	Not Applicable*	DISEASE CONTROLLED
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						

<sup>\*</sup> In case of surgical history, the "Not Applicable" box for "Persistence of symptoms" must be ticked.

symptoms persist, and disease is not controlled

"yes" means: "no" means: symptoms do not persist "not applicable": use in case of surgical history

"disease controlled" means: condition still persists, but is controlled (by medication for example)

XT	6 ,	XRP6258	EFC6193
Confide	ntial ■ FINAL ■ 21-Nov-2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>7</b> Page	
BASELINE	V 00	·				

### **HEMATOLOGY**

LABH\_1

To be performed within 28 days prior to randomization.

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10º/L	
Lymphocytes		10º/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 7 XRP6258 EFC6193

(RP62 FC61		Centre No.	Subject No.	8 Page
Basi	ELINE V 00			
ВІО	CHEMISTRY			LAB
o be p	performed within 28 days prior t	o randomization.		
Date o	of sampling: 니니 니니니니			
	day month	year		
	TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT,
	Sodium		mmol/L	
	Potassium		mmol/L	
	SGOT (AST)		U/L	
	SGPT (ALT)		U/L	
	Alkaline phosphatase		U/L	
	Total bilirubin		mg/dL	
	BUN		mg/dL	
	Creatinine		mg/dL	
	Glucose		mg/dL	
	Chloride		mmol/L	
	Bicarbonate		mmol/L	
	TACTERONE			
	STOSTERONE			LAB
be p	performed within 28 days prior t	o randomization.		
Oate o	of sampling:	year		
	Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT,
- 1	Testosterone		ng/dL	

NO

8

EFC6193

XRP6258

— NO 9		, XRP6258	, EFC	0400
	PSA PSA		ng/mL	
DATE OF SAMPLING day month year	TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
The fourth confirmatory PSA sl	hould be taken PSA-1 for anno		or to randomiz	ation.
PSA - 4				LABH_1
	PSA		ng/mL	
DATE OF SAMPLING day month year	TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
·	SA-1 for anno		auys unter tile	- Incasure.
<b>PSA - 3</b> The third confirmatory PSA me	pasiire miiet ha	obtained at least 7	days after the	LABH_1
	<u> </u>			
	PSA		ng/mL	
DATE OF SAMPLING day month year	TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT,
The first rising PSA should be t  See F	aken at least 7 PSA-1 for anno		ence value.	
PSA - 2			_	LABH_1
	PSA		ng/mL	
DATE OF SAMPLING day month year	TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT,
PSA - 1				LABH_1
l				
<b>BASELINE</b> V	Country No.	Centre No.   Subject N	0.	Page
(RP6258 EFC6193			NO	9

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO 10	<b>)</b> nge	
BASELINE	V 00					
PHYSICAL EXA	AMINATIO	N		PHY	/SEXAM_1	
• Date performed: LLL day	month yea	*				
* If clinically relevant, pleas	e report on the Sigi	ns and Syn	nptoms and/or	Medical Histo	ory forms.	
VITAL SIGNS					VITAL_1	
Please record below the assessme	nt performed the close	st to first ad	ministration of st	udy drug.		
Date performed: LLL L	month year					
Height: LILL cm			We	ight: 니니스	」.	
- Blood pressure: Systol	ic LLL mm	nHg / D	Diastolic LLL	⊔⊔ mmHg		
- Heart rate:	⊔∟ beats/min					
- Temperature:	°C . ∟ . ∟		_	_		_
ECOG Performance Status	(tick appropriate bo	ox):	Oral 🗖	Rectal 🗖	Auricula	· 🔲
(	2 3	4				

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	11 Page	
BASELINE	V 00					
ECG						ECG_1
To be performed within 28 days	prior to the fir	st study drug ac	lministration.			
• Date performed: LLL L	month	year				
• ECG: Normal	A	Abnormal* 🗖				
If abnormal, specify:						

 NO
 11
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-NOV-2006

<sup>\*</sup> If clinically relevant, please report on the Signs and Symptoms and/or Medical History forms.

XRP6258 EFC6193	Country No.   Centre	No.   Subject No.	12 Page
BASELINE	V 00		
			-
ECHOCARDIC	GRAPHY		ECHOCARD_1
To be performed within 28 of NOT DONE	ays prior to the first study d	Irug administration.	
• Date performed: Light day	month year	I	
• 2D-Echocardiography:	Normal $\Box$	Abnormal* 🗖	
- Left ventricular ejection f	action (LVEF)	%	
- Lower Limit Normal of L	EF LL	%	
* If clinically relevant, p	ease report on the Signs a	nd Symptoms and/or Me	dical History forms.
* If clinically relevant, p	, c		dical History forms.  MUGA_1
RADIONUCLI To be performed within 28 o	DE VENTRICU	JLOGRAPHY	·
RADIONUCLI	<b>DE VENTRICU</b> ays prior to the first study d	JLOGRAPHY	·
RADIONUCLI To be performed within 28 of NOT DONE  • Date performed:	DE VENTRICU  ays prior to the first study of  month year	JLOGRAPHY	MUGA_1
RADIONUCLI  To be performed within 28 of NOT DONE  • Date performed: Light day  • Radionuclide Ventricular	DE VENTRICU  ays prior to the first study of  month year  graphy: Normal	JLOGRAPHY  Irug administration.  Abnormal*	MUGA_1
RADIONUCLI  To be performed within 28 of NOT DONE  • Date performed:	DE VENTRICU  ays prior to the first study of  month year  graphy: Normal  action (LVEF)	JLOGRAPHY  Irug administration.  Abnormal*	MUGA_1
RADIONUCLI  To be performed within 28 of NOT DONE □  • Date performed: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	DE VENTRICU  ays prior to the first study of  month year  graphy: Normal  action (LVEF)	Irug administration.  Abnormal*	MUGA_1

* METHOD CODES:			
1 - CT Scan	3 - MRI	5 - Scintigraphy	
2 - Spiral CT	4 - PET	7 - Ultrasound	
8 - X-Ray	10 - Physical Exam	99 - Other	
** LOCATION:			
1 - Abdominal	3 - Head	5 - Abdomen/Pelvis	
2 - Chest	4 - Pelvis	99 - Other	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	13 Page
BASELINE	V 00				

# BASELINE TUMOR EVALUATION METHOD OF O.ASSESS\_1 ASSESSMENT

Метнод*	Location** (sites)	<b>D</b> ATE Day Month Year	NORMAL	IF ABNORMAL, SPECIFY:
			۵	Tumor related Other:
				Tumor related Other:
				Tumor related Other:
				Tumor related Other:
				Tumor related Other:
				Tumor related Other:
				Tumor related Other:
99 - Other Specify:				Tumor related Other:
99 - Other Specify:				Tumor related Other:
99 - Other Specify:				Tumor related Other:

NO	13	XRP6258	EFC6193
0 6 -1 -	-1'-1 - FINIAL - 21 NOV 2006	san	ofi aventis

Loc	ATION:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan3 - MRI5 - Scintigraphy2 - Spiral CT4 - PET7 - Ultrasound8 - X-Ray10 - Physical Exam99 - Other

	BASI	ELINE TU	JMOR MEAS	GUREMENTS		O.ASSESS_2		_	BASELINE	XRP6258 EFC6193
NO 14 Confidential FINAL	LESION NUMBER	LOCATION (site) *	LESION DESCRIPTION (subsite)	DATE OF ASSESSMENT Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	Non Target			93
ential 1	1	LJLJ.LJLJ								
14 FINA	2									
	3	<u> </u>							<	
21-NOV-2006	4	<u></u>							00	Country No.
·-2006	5	L.L.								
	6	<u></u>								Centre No.
	7									No.
XRP6258	8	<u></u>								ا س ا
5258	9	<u></u>								Subject No
sanofi	10	LJLJ.LJL								
-	11	<u></u>								O O
EFC6193	12									
93	13	<u></u>								14 Page
	14									
Ī										

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	15 Page	01
BASELINE	V 00					

## SIGNS AND SYMPTOMS PRESENT AT BASELINE O.SYMPTOM\_1

None  $\square$ 

	SIGNS AND SYMPTOMS	DATE OF ONSET  Day Month Year	Grade (1 - 4)
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

XT 15	1	XRP6258	EFC6193	
Confidential = El	NIAL = 21 NOV 2006	san	ofi aventis	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	15 Page	02
BASELINE	v 00	See Pag	e 34			

## SIGNS AND SYMPTOMS PRESENT AT BASELINE O.SYMPTOM\_1

	SIGNS AND SYMPTOMS	<b>DATE OF ONSET</b> Day Month Year	Grade (1 - 4)
1			<u> </u>
2			
3			
4			
5			
6			
7			
8			
9			
10			

XT	15	XRP6258	_ EFC6193
Confide	ential = FINIAL = 21 NOV 2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	15 Page	
BASELINE	V 00	See Pa	ge 34			

### SIGNS AND SYMPTOMS PRESENT AT BASELINE O.SYMPTOM\_1

	SIGNS AND SYMPTOMS	DATE OF ONSET	Grade (1 - 4)
		Day Month Year	(1 - 4)
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

/\ I	13	1	7111 0Z30	
XT	15		XRP6258	EFC6193

XRP6258 EFC6193	Country N	o. C	entre No.	Subject	No.	T 16		01
BASELINE	V 0(							
(!)	Excludin	G PRIOR	ANTI-CAN	CER THI	ERAPIES.		_	
PRIOR MED	CATION						O.ME	D_8
NONE  Record any medications to been taken within 30 days on the Concomitant Medi	s prior to the first tr	•	,					
MEDICATION			ART DATE	Year	Day	END DATE  Month Year		Ongoing
1.	L							
2.	L							
3.	L							
4.	L							
5.	L							
6.	L							
7.	L							
8.	L							
9.	L							
XT 1	6		, X	RP625	B ,	EFC6193		

XRP62 EFC6	1 11	ry No. Centre I	No.   Subject	No.	Γ 16 Page	
Basi	ELINE V		See Page 3	<b>37</b>		
	Exclud	ING PRIOR ANT	I-CANCER TH	ERAPIES.		
PRI	OR MEDICATIO	N			0.1	MED_8
☐ Nor						
been tak	any medications taken within 30 en within 30 days prior to the first oncomitant Medication page.					
	MEDICATION	START		Day	END DATE	Ongoing
		Day Month	Year	,	Month Year	
1.						
2.						
3.						
4.						
5.						
6.						
7.						
8.						_ □
9.						_ 🗖
	XT 16 ,		XRP625	8 ,	EFC6193	

l .	P6258 C6193	Country No.	Centre No.	Subject No.	NO	<b>17</b> Page	
Ва	SELINE	V 00					
IN	CLUSION C	RITERIA					CRIT_1
Th	e Patient must have:					Y	'ES N
re re m Ta	Piagnosis of histologice fractory to hormone egimen. Patient must nonths after prior horm axotere®-containing	therapy and previ have documented mone therapy and therapies	ously treated of the progression disease progr	with a Taxoter of disease dur ession during	e®-contai ing or wit or after	ning hin 6	<b>_</b> [
· I do m sc cl le · I le re ta th th	atient must have either Patient with measurable demonstrating at least one wast measure at least 10 mean or MRI (chest, abdome early defined lung lesion sion, and bone lesions with Patient with non-measural sion. [Rising PSA is defined ference value (measure 1) ken at least 7 days after the reference level) to be gree 2nd measure. If this is reseasure. The third (or the ference the signal of	visceral or soft tissue rate in the longest diamen, pelvis) or 20 mm of surrounded by aerated. If be considered non-ble disease must have ed as at least two consumer reference value. A freater than the second not the case, a fourth fourth) confirmatory Ps	umented progress metastatic lesion neter (or two time on conventional of d lung. (Previousl measurable disea documented risi secutive rises in Feek apart. The first third confirmator measure and it r PSA measure is re SA should be take	ion of disease by including new less the slice thickness the slice thickness or Chest X-ray y irradiated lesionse).  The property of the prope	PRECIST critesion). This ess) on spiral for biopsy parts, primary pappearance ented over a asure 2) shour required (2) at least 7 days and be gress prior to raise.	eria lesion I CT proven, prostate of new ald be ad beyond ays after eater than t	n]
(L es m al al (L C w es st th	eceived prior castration. H-RH) agonist with of stramustine, or other mandatory. However, bove 5 ng/mL at the lantiandrogen withdrave. H-RH agonist treatmental blocal utamide moved and an antiandrogen an antiandrogen is occurs because the which is allowing the antibit it)	or without antiand hormonal agents. if the patient has last administration val syndrome* should continue or flutamide must have been stop triandrogen withdreen such as chloring antiandrogen to standrogen to stand	frogen, antiand (A prior treat been treated was of antiandrogould be confinue during the st have been soped at least 6 frawal syndrommadinone ace induced a ntimulate prosta	drogen withdrement by antial with antiandrogens, presence med prior to the study treatment topped at lead weeks prior the is a decrease tate, flutamide nutation in the ate cancer ground antial with antigen with a steement and a steement a steement and a steement a steement and a steement and a steement a steement and a steement and a steement a steement and a steement and a steement and a steement a steement a steement and a steement a steeme	awal, mor ndrogen is gens, <u>and</u> or absend he study e nt period. st 4 weeks o, the last se in PSA s e, or bicalu e androger wth rather	prior to, PSA prior to, PSA een upor utamide; than	with
4. L	ife expectancy > 2 m	onths				[	
5. E	astern Cooperative O	ncology Group (E	COG) perform	nance status 0	- 2	[	
6. A	ge ≥ 18 years					[	
	IF THE ANSWER TO	ANY OF THE INCLUSION	I CRITERIA IS NO,	THE SUBJECT IS I	NOT ELIGIB	LE FOR THE	STUDY.
L	NO 17		. >	(RP6258	. FF	C6193	_
	Confidential ■ FIN		1		nofi av		

XRP62 EFC61			Country No	. Centre	No.	Subject No.	NO	<b>17</b> . Page	01
Base	LINE		V 00	]					
INC	LUS	ION C	RITERI	A					CRIT_1
The P	atient m	ust have:						•	YES N
horm Patie horm regin 2. Patie	one thera nt must ha one thera nen nt must ha	py and previous py and disease of the control of th	or cytologically ously treated w ted progression on the progression of	ith a Taxoterd of disease d during or afte  n-measurable	e® (or doc uring or w er Taxotere  e disease .	etaxel)-conta ithin 6 mont ® (or doceta	ining regime hs after prio xel)-containi 	en. r ng · · ·	<b>-</b>
demo must scan clearl lesior · Patic lesior refere taken the re the 20 meas	onstrating a measure a or MRI (ch y defined n, and bon ent with n n. [Rising f ence value at least 7 eference le nd measur ure. The th	at least one vist least 10 mm lest, abdomen lung lesion sure lesions will on-measurable PSA is defined (measure 1) that days after the vel) to be greate. If this is no nird (or the found	ease must have sceral or soft tiss in the longest of pelvis) or 20 murrounded by aer be considered redisease must has at least two aken at least one reference value ater than the sect the case, a fouurth) confirmator	sue metastatic diameter (or two nm on conver rated lung. (Pro non-measurab nave documer consecutive ri e week apart. A third conf nond measure rth PSA measury PSA should	lesion (incovo times the attional CT of reviously in le disease). Inted rising Fases in PSA. The first rising and it musure is requibe taken v	luding new lete slice thicknown Chest X-ray radiated lesion PSA levels or sto be documed in gradiated lesion PSA (measure is to be obtained to be take within 4 week	esion). This less) on spiral for biopsy pens, primary pensenged over a sure 2) shourequired (2n at least 7 da en and be gress prior to ran	esion CT roven, rostate of new Id be d beyond ys after eater than domization	the 2nd on]
agon other has b antia to the Chloi bical antia chloi induc	ist with or hormona een treate ndrogens, e study en rmadinon- utamide r indrogen v rmadinone ced a mut	without antial agents. (A ped with antial presence or try). (LH-RH er acetate or finust have been withdrawal syes acetate, flut ation in the a	orchiectomy a androgen, antia prior treatment ndrogens, and F absence of antia agonist treatma lutamide must be en stopped at lea androme is a de amide, or bical androgen recept er than inhibit	androgen with by antiandrogen with above androgen with entire should contain the been stopped to the beast 6 weeks and accrease in PS, but amide; this act of which is a stopped to the beast of which is a stopped to the beast of the beast o	hdrawal, n gen is not 5 ng/mL a thdrawal s ontinue du opped at le prior to, th A seen upo s occurs be allowing th	monotherapy mandatory. It the last adn yndrome* sh ring the stud- east 4 weeks ee last PSA even stopping a recause the an ire antiandrog	with estramed However, if hinistration could be conducted treatment prior to, what aluation.) (In antiandrogen lien to stimul	ustine, or the patie of firmed proeriod. ile * The gen such has ate	nt
4. Life e	expectanc	y > 2 months							
			ogy Group (ECC self-care, and up						
6. Age 2	≥ 18 years								
	IF THE	ANSWER TO A	NY OF THE INCLU	SION CRITERIA	ıs <b>NO</b> , THI	E SUBJECT IS N	IOT ELIGIBI	E FOR TH	E STUDY.
<u> </u>	NO	17.01	ı		XRI	P6258		C6193	
525	Confide	ential ■ E2A	2 ■ 05-Oct-20	007		sar	nofi ave	entis	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	18 Page	
BASELINE	V 00					
EXCLUSION CF	RITERIA				CRI	T_2
<ol> <li>Previous treatment with m</li> <li>Prior radiotherapy to ≥ 40</li> <li>Prior surgery, radiation, ch</li> </ol>	% of bone ma	rrow				No □
weeks prior to enrollment 4. Active secondary cancer i	in the study . ncluding prior	malignancy f	rom which the	 e patient ha		
disease-free for ≤ 5 years cancer before 4 weeks pri 5. Known brain or leptomen	or to entry car ingeal involve	be eligible to	the study) .		🗖	
<ul><li>6. History of severe hyperser drugs</li><li>7. History of severe hyperser</li><li>8. Other concurrent serious</li><li>9. Inadequate organ function</li></ul>	nsitivity reaction	on (≥ grade 3) cal conditions	or intolerance	to prednise	one	<u> </u>
and serum chemistries at 6  Neutrophils ≤ 1.5 x 10 <sup>9</sup> Hemoglobin ≤ 10 g/dL  Platelets ≤ 100 x 10 <sup>9</sup> /L  Total bilirubin ≥ Upper  AST (SGOT) ≥ 1.5 x UL  ALT (SGPT) ≥ 1.5 x UL	enrollment: P/L limit of norma N	,	mg peripiicia	. 5.000		
<ul> <li>Creatinine ≥ 1.5 x ULN</li> <li>10. Uncontrolled cardiac arrh congestive heart failure, o allowed</li></ul>	ythmias, angir r myocardial i	nfarction with	in last 6 mont	hs is also n	ot _	
<ul><li>11. Left ventricular ejection fr (MUGA) scan or echocard</li><li>12. Uncontrolled diabetes me</li></ul>	action (LVEF) 5 diogram dlitus	50% by multi-	gated radionu	clide angio	graphy	
<ul><li>13. Active uncontrolled Gastr</li><li>14. Active infection requiring</li><li>15. Participation in another of</li></ul>	systemic antib	iotic or anti-fu	ıngal medicat	ion	🗖	
<ul><li>15. Participation in another cl prior to study enrollment</li><li>16. Concurrent or planned tre</li></ul>					<b></b>	
(A one-week washout per treatments)				,		
IF THE ANSWER TO ANY OF THE EXC		YES, THE SUBJE			STUDY.	
NO 18	1		(RP6258	_ EFC	6193	

		1	1					
XRP6258					NO	18	.01	
EFC6193		Country No.	Centre No.	Subject No.	1	Page		
BASELINE		v 00						
								_
EXCLUS	ON CI	RITERIA					CRIT_2	
							YES	No
1a. Previous treatm								
2a. Previous treatm	ent with less	than 3 cycles o	r <225 mg/m <sup>2</sup> o	cumulative dose	e of Taxotere	e®		
3a. Prior radiothera						• • •	_	_
bone-seeking ra	adio-isotope	(samarium-153,	strontium-89, o	r P-32) is allow	ed, but 8 we	eeks		
must have elap	sed atter sam ior to first sti	arium-153 or P- udy drug admini	·32 and 12 weel stration	ks must have el	apsed after			
4a. Prior surgery, ra	diation, che	motherapy, or ot	her anti-cancer	therapy within	4 weeks pri	or to	_	_
enrollment in t	ne study	· · · · · · · · · · · · · · ·					H	
<ul><li>5a. Active grade ≥2</li><li>6a. Active grade ≥2</li></ul>								
7a. Active seconda							_	_
disease-free for	≤ 5 years (H	owever, adequa	tely treated supe	erficial basal ce	ell skin			
8a. Known brain o		to entry can be					<u> </u>	7
9a. History of seve								ā
10a. History of seve	re hypersensi	tivity reaction (≥	grade 3) or inte	olerance to pre	dnisone			
11a. Other concurre							ш	Ц
12a. Inadequate org		s evidenced by	the following pe	eripheral blood	counts, and	serum		
<ul> <li>Neutrophils</li> </ul>	_							
· Hemoglobin								
<ul> <li>Platelets ≤ 10</li> <li>Total bilirubi</li> </ul>		mit of normal (U	IN)					
· AST (SGOT)		int of normal (e	21 1/					
· ALT (SGPT) ≥								
<ul> <li>Creatinine ≥</li> <li>13a.Uncontrolled c</li> </ul>		hmias angina n				··· ισestiv <i>e</i>	, 	
		infarction withir						
14a. Left ventricular								
(MUGA) scan of 15a. Uncontrolled d		ogram					<u> </u>	7
16a. Active uncontrol							ā	ā
17a. Active infection								
18a. Participation in		ical trial with an			0 days prior	•	П	
19a.Concurrent or					0 3A4/5 (A d	one-	_	_
week washout	period is nec	essary for patien	its who are alrea	ady on these tre	eatments) .			
20a. For patient enro		Jnited Kingdom, reproductive po						
		eption, described						
IF THE ANSWER TO A	NY OF THE EXC	CLUSION CRITERIA IS	YES, THE SUBJEC	T IS NOT ELIGI	BLE FOR THE	STUDY.		
			,					
NO	18.01	1	, X	(RP6258	EFC	6193		
					מונים	otic.		

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	19 Page
CYCLE 1	V 01		Date of visit:	day / m	onth year
PHYSICAL EX	AMINATI	ON			PHYSEXAM_2
NONE NOT SUE	<b>BMITTED</b>				
To be done if the screening	g exam is more th	an 5 days fro	m study drug	administra	tion
Date performed: Lay	month ye	ar			
Were there any clinically	y significant chan	ges from the	previous evalu	uation?	Yes* ☐ No ☐
*If yes, please complete Otherwise, complete th			if performed	prior the fi	rst dose.
VITAL SIGNS	See Page	e 27			VITAL 1
NOT DONE					VITAL_1
To be done if the screenin	g evam is more th	aan 5 days fr	om etudy drug	, administra	tion
To be done if the screening	g exam is more ti	ian 5 days in	om study urug	, administra	uon.
Weight: LLL.L	kg				
- Blood pressure: Syste	olic LLLL ı	mmHg / E	Diastolic 🔲		Hg
- Heart rate:	⊔⊔ beats/min				
- Temperature:	∟ °C				
	(tick appropriate	e box):	Oral 🗖	Rectal [	Auricular 🗖
ECOG Performance State					
$\begin{array}{cccc} 0 & 1 & 2 \\ \hline \Box & \hline \end{array}$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$				
NO 19	ı	, >	(RP6258	EFC	6193

Page 43/525 Confidential ■ FINAL ■ 21-NOV-2006

sanofi aventis

XRP62 EFC61		Country No.	Centre No.	Subject No.	20 Page			
Cyc	LE 1 - DAY 1	V 01						
		See Page 2	4					
HEMATOLOGY LABH_1								
	Ione if the screening e of sampling:	xam is more	than 5 days from	study drug admir	nistration			
	Test		VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY			
	WBC			10º/L				
	RBC			10 <sup>6</sup> /mm <sup>3</sup>				

10°/L

10<sup>9</sup>/L

10<sup>9</sup>/L

10<sup>9</sup>/L

Lymphocytes 10°/L

Platelets 10°/L

Hemoglobin g/dL

PSA

See Page 26

LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

	NO	20		XRP6258	EFC6193		
-	Confidential ■ FINAL ■ 21-NOV-2006			sanofi aventis			

Neutrophils

Eosinophils

Basophils

Monocytes

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	21 Page	
CYCLE 1 - DAY 1	V 01					

See Page 25

### **BIOCHEMISTRY**

LABB\_1

To be done if the screening exam is more than 5 days from study drug administration

Date of sampling:			
	day	month	year

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 21 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	22 Page	
CYCLE 1 - DAY 8	V 01					
	See Page 24					
<b>HEMATOLOGY</b>					LABH_1	

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 22 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	23 Page	
CYCLE 1 - DAY 15	V 01					
HEMATOLOGY	See Page 24				LABH_1	

Date of sampling:	ШШ		
	day	month	year

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 23 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	24 Page	
CYCLE 1	V 01					

#### **SPECIFIC CONCOMITANT MEDICATION** SPMED\_1

Ν	one	Г

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION	1	SAGE		START DA	.TE	END DATE		
	MEDICATION	Number of Units	Unit	day	month	year	day month year		
1									
2									
3									
-			 						
4									
5				шш					
6									
7									
8							UU UUU UUUU		
9									
10									

NO	24		XRP6258	EFC6193
Confide	ontial ■ EINIAI ■	21 NOV 2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	25 Page	
CYCLE 1	V 01					

#### **INVESTIGATIONAL PRODUCT ADMINISTRATION** ADMIN\_1

Treatment Name	DATE AND TIME OF DOSING						ACTUAL Dose Given
		day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start L	JLJ L_					
☐ Mitoxantrone	End						
IF DOSE DELAYED AND	OR REDU	UCED AN	id/or interi	RUPTED, SPECIFY R	EASON:		
☐ AE: Specify on AE form							
☐ Other:							

Dose change: interruption only at Cycle 1(delay and/or reduction are not applicable).\*

\*IF DOSE INTERRUPTED:

Treatment Name		DATE A	ND TIME OF DOSI	NG	Intended Dose	ACTUAL DOSE
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	GIVEN (mg)
☐ XRP6258	Start L L					
☐ Mitoxantrone	End				NA	

NO	25		XRP6258	EFC6193
Confide	ntial ■ FINIAL ■	21-NOV-2006	san	ofi aventis

XRP6258 EFC6193				NO	26	
21 00100	Country No.	Centre No.	Subject No.	1	Page	
CYCLE 1	V 01	See Pag	ge 49			

### INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

	Treatment Name		DATE OF DOS	SING	Intended Dose	ACTUAL DOSE
		day	month	year	(mg)	GIVEN (mg)
	Prednisone	Start				
	Prednisolone	End LL				
IF DOSE DEL	AYED AND/OR REDUCED	and/or interru	PTED, SPECIFY RI	EASON:		
☐ AE: Specif	fy on AE form					
Other:						

Dose change: interruption only at Cycle 1(delay and/or reduction are not applicable).\*

\*IF DOSE INTERRUPTED:

Treatment Name	DATE OF DOSING	Intended Dose	ACTUAL DOSE GIVEN
	day month year	(mg)	(mg)
☐ Prednisone	Start		
☐ Prednisolone	End	NA	

NO	26	1	XRP6258	EFC6193
			500	of: avootic

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>27</b> Page	
CYCLE 1	V 01					

# **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 27 XRP6258 EFC6193

XRP6258
Country No. Centre No. Subject No. Page  CYCLE 1  V 0 1  See Page 29
ECHOCARDIOGRAPHY ECHOCARD_1
LONGOARDIOCRAFIII
NOT DONE
• Date performed: LLLLLL wonth year
• 2D-Echocardiography: Normal □ Abnormal* □
- Left ventricular ejection fraction (LVEF)
- Lower Limit Normal of LVEF
RADIONUCLIDE VENTRICULOGRAPHY  NOT DONE
• Date performed: LLLLLLL day month year
• Radionuclide Ventriculographyy: Normal  Abnormal*
- Left ventricular ejection fraction (LVEF)
- Lower Limit Normal of LVEF
* If clinically relevant, please report on the Signs and Symptoms form if performed prior first dose. Otherwise complete the Adverse Event form.

XRP6258 EFC6193				NO	29	
	Country No.	Centre No.	Subject No.		Page	
CYCLE 1	V 01					

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1		
3.		
4		
5.		
6.	L	
7.		

NO 29 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	) Colon	30	Other
11.0	1 Regional Lymph Nodes	20.20	) Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	30 Page	
CYCLE 1	V 01					

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4	LJLJ.LJLJ	□□□□□□□□□□□□□□□□ Not Done			
5		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		LJLJ mm	
6		□□□□□□□□□□□□□□□□□ Not Done			
7	LJLJ.LJ	□□□□□□□□□□□□□□□□□ Not Done			
8	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
9		□□ □□□ □□□□□ □ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□□ Not Done			
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
14	<u> </u>	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		mm	

NO 30 XRP6258 EFC6193

(RP6258 EFC6193	Country No. Centre No.	Subject No.   NO 31	
CYCLE 1	V 01		
	NOT SUBMIT	TED	_
PHARMAC	COKINETIC - BLOOD SAM	PLING (SCHEDULE 1	<b>l)</b> PK_1
NOT APPL	ICABLE		
SAMPLE	THEORETICAL	SAMPLE DATE	SAMPLE TIME
ID	TIME	day month year	24 hour clock
P00	Prior to Infusion of XRP6528		
P01	30 minutes before end of infusion		
P02	5 minutes post end of Infusion		
P03	1 hour post end of infusion		
P04	6-10 hours post end of infusion		
P05	24-72 hours post end of infusion		
PHARMAC	COKINETIC - BLOOD SAM		
PHARMAC NOT APPL	COKINETIC - BLOOD SAM LICABLE THEORETICAL		2) PK_1 SAMPLE TIME
PHARMAC Not Appl	COKINETIC - BLOOD SAM	PLING (SCHEDULE 2	<b>2)</b> <i>PK</i> _1
PHARMAC NOT APPL	COKINETIC - BLOOD SAM LICABLE THEORETICAL	PLING (SCHEDULE 2	SAMPLE TIMI 24 hour clock
PHARMAC  NOT APPL  SAMPLE  ID	COKINETIC - BLOOD SAM LICABLE THEORETICAL TIME	PLING (SCHEDULE 2  SAMPLE DATE day month year	SAMPLE TIME 24 hour clock
PHARMAC  NOT APPL  SAMPLE ID  P00	COKINETIC - BLOOD SAM  ICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock
PHARMAC  NOT APPL  SAMPLE ID  P00  P01	COKINETIC - BLOOD SAM  LICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock  LJLL: LJLL  LJLL: LJLL
PHARMAC  NOT APPL  SAMPLE ID  P00  P01  P02	COKINETIC - BLOOD SAM  ICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion	SAMPLE DATE day month year	2) <i>PK_1</i> SAMPLE TIMI 24 hour clock
PHARMAC  NOT APPL  SAMPLE ID  P00  P01  P02  P03	COKINETIC - BLOOD SAM  LICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion  2 hours post end of infusion	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock  LILL: LILL  LILL: LILL  LILL: LILL  LILL: LILL
PHARMAC  NOT APPL  SAMPLE ID  P00  P01  P02  P03  P04	COKINETIC - BLOOD SAM  ICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion  2 hours post end of infusion  8-12 hours post end of infusion	SAMPLE DATE day month year  LILI LILI LILILI LILILI LILI LILILI LILI LILILI LILI L	SAMPLE TIME 24 hour clock  LILL: LILL  LILL: LILL  LILL: LILL  LILL: LILL
PHARMAC  Not Appl  SAMPLE ID  P00  P01  P02  P03  P04	COKINETIC - BLOOD SAM  ICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion  2 hours post end of infusion  8-12 hours post end of infusion	SAMPLE DATE day month year  LILI LILI LILILI LILILI LILI LILILI LILI LILILI LILI L	SAMPLE TIME 24 hour clock  LJL : LJL  LJL : LJL  LJL : LJL  LJL : LJL

XRP6258 EFC6193	Country No. Centre No.	Subject No. NO 31	.01
CYCLE 1	V 01		
	NOT SUBMITT	ED	_
PHARMA	COKINETIC - BLOOD SAMP	PLING (SCHEDULE 1	) PK_1
NOT AP	PLICABLE		
SAMPLE ID	THEORETICAL TIME	SAMPLE DATE day month year	SAMPLE TIME 24 hour clock
P00	Prior to Infusion of XRP6528		
P01	30 minutes before end of infusion		
P02	5 minutes post end of Infusion		
P03	1 hour post end of infusion		
P04	6-10 hours post end of infusion		
P04	6-10 hours post end of infusion  24-168 hours post end of infusion		
P05	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP		
PHARMA  Not Apple	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL		PK_1  SAMPLE TIME
PHARMA  NOT AP  SAMPLE ID	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL  TIME	PLING (SCHEDULE 2	2) PK_1
PHARMA  Not Apple	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL	PLING (SCHEDULE 2	PK_1  SAMPLE TIME
PHARMA  NOT APPLE ID	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL  TIME	PLING (SCHEDULE 2  SAMPLE DATE day month year	PK_1  SAMPLE TIME 24 hour clock
PHARMA  Not Apple ID P00	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528	SAMPLE DATE day month year	SAMPLE TIME 24 hour clock
PHARMA  Not Apple ID  P00  P01	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion	SAMPLE DATE day month year	SAMPLE TIME 24 hour clock
PO5  PHARMA  NOT API  SAMPLE ID  P00  P01  P02	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion	SAMPLE DATE day month year	2) <i>PK_1</i> SAMPLE TIME 24 hour clock
PO5  PHARMA  NOT API  SAMPLE ID  P00  P01  P02  P03	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion  2 hours post end of infusion	SAMPLE DATE day month year	2) <i>PK_1</i> SAMPLE TIME 24 hour clock
PHARMA Not Appl SAMPLE ID P00 P01 P02 P03 P04	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion  2 hours post end of infusion  8-12 hours post end of infusion	SAMPLE DATE day month year	2) <i>PK_1</i> SAMPLE TIME 24 hour clock  LILL: LILL
PO5  PHARMA  Not Apple ID  P00  P01  P02  P03  P04	24-168 hours post end of infusion  COKINETIC - BLOOD SAMP  PLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion  2 hours post end of infusion  8-12 hours post end of infusion  24-168 hours post end of infusion	SAMPLE DATE day month year	2) <i>PK_1</i> SAMPLE TIME 24 hour clock  LILL: LILL  LILL: LILL

FC6193	Country No. Centre No.	Subject No.   NO 32	
CYCLE 1	V 01		
	NOT SUBMITTE	D	_
PHARMA	COKINETIC - BLOOD SAME	PLING (SCHEDULE 3	B) PK_1
NOT APP	PLICABLE		
SAMPLE ID	THEORETICAL TIME	SAMPLE DATE day month year	SAMPLE TIME 24 hour clock
P00	Prior to Infusion of XRP6528		
P01	30 minutes before end of infusion		
P02	20 minutes post end of Infusion		
P03	3 hours post end of infusion		<u> </u>
P04	10-14 hours post end of infusion		
B05	24.72 hours part and of infusion		 
P05	24-72 hours post end of infusion		
	COKINETIC - BLOOD SAME		<b>!)</b> PK_1
PHARMA  Not App	COKINETIC - BLOOD SAMF	PLING (SCHEDULE 4	<b>!)</b> PK_1
PHARMA  NOT APP  SAMPLE	COKINETIC - BLOOD SAMF PLICABLE THEORETICAL	PLING (SCHEDULE 4	SAMPLE TIMI 24 hour clock
PHARMA  Not App  SAMPLE ID	COKINETIC - BLOOD SAMF PLICABLE THEORETICAL TIME	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock
PHARMA  NOT APP  SAMPLE ID  P00	COKINETIC - BLOOD SAME  PLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock
PHARMA Not App SAMPLE ID P00 P01	COKINETIC - BLOOD SAME  PLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion	SAMPLE DATE day month year	SAMPLE TIME 24 hour clock  LILL: LILL  LILL: LILL
PHARMA NOT APP SAMPLE ID P00 P01 P02	COKINETIC - BLOOD SAME  PLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion	SAMPLE DATE day month year	SAMPLE TIME
PHARMA Not App SAMPLE ID P00 P01 P02 P03	COKINETIC - BLOOD SAME  PLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion  4 hours post end of infusion	SAMPLE DATE day month year	SAMPLE TIME 24 hour clock  LILL: LILL  LILL: LILL  LILL: LILL
PHARMA Not App SAMPLE ID P00 P01 P02 P03 P04	COKINETIC - BLOOD SAME  PLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion  4 hours post end of infusion  12-24 hours post end of infusion	SAMPLE DATE day month year  LILL LIL	SAMPLE TIME 24 hour clock

CYCLE	Country No. Centre No.  V 01	Subject No.   Pag	2 .01 ge
	NOT SUBMITTED	· ·	-
PHARM	ACOKINETIC - BLOOD SAME	PLING (SCHEDULE 3	<b>B)</b> PK_1
☐ Not A	APPLICABLE		
SAMPLE ID	THEORETICAL TIME	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock
P00	Prior to Infusion of XRP6528		
P01	30 minutes before end of infusion		
P02	20 minutes post end of Infusion		
P03	3 hours post end of infusion		
P04	10-20 hours post end of infusion		
P05	24-168 hours post end of infusion		
PHARM	ACOKINETIC - BLOOD SAMF	PLING (SCHEDULE 4	<b>l)</b> PK_1
PHARM.  Not A	ACOKINETIC - BLOOD SAME APPLICABLE THEORETICAL	PLING (SCHEDULE 4	SAMPLE TIM
PHARM.	ACOKINETIC - BLOOD SAMF	PLING (SCHEDULE 4	SAMPLE TIM 24 hour clock
PHARM  Not A  SAMPLE ID	ACOKINETIC - BLOOD SAMF APPLICABLE THEORETICAL TIME	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock
PHARM Not A  SAMPLE ID P00	ACOKINETIC - BLOOD SAME APPLICABLE THEORETICAL TIME Prior to Infusion of XRP6528	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock
PHARM  Not A  SAMPLE ID  P00  P01	ACOKINETIC - BLOOD SAME APPLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock  LILL: LILL  LILL: LILL
PHARM  Not A  SAMPLE ID  P00  P01  P02	ACOKINETIC - BLOOD SAME APPLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion	SAMPLE DATE day month year	SAMPLE TIME 24 hour clock
PHARM  Not A  SAMPLE ID  P00  P01  P02  P03	ACOKINETIC - BLOOD SAME APPLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion  4 hours post end of infusion	SAMPLE DATE day month year	SAMPLE TIMI

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	33 Page	01
CYCLE 1	V 01					

# **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	End Date
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XT	33	XRP6258	EFC6193
O	antial = FINIAL = 21 NOV 2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	33 Page	02
CYCLE 1	V 01	See Pa	ige 60			

# **CONCOMITANT MEDICATION**

O.MED\_9

	MEDICATION	Start Date			END DATE		
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□ L □ Ongo	
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□ L □ Ongo	ing
6.			□□□□□□□□ □□ Ongoi			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
8.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□ L □ Ongo	ing
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□ L □ Ongo	
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	

		cao	of: avootic
XT	33	XRP6258	EFC6193

XRP6258 EFC6193	Country No. Centre No. S	Subject No.   AT 601 Page
CYCLE 1	v 01   000	
ADVERSE EVI	ENT FORM	0.1_AE_1
1. Adverse Event Diagnosis	AE form no:	AE form no: 1011-1012  AE ref. no: 1-11-1012
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	1 Date of start: LL	day month year
3= Ongoing with change  3. GRADE (1 - 4)	1 2 3 4 [	
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No C	Yes No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes 🔲 No 🗅	Yes 🗖 No 🗖
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
3. Seriousness Criteria	Yes No C - Date event became serious:	Yes No Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that app	ly:   IF YES
	Resulting in death	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event
Investigator's name, date of repo	ort and signature: Monitoring	representative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study trea	ment?
		6258 EFC6193

XRP6258 EFC6193		XT 601 02
CYCLE 1		ee Page 62
		ee i age oz
ADVERSE EVI	ENT FORM	0.1_AE_1
1.	AE form no: [0][1]-[0][3]	AE form no: [ <b>0</b> ][ <b>1</b> ]-[ <b>0</b> ][ <b>4</b> ]
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
2. STATUS OF AE	1 Date of start:	□ Date of start: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□
1= New 2= Ongoing from previous period without change	day month year 2  (do not complete the remaining items in the column	· · · · · · · · · · · · · · · · · · ·
3= Ongoing with change	3 🗖	3 🗖
3. GRADE (1 - 4)	1	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes No No
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted
STUDY TREATMENT	0 1 2 3 4 5	0
6. Corrective Treatment/Therapy	Yes 🔲 No 🗖	Yes 🗖 No 🗖
7. OUTCOME 1= Recovered	1 □ <b>〕</b> Date: □□ □□□ □□□□ vear	」
4= Recovered with sequelae	4 D Specify sequelae:	
2= Recovering	2 🔲	_   2 <b>_</b>
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	5 Date of death: LL LLL LLL L	5 Date of death: LL LLL wonth year
6= Unknown	6	
8. SERIOUSNESS CRITERIA	Yes U No U  Output - Date event became serious:	Yes U No U  Output  Output  Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	□ IF YES	⇒ IF YES   Li
FORM	- Tick below all criteria that apply	I I
	Resulting in death	Resulting in death
	Life-threatening	Life-threatening
	Requiring/prolonging hospitalization	Requiring/prolonging hospitalization
	Congenital anomaly/birth defect	Congenital anomaly/birth defect
	Other medically important event	Other medically important event
Investigator's name, date of repo	ort and signature: Monitoring re	presentative's name, date of receipt:

XT 601 , XRP6258 , EFC6193

\* Is there a reasonable possibility that the AE was caused by study treatment?

XRP6258 EFC6193	Country No.   Centre No.	Subje	XT	601 Page	03
CYCLE 1	V 01		Page 62		
ADVERSE EVI	ENT FORM			O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no:   <b>0</b>   <b>1</b>   <b>1</b>   <b>0</b>   <b>1</b>   <b>1</b>		AE form	n no: [ <b>0</b> ][ <b>1</b> ]-[ <b>0</b> ][ <b>6</b>	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL LL day month 2 (do not complete the remaining items	year	1 Date of start: 2 (do not comple	day month Lete the remaining items in	year
3. GRADE (1 - 4)	1 2 3 3	4 🗆	1 2 2		4 🗖
ACTION TAKEN WITH     STUDY TREATMENT*      ACTION TAKEN WITH     STUDY TREATMENT	Yes No  0= None / 1= Permanently discontinued / 2= 3= Dose reduced / 4= Delayed and reduced /  0 1 2 3 4		3= Dose reduced / 4=	nently discontinued / 2= Delayed and reduced / 5= 2	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖 No		Yes 🗖	l No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL Lday month 4 Specify sequelae:	year	1 Date: 4 Specify s	day month	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	UUU year	2	h:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	ia that apply:	Resulting in deat	No  Date event became se  Limit Limi	year  a that apply:
Investigator's name, date of repo	Persistent/significant disability/incapac Congenital anomaly/birth defect Other medically important event ort and signature: Mc possibility that the AE was caused by	onitoring repr	Congenital anom Other medically esentative's name	cant disability/incapacity naly/birth defect important event e, date of receipt:	🗖

 XT
 601
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-NOV-2006
 sanofi aventis

XRP6258 EFC6193	Country No. Centre No. Subjet	Tot No.   Page   Page   D   A   Page   D   Page	
CYCLE 1	v 60 000	e Page 62	
ADVERSE EVI	ENT FORM	O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: [0][1]-[0][7] AE ref. no: []-[]-	AE form no: [ <b>0</b> ][ <b>1</b> ]-[ <b>0</b> ][ <b>8</b> ] AE ref. no: []-[]-	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: Lay month year 2 (do not complete the remaining items in the column) 3	
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4 🔲	1	
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes No 🗆	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed       0= None / 1= Permanently discontinued / 2= Delayed         3= Dose reduced / 4= Delayed and reduced / 5= Interrupted       3= Dose reduced / 4= Delayed and reduced		
6. CORRECTIVE TREATMENT/THERAPY	Yes No 🗆	Yes No 🗆	
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered  5 = Fatal (complete the death report form)  6 = Unknown	1 Date: Lay Month year 4 Specify sequelae: 2	1 Date: day month year  4 Specify sequelae:  2	
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes	
Investigator's name, date of repo	ort and signature: Monitoring representation	esentative's name, date of receipt:	

EFC6193 601 XRP6258 XT sanofi aventis

XRP6258 EFC6193	Country No. Centre No. Subje	Tot No.   XT 601 05		
CYCLE 1	V 01 Se	ee Page 62		
ADVERSE EV	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no:	AE form no: 1011-110  AE ref. no: 11-11		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL LLL year  2 (do not complete the remaining items in the column)  3		
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes 🗖 No 🗖		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0			
6. Corrective Treatment/Therapy	Yes No D	Yes		
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL year  4 Specify sequelae:	1 Date: LL LLL LLL year 4 Specify sequelae:		
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No C  - Date event became serious:    Solitor   Continue   Con	Yes □ No □  - Date event became serious:  □ IF YES     □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □		
Investigator's name, date of rep	Resulting in death	Resulting in death		

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 601 | XRP6258 | EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 601 06
CYCLE 1	V 01 Se	ee Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.	AE form no: [ <b>0</b> ][ <b>1</b> ]-[ <b>1</b> ][ <b>1</b> ]	AE form no: [0][1]-[1][2]
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
2. STATUS OF AE	1 Date of start: LL LLL year	1 Date of start: LL LLL Lyear
2= Ongoing from previous period without change 3= Ongoing with change	2 (do not complete the remaining items in the column) 3	2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes No No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes  No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLL LLL year 4 Specify sequelae:	1 Date: LLL LLLL year 4 Specify sequelae:
2= Recovering	2 🔲	2 🗖
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form) 6= Unknown	5 Date of death:	5 Date of death: LL LLL year
8. SERIOUSNESS CRITERIA	Yes	Yes No C - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	→ IF YES	Tick below all criteria that apply:
	Resulting in death	Resulting in death

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 601 , XRP6258 , EFC6193

Investigator's name, date of report and signature:

Monitoring representative's name, date of receipt:

XRP6258		] XT 601
EFC6193	Country No. Centre No. Subje	ct No.   Page
CYCLE 1	V 01 Se	ee Page 62
ADVERSE EVI	ENT FORM	0.1_AE_1
1.	AE form no:	AE form no:
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
S		
2. STATUS OF AE 1= New	1 Date of start: LLLLLL year	1 Date of start: LLLLLL LLLL day month year
2= Ongoing from previous period without change	2 (do not complete the remaining items in the column)	2 (do not complete the remaining items in the column)
3= Ongoing with change	3 🗖	3 🗖
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No No	Yes  No
7. OUTCOME  1= Recovered	1 <b>1</b> Date:	
4= Recovered with sequelae	day month year  4  Specify sequelae:	day month year  4  Specify sequelae:
2= Recovering		2 🗖
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	5 Date of death:	5 Date of death: U U U U U U U U U U U U U U U U U U U
6= Unknown	6 🖸	6 🔲
8. SERIOUSNESS CRITERIA	Yes  \( \begin{align*} \text{No} & \Boxed \\ \end{align*} \)  \( \begin{align*} \text{Ves} & \text{No} & \Boxed \\ \end{align*} \)  \( \begin{align*} \text{Ves} & \text{Date event became serious:} \end{align*} \)	Yes  No  No  To Date event became serious:
IF YES, COMPLETE THIS SECTION	⇒ IF YES	
AND THE SAE COMPLEMENTARY FORM	- Tick below all criteria that apply:	day month year - Tick below all criteria that apply:
	Resulting in death	Resulting in death
	Life-threatening	Life-threatening
	Requiring/prolonging hospitalization	Requiring/prolonging hospitalization
	Congenital anomaly/birth defect	Congenital anomaly/birth defect
Investigator's name, date of repo	Other medically important event	Other medically important event
on the state of teps		see a marrie of date of receipt.
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?

EFC6193 XT 601 XRP6258 sanofi aventis Confidential ■ FINAL ■ 17-Oct-2006

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO 34	
CYCLE 2	V 02		Date of visit:	day month	/ Dayear
				See Page	<u> </u>
PHYSICAL	EXAMINAT	ION PHYS	EXAM_2		
None $\square$					
Date performed: Lda		J L J L J year			
Were there any clining	ically significant cha	nges from the	previous evalua	ation? Yes*	□ No □
* If yes, please com	plete Adverse Event	form.			
		See Page 27			
VITAL SIGN	IS				VITAL_1
NOT DONE					
Weight: ШШШ	. Ш kg				
- Blood pressure:	Systolic LILL	mmHg / E	Diastolic LL	mmHg	
- Heart rate:	□□□ beats/mir	1			
	□□.□ °C				
- Temperature:	(tick appropria		Oral 🔲	Rectal 🔲	Auricular 🔲
ECOG Performance					
0 1 2					
L NO 3	34 ,	, >	(RP6258	_ EFC6193	

Page 69/525 Confidential ■ FINAL ■ 21-NOV-2006

sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.	NO	35 Page	
CYCLE 2 - DAY 1	V 02	See Page 24			

# **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

PSA

See Page 26

LABH\_1

DATE OF SAMPLING day month year	Test	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

 NO
 35
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-NOV-2006
 sanofi aventis

XRP6258 EFC6193		NO	36
EFC0193	Country No.	Centre No.   Subject No.	Page
CYCLE 2 - DAY 1	V 02	See Page 25	

# **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 36 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	37 Page	
CYCLE 2 - DAY 8	V 02	See Pag	ne 24			

# **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 37 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	38 Page	
CYCLE 2 - DAY 15	V 02	See Pag	ge 24			

### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 38 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No.	39 Page
CYCLE 2	V 02	See Page 48	T age

#### **SPECIFIC CONCOMITANT MEDICATION** SPMED\_1

N	one	, [

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION	Dosage			START DA	<b>TE</b>	END DATE
	MEDICATION	Number of Units	Unit	day	month	year	day month year
1							
2							
3							
4							
5							
6							
7							
8							
9							
-							
10					_		

NO	39 ,	XRP6258	EFC6193
Confido	ntial ■ FINIAL ■ 21 NOV 2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No.	O 40 Page
CYCLE 2	V 02	See Page 49	

#### INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

Treatment Name	Date and Time of Dosing			Intended Dose	ACTUAL DOSE GIVEN	
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start					
☐ Mitoxantrone	End					
IF DOSE DELAYED AND	OR REDUCED	AND/OR INTERI	RUPTED, SPECIFY	REASON:		
☐ AE: Specify on AE fo	rm					
Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name	Date and Time of Dosing			Intended Dose	ACTUAL DOSE GIVEN	
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start					
☐ Mitoxantrone	End				NA	

NO 40 , XRP6258 , EFC61		. 5		anosi aventis
	NO	40	XRP6258	_ EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page
CYCLE 2	V 02	See Page 49

#### **INVESTIGATIONAL PRODUCT ADMINISTRATION** ADMIN\_1

	TREATMENT NAME	DATE OF DOSING			Intended Dose	ACTUAL DOSE GIVEN	
		day	month	year	(mg)	(mg)	
	Prednisone	Start L					
	Prednisolone	End LL					
IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:							
☐ AE: Specify on AE form							
Other:							

IF DOSE INTERRUPTED, complete below:

Treatment Name	DATE OF DOSING	Intended Dose	ACTUAL DOSE GIVEN
	day month year	(mg)	(mg)
☐ Prednisone	Start		
☐ Prednisolone		NA	

NO	41	XRP6258	EFC6193
		500	of: avootic

XRP6258 EFC6193			NO 4	12
EFC0193	Country No.	Centre No.   Subject No.	Į F	Page
CYCLE 2	V 02	See Page 51		

#### **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 42 XRP6258 EFC6193

Locat	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	Regional Lymph Nodes	20.20	Rectum		
11.02	Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	43 Page	
CYCLE 2	V 02	See Pa	ge 55			

#### **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	DATE OF ASSESSMENT Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	LJLJ.LJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□ □□□□□□□□□□□□ Not Done		mm	
3	LJLJ.LJ	Not Done			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.L	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
6		□ Not Done			
7		□ Not Done			
8		□ Not Done			
9		□□ □□□□□□□□□□□□□ Not Done			
10	LJLJ.LJLJ	□□ □□□□□□□□□□□□□ Not Done			
11		□ Not Done			
12	LJLJ.LJ	□□ □□□□□□□□□□□□ Not Done			
13		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
14	L.L.L	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 43 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	<b>44</b> Page	
CYCLE 2	V 02	See Page 53	1	1 1.90	

#### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1.	Ш	
2.		
3.		
4		
5.		
7	Ш	

NO 44 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	45 Page
CYCLE 2	V 02	See P	age 29		
					_
ECHOCARDIO	RAPHY	•			ECHOCARD_1
NOT DONE					
• Date performed: LLL L	month	year			
• 2D-Echocardiography:	Normal $\Box$		Abnormal*		
- Left ventricular ejection frac	tion (LVEF)	<u>.</u>	%		
- Lower Limit Normal of LVEF		اللا	. [_] %		
RADIONUCLID	E VENT	RICULO	OGRAP	HY	MUGA_1
NOT DONE					
• Date performed: LLL L	month	year			
• Radionuclide Ventriculogr	aphyy: Norma	al 🗖	Abno	ormal* 🗖	
- Left ventricular ejection frac	tion (LVEF)	<u> </u>	. 🔲 %		
- Lower Limit Normal of LVEF		. لــالــا	. 🔲 %		
* If clinically relevant, ple	ease complete	the Adverse	Event form.		

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	<b>46</b> Page	01
CYCLE 2	V 02	See Pa	ge 60			

#### **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	End Date
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XRP6258 XT46 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	46 Page	02
CYCLE 2	V 02	See Pa	age 60			

### **CONCOMITANT MEDICATION**

O.MED\_9

	MEDICATION	Start Date		END DATE			
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□ L □ Ongo	
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□ L □ Ongo	ing
6.			□□□□□□□□ □□ Ongoi			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
8.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□ L □ Ongo	ing
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□ L □ Ongo	
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	

XT	46	XRP6258	EFC6193
Confide	ontial ■ FINIAL ■ 21 NOV 2006	san	ofi aventis

XRP6258 EFC6193	Country No. Centre No.	Subje	oct No.	602 Page	01
CYCLE 2	V 02 0		See Page	<b>62</b>	
ADVERSE EVI	ENT FORM			O.1_AE_1	
☐ NONE	AE form no:   <b>0</b>    <b>2</b>  -  <b>0</b>    <b>1</b>			form no: [0][2]-[0	119 1
Adverse Event Diagnosis	AE ref. no:			ref. no: LJL-L	
2. STATUS OF AE 1= New	1 Date of start:	year	1 Date of sta	rt; LJL LJL day month	year
2= Ongoing from previous period without change 3= Ongoing with change	2 (do not complete the remaining items and 3 )	n the column)	2	omplete the remaining ite	ms in the column)
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲	4 🔲	1 🔲 💢	2 🔲 3 🖵	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No		Yes	□ N	o 🗖
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinued / 2= I 3= Dose reduced / 4= Delayed and reduced / 5: 0  1  2  3  4  5	= Interrupted		ermanently discontinued / / 4= Delayed and reduced 2  3	
6. Corrective Treatment/Therapy	Yes 🔲 No		Yes	□ N	o 🗖
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL Month 4 Specify sequelae:	year	1 Date 4 Spec	: LL LLL day month ify sequelae:	,
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	year	2	death:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes No No - Date event became so		Yes	Date event becam	ne serious:
FORM	- Tick below all criteria  Resulting in death		Life-threaten Requiring/pr Persistent/sig Congenital a	- Tick below all cri death	pacity
Investigator's name, date of repo			L	nme, date of recei	
* Is there a reasonable XT 602	possibility that the AE was caused by s	tudy treatmen		EFC6193	_

XRP6258		T 602 02
EFC6193	Country No.   Centre No.   Subje	oct No.   Page
CYCLE 2	V DO DO _	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.	AE form no: [0][2]-[0][3]	AE form no: [0][2]-[0][4]
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
2. STATUS OF AE	1 Date of start: LL	1 Date of start:
2= Ongoing from previous period without change 3= Ongoing with change	3	3
3. GRADE (1 - 4)	1	1 🗆 2 🗔 3 🗔 4 🗔
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗖	Yes 🗖 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes  No	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date:	1 Date: LL LL LLL year 4 Specify sequelae:
2= Recovering	2 🗖	
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	5 Date of death: U UUU Vear	5 Date of death:
6= Unknown	6 <b></b>	6 🗖
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes □ No □  - Date event became serious:  □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □	Yes □ No □  - Date event became serious:  □ IF YES     □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
FORM	- Tick below all criteria that apply:  Resulting in death	- Tick below all criteria that apply:  Resulting in death

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 602 , XRP6258 , EFC6193

Investigator's name, date of report and signature:

Monitoring representative's name, date of receipt:

XRP6258 EFC6193			][ хт	602	03
		stre No. Subje	ct No.	Page	
CYCLE 2	V 02 LI		See Page 62		
ADVERSE EV	ENT FORM			0.1_AE_1	
1.	AE form no: <b>0 2</b>	]- <mark>0                                    </mark>	AE form	no: <b>0 2</b> - <b>0 6</b>	
Adverse Event Diagnosis	AE ref. no:	J-L_	AE ref. no:		<u> </u>
2. STATUS OF AE	1 Date of start:		1 Date of start:		
1= New 2= Ongoing from previous period without change		month year	2 \(\square\) (do not complete	day month	year
3= Ongoing with change	3 🗖		3 🗖		
3. GRADE (1 - 4)	1 2 3	4 🗆	1 2 2	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🚨	No 🚨	Yes 🗖	No	
5. ACTION TAKEN WITH	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and re			ntly discontinued / 2= De Delayed and reduced / 5=	
STUDY TREATMENT	0 1 2 3 3			3 4 0	· · _
6. Corrective Treatment/Therapy	Yes 🗖	No 🚨	Yes 🗖	No	٥
7. OUTCOME 1= Recovered	1 Date:	month year	1 <b>D</b> Date:	day month	J L J L J
4= Recovered with sequelae	4 🗖 🕽 Specify sequelae:		4 🗖 🕽 Specify se	quelae:	
2= Recovering	2 🗖		2 🗖		
3= Not recovered	3 🗖		3 🗖		
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: LiL L day	month year	5  Date of death:	day month	year
8. SERIOUSNESS CRITERIA	Yes 📮	No 🔲	Yes 🗆	No ate event became se	rious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	□ IF YES		⇒ IF YES		
FORM	- Tick below a	I criteria that apply:	L - Tio	ck below all criteria	that apply:
	Resulting in death	Life-threatening Requiring/prolongi Persistent/significa Congenital anoma	ng hospitalization  nt disability/incapacity ly/birth defect  nportant event		
Investigator's name, date of repo	J	<b></b>	esentative's name,	·	··· <del>-</del>

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 602 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subject	XT 602 04
CYCLE 2	V 02	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: \0]\2]-\0]\7\ AE ref. no: \	AE form no: [ <b>0</b> ][ <b>2</b> ]-[ <b>0</b> ][ <b>8</b> ] AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL	1 Date of start: Lay month year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗖	Yes No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🔲 No 🗖	Yes  No
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered	1 Date: LL LLL year 4 Specify sequelae:	1  Date: LL LLL year 4  Specify sequelae:
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: U UUU Vear	5 Date of death: LL LLL year  6 D
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Compared to the No Compar	Yes No Compared to the No Compar
	Resulting in death	Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring repre	esentative's name, date of receipt:

XT 602 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 602 05
CYCLE 2	v 02   UUU	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \0 2 -\0 9  AE ref. no: \      -	AE form no:   <b>0</b>   <b>2</b>  -  <b>1</b>    <b>0</b>    AE ref. no:    -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL Lyear 2 (do not complete the remaining items in the column) 3	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1 🗆 2 🗔 3 🗔 4 🗔
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No C	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0 1 2 3 4 5 5
6. Corrective Treatment/Therapy	Yes No No	Yes No No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL
2= Recovering	2 🗖	2 🗖
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	Date of death:	5 Date of death:
6= Unknown	6 🔲	6 🗖
8. SERIOUSNESS CRITERIA	Yes  No  \( \begin{align*} \text{No} & \begin{align*} \text{V} & \text{Solution} & \	Yes No C - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that apply:  Resulting in death	Tick below all criteria that apply:  Resulting in death
Investigator's name, date of repo	Congenital anomaly/birth defect	Congenital anomaly/birth defect

EFC6193 602 XRP6258 XT

XRP6258 EFC6193	Country No.	Centre No.	Subje		ΚΤ	602 Page	06
CYCLE 2	V 02			<mark>See Pag</mark> e	e 62		
ADVERSE EVI	ENT FORI	VI				O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: AE ref. no:	0 2 - 1 1			AE form no: AE ref. no:	0 2 -1 2	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		wonth e remaining items in t	year	1	da	L L L L ay month e remaining items in	year
3. GRADE (1 - 4)	1 🔲 2 🔲	3 🗖	4 🔲	1 🔲	2 🗖	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No		Yes		No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently of 3= Dose reduced / 4= Delay				ced / 4= Delay	discontinued / $2=D$ yed and reduced / $5=$ $3 \square 4 \square$	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No		Yes		No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	_ }	ay month	year	<sup>-</sup> }	d	L LL L ay month Plae:	year
2= Recovering	2 🗖			2 🗖			
3= Not recovered	3 Detection			3 🔲	of doothy I		
5= Fatal (complete the death report form) 6= Unknown	5  Date of death: L	ay month	year	5 <b>□</b> Date 6 <b>□</b>		ay month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes		Resulting in death			erious:	
Investigator's name, date of repo	Other medically impo	rtant event	oring repr	Other m esentative's	edically impo	irth defectrtant eventte of receipt:	

XRP6258 EFC6193			] XT	602	
CYCLE 2	V 02	tre No. Subje	See Page 62	Page	
ADVERSE EVI	ENT FORM			O.1_AE_1	_
1. Adverse Event Diagnosis	AE form no:	- <u>                                     </u>	AE form (	no:     -	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		onth year  og items in the column)		day month you the remaining items in the co	ear
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 🔲 2 🖵	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No 🗖	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0		3= Dose reduced / 4= [	ntly discontinued / 2= Delayed Delayed and reduced / 5= Interru	
6. Corrective Treatment/Therapy	Yes 📮	No 🗖	Yes 🗖	No 🗖	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		nonth year	1 Date: 4 Specify se		ear
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI	2	day month y	J L J
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event be  IF YES - Date event be  Limit Limit day month - Tick below all	No	⇒ IF YES	No late event became serious	::   <u> </u>
	Resulting in death	ation	Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anoma	ing hospitalization	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name,	date of receipt:	
* Is there a reasonable	possibility that the AE was caus	ed by study treatmer	nt?		

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO 47	
CYCLE 3	V 03		Date of visit:	day month	J/                       year
	See Page	<del>2</del> 43			
PHYSICAL EXA				PHY	SEXAM_2
None 🗖					
Date performed: LLL LL day	month year				
• Were there any clinically s	ignificant change	es from the p	orevious evalu	ation? Yes	* 🔲 No 🔲
* If yes, please complete A	dverse Event for	m.			
VITAL SIGNS	See Page 27				VITAL_1
NOT DONE					-
Weight: ШШШ . Ш	kg				
- Blood pressure: Systolic	c LJLJ mr	mHg / D	iastolic LLL	mmHg	
	∟∟ beats/min	0 ,		J	
- Temperature: LILI	. L °C (tick appropriate b	oox).	Oral 🔲	Rectal 🔲	Auricular 🗖
<b>ECOG Performance Status</b>	(пек арргориме к	, ox,		Rectur <b>_</b>	/ turredian
$\begin{array}{cccc} 0 & 1 & 2 \\ \square & \square & \square \end{array}$	3 4 <b>-</b>				
					_

Confidential ■ FINAL ■ 21-NOV-2006

47

NO

XRP6258 sanofi aventis

EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	48 Page	
CYCLE 3 - DAY 1	V 03					
HEMATOLOGY	See Page 24	1			LABH_	1
Date of sampling:						

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

PSA

See Page 26

LABH\_1

d	DATE OF SAMPLING lay month year	Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
		PSA		ng/mL	

Confido	ntial ■ FINIAL ■ 21 N	OV 2006	sar	nofi aventis	
NO	48		XRP6258	_ EFC6193	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	49 Page	
CYCLE 3 - DAY 1	V 03	See Pag	ge 25			

#### **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 49 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	50 Page	
CYCLE 3 - DAY 8	V 03	See Pa	ige 24			

### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 50 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>51</b> Page	
CYCLE 3 - DAY 15	V 03	See Pa	age 24			

### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10 <sup>9</sup> /L	
Eosinophils		10 <sup>9</sup> /L	
Basophils		10 <sup>9</sup> /L	
Monocytes		10 <sup>9</sup> /L	
Lymphocytes		10 <sup>9</sup> /L	
Platelets		10 <sup>9</sup> /L	
Hemoglobin		g/dL	

NO 51 XRP6258 EFC6193

XRP6258 EFC6193			NO	52	
	Country No.	Centre No.   Subject No.		Page	
CYCLE 3	V 03	See Page 48			

#### SPECIFIC CONCOMITANT MEDICATION SPMED\_1

Ν	O	ne	Г

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION		SAGE		START DA	<b>TE</b>	End date	
	MEDICATION	Number of Units	Unit	day	month	year	day month year	
1								
2								
3								
4								
5								
6								
7								
8								
9								
-								
10					_			

NO	52	XRP625	8 <sub> </sub> EFC6193
Confide	ntial ■ FINIAL ■ 21 N	006	sanofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page
CYCLE 3	V 03	See Page 49

## INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

Treatment Name	Date and Time of Dosing					ACTUAL DOSE GIVEN
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start L			LL: LL		
☐ Mitoxantrone	End					
IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:						
☐ AE: Specify on AE form						
☐ Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name		Intended Dose	ACTUAL DOSE GIVEN			
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start					
☐ Mitoxantrone	End				NA	

NO	NO 53 <sub> </sub>		XRP6258	EFC6193
			500	ofi aventic

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page	
CYCLE 3	V 03	See Page 49	

## INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

	TREATMENT NAME		Intended Dose	ACTUAL DOSE GIVEN				
		day	month	year	(mg)	(mg)		
	Prednisone	Start						
	Prednisolone	End L						
IF DOSE DEL	IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:							
☐ AE: Specify on AE form								
Other:								

IF DOSE INTERRUPTED, complete below:

Treatment Name		Intended Dose	ACTUAL Dose Given		
	day	month	year	(mg)	(mg)
☐ Prednisone	Start				
☐ Prednisolone	End L			NA	

NO	54	XRP6258	_ EFC6193
0 " 1	4 1 - FD141 - 64 N		anofi aventis

XRP6258 EFC6193				NO	55	
	Country No.	Centre No.	Subject No.		Page	
CYCLE 3	V 03	See Pag	<mark>je 51</mark>			

# **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 55 XRP6258 EFC6193

Locat	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	Regional Lymph Nodes	20.20	Rectum		
11.02	Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
CYCLE 3	V 03	See Page 55

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.L.	□□□□□□□□□□□□□□□□ Not Done			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJLJ	Not Done			
4		□□□□□□□□□□□□□□□□ Not Done			
5	L.L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□ Not Done			
7	L.L.L.	□□□□□□□□□□□□□□□ Not Done			
8	L.I	□ Not Done			
9		□□ □□□ □□□□□ □ Not Done			
10	LILI.LILI	□□□□□□□□□□□□□□□□ Not Done		L_ L_  mm	
11		□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□ □□□□□ □ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 56 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	57 Page	
CYCLE 3	V 03	See Pa	age 53			

#### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		LILL. LILL
3.		
4.		لــالــا . لــالــا
5		
6.		
7		

NO 57 XRP6258 EFC6193

XRP6258				NO	58
EFC6193	Country No.	Centre No.	Subject No.		Page
CYCLE 3	V 03	See	Page 29		
					_
<b>ECHOCARDIO</b>	GRAPHY	<b>1</b>			ECHOCARD_1
NOT DONE					
• Date performed: Lay	month	year			
2D-Echocardiography:	Normal $\Box$		Abnormal*		
- Left ventricular ejection frac	ction (LVEF)		• 📖 %		
Lower Limit Normal of LVE	F		. 🔲 %		
RADIONUCLID	E VENT	RICUL	OGRAP	HY	MUGA_1
• Date performed: Lay	month	year			
<ul> <li>Radionuclide Ventriculog</li> <li>Left ventricular ejection fraction</li> </ul>		nal 🗖		ormal* 🗖	
- Lower Limit Normal of LVE					
* If clinically relevant, pl	ease complete	the Adverse	Event form.		

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	59 Page	01
CYCLE 3	V 03	See Pa	age 60			

#### **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	END DATE
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

59 XRP6258 XTEFC6193 sanofi aventis

CYCLE 3	V 03	Centre No.	Subject No.	1	Page	
XRP6258 EFC6193				XT	59	02

#### **CONCOMITANT MEDICATION**

O.MED\_9

	Medication	START DATE		End Date			
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШ bing		□□□□ L □ Ongo	⊔⊔Ш ing
2.			□□□ l □ Ongo	⊔⊔Ш bing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ШШШ ving		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ШШШ ing
4.			□□□ l □ Ongo	⊔⊔Ш bing		□□□ L □ Ongo	ப்பட்ட ing
5.			□□□ l □ Ongo	⊔ШШШ bing		⊔⊔⊔ L □ Ongo	ப்பட்பட் ing
6.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	bing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ululul ping		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ululul ing
8.			□ Ongo	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing ing
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ЫШШ bing		□□□□ L □ Ongo	⊔ШШ ing
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШ Jing		□□□□ L □ Ongo	⊔⊔Ш Jing

XRP6258 EFC6193		tre No. Subjec	T XT	603 Page	0[1
CYCLE 3  ADVERSE EVI	V 03 L		See Page 62	0.1_AE_1	_
None					
1. Adverse Event Diagnosis	AE form no:   <b>0</b>   <b>3</b> AE ref. no:	-  <b>0</b>   1    -	AE form no: 1013-012  AE ref. no: 1-11		
2. STATUS OF AE 1= New	1 Date of start:	LILI LILI LI	1 Date of start:	day month	J
2= Ongoing from previous period without change 3= Ongoing with change	2 (do not complete the remaini	ng items in the column)	2  (do not comple	ete the remaining items in	the column
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖵	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 📮	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0 1 1 2 3 3	luced / 5= Interrupted	3= Dose reduced / 4=	nently discontinued / 2= De Delayed and reduced / 5= 2  3  4  4	Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 📮	No 🗖	Yes 🗖	No	
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  1  Date: Lill Lill Lill Lill Lill Lill Lill Lil		1 Date: LL LL LLL year 4 Specify sequelae:			
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILI	2	n:	J∐∐L year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM		No	⇒ IF YES	No  Date event became ser  LLLLLLL  day month  Fick below all criteria	J L L L J
	Resulting in death		Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event		
Investigator's name, date of repo	Monitoring repre	Monitoring representative's name, date of receipt:			
* Is there a reasonable	possibility that the AE was caus				

XRP6258 EFC6193		XT 603 02		
CYCLE 3	V 03 Centre No. Subject	See Page 62		
ADVERSE EVI	ENT FORM	O.1_AE_1		
1.  Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin{align*} \begin{align*} \left( 0 \right) \\ \left( 3 \right) \\ \left( 1 \right) \\ \left(	AE form no:   <b>0</b>   <b>3</b>   <b>0</b>   <b>4</b>   AE ref. no:   -		
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3 D		
3. GRADE (1 - 4)	1 2 3 4 4	1 🔲 2 🔲 3 🔲 4 🔲		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No 🗆		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
7. OUTCOME	Yes No D	Yes  No		
1= Recovered 4= Recovered with sequelae 2= Recovering	1 Date: LL	Date: LL		
3= Not recovered	3 🗖	3 🗖		
5= Fatal (complete the death report form) 6= Unknown	5 ☐ Date of death: ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐	5 Date of death: U UUU year 6 D		
8. SERIOUSNESS CRITERIA	Yes	Yes No C - Date event became serious:		
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that apply:	→ IF YES     Solution   Control   C		
	Resulting in death	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event		
Investigator's name, date of report and signature:  * Is there a reasonable possibility that the AE was caused by study treatment?  * Is there a reasonable possibility that the AE was caused by study treatment?				

XT 603 XRP6258 EFC6193

XRP6258 EFC6193		XT 603 03			
CYCLE 3	V 03 Centre No. Subje	See Page 62			
ADVERSE EV	ENT FORM	O.1_AE_1			
1. Adverse Event Diagnosis	AE form no: [0] 3]-[0] [5] AE ref. no: []-[]-	AE form no: [0] [3]-[0] [6] AE ref. no: []-[]-			
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3 D	1 Date of start: LLL LLL LLL LLL LLL LLL LLL LLL LLL L			
3. GRADE (1 - 4)	1	1 🗆 2 🗔 3 🗔 4 🗔			
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖	Yes No C			
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0			
6. CORRECTIVE TREATMENT/THERAPY	Yes No 🗆	Yes No D			
1= Recovered 4= Recovered with sequelae 2= Recovering	1  Date: LL	Date: LL			
3= Not recovered	3 🗖	3 🗖			
5= Fatal (complete the death report form) 6= Unknown	5 Date of death:	5 Date of death:			
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes No C  - Date event became serious:    If Yes	Yes No C  - Date event became serious:    Solition   Date   Date			
AND THE SAE COMPLEMENTARY FORM	- Tick below all criteria that apply:	- Tick below all criteria that apply:			
	Resulting in death	Resulting in death			
Investigator's name, date of report and signature:  Monitoring representative's name, date of receipt:					
* Is there a reasonable	possibility that the AE was caused by study treatment	nt?			

XT 603 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cent	tre No.   Subje	XT	603 Page	04
CYCLE 3	v 03		See Page 62	_	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>0</b> ] <b>3</b> AE ref. no: <b>1</b>	- <mark> 0  7 </mark>  -	AE for	m no:   <mark>0  3 - 0  8</mark> no:    -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		JUUUU nonth year ng items in the column)	1 Date of start: 2 (do not comp	day month left the remaining items in	year
3. GRADE (1 - 4)	_	<u> </u>	1 2 2		4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*  5. ACTION TAKEN WITH STUDY TREATMENT	Yes		3= Dose reduced / 4	anently discontinued / 2= 0 4= Delayed and reduced / 5= 2  3  4  4	= Interrupted
6. Corrective Treatment/Therapy	Yes 📮	No 🗖	Yes	No No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		oonth year	1 Date: 4 Specify	day month sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI nonth year	2	th:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event bed - Date event bed - Date event bed - Date event bed - Tick below all - Tick below all - Resulting in death	year criteria that apply:	⇒ IF YES { L	No Date event became se	year a that apply:
Investigator's name, data of repo	Life-threatening	ation	Life-threatening Requiring/prolo Persistent/signifi Congenital anor Other medically	nging hospitalization icant disability/incapacit maly/birth defect	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name	e, date of receipt:	

XT 603 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 603 05
CYCLE 3	v 03	See Page 62
ADVERSE EV	ENT FORM	0.1_AE_1
1. Adverse Event Diagnosis	AE form no:   <b>0</b>   <b>3</b>  - <b> 0</b>   <b>9</b>    AE ref. no:   - - - -	AE form no: [0][3]-[1][0] AE ref. no: []-[]-
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column)	Date of start: LLL LLLL year  2  (do not complete the remaining items in the column)  3  \[ \begin{align*}  \text{ \tex{ \text{ \
3. GRADE (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT*	1	1
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0 1 2 3 4 5 5	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes No C
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date: LIL LIL LIL LIL LIL LIL LIL LIL LIL LI	Date: Liling Liling Month year  Specify sequelae:
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No - Date event became serious:  If Yes - Date event became serious:  Light Heritage And American Serious:  - Tick below all criteria that apply:	Yes One No One of the Pres Serious:  - Date event became serious:  - Date event became serious:  - Tick below all criteria that apply:
Investigator's name, date of rep	Resulting in death	Resulting in death
'		

XT 603 XRP6258 EFC6193

\* Is there a reasonable possibility that the AE was caused by study treatment?

XRP6258 EFC6193	Country No.   Centre No.   Subjection	XT 603 06	
CYCLE 3	v na nn	See Page 62	
ADVERSE EVI	ENT FORM	0.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>[0][3]-[1][1]</b> AE ref. no: <b>[]]-[]</b>	AE form no: [0]3-[1]2 AE ref. no: []-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	
3. GRADE (1 - 4)	1	1	
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No 🗆	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	
6. CORRECTIVE TREATMENT/THERAPY	Yes No 🗆	Yes No 🗆	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)	1 Date: LLL LLLL Agy month year 4 Specify sequelae:		
6= Unknown	6 🗆	6 0	
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes	
Investigator's name, date of repo	Congenital anomaly/birth defect	Congenital anomaly/birth defect	

EFC6193 603 XRP6258 XT

XRP6258		☐ XT 603 ☐ ☐
EFC6193	Country No. Centre No. Subje	ect No. Page
CYCLE 3	v 03 100 _	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: LL-LL AE ref. no: LL-LL	AE form no: LL-LL AE ref. no: LL-LL
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: L L L L L L L L L L L L L L L L L L L	1 Date of start: L L L L L L L L L L L L L L L L L L L
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No No	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes  No  No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: U UU UUU year 4 D Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes No C  - Date event became serious:    Solitor   Date   Date	Yes □ No □  - Date event became serious: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□
FORM	- Tick below all criteria that apply:  Resulting in death	- Tick below all criteria that apply:  Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring repr	resentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmen	nt?

XRP6258 EFC6193	Country No. Centre N	lo. Subject No.	NO 60	) e
CYCLE 4	v 04	Date of visit:	day month	/ Quar
		See Page 43		$\neg$
PHYSICAL EXA	AMINATION	See Fage 43	PHYS	EXAM_2
NONE				
Date performed: Lay	month year			
Were there any clinically	significant changes from	the previous evalu	uation? Yes*	No 🗆
*If yes, please complete A	Adverse Event form.			
VITAL SIGNS	See Page 27			VITAL_1
NOT DONE				
Weight: ШШШ. Ш	kg			
- Blood pressure: Systol	ic LLL mmHg	/ Diastolic 📖	mmHg	
- Heart rate: LIL	⊔∟ beats/min			
- Temperature:	J.∐ °C			
'	(tick appropriate box):	Oral 🔲	Rectal	Auricular 🔲
<b>ECOG Performance Status</b>	i			
0 1 2	3 4			

EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	61 Page	
CYCLE 4 - DAY 1	V 04					
	See Page	24				_
<b>HEMATOLOGY</b>		<del></del>			LABH_	1
Date of sampling:	month	year				

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

PSA

See Page 26

LABH\_1

DATE OF SAMPLING day month year	Test	<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

<u>L</u>	NO	61	ı	XRP6258	EFC6193
Page 114/525	Confider	itial ■ FINAL ■ 21-NOV-2006		san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	62 Page	
CYCLE 4 - DAY 1	V 04	See Pa	ige 25		-	

#### **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 62 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	63 Page	
CYCLE 4 - DAY 8	V 04		age 24		. ago	

## **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 63 XRP6258 EFC6193

XRP6258 EFC6193			NO	64	
EFC0193	Country No.	Centre No.   Subject No.	1	Page	
CYCLE 4 - DAY 15	V 04	See Page 24			

### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 64 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.	65 Page
CYCLE 4	V 04	See Page 48	

#### **SPECIFIC CONCOMITANT MEDICATION** SPMED\_1

Ν	one	, $\square$

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION		SAGE		START DA	<b>TE</b>	END DATE	
	MEDICATION	Number of Units	Unit	day	month	year	day month year	
1								
2								
3								
4								
5								
6								
7								
8								
9								
-								
10					_			

NO	65		XRP6258	EFC6193
Confide	ntial ■ FINAL I	■ 21-NOV-2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	66 Page	
CYCLE 4	V 04	See Page 49		T age	

## INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

Treatment Name	DATE AND TIME OF DOSING				Intended Dose	ACTUAL DOSE GIVEN	
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)	
☐ XRP6258	Start L			LL: LL			
☐ Mitoxantrone	End						
IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:							
☐ AE: Specify on AE form							
Other:							

IF DOSE INTERRUPTED, complete below:

TREATMENT NAME	DATE AND TIME OF DOSING				Intended Dose	ACTUAL DOSE
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	GIVEN (mg)
☐ XRP6258	Start L					
☐ Mitoxantrone	End				NA	

NO 66 . XRP6258 . EFC6193			7.1.11 0200	
	NO	66	XRP6258	EFC6193

XRP6258 EFC6193				NO	67	
LI 00133	Country No.	Centre No.	Subject No.		Page	
CYCLE 4	V 04	See Pa	ge 49			

## INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

	TREATMENT NAME	DATE OF DOSING			Intended Dose	ACTUAL DOSE GIVEN		
		day	month	year	(mg)	(mg)		
	Prednisone	Start L						
	Prednisolone	End LL						
IF DOSE DEL	IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:							
☐ AE: Specify on AE form								
Other:								

IF DOSE INTERRUPTED, complete below:

Treatment Name	DATE OF DOSING	Intended Dose	ACTUAL DOSE GIVEN
	day month year	(mg)	(mg)
☐ Prednisone	Start		
☐ Prednisolone	End	NA	

NO	67	, XRP6258	EFC6193
o		san	ofi aventis

XRP6258 EFC6193			NO	68	
LI C0193	Country No.	Centre No.   Subject No.	1	Page	
CYCLE 4	V 04	See Page 51			

### **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 68 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	) Colon	30	Other
11.0	1 Regional Lymph Nodes	20.20	) Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193		NO	69
EFC0193	Country No.	Centre No.   Subject No.	Page
CYCLE 4	V 04	See Page 55	

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.L.	□□□□□□□□□□□□□□□□ Not Done			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJLJ	Not Done			
4		□□□□□□□□□□□□□□□□ Not Done			
5	L. L. L.	□□ □□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□ Not Done			
7	L.L.L.	□□□□□□□□□□□□□□□ Not Done			
8	L.I	□ Not Done			
9		□□ □□□ □□□□□ □ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		L_ L_  mm	
11		□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 69 , XRP6258 , EFC6193

XRP6258 EFC6193				NO	70	
E1 00100	Country No.	Centre No.	Subject No.		Page	
CYCLE 4	V 04	See Pa	ige 53			

#### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		LILL . LILL
3.		니니. 니니
4		LJLJLJ
5.		
6		LJLJ. LJLJ
7	Ш	니니니 . 니니

XRP6258 NO 70 EFC6193

XRP6258  EFC6193  Courty No.	71
CYCLE 4 V 0 4	Page
See Page 29	
ECHOCARDIOGRAPHY	ECHOCARD_1
NOT DONE	
• Date performed: UUUUU Uuu usaar month year	
• <b>2D-Echocardiography:</b> Normal $\square$ Abnormal* $\square$	
- Left ventricular ejection fraction (LVEF) %	
- Lower Limit Normal of LVEF	
RADIONUCLIDE VENTRICULOGRAPHY  NOT DONE	MUGA_1
• Date performed: LLLLLLL LLLL wear	
• Radionuclide Ventriculographyy: Normal ☐ Abnormal* ☐	
- Left ventricular ejection fraction (LVEF) %	
- Lower Limit Normal of LVEF %	
* If clinically relevant, please complete the Adverse Event form.	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	 72 Page	
CYCLE 4	V 04	See Pa	age 60		

### **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	End Date
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

CYCLE 4	V 04	See Pa	ge 60			
LFC0193	Country No.	Centre No.	Subject No.	I	Page	
XRP6258 EFC6193				XT	72	02

### **CONCOMITANT MEDICATION**

O.MED\_9

	MEDICATION	Start Date		MEDICATION START DATE END DATE		ГЕ	
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□ L □ Ongo	
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□ L □ Ongo	ing
6.			□□□□□□□□ □□ Ongoi			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
8.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□ L □ Ongo	ing
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□ L □ Ongo	
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	

<u> </u>		7(1(1 0200	
ΧT	72	XRP6258	_ EFC6193

XRP6258 EFC6193	Country No. Centre	No. Subje	ct No.	604 Page	01
CYCLE 4	v 04 🗆		See Page 62	2	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no:		AE fo AE ref	rm no: [ <b>0]4]-[0</b> ][2 . no: []-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LL day month 2 (do not complete the remaining it	year year tems in the column)	1	day month plete the remaining items	
3. GRADE (1 - 4)	1 2 3 3	4 🗆	1 🗖 2 🛭	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*  5. ACTION TAKEN WITH STUDY TREATMENT	Yes		0= None / 1= Perm	namently discontinued / 2= 4= Delayed and reduced / 5 2  3  4	5= Interrupted
6. CORRECTIVE TREATMENT/THERAPY 7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown			1  Date: 4  Specify 2  3	No	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM		riteria that apply:	Yes  IF YES  Resulting in de Life-threatenin, Requiring/prole Persistent/signin Congenital and	No Date event became s  An	a that apply:
Investigator's name, date of repo			L	ne, date of receipt:	
* Is there a reasonable XT 604	possibility that the AE was caused	by study treatmer		EFC6193	_

XRP6258		T			
EFC6193	Country No. Centre No. Subje	ct No.   Page			
CYCLE 4	V 04 000	See Page 62			
ADVERSE EV	ENT FORM	O.1_AE_1			
		I			
1. Adverse Event	AE form no: [0][4]-[0][3]	AE form no: [0][4]-[0][4]			
DIAGNOSIS	AE ref. no:	AE ref. no:			
2. STATUS OF AE	1 □ Date of start: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	1 □ Date of start: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
1= New 2= Ongoing from previous period without change	day month year  2  (do not complete the remaining items in the column)	day month year 2  (do not complete the remaining items in the column)			
3= Ongoing with change	3 🗖	3 🗖			
3. GRADE (1 - 4)	1 2 3 4 1	1			
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗆	Yes 🔲 No 🚨			
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  0			
6. CORRECTIVE TREATMENT/THERAPY  7. OUTCOME	Yes No D	Yes No D			
1= Recovered	1 Date: LL LL LL year	1 Date: LL LL LL LL L			
4= Recovered with sequelae	4 🗖 🕽 Specify sequelae:	4 🗖 🕽 Specify sequelae:			
2= Recovering	2 🗖	2 🗆			
3= Not recovered	3 🗖	3 🗖			
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: LL LL LLL year	6 Date of death:			
8. SERIOUSNESS CRITERIA	Yes No No	Yes No No			
IF YES, COMPLETE THIS SECTION	- Date event became serious:	→ IF YES - Date event became serious:			
AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that apply:	Tick below all criteria that apply:			
	Resulting in death	Resulting in death			
	Life-threatening	Life-threatening			
	Persistent/significant disability/incapacity	Persistent/significant disability/incapacity			
	Congenital anomaly/birth defect	Congenital anomaly/birth defect			
Investigator's name, date of rep	Investigator's name, date of report and signature:  Monitoring representative's name, date of receipt:				
* Is there a reasonable	possibility that the AE was caused by study treatmen	nt?			

XT 604 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No.	XT 604 03
CYCLE 4	V 04	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin	AE form no: 0 4 - 0 6 AE ref. no:
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	1 Date of start: LLL LLL year  2 (do not complete the remaining items in the colu	day month year
3= Ongoing with change	3 🗖	3 🗖
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4	1     2     3     4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes 🗆 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  0
6. Corrective Treatment/Therapy	Yes No 🗆	Yes No No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLL LLL year 4 Specify sequelae:	day month year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes □ No □  - Date event became serious:  □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □	day month year
Investigator's name, date of rep	- Tick below all criteria that app  Resulting in death	Resulting in death

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 604 XRP6258 EFC6193

XRP6258		T
EFC6193	Country No. Centre No. Subje	ct No.   Page
CYCLE 4	V 04 000	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1.	AE form no: <b>0 4 - 0 7</b>	AE form no: <b>0 4 -0 8</b>
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
2. STATUS OF AE 1= New	1 Date of start: LL LLL year	1 Date of start: LL LLL year
2= Ongoing from previous period without change	2 (do not complete the remaining items in the column)	2 (do not complete the remaining items in the column)
3= Ongoing with change	3 🗖	3 🗖
3. GRADE (1 - 4)	1 🗆 2 🗔 3 🔲 4 🗔	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes No 🗆
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted
	0 0 1 0 2 0 3 0 4 0 5 0	0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖 No 🗖	Yes 🔲 No 🗖
7. OUTCOME 1= Recovered	1 □	1 🗖 🕽 Date: 📙 🗀 🗀 U
4= Recovered with sequelae	4 🗖 Specify sequelae:	4  Specify sequelae:
2= Recovering	2 🗖	2 🗖
3= Not recovered	3 🗖	
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: U UU U U U Vear  6 D	5 Date of death:
8. SERIOUSNESS	Yes No D	Yes No D
CRITERIA	- Date event became serious:	- Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE <b>SAE</b> COMPLEMENTARY FORM	⇒ IF YES	→ IF YES
	Resulting in death	Resulting in death
	Life-threatening	Life-threatening
	Persistent/significant disability/incapacity $lacksquare$	Persistent/significant disability/incapacity $lacksquare$
	Congenital anomaly/birth defect	Congenital anomaly/birth defect
Investigator's name, date of rep		esentative's name, date of receipt:
		, - r ·

XT 604 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 604 05
CYCLE 4	V 04	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no:   <b>0</b>   <b>4</b>  -  <b>0</b>   <b>9</b>    AE ref. no:           -	AE form no: [0] [4] - [1] [0] AE ref. no: [] - [] -
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No No	Yes  No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	Date: U U U U U U U U U U U U U U U U U U U	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Companies N	Yes  No  - Date event became serious:  IF YES
Investigator's name, date of rep	Resulting in death	Resulting in death

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 604 0 6
CYCLE 4	V 04	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: [ <b>0</b> ][ <b>4</b> ]-[ <b>1</b> ][ <b>1</b> ] AE ref. no: []-[]-	AE form no:   <b>0</b>   <b>4</b>  -  <b>1</b>   <b>2</b>    AE ref. no:       -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 📮	Yes 🗖 No 🗖
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes 🔲 No 🗖	Yes  No
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering	1 Date: LL LLL LLL LLL LLL LLL LLL LLL LLL LL	1 Date: LL
3= Not recovered  5= Fatal (complete the death report form)	3 ☐ 5 ☐ Date of death: ☐☐ ☐☐☐ ☐☐☐☐☐	3
6= Unknown	day month year	day month year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes No C - Date event became serious:	Yes □ No □  - Date event became serious: □ IF YES { □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
AND THE SAE COMPLEMENTARY FORM	day month year  - Tick below all criteria that apply:	day month year  - Tick below all criteria that apply:
	Resulting in death	Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt:

EFC6193 604 XRP6258 XT

XRP6258 EFC6193	Country No. Centre N	o. Subje	act No.	604 Page	
CYCLE 4	v 04		See Page 62		
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: L_  - AE ref. no: L_ _ -		AE form r AE ref. no:	no: ШЫ-ШЬ	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL LL May month 2 (do not complete the remaining item 3	year	1 Date of start: 2 (do not complete 3 D	day month the the remaining items in	year
3. GRADE (1 - 4)	1 2 3 3	4 🗖	1 🔲 2 🖸	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No	. 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 3= Dose reduced / 4= Delayed and reduced 0		0= None / 1= Permanen 3= Dose reduced / 4= D 0		= Interrupted
6. Corrective Treatment/Therapy	Yes 🔲 No	) <b>U</b>	Yes 🗖	No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date: LIL LIL day month  Specify sequelae:  2  3  5  Date of death: LIL LIL day month	year	_ }	day month quelae:	year year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes □ No  - Date event becam  ⇒ IF YES		Yes 🗖	No ate event became se	erious:
FORM  Investigator's name, date of repo	- Tick below all crit  Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incap  Congenital anomaly/birth defect  Other medically important event	eria that apply:	- Tic Resulting in death Life-threatening Requiring/prolongi Persistent/significar Congenital anomal	ck below all criteria ng hospitalization nt disability/incapacit ly/birth defect nportant event	a that apply:
	possibility that the AE was caused b			aute of receipt.	

EFC6193 XT 604 XRP6258

XRP6258 EFC6193 CYCLE 5	Country No. Centre No. V 05	Subject No.  Date of visit:	NO 73 Page	/ Day
PHYSICAL EXA	MINATION	See Page 43	,	EXAM_2
· ·   · · · · · · · · · · · · · · · · ·	month year			
Were there any clinically s  *If yes, please complete A		the previous evalua	ation? Yes*	□ No □
VITAL SIGNS NOT DONE	See Page 27			VITAL_1
Weight: LLL L		/ Diastolic L.J.L.	니니 mmHg	
- Heart rate: LL	<ul><li> beats/min</li><li>. □ °C</li><li>(tick appropriate box):</li></ul>	Oral 🗖	Rectal 🔲	Auricular 🗖
ECOG Performance Status  0 1 2	3 4			

Page 135/525 Confidential ■ FINAL ■ 21-NOV-2006

73

NO

sanofi aventis

EFC6193

XRP6258

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>74</b> Page
CYCLE 5 - DAY 1	V 05				
HEMATOLOGY	See Pag	ge 24			LABH_1

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10º/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10 <sup>9</sup> /L	
Eosinophils		10 <sup>9</sup> /L	
Basophils		10 <sup>9</sup> /L	
Monocytes		10 <sup>9</sup> /L	

year

Date of sampling: UU UUU UUUU

Lymphocytes

Hemoglobin

Platelets

Page 136/525

month

PSA

See Page 26

LABH\_1

10<sup>9</sup>/L

10<sup>9</sup>/L

g/dL

DATE OF SAMPLING day month year	Test	<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO	74	ı	XRP6258	_ EFC6193
Confide	ntial ■ FINAL ■ :	21-NOV-2006	sar	nofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>75</b> Page	
CYCLE 5 - DAY 1	V 05	See Pa	ae 25			

#### **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 75 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page
CYCLE 5 - DAY 8	V 05	See Page 24

### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 76 XRP6258 EFC6193

XRP6258 EFC6193				NO	77	
	Country No.	Centre No.	Subject No.		Page	
CYCLE 5 - DAY 15	V 05	See Pa	age 24			

## **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 77 XRP6258 EFC6193

XRP6258 EFC6193		
EFC0193	Country No.	Centre No. Subject No. Page
CYCLE 5	V 05	See Page 48

#### **SPECIFIC CONCOMITANT MEDICATION** SPMED\_1

Ν	one	

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION	1	SAGE		START DA	ATE .	END DATE	
	MEDICATION	Number of Units	Unit	day	month	year	day month year	
1								
2			 	1 11 11				
<u> </u>			 					
3			 					
4								
5			 					
6			 	ا لــالــا				
7			 				UU UUU UUUU	
8							UU UUU UUUU	
9								
10								

NO	78	XRP6258	EFC6193	
Confident	tial ■ FINIAL ■ 21-NOV-2006	san	nofi aventis	

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page	
CYCLE 5	V 05	See Page 49	

#### INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

Treatment Name	Date and Time of Dosing			Intended Dose	ACTUAL DOSE GIVEN	
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start  _					
☐ Mitoxantrone	End					
IF DOSE DELAYED AND	OR REDUCE	D AND/OR INTER	RRUPTED, SPECIFY	REASON:		
☐ AE: Specify on AE form						
Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name		Intended Dose	ACTUAL DOSE GIVEN			
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start					
☐ Mitoxantrone	End				NA NA	

NO 79 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	80 Page	
CYCLE 5	V 05	See Page 49			

#### **INVESTIGATIONAL PRODUCT ADMINISTRATION** ADMIN\_1

	TREATMENT NAME		DATE OF DOS	ING	Intended Dose	ACTUAL DOSE GIVEN	
		day	month	year	(mg)	(mg)	
	Prednisone	Start					
	Prednisolone	End L					
IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:							
☐ AE: Specify on AE form							
Other:							
<u> </u>	•						

IF DOSE INTERRUPTED, complete below:

Treatment Name	DATE OF DOSING	Intended Dose	ACTUAL DOSE GIVEN
	day month year	(mg)	(mg)
☐ Prednisone	Start		
☐ Prednisolone		NA	

NO	80 ,	XRP6258	_ EFC6193
Confide	ntial ■ FINAL ■ 21-NOV-2	sa	nofi aventis

XRP6258 EFC6193	Country No.	Contro No.	Cubicat No.	NO	81 Barr
	Country No.	Centre No.	Subject No.		Page
CYCLE 5	V 05	See P	age 51		

### **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 81 XRP6258 EFC6193

Loca	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	Regional Lymph Nodes	20.20	Rectum		
11.02	Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193		NO	82
EFC0193	Country No.	Centre No.   Subject No.	Page
CYCLE 5	V 05	See Page 55	

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.L.	□□□□□□□□□□□□□□□□ Not Done			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJLJ	Not Done			
4		□□□□□□□□□□□□□□□□ Not Done			
5	L. L. L.	□□ □□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□ Not Done			
7	L.L.L.	□□□□□□□□□□□□□□□ Not Done			
8	L.I	□ Not Done			
9		□□ □□□ □□□□□ □ Not Done			
10	LILI.LILI	□□□□□□□□□□□□□□□□ Not Done		L_ L_  mm	
11		□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 82 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No. Sub	ject No.	D 83 Page
CYCLE 5	V 05	See Page 53	<u>.                                    </u>	

#### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		LILL . LILL
3.		니니. 니니
4		LJLJLJ
5.		
6.		LJLJ. LJLJ
7	Ш	니니니 . 니니

NO 83 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	84 Page
CYCLE 5	V 05	See Pa	age 29		
ECHOCARDIO	RAPHY	•			ECHOCARD_1
🗖					
NOT DONE ☐  • Date performed: ☐☐☐ ☐☐☐ ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐	month	year			
• 2D-Echocardiography:	Normal $\Box$	,	Abnormal* [	ם	
- Left ventricular ejection frac	tion (LVEF)	<u> </u>			
- Lower Limit Normal of LVEF	:	<u> </u>	%		
RADIONUCLID	E VENT	RICULO	GRAPH	ΙΥ	MUGA_1
RADIONUCLID  NOT DONE □  • Date performed: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	E VENTI	<b>RICULO</b> LUL  year	GRAPH	ΙΥ	MUGA_1
NOT DONE   • Date performed: Lay  • Radionuclide Ventriculogr	aphyy: Norma	year	Abnoi	<b>IY</b> rmal* □	MUGA_1
NOT DONE   • Date performed: LLL L	aphyy: Norma	<b>  </b> year	Abnoi 1 %		MUGA_1
NOT DONE  • Date performed: Lay  • Radionuclide Ventriculogr  - Left ventricular ejection frac	month  aphyy: Normation (LVEF)	year  Al	Abnoi <u></u>		MUGA_1
NOT DONE  Date performed: Lay  Radionuclide Ventriculogr Left ventricular ejection fract Lower Limit Normal of LVER	month  aphyy: Normation (LVEF)	year  Al	Abnoi <u></u>		MUGA_1
NOT DONE  Date performed: Lay  Radionuclide Ventriculogr Left ventricular ejection fract Lower Limit Normal of LVER	month  aphyy: Normation (LVEF)	year  Al	Abnoi <u></u>		MUGA_1

CYCLE 5	V 05	Centre No.	Subject No.		Page	
XRP6258 EFC6193				XT	85	01

#### **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	End Date
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XRP6258 XT85 EFC6193 sanofi aventis

CYCLE 5	V 05	Centre No.	Subject No.	<u> </u>	Page	
XRP6258 EFC6193				XT	85	02

## **CONCOMITANT MEDICATION**

O.MED\_9

	Medication	Start Date			END DATE		
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШ ing
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШШ ing		□□□ L □ Ongo	⊔ШШ ing
6.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
8.			□□□□ l Ongo	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing

0 " 1	# I = 50 I I = 04 NOV 000	_	sand	ofi aventis
 XT	85	, XRF	P6258	EFC6193

XRP6258 EFC6193	Country No. Cent	tre No. Subje	Ct No.	605 Page	01
CYCLE 5	V 05		See Page 6	2	
ADVERSE EVI	ENT FORM			0.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>0 5</b> AE ref. no:	- <u> 0   1  </u> 	AE fo AE ref	orm no:   <b>0</b>   <b>5</b>   <b>-0</b>   <b>2</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LL day m 2 (do not complete the remaining	onth year  og items in the column)	1	day month mplete the remaining items	
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 🗖 2	<b>3</b>	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*  5. ACTION TAKEN WITH STUDY TREATMENT	Yes    0= None  / 1= Permanently discontinued 3= Dose reduced  / 4= Delayed and red  0		0= None / 1= Perm	nanently discontinued / 2= 4= Delayed and reduced / 5	= Interrupted
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae 2 = Recovering 3 = Not recovered 5 = Fatal (complete the death report form) 6 = Unknown	4 □		1	No  Li   I   I   I    y sequelae:  ath: Li   Li    day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event bed ay month	year  criteria that apply:  ation   neapacity	Yes  IF YES  Resulting in de Life-threatenin Requiring/prol Persistent/signing Congenital and	No - Date event became s - Date event became s - Tick below all criteri eath	year  a that apply:
Investigator's name, date of repo			L	ne, date of receipt:	<del>-</del>
* Is there a reasonable  XT 605	possibility that the AE was cause	ed by study treatmer  XRP62		EFC6193	_

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 605 02
CYCLE 5	V 05	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.	AE form no: [ <b>0</b> ][ <b>5</b> ]-[ <b>0</b> ][ <b>3</b> ]	AE form no: [0][5]-[0][4]
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4 🔲	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🔲 No 🗖	Yes 🗆 No 🗅
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: U U U U U U U U U U U U U U U U U U U	1 Date: LL LL LL L L L L L L L L L L L L L L
2= Recovering	2 🗖	2 🗖
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form) 6= Unknown	5 Date of death:	5 Date of death:
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes No Compared to the Property of the Propert	Yes □ No □  - Date event became serious:  □ IF YES     □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
AND THE SAE COMPLEMENTARY FORM	day month year  - Tick below all criteria that apply:  Resulting in death	day month year  - Tick below all criteria that apply:  Resulting in death
	Life-threatening	Life-threatening

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 605 XRP6258 EFC6193

Investigator's name, date of report and signature:

Monitoring representative's name, date of receipt:

XRP6258 EFC6193	Country No.   Centre No.   Subjection	Tot No.   XT 605   03		
CYCLE 5	v 05	See Page 62		
ADVERSE EVI	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no: [0][5]-[0][5] AE ref. no: []-[]-	AE form no: [0][5]-[0][6] AE ref. no: []-[]		
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL LLL year  2 (do not complete the remaining items in the column)  3	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3		
3. GRADE (1 - 4)	1	1 🗆 2 🗔 3 🗔 4 🗔		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No D		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0			
6. CORRECTIVE TREATMENT/THERAPY	Yes No 🗆	Yes No D		
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date:	1 Date: Li Li Li Li Li Li Li Li Specify sequelae:		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes		
Investigator's name, date of repo		esentative's name, date of receipt:		
* Is there a reasonable	possibility that the AE was caused by study treatment	nt?		

XT 605 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	Tot No.   XT 605   04   14   15   15   15   15   15   15   1
CYCLE 5	v 05	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \0 5 -\0 7  AE ref. no: \  \  \  \  \  \  \  \  \  \  \	AE form no:   <b>0</b>   <b>5</b>  - <b>0</b>   <b>8</b>    AE ref. no:   -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLL LLL LLL LLL LLL LLL LLL LLL L
3. GRADE (1 - 4)	1 🗆 2 🗔 3 🔲 4 🗔	1 🗆 2 🗔 3 🔲 4 🗔
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering	Date: LLL LLLL year  Specify sequelae:	1 Date: LLL LLLL year 4 Specify sequelae:
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	5 ☐ Date of death: ☐☐ ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐	5  Date of death:
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Compared to the Property of the Propert	Yes No Service
Investigator's name, date of repo	Resulting in death	Resulting in death
	possibility that the AF was caused by study treatmen	· 

XT 605 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 605 05
CYCLE 5	V 05 000	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin	AE form no: [0][5]-[1][0] AE ref. no: []-[]-
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL	Date of start: LL LLL year  2  (do not complete the remaining items in the column)  3
3. GRADE (1 - 4)  4. RELATIONSHIP TO STUDY TREATMENT*	1	1
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖 No 🗖	Yes 🗖 No 🗖
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered  5 = Fatal (complete the death report form)  6 = Unknown	1 Date: Local Manager Local Ma	Date:
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes
Investigator's name, date of rep	ort and signature: Monitoring repr	resentative's name, date of receipt:

EFC6193 XT 605 XRP6258

\* Is there a reasonable possibility that the AE was caused by study treatment?

XRP6258 EFC6193	Country No. Centre No. Subje	XT 605 06
CYCLE 5	V 05 0	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [ <b>0</b> ][ <b>5</b> ]-[ <b>1</b> ][ <b>1</b> ]  AE ref. no: []-[]-	AE form no: [0][5]-[1][2] AE ref. no: [][-[][]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL LLL year  2 (do not complete the remaining items in the column)  3
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes 🔲 No 🗖	Yes 🔲 No 🚨
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering	1 Date: ULL Wear  4 Specify sequelae:	1 Date: LL LLL year 4 Specify sequelae:
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: LL LL LL year 6 D	5 Date of death:
8. SERIOUSNESS CRITERIA	Yes	Yes
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that apply:	Tick below all criteria that apply:
	Resulting in death	Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt:

XT 605 XRP6258 EFC6193

XRP6258		☐ XT 605 ☐ ☐			
EFC6193	Country No. Centre No. Subje	ect No.   Page			
CYCLE 5	V 05 0	See Page 62			
ADVERSE EV	ENT FORM	0.1_AE_1			
1.	AE form no:	AE form no:			
Adverse Event	AE ref. no:	AE ref. no:			
Diagnosis					
2. STATUS OF AE	1 <b>D</b> Date of start:	1 <b>D</b> Date of start:			
1= New	day month year  2  (do not complete the remaining items in the column)	day month year  2  (do not complete the remaining items in the column)			
2= Ongoing from previous period without change	3 🗖	3 🗖			
3= Ongoing with change	-	-			
3. GRADE (1 - 4)	1	1 2 3 4 4			
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No D			
5. ACTION TAKEN WITH	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted			
STUDY TREATMENT	0 1 2 3 4 5 5				
6. Corrective Treatment/Therapy	Yes No No	Yes No D			
7. OUTCOME 1= Recovered	1 <b>D D</b> Date:	1 Date:			
4= Recovered with sequelae	day month year  Specify sequelae:	day month year  4  Specify sequelae:			
2= Recovering 3= Not recovered	3 🗖	3 🗆			
5= Fatal (complete the death report form)	5 🔲 Date of death: 📙 📙 📗	5 🔲 Date of death: 📖 📖 📖 📗			
6= Unknown	day month year	day month year			
8. SERIOUSNESS	Yes 🔲 No 🗖	Yes No D			
CRITERIA	- Date event became serious:	- Date event became serious:			
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	TF YES Cay month year	TF YES Cay month year			
FORM	- Tick below all criteria that apply:	- Tick below all criteria that apply:			
	Resulting in death	Resulting in death			
	Requiring/prolonging hospitalization	Requiring/prolonging hospitalization			
	Persistent/significant disability/incapacity	Persistent/significant disability/incapacity			
	Congenital anomaly/birth defect	Congenital anomaly/birth defect			
Investigator/o name data of	Other medically important event	Other medically important event			
investigator's name, date of repo	Investigator's name, date of report and signature:  Monitoring representative's name, date of receipt:				
* Is there a reasonable possibility that the AE was caused by study treatment?					

XT 605 , XRP6258 , EFC6193

XRP6258			NO 86	
EFC6193	Country No. Centre	No. Subject No.	Page	
CYCLE 6	v 06   C	Date of visit:	day month	year
		Con David 42	1	
PHYSICAL EX	MINATION	See Page 43	PHYSE	XAM_2
NONE				
Date performed: LL day	month year			
Were there any clinicall	y significant changes fror	n the previous evalu	ation? Yes* [	□ No □
*If yes, please complete	Adverse Event form.			
VITAL SIGNS	See Page 27			VITAL_1
NOT DONE				
Weight: ШШШ. L	l kg			
- Blood pressure: Syst	olic LLL mmHg	/ Diastolic L_L	⊔∟ mmHg	
- Heart rate: └──↓	⊥∟ beats/min			
- Temperature: └──↓				
- Temperature.	(tick appropriate box):	Oral 🗖	Rectal	Auricular 🗖
ECOG Performance State				
$\begin{array}{cccc} 0 & 1 & 2 \\ \hline & \hline & \hline & \hline \end{array}$	3 4			
NO 86	1	XRP6258	_ EFC6193	

Page 157/525 Confidential ■ FINAL ■ 21-NOV-2006

sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	87 Page		
CYCLE 6 - DAY 1	V 06						
HEMATOLOGY	See Pag	ge 24				LABH_1	
Date of sampling: 니니 L							

day

month

year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10 <sup>9</sup> /L	
Basophils		10°/L	
Monocytes		10 <sup>9</sup> /L	
Lymphocytes		10 <sup>9</sup> /L	
Platelets		10°/L	
Hemoglobin		g/dL	

PSA

See Page 26

LABH\_1

DATE OF SAMPLING day month year	Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

L	NO	87	, XRP6258	EFC6193
Page 158/525	Confider	ntial ■ FINAL ■ 21-NOV-2006	san	ofi aventis

XRP6258 EFC6193				NO	88
EFC0193	Country No.	Centre No.	Subject No.		Page
CYCLE 6 - DAY 1	V 06	See Pa	ge 25		

#### **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

TEST	<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 88 XRP6258 EFC6193

XRP6258 EFC6193			NO	89	
EFC0193	Country No.	Centre No.   Subject No.	1	Page	
CYCLE 6 - DAY 8	V 06	See Page 24			

#### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 89 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	90 Page	
CYCLE 6 - DAY 15	V 06	See P	Page 24			

### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 90 XRP6258 EFC6193

XRP6258 EFC6193			NO	91
EFC0193	Country No.	Centre No.   Subject No.	I	Page
CYCLE 6	V 06	See Page 48		

#### **SPECIFIC CONCOMITANT MEDICATION** SPMED\_1

Ν	one	, $\square$

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION	1	SAGE		START DA	ATE .	END DATE	
	MEDICATION	Number of Units	Unit	day	month	year	day month year	
1								
2			 	1 11 11				
<u> </u>			 					
3			 					
4								
5			 					
6			 	ا لــالــا				
7			 				UU UUU UUUU	
8							UU UUU UUUU	
9								
10								

NO	91	ı	XRP6258	EFC6193	
Confider	ntial ■ FINAL ■ 21-NOV-2006		san	ofi aventis	

XRP6258 EFC6193	Country No.	Centre No.   Subject No.	NO 92 Page
CYCLE 6	V 06	See Page 49	-

### INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

Treatment Name	DATE AND TIME OF DOSING				Intended Dose	ACTUAL DOSE GIVEN		
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)		
☐ XRP6258	Start  _							
☐ Mitoxantrone	End							
IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:								
☐ AE: Specify on AE form								
☐ Other:								

IF DOSE INTERRUPTED, complete below:

Treatment Name		Intended Dose	ACTUAL DOSE GIVEN			
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start					
☐ Mitoxantrone	End				NA	

NO 92 XRP6258 EFC6193			The same of the sa	
	NO	92	XRP6258	EFC6193

XRP6258 EFC6193			NO	93	
	Country No.	Centre No.   Subject N	10. <sub> </sub>	Page	
CYCLE 6	V 06	See Page 49			

#### INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

	TREATMENT NAME	Date of Dosing			Intended Dose	ACTUAL DOSE GIVEN			
		day	month	year	(mg)	(mg)			
	Prednisone	Start							
	Prednisolone	End L							
IF DOSE DEL	IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:								
☐ AE: Specify on AE form									
Other:									

IF DOSE INTERRUPTED, complete below:

Treatment Name	DATE OF DOSING	Intended Dose	ACTUAL DOSE GIVEN
	day month year	(mg)	(mg)
☐ Prednisone	Start		
☐ Prednisolone		NA	

NO 93 . XRP6258 . EFC6193			Maria Victoria Ave	
	NO	93	XRP6258	EFC6193

XRP6258 EFC6193			] NO	94	
EFC0193	Country No.	Centre No.   Subject N	o. <sub> </sub>	Page	
CYCLE 6	V 06	See Page 51			

#### **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 94 XRP6258 EFC6193

Loca	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	) Colon	30	Other
11.01	Regional Lymph Nodes	20.20	) Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193		NO	95
EFC0193	Country No.	Centre No.   Subject No.	Page
CYCLE 6	V 06	See Page 55	

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.L.	□□□□□□□□□□□□□□□□ Not Done			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJLJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□ Not Done			
5	L. L. L.	□□ □□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□ Not Done			
7	L.L.L.	□□□□□□□□□□□□□□□ Not Done			
8	L.I	□ Not Done			
9		□□ □□□ □□□□□ □ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		L_ L_  mm	
11		□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 95 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page	
CYCLE 6	V 06	See Page 53	

#### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1		
		LILL . LILL
3.		
4		
5.		
6.		
7.		

NO 96 XRP6258 EFC6193

XRP6258 EFC6193				NO	97
CYCLE 6	V 06	Centre No.	Subject No.		Page
		See F	Page 29		
ECHOCARDIO	GRAPHY				ECHOCARD_1
NOT DONE					
• Date performed: LLL I	month	year			
• 2D-Echocardiography:	Normal $\Box$		Abnormal*	<b>_</b>	
- Left ventricular ejection fra	ction (LVEF)	Ш.	%		
- Lower Limit Normal of LVE	F	<u> </u>	%		
RADIONUCLID	E VENT	RICULO	OGRAPI	łΥ	MUGA_1
NOT DONE					
• Date performed: Lill day	month	year			
• Radionuclide Ventriculog	raphyy: Norm	al 🗖	Abno	rmal* 🔲	
- Left ventricular ejection frac	ction (LVEF)	<u> </u>	<u></u> %		
- Lower Limit Normal of LVE	F	<u> </u>	<u></u> %		
* If clinically relevant, pl	lease complete	the Adverse I	Event form.		

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	98 Page	01
CYCLE 6	V 06	See P	age 60			

#### **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	END DATE
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XRP6258 XT98 EFC6193 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	98 Page	0[2]
CYCLE 6	V 06	See P	age 60			

#### **CONCOMITANT MEDICATION**

O.MED\_9

	Medication	START DATE		END DATE			
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	LILLILLI Ding		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	LILLILLI Ding		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	LILLILLI Ding		□□□ L □ Ongo	ing
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	LILLLI Ding		□□□ L □ Ongo	⊔⊔Ш ing
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	LILLILLI Ding		□□□ L □ Ongo	JUUU ing
6.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	LILILI Ding		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
7.				Ding		□□□□ L □ Ongo	ing
8.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	Ding		□□□□ L □ Ongo	ing
9.			□□□□ ☐ Ongo	LILILI Ding		□□□ L □ Ongo	ப்பட்ட ing
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	LILILI Ding		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	

XRP6258 EFC6193	Country No. Cer	tre No. Subje	ct No.	606 Page	01
CYCLE 6	v 06		See Page	62	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>\0</b> ] <b>\6</b> AE ref. no: <b>\\</b>	- <mark> 0   1  </mark>  -		form no:  0  6 - 0 ref. no:         -	
2. STATUS OF AE 1= New	1 Date of start: LLL day  2 (do not complete the remaini	nonth year	1  Date of sta	art: day month	
2= Ongoing from previous period without change 3= Ongoing with change	3 🗖		3 🗖		
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 🗖	2 🔲 3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🚨	Yes	□ No	) <b></b>
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0	duced / 5= Interrupted		ermanently discontinued / / 4= Delayed and reduced 2  3	
6. Corrective Treatment/Therapy	Yes 📮	No 🚨	Yes	☐ No	) <b>[</b>
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL Lday  4 Specify sequelae:	month year	1 Date 4 Spec	e: day month cify sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI month year	2	death:	J LJLJL year
8. SERIOUSNESS CRITERIA  If yes, complete this section AND THE SAE COMPLEMENTARY FORM		No	Yes	Date event became Lill Lill Lill Lill Lill Lill Lill Lil	e serious:
	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defed	Life-threater Requiring/p Persistent/si Congenital	death	acity	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's na	ame, date of receip	ot:
* Is there a reasonable possibility that the AE was caused by study treatment?					
XT 606	ı	XRP62	58	EFC6193	_

XRP6258				<u> </u>	 XT	606	02
EFC6193	Country No.	Centre No.	LJL <sub>I</sub> Subje	ect No.	Λ1	Page	ال ال
CYCLE 6	V 06			See Pa	ge 62		
ADVERSE EV	ENT FOR	M				O.1_AE_1	
1. Adverse Event Diagnosis	AE form no AE ref. no:	: <u>[0][6]-[0][3</u>			AE form no: AE ref. no:	0 6-0 4	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: L 2 (do not complete t	day month the remaining items	year	1	C	day month tems i	year
3. GRADE (1 - 4)	1 🔲 2 🔲	3 🗖	4 🔲	1 🔲	2 🗖	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No		Yes	. 🗆	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently 3= Dose reduced / 4= Del 0	layed and reduced / 5	= Interrupted	rrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted			= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No		Yes		No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	1 Date:			day month year  Specify sequelae:  2			year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No No Service Fig. 1. No			Yes  IF YES  Resultin Life-thre Requirir Persister Congen	- Date	No event became so                            below all criteria  hospitalization disability/incapacite ortant event	a that apply:
Investigator's name, date of rep	ort and signature:	Moi	nitoring repr	esentative's	s name, da	ate of receipt:	

XT 606 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subie	ect No.	XT	606 Page	03
CYCLE 6	V 06				age 62		
ADVERSE EVI	ENT FOR	M				O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no AE ref. no:	: [0][6]-[0][5			AE form no AE ref. no:	: <u> 0  6 - 0  6</u>	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		day month	year	1		day month le remaining items i	year
3. GRADE (1 - 4)	1 🔲 2 🔲	3 🗖	4 🔲	1 🔲	2 🗖	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No		Y	'es 🔲	No	۵
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently 3= Dose reduced / 4= Del 0	layed and reduced / 5	= Interrupted				= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No		Y	'es 🔲	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	Specify sequence of the sequen	day month uelae:	year	1	Specify sequ	day month  Jelae:  July Light	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes			Result Life-th Requi Persist Conge	aby Tick ting in death reatening ring/prolonging tent/significant enital anomaly/	No e event became se below all criteria g hospitalization disability/incapacit/birth defect	year  a that apply:
Investigator's name, date of report and signature:  * Is there a reasonable possibility that the AE was caused by study treatment?  * Is the a reasonable possibility that the AE was caused by study treatment?							

EFC6193 606 XRP6258 XT

VDD0050					
XRP6258 EFC6193	Country No. Centre No. Subject	Tot No.   Page   O 4			
CYCLE 6	v 06   00	See Page 62			
ADVERSE EVI	ENT FORM	O.1_AE_1			
1.  Adverse Event Diagnosis	AE form no: \0\6\-\0\17\ AE ref. no: \\-\-\-\-\	AE form no:   <b>0</b>   <b>6</b>  - <b>10</b>   <b>8</b>   AE ref. no:   -			
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL			
3. GRADE (1 - 4)	1 🗆 2 🗔 3 🔲 4 🗔	1 2 3 4 4			
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No D			
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0			
6. Corrective Treatment/Therapy	Yes No 🗆	Yes 🔲 No 🗖			
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered  5 = Fatal (complete the death report form)  6 = Unknown	1 Date: Li	1 Date: day month year 4 Specify sequelae: 2			
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes			
Investigator's name, date of report and signature:  * Is there a reasonable possibility that the AE was caused by study treatment?  * Monitoring representative's name, date of receipt:  * Is there a reasonable possibility that the AE was caused by study treatment?					

s there a reasonable possibility that the ria caused by stady treatment

XT 606 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	Tot No.   AT 606   05   10   10   10   10   10   10   10
CYCLE 6	v 06 000	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: <b>[0][6]-[0][9</b> ] AE ref. no: <b>[]]-[]</b>	AE form no: [0][6]-[1][0] AE ref. no: []-[]-
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL LLL year  2 (do not complete the remaining items in the column)  3	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1 🗆 2 🗔 3 🗔 4 🗔
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗆	Yes No C
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No 🗆	Yes No D
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date: LL LLL LLL LLL LLL LLL LLL LLL LLL LL	1 Date: LL
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes No Solution No	Yes □ No □  - Date event became serious:    □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
FORM  Investigator's name, date of repo	- Tick below all criteria that apply:  Resulting in death	- Tick below all criteria that apply:  Resulting in death
* Is there a reasonable	possibility that the AE was caused by study treatmen	nt?

EFC6193 606 XRP6258 XT

XRP6258 EFC6193	Country No. Centre No. Subje	XT 606 06		
CYCLE 6	V 06	See Page 62		
ADVERSE EV	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no: [0] 6]-[1] 1 AE ref. no: []-[]	AE form no: [0] [6] - [1] [2] AE ref. no: [] - []		
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3		
3. GRADE (1 - 4)	1	1		
Action Taken with     Study Treatment*      Action Taken with     Study Treatment	Yes □ No □  0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  0 □ 1 □ 2 □ 3 □ 4 □ 5 □	Yes □ No □  0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  0 □ 1 □ 2 □ 3 □ 4 □ 5 □		
6. Corrective Treatment/Therapy	Yes 🔲 No 🗖	Yes No No		
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: U U U U U U U U U U U U U U U U U U U	Date: LIL LIL LIL year  4  Specify sequelae:		
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Company No Comp	Yes No Compared to the No Compar		
Investigator's name, date of rep	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect	Resulting in death		
investigator s name, date of rep	or and signature. Monitoring tept	eschauve's hame, date of receipt.		

XT 606 XRP6258 EFC6193

\* Is there a reasonable possibility that the AE was caused by study treatment?

XRP6258 EFC6193 CYCLE 6	v 06   111 _	XT 606 Page		
ADVERSE EVI		See Page 62  0.1_AE_1		
1. Adverse Event Diagnosis	AE form no: LLL-LLL AE ref. no: LLL-LLL	AE form no: LJ-LJ- AE ref. no: LJ-LJL		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3		
3. GRADE (1 - 4)	1	1 🗆 2 🗔 3 🗔 4 🗔		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes	Yes 🗖 No 🗖		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
6. Corrective Treatment/Therapy	Yes No No	Yes No D		
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL LL LL year  4 D Specify sequelae:		
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No C  - Date event became serious:    Solution   Date   Date	Yes □ No □  - Date event became serious:  □ IF YES  □   □   □   □   □   □   □   □   □   □		
FORW	- Tick below all criteria that apply:  Resulting in death	- Tick below all criteria that apply:  Resulting in death		
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt:		
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?		

XT 606 XRP6258 EFC6193

			T	1	
XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO 99	e
CYCLE 7	V 07		Date of visit:	day month	/ Dayear
		<u> </u>	See Page 43		$\neg$
PHYSICAL EXA	MINATI			PHYS	EXAM_2
None 🗖					
Date performed:	month ye	<b>L</b>			
• Were there any clinically s	ignificant chan	ges from the	previous evalu	ation? Yes*	No 🗆
*If yes, please complete A	dverse Event fo	orm.			
VITAL SIGNS	See Page	<b>27</b>			LUTAL 4
NOT DONE					VITAL_1
Weight: ШШШ. Ш	kg				
- Blood pressure: Systolic		mmHg / [	Diastolic LL	⊔⊔ mmHg	
- Heart rate: LL	∟ beats/min				
- Temperature: LILI	.∟ °С				
	(tick appropriat	e box):	Oral 🗖	Rectal 🔲	Auricular 🗖
ECOG Performance Status 0 1 2	3 4				

Page 179/525 Confidential ■ FINAL ■ 21-NOV-2006

99

NO

sanofi aventis

EFC6193

XRP6258

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	100 Page	
CYCLE 7 - DAY 1	V 07					
HEMATOLOGY	See Pa	ge 24			LAE	BH_1

Date of sampling:			
, ,	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

	See Page 26	
PSA		LABH_1
		_

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

	NO	100	XRP6258	_ EFC6193		
,	Confidential ■ FINAL ■ 21-NOV-2006		one sanofi aven			

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	101 Page	
CYCLE 7 - DAY 1	V 07	See I	Page 25			

#### **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 101 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No.	O 102
CYCLE 7 - DAY 8	V 07	See Page 24	, age

#### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 102 XRP6258 EFC6193

CYCLE 7 - DAY 15	V 07	See Page 24	·		
EFC6193	Country No.	Centre No.   Subject No.	1	Page	J
XRP6258			NO	103	

#### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 103 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject N	NO NO	104 Page	
CYCLE 7	V 07	See Page 48			

#### SPECIFIC CONCOMITANT MEDICATION SPMED\_1

Ν	O	ne	Г

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION	1	SAGE		START DA	ATE .	END DATE
	MEDICATION	Number of Units	Unit	day	month	year	day month year
1							
2			 	1 11 11			
<u> </u>			 				
3			 				
4							
5			 				
6			 	ا لــالــا			
7			 				UU UUU UUUU
8							UU UUU UUUU
9							
10							

NO	104		XRP6258	EFC6193
Confid	ontial = FINIAL =	■ 21 NOV 2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	105 Page	
CYCLE 7	V 07	See Page 49			

#### INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

Treatment Name		Date a	ND TIME OF <b>D</b> OSI	NG	Intended Dose	ACTUAL Dose Given
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start L					
☐ Mitoxantrone	End					
IF DOSE DELAYED AND	O/OR REDUCED A	.ND/OR INTERI	RUPTED, SPECIFY	REASON:	'	
☐ AE: Specify on AE fo	orm					
Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name		Date at	ND TIME OF <b>D</b> OSI	NG	Intended Dose	ACTUAL DOSE GIVEN
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start L					
☐ Mitoxantrone	End				NA	

NO	105	XRP6258	EFC6193

XRP6258 EFC6193				NO	106
	Country No.	Centre No. S	ubject No.		Page
CYCLE 7	V 07	See Page 4	<del>19</del>		

#### **INVESTIGATIONAL PRODUCT ADMINISTRATION** ADMIN\_1

	TREATMENT NAME		DATE OF DOS	ing	Intended Dose	ACTUAL DOSE GIVEN
		day	month	year	(mg)	(mg)
	Prednisone	Start				
	Prednisolone	End L				
IF DOSE DEL	AYED AND/OR REDUCED	and/or interru	PTED, SPECIFY RE	EASON:		
☐ AE: Specif	fy on AE form					
Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name	DATE OF DOSING	Intended Dose	ACTUAL DOSE GIVEN
	day month year	(mg)	(mg)
☐ Prednisone	Start		
☐ Prednisolone	End	NA	

NO	106	XRP6258	EFC6193
		500	of: avootic

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	107 Page	
CYCLE 7	V 07	See P	age 51		- 3	

#### **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 107 XRP6258 EFC6193

Locat	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	Regional Lymph Nodes	20.20	Rectum		
11.02	Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193		NO 108
LFC0193	Country No.	Centre No.   Subject No.   Page
CYCLE 7	V 07	See Page 55

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ Not done

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	LJL.LJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□ Not Done			
3	LL.LL	Not Done		L L  mm	
4	LL.LL	□ Not Done		mm	
5		□ Not Done			
6		□ Not Done			
7		□ Not Done			
8		□□ □□□□□□□□□□□□□ Not Done		∟∟∟ mm	
9		□ □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
10	LIL.LIL	□ Not Done			
11		□ Not Done			
12	L. L. L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
13	LILI.LILI	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
14	<u> </u>	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		mm	

NO 108 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No.	] NO	109 Page	
CYCLE 7	V 07	See Page 53			

#### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		LILL . LILL
3.		니니. 니니
4		LJLJLJ
5.		
6		LJLJ. LJLJ
7	Ш	니니니 . 니니

NO 109 , XRP6258 , EFC6193

XRP6258 EFC6193  Country No.  Centre No.  Subject No.	110 Page
<b>CYCLE 7</b> V 07  See Page 29	
	<u>-</u>
ECHOCARDIOGRAPHY	ECHOCARD_1
NOT DONE	
• Date performed: LILILILILILILILILILILILILILILILILILILI	
• 2D-Echocardiography: Normal $\square$ Abnormal* $\square$	
- Left ventricular ejection fraction (LVEF) %	
- Lower Limit Normal of LVEF	
* If clinically relevant, please complete the Adverse Event form.  RADIONUCLIDE VENTRICULOGRAPHY	MUGA_1
NOT DONE	
• Date performed: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL	
• Radionuclide Ventriculographyy: Normal ☐ Abnormal* ☐	
- Left ventricular ejection fraction (LVEF) %	
- Lower Limit Normal of LVEF	
* If clinically relevant, please complete the Adverse Event form.	

XRP6258 NO 110 EFC6193 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	<b>111</b> Page	01
CYCLE 7	V 07	See Pa	age 60			

#### **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	End Date
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XRP6258 XT111 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	<b>111</b> Page	02
CYCLE 7	V 07	See F	Page 60			

#### **CONCOMITANT MEDICATION**

O.MED\_9

	Medication	START DATE		END DATE		ГЕ	
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШ ing
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШШ ing		□□□ L □ Ongo	⊔ШШ ing
6.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
8.			□□□□ l Ongo	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing

<u> </u>	111			osi aventis
ΧT	111		XRP6258	EFC6193

XRP6258 EFC6193	Country No.   Cen	tre No.   Subje	XT	607 Page	01
CYCLE 7	v 07		See Page 62		
ADVERSE EVI	ENT FORM			O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no: LOLZ AE ref. no: LL	- <mark> 0   1  </mark> 	AE form AE ref. no	no: [ <b>0</b> ] <b>7</b> ]-[ <b>0</b> ] <b>2</b> ]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	1 Date of start: LLL Lday r 2 (do not complete the remaining	nonth year ng items in the column)	<ul><li>1 □ Date of start:</li><li>2 □ (do not comple</li></ul>	day month te the remaining items in	
3= Ongoing with change	3 🗖		3 🗖	2.0	
3. GRADE (1 - 4)  4. RELATIONSHIP TO STUDY TREATMENT*	1	No	1	3 <b>\(\sigma\)</b>	4 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec 0	d / 2= Delayed luced / 5= Interrupted	0= None / 1= Permane 3= Dose reduced / 4=	ently discontinued / 2= Del Delayed and reduced / 5= I	layed
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering	4  Specify sequelae:	nonth year	2 🗆	day month equelae:	year
3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	3 Date of death:	LILI LILILI month year	3	:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	l '	No □ came serious: □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □	□ IF YES {	No Pate event became ser  All LILI LILI Bay month y  ick below all criteria t	] L L L L L L L L L L L L L L L L L L L
	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec	ation	Life-threatening . Requiring/prolong Persistent/significa Congenital anom	ging hospitalization ant disability/incapacity aly/birth defect	
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's name,	, date of receipt:	
	* Is there a reasonable possibility that the AE was caused by study treatment?				
XT 607		XRP62	ეგ <sup> </sup> F	FC6193	

XRP6258 EFC6193		XT 607 02
CYCLE 7	V 07 Centre No. Subje	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: <b>[0][7]-[0][3</b> ] AE ref. no: <b>[]]-[]</b>	AE form no:   <b>0</b>   <b>7</b>   <b>0</b>   <b>4</b>    AE ref. no:   -
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: Lay	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3 D
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗖	Yes No 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL LL L L L L L L L L L L L L L L	1 Date: LL LLL year  4 D Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No No In Pres Serious:  - Date event became serious:  - Date event became serious:  - Tick below all criteria that apply:	Yes No No Compared Property Pr
Investigator's name, date of repo	Resulting in death	Resulting in death

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 607 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Su	bject No.   XT 607 03
CYCLE 7	v 07	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [0][7]-[0][5] AE ref. no: []-[]-	AE form no:   <b>0</b>   <b>7</b>  - <b>0</b>   <b>6</b>    AE ref. no:           -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL Lyear 2 (do not complete the remaining items in the column 3	day month year
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🚨	Yes 🔲 No 🚨
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes  No	Yes No No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes No C  - Date event became serious:    Solition   So
Investigator's name, date of repo	ort and signature: Monitoring re	presentative's name, date of receipt:

 $\ ^*$  Is there a reasonable possibility that the AE was caused by study treatment?

XT 607 , XRP6258 , EFC6193

XRP6258 EFC6193		XT 607 04		
		ect No. Page		
CYCLE 7	V 07   LLL	See Page 62		
ADVERSE EV	ENT FORM	0.1_AE_1		
1.	AE form no: [0][7]-[0][7]	AE form no: 0 7 -0 8		
Adverse Event Diagnosis	AE ref. no:	AE ref. no:		
2. STATUS OF AE	1 □ Date of start: □□ □□□ □□□□	1 Date of start:		
1= New	1 ☐ Date of start: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐	Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL		
2= Ongoing from previous period without change	3 🗖	3 🗖		
3= Ongoing with change				
3. GRADE (1 - 4)	1			
4. RELATIONSHIP TO STUDY TREATMENT*	Yes  No	Yes No D		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted		
CTOST TREATMENT	0 1 2 3 4 5	0 1 2 3 4 5 5		
6. Corrective Treatment/Therapy	Yes 🗆 No 🗅	Yes No D		
7. OUTCOME 1= Recovered	1 □ <b>〕</b> Date: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	1 Date: UU UUU UGA month year		
4= Recovered with sequelae	4 D Specify sequelae:	4 D Specify sequelae:		
2= Recovering	2 🔲	2 🔲		
3= Not recovered	3 🗖	3 🗖		
5= Fatal (complete the death report form)	5 Date of death:	5 Date of death:		
6= Unknown	6 □ Yes □ No □	6		
8. SERIOUSNESS CRITERIA	Yes	Yes U No U  Output Date event became serious:		
IF YES, COMPLETE THIS SECTION	⇒ IF YES     □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⇒ IF YES		
AND THE SAE COMPLEMENTARY FORM	- Tick below all criteria that apply:	- Tick below all criteria that apply:		
	Resulting in death	Resulting in death		
	Life-threatening	Life-threatening		
	Persistent/significant disability/incapacity $lacksquare$	Persistent/significant disability/incapacity		
	Congenital anomaly/birth defect	Congenital anomaly/birth defect		
Investigator's name, date of rep		resentative's name, date of receipt:		
date of tep	The state of the s	and a manage of the company		
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?		

EFC6193 607 XRP6258 XT

XRP6258 EFC6193	Country No. Centre No. Subje	XT 607 05
CYCLE 7	v 07	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: 017-019  AE ref. no: 11-11	AE form no: 017-110 AE ref. no: 11-11
2. STATUS OF AE	1 Date of start: LL LLL year	1 Date of start: LIL LIL Jugar
2= Ongoing from previous period without change 3= Ongoing with change	2  (do not complete the remaining items in the column) 3	2  (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 4	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes 🔲 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted
6. Corrective Treatment/Therapy	9 0 1 0 2 0 3 0 4 0 5 0 Yes 0 No 0	9 0 1 0 2 0 3 0 4 0 5 0 Yes 0 No 0
7. OUTCOME  1= Recovered  4= Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL LLL year  Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Compared to the No Compar	Yes No C  - Date event became serious:    If Yes
Investigator's name, date of rep	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event  resentative's name, date of receipt:

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 607 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cent	re No. Subje	ct No.	607 Page	06
CYCLE 7	V 07		See Page 62		
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: 0]7		AE forn AE ref. r	n no:   <b>0 7-1 2</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change		nth year g items in the column)	1 ☐ Date of start: 2 ☐ (do not compl	day month lete the remaining items i	year
3= Ongoing with change	3 🗆		3 🗖		4.0
3. GRADE (1 - 4)  4. RELATIONSHIP TO STUDY TREATMENT*	1	No 🔲	1  2		4 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and redu 0 1 1 2 3 3		3= Dose reduced / 4	nently discontinued / 2= E = Delayed and reduced / 5= 2	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🚨	Yes 🗆	<b>l</b> No	
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered	Date: LL LL day m  Specify sequelae:  2	nnth year	1	day month sequelae:	
5= Fatal (complete the death report form) 6= Unknown	5  Date of death: LIL LIL day m	onth year	5  Date of deat	h:     day month	year
8. SERIOUSNESS CRITERIA	Yes - Date event bed	No  ame serious:	Yes 🗆	No  No Date event became se	erious:
IF YES, COMPLETE THIS SECTION AND THE <b>SAE</b> COMPLEMENTARY FORM	Resulting in death	🗖	Resulting in dea Life-threatening	day month  Tick below all criteria  th	that apply:
Investigator's name, date of rep	Requiring/prolonging hospitaliza Persistent/significant disability/in Congenital anomaly/birth defect Other medically important even	capacity	Persistent/signifi Congenital anon Other medically	nging hospitalization	y 🗖 🗖

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 607 , XRP6258 , EFC6193

XRP6258 EFC6193		XT 607		
	Country No. Centre No. Subje	ect No.   Page		
CYCLE 7	V 0]7   LLL	See Page 62		
	TIT FORM	24.55.4		
ADVERSE EVI	ENT FORIVI	0.1_AE_1		
	1	1		
Adverse Event	AE form no: LL-LL	AE form no: UL-UL  AE ref. no: UL-UL		
DIAGNOSIS	At ref. no:	At ref. no:		
2. STATUS OF AE 1= New	1 Date of start:	1 Date of start: LLL LLLL year		
2= Ongoing from previous period without change	2 (do not complete the remaining items in the column)	2 (do not complete the remaining items in the column)		
3= Ongoing with change	3 🗖	3 🗖		
3. GRADE (1 - 4)	1 🗆 2 🗔 3 🗔 4 🗔	1 🗆 2 🗔 3 🔲 4 🔲		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No No	Yes No D		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
6. Corrective Treatment/Therapy		Yes No D		
7. OUTCOME 1= Recovered	1 <b>D</b> Date:	1 <b>D</b> Date: LL LLL LLL		
1= Recovered 4= Recovered with sequelae	day month year  4  Specify sequelae:	day month year 4  Specify sequelae:		
2= Recovering	2 🗖	2 🗖		
3= Not recovered	3 🗖	3 🗖		
5= Fatal (complete the death report form)	5 Date of death: LL LL LL year	5 Date of death:		
6= Unknown	Yes No D	Yes No D		
8. SERIOUSNESS CRITERIA	- Date event became serious:	- Date event became serious:		
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	⇒ IF YES	⇒ IF YES      □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □		
FORM	- Tick below all criteria that apply:	- Tick below all criteria that apply:		
	Resulting in death	Resulting in death		
	Life-threatening	Life-threatening		
	Persistent/significant disability/incapacity	Persistent/significant disability/incapacity		
1	Congenital anomaly/birth defect	Congenital anomaly/birth defect		
tiester/s name date of ren	Other medically important event	Other medically important event		
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt.		
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?		

\_\_\_ EFC6193 XT 607 XRP6258

				1	
XRP6258 EFC6193				NO 112	
	Country		1	Page	
CYCLE 8	V [0]	8   UUL	Date of visit:	day month	year
		_	Day Day 10		$\neg$
PHYSICAL	EXAMINA	ATION E	See Page 43	PHYS	EXAM_2
NONE					
Date performed:		year			
Were there any clin	ically significant	changes from t	he previous eval	uation? Yes*	□ No □
*If yes, please comp	olete Adverse Ev	ent form.			
	See	Page 27			
VITAL SIGN	IS				VITAL_1
NOT DONE					
Weight: LILL	. Ш kg				
- Blood pressure:	Systolic LLL	⊫ mmHg /	Diastolic 🗀	∟∟ mmHg	
- Heart rate:	∟∟∟ beats	s/min			
Topanoraturo		°C			
- Temperature:	(tick app	°C	Oral 🔲	Rectal 🗖	Auricular 🔲
ECOG Performance		Topridie Soxy.	orar 🕳	neetai 🕳	/ tarrearar 🕳
0 1 2		4			

XRP6258 NO 112 EFC6193 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	113 Page		
CYCLE 8 - DAY 1	V 08						
HEMATOLOGY	See Pa	age 24				LABH_1	

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

# PSA See Page 26 LABH\_1

DATE OF SAMPLING day month year	Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO	113	XRP6258	_ EFC6193
Confide	ential ■ FINAL ■ 21-NOV-2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>114</b> Page	
CYCLE 8 - DAY 1	V 08	See F	Page 25			

#### **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 114 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	115 Page	
CYCLE 8 - DAY 8	V 08	See	Page 24			

### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 115 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	116 Page	
CYCLE 8 - DAY 15	V 08	See	Page 24			

#### **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 116 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.	NO	<b>117</b> Page	
CYCLE 8	V 08	See Page 48	,		

#### SPECIFIC CONCOMITANT MEDICATION SPMED\_1

N	one	

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION	DOSAGE Number	START DATE	END DATE		
$\vdash$		of Units Unit	day month year	day month year		
1						
2						
3						
4						
5		1				
6						
7						
8						
9						
10						

NO	117	ı	ı	XRP6258	EFC6193
Confidential ■ FINAL ■ 21-NOV-2006			san	ofi aventis	

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page
CYCLE 8	V 08	See Page 49

### INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

Treatment Name	DATE AND TIME OF DOSING			Intended Dose	ACTUAL DOSE GIVEN		
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)	
☐ XRP6258	Start L			LL: LL			
☐ Mitoxantrone	End						
IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:							
☐ AE: Specify on AE form							
Other:							

IF DOSE INTERRUPTED, complete below:

Treatment Name	Date and Time of Dosing				Intended Dose	ACTUAL DOSE GIVEN
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start					
☐ Mitoxantrone	End				NA	

 NO
 118
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-NOV-2006
 Sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
CYCLE 8	V 08	See Page 49

#### INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

	TREATMENT NAME	DATE OF DOSING			Intended Dose	ACTUAL DOSE GIVEN		
		day	month	year	(mg)	(mg)		
	Prednisone	Start						
	Prednisolone	End L						
IF DOSE DEL	IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:							
☐ AE: Specify on AE form								
Other:								

IF DOSE INTERRUPTED, complete below:

Treatment Name	DATE OF DOSING			Intended Dose	ACTUAL DOSE GIVEN
	day	month	year	(mg)	(mg)
☐ Prednisone	Start				
☐ Prednisolone	End L			NA	

NO 119 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject I	NO NO	120 Page	
CYCLE 8	V 08	See Page 51	 ]	<u> </u>	

#### **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 120 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	I Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	121 Page	
CYCLE 8	V 08	See Page 55		T age	

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJLJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□ Not Done			
5	L. L. L.	□□ □□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□ Not Done			
7	L.L.L.	□□□□□□□□□□□□□□□ Not Done			
8	L.I	□ Not Done			
9		□□ □□□ □□□□□ □ Not Done			
10	LILI.LILI	□□□□□□□□□□□□□□□□ Not Done		L_ L_  mm	
11	LJLJ-LJLJ	□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 121 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.	NO 122
CYCLE 8	V 08	See Page 53	

#### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1		
		LILL . LILL
3		
4		
5.	Ш	
6.	Ш	
7		

NO 122 XRP6258 EFC6193

VDD0050					
XRP6258 EFC6193	Country No.	Contro No	Subject No.	NO	123
CYCLE 8	V 08	See P	Subject No.		Page
ECHOCARDIO	GRAPHY				ECHOCARD_1
NOT DONE					
• Date performed: LL I	month	year			
• 2D-Echocardiography:	Normal $\Box$		Abnormal* [	<b>-</b>	
- Left ventricular ejection fra	ction (LVEF)	<u> </u>	<u> </u>		
- Lower Limit Normal of LVE	F	<u> </u>	<u></u> %		
* If clinically relevant, pl	ease complete t	the Adverse E	event form.		
* If clinically relevant, pl	·			ΗΥ	MUGA_1
RADIONUCLID	·			ΗΥ	MUGA_1
RADIONUCLID  NOT DONE   • Date performed:	E VENTI	RICULO	Abno	<b>-IY</b> rmal* □	MUGA_1
RADIONUCLID  NOT DONE  Date performed: Lay  Radionuclide Ventriculog  Left ventricular ejection frac	E VENTI  With the second section (LVEF)  F	RICULO  year  LILI  LILI	Abno		MUGA_1
RADIONUCLID  NOT DONE  • Date performed: Late   Lat	E VENTI  With the second section (LVEF)  F	RICULO  year  LILI  LILI	Abno		MUGA_1
RADIONUCLID  NOT DONE  • Date performed: Late   Lat	E VENTI  With the second section (LVEF)  F	RICULO  year  LILI  LILI	Abno		MUGA_1

XRP6258 EFC6193				XT	124	01
	Country No.	Centre No.	Subject No.		Page	
CYCLE 8	V 08	See P	age 60			

#### **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	End Date
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XT	124	ı	XRP6258	EFC6193
Confide	ntial ■ FINAL ■	I 21-NOV-2006	san	ofi aventis

XRP6258 EFC6193				XT	124	02
	Country No.	Centre No.	Subject No.		Page	
CYCLE 8	V 08	See	Page 60			

#### **CONCOMITANT MEDICATION**

O.MED\_9

	MEDICATION		START DAT	E	End Date		E
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□				
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			Ongo	
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			Ongo	
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□				
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
6.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□				
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			Ongo	
8.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			Ongo	
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□				
10.						Ongo	

XRP6258 EFC6193	Country No. Cen	tre No.   Subje	T XT	608 Page	01	
CYCLE 8	v 08 🗆		See Page 62	<u>!</u>		
ADVERSE EVI	ENT FORM			O.1_AE_1		
1.  Adverse Event Diagnosis	AE form no: <b>1018</b> AE ref. no: <b>11</b>	- <mark> 0   1  </mark> 	AE form AE ref. n	n no:   <mark>0 8 -0 2</mark> o:   -		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	1 Date of start: LLL Lday r 2 (do not complete the remaining	nonth year ng items in the column)	1 ☐ Date of start: 2 ☐ (do not comple	day month ete the remaining items in		
3= Ongoing with change  3. GRADE (1 - 4)	1 2 3	<u> </u>	1 2 2	3 🗖	4 🗖	
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲	No 🔲	Yes			
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec 0  1  2  3	luced / 5= Interrupted	0= None / 1= Permar 3= Dose reduced / 4=	nently discontinued / 2= De Delayed and reduced / 5= I	layed nterrupted	
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	No		
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL Lday r 4 Specify sequelae:	month year		day month equelae:	year	
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	Conth year	2	n:	year	
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	l '	No Grame serious:	□ IF YES	No Date event became ser	] L ] L ] rear	
	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec	tation	Life-threatening Requiring/prolon Persistent/signific Congenital anom	h ging hospitalization ant disability/incapacity haly/birth defect important event	🗆	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name	, date of receipt:		
* Is there a reasonable possibility that the AE was caused by study treatment?  XT 608   XRP6258   EFC6193						
<u> </u>		_ ANT UZ:	JO   E	1 00130		

XRP6258 EFC6193 CYCLE 8	Country No. Centre No. Subje	XT 608 02  ect No.   Page  See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [ <b>0</b> ][ <b>8</b> ]-[ <b>0</b> ][ <b>3</b> ] AE ref. no: []-[]-	AE form no:   <b>0</b>   <b>8</b>  -  <b>0</b>   <b>4</b>    AE ref. no:    -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No No	Yes No 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No No	Yes 🔲 No 🚨
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: U U U U U U U U U U U U U U U U U U U	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown  8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	2	2
Investigator's name, date of repo	J	resentative's name, date of receipt:

XT 608 | XRP6258 | EFC6193

XRP6258				<u> </u>	ΧT	608	03
EFC6193	Country No.	Centre No.	Subjec	ct No.		Page	
CYCLE 8	V 08			See P	age 62	]	
ADVERSE EVI	ENT FORM	ı				O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no: L AE ref. no: L	0] 8]-[0] [5]			AE form no AE ref. no:	: [0][8]-[0][6 []-[]	
2. STATUS OF AE	1 Date of start:		year	1 Date of		day month	year
2= Ongoing from previous period without change	2 (do not complete the re	emaining items in th	e column)	2 🔲 (do n	ot complete tl	he remaining items i	n the column)
3= Ongoing with change	3 🗖			3 🗖			
3. GRADE (1 - 4)	1 🔲 2 🔲	3 🗖	4 🔲	1 🔲	2 🗖	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No		Yes		No	
5. Action Taken with	0= None / 1= Permanently disc 3= Dose reduced / 4= Delayed					discontinued / 2= E ayed and reduced / 5=	
STUDY TREATMENT	0 🗖 1 🗖 2 🗖	3 🗖 4 🗖	5 🗖	0 🗖 1	2 🗆	3 🗖 4 🗔	5 🗖
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No I		Yes		No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)		e:		4	pecify sequ	day month telae:	
6= Unknown	6   day	month —	year	6 <b></b>		day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY		No [ ent became serio		Yes IF YES	- Date	No event became se	
FORM  Investigator's name, date of repo	Resulting in death Life-threatening Requiring/prolonging hos Persistent/significant disal Congenital anomaly/birth Other medically importa	pitalization bility/incapacity . ı defect		Life-thre Requirir Persister Congeni Other m	g in death	hospitalization disability/incapacity birth defect ortant event ate of receipt:	

EFC6193 608 XRP6258  $\mathsf{XT}$ 

\* Is there a reasonable possibility that the AE was caused by study treatment?

XRP6258 EFC6193 CYCLE 8	Country No. Centre No. Subje	XT 608 04  See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \0\8\-\0\7\ AE ref. no: \ \_\-\_\	AE form no: [0][8]-[0][8]  AE ref. no: []-[]-
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay Month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes  No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🔲 No 🗖	Yes No 🗆
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered	1 Date: LLL LLL LLL LLL LLL LLL LLL LLL LLL L	1 Date: Lay month year 4 Specify sequelae:
5= Fatal (complete the death report form)	5 Date of death: U UUU UUU	5 Date of death: U UU Vear
6= Unknown	6 🗖	6 🗖
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes O No O To Date event became serious:  - Persitent per a	Yes O No O To Date event became serious:  - Persitent serious: - Date event became serious: -
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt:

XT 608 XRP6258 EFC6193

XRP6258 EFC6193		XT 608 05
CYCLE 8	V 08   LLL	See Page 62
ADVERSE EVI	ENT FORM	0.1_AE_1
1. Adverse Event Diagnosis	AE form no: [0][8]-[0][9] AE ref. no: []-[]	AE form no: [0][8]-[1][0] AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3 D	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3 D
3. GRADE (1 - 4)	1	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes No D	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL	1 Date: LL LLL year  4 D Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA	Yes No No C - Date event became serious:	Yes No O - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	□ IF YES □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □	Terror Trick below all criteria that apply:  Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring repr	resentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?

XT 608 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 608 06
CYCLE 8	V 08	See Page 62
ADVERSE EVE	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \0\8\-\1\1\	AE form no: [0][8]-[1][2] AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lili Lili year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLLLL LLLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes  No	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes No D
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown  8. SERIOUSNESS	2	2
CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	→ IF YES   - Date event became serious:    □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □	- Date event became serious:  □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□
	Life-threatening	Life-threatening
Investigator's name, date of repo	ort and cignatures   Manitaring room	esentative's name, date of receipt:

XRP6258 \_ EFC6193 XT 608

XRP6258 EFC6193	Garage No.		XT	608	
CYCLE 8	V 08	Subje	See Page 62	Page	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no: LLL-L		AE form I AE ref. no:	no:     -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LL Lday mon 2 (do not complete the remaining	,		day month e the remaining items in	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖵	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🚨	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and reduc		3= Dose reduced / 4= [	ntly discontinued / $2 = De$ Delayed and reduced / $5 = U$	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL day mon Specify sequelae:	,	1 Date: 4 Specify see	day month quelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2		2	day month	J L J L J
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	year	⇒ IF YES	No ate event became ser	J L J L J
	Resulting in death	ion	Life-threatening Requiring/prolongi Persistent/significa Congenital anoma	ing hospitalization nt disability/incapacity ly/birth defect nportant event	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name,	date of receipt:	
* Is there a reasonable	possibility that the AE was caused	l by study treatmer	nt?		

Page 222/525 Confidential ■ FINAL ■ 17-Oct-2006

		1	1	
XRP6258 EFC6193	Country No.   Centre	No. Subject No.	NO 125	
CYCLE 9	V 09	Date of visit:		year year
		See Page 43		
PHYSICAL EXA	AMINATION	Occ 1 age 40		EXAM_2
None $\square$				
Date performed: Lay	month year			
Were there any clinically	significant changes fror	n the previous evalu	uation? Yes*	□ No □
*If yes, please complete A	Adverse Event form.			
VITAL SIGNS	See Page 27			MITAL 4
NOT DONE				VITAL_1
Weight: LILILI . LI	kg			
- Blood pressure: Systol	ic LLL mmHg	/ Diastolic Ш	ニニ mmHg	
- Heart rate:	⊔∟ beats/min			
- Temperature:	°C . ∟ . ∟			
ECOG Performance Status	(tick appropriate box):	Oral 🗖	Rectal	Auricular 🗖
0 1 2	3 4			

Page 223/525 Confidential ■ FINAL ■ 21-NOV-2006

125

NO

sanofi aventis

EFC6193

XRP6258

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	126 Page		
CYCLE 9 - DAY 1	V 09						
HEMATOLOGY	See	Page 24				LABH_1	

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

PSA

LABH\_1

DATE OF SAMPLING day month year	Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO	126		XRP6258	EFC6193
Confide	Confidential ■ FINAL ■ 21-NOV-2006		san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	127 Page	
CYCLE 9 - DAY 1	V 09	See I	Page 25			

## **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 127 XRP6258 EFC6193

XRP6258 EFC6193			NO	128	
EFC0193	Country No.	Centre No.   Subject No.		Page	
CYCLE 9 - DAY 8	V 09	See Page 24			

# **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 128 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	129 Page	
CYCLE 9 - DAY 15	V 09	See	Page 24			

# **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 129 XRP6258 EFC6193

XRP6258 EFC6193			NO	130	
LFC0193	Country No.	Centre No.   Subject No.	1	Page	
CYCLE 9	V 09	See Page 48			

#### **SPECIFIC CONCOMITANT MEDICATION** SPMED\_1

Ν	one	Г

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION	1	SAGE		START DA	ATE .	END DATE
	MEDICATION	Number of Units	Unit	day	month	year	day month year
1							
2			 	1 11 11			
<u> </u>			 				
3			 				
4							
5			 				
6			 	ا لــالــا			
7			 				UU UUU UUUU
8							UU UUU UUUU
9							
10							

<b>VO</b>	130	XRP6258	EFC6193
		 san	ofi aventic

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	131 Page	
CYCLE 9	V 09	See	Page 49			

#### **INVESTIGATIONAL PRODUCT ADMINISTRATION** ADMIN\_1

Treatment Name		Date a	ND TIME OF <b>D</b> OSI	NG	Intended Dose	ACTUAL Dose Given
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start L					
☐ Mitoxantrone	End					
IF DOSE DELAYED AND	O/OR REDUCED A	.ND/OR INTERI	RUPTED, SPECIFY	REASON:	'	
☐ AE: Specify on AE fo	orm					
Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name		Date a	ND TIME OF DOSII	NG	Intended Dose	ACTUAL DOSE GIVEN
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start					
☐ Mitoxantrone	End				NA	

NO	131	XRP6258	EFC6193
		500	of: avootic

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	132 Page	
CYCLE 9	V 09	See Page 49			

# INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

	TREATMENT NAME		DATE OF DOS	ing	Intended Dose	ACTUAL DOSE GIVEN
		day	month	year	(mg)	(mg)
	Prednisone	Start				
	Prednisolone	End L				
IF DOSE DEL	AYED AND/OR REDUCED	and/or interru	PTED, SPECIFY RE	EASON:		
☐ AE: Specif	fy on AE form					
Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name	DATE OF DOSING	Intended Dose	ACTUAL DOSE GIVEN
	day month year	(mg)	(mg)
☐ Prednisone	Start		
☐ Prednisolone	End	NA	

NO 132 , XRP6258 ,	EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
CYCLE 9	V 09	See Page 51

# **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 133 XRP6258 EFC6193

Loca	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	) Colon	30	Other
11.01	Regional Lymph Nodes	20.20	) Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193		NO 134
	Country No.	Centre No. Subject No. Page
CYCLE 9	V 09	See Page 55

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.L.	□□□□□□□□□□□□□□□□ Not Done			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJLJ	Not Done			
4		□□□□□□□□□□□□□□□□ Not Done			
5	L. L. L.	□□ □□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□ Not Done			
7	L.L.L.	□□□□□□□□□□□□□□□ Not Done			
8	L.I	□ Not Done			
9		□□ □□□ □□□□□ □ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		L_ L_  mm	
11		□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 134 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	135 Page	
CYCLE 9	V 09	See P	Page 53			

## **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		LILL. LILL
3.		
4.		لــالــا . لــالــا
5		
6.		
7		

NO 135 , XRP6258 , EFC6193

XRP6258				NO	136
CYCLE 9	V 09	Centre No.	Subject No.		Page
		See P	age 29		_
ECHOCARDIO	GRAPHY				ECHOCARD_1
NOT DONE					
Date performed: LL day	month	year			
2D-Echocardiography:	Normal $\Box$	Al	onormal* 🗖		
Left ventricular ejection fra	ction (LVEF)	Ш <b>.</b> . L			
Lower Limit Normal of LVE	∃F	LL . L	」 %		
RADIONUCLID	E VENT	RICULO	GRAPH	Y	MUGA_1
Date performed: LLL day	month	year			
Radionuclide Ventriculog	graphyy: Norma	al 🗖	Abnorr	nal* 🔲	
Left ventricular ejection fra	ction (LVEF)		<b>」</b> ‰		
,					
Lower Limit Normal of LVE	EF .	ШШ . L	」 %		
,					
Lower Limit Normal of LVE					
Lower Limit Normal of LVE					

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	137 Page	01
CYCLE 9	V 09	See	Page 60			

# **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	End Date
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XRP6258 XT137 EFC6193 sanofi aventis

CYCLE 9	V 09	See	Page 60			
EFC0193	Country No.	Centre No.	Subject No.	I	Page	
XRP6258 EFC6193				XT	137	02

# **CONCOMITANT MEDICATION**

O.MED\_9

	Medication	START DATE			END DAT	ГЕ	
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШ ing
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШШ ing		□□□ L □ Ongo	⊔ШШ ing
6.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
8.			□□□□ l Ongo	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing

XT 137   XRP6258   EFC6193			and countries	of aventic
	XT	137	, XRP6258	_ EFC6193

XRP6258 EFC6193	Country No. Cent	re No.   Subje	XT	609 Page	01
CYCLE 9	v 09 🗆		See Page 62	:	
ADVERSE EVI	ENT FORM			0.1_AE_1	_
1. Adverse Event Diagnosis	AE form no: <b>[0] 9</b> AE ref. no: <b>[]</b>	- <u>(0   1  </u> -	AE form AE ref. no	no:   <b>0 9- 0 2</b> o:   - -	
2. STATUS OF AE	1 Date of start: LL LL day m 2 (do not complete the remaining	onth year  g items in the column)	1  Date of start:  2  (do not comple	day month	
2= Ongoing from previous period without change 3= Ongoing with change	3 🗖		3 🗖		
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 🔲 2 🖸	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and red		3= Dose reduced / 4=	ently discontinued / 2= Delay Delayed and reduced / 5= Into Part 2	
6. Corrective Treatment/Therapy	Yes 📮	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL Ll day m Specify sequelae:	oonth year	1 Date: 4 Specify so	day month Lile	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	nonth year	2	:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event bed ay month		□ IF YES {	No Date event became serio	 r
	Resulting in death  Life-threatening  Requiring/prolonging hospitaliz.  Persistent/significant disability/in  Congenital anomaly/birth defec  Other medically important ever	ation	Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anom	ging hospitalization ant disability/incapacity aly/birth defect important event	
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's name,	, date of receipt:	
* Is there a reasonable	possibility that the AE was cause	ed by study treatmer	nt?		
XT 609		XRP62	58 , E	FC6193	

XRP6258 EFC6193	Country No.   Centre No.   Subje	Tot No.   XT 609 02
CYCLE 9	v 09	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin	AE form no:   <b>0</b>   <b>9</b>  - <b> 0</b>   <b>4</b>    AE ref. no:         -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*  5. ACTION TAKEN WITH STUDY TREATMENT	Yes No No On the None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted Oo 1 1 2 3 4 5 0	Yes     No       0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted       0 □ 1 □ 2 □ 3 □ 4 □ 5 □
6. Corrective Treatment/Therapy	Yes No D	Yes  No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown  8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	2	2
Investigator's name, date of repo	Life-threatening	Life-threatening

XT 609 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	ct No.	609 Page	03
CYCLE 9	v 09		See Page 62		
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>[0] 9</b> AE ref. no: <b>[]</b>	- <u> 0  5 </u> - <u> </u>	AE form AE ref. no:	no:   <mark>0  9 - 0  6</mark> :    -	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		onth year  ng items in the column)	1 Date of start: 2 (do not complet) 3	day month e the remaining items in	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖵	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec 0 1 1 2 3 3	uced / 5= Interrupted  4	3= Dose reduced / 4= I 0	ntly discontinued / 2= D Delayed and reduced / 5=  3 4	Interrupted 5
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🗖	Yes 🗖	No	
1= Recovered 4= Recovered with sequelae		nonth year	1 Date: 4 Specify se	day month quelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2 □ 3 □ 5 □ Date of death: □□□□ day	nonth year	2	LLL LLLL L	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event be  IF YES - Date event be  Light below all  Tick below all	No came serious:	⇒ IF YES	No ate event became se  month ck below all criteria	year
Investigator's name, date of repo	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec Other medically important ever	Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anoma	ing hospitalization nt disability/incapacity ly/birth defect nportant event	0	
	possibility that the AE was caus				

EFC6193 XT 609 XRP6258

XRP6258 EFC6193 CYCLE 9	Country No. Centre	No. Subject	XT xt No.	609 Page	04
ADVERSE EV	ENT FORM			0.1_AE_1	_
1. Adverse Event Diagnosis	AE form no: \_0   \_9   -\_		AE foi AE ref.	m no:   <b>0   9   -   0    </b> no:           -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LL day montf 2 (do not complete the remaining in	<i>'</i>	1  Date of start: 2  (do not compared to the c	day month  olete the remaining items	year
3. GRADE (1 - 4)	1 2 3 3	4 🗖	1 🗖 2 🗓	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 N	No 🗖	Yes [	□ No	
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinued / 3= Dose reduced / 4= Delayed and reduce 0 1 2 3 1			anently discontinued / 2= 4= Delayed and reduced / 5 2	5= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖 N	No 🗖	Yes [	no No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered 5= Fatal (complete the death report form)	Date: LL LL Month  A Date: LL LL Month  A Specify sequelae:  2		2 🗆	day month sequelae:  ath: day month	year 
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM		year riteria that apply:	Yes  IF YES  Resulting in de Life-threatening Requiring/prole Persistent/signi Congenital and	No Date event became state when the came state	a that apply:
Investigator's name, date of repo	ort and signature:	Monitoring repre	esentative's nam	ne, date of receipt:	
	possibility that the AE was caused				

XRP6258 EFC6193	Country No. Centr	re No. J Subje	XT	609 Page	05
CYCLE 9	v 09		See Page 62	]	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no:   <b>0</b>    <b>9</b>  - AE ref. no:     -		AE form AE ref. n	n no:   <b>0  9 - 1  0</b> o:    -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL Lday mc 2 (do not complete the remaining	year g items in the column)	1 Date of start: 2 (do not comple	day month tete the remaining items i	
3. GRADE (1 - 4)	1 🗖 2 🗖 3 🗓	4 🗆	1 🗖 2 🗖	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲	No 🔲	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and redu 0		3= Dose reduced / 4=	nently discontinued / 2= I Delayed and reduced / 5: 2  3  4  4	= Interrupted
6. Corrective Treatment/Therapy	Yes 📮	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered 5= Fatal (complete the death report form)	4 ☐		2 🔲	day month sequelae:	year
6= Unknown	6 🗖		6 🗖		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes □ No □  - Date event became serious:  □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □		⇒ IF YES	No Date event became so  LL LLL LL  day month  Fick below all criteria	year
	Resulting in death Life-threatening Requiring/prolonging hospitaliza Persistent/significant disability/in Congenital anomaly/birth defect Other medically important event	Life-threatening Requiring/prolon Persistent/signific Congenital anom	hging hospitalization cant disability/incapacit naly/birth defect important event		
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name	, date of receipt:	

EFC6193 609 XRP6258 XT

XRP6258 EFC6193	Country No. Centre No.	Subjec	t No.	609 Page	0[6
ADVERSE EV			See Page 62	O.1_AE_1	_
1. Adverse Event Diagnosis	AE form no:   <b>0</b>   <b>9</b>  -  <b>1</b>   <b>1</b>    AE ref. no:       -		AE form r AE ref. no:	no:   <b>0  9 - 1  2</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL	year	1  Date of start: 2  (do not complete	day month e the remaining items i	year
3. GRADE (1 - 4)	1 2 3 3	4 🔲	1 🔲 2 🔲	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No		Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Dela 3= Dose reduced / 4= Delayed and reduced / 5= Ir		0= None / 1= Permaner 3= Dose reduced / 4= E 0		= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖 No		Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL L  day month  Specify sequelae:			day month quelae:	
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	year	2	day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No  - Date event became seried ay month ye  - Tick below all criteria the	L	⇒ IF YES	No  Ite event became so  It I I I I I I I  Immorth  Ck below all criteria	year
	Resulting in death Life-threatening Requiring/prolonging hospitalization Persistent/significant disability/incapacity Congenital anomaly/birth defect Other medically important event		Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event		
Investigator's name, date of rep	ort and signature: Monit	oring repre	esentative's name,	date of receipt:	
* Is there a reasonable	possibility that the AE was caused by stud	ly treatmen	t?		

XRP6258 | EFC6193 XT 609 Page 243/525 Confidential ■ FINAL ■ 21-NOV-2006

XRP6258 EFC6193	Country No. Cen	tre No. Subje	Ct No.	609 Page	
ADVERSE EVI			See Page 62	0.1_AE_1	_
1. Adverse Event Diagnosis	AE form no: LIL	- <b> </b>	AE forn AE ref. r	n no:       -       no:         -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nonth year ng items in the column)	1  Date of start: 2  (do not compi	day month  lete the remaining items i	year
3. GRADE (1 - 4)	1 🗖 2 🗖 3	4 🗆	1 2 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🚨	No 🚨	Yes 🗆	<b>N</b> o	
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0  1  2  3	luced / 5= Interrupted	3= Dose reduced / 4	nently discontinued / 2= I = Delayed and reduced / 5: 2	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗆	<b>l</b> No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered	4 □		2 🗆	day month sequelae:	
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: 4ay day	month year	5 Date of deat	h:   day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	'	year  I criteria that apply:	Resulting in dea Life-threatening Requiring/prolor Persistent/signific	No  Date event became so  Limited with the control of the control	year  a that apply:
Investigator's name, date of repo	Other medically important eve	nt	Other medically	important evente, date of receipt:	
* Is there a reasonable	possibility that the AE was caus	ed by study treatmen	nt?		

sanofi aventis

XRP6258 EFC6193	Country No. Centre N	lo. Subject No.	NO 138	9
CYCLE 10	v 10	Date of visit:		/ Quar
		See Page 43	3	
PHYSICAL EX	CAMINATION		 PHYS	EXAM_2
NONE				
Date performed: Lay	month year			
Were there any clinical	ly significant changes from	the previous evalu	uation? Yes*	No 🗆
*If yes, please complete	e Adverse Event form.			
VITAL SIGNS	See Page 27			VITAL_1
NOT DONE				
Weight: ШШШ. L	J kg			
- Blood pressure: Syst	rolic LLL mmHg	/ Diastolic 📖	שו∟ mmHg	
- Heart rate:	∟∟∟ beats/min			
- Temperature: Ш	∟.∟ °C			
	(tick appropriate box):	Oral 🗖	Rectal 🔲	Auricular 🔲
<b>ECOG Performance Stat</b>	us			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	3 4			
	<b>.</b>			

Page 245/525 Confidential ■ FINAL ■ 21-NOV-2006

138

NO

sanofi aventis

EFC6193

XRP6258

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	139 Page		
CYCLE 10 - DAY 1	V 10						
See Page 24 HEMATOLOGY LABH_1							
Date of sampling: 니니 L							

year

month

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10 <sup>9</sup> /L	
Eosinophils		10 <sup>9</sup> /L	
Basophils		10 <sup>9</sup> /L	
Monocytes		10 <sup>9</sup> /L	
Lymphocytes		10 <sup>9</sup> /L	
Platelets		10 <sup>9</sup> /L	
Hemoglobin		g/dL	

# See Page 26 PSA LABH\_1

DATE OF SAMPLING day month year	Test	<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO	139		XRP6258	EFC6193
Confide	ntial ■ FINAL I	■ 21-NOV-2006	sand	ofi aventis

XRP6258 EFC6193				NO	140	
EFC0193	Country No.	Centre No.	Subject No.	I	Page	
CYCLE 10 - DAY 1	V 10	See F	Page 25			

## **BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

NO 140 , XRP6258 , EFC6193

XRP6258 EFC6193				NO	141	
EFC0193	Country No.	Centre No.	Subject No.		Page	
CYCLE 10 - DAY 8	V 10	See	Page 24			

# **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 141 XRP6258 EFC6193

XRP6258 EFC6193				NO	142	
LFC0193	Country No.	Centre No.	Subject No.	1	Page	
CYCLE 10 - DAY 15	V 10	See	Page 24			

# **HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

NO 142 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject	No. NO	143 Page	
CYCLE 10	V 10	See Page 48	1		

# SPECIFIC CONCOMITANT MEDICATION SPMED\_1

Ν	one	Г

• Please record all premedication administered prior to study drug XRP6258 or Mitoxantrone infusion or tick "None".

	MEDICATION	1	SAGE		START DA	ATE .	END DATE	
	MEDICATION	Number of Units	Unit	day	month	year	day month year	
1								
2			 	1 11 11				
<u> </u>			 					
3			 					
4								
5			 					
6			 	ا لــالــا				
7			 				UU UUU UUUU	
8							UU UUU UUUU	
9								
10								

NO	143		XRP6258	EFC6193
Confid	ontial = FINIAL =	■ 21 NOV 2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
CYCLE 10	V 10	See Page 49

# INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

Treatment Name		Date a	ND TIME OF DOSI	NG	Intended Dose	ACTUAL DOSE GIVEN
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start			<u> </u>		
☐ Mitoxantrone	End					
IF DOSE DELAYED AND	OOR REDUCE	D AND/OR INTER	RUPTED, SPECIFY	REASON:		
☐ AE: Specify on AE fo	orm					
Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name		Date an	ND TIME OF DOS	ING	Intended Dose	ACTUAL DOSE GIVEN
	day	month	year	24-hour clock	(mg/m <sup>2</sup> )	(mg)
☐ XRP6258	Start					
☐ Mitoxantrone	End				NA	

110 111   7111 0200   21
NO 144 , XRP6258 , EF

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	145 Page	
CYCLE 10	V 10	See Page 49			

## INVESTIGATIONAL PRODUCT ADMINISTRATION ADMIN\_1

	TREATMENT NAME	DATE OF DOSING		Intended Dose	ACTUAL DOSE GIVEN	
		day	month	year	(mg)	(mg)
☐ Prednisone		Start				
	Prednisolone	End L				
IF DOSE DELAYED AND/OR REDUCED AND/OR INTERRUPTED, SPECIFY REASON:						
AE: Specif	fy on AE form					
Other:						

IF DOSE INTERRUPTED, complete below:

Treatment Name	DATE OF DOSING	Intended Dose	ACTUAL DOSE GIVEN
	day month year	(mg)	(mg)
☐ Prednisone	Start Start		
☐ Prednisolone	End	NA	

110   7111 0200   21
NO 145 , XRP6258 , EF

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
CYCLE 10	V 10	See Page 51

# **BATCH NUMBERS**

O.BATCH\_1

	Drug Name	Batch Number
1		
2		
3		
4		
5		

NO 146 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	) Colon	30	Other
11.0	1 Regional Lymph Nodes	20.20	) Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193		NO 147
21 00100	Country No.	Centre No. Subject No. Page
CYCLE 10	V 10	See Page 55

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	LJL.LJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□ Not Done			
3	L.L.	Not Done		L L  mm	
4	LL.LL	□ Not Done			
5		□ Not Done			
6		□ Not Done			
7		□ Not Done			
8		□□□□□□□□□□□□□□□□ Not Done		∟∟∟ mm	
9		□ □ □ □ □ □ □ □ □ □ Not Done			
10	LIL.LIL	□ Not Done			
11		□ Not Done			
12	L. L. L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
13	LILI.LI	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
14	<u> </u>	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		mm	

NO 147 , XRP6258 , EFC6193

CYCLE 10	V 10	Soci	Page 53			
EFC6193	Country No.	Centre No.	Subject No.	ı	Page	
XRP6258				NO	148	

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current cycle (7 days prior to dosing Day 1)

Date (Day Month Year)	PPI	Analgesic Score
1		
2.		
3		
4		
5.		
		LILL . LILL
7	Ш	

NO 148 , XRP6258 , EFC6193

XRP6258 EFC6193				NO	149
CYCLE 10	V 10	See Pa	Subject No.		Page
ECHOCARDIO	GRAPHY				ECHOCARD_1
NOT DONE					
• Date performed: LLL L	month yea				
• 2D-Echocardiography:	Normal $\square$	A	bnormal* [	ם	
- Left ventricular ejection frac	ction (LVEF)	<u> </u>			
- Lower Limit Normal of LVE	F				
RADIONUCLID	E VENTR	ICULO:	GRAPI	ΙΥ	MUGA_1
NOT DONE   • Date performed:			GRAPI	ΙΥ	MUGA_1
NOT DONE   • Date performed: Lay	month yea	 ır		<b>IY</b> rmal* □	MUGA_1
NOT DONE   • Date performed: Lay  • Radionuclide Ventriculogi	month yea	 ır	Abno		MUGA_1
NOT DONE   • Date performed: LLL L	month year raphyy: Normal ction (LVEF)	ar	Abno ⊔ %		MUGA_1
NOT DONE  • Date performed: Lay  • Radionuclide Ventriculog  - Left ventricular ejection frac	month year raphyy: Normal ction (LVEF)		Abno ⊔ % ⊔ %		MUGA_1
NOT DONE  Date performed: Lay  Radionuclide Ventriculogo Left ventricular ejection fraction fractions Lower Limit Normal of LVE	month year raphyy: Normal ction (LVEF)		Abno ⊔ % ⊔ %		MUGA_1
NOT DONE  Date performed: Lay  Radionuclide Ventriculogo Left ventricular ejection fraction fractions Lower Limit Normal of LVE	month year raphyy: Normal ction (LVEF)		Abno ⊔ % ⊔ %		MUGA_1

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	150 Page	01
CYCLE 10	V 10	See	Page 60			

# **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	END DATE
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XRP6258 XT150 EFC6193

XRP6258 EFC6193				XT	150	02
LI C0193	Country No.	Centre No.	Subject No.		Page	
CYCLE 10	V 10	See	Page 60			

# **CONCOMITANT MEDICATION**

O.MED\_9

	Medication	START DATE			END DATE			
		Day	Month	Year	Day	Month	Year	
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing	
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing	
3.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ШШШ ing	
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ப்பட்ட Jing	
5.			□□□ l	⊔ШШ ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ப்பட்பட் ing	
6.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing	
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ululul ing	
8.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing ing	
9.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔ШШ ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing	
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing		□□□□ L □ Ongo	⊔⊔Ш Jing	

XRP6258 EFC6193	Country No. Cer	tre No. Subje	Ct No.	610 Page	01
CYCLE 10	v 🔲 🗎		See Page	62	_
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: L1 L0 AE ref. no: L1	j- <mark>[0] [1]</mark> J-		form no: 1101-1012 ef. no: 11-11	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	2 (do not complete the remaini	month year ng items in the column)		t:	
3= Ongoing with change  3. GRADE (1 - 4)	1 2 3	<b>4</b>	1 2	3 🗆	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🚨	Yes	□ No	
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinuu 3= Dose reduced / 4= Delayed and red 0  1  2  3	duced / 5= Interrupted		rmanently discontinued / 2= / 4= Delayed and reduced / 5 2	5= Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 📮	Yes	□ No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL Lday 4 Specify sequelae:	nonth year	1  Date:	day month fy sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI month year	2	eath:	L] L] L year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM		No	Yes	No - Date event became s - Date wonth - Tick below all criteri	year
	Resulting in death	ration	Life-threateni Requiring/pro Persistent/sig Congenital a	death ng olonging hospitalization nificant disability/incapaci nomaly/birth defect ally important event	ty
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's na	me, date of receipt:	
* Is there a reasonable	possibility that the AE was caus	l sed by study treatmer	nt?		
XT 610	I	XRP62	58 ,	EFC6193	

XRP6258 EFC6193	Country No	o. Centre No.	Subje	ect No.	XT	610 Page	02
CYCLE 10	V 10			See Pa	age 62		
ADVERSE EV	ENT FO	RM				O.1_AE_1	
1. Adverse Event Diagnosis	AE for	m no: [1][0]-[0][: no: []-[]			AE form n AE ref. no:	no: [1][0]-[0][4	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1	day month  plete the remaining items	year			day month the remaining items	year
3. GRADE (1 - 4)	1 🗖 2 🕻	3 🗖	4 🗖	1 🗖	2 🗖	3 🗖	4 🗖
Action Taken with     Study Treatment	0= None / 1= Perm	anently discontinued / 2= 4= Delayed and reduced / 2  3  4		0= None / 3= Dose rec		No  tly discontinued / 2= lelayed and reduced / 5  3  4  4	= Interrupted
6. CORRECTIVE TREATMENT/THERAPY 7. OUTCOME	Yes [	☐ No	0	Ye	es 🗖	No	
1= Recovered	1 <b>D</b> Date:	day month	<b>UUU</b>	10}	Date:	day month	L L L L L L J year

4 Specify sequelae: \_ 4 Specify sequelae: \_ 4= Recovered with sequelae 2 2 2= Recovering 3 3 3= Not recovered 5 **D** Date of death: \_\_\_\_ \_\_\_\_ 5 Date of death: 5= Fatal (complete the death report form) 6 🔲 6 🔲 6= Unknown 8. SERIOUSNESS - Date event became serious: - Date event became serious: day month year day month year IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM - Tick below all criteria that apply: - Tick below all criteria that apply: Resulting in death . . . . . . .  $\Box$ Resulting in death ..... Life-threatening ..... Requiring/prolonging hospitalization . . . . . . Requiring/prolonging hospitalization ..... Persistent/significant disability/incapacity . .  $\Box$ Persistent/significant disability/incapacity . . Congenital anomaly/birth defect . . . . . . . . . Congenital anomaly/birth defect . . . . . . . . Other medically important event  $\ldots$ Other medically important event ..... Investigator's name, date of report and signature: Monitoring representative's name, date of receipt: \* Is there a reasonable possibility that the AE was caused by study treatment?

EFC6193 XT610 XRP6258

XRP6258 EFC6193	Country No. Centre No.	Subject N	XT	610 Page	03
CYCLE 10	v 10		See Page 62	]	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: [1][0]-[0][5] AE ref. no: []-[]		AE form r AE ref. no:	no:   <b>1  0 - 0  6</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LL Lyes 2 (do not complete the remaining items in the co	olumn) 2	Date of start:	day month the remaining items i	year
3. GRADE (1 - 4)	1 🗆 2 🗔 3 🗔	4 🔲 1	2 🗆	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🚨		Yes 🗖	No	٥
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrup	oted 3	D= None / 1= Permanen B= Dose reduced / 4= D	relayed and reduced / 5=	= Interrupted
6. Corrective Treatment/Therapy	Yes No No		Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL LL LL Lday month ye  4 D Specify sequelae:	ar	- }	day month	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	3 	2	L]L]L]L]l day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes Onte event became serious:  - Date event became serious: - Date event became serious: - Date event became serious: - Date event became serious: - Date event became serious: - Date event became serious: - Date event became serious: - Persistent became serious: - Date event	ipply:	Yes	No te event became so te event became so from the content of the c	that apply:
Investigator's name, date of repo	ort and signature: Monitorin	ng represe	entative's name,	date of receipt:	

 $\ ^*$  Is there a reasonable possibility that the AE was caused by study treatment?

XT 610 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	ct No.	610 Page	04
CYCLE 10	v 10		See Page 62		
ADVERSE EVI	ENT FORM			O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no: [1] [0] AE ref. no: []	-  <b>0</b>    <b>7</b>    -	AE form AE ref. no:	no: 10-08	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		nonth year  ng items in the column)	1 Date of start: 2 (do not complete 3	day month  e the remaining items in	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖵	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec 0	luced / 5= Interrupted	3= Dose reduced / 4= [	ntly discontinued / 2= Delayed and reduced / 5=	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🚨	Yes 🗖	No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown  8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	4  Specify sequelae:	No Came serious:	Specify se  2	quelae:    Juli   Land   Land	year  year  year  rious:
Investigator's name, date of repo	Resulting in death  Life-threatening  Requiring/prolonging hospitaliz  Persistent/significant disability/i  Congenital anomaly/birth defect  Other medically important every  ort and signature:  possibility that the AE was caus	ation   ncapacity   t   Monitoring repr	Life-threatening Requiring/prolong Persistent/significa Congenital anoma Other medically ir esentative's name,	ing hospitalization nt disability/incapacity ly/birth defect nportant event date of receipt:	🗆

XT 610 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Centre No.	XT 610   05   Subject No.   Page
CYCLE 10	v 10	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [1][0]-[0][9] AE ref. no: [][-[][-	AE form no: [1][0]-[1][0] AE ref. no: []-[]-
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLL LLL LLL LLL LLL LLL LLL LLL LLL L	day month year
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 1	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0 1 1 2 1 3 1 4 5 1
6. Corrective Treatment/Therapy	Yes No 🗆	Yes 🗖 No 🗖
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date:	day month year  4  Specify sequelae:
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes
Investigator's name, date of repo	ort and signature: Monitoring  possibility that the AE was caused by study tre	g representative's name, date of receipt:

XT 610 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Centre N	No. Subje	act No.	610 Page	06
CYCLE 10	v 10   00		See Page 6	2	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: [1][0]-[1 AE ref. no: [][-		AE fon AE ref.	m no: [1][0]-[1][2 no: []-[]	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLL LLL day month 2 (do not complete the remaining ite	year ems in the column)	1 Date of start: 2 (do not comp	day month L	year
3. GRADE (1 - 4)	1 2 3 3	4 🗖	1 🗖 2 🗔	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 N	o 🗖	Yes	<b>N</b> o	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 3= Dose reduced / 4= Delayed and reduced 0			anently discontinued / 2= D 4= Delayed and reduced / 5= 2	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖 N	o 🗖	Yes	No No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)	Date: LL LLL day month  Specify sequelae:  2		2 🗆	th:	year
6= Unknown	day month	year	6 🗖	day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	ne serious:	⇒ IF YES {	No Date event became se	year
Investigator's name, date of repo	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incap  Congenital anomaly/birth defect  Other medically important event  ort and signature:	pacity	Life-threatening Requiring/prolo Persistent/signifi Congenital anoi Other medically	ath	
* Is there a reasonable	possibility that the AE was caused l	oy study treatmer	nt?		

XT 610 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Contro No. Subject	XT 610
CYCLE 10	V 10 Centre No. Subject	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event  Diagnosis	AE form no: LLL-LLL AE ref. no: LLL-LLL	AE form no: LL-LL AE ref. no: LL-LL
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LLL year  2 (do not complete the remaining items in the column)  3	Date of start: LL LLL year  2 (do not complete the remaining items in the column)  3
3. GRADE (1 - 4)	1	1
ACTION TAKEN WITH     STUDY TREATMENT*	Yes No D  0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted    0 D 1 D 2 D 3 D 4 D 5 D	Yes No One None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted Oor 1 Or 2 Or 3 Or 4 Or 5 Or 5
6. Corrective Treatment/Therapy	Yes No D	Yes 🔲 No 🚨
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: U UU UUU year 4 D Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown  8. Seriousness Criteria  If yes, complete this section and the SAE complementary FORM	2	2
Investigator's name, date of repo	Requiring/prolonging hospitalization	Requiring/prolonging hospitalization Persistent/significant disability/incapacity Ongenital anomaly/birth defect Other medically important event Presentative's name, date of receipt:

XT 610 XRP6258 EFC6193

(RP6258 FC6193	Country No.   Centre No.	o. Subject No.	NO 501	
ND OF TREATMENT	99			
END OF TREATM	IENT O.ENDTT_2	?		
Main reason for stopping trea	tment (tick "✓" one	box only):		
- Completed study treatment p	eriod			
- Lack of efficacy				
- Disease progression*	• • • • • • • • • • • • • • • • • • • •			
- Adverse event* (complete AE	form)			
- Poor compliance to protocol				
- Subject lost to follow-up				
- Other reason	• • • • • • • • • • • • • • • • • • • •			
If other reason, specify: _				
_				
- Subject request				
This box should be check			onsent and none	
of the above reasons are	present especially ad	lverse event.		
Specify:				
* In case of an adverse event	complete the Advers	se Event form.		
"I, the undersigned, certify that To the best of my knowledge,	•		s on the CRF for this	subject.
, ,				
Investigator signature:		Date: L		
			day month	year
NO 501	1	XRP6258	EFC6193	
Confidential ■ FINAL ■ 2	21 NOV 2006	so	nofi aventis	

XRP6258         Image: Country No.         NO         151           EFC6193         Country No.         Centre No.         Subject No.         Page
END OF TREATMENT V 80 Date of visit: day / month / month / wear
See Page 43
PHYSICAL EXAMINATION PHYSEXAM_2
None
Date performed: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL
• Were there any clinically significant changes from the previous evaluation? Yes* $\square$ No $\square$
*If yes, please complete the Adverse Event form.
See Page 27
VITAL SIGNS  VITAL_1
NOT DONE
Weight: LILILI . LJ kg
- Blood pressure: Systolic       mmHg / Diastolic     mmHg
- Heart rate: LILILI beats/min
- Temperature: ☐☐ . ☐ °C
(tick appropriate box): Oral $\square$ Rectal $\square$ Auricular $\square$
ECOG Performance Status
$\begin{array}{cccccccccccccccccccccccccccccccccccc$

NO 151 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	152 Page	
END OF TREATMENT	V 80					
See Page 24 HEMATOLOGY LABH_1						
Date of sampling:	month					

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10 <sup>9</sup> /L	
Basophils		10°/L	
Monocytes		10 <sup>9</sup> /L	
Lymphocytes		10 <sup>9</sup> /L	
Platelets		10 <sup>9</sup> /L	
Hemoglobin		g/dL	

PSA

See Page 26

LABH\_1

DATE OF SAMPLING day month year	Test	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

	NO 152	XRP6258   EFC6193	
Page 269/525	Confidential ■ FINAL ■ 21-NOV-2006	sanofi aventis	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	153 Page		
END OF TREATMENT	V 80						
See Page 25 BIOCHEMISTRY  LABB_1							
Date of sampling:	month	year					

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

TESTOSTERONE	LABB_1
Date of sampling: LLLLLL Lyear Month year	

Test	<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Testosterone		ng/dL	

NO	153	I	XRP6258	EFC6193
Confid	ontial = FINIAL I	■ 21 NOV 2006	san	ofi aventis

· Loca	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>154</b> Page	
END OF TREATMENT	V 80	See F	Page 55			

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ Not done

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	L.I.I.I.I.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		∟∟∟ mm	
8		□□ □□□ □□□□□ □ Not Done			
9		□□□□□□□□□□□□□□□□ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done			
12	L. L. L.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 154 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	155 Page	
END OF TREATMENT	V 80	See	Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to End of Treatment visit (7 days prior to End of Treatment visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		
3.		
4		
5.	Ш	
6.	L	
7.		

NO 155 XRP6258 EFC6193

Centre No.	Subject No.	NO	156 Page	
See Pa	age 28			
				ECG_1
ormal* 🔲				
		See Page 28	See Page 28	See Page 28

\* If clinically relevant, please report on the Adverse Event form.

XRP6258			
EFC6193		NO	157
	Country No. Centre No.	Subject No.	Page
END OF TREATMENT	V 8 0 See	Page 29	
			_
ECHOCARDIOG	RAPHY ECHOCARI	D_1	
NOT DONE			
• Date performed: LL L	month year		
• 2D-Echocardiography:	Normal 🗖	Abnormal* □	
- Left ventricular ejection fraction	on (LVEF)	<u> </u>	
- Lower Limit Normal of LVEF	<u> </u>	<u> </u>	
* If clinically relevant, please  RADIONUCLIDE	·		MUGA_1
NOT DONE			
_	month year		
NOT DONE ☐  • Date performed: ☐☐ ☐	,	Abnormal* 🗖	
NOT DONE ☐  • Date performed: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐	ohy: Normal 🗖		
NOT DONE   • Date performed: Lay Lay  • Radionuclide Ventriculogra	ohy: Normal 🗖	<u> </u>	
NOT DONE   • Date performed: Lay  • Radionuclide Ventriculograph - Left ventricular ejection fraction	ohy: Normal ☐ on (LVEF) ☐ ☐ .	<ul><li></li></ul>	
NOT DONE  • Date performed: Lay  • Radionuclide Ventriculograph  - Left ventricular ejection fraction  - Lower Limit Normal of LVEF	ohy: Normal ☐ on (LVEF) ☐ ☐ .	<ul><li></li></ul>	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	158 Page	01
END OF TREATMENT	V 80	See	Page 60			

# **CONCOMITANT MEDICATION**

O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	END DATE
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XT	158	XRP6258	EFC6193
0 6 -1		san	ofi aventis

XRP6258 EFC6193				XT	158	02
21 00 100	Country No.	Centre No.	Subject No.	I	Page	
END OF TREATMENT	V 80	See	Page 60			

# **CONCOMITANT MEDICATION**

O.MED\_9

	Medication	START DATE			END DAT	Γ <b>E</b>	
		Day	Month	Year	Day	Month	Year
1.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing		□□□□ L □ Ongo	⊔ШШ ing
2.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⊔⊔Ш ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
3.			□□□□ l	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
4.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□ L □ Ongo	ing
5.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing ing		□□□□ L □ Ongo	ing
6.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
7.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
8.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
9.			□□□□ l	ing		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing
10.			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	ing

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>159</b> Page
Follow-up 1	V 81		Date of visit:	ay/	month year
			See Pag	<mark>je 12</mark>	_
FOLLOW-UP 1					O.FOLLOWUP_2
Subject condition (tick "✓"  ☐ Alive ☐ Lost to follow-up ☐ Dead (complete Death form)  Progression		·):			
Has the subject had disease	e progression?	(tick "✓" one	box only)		
Unknown	1 0	•	,,		
☐ Previously reported pro	ogression				
■ No *					
☐ Yes **					
* If NO please complete	the Turne or A.A	looguromeent n	ngo DCA Daim	Intonsite	· Assassment forms

- If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- If YES, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

NO XRP6258 159 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	160 Page	
FOLLOW-UP 1	V 81					

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

■ None		Unknown
--------	--	---------

Drug/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			۰
2.			٥
3.			٥
4.			
5.			٥
6.			٥
7.			٥
8.			
9.			٥
10.			

			san	ofi aventic
NO	160	1	XRP6258	EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	<b>161</b> Page	
FOLLOW-UP 1	V 81	See Page 26			

PSA LABH\_1

DATE OF SAMPLING day month year	Test	<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 161 XRP6258 EFC6193

* Loca	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	Regional Lymph Nodes	20.20	Rectum		
11.02	? Distant Lymph Nodes	21	Adrenal		

### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

### \*\*\*RESPONSE OF NON-TARGET CODES:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 1	V 81	See Page 55

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.I.L.I.L.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□ □□□ □□□□□ □ Not Done		mm	
3		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		L L  mm	
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5		□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□ Not Done			
8		□□□□□□□□□□□□□□□□ Not Done			
9	L	□□ □□□ □□□□□ □ Not Done			
10		□□□□□□□□□□□□□□□ Not Done			
11		□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14	L.L.L	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 162 , XRP6258 , EFC6193

XRP6258 EFC6193				NO	163	
21 00 100	Country No.	Centre No.	Subject No.	I	Page	
FOLLOW-UP 1	V 81	See I	Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		
3.		
4		
5.	Ш	
6.	L	
7.		

NO 163 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cer	tre No. Subje	ct No.	681 Page	01
Follow-up 1	V 81		See Page	<mark>62</mark>	
ADVERSE EVI	ENT FORM			0.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>L8</b> L <b>1</b> AE ref. no: <b>L</b> 1	- <mark> 0  1</mark>  -		orm no:   <b>8   1   - 10   12</b> ef. no:         -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	1 Date of start: LLLL day 1 2 (do not complete the remaini 3	nonth year ng items in the column)	1  Date of start 2  (do not cor	day month	
3= Ongoing with change  3. GRADE (1 - 4)		<b>4</b>		3 🗆	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes	□ No	
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0	duced / 5= Interrupted		manently discontinued / 2= 4= Delayed and reduced / 5 2  3  4 [	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes	□ No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL Lday  4 Specify sequelae:	month year	1 Date:	day month	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI month year	2	eath:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM		No	Yes	No - Date event became s - Date event became s - Tick below all criteric	year
	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defed	ration   ncapacity	Life-threateni Requiring/pro Persistent/sigr Congenital ar	leath  ng  longing hospitalization  nificant disability/incapaci  nomaly/birth defect  lly important event	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's nai	me, date of receipt:	
	possibility that the AE was caus	, ,			
XT 681	1	XRP62	58	EFC6193	

XRP6258 EFC6193				XT	681	02
Follow-up 1	V 81	Centre No.	Subject	See Page	Page <b>62</b>	_
ADVERSE EVI	ENT FOR	M			O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no: AE ref. no:	8 1 - 0 3			orm no: [ <b>8</b> ][ <b>1</b> ]-[ <b>0</b> ][ f. no: [][-[][	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		day month the remaining items in	the column)	1 Date of start 2 (do not cor	:	year
3. GRADE (1 - 4)	1 🔲 2 🔲	3 🗖	4 🔲	1 🗖 2	3 🗆	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No		Yes	□ No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently 3= Dose reduced / 4= Del 0	ayed and reduced / 5=	Interrupted		manently discontinued / 2= 4= Delayed and reduced / 2	
6. Corrective Treatment/Therapy	Yes 🗖	No		Yes	□ No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered	4 □ <b>J</b> Specify sequence 2 □ 3 □	JL LLL L day month uelae:	year	2 🗆	day month fy sequelae:	
5= Fatal (complete the death report form) 6= Unknown	5 ☐ Date of death: ☐ 6 ☐	day month	year	<ul><li>5 □ Date of do</li><li>6 □</li></ul>	eath: day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	⇒ If YES	No event became se	J L J	Yes	No - Date event became	year
	Resulting in death Life-threatening Requiring/prolonging Persistent/significant Congenital anomaly/	hospitalization disability/incapacity birth defect	0	Life-threateni Requiring/pro Persistent/sign Congenital ar	leath  Ilonging hospitalization  Ilonging hospitalization  Ilificant disability/incapac  Ilificant disability/incapac  Ilificant disability/incapac	
Investigator's name, date of repo	ort and signature:	Mon	itoring repres	sentative's na	me, date of receipt:	

XT 681 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subject	XT 681 03
Follow-up 1	V 81	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [8][1]-[0][5] AE ref. no: []-[]-	AE form no: [8] 1] - [0] [6] AE ref. no: [] - []
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: Lay month year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes	Yes

**O**UTCOME 1 Date: 1= Recovered Specify sequelae: Specify sequelae: 4= Recovered with sequelae 2 2 2= Recovering  $3 \square$ 3 3= Not recovered 5 **D** Date of death: \_\_\_\_ \_\_\_\_ 5 Date of death: 5= Fatal (complete the death report form) 6 🔲 6 🔲 6= Unknown 8. **S**ERIOUSNESS CRITERIA - Date event became serious: - Date event became serious: day month year day month year IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM - Tick below all criteria that apply: - Tick below all criteria that apply: Requiring/prolonging hospitalization . . . . . . Requiring/prolonging hospitalization . . . . Persistent/significant disability/incapacity . .  $\Box$ Persistent/significant disability/incapacity . . . Congenital anomaly/birth defect . . . . . . . . Congenital anomaly/birth defect . . . . . . . Other medically important event  $\dots$ Other medically important event ..... Investigator's name, date of report and signature: Monitoring representative's name, date of receipt: \* Is there a reasonable possibility that the AE was caused by study treatment?

XT681 XRP6258 EFC6193

XRP6258 EFC6193			11 1		
	Country No. Cen	tre No. Subje	Lt No.	681 Page	0 4
Follow-up 1	V 81		See Page 62	]	
ADVERSE EVE	NT FORM			O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no: <b>8 1</b> AE ref. no:	- <u> 0</u>	AE form r AE ref. no:	no:  8 1 - 0 8	
1= New 2= Ongoing from previous period without change		onth year  ng items in the column)	1 Date of start: 2 (do not complete	day month to the remaining items in	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖸	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲	No 🗖	Yes 🗖	No	
ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0		0= None / 1= Permanen 3= Dose reduced / 4= D 0		= Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 📮	No 🗖	Yes 🗖	No	
1= Recovered 4= Recovered with sequelae  2= Recovering 3= Not recovered 5= Fatal (complete the death report form)	Specify sequelae:  2	Onnonth year	4	day month quelae:  day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes  - Date event be - Date event be - Date event be - Date event be - Tick below all - Tick below all - Tick below all - Resulting in death - Life-threatening - Requiring/prolonging hospitaliz - Persistent/significant disability/it - Congenital anomaly/birth defect - Other medically important even	riteria that apply:	→ IF YES	No  Ite event became se  I III III  I II  I III  I II  I III  I II  I III  I II	year  that apply:
Investigator's name, date of report	t and signature:  ossibility that the AE was caus		esentative's name,	date of receipt:	

XT 681 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.   Cer	tre No. J Subje	XT	681 Page	0[5
Follow-up 1	V 81		See Page 62	_	
ADVERSE EV	ENT FORM			0.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>811</b> AE ref. no: <b>1</b>	- <mark> 0  9 </mark>  -	AE form AE ref. no:	no:   <b>8</b>   <b>1</b>  - <b>1</b>   <b>0</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nonth year ng items in the column)	1   Date of start: 2   (do not complete 3	day month e the remaining items in	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 2 2	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🔲	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0	luced / 5= Interrupted	3= Dose reduced / 4= [	ntly discontinued / 2= Delayed and reduced / 5=	Interrupted
6. Corrective Treatment/Therapy	Yes 🔲	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		month year	- }	LLL LLLL L day month quelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILILI year	2	day month	year
8. SERIOUSNESS CRITERIA	Yes - Date event be	No 🗖	Yes 🗖	No ate event became se	rious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/ Congenital anomaly/birth defee	I criteria that apply:	- Tio Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anoma	ck below all criteria ing hospitalization int disability/incapacity ly/birth defect	0
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's name,	date of receipt:	
* Is there a reasonable	possibility that the AE was caus	ed by study treatmer	nt?		

XT 681 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 681 06
Follow-up 1	V 81 000	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: <b>[8] 1]</b> - <b>[1] 1</b> AE ref. no: <b>[]</b> - <b>[]</b>	AE form no:   <b>8</b>   <b>1</b>  - <b>1</b>   <b>2</b>    AE ref. no:       -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖	Yes 🗆 No 🖵
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes 🔲 No 🚨	Yes 🔲 No 🗖
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered	Date: J J J J J J J J J J J J J J J J J J J	Date: LL
5= Fatal (complete the death report form)	5 Date of death: U UU UUU year	5 Date of death: U U U U U U U U U U U U U U U U U U U
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Solution No	Yes No Solution No
	Resulting in death	Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt:

XRP6258 EFC6193	Country No. Centre No. Subje	XT 681 Page
FOLLOW-UP 1	V 81   LLL	See Page 62
ADVERSE EVI	EN I FURIVI	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: LL-LL AE ref. no: LL-LL	AE form no: LJL-LJL AE ref. no: LJL-LJL
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LL Lyear  2 (do not complete the remaining items in the column)  3	Date of start: Lay Lay month year    Quantification   Qua
3. GRADE (1 - 4)	1	1 🗆 2 🖸 3 🔲 4 🗓
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No C	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: ULL ULL year 4 D Specify sequelae:	1 Date: LLL LLLL year 4 D Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA	Yes  No  O - Date event became serious:	Yes  No  No  C  - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE <b>SAE</b> COMPLEMENTARY FORM	Tick below all criteria that apply:	Tick below all criteria that apply:  Resulting in death
	Life-threatening	Life-threatening
Investigator's name, date of repo	ort and signature: Monitoring repr	resentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmer	11?

XRP6258 EFC6193				NO	164
	Country No.	Centre No.	Subject No.		Page
Follow-up 2	V 82		Date of visit:	day /	month year See Page 12
	See Page 27	8			
FOLLOW-UP 2					O.FOLLOWUP_2
<b>Subject condition</b> (tick "✓	" one box only	·):			
_	one 20% only	,.			
☐ Alive					
☐ Lost to follow-up					
☐ Dead (complete Death t	form)				
Dead (complete Death )	OIIII)				
Progression					
Has the subject had diseas	e progression?	(tick "✓" one	box only)		
☐ Unknown					
☐ Previously reported pre	ogression				
☐ No *					
☐ Yes **					

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

 NO
 164
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-NOV-2006
 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	165 Page	
Follow-up 2	V 82	See Page 279			

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

	None		l Unknown
--	------	--	-----------

Drug/Regimen/Agent	START DATE	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			٥
4.			٥
5.			
6.			٥
7.			
8.			٥
9.			
10.			

NO	165	XRP6258	EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 2	V 82	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 166 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	I Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

## \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	167 Page	
Follow-up 2	V 82	See I	Page 55			

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ Not done

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	L.I.I.I.I.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		∟∟∟ mm	
8		□□ □□□ □□□□□ □ Not Done			
9		□□□□□□□□□□□□□□□□ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done			
12	L. L. L.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 167 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	168 Page	
FOLLOW-UP 2	V 82	See	Page 53			

## **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
3.		
4		
5.		
7.		

NO 168 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Centre N	lo. Subje	ct No.	682 Page	01
FOLLOW-UP 2  ADVERSE EVI	V 82 LL		See Page 62	0.1_AE_1	_
☐ NONE					
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin		AE fori AE ref.	m no: [8]2]- <mark>0]2</mark> no: []-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	day month  2	year ms in the column)	<i>'</i>	day month Lete the remaining items in	year
3= Ongoing with change	3 🗆		3 🗖	2.0	
3. GRADE (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT*	1	4 🗆	1		4 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 3= Dose reduced / 4= Delayed and reduced 0 1 2 3 1	2= Delayed	0= None / 1= Perma	anently discontinued / 2= Du l= Delayed and reduced / 5= 2  3  4	elayed Interrupted
6. Corrective Treatment/Therapy	Yes 🔲 No	) <b></b>	Yes	<b>1</b> No	
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered  5 = Fatal (complete the death report form)	Date: LL		2	th:	year
6= Unknown  8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	e serious:	⇒ IF YES {	Date event became se	J L J L J
	Resulting in death Life-threatening Requiring/prolonging hospitalization Persistent/significant disability/incap Congenital anomaly/birth defect Other medically important event	acity	Resulting in dea Life-threatening Requiring/prolo Persistent/signifi Congenital anoi	nging hospitalization icant disability/incapacity maly/birth defect y important event	0
Investigator's name, date of report and signature:  Monitoring representative's name, date of receipt:					
* Is there a reasonable	possibility that the AE was caused b	y study treatmer		FC6193	_

XRP6258 EFC6193		XT 682 02			
	Country No. Centre No. Subje	ct No.   Page			
FOLLOW-UP 2	V 8 2   LLL	See Page 62			
	<u> </u>				
ADVERSE EVI	ENT FORM	0.1_AE_1			
1.	AE form no: [8][2]-[0][3]	AE form no: [8][2]-[0][4]			
Adverse Event	AE ref. no:	AE ref. no:			
Diagnosis					
2. STATUS OF AE	1 <b>D</b> Date of start:	1 🔲 Date of start: 🔠 🗀 🗀 🗀 🗀			
1= New 2= Ongoing from previous period without change	day month year  2  (do not complete the remaining items in the column)	day month year  2			
3= Ongoing with change	3 🗖	3 🗖			
3. GRADE (1 - 4)	1	1 0 2 0 3 0 4 0			
4. RELATIONSHIP TO STUDY TREATMENT*	Yes  No	Yes No 🗖			
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted				
STODY TREATMENT	0 1 2 3 4 5	0 1 2 3 4 5 5			
6. Corrective Treatment/Therapy	Yes 🗖 No 🗖	Yes No 🗆			
7. OUTCOME 1= Recovered	1 <b>D D</b> Date:	1 <b>□                                   </b>			
4= Recovered with sequelae	day month year  4  Specify sequelae:	4  Specify sequelae:			
2 Pi	2 🗆	2 🗖			
2= Recovering 3= Not recovered	3 🗖	3 🗖			
5= Fatal (complete the death report form)	5 Date of death: U UUU UUUU	5 Date of death: UU UUU UUUU			
6= Unknown	6 🗖	6 🗖			
8. SERIOUSNESS CRITERIA	Yes  No  No  To Date event became serious:	Yes  \( \bigcap \) No \( \bigcap \)  \( \bigcap \) - Date event became serious:			
IF YES, COMPLETE THIS SECTION		⇒ IF YES     □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □			
AND THE SAE COMPLEMENTARY FORM	day month year  - Tick below all criteria that apply:	day month year - Tick below all criteria that apply:			
	Resulting in death	Resulting in death			
	Life-threatening	Life-threatening			
	Requiring/prolonging hospitalization	Requiring/prolonging hospitalization			
	Congenital anomaly/birth defect	Congenital anomaly/birth defect			
	Other medically important event	Other medically important event			
Investigator's name, date of repo	Investigator's name, date of report and signature:  Monitoring representative's name, date of receipt:				
* le thora a rascanabla	possibility that the AE was caused by study treatmen	st2			
is uiere a reasoriable	possibility that the AL was caused by study freatment	ru:			

XT 682 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 682 03
Follow-up 2	V 82	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: <b>[8][2]-[0][5</b> ] AE ref. no: <b>[]]-[]</b>	AE form no:   <b>8</b>   <b>2</b>  -  <b>0</b>   <b>6</b>    AE ref. no:   -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL
3. GRADE (1 - 4)	1	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes No 🗆	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL LLL year 4 Specify sequelae:	1 Date: LL LLL year 4 Specify sequelae:
2= Recovering	2 🔲	2 🗖
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	5 Date of death: U UUU UUU wear	5 Date of death: U UU UUU year
6= Unknown	6 <b></b>	6 🗖
8. SERIOUSNESS	Yes No D	Yes No D

IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY **FORM** - Tick below all criteria that apply: Life-threatening . . . . . . . . . . . . . . . . . Life-threatening . . . . .  $\Box$ Requiring/prolonging hospitalization  $\dots$ Requiring/prolonging hospitalization . . . . . Persistent/significant disability/incapacity  $\dots$ Persistent/significant disability/incapacity . .  $\Box$ Congenital anomaly/birth defect . . . . . . . .  $\Box$ Congenital anomaly/birth defect . . . . . . . . Other medically important event  $\dots$ Other medically important event .....

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 682 | XRP6258 | EFC6193

Investigator's name, date of report and signature:

Monitoring representative's name, date of receipt:

XRP6258 EFC6193	Country No. Centre No. Subje	XT 682 04
Follow-up 2	V 82 000	See Page 62
ADVERSE EV	ENT FORM	0.1_AE_1
1. Adverse Event Diagnosis	AE form no:   <b>8</b>   <b>2</b>  - <b>0</b>   <b>7</b>   AE ref. no:   -	AE form no:   <b>8</b>   <b>1</b>  - <b>1</b> 0  <b>8</b>   AE ref. no:   - - - -
2. STATUS OF AE 1= New	1 Date of start: LL LLL LLL year	1 Date of start:
2= Ongoing from previous period without change	2 (do not complete the remaining items in the column)	2 (do not complete the remaining items in the column)
3= Ongoing with change	3 🗖	3 🗖
3. GRADE (1 - 4)	1 2 3 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖	Yes No 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted
	0 0 1 0 2 0 3 0 4 0 5 0	0 1 2 3 4 5
6. Corrective Treatment/Therapy	Yes 🗖 No 🗖	Yes 🗖 No 🗖
7. OUTCOME  1= Recovered  4= Recovered with sequelae	1 Date: LL LLL year  Specify sequelae:	1 Date: LL LLL year 4 D Specify sequelae:
2= Recovering	2 🗖	2 🗖
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	5 Date of death: U U U U U U U U U U U U U U U U U U U	5 Date of death: LL LLL year month year
6= Unknown	6 □ Yes □ No □	Yes No D
8. SERIOUSNESS CRITERIA	- Date event became serious:	- Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	⇒ IF YES      □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	⇒ IF YES
FORM	- Tick below all criteria that apply:	- Tick below all criteria that apply:
	Resulting in death	Resulting in death
	Life-threatening	Life-threatening
	Persistent/significant disability/incapacity	Persistent/significant disability/incapacity
	Congenital anomaly/birth defect	Congenital anomaly/birth defect
	Other medically important event	Other medically important event
Investigator's name, date of rep	on and signature:   Monitoring repr	resentative's name, date of receipt:

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 682 | XRP6258 | EFC6193

XRP6258 EFC6193 FOLLOW-UP 2	Country No. Cen	tre No. Subjec	XT	682 Page	0[5
ADVERSE EV			See Page 62	O.1_AE_1	_
1. Adverse Event Diagnosis	AE form no: <b>812</b> AE ref. no: <b>1</b>	- <mark> 0  9 </mark>  -	AE form n AE ref. no:	0: <b>[8][2]-[1][0</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nonth year ng items in the column)	1  Date of start: L 2  (do not complete	day month the remaining items in	year
3. GRADE (1 - 4)	1 🗖 2 🗖 3	4 🗆	1 🔲 2 🔲	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red	luced / 5= Interrupted	0= None / 1= Permanent 3= Dose reduced / 4= D 0	elayed and reduced / 5=	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🚨	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL day n 4 Specify sequelae:	nonth year		day month	
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	nonth year	2	day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	<b>I</b> '	No	⇒ IF YES	No te event became se	<b>JLI</b>
	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec	ation $\square$ ncapacity $\square$	Life-threatening Requiring/prolongin Persistent/significan Congenital anomal	ng hospitalization it disability/incapacity y/birth defect portant event	
Investigator's name, date of rep	ort and signature:	Monitoring repre	sentative's name, o	date of receipt:	
*1.1	possibility that the AE was caus		2		

XT 682 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 682 06		
Follow-up 2	V 82	See Page 62		
ADVERSE EV	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no: [8] 2]-[1] 1  AE ref. no: []-[]-	AE form no:   <b>8</b>   <b>2</b>  -  <b>1</b>    <b>2</b>    AE ref. no:    -		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LL LL Lyear 2 (do not complete the remaining items in the column) 3	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL		
3. GRADE (1 - 4)	1 2 3 4 4	1		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes No D		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0 1 2 2 3 4 5 5	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
6. Corrective Treatment/Therapy	Yes No D	Yes No D		
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: ULL ULL year 4 D Specify sequelae:	1 Date: LL LL LL LL L L L L L L L L L L L L L		
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Company No Comp	Yes No Control No Cont		
	Resulting in death Resulting in death			
Investigator's name, date of report and signature:  Monitoring representative's name, date of receipt:				
* Is there a reasonable	possibility that the AE was caused by study treatmen	nt?		

XT 682 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 682		
Follow-up 2	V 82	See Page 62		
ADVERSE EVI	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no: LLL-LLL  AE ref. no: LLL-LLL	AE form no: LJL-LJL AE ref. no: LJL-LJL		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LL LL year 2 (do not complete the remaining items in the column) 3	Date of start: LLL LLLL year  2  (do not complete the remaining items in the column)  3		
3. GRADE (1 - 4)	1	1 🗆 2 🖸 3 🗖 4 🗖		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No D		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
6. Corrective Treatment/Therapy	Yes No D	Yes No D		
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year  4 D Specify sequelae:	1 Date: LLL LLL LLL LLL LLL LLL LLL LLL LLL L		
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2		
8. SERIOUSNESS CRITERIA	Yes  No  No  C - Date event became serious:	Yes  No  No  C		
IF YES, COMPLETE THIS SECTION AND THE <b>SAE</b> COMPLEMENTARY FORM	Tick below all criteria that apply:  Resulting in death			
	Requiring/prolonging hospitalization			
Investigator's name, date of repo	ort and signature: Monitoring repr	resentative's name, date of receipt:		
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?		

XT 682 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	169 Page	
Follow-up 3	V 83		Date of visit:	day /	month / [	year
			1	·	ee Page 12	
	See Page 27	8				
FOLLOW-UP 3					O.FOLLOWUP	_2_2
Subject condition (tick "v	✓" one box only	<i>y</i> ):				
☐ Alive						
☐ Lost to follow-up						
☐ Dead (complete Death	form)					
,						
Progression						
Has the subject had disea	se progressions	? (tick " <b>√</b> " one	box only)			
☐ Unknown						
☐ Previously reported p	rogression					
□ No *						
☐ Yes **						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

 NO
 169
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-NOV-2006
 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
Follow-up 3	V 83	See Page 279

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

■ None	■ Unknown
--------	-----------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			۵
4.			
5.			٥
6.			٥
7.			
8.			۵
9.			
10.			

NO	170	XRP6258	EFC6193
04:-1-	ontial = FINIAL = 21 NOV/ 2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 3	V 83	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 171 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	NO 172  Centre No.   Subject No.   Page
FOLLOW-UP 3	V 83	See Page 55

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□ Not Done			
3	L.L.	Not Done			
4	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□ Not Done			
6		□ Not Done			
7		□ Not Done			
8		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
9		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
10	LILI.LILI	□ Not Done		LJLJ mm	
11	L_  L_  .L_	□ Not Done			
12		□ Not Done			
13	L.I.I.I.I.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 172 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>173</b> Page	
FOLLOW-UP 3	V 83	See F	Page 53			

## **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		LJLL . LJL
3.		
4		
5.	Ш	
6.	L	
7.	Ш	

NO 173 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	XT	683 Page	01
FOLLOW-UP 3	V 83		See Page 6	<mark>62</mark>	_
ADVERSE EVI	ENT FORM			O.1_AE_1	
☐ NONE			ı		
1. Adverse Event Diagnosis	AE form no: <b>8</b> 1 <b>3</b> AE ref. no: <b>1</b>	- <b>(0</b>	AE fo	orm no:   <b>8   3   0</b>   2 f. no:         -	
2. STATUS OF AE	1 Date of start:	LILI LILILI	1  Date of start:	day month	
2= Ongoing from previous period without change 3= Ongoing with change	2 (do not complete the remaining 3 )	ng items in the column)	2  (do not con	nplete the remaining items	
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🗖 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 📮	No 🗖	Yes	□ No	
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0	luced / 5= Interrupted		manently discontinued / 2= 4= Delayed and reduced / 5 2	
6. Corrective Treatment/Therapy	Yes 🔲	No 🗖	Yes	□ No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLLL Aday Specify sequelae:	nonth year	1 Date:	day month y sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LLL LLLLL month year	2	eath:	∐∐∐ year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes - Date event be day month	No 🗖 ecame serious:		No - Date event became s	
FORM	- Tick below al  Resulting in death	tation	Life-threatenir Requiring/pro Persistent/sign Congenital an	- Tick below all criterieath  g longing hospitalization ificant disability/incapaciomaly/birth defect  lly important event	ty
Investigator's name, date of repo			L	me, date of receipt:	
* Is there a reasonable XT 683	possibility that the AE was caus	ed by study treatmer		EFC6193	

XRP6258 EFC6193	Country No.   Centre No.   Subje	Tict No.   XT 683 0 2
FOLLOW-UP 3	V 83	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin	AE form no: [8]3]-[0]4] AE ref. no: []-[]
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT*	1	1
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLL LLLL year 4 Specify sequelae:	1 Date: LL LLL year 4 Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2 ☐ 3 ☐ 5 ☐ Date of death: ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No C  - Date event became serious:    Solution of the property of the prop	Yes No No In Pres Serious:  - Date event became serious:  - Date event became serious:  - Date event became serious:  - Tick below all criteria that apply:
Investigator's name date of ren	Resulting in death	Resulting in death

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 683 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Sub	XT 683 03
FOLLOW-UP 3	V 83	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [8]3-[0]5  AE ref. no: []-[]	AE form no: [8]3-0[6] AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL	day month year
3. GRADE (1 - 4)	1 2 3 4 4	1
4. RELATIONSHIP TO STUDY TREATMENT	Yes No No	Yes 🗆 No 🖵
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therai	Yes 🗖 No 🗖	Yes  No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1  Date: LL LL LL LL LA Jear Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA	Yes No O - Date event became serious:	Yes
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	day month year  - Tick below all criteria that apply:  Resulting in death	Resulting in death
Investigator's name, date of re	port and signature: Monitoring re	L

XT 683 | XRP6258 | EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	ct No.	683 Page	04
Follow-up 3	V 83		See Page 62		
ADVERSE EV	ENT FORM			0.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \[ \begin{array}{c c} \begin{array}{c c} \B & \le & \end{array} \]  AE ref. no: \[ \begin{array}{c c} \begin{array}	- <mark> 0  7</mark>  -	AE form AE ref. no	no:   <b>8 3 -10 8</b> :         -	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		nonth year ng items in the column)	1   Date of start: 2   (do not complet	day month le the remaining items in	year
3. GRADE (1 - 4)	1 🔲 2 🔲 3	4 🗆	1 2 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 📮	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec 0	luced / 5= Interrupted	3= Dose reduced / 4= 1	ntly discontinued / 2= D Delayed and reduced / 5=	= Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🚨	Yes 🗖	No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown  8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	4  Specify sequelae:	No Grand serious:    Came serious:	2	equelae:  How month  No ate event became sell with the companion of the co	erious:
Investigator's name, date of repo	Life-threatening	ation  ncapacity  nt	Requiring/prolong Persistent/significa Congenital anoma Other medically in esentative's name,	ing hospitalization unt disability/incapacity aly/birth defect mportant event date of receipt:	🗆 y 🗅

XT 683 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	ct No.	683 Page	05
Follow-up 3	v 83		See Page 62		
ADVERSE EVI	ENT FORM			0.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \_ <b>8</b> \_ <b>3</b> AE ref. no: \_\_\_	- <mark> 0  9 </mark>  - _	AE form AE ref. no	no: <b> 8 3-1 0</b> :   -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nonth year ng items in the column)	1   Date of start: 2   (do not complet	day month te the remaining items in	year
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 2 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0	luced / 5= Interrupted	3= Dose reduced / 4=	ently discontinued / 2= D Delayed and reduced / 5=	= Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🗖	Yes 🗖	No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	4  Specify sequelae: 2		2 🗆	equelae:  day month  equelae:  day month	year year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes - Date event be		Yes ☐  → IF YES   → IF YES	No ate event became se	
AND THE SAE COMPLEMENTARY FORM  Investigator's name, date of repo	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec	I criteria that apply:	- Ti Resulting in death Life-threatening . Requiring/prolong Persistent/significa Congenital anoma	ick below all criteria ick below all criteria iging hospitalization ant disability/incapacity aly/birth defect important event date of receipt:	
* Is there a reasonable	possibility that the AE was caus	ed by study treatmer	nt?		

XRP6258 EFC6193 XT 683

XRP6258 EFC6193	Country No. Cen	tre No. Subje	ct No.	683 Page	06
FOLLOW-UP 3	V 83		See Page 62	. ago	
ADVERSE EV	ENT FORM			0.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin{align*} \begin{align*} \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	]-[ <b>1</b> ][ <b>1</b> ]	AE form AE ref. no	no: [ <b>8]</b> [3]-[1][2	
2. STATUS OF AE  1= New  2= Ongoing from previous period without chan  3= Ongoing with change	day n	nonth year ng items in the column)	1 Date of start: 2 (do not complet	day month te the remaining items ir	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 2 2	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT	* Yes 🗖	No 🚨	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec	duced / 5= Interrupted	3= Dose reduced / 4=	ently discontinued / 2= D Delayed and reduced / 5=	Interrupted
6. Corrective Treatment/Thera	Yes 🗖	No 📮	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		month year	1 Date: 4 Specify se	day month equelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI month year	2	: L day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTIO AND THE SAE COMPLEMENTAR' FORM	day month	year	⇒ IF YES	No ate event became se	year
PORM	Resulting in death	ration  ncapacity	Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anoma	ck below all criteria  ging hospitalization ant disability/incapacity aly/birth defect mportant event	0
Investigator's name, date of re	port and signature:	Monitoring repr	esentative's name,	date of receipt:	

XT 683 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Sul	XT 683
Follow-up 3	v 83 🗆	See Page 62
ADVERSE EVI	ENT FORM	0.1_AE_1
1. Adverse Event Diagnosis	AE form no: LJLJ-LJLJ AE ref. no: LJLJ-LJLJ	AE form no: LLL-LLL AE ref. no: LLL-LLL
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL	day month year
3. GRADE (1 - 4)	1	1 2 3 4 4
ACTION TAKEN WITH     STUDY TREATMENT*      ACTION TAKEN WITH     STUDY TREATMENT	Yes No One None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted One of the None of th	Yes No One None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted One on 1 One of 2 One of 3 One of 4 One of 5 One
6. Corrective Treatment/Therapy	Yes No 🗆	Yes No D
7. QUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered  5 = Fatal (complete the death report form)	1 Date: LL	day month year  4
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes  No  Service  Yes  No  Service  Yes  No  Service  Yes  Yes  Service  Yes  Yes  Service  Yes  Yes  Service  Yes  Yes  Yes  Yes  Yes  Yes  Yes  Y	Yes
Investigator's name, date of repo		presentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatm	ent?

XRP6258 EFC6193 XT 683

XRP6258 EFC6193				NO	174	
	Country No.	Centre No.	Subject No.		Page	
FOLLOW-UP 4	V 84		Date of visit:	aday /	month /	year
				See	Page 12	
	See Page 27	<mark>78</mark>				
FOLLOW-UP 4					O.FOLLOWUP	_2
<b>Subject condition</b> (tick "✓"	one box only	/):				
☐ Alive						
☐ Lost to follow-up						
☐ Dead (complete Death for	orm)					
·						
Progression						
Has the subject had disease	e progression?	? (tick "✓" one	box only)			
☐ Unknown						
☐ Previously reported pro	ogression					
□ No *	.0					
_						
☐ Yes **						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

NO 174 XRP6258 EFC6193

Confidential FINAL 21-NOV-2006 Sanofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject	No. NO	175 Page	
FOLLOW-UP 4	V 84	See Page 27	)		

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

	None		l Unknown
--	------	--	-----------

Drug/Regimen/Agent	START DATE	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			٥
4.			٥
5.			
6.			٥
7.			
8.			٥
9.			
10.			

				500	of: avootic
_	NO	175	1	XRP6258	EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 4	V 84	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	I Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

## \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 4 V 8		See Page 55

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ Not done

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L. L L. L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
8		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
9		□□ □□□ □□□□□ □ Not Done			
10	LJLJ.LJ	□□ □□□□□□□□□□□□ Not Done			
11	L_  L_  . L_  L_	□□□□□□□□□□□□□□□□ Not Done			
12	L_  L	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□ □□□□□ □ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 177 XRP6258 EFC6193

XRP6258 EFC6193				NO	178	
	Country No.	Centre No.	Subject No.		Page	
FOLLOW-UP 4	V 84	See P	age 53			

## **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
	Ш	
2.		LJLJ. LJLJ
3.		
4.		
5.		
6.		
7.		니니니.니니

NO 178 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Centre	No.   Subje	XT	684 0 1		
Follow-up 4	V 84		See Page 62			
ADVERSE EVI	ENT FORM			O.1_AE_1		
1. Adverse Event Diagnosis	AE form no: <b>[8][4]-</b> [ AE ref. no: <b>[]</b> ]-[		AE form r AE ref. no:	no:   <b>8  4 - 0  2</b>    _  -		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	1 Date of start: LLL LLL day mon 2 (do not complete the remaining	th year items in the column)		day month year e the remaining items in the column)		
3= Ongoing with change  3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 2 2	3 🔲 4 🖸		
4. RELATIONSHIP TO STUDY TREATMENT*  5. ACTION TAKEN WITH STUDY TREATMENT	Yes  0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and reduce  0		3= Dose reduced / 4= E	No		
6. CORRECTIVE TREATMENT/THERAPY 7. OUTCOME 1 = Recovered	1 ☐ 】 Date: ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐	No 🗖	<b>}</b>	No 🗖		
4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	4 ☐ Specify sequelae:  2 ☐  3 ☐  5 ☐ Date of death: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		2 🗆	quelae:		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event because of the Yes - Date event because of th	year	⇒ IF YES	No Late event became serious:  Lack Event became serious:  Lack Event became serious:  Lack Event became serious:  No Lack Event Became serious:		
	Resulting in death	on	Resulting in death			
Investigator's name, date of repo			esentative's name,	date of receipt:		
* Is there a reasonable  XT 684	possibility that the AE was caused	by study treatmer				

XRP6258 EFC6193	Country No.	Centre No.	Subje	ct No.	XT	684 Page	02
Follow-up 4	V 84			See Pa	ge 62		
ADVERSE EVI	ENT FOR	M				O.1_AE_1	
1. Adverse Event Diagnosis	AE form no AE ref. no:	: <b>(8)(4)-(0)(3</b>			AE form no: AE ref. no:	8 4 - 0 4	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 □ Date of start: □ 2 □ (do not complete t	day month the remaining items in	year	1	da	L L L L ay month e remaining items in	year
3. GRADE (1 - 4)	1 2 2	3 🗖	4 🔲	1 🔲	2 🗖	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No		Yes	, 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted			0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  0			
6. Corrective Treatment/Therapy	Yes 🗖	No		Yes	· •	No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering	Specify sequence 2 $\square$	JLJ LJLJL L day month uelae:	year	4 🗆 } s	da		year
3= Not recovered	3 □ 5 □ Date of death: □		11 11 11 1	3			
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: LL LLL LLL Gay month year			day month year			
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes			Yes			
Other medically important event							

XT 684 XRP6258 EFC6193

			ı		
XRP6258 EFC6193	Country No. Cen	ntre No. Subje	ct No.	684 Page	03
Follow-up 4	v 84		See Page 62		
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>8</b> 1 <b>4</b> AE ref. no: <b>1</b>	J- <b>0</b>	AE form n AE ref. no:	o: <b>8 4 - 0 6</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nonth year ng items in the column)	1 Date of start: L 2 (do not complete	day month the remaining items in	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 2 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 📮	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0  1  2  3	duced / 5= Interrupted	0= None / 1= Permanent 3= Dose reduced / 4= D 0	elayed and reduced / 5= I	
6. Corrective Treatment/Therapy	Yes 🗖	No 🚨	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		month year	<b>-</b> }	day month puelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2		2	day month	J L L L J
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes - Date event be - Date event be day month		Yes - Dat	No te event became ser	ious:
AND THE SAE COMPLEMENTARY FORM	- Tick below al  Resulting in death  Life-threatening  Requiring/prolonging hospitaliz  Persistent/significant disability/i  Congenital anomaly/birth defectory  Other medically important ever	Il criteria that apply:	- Tic Resulting in death Life-threatening Requiring/prolongin Persistent/significan Congenital anomal Other medically im	k below all criteria t ng hospitalization nt disability/incapacity y/birth defect	that apply:
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name, o	date of receipt:	
* Is there a reasonable	possibility that the AE was caus	l sed by study treatmer	nt?		

\_ EFC6193 XT 684 XRP6258

XRP6258 EFC6193	Country No. Centre	No. Subje	xT	684 Page	04
FOLLOW-UP 4	V 84   LL		See Page 62	2	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin		AE form AE ref. n	n no:   <b>8 4 - 0 8</b> o:    -	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: Lay month 2 (do not complete the remaining it	,	1  Date of start: 2  (do not comple	day month ete the remaining items	year
3. GRADE (1 - 4)	1	4 🗆	1 🗆 2 🗅	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 N	No 🗖	Yes 🗖	l No	٥
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 3= Dose reduced / 4= Delayed and reduce		3= Dose reduced / 4=	nently discontinued / 2=   = Delayed and reduced / 5 2	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖 N	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL day montl 4 Specify sequelae:		1 Date: 4 Specify s	day month	
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2		2	n:	UUU year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes ☐ N  - Date event becar    Jif Yes		⇒ IF YES { L	No Date event became s	erious:
FORM	- Tick below all cr Resulting in death	on	Resulting in deat Life-threatening Requiring/prolon Persistent/signific Congenital anom	Fick below all critering the second of the s	
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's name	, date of receipt:	
* Is there a reasonable	possibility that the AE was caused	by study treatmer	nt?		

XRP6258 | EFC6193 684

XRP6258 EFC6193	Country No. Cent	re No. Subje	ct No.	684 Page	05
Follow-up 4	V 84		See Page 62	]	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>8</b> 1 <b>4</b> 1  AE ref. no: <b>1</b>	-i <b>0</b>   <b>9</b>   -LLL	AE form AE ref. n	n no: [ <b>8</b> ] <b>4</b> ]-[ <b>1</b> ][ <b>0</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		onth year g items in the column)	<ul><li>1 □ Date of start:</li><li>2 □ (do not completed)</li><li>3 □</li></ul>	day month lete the remaining items i	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🗆	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗆	<b>N</b> o	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and reduced 0 1 2 3 3		3= Dose reduced / 4=	nently discontinued / 2= I = Delayed and reduced / 5	= Interrupted
6. Corrective Treatment/Therapy	Yes 📮	No 🗖	Yes 🗆	l No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering		onth year	1  Date: 4  Specify s	day month sequelae:	year
3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	3 □ 5 □ Date of death: □□□□□□ 6 □	onth year	3	h:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	year criteria that apply:	☐ IF YES	No Date event became so  LULLULL  day month  Fick below all criteria	year  a that apply:
Investigator's name, date of rep	Requiring/prolonging hospitaliza Persistent/significant disability/ir Congenital anomaly/birth defect Other medically important even	ation	Requiring/prolon Persistent/signific Congenital anon	ging hospitalization cant disability/incapacit naly/birth defect important event	y 🗆
* Is there a reasonable	possibility that the AE was cause	ed by study treatmer	nt?		

XRP6258 EFC6193	Country No. Centr	re No. Subje	Ct No.	684 Page	06
Follow-up 4	V 84		See Page 62	<u>!</u>	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin		AE form AE ref. no	no: [8][4]-[1][2 : []-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nth year g items in the column)	1 Date of start: 2 (do not complet	day month te the remaining items in	year
3. GRADE (1 - 4)	1 2 2 3 [	4 🗆	1 🔲 2 🖵	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and redu		3= Dose reduced / 4=	ntly discontinued $/$ 2= $\Box$ Delayed and reduced $/$ 5= $\Box$ 3 $\Box$ 4 $\Box$	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🚨	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		nnth year	1 Date: 4 Specify se	day month cquelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	JL LLL onth year	2	day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes ☐ - Date event bec  □ IF YES   - Date event bec □ □ □ □ □ □ □ □ day month - Tick below all	No  ame serious:	⇒ IF YES { ⊔	No ate event became so I	year
	Resulting in death				
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name,	date of receipt:	
* Is there a reasonable	possibility that the AE was cause	d by study treatmer	nt?		

XT 684 XRP6258 EFC6193

XRP6258 EFC6193 FOLLOW-UP 4	Country No. Centre No. Subjet	XT 684 Page  See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: LL-LL  AE ref. no: LL-LL	AE form no: LJLJ-LJLJ AE ref. no: LJLJ-LJLJ
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLLLL LLLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLL LLL LLL LLL LLL LLL LLL LLL L
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No No	Yes  No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No 🗖	Yes No No
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)	Date:	Date: LLL LLL LLL LLL LLL LLL LLL LLL LLL L
6= Unknown  8. SERIOUSNESS CRITERIA	Yes No C - Date event became serious:	Yes No C - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that apply:  Resulting in death Life-threatening Requiring/prolonging hospitalization Persistent/significant disability/incapacity Congenital anomaly/birth defect Other medically important event	Tick below all criteria that apply:  Resulting in death
Investigator's name, date of rep	ort and signature: Monitoring repr	resentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmen	nt?

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	179 Page	
FOLLOW-UP 5	V 85		Date of visit:	day See	month year Page 12	
	See Page 2	<mark>78</mark>				
FOLLOW-UP 5					O.FOLLOWUP_2	
<b>Subject condition</b> (tick "✓"	one box only	·):				
☐ Alive	•					
_						
Lost to follow-up						
☐ Dead (complete Death for	orm)					
Progression						
Has the subject had disease	e progression?	(tick " <b>√</b> " one	box only)			
☐ Unknown			·			
_						
☐ Previously reported pro	ogression					
■ No *						
☐ Yes **						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

NO 179 XRP6258 EFC6193

Confidential FINAL 21-May-2008 Sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 5	V 85	See Page 279

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

■ None		Unknown
--------	--	---------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			۵
2.			
3.			٥
4.			
5.			
6.			٥
7.			
8.			
9.			
10.			٥

NO 100	
NO 180 , XRP6258	EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 5	V 85	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	182 Page	
FOLLOW-UP 5	V 85	See F	Page 55			

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	L.I.I.I.I.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		∟∟∟ mm	
8		□□ □□□ □□□□□ □ Not Done			
9		□□□□□□□□□□□□□□□□ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done			
12	L. L. L.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 182 , XRP6258 , EFC6193

XRP6258 EFC6193				NO	183	
	Country No.	Centre No.	Subject No.		Page	,
FOLLOW-UP 5	V 85	See	Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
3.		
4		
5.		
7		

NO 183 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cent	re No. Subje	ct No.	685 Page	0[1
FOLLOW-UP 5  ADVERSE EVI	V 85 LL		See Page 6	0.1_AE_1	_
☐ NONE					
1. Adverse Event Diagnosis	AE form no: L8 L5 L AE ref. no: L1 L1	- <u>[0] [1]</u> 	AE for AE ref.	m no: [8]5]- <mark> 0] 2</mark> no: []-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change		onth year g items in the column)	1 Date of start: 2 (do not comp	day month colete the remaining items in	year
3= Ongoing with change  3. GRADE (1 - 4)	1 2 3		1 2 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 📮	No 🗖	Yes [	No	<u> </u>
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and reduced 0 \( \bigcup 1 \) \( \bigcup 2 \) \( \bigcup 3 \) \( \bigcup \)			anently discontinued / 2= De 4= Delayed and reduced / 5= 2  3  4	Interrupted
6. Corrective Treatment/Therapy	Yes 📮	No 🔲	Yes [	n <sub>o</sub>	
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered	Date: LL LL day m Specify sequelae: 2	onth year	1  Date: 4  Specify 2  3	LL LLL L day month sequelae:	year
5= Fatal (complete the death report form) 6= Unknown	5 🔲 Date of death: 📖 📖	oonth year		ith:     day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event bed day month - Tick below all	No	⇒ IF YES {	No Date event became ser                          day month   Tick below all criteria	JLJ LJ year
	Resulting in death Life-threatening Requiring/prolonging hospitalize Persistent/significant disability/ir Congenital anomaly/birth defect Other medically important even	ation	Life-threatening Requiring/prolo Persistent/signif Congenital ano	ath  gonging hospitalization  cicant disability/incapacity  maly/birth defect  y important event	•
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's nam	e, date of receipt:	
* Is there a reasonable XT 685	possibility that the AE was cause	ed by study treatmer		EFC6193	_

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 685 02
FOLLOW-UP 5	V 85	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \( \begin{align*} \begin{align*} \begin{align*} \	AE form no: [8]5]-[0]4] AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3 \( \begin{align*}     &  \text{ \ \text{ \  \text{ \text{ \text{ \text{ \text{ \text{ \text{ \text{ \text{	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT*	1	1
5. ACTION TAKEN WITH STUDY TREATMENT	Yes	Yes
6. Corrective Treatment/Therapy	Yes No No	Yes No 🗆
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: ULL ULL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No C  - Date event became serious:    If Yes	Yes  No  No  Pare Property  No
Investigator's name, date of repo	Life-threatening	Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event  resentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?

XRP6258 EFC6193 XT 685

XRP6258 EFC6193	Country No.   Centre No.   Subjection	XT 685 03
FOLLOW-UP 5	v 85	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin	AE form no: \[ \begin{align*} \begin
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL	1 Date of start: Law Manner Law
3. GRADE (1 - 4)	1 2 3 4 4	1 🗆 2 🗔 3 🗔 4 🗔
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No 🗖	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLL LLL year 4 Specify sequelae:	1 Date: LL LLL year 4 Specify sequelae:

2 2 2= Recovering 3 3 🔲 3= Not recovered 5 Date of death: 5 **D** Date of death: \_\_\_\_ \_\_\_\_ 5= Fatal (complete the death report form) 6 🔲 6 🔲 6= Unknown No 8. SERIOUSNESS CRITERIA - Date event became serious: - Date event became serious: day month year day month year IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM - Tick below all criteria that apply: - Tick below all criteria that apply: Resulting in death . . . . . . . . . . . . .  $\Box$ Life-threatening . . . . .  $\Box$ Life-threatening ..... Requiring/prolonging hospitalization . . . . . . Requiring/prolonging hospitalization . . . . Persistent/significant disability/incapacity . .  $\Box$ Persistent/significant disability/incapacity . . . Congenital anomaly/birth defect . . . . . . . . . Congenital anomaly/birth defect . . . . . . . Other medically important event  $\dots$ Other medically important event ..... Investigator's name, date of report and signature: Monitoring representative's name, date of receipt: \* Is there a reasonable possibility that the AE was caused by study treatment?

XT EFC6193 685 XRP6258

XRP6258			] хт	685	04
FOLLOW-UP 5	V 85	tre No. Subje	See Page 62	Page	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1.  Adverse Event Diagnosis	AE form no: \( \begin{array}{c ccc} & & \left & \\ & & & \end{array} \)  AE ref. no: \( \begin{array}{c ccc} & & & & & & & & \\ & & & & & & & & & &	- <mark> 0  7</mark>  -	AE form AE ref. no	no: <b>[8][5]- 0][8</b> o: []-[]	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		nonth year ng items in the column)	1 Date of start: 2 (do not complet) 3	day month te the remaining items i	year
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 2 2	3 🗖	4 🗖
Action Taken with Study Treatment	Yes   0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec  0	luced / 5= Interrupted	3= Dose reduced / 4=	No  ently discontinued / 2= E Delayed and reduced / 5=  3	= Interrupted
6. Corrective Treatment/Therapy	Yes 📮	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		nonth year	Date: 4 Specify se	LLL LLLL L day month equelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI ponth year	2	:	_   year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	year  I criteria that apply:	TIF YES   Resulting in death	No ate event became so ILI LILI LIL lay month ick below all criteria	year  that apply:
Investigator's name, date of repo	Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec Other medically important ever	ation	Requiring/prolong Persistent/significa Congenital anoma	ging hospitalization ant disability/incapacit aly/birth defect mportant event	🗆 y 🗅
* Is there a reasonable	possibility that the AE was caus	ed by study treatmer	nt?		

XT 685 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 685 05
FOLLOW-UP 5	V 85	See Page 62
ADVERSE EVE	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE ref. no: LU-LU	AE form no:   <b>8</b>   <b>5</b>  - <b>1</b>   <b>0</b>    AE ref. no:   -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL LLL year 2 (do not complete the remaining items in the column) 3 D	1 Date of start: LL LLL LLL LLL LLL LLL LLL LLL LLL LL
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4 🔲	1 2 3 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes  No	Yes No 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes  No	Yes No D
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: LIL LILL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown  8. SERIOUSNESS	2	2
CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	- Date event became serious:    U	→ IF YES   - Date event became serious:    □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
	Resulting in death	Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt:

XT 685 | XRP6258 | EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 685 06
FOLLOW-UP 5	V 85	See Page 62
ADVERSE EVE	INT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: [8][5]-[1][1] AE ref. no: []-[]-	AE form no:  8 5 - 1 2  AE ref. no:
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3 D	1 Date of start: L L L L L L L L L L L L L L L L L L L
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4 🔲	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No C
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No C	Yes No O
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: Lill Lill year 4 D Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA	Yes	Yes
If yes, complete this section and the SAE complementary form	Tick below all criteria that apply:  Resulting in death	Tick below all criteria that apply:  Resulting in death
Investigator's name, date of repo	rt and signature.   Monitoring ren	resentative's name, date of receipt:

XT 685 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	184 Page
FOLLOW-UP 6	V 86		Date of visit:	day /	month year
					See Page 12
	See Page	<b>278</b>			
FOLLOW-UP 6					O.FOLLOWUP_2
Subject condition (tick "✓"	one box only	·):			
☐ Alive					
☐ Lost to follow-up					
☐ Dead (complete Death fo	orm)				
Progression					
Has the subject had disease	e progression?	(tick "✔" one	box only)		
☐ Unknown					
☐ Previously reported pro	gression				
■ No *					
☐ Yes **					

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

NO 184 XRP6258 EFC6193

Confidential FINAL 21-May-2008 Sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 6	V 86	See Page 279

## POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

☐ NONE	☐ Unknown
--------	-----------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			٥
4.			٥
5.			
6.			٥
7.			
8.			٥
9.			
10.			

NO 185 , XRP6258 , EFC6193					of: avootic
	NO	185	ı	XRP6258	EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 6	V 86	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 186 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	187 Page	
FOLLOW-UP 6	V 86	See	Page 55			

### **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	L.I.I.I.I.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		∟∟∟ mm	
8		□□ □□□ □□□□□ □ Not Done			
9		□□□□□□□□□□□□□□□□ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done			
12	L. L. L.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 187 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	188 Page	
FOLLOW-UP 6	V 86		Page 53		. age	

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
3.		
4		
5.		
7		

NO 188 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	XT	686 0	1
Follow-up 6	v 86   [		See Page 62		
ADVERSE EV	ENT FORM			O.1_AE_1	
☐ NONE					
1.	AE form no: <b>86</b>	-0 1	AE form	no: 8 6 -0 2	_
Adverse Event Diagnosis	AE ref. no:	J-L.L.	AE ref. n	0:    -	
2. STATUS OF AE	1 Date of start:	nonth year	1 Date of start:	day month year	Ш
2= Ongoing from previous period without change	2 (do not complete the remaining	0	- '	ete the remaining items in the colum	
3= Ongoing with change	3 ☐ If grade changes, date of change: ☐ ☐ ☐ ☐	nonth year	3 If grade changes date of change	5, :	Ш
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖵	3 🗖 4 🗔	<u> </u>
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🚨	Yes 🗖	No 🚨	
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red			ently discontinued / 2= Delayed Delayed and reduced / 5= Interrupted	
STUDY TREATMENT	0 0 1 0 2 0 3 0	4 🗖 5 🗖	0 1 1 2	2 🔲 3 🔲 4 🔲 5	_
6. Corrective Treatment/Therapy	Yes 🔲	No 🗖	Yes 🗖	No 🗖	
7. OUTCOME 1= Recovered	1 <b>□ )</b> Date: □□□	nonth year	1 <b>D</b> Date:	day month year	Ш
4= Recovered with sequelae	4 🗖 🕈 Specify sequelae:		4 🗖 🕽 Specify s	day month year equelae:	
2= Recovering	2 🗖		2 🗖		_
3= Not recovered	3 🗖		3 🗖		
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: LL L	nonth year	5 Date of death	n:	Ш
8. SERIOUSNESS	Yes 🗖	No 🗖	Yes 🗖	No 🗖	_
CRITERIA	- Date event be	came serious:		Date event became serious:	
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	☐ IF YES	,	⇒ IF YES	day month year	
FORM	- Tick below al	I criteria that apply:	<b>\</b> -T	ick below all criteria that appl	ly:
	Resulting in death Life-threatening		Resulting in death		
	Requiring/prolonging hospitaliz		Requiring/prolonging hospitalization		
	Persistent/significant disability/i		Persistent/significant disability/incapacity		
	Congenital anomaly/birth defection Other medically important ever			aly/birth defect	
Investigator's name, date of rep	J		esentative's name		
* Is there a reasonable	possibility that the AE was caus	ed by study treatmer	nt?		_
	The state of the s	, ,		F00400	
XT 686		XRP62	00   E	FC6193	

XRP6258 EFC6193	Country No. Cer	ntre No.   Subje	T XT	686 Page	02
Follow-up 6	v 86		See Page 62	_	
ADVERSE EVE	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>8</b> 1 <b>6</b> AE ref. no: <b>1</b>	- <mark> 0  3</mark>    -	AE form AE ref. no	no: [ <b>8][6]-[0][4</b> : [][-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		month year ng items in the column)	1 Date of start: 2 (do not complet) 3	day month le the remaining items i	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖵	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🚨	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0 1 1 2 3 3	duced / 5= Interrupted	3= Dose reduced / 4=	ently discontinued / 2= IDelayed and reduced / 5:	= Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 🔲	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		Month year	1 Date: 4 Specify se	day month	year
2= Recovering	2 🗖		2 🗖		
3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	3 ☐ 5 ☐ Date of death: ☐ ☐ ☐ ☐ ☐ ☐	month year	3 ☐ 5 ☐ Date of death: 6 ☐	day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes - Date event be	No 🗖 ecame serious:	Yes ☐  F Yes   IF Yes    □	No ate event became s	erious:
AND THE SAE COMPLEMENTARY FORM	day month	l criteria that apply:	d	ck below all criteria	year a that apply:
Resulting in death			ing hospitalization ant disability/incapacit aly/birth defect	<b></b> y <b></b>	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name,	date of receipt:	

XT 686 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	ct No.	686 Page	03
FOLLOW-UP 6	V 86		See Page 62		
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>86</b> AE ref. no: <b>6</b>	- <mark> 0  5</mark>  - _	AE form AE ref. no.	no: 86-06	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		nonth year ng items in the column)	1 Date of start: 2 (do not complet) 3	day month e the remaining items ir	year
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 🔲 2 🗖	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 📮	No 🚨	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0	luced / 5= Interrupted  4	3= Dose reduced / 4= I 0	ntly discontinued / 2= D Delayed and reduced / 5=  3 4	Interrupted 5
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🗖	Yes 🗖	No	
1= Recovered 4= Recovered with sequelae		month year	1 Date: 4 Specify se	day month quelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2 □ 3 □ 5 □ Date of death: □□□□ day  6 □	LLL LLLLL month year	2	day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes - Date event be		⇒ IF YES	No ate event became se	erious:
FORM	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec Other medically important ever	ration	Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anoma Other medically ir	ing hospitalization  Int disability/incapacity  Ity/birth defect  Inportant event	0
Investigator's name, date of report states of report states a reasonable states a reas	ore and signature:  possibility that the AE was caus		esentative's name,	uale of receipt:	

XT 686 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cent	tre No.   Subje	XT	686 Page	04
FOLLOW-UP 6	V 86		See Page 6	2	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>8 6</b> AE ref. no:	- <mark> 0</mark>   7   -	AE form	n no:   <b>8 6 - 0 8</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nonth year ng items in the column)	1 Date of start: 2 (do not comple	day month lete the remaining items in	year
3. GRADE (1 - 4)		<u> </u>	1 2 2		4 🗖
ACTION TAKEN WITH     STUDY TREATMENT*  5. ACTION TAKEN WITH     STUDY TREATMENT	Yes	luced / 5= Interrupted	3= Dose reduced / 4=	nently discontinued / 2= E = Delayed and reduced / 5= 2  3  4  4	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	l No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae		nonth year	1 Date: 4 Specify s	day month sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILILI month year	2	h:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event be  IF YES - Date event be  Lilian India  day month  - Tick below all		⇒ IF YES	No  Date event became so  LL LL LL  day month  Tick below all criteria	year
	Life-threatening			th	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name	, date of receipt:	

EFC6193 XT 686 XRP6258

XRP6258 EFC6193	Country No. Centre No.	Subje	T XT	686 Page	05
FOLLOW-UP 6	V 86		See Page 62	2	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \( \begin{align*} \begin		AE form AE ref. n	n no:   <b>8 6 - 1  0</b> o:    -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL	year	<ul><li>1 □ Date of start:</li><li>2 □ (do not completed)</li><li>3 □</li></ul>	day month ete the remaining items	year
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲	4 🔲	1 2 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🕻	נ	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
6. Corrective Treatment/Therapy	Yes 🔲 No 🕻	]	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL LL Ay month  4 Specify sequelae:	year	1 Date: 4 Specify s	day month	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	year	2	n:	<b>UUU</b> year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes ONO ONO ONO ONO ONO ONO ONO ONO ONO ON	is:	⇒ IF YES	No Date event became s III IIII III day month Fick below all criteri	year
	Resulting in death Life-threatening Requiring/prolonging hospitalization Persistent/significant disability/incapacity Congenital anomaly/birth defect Other medically important event	Life-threatening . Requiring/prolon Persistent/signific Congenital anom	h ging hospitalization ant disability/incapaci naly/birth defect important event	iy 🗆	
Investigator's name, date of repo	ort and signature: Monitor	ring repr	esentative's name	, date of receipt:	
* Is there a reasonable	possibility that the AE was caused by study	treatmen	nt?		

XT 686 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Cent	tre No. Subje	Ct No.	686 Page	0[6
FOLLOW-UP 6	V 86		See Page 62	!	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>8 6</b> AE ref. no:	-[1][1]	AE form AE ref. no:	no:  8 6 - 1 2 :   - -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		g items in the column)	1  Date of start: 2  (do not complet) 3	day month e the remaining items in	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🔲	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No	٥
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and red		3= Dose reduced / 4= [	ntly discontinued / 2= D Delayed and reduced / 5=	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		nonth year		LLL LLLL L day month quelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	DI IIII	2	LILI LILI L day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	No	⇒ IF YES	No ate event became se  month ck below all criteria	year
	Resulting in death			ing hospitalization nt disability/incapacity ly/birth defect	
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's name,	date of receipt:	
* Is there a reasonable	possibility that the AE was cause	ed by study treatmer	nt?		

XT 686 , XRP6258 , EFC6193

XRP6258 EFC6193				NO	189	
	Country No.	Centre No.	Subject No.	1	Page	
FOLLOW-UP 7	V 87		Date of visit:	aday / [	month / [	year
		-	-	Se	ee Page 12	
	See Page 278	8				
FOLLOW-UP 7		_			O.FOLLOWUP_	2
Subject condition (tick "v	one box only	y):				
☐ Alive						
_						
Lost to follow-up						
☐ Dead (complete Death	form)					
, p	- ,					
Progression						
Has the subject had disea	se progression?	? (tick "✔" one	box only)			
☐ Unknown						
☐ Previously reported p	rogression					
□ No *						
☐ Yes **						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

 NO
 189
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-May-2008
 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.	NO 190
FOLLOW-UP 7	V 87	See Page 279	<u> </u>

## POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

Ц	None		Unknown
---	------	--	---------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			۵
2.			
3.			٥
4.			
5.			
6.			٥
7.			
8.			
9.			
10.			٥

NO	190		XRP6258	EFC6193
Confide	ontial ■ FINIAL ■	■ 21 May 2008	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 7	V 87	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 191 , XRP6258 , EFC6193

Location:					
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	I Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	192 Page	
FOLLOW-UP 7	V 87	See	Page 55			

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L. L L. L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
7		□□□□□□□□□□□□□□□□ Not Done			
8		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
9		□□ □□□ □□□□□ □ Not Done			
10	LJLJ.LJ	□□ □□□□□□□□□□□□ Not Done			
11	L_  L_  . L_  L_	□□□□□□□□□□□□□□□□ Not Done			
12	L_  L	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□ □□□□□ □ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 192 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	193 Page	
FOLLOW-UP 7	V 87	Se	e Page 53	1	3.	

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
		لــالــا . لــالــا
3.		
4		
5.		
6.		
7.		

NO 193 XRP6258 EFC6193

XRP6258 EFC6193		tre No. Subje	t No.	687 Page	01
ADVERSE EVI	V 87 L		See Page 6	0.1_AE_1	_
1. Adverse Event Diagnosis	AE form no: <b>8 7</b> AE ref. no:	-i <mark>0   1  </mark>   _	AE fo	orm no: [8][7]-[0][2 f. no:	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		•		day month  nplete the remaining items in  nges,  nge day month	year n the column)
3. GRADE (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT*		0 4 0		3	4 🗆
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0  1  2  3	d / 2= Delayed	0= None / 1= Perm	manently discontinued / 2= E 4= Delayed and reduced / 5= 2  3  4	Pelayed = Interrupted
<ul><li>6. CORRECTIVE TREATMENT/THERAPY</li><li>7. OUTCOME</li><li>1 = Recovered</li><li>4 = Recovered with sequelae</li></ul>	Yes  Date:	No U	1 <b> )</b> Date:	No Light Light Light Month  y sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	nonth year	2	eath:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event be The Yes - Date event be Aday month Tick below all	No	⇒ IF YES	No - Date event became se	year
Resulting in death			Resulting in death		
Investigator's name, date of repo			L	me, date of receipt:	
* Is there a reasonable XT 687	possibility that the AE was caus	ed by study treatmer		EFC6193	_

XRP6258			
EFC6193	Country No. Centre No. Subje	XT 687   0 2  ect No.   Page	
Follow-up 7	V 87	See Page 62	
ADVERSE EV	ENT FORM	O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin	AE form no: <b>[8]</b> [ <b>7]</b> - <b>[0]</b> [ <b>4</b> ]  AE ref. no: <b>[]</b>	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: L L L L L L L L L L L L L L L L L L L	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	
3. GRADE (1 - 4)	1	1	
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗆	Yes 🔲 No 🗖	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
6. CORRECTIVE TREATMENT/THERAPY	Yes  No	Yes 🗖 No 🗖	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date:	Date:	
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes	
Investigator's name, date of rep		esentative's name, date of receipt:	
* Is there a reasonable	possibility that the AE was caused by study treatment	nt?	

XT 687 XRP6258 EFC6193

XRP6258 EFC6193  FOLLOW-UP 7  ADVERSE EVI	Country No. Centre No. Subject V 87	XT 687 03 ct No. Page  See Page 62  0.1_AE_1
1. Adverse Event	AE form no: <b>\8\7-\0\5</b> AE ref. no: <b>\\-\-\</b>	AE form no: \[ \begin{align*} \begin
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: Lay month year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes  No	Yes 🔲 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes No 🗖	Yes No 🗖
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date:	1 Date: day month year 4 Specify sequelae:
8. SERIOUSNESS	Yes No D	Yes No 🗆
CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	- Date event became serious:  - Date event became serious:  - Tick below all criteria that apply:  Resulting in death	- Date event became serious:  - Date event became serious:  - Tick below all criteria that apply:  Resulting in death
Investigator's name, date of repo	Other medically important event	Other medically important event

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 687 XRP6258 EFC6193

XRP6258 EFC6193			][ хт	687	04
	Country No. Centr	e No. Subje	ect No.	Page	
FOLLOW-UP 7	V 8 7   LL		See Page 6	2	
<b>ADVERSE EV</b>	ENT FORM			O.1_AE_1	
1.	AE form no: <b>8 7</b> -	. <u>0 [7]</u>	AE form	no: <b>8 7 -0 8</b>	]
Adverse Event	AE ref. no:		AE ref. no		
Diagnosis					
2. STATUS OF AE			1 Date of start:		
1= New	day mo 2  (do not complete the remaining	g items in the column)	2 🔲 (do not comple	day month ete the remaining items ir	year n the column)
2= Ongoing from previous period without change	3 🗖		3 🗖	v	
3= Ongoing with change	_		_		
3. GRADE (1 - 4)	1 2 3 3	4 🗆	1 2 2	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and redu			ently discontinued / 2= D Delayed and reduced / 5=	
STUDY TREATMENT	0 0 1 0 2 0 3 0	4 🔲 5 🔲	0 1 2	3 4	5 🗖
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🚨	Yes 🗖	No	
7. OUTCOME 1= Recovered	1 <b>☐                                   </b>		1 <b>D</b> Date:		
4= Recovered with sequelae	4 Specify sequelae:	onth year	4 D Specify so	day month equelae:	year
2= Recovering 3= Not recovered	2 🗖		3 🗖		
5= Fatal (complete the death report form)	5 🔲 Date of death: 📖 📖				
6= Unknown	6 🗖	onth year	6 🗖	day month	year
8. SERIOUSNESS	Yes 📮	No 🔲	Yes 🗖	No	
CRITERIA	- Date event bec	ame serious:		ate event became se	
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	IF YES   day month	year		day month	
FORM		criteria that apply:		ick below all criteria	_ ' '
	Resulting in death		1		
	Requiring/prolonging hospitaliza		ging hospitalization		
	Persistent/significant disability/in	Persistent/significant disability/incapacity			
	Congenital anomaly/birth defect Other medically important event	_ ~	aly/birth defect important event		
Investigator's name, date of repo	J		esentative's name		· · · · <b>-</b>
investigator's name, date of repo	on and signature.	Monitoring repr	cocmative s name,	, date of receipt.	
* Is there a reasonable	possibility that the AE was cause	d by study treatmer	nt?		

XT 687 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No.   Subje	XT	687 Page	0[5
Follow-up 7	V 87		See Page 62		
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \( \begin{array}{c c} 8 \cdot 7 \\ AE ref. no: \cdot \	j- <mark>0  9  </mark> J	AE form AE ref. no	no: [8][7]-[1][0 : []-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nonth year ng items in the column)	_	day month e the remaining items in	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 2 2	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 📮	No 🛚	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec 0   1   2   3	duced / 5= Interrupted	3= Dose reduced / 4= I	ntly discontinued / 2= De Delayed and reduced / 5=	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🚨	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		month year	- }	day month cquelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI month year	2	LILI LILI L day month	year
8. SERIOUSNESS CRITERIA	Yes ☐ - Date event be	No 🗖 ecame serious:		No ate event became ser	rious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	day month	year  I criteria that apply:	- Ti Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anoma	ay month ck below all criteria ing hospitalization int disability/incapacity ily/birth defect	0
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name,	date of receipt:	
* Is there a reasonable	possibility that the AE was caus	 sed by study treatmer	nt?		

XRP6258 EFC6193 XT 687 sanofi aventis

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 687 06
FOLLOW-UP 7	V 87	See Page 62
ADVERSE EVE	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: <b>[8] [7]</b> - <b>[1] [1]</b> AE ref. no: <b>[]</b> - <b>[]</b> - <b>[]</b>	AE form no:   <b>8</b>   <b>7</b>  - <b>1</b>   <b>2</b>    AE ref. no:   -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL LLL LLL LLL LLL LLL LLL LLL LLL LL
3. GRADE (1 - 4)	1	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes  No	Yes No U
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes O No O - Date event became serious:	Yes O No O - Date event became serious:
AND THE SAE COMPLEMENTARY FORM	day month year  - Tick below all criteria that apply:  Resulting in death	day month year  - Tick below all criteria that apply:  Resulting in death
1+:+/a mamaa data of rong	ort and signature: Monitoring repr	esentative's name, date of receipt:

XRP6258 EFC6193	O O O O		Ochica t Na	NO	194	
	Country No.	Centre No.	Subject No.		Page	$\overline{}$
FOLLOW-UP 8	V 88		Date of visit:	LLL / L	month year	
		•		Se	ee Page 12	
	See Page 27	78				
FOLLOW-UP 8					O.FOLLOWUP_2	
Subject condition (tick "✓"	one box only	<i>י</i> ):				
☐ Alive						
☐ Lost to follow-up						
☐ Dead (complete Death f	orm)					
Progression						
Has the subject had disease	e progression?	' (tick "✔" one	box only)			
☐ Unknown						
☐ Previously reported pro	ogression					
□ No *						
☐ Yes **						

- If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- If YES, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

XRP6258 NO 194 EFC6193 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page
Follow-up 8	V 88	See Page 279

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

■ None	■ Unknown
--------	-----------

Drug/Regimen/Agent	START DATE	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			
2.			
3.			
4.			
5.			۵
6.			٥
7.			
8.			٥
9.			
10.			۰

NO	195		XRP6258	EFC6193
Confid	ontial = EINIAL =	L 21 May 2009	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page	
Follow-up 8	V 88	See Page 26	

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 196 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	I Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	197 Page	
FOLLOW-UP 8	V 88	See F	Page 55			

## **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LILI.LILI	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		∟∟∟ mm	
8		□□ □□□ □□□□□ □ Not Done			
9		□□□□□□□□□□□□□□□□ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done			
12	L. L. L.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 197 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	198 Page	
FOLLOW-UP 8	V 88	See I	Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
3.		
4		
5.		
7.		

NO 198 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	Ct No.	688 01
Follow-up 8	V 88 [		See Page 62	2
ADVERSE EV	ENT FORM			O.1_AE_1
☐ NONE				
1. Adverse Event Diagnosis	AE form no: <b>\8\\8</b> AE ref. no: <b>\\$\</b>	-  <mark>0  1</mark>  -	AE form AE ref. no	no: [ <b>8</b> ] <b>8</b> ]-[ <b>0</b> ][ <b>2</b> ] o: []-[]
2. STATUS OF AE	1 Date of start:		1 Date of start:	day month year
2= Ongoing from previous period without change	2 (do not complete the remaining a lift grade changes, date of change			te the remaining items in the column)
3= Ongoing with change  3. GRADE (1 - 4)		nonth year 4	date of change	day month year
4. RELATIONSHIP TO STUDY TREATMENT*	Yes $\square$	No D	Yes 🖸	No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec 0		3= Dose reduced / 4=	ently discontinued / 2= Delayed Delayed and reduced / 5= Interrupted
6. Corrective Treatment/Therapy	Yes 🚨	No 🗖	Yes 🗖	No 🗖
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL Lday r 4 Specify sequelae:	nonth year	1 Date: 4 Specify se	day month year equelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LL LLLLI	2	day month year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes - Date event be			No late event became serious:
FORM	l '	criteria that apply:	- Ti Resulting in death Life-threatening . Requiring/prolong Persistent/significa Congenital anoma	ick below all criteria that apply:
Investigator's name, date of rep	J		L esentative's name,	
	possibility that the AE was caus	, ,		
XT 688	1	XRP62	58 <sub> </sub> El	FC6193

XRP6258 EFC6193	Country No.   Centre No.   Subj	XT 688 02
FOLLOW-UP 8	V 88	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \[ \bar{8} \bar{8} - \bar{0} \] \[ 3 \]  AE ref. no: \[ \bar{1} \bar{1} - \bar{1} \bar{1} \]	AE form no: [8][8]-[0][4]  AE ref. no: []-[]-
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes  No	Yes • No •
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAP	Yes No 🗆	Yes No No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes ONO ONE OF THE PROOF OF THE	Yes ONO ONE OF THE PROOF OF THE
	Resulting in death	Resulting in death
Investigator's name, date of rep	port and signature: Monitoring ren	resentative's name, date of receipt:

XT 688 XRP6258 EFC6193

		1	1		
XRP6258 EFC6193	Country No.   Cen	tre No. I Subje	Tot No.	688 Page	03
Follow-up 8	V 88		See Page 62		
ADVERSE EVI	ENT FORM			0.1_AE_1	
1.  Adverse Event Diagnosis	AE form no: <b>88</b>	- <mark> 0</mark>   5   - _	AE form AE ref. no	no: <b>8 8 - 0 6</b>	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		nonth year ng items in the column)	1 Date of start: 2 (do not completed) 3	day month te the remaining items in	year
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 🔲 2 🔲	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 📮	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec	luced / 5= Interrupted  4	3= Dose reduced / 4= 0	ently discontinued / 2= D Delayed and reduced / 5=	Interrupted 5
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🗖	Yes 🗖	No	
1= Recovered 4= Recovered with sequelae		nonth year	1 Date: 4 Specify se	day month equelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2 □ 3 □ 5 □ Date of death: □□□□ day	UUUUU	2	:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes - Date event be - Date worth be day month	No	⇒ IF YES { ∟	No ate event became se	erious:
FORM	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec Other medically important ever	ation	Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anoma Other medically i	ck below all criteria ging hospitalization ant disability/incapacity aly/birth defect mportant event	
Investigator's name, date of report street in the street and street areasonable	ort and signature:  possibility that the AE was caus		esentative's name,	uate of receipt:	

XT 688 | XRP6258 | EFC6193

XRP6258 EFC6193 FOLLOW-UP 8	Country No. Centre No.	Subjec	XT t No.   See Page 6	688 Page	04
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin		AE form AE ref. no	no: [8][8]-[0][8	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL Lday month y 2 (do not complete the remaining items in the of	ear	1 Date of start: 2 (do not completed) 3	day month te the remaining items in	year
3. GRADE (1 - 4)	1 2 3 3	4 🔲	1 🔲 2 🖸	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖		Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interm 0		3= Dose reduced / 4=	ently discontinued $/$ 2= $\square$ Delayed and reduced $/$ 5= $\square$ 3 $\square$ 4 $\square$	Interrupted
6. Corrective Treatment/Therapy	Yes No 🗆		Yes 🗖	No	٥
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1  Date: LL LL LL LL day month y  4  Specify sequelae:	/ear	Date: 4  Specify se	day month equelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown		JLJLJ year	2	: LLL LLLL   day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes ONO ONO ONO ONO ONO ONO ONO ONO ONO ON	apply:	⇒ IF YES {	No late event became se lill lill lill lay month lick below all criteria	year that apply:
Investigator's name, date of rep	Life-threatening Requiring/prolonging hospitalization Persistent/significant disability/incapacity Congenital anomaly/birth defect Other medically important event		Life-threatening . Requiring/prolong Persistent/significa Congenital anom.	ging hospitalization ant disability/incapacity aly/birth defect mportant event	
investigator's name, date of rep	ort and signature.	ng repre	semanve s name,	uate of receipt:	

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 688 | XRP6258 | EFC6193

XRP6258 EFC6193	Country No. Centre No.	Subject No.   Page   D 5
FOLLOW-UP 8	V 88	See Page 62
ADVERSE E\	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \[ \bar{8} \cdot \bar{8} \cdot \bar{9} \cdot \]  AE ref. no: \[ \bar{1} \cdot	AE form no: [8]8-[1]0 AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without char 3= Ongoing with change	2 \(\int \) (do not complete the remaining items in the	ar day month year
3. GRADE (1 - 4)	1	4 🔲 1 🖸 2 🔲 3 🖫 4 🔲
4. RELATIONSHIP TO STUDY TREATMENT	* Yes 🗖 No 🗖	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interm 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 5
6. CORRECTIVE TREATMENT/THERA	Yes No 🗆	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1  Date: LL LL LL LL Aday month y  Specify sequelae:	ear day month year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTIO AND THE SAE COMPLEMENTAR	day month year	☐ IF YES
FORM	- Tick below all criteria that  Resulting in death	Resulting in death
Investigator's name, date of re	port and signature: Monitori	ng representative's name, date of receipt:

XT 688 | XRP6258 | EFC6193

XRP6258 EFC6193 FOLLOW-UP 8	Country No. Centre No. Subje	XT 688 06 Page  See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: [8] 8]-[1] 1  AE ref. no: []-[]	AE form no:   <b>8</b>   <b>8</b>  -  <b>1</b>   <b>2</b>    AE ref. no:       -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL
3. GRADE (1 - 4)	1 2 3 4	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🖫	Yes 🗆 No 🖵
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖 No 🗖	Yes 🗖 No 🗖
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae 2 = Recovering	1 Date: U U U Vear 4 Specify sequelae: 2	Date: LL LLL year  A Date: Specify sequelae:
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	5 Date of death:	5 Date of death: U UUU Uuu
6= Unknown	6 0	6 0
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes Onto No Onto Test Section 1. No Onto Test Section 2. No Onto Test Section	Yes  No  No  To Date event became serious:  IF YES
Investigator's name, date of repo	Congenital anomaly/birth defect	Congenital anomaly/birth defect

EFC6193 688 XRP6258 XT

XRP6258 EFC6193		On the second	Outries 1 No.	NO	199	
Follow-up 9	V 89	Centre No.	Subject No.  Date of visit:		Page /	
				day	month See Page 12	year
	See Page 278	<u> </u>				
FOLLOW-UP 9					O.FOLLOWUP_2	•
<b>Subject condition</b> (tick "✓"	one box only	):				
☐ Alive						
☐ Lost to follow-up						
☐ Dead (complete Death fo	orm)					
Progression						
Has the subject had disease	e progression?	(tick "✔" one	box only)			
☐ Unknown			·			
_	ograssion					
Previously reported pro	gression					
No *						
☐ Yes **						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

 NO
 199
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-May-2008
 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 9	V 89	See Page 279

## POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

■ None		Unknown
--------	--	---------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			۵
4.			
5.			٥
6.			۰
7.			
8.			۵
9.			
10.			

NO	200	XRP6258	EFC6193
Confide	ontial ■ FINIAL ■ 21 May 2008	san	ofi aventis

XRP6258 EFC6193	Country No.	NO 201  Centre No.   Subject No.   Page
FOLLOW-UP 9	V 89	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	I Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	202 Page	
FOLLOW-UP 9	V 89	See Page 55		. age	

## **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
3	LILI.LILI	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4	L.I.I.I.I.I	□□ □□□ □□□□□ □ Not Done			
5	L.L.L	□ Not Done			
6		□ Not Done			
7		□□□□□□□□□□□□□□□□ Not Done			
8		□□□□□□□□□□□□□□□□ Not Done			
9		□□ □□□ □□□□□ □ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done			
11	L_  L_	□□□□□□□□□□□□□□□□ Not Done			
12	L.L.	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□ □□□□□ □ Not Done			
14		□ Not Done			

NO 202 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	203 Page	
FOLLOW-UP 9	V 89	See	Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1	Ш	
		لــالــا . لــالــا
3.		
4.		
5.		
6.		
7.		

NO 203 | XRP6258 | EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	oct No.	689 Page	01
Follow-up 9	v 89		See Page 62		
ADVERSE EV	ENT FORM			0.1_AE_1	
☐ NONE					
1. Adverse Event Diagnosis	AE form no: [8] 9 AE ref. no: []	j-[ <b>0</b> ][ <b>1</b> ] 	AE form	no:   <b>8 9 -0 2</b> o:   -	
2. STATUS OF AE	· _	nonth year	1  Date of start:	day month	,
2= Ongoing from previous period without change 3= Ongoing with change	3  If grade changes, date of change:			ete the remaining items in	
3. GRADE (1 - 4)		4 🗆	1 🗆 2 🖵	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🚨	No 🗖	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec	luced / 5= Interrupted	3= Dose reduced / 4=	ently discontinued / 2= D Delayed and reduced / 5= 2	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL L day r Specify sequelae:	nonth year	1 Date: 4 Specify s	day month equelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	UU UUUU	2	n:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes ☐ - Date event be   □   □   □   □   □   □   □   □   □   □			No Date event became se	
FORM	- Tick below al  Resulting in death	tation	Resulting in deat Life-threatening . Requiring/prolon Persistent/signific Congenital anom	ick below all criteria  h ging hospitalization ant disability/incapacity aly/birth defect important event	0
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's name	, date of receipt:	
* Is there a reasonable	possibility that the AE was caus	ed by study treatmer	nt?		

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 689 02
FOLLOW-UP 9	v 89	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin	AE form no: [8]9]-[0]4] AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT*	1	1
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes  No	Yes No 🗖
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown  8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	2	2
Investigator's name, date of repo	Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect	Requiring/prolonging hospitalization Persistent/significant disability/incapacity Congenital anomaly/birth defect Other medically important event essentative's name, date of receipt:

XT 689 , XRP6258 , EFC6193

3. GRADE (1 - 4) 1 4. RELATIONSHIP TO STUDY TREATMENT*					1 <b>(</b> ) 0= None		No  No  ntly discontinued / 2= Delayed and reduced /	
3. GRADE (1 - 4) 1	1 🔲 2							
		<u> </u>	3 🗖	4 🔲		2 🗖	3 🗖	4 🗆
	<i>y</i> <b>_</b>				) <b>_</b>			
3= Ongoing with change	3 🔲				3 🔲			
2= Ongoing from previous period without change	2 \(\begin{aligned} \text{ (do not con} \)	mplete the re	emaining items	in the column)	2 🔲 (	do not complet	e the remaining items	in the columi
2. STATUS OF AE	1 Date of start	: LJL day	month	year	1 🔲 [	Date of start:	day month	year
Diagnosis —								
Adverse Event	AE ic		8] <b>9</b> ]- <b>0</b> ] [5			AE ref. no:	no: [ <b>8] 9]-[0</b> ] [ : []-[][	

1= Recovered 4 Specify sequelae: 4= Recovered with sequelae 2 2 2= Recovering  $3 \square$ 3 3= Not recovered 5 **D** Date of death: \_\_\_\_ \_\_\_\_ 5 **D** Date of death: \_\_\_\_ \_\_\_ 5= Fatal (complete the death report form) 6 🔲 6 🔲 6= Unknown 8. **S**ERIOUSNESS CRITERIA - Date event became serious: - Date event became serious: day month year day month year IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM - Tick below all criteria that apply: - Tick below all criteria that apply: Life-threatening . . . .  $\Box$ Life-threatening ..... Requiring/prolonging hospitalization . . . . . . Requiring/prolonging hospitalization . . . . Persistent/significant disability/incapacity . .  $\Box$ Persistent/significant disability/incapacity . . . Congenital anomaly/birth defect . . . . . . . . Congenital anomaly/birth defect . . . . . . . Other medically important event  $\dots$ Other medically important event ..... Investigator's name, date of report and signature: Monitoring representative's name, date of receipt: \* Is there a reasonable possibility that the AE was caused by study treatment?

XT EFC6193 689 XRP6258

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 689 04
Follow-up 9	v 89	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: \[ \begin{align*} \begin	AE form no:   <b>8</b>   <b>9</b>  - <b>10</b>   <b>8</b>   AE ref. no:   -
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes  No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No No	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: LL LLL year 4 Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown  8. SERIOUSNESS CRITERIA	2	2
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that apply:  Resulting in death	Tick below all criteria that apply:  Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmen	nt?

XT 689 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cent	re No. Subje	Ct No.	689 Page	05
FOLLOW-UP 9	v 89		See Page 6	5 <mark>2</mark>	
ADVERSE EV	ENT FORM			0.1_AE_1	
1. Adverse Event Diagnosis	AE form no: 819 AE ref. no:	- <u>(0</u>	AE for AE ref.	m no: <b>[8] 9]-[1] 0</b> no: <b>[] - [</b> ]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		onth year g items in the column)	1 Date of start: 2 (do not comp	day month lolete the remaining items i	year
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 🗖 2 🕻	3 🗆	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes [	No No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and redu 0			anently discontinued / 2= E 4= Delayed and reduced / 5= 2  3  4  5	= Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🗖	Yes [	<b>N</b> o	
7. OUTCOME 1= Recovered 4= Recovered with sequelae		onth year	1 Date: 4 Specify	day month sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2		2	ath:	year
8. SERIOUSNESS CRITERIA	Yes - Date event bed	No 🔲 came serious:		No Date event became so	erious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	day month	ation	Resulting in de Life-threatening Requiring/prolo Persistent/signil Congenital ano	day month Tick below all criteria ath 3 onging hospitalization ficant disability/incapacit smaly/birth defect y important event	y □
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's nam	e, date of receipt:	

XT 689 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. S	XT 689 0 6
Follow-up 9	V 89	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: <b>89-111</b> AE ref. no: <b></b>	AE form no:   <b>8</b>   <b>9</b>  -  <b>1</b>   <b>2</b>    AE ref. no:   -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLLLL LLLL year 2 (do not complete the remaining items in the columns)	day month year
3. GRADE (1 - 4)	1 2 3 4 5	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖	Yes 🔲 No 🖵
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0 1 1 2 1 5 5	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No 🗆	Yes No C
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: U U U U U U V V V V V V V V V V V V V	day month year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No No Compared Property Pr	Yes No No Compared Property Pr
	Resulting in death	Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring r	epresentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treat	ment?

XT 689 XRP6258 EFC6193

XRP6258 EFC6193				NO	204	
	Country No.	Centre No.	Subject No.		Page	
FOLLOW-UP 10	V 90		Date of visit:	day /	month / Que	ar
			•		See Page 12	
	See Page	<b>278</b>				
FOLLOW-UP 10					O.FOLLOWUP_2	
<b>Subject condition</b> (tick "✓"	one box only	/):				
☐ Alive						
☐ Lost to follow-up						
_	. ,					
☐ Dead (complete Death f	orm)					
Progression						
Has the subject had diseas	e progression?	? (tick "✓" one	box only)			
☐ Unknown						
☐ Previously reported pro	ogression					
□ No *						
☐ Yes **						

- If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- If YES, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

XRP6258 NO 204 EFC6193 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page
Follow-up 10	V 90	See Page 279

### POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

☐ NONE ☐ UNKNOWN

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			۵
3.			٥
4.			۵
5.			٥
6.			٠
7.			
8.			٠
9.			
10.		 	

NO	205	l	XRP6258	EFC6193
Confide	ntial ■ FINIAL I	■ 21 May 2008	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	206 Page	
Follow-up 10	V 90	See Page 26			

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	207 Page	
Follow-up 10	V 90	See	Page 55			

## **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ Not done

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LILI.LILI	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		∟∟∟ mm	
8		□□ □□□ □□□□□ □ Not Done			
9		□□□□□□□□□□□□□□□□ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done			
12	L. L. L.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 207 XRP6258 EFC6193

XRP6258 EFC6193				NO	208	
LI 00193	Country No.	Centre No.	Subject No.	I	Page	
FOLLOW-UP 10	V 90	See	Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.	Ш	
2.		
3.		
4		
5.		
7	Ш	

NO 208 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Cent	re No. Subje	Ct No.	690 Page	01
FOLLOW-UP 10	v 90   [		See Page	62	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>90</b> AE ref. no: <b>1</b>	-i <b>0</b>   <b>1</b>     _	AE foi AE ref.	m no:   <b>9 0 - 0 2</b> no:    -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	2 (do not complete the remaining	onth year  g items in the column)		day month  clete the remaining items in  ges, day month	year n the column)
3= Ongoing with change  3. GRADE (1 - 4)	1	onth year	1 2 2	3 🗖	4 🗖
RELATIONSHIP TO STUDY TREATMENT*     ACTION TAKEN WITH     STUDY TREATMENT	Yes		0= None / 1= Perm	anently discontinued / 2= 0 4= Delayed and reduced / 5= 2 3 3 4 0	Interrupted
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	Yes  Date: LL LL LL day m  Specify sequelae:	No unth year	1 <b>D</b> Date:	No Light Hard Light Hard May month y sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	3 ☐ 5 ☐ Date of death: ☐ ☐ ☐ ☐		3 🗖	ath: [ day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes ☐ - Date event bee day month - Tick below all	No came serious:	⇒ IF YES	No Date event became se	year
	Resulting in death	Resulting in death			
Investigator's name, date of repo			esentative's nam	ne, date of receipt:	
* Is there a reasonable XT 690	possibility that the AE was cause	ed by study treatmer		EFC6193	_

XRP6258 EFC6193	Country No.	Centre No.	Subject N	XT	690 Page	02
Follow-up 10	V 90			See Page	<mark>62</mark>	
ADVERSE EV	ENT FORM	1			O.1_AE_1	
1. Adverse Event Diagnosis		9 0 - 0  3		AE fo	m no: [ <b>9</b> ][ <b>0</b> ]- <b>[0</b> ][4	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Light day 2 (do not complete the light)	month LIL	e column) 2	Date of start:  (do not com	day month  plete the remaining items	year
3. GRADE (1 - 4)	1 🔲 2 🖸	3 🗖		2 [	3 🗖	4 🗖
Action Taken with     Study Treatment*      Action Taken with     Study Treatment	Yes  0= None / 1= Permanently dis 3= Dose reduced / 4= Delayer  0	continued / 2= Delay	errupted 3	0= None / 1= Perm	nanently discontinued / 2= 4= Delayed and reduced / 5 2  3  4	
6. Corrective Treatment/Therapy	Yes 🗖	No [		Yes [	☐ No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date: LLL day  Specify sequela  2		year 2	2 🗆	day month  ' sequelae:  ath: UU UUU day month	
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick be  Resulting in death  Life-threatening  Requiring/prolonging hor  Persistent/significant distance and the congenital anomaly/birt  Other medically importa	rent became serior	at apply:	Resulting in de Life-threatening Requiring/prole Persistent/signi Congenital and	No Date event became s  Aday month  Tick below all criteriath  Gonging hospitalization ficant disability/incapacionaly/birth defect  by important event	year  a that apply:
Investigator's name, date of repo	ort and signature:	Monito	oring represe	entative's nam	ne, date of receipt:	

XT 690 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 690 03
Follow-up 10	v 90	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
Adverse Event Diagnosis	AE form no: [9] 0 - 0   5    AE ref. no:	AE form no: [9] [0] -[0] [6] AE ref. no: [] -[] -[]
Pixenosis		
2. STATUS OF AE 1= New	1 Date of start:	1 Date of start: LL LL LL LL LL day month year
2= Ongoing from previous period without change	2  (do not complete the remaining items in the column)	2  (do not complete the remaining items in the column)
3= Ongoing with change	3 🗖	3 🗖
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted
	0 1 2 3 4 5 5	0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🔲 No 🚨	Yes No 🗖
7. OUTCOME 1= Recovered	1 Date: UU UUU UUUU day month year	1 Date: LL LL LL L
4= Recovered with sequelae	4 🗆 🕽 Specify sequelae:	4 D Specify sequelae:
2= Recovering	2 🗖	2 🗖
3= Not recovered	3	3
5= Fatal (complete the death report form) 6= Unknown	day month year	day month year
8. SERIOUSNESS	Yes No No	Yes No No
CRITERIA  IF YES, COMPLETE THIS SECTION	□ IF YES - Date event became serious:	- Date event became serious:
AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that apply:	Tick below all criteria that apply:
	Resulting in death	Resulting in death
	Life-threatening	Life-threatening
	Persistent/significant disability/incapacity	Persistent/significant disability/incapacity
	Congenital anomaly/birth defect	Congenital anomaly/birth defect
Investigator's name, date of repo	J	esentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?

EFC6193 690 XRP6258 XT

XRP6258 EFC6193	Country No.	Centre No	Subi	ect No.	(T	690	04
FOLLOW-UP 10	V 90		. Subje		age 62	Page	
ADVERSE EV	ENT FOR	RM				O.1_AE_1	
1. Adverse Event Diagnosis	AE form n AE ref. no:	o: [ <b>9][0]-[0</b> ]			AE form no: AE ref. no:	9 0 -0 8	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change	_	day month	year	1	day	y month	year
3= Ongoing with change	3 🗖			3 🗖			
3. GRADE (1 - 4)	1 🛘 2 🖵	3 🗖	4 🗖	1 🔲	2 🗖	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No		Yes		No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanen 3= Dose reduced / 4= D 0  1  2	elayed and reduced /			ed / 4= Delaye	iscontinued / $2=\Box$ ed and reduced / $5=$ 3 $\Box$ 4 $\Box$	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No No		Yes		No No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)	1  Date: 4  Specify sec	day month quelae:	year	1	rate: LLL day pecify sequel	ULLE y month lae:	JULI year
6= Unknown  8. SERIOUSNESS CRITERIA		No te event became	serious:	6 🗆 Yes		No event became se	
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Resulting in death Life-threatening Requiring/prolongin Persistent/significan Congenital anomal Other medically im	k below all crite  ng hospitalization  nt disability/incapar y/birth defect	year ria that apply:	Life-threa Requiring Persisten Congenit Other me	- Tick be tin death atening g/prolonging h t/significant di tal anomaly/bit edically impor	elow all criteria	that apply:
Investigator's name, date of rep	ort and signature:	M	onitoring rep	resentative's	name, date	e of receipt:	

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 690 | XRP6258 | EFC6193

XRP6258		
EFC6193	Country No. Centre No. S	XT 690   0 5  Subject No.   Page
Follow-up 10	v 90	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1.	AE form no: [9][0]-[0][9]	AE form no: 19101-110
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
2. STATUS OF AE	1 Date of start: LLL LLL Lgay month year	☐ 1 ☐ Date of start: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
2= Ongoing from previous period without change 3= Ongoing with change	2  (do not complete the remaining items in the column 3	nn) 2  (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 [	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes 🗖 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	
6. Corrective Treatment/Therapy	Yes	Yes
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1  Date:	1 Date: LL
2= Recovering 3= Not recovered	2 🔲	
5= Fatal (complete the death report form) 6= Unknown	5 Date of death:	Date of death: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐
8. SERIOUSNESS CRITERIA	Yes	Yes  No  No  - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	☐ IF YES	ly:    Signature   If Yes   If
	Resulting in death	Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring  possibility that the AE was caused by study trea.	representative's name, date of receipt:

XT 690 , XRP6258 , EFC6193

XRP6258 EFC6193 FOLLOW-UP 10	Country No. Cen V 90	tre No. Subjec	XT t No.  See Page 62	690 Page	06
ADVERSE EV	ENT FORM		oce rage uz	O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>90</b> AE ref. no: <b>1</b>	- <u>1111</u>  -111	AE form r AE ref. no:	no: [9]0-[1]2	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		noonth year ng items in the column)	1  Date of start: 2  (do not complete	day month e the remaining items in	year
3. GRADE (1 - 4)	1 🗖 2 🗖 3	4 🗆	1 2 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🚨	No 🗖	Yes 📮	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec	luced / 5= Interrupted	0= None / 1= Permaner 3= Dose reduced / 4= E 0		Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL Lday r Specify sequelae:	nonth year	}	LL LLL L day month quelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	nonth year	2	day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event be  IF YES   - Date event be    Li   Li   Li   Li   Li   Li   Li   L		⇒ IF YES	No  Ite event became se  I III III  Month  Ck below all criteria	year
	Resulting in death  Life-threatening  Requiring/prolonging hospitaliz  Persistent/significant disability/i  Congenital anomaly/birth defec	ation $\square$ ncapacity $\square$	Life-threatening Requiring/prolongi Persistent/significat Congenital anoma	ng hospitalization  nt disability/incapacity ly/birth defect  nportant event	
Investigator's name, date of repo	ort and signature:	Monitoring repre	esentative's name,	date of receipt:	
* Is there a reasonable	possibility that the AE was caus		:2		

XT 690 XRP6258 EFC6193

XRP6258 EFC6193	Country No	Centre No.	Subject No.	NO	209 Page	
Follow-up 11	V 91	Centre No.	Date of visit:	day/		ear
	ı		ı	,	See Page 12	<u> </u>
	See Page	<b>278</b>				
FOLLOW-UP 11					O.FOLLOWUP_2	
Subject condition (tick "✓"	one box only	<i>י</i> ):				
☐ Alive						
☐ Lost to follow-up						
☐ Dead (complete Death fo	orm)					
Progression						
Has the subject had disease	e progression?	' (tick "✓" one	box only)			
☐ Unknown						
☐ Previously reported pro	ogression					
□ No *	O					
☐ Yes **						
<u> </u>						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

NO 209 XRP6258 EFC6193

Confidential FINAL 21-May-2008 Sanofi aventis

XRP6258 EFC6193			NO	210	
	Country No.	Centre No. Subject No.		Page	
FOLLOW-UP 11	V 91	See Page 279			

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

	None		l Unknown
--	------	--	-----------

Drug/Regimen/Agent	START DATE	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			٥
4.			٥
5.			
6.			٥
7.			
8.			٥
9.			
10.			

NO	210	XRP6258	EFC6193
0	antial = FINIAL = 21 NA 2000	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	<b>211</b> Page	
Follow-up 11	V 91	See Page 26			

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193		NO 212
21 00 100	Country No.	Centre No. Subject No. Page
FOLLOW-UP 11	V 91	See Page 55

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	L.I.I.I.I.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		∟∟∟ mm	
8		□□ □□□ □□□□□ □ Not Done			
9		□□□□□□□□□□□□□□□□ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done			
12	L. L. L.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 212 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	213	
FOLLOW-UP 11	V 91		Page 53		. age	

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		
3.		
4		
5.	Ш	
6.	L	
7.		

NO 213 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cent	tre No. Subje	ct No.	691 Page	0[1
FOLLOW-UP 11	V 91		See Page	<b>62</b>	_
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: 911 AE ref. no:	- <u>[0                                    </u>	AE for AE ref.	m no: 911-012 no: 11-11	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		onth year  ng items in the column)	1 Date of start: 2 (do not comp	day month  olete the remaining items in	year
3. GRADE (1 - 4)		4 🗆	1 🔲 2 🕻		4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*  5. ACTION TAKEN WITH STUDY TREATMENT	Ves U  0= None / 1= Permanently discontinued 3= Dose reduced / 4= Delayed and red  0  1  2  3		0= None / 1= Perm	anently discontinued / 2= De 4= Delayed and reduced / 5= 2  3  4    4	Interrupted
6. CORRECTIVE TREATMENT/THERAPY 7. OUTCOME 1= Recovered 4= Recovered with sequelae	Yes  Date: LL LL  day m  Specify sequelae:	No U	1 Date:	No No Light Light Light Month sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	nonth year	2	tth: L.J.L.J.L.J.L.J.L.J.L.J.L.J.L.J.L.J.L.J	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event ber day month - Tick below all		⇒ IF YES	No Date event became ser                            day month  Tick below all criteria	уеаг
	Resulting in death	ation	Resulting in de Life-threatening Requiring/prolo Persistent/signit Congenital ano	ath	
Investigator's name, date of repo			L	e, date of receipt:	
* Is there a reasonable  XT 691	possibility that the AE was cause	ed by study treatmer		EFC6193	_

XRP6258 EFC6193	Country No.   Centre No.   Sub	XT 691 02
Follow-up 11	v 91	See Page 62
ADVERSE EVI	ENT FORM	0.1_AE_1
1.  Adverse Event Diagnosis	AE form no:   <b>9</b>   <b>1</b>  - <b> 0</b>   <b>3</b>   AE ref. no:   - -	AE form no: [9][1]-[0][4]  AE ref. no: [][-[][
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	day month year
3. GRADE (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT*	1	1
5. ACTION TAKEN WITH STUDY TREATMENT	Ves No No One / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted    0	Yes  No  O= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  O  1  2  3  4  5  5
6. Corrective Treatment/Therapy	Yes No 🗆	Yes No D
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	1 Date: day month year 4 Specify sequelae: 2 3 5 Date of death: day month year 6 0	4
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes One No One Present Serious:  - Date event became serious:  - D	Yes No Solution No
Investigator's name, date of repo	Requiring/prolonging hospitalization Persistent/significant disability/incapacity Congenital anomaly/birth defect Other medically important event	Requiring/prolonging hospitalization Persistent/significant disability/incapacity Congenital anomaly/birth defect Other medically important event Dresentative's name, date of receipt:

XT 691 , XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subj	XT 691 03
Follow-up 11	v 91	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1.	AE form no: [9][1]-[0][5]	AE form no:  9 1- 0 6
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
DIAGNOSIS		
2. STATUS OF AE 1= New	1 Date of start:	1 ☐ Date of start: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
2= Ongoing from previous period without change	2 (do not complete the remaining items in the column)	2 (do not complete the remaining items in the column)

3 🗖 3 🗖 3= Ongoing with change 1 🔲 2 3 4 🔲 1 🔲 2 🗆 3 🗖 4 🔲 **GRADE** (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT\* Yes No Yes No 0= None / 1= Permanently discontinued / 2= Delayed 0= None / 1= Permanently discontinued / 2= Delayed **ACTION TAKEN WITH** 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted STUDY TREATMENT 0 🔲 1 🔲 2 🗖 3 🗖 4 5 0 1 1 2 🔲 3 🔲 4 5 6. Corrective Treatment/Therapy Yes No Yes No **O**UTCOME day month year 10) Date: Date: 1= Recovered Specify sequelae: \_ Specify sequelae: 4= Recovered with sequelae 2 2 2= Recovering 3 🔲 3 3= Not recovered 5  $\square$  Date of death:  $\square$   $\square$   $\square$   $\square$   $\square$ 5 **D** Date of death: \_\_\_\_ \_\_\_ 5= Fatal (complete the death report form) 6 🔲 6 🔲 6= Unknown 8. **S**ERIOUSNESS - Date event became serious: - Date event became serious: day month year day month year IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY **FORM** - Tick below all criteria that apply: - Tick below all criteria that apply: Life-threatening . . . . .  $\square$ Life-threatening ..... Requiring/prolonging hospitalization . . . . Persistent/significant disability/incapacity . . Persistent/significant disability/incapacity . . . Congenital anomaly/birth defect . . . . . . . . Congenital anomaly/birth defect . . . . . . . . Other medically important event ...... Other medically important event ..... Investigator's name, date of report and signature: Monitoring representative's name, date of receipt:

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 691 , XRP6258 , EFC6193

XRP6258 EFC6193 FOLLOW-UP 11	Country No. Centre No. Subje	XT 691 04  See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no:   <b>9</b>   <b>1</b>  - <b>0</b>   <b>7</b>   AE ref. no:   -	AE form no:   <b>9 1 - 0 8</b>   AE ref. no:   - - - - -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes 🗆 No 🖵
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes No 🗖	Yes 🗖 No 🗖
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL LLL year 4 D Specify sequelae:	1 Date: LL LLL year 4 Specify sequelae:
2= Recovering	2 🗖	2 🗖
3= Not recovered	3 🗖	3 🗖
5= Fatal (complete the death report form)	5 Date of death: U UUU UUU	5 Date of death: LL LLL LLL Gay month year
6= Unknown	6 □ Yes □ No □	6
8. SERIOUSNESS CRITERIA	Yes  No  - Date event became serious:	Yes
IF YES, COMPLETE THIS SECTION AND THE <b>SAE</b> COMPLEMENTARY FORM	Tick below all criteria that apply:  Resulting in death	Tick below all criteria that apply:  Resulting in death
Investigator's name, date of repo	Other medically important event U  ort and signature: Monitoring repr	Other medically important event

XT 691 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 691 05
FOLLOW-UP 11	V 91 000	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no:	AE form no: 1911-110 AE ref. no: 11-11
2. STATUS OF AE	1 □ Date of start: □□ □□□ □□□□	1 Date of start:
1= New 2= Ongoing from previous period without change 3= Ongoing with change	day month year  2 (do not complete the remaining items in the column)  3	day month year  2  (do not complete the remaining items in the column)  3
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4 🛄	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🚨	Yes No 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  0
6. Corrective Treatment/Therapy	Yes No	Yes No No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: UL ULU Year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes □ No □  - Date event became serious:  □ IF YES     U   U   U   U   U   U   U   U   U	Yes □ No □  - Date event became serious:  □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
Investigator's name, date of rep	Resulting in death	Resulting in death

XRP6258 EFC6193	Country No. Centre No. Sul	XT 691 06		
FOLLOW-UP 11	V 91	See Page 62		
ADVERSE EVI	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no: <b>[9][1]-[1][1</b> ] AE ref. no: <b>[]]-[]</b>	AE form no: [9][1]-[1][2] AE ref. no: [][-[][-		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL	day month year		
3. GRADE (1 - 4)	1	1 2 3 4 4		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes No D		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
6. Corrective Treatment/Therapy	Yes No 🗆	Yes  No		
7. OUTCOME 1 = Recovered 4 = Recovering	Date: LLL LLL year  4  Specify sequelae:	Date: LL		
2= Recovering 3= Not recovered	3 🗖	3 🗖		
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: LL LLL LLL LLL LLL LLL LLL LLL LLL LL	5 Date of death: LL LL LL LL LL LL year 6 D		
8. SERIOUSNESS CRITERIA	Yes	Yes No C - Date event became serious:		
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	→ IF YES     Solution   Control   C	→ IF YES		
	Resulting in death	Resulting in death		
Investigator's name, date of repo	ort and signature: Monitoring re	presentative's name, date of receipt:		

XT 691 , XRP6258 , EFC6193

			_			
XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	214 Page	
Follow-up 12	V 92		Date of visit:	day /		rear
				(	See Page 12	
FOLLOW-UP 12	See Page	<del>278</del>			O.FOLLOWUP_2	
<b>Subject condition</b> (tick "✓"	one box only	/):				
☐ Alive						
☐ Lost to follow-up						
☐ Dead (complete Death fo	orm)					
Progression						
Has the subject had disease	e progression?	? (tick "✓" one	box only)			
☐ Unknown						
☐ Previously reported pro	ogression					
□ No*						
☐ Yes **						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

NO 214 XRP6258 EFC6193

Confidential FINAL 21-May-2008 Sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	215 Page	
Follow-up 12	V 92	Se	e Page 279			

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

	None		l Unknown
--	------	--	-----------

Drug/Regimen/Agent	START DATE	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			٥
4.			٥
5.			
6.			٥
7.			
8.			٥
9.			
10.			

NO	215	<sub>1</sub> XRP6258	EFC019
NO	215	VDD6250	EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
Follow-up 12	V 92	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 216 XRP6258 EFC6193

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

# \*\*\*RESPONSE OF NON-TARGET CODES:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	217 Page	
Follow-up 12	V 92	See	Page 55			

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.I.L.I.L.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□ □□□ □□□□□ □ Not Done		mm	
3		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		L L  mm	
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5		□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□ Not Done			
8		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
9	L	□□ □□□ □□□□□ □ Not Done			
10		□□□□□□□□□□□□□□□ Not Done			
11		□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14	L.L.L	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 217 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	218 Page	
FOLLOW-UP 12	V 92	Sec	e Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1	Ш	
		لــالــا . لــالــا
3.		
4.		
5.		
6.		
7.		

NO 218 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	XT	692 0 1
FOLLOW-UP 12	v 92		See Page 62	2
ADVERSE EV	ENT FORM			O.1_AE_1
☐ NONE				
1.  Adverse Event  Diagnosis	AE form no: 1912  AE ref. no:	-[ <b>0</b>	AE form AE ref. no	no: [9][2]-[0][2] o: []-[]
2. STATUS OF AE	· _	nonth year	1 Date of start:	day month year
2= Ongoing from previous period without change 3= Ongoing with change	3  If grade changes, date of change:			te the remaining items in the column)  ':
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖸	3 🗖 4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🗖	Yes 🗖	No 🚨
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red		3= Dose reduced / 4=	ently discontinued / 2= Delayed Delayed and reduced / 5= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	No 🚨
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL day n Specify sequelae:	nonth year	1 Date: 4 Specify so	day month year equelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI nonth year	2	:
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes ☐ - Date event be	No Came serious:		No □  Nate event became serious:  U□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□
FORM	Resulting in death	ation	Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anom	ick below all criteria that apply:  n
	Other medically important ever	11		•
Investigator's name, date of rep	J,		esentative's name,	
	J,	Monitoring repr		

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 692 02
FOLLOW-UP 12	v 92	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no:	AE form no:
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLLL LLLL year 2 (do not complete the remaining items in the column) 3 D
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4 🗀	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 📮	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0

6. CORRECTIVE TREATMENT/THERAPY Yes **O**UTCOME 1 🔲 🕽 Date: 1= Recovered Specify sequelae: Specify sequelae: 4= Recovered with sequelae 2 🔲 2 2= Recovering 3 3 3= Not recovered 5 **D** Date of death: \_\_\_\_ \_\_\_\_ 5 **D** Date of death: \_\_\_\_ \_\_\_ 5= Fatal (complete the death report form) 6 🔲 6 🔲 6= Unknown No 8. SERIOUSNESS CRITERIA - Date event became serious: - Date event became serious: day month year day month year IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM - Tick below all criteria that apply: - Tick below all criteria that apply: Life-threatening ..... Requiring/prolonging hospitalization . . . . . . Requiring/prolonging hospitalization . . . . Persistent/significant disability/incapacity . . Persistent/significant disability/incapacity Congenital anomaly/birth defect . . . . . . . . Congenital anomaly/birth defect . . . . . . . . Other medically important event . . . . . . . . . . Other medically important event ..... Investigator's name, date of report and signature: Monitoring representative's name, date of receipt: \* Is there a reasonable possibility that the AE was caused by study treatment?

XT692 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subjection	XT 692 03
FOLLOW-UP 12	V 92	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [9][2]-[0][5] AE ref. no: []-[]-	AE form no:   <b>9</b>   <b>2</b> - <b>0</b>   <b>6</b>   AE ref. no:   -
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3 D
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖	Yes 🔲 No 🗬
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0 1 1 2 1 5 1 5 1	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No 🗆	Yes No 🗆
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL LLL year 4 Specify sequelae:	1 Date: LLL LLLL year 4 Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes □ No □  - Date event became serious:  □ □ □ □ □ □ □ □ □ □ □ □ □ day month year  - Tick below all criteria that apply:	Yes No C  - Date event became serious:    Solition   Date   Date
Investigator's name, date of repo	Resulting in death	Resulting in death

XT 692 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Ce	ntre No. Subject N	XT	692 Page	04
FOLLOW-UP	12 v 92	S	See Page 62		
ADVERSE	EVENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>9</b> 12 AE ref. no: <b>1</b>	1-(0);7; 1-[]	AE form no AE ref. no:	: 19121-1018	
2. STATUS OF AE 1= New 2= Ongoing from previous period with	day  2	month year		day month	year
3= Ongoing with change	3 🗖	3	3 🗖		
3. GRADE (1 - 4)	1 2 2 3	3 4 1 1	2 🗆	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREA	TMENT* Yes 🗖	No 🗖	Yes 📮	No	
5. ACTION TAKEN WIT STUDY TREATMENT	3= Dose reduced / 4= Delayed and re	educed / 5= Interrupted 3	0= None / 1= Permanently 3= Dose reduced / 4= Del	ayed and reduced / 5=	Interrupted
6. Corrective Treatment/	HERAPY Yes	No 🗖	Yes 📮	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering 3= Not recovered	1  Date: LL Lday 4  Specify sequelae: 2	month year 4	Date: L Specify sequ	JL LLL L day month uelae:	year
5= Fatal (complete the death repo	t form) $\begin{bmatrix} 5 & \Box \\ 6 & \Box \end{bmatrix}$ Date of death: $\Box \Box \Box \Box \Box$	month year		day month	year
8. SERIOUSNESS CRITERIA	Yes 📮	No 🗖 ecame serious:	Yes 🔲	No e event became ser	ious:
IF YES, COMPLETE THIS SI AND THE SAE COMPLEME FORM	NTARY day mont	Il criteria that apply:	day	below all criteria	year
	Resulting in death	zation	Resulting in death	g hospitalization disability/incapacity birth defect ortant event	
investigator's name, date	of report and signature:	Monitoring represe	emanve's name, d	ate of receipt:	

XT 692 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No.	Subje	Ct No.	692 Page	05
FOLLOW-UP 12	V 92		See Page	62	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: 912-019 AE ref. no: 11-11		AE form AE ref. no	no:   <b>9 2-1 0</b> :   -	
2. STATUS OF AE	1 Date of start: LL LL L L L L L L L L L L L L L L L L	year	1 Date of start: 2 (do not complete	day month	year
2= Ongoing from previous period without change 3= Ongoing with change	3 🗖		3 🗖		
3. GRADE (1 - 4)	1 2 3 3	4 🗖	1 2 2	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No		Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Do 3= Dose reduced / 4= Delayed and reduced / 5= 0  1  2  3  4	Interrupted	3= Dose reduced / 4=	ntly discontinued $/$ 2= $\square$ Delayed and reduced $/$ 5= $\square$ 3 $\square$ 4 $\square$	Interrupted
6. Corrective Treatment/Therapy	Yes 🗖 No		Yes 🗖	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 ☐ } Date: ☐☐ ☐☐ ☐☐ ☐☐☐ ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐	year	1 Date: 4 Specify se	day month	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	J L J L J	2	day month	year
8. SERIOUSNESS CRITERIA	Yes No  - Date event became set			No ate event became se	
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	- Tick below all criteria	that apply:	- Ti		that apply:
	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event		Life-threatening . Requiring/prolong Persistent/significa Congenital anoma Other medically i	ing hospitalization int disability/incapacit ily/birth defect	
Investigator's name, date of rep	ort and signature: Mon	itoring repr	esentative's name,	date of receipt:	

XT 692 XRP6258 EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 692 06
FOLLOW-UP 12	v 92	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [9][2]-[1][1] AE ref. no: []-[]-	AE form no: [9][2]-[1][2] AE ref. no: []-[]-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4) 4. RELATIONSHIP TO STUDY TREATMENT*	1	1
5. Action Taken with Study Treatment	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	Ves No
6. Corrective Treatment/Therapy	Yes No 🗆	Yes No 🗆
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: ULL Wear  4 Specify sequelae:	1 Date: LL LLL year 4 Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA	Yes No O - Date event became serious:	Yes No C - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM  Investigator's name, date of repo	Tick below all criteria that apply:  Resulting in death	Tick below all criteria that apply:  Resulting in death
		esentative's name, date of receipt:

XT 692 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	219 Page	
Follow-up 13	V 93	Centre No.	Date of visit:	day /	month rage	year
			1	Se	ee Page 12	
	See Page 2	<b>278</b>				
FOLLOW-UP 13					O.FOLLOWUP_	2
Subject condition (tick "✓"	one box only	y):				
☐ Alive						
☐ Lost to follow-up						
☐ Dead (complete Death fo	orm)					
Progression						
Has the subject had disease	e progression?	? (tick "✓" one	box only)			
☐ Unknown						
☐ Previously reported pro	gression					
□ No *						
☐ Yes **						

- If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- If YES, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

XRP6258 NO 219 EFC6193 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
Follow-up 13	V 93	See Page 279

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

	None		Unknown
--	------	--	---------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			
4.			
5.			٥
6.			
7.			٥
8.			
9.			٥
10.			

NO	220	XRP6258	EFC6193
0	antial = FINIAL = 21 M 2000	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 13	V 93	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No. Subject No.	NO	222 Page	
Follow-up 13	V 93			i age	
I OLLOW OF TO	, <u>a</u>	See Page 55			

# **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	L	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5		□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□ Not Done			
8		□□ □□□ □□□□□ □ Not Done		LJLJ mm	
9		□□ □□□ □□□□□ □ Not Done			
10	LJLJ.LJLJ	□□□□□□□□□□□□□□□ Not Done			
11		□□□□□□□□□□□□□□□□ Not Done			
12	L.I.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□ Not Done			ШШ

NO 222 XRP6258 EFC6193

XRP6258 EFC6193				NO	223	
21 00100	Country No.	Centre No.	Subject No.	I	Page	
Follow-up 13	V 93	See Pa	ge 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.	Ш	
2.		
3.		
4		
5.		
7.	Ш	

NO 223 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	oct No.	693 Page	01
Follow-up 13	v 93 🗆		See Page 6	52 	
ADVERSE EV	ENT FORM			0.1_AE_1	
☐ NONE					
1.  Adverse Event Diagnosis	AE form no: <b>1913</b> AE ref. no: <b>11</b>	-  <b>0</b>    <b>1</b>    -	AE for AE ref.	m no:  9 3 - 0 2 no:   -	
2. STATUS OF AE	· ·	month year	1 Date of start:	day month	
2= Ongoing from previous period without change 3= Ongoing with change	2 ☐ (do not complete the remaining items in the column)  3 ☐ If grade changes, date of change: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		2 ☐ (do not complete the remaining items in the column)  3 ☐ If grade changes, date of change: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		
3. GRADE (1 - 4)	1 🗖 2 🗖 3	4 🗆	1 🗖 2 🕻	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🚨	Yes [	<b>N</b> o	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0	duced / 5= Interrupted		anently discontinued / 2= I 4= Delayed and reduced / 5 2	= Interrupted
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes [	No No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL Lday Specify sequelae:	month year	1 Date: 4 Specify	day month sequelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	□□ □□□□ month year	2	th: day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes - Date event be			No Date event became s	
FORM	- Tick below all criteria that apply:  Resulting in death		- Tick below all criteria that apply:  Resulting in death		
Investigator's name, date of rep	J	·	L	e, date of receipt:	
			s+2		
* Is there a reasonable	possibility that the AE was caus	ea by study treatmer	n:		

XRP6258 EFC6193		XT 693 02
EFC0193	Country No. Centre No. Subje	ct No.   Page
FOLLOW-UP 13	V 93	See Page 62
ADVERSE EV	/ENT FORM	O.1_AE_1
1.	AE form no: [9][3]-[0][3]	AE form no: 1913-1014
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
2. STATUS OF AE	1 Date of start: LL LLL year	1 Date of start:
2= Ongoing from previous period without cha	2  (do not complete the remaining items in the column)	2 (do not complete the remaining items in the column)
3= Ongoing with change	3 4	
3. GRADE (1 - 4)	1 🗆 2 🗔 3 🗔 4 🗔	1
4. RELATIONSHIP TO STUDY TREATMEN	* Yes • No •	Yes 🗖 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted
6. Corrective Treatment/Ther	0	Yes
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL	1 Date: LLL LLL LLL LLL LLL LLL LLL LLL LLL L
2= Recovering	2 🗆	2 🗖
3= Not recovered 5= Fatal (complete the death report form	3	5 Date of death: LL LLL year
8. SERIOUSNESS CRITERIA	Yes  No  O  O  O  O  O  O  O  O  O  O  O  O  O	Yes  No  O - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARE FORM		☐ IF YES
	Resulting in death	Resulting in death
Investigator's name, date of i	eport and signature: Monitoring repr	esentative's name, date of receipt:

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 693 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No.	XT 693 03
FOLLOW-UP 13	v 93 🗆	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: 1913-1015 AE ref. no: 11-11	AE form no: \( \begin{align*} 9 \cdot 3 - \begin{align*} 0 \cdot 6 \\ AE ref. no: \cdot \cdot \cdot - \cdot
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL	ar day month year
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🖫	4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖	Yes 🔲 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interru	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 5
6. Corrective Treatment/Therapy	Yes • No •	Yes 🗖 No 🗖
7. OUTCOME 1= Recovered 4= Recovered with sequelae 2= Recovering		Date: LLL LLL LLL LLL LLL LLL LLL LLL LLL L
3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	3 ☐ 5 ☐ Date of death: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	3 Date of death: U U U Wear  6 D
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes One of the No One of the Yes One	apply: Sir Yes \ \begin{array}{llll} \begin{array}{lll} \begin{array}{llll} arr
Investigator's name, date of repo	Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event	Requiring/prolonging hospitalization

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 693 | XRP6258 | EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subje	Ct No.	693		04
FOLLOW-UP 13	V 93			See Pag	e 62		
ADVERSE EVE	ENT FOR	M			0.1_1	4 <i>E_1</i>	
1. Adverse Event Diagnosis	AE form no: AE ref. no:	93-07			form no: 1915 ref. no: LL	3]-[ <b>0</b> ][8	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		ll	year	1		month	year o the column)
3. GRADE (1 - 4)	1 🔲 2 🔲	3 🗖	4 🔲	1 🗖	2 🗖	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No		Yes		No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently 3= Dose reduced / 4= Dela 0  1  2  1	yed and reduced / 5=	Interrupted		rermanently discontinuted / 4= Delayed and recommendation / 2  3  5	educed / 5=	Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No		Yes		No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	_ }	JL LLL L Jay month elae:	year	1 Date 4 Speci		month	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form)		JLJ LJLJ L day month	year		death: L_  L_  day	JLJLJ L	JLJ LL year
8. SERIOUSNESS CRITERIA  If yes, complete this section and the SAE complementary FORM	⇒ IF YES	No event became se	<b>J L J</b> year	Yes  Yes	- Date event be day mont	ILI LIL	J L L L year
	Resulting in death Life-threatening Requiring/prolonging Persistent/significant of Congenital anomaly/b Other medically impo	hospitalization lisability/incapacity irth defect ortant event		Life-threater Requiring/p Persistent/si Congenital	death ning rolonging hospital gnificant disability anomaly/birth defo cally important ev	ization /incapacity	0
Investigator's name, date of repo		Mon	itoring repr	esentative's n	ame, date of r	eceipt:	

XRP6258		
EFC6193	Country No.   Centre No.   Subj	XT 693
Follow-up 13	V 93	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1.	AE form no: [9][3]-[0][9]	AE form no: [9][3]-[1][0]
Adverse Event Diagnosis	AE ref. no:	AE ref. no:
2. STATUS OF AE	1 Date of start: LL LLL year	1 Date of start:
2= Ongoing from previous period without change 3= Ongoing with change	2  (do not complete the remaining items in the column)	2  (do not complete the remaining items in the column)
3. GRADE (1 - 4)	1	1 2 3 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No No	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes	Yes
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1  Date: UL UL UL Vear 4  Specify sequelae:	1 Date: LL LL LL LL year 4 D Specify sequelae:
2= Recovering 3= Not recovered	2 🔲	
5= Fatal (complete the death report form) 6= Unknown	5 Date of death: LL LL LL LL year	5 Date of death: U U U year
8. SERIOUSNESS CRITERIA	Yes No No C	Yes No No C - Date event became serious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	⇒ IF YES	Tick below all criteria that apply:
	Resulting in death	Resulting in death
Investigator's name, date of repo	ort and signature: Monitoring rep  possibility that the AE was caused by study treatme	resentative's name, date of receipt:

XT 693 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 693 06
FOLLOW-UP 13	v 93	See Page 62
ADVERSE EV	ENT FORM	0.1_AE_1
1. Adverse Event Diagnosis	AE form no: [9][3]-[1][1]  AE ref. no: []-[]-	AE form no:  9 3 - 1  2  AE ref. no:
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes No D	Yes No D
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered  5 = Fatal (complete the death report form)  6 = Unknown	Date: LL	Date: LL
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes □ No □  - Date event became serious:  □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □	Yes □ No □  - Date event became serious:  □ IF YES     □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
FORM  FORM  Investigator's name, date of repo	- Tick below all criteria that apply:  Resulting in death	- Tick below all criteria that apply:  Resulting in death

XT 693 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	224 Page	
Follow-up 14	V 94		Date of visit:	aday /		ear
٩	ee Page 278	1			See Page 12	
FOLLOW-UP 14	ee i age zio	ı			O.FOLLOWUP_2	
Subject condition (tick "✓"  Alive  Lost to follow-up  Dead (complete Death form)  Progression		·):				
Has the subject had diseas	e progression?	(tick "✔" one	box only)			
☐ Unknown						
☐ Previously reported pro	ogression					
■ No *						
☐ Yes **						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

NO 224 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page
Follow-up 14	V 94	See Page 279

## POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

■ None		Unknown
--------	--	---------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			۵
4.			
5.			٥
6.			۰
7.			
8.			۵
9.			
10.			

NO	225	I	XRP6258	EFC6193
Confide	ntial = FINI	AL = 21 May 2009	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	226 Page	
Follow-up 14	V 94	See	Page 26			

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 226 XRP6258 EFC6193

Loca	ation:	* Location:					
01	Skin	12	Liver	22	Mediastinum		
02	Muscle/Soft Tissue	13	Stomach	23	Uterus		
03	Bone	14	Pancreas	24	Abdomen		
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract		
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis		
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum		
07	Head/Neck	17	Bladder	28	Testis		
80	Esophagus	18	Prostate	29	Thorax		
09	Breast	19	Cervix	29.01	Pleura		
10	Lungs	20.10	Colon	30	Other		
11.0	Regional Lymph Nodes	20.20	Rectum				
11.02	2 Distant Lymph Nodes	21	Adrenal				

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	<b>227</b> Page	
Follow-up 14	V 94	See	Page 55			

## **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1		□ Not Done			
2		□ Not Done			
3		Not Done		LJLJ mm	
4		□ Not Done			
5		□ Not Done			
6		□ Not Done			
7		□ Not Done			
8		□□□□□□□□□□□□□□□□ Not Done			
9		□ Not Done		LJLJ mm	
10	L.L.	□ Not Done			
11	L_  L_  .L_	□ Not Done			
12	L  L	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
13	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
14	LL.LL	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		mm	

NO 227 XRP6258 EFC6193

XRP6258 EFC6193				NO	228	
EFC0193	Country No.	Centre No.	Subject No.	I	Page	
Follow-up 14	V 94	See	Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		
3.		
4		
5.	Ш	
6.	L	
7.		

NO 228 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cen	tre No. Subje	Ct No.	694 0 1
Follow-up 14	V 94		See Page 62	_
ADVERSE EV	ENT FORM			O.1_AE_1
☐ NONE				
1. Adverse Event Diagnosis	AE form no: <b>94</b> AE ref. no: <b>1</b>	-  <mark>0  1 </mark>  -	AE form AE ref. no	no: [ <b>9][4]-[0][2</b> ]
2. STATUS OF AE	· · · · · · · · · · · · · · · · · · ·	nonth year	1 Date of start:	day month year
2= Ongoing from previous period without change 3= Ongoing with change	3  If grade changes, date of change:			te the remaining items in the column)  Light Hamman day month year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 2 2	3 🔲 4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 📮	Yes 🗖	No 📮
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec	luced / 5= Interrupted	3= Dose reduced / 4=	ently discontinued / 2= Delayed Delayed and reduced / 5= Interrupted  3 4 5 5
6. Corrective Treatment/Therapy	Yes 🗖	No 🗖	Yes 🗖	No 🗖
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLL Lday r Specify sequelae:	nonth year	1 Date: 4 Specify se	day month year equelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	UU UUU	2	day month year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY	Yes ☐ - Date event be	No Came serious:		No □ ate event became serious: I□ □□□ □□□□ Iay month year
FORM	- Tick below al  Resulting in death	ation	Resulting in death Life-threatening Requiring/prolong Persistent/significa Congenital anoma	ck below all criteria that apply:
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's name,	date of receipt:
* Is there a reasonable possibility that the AE was caused by study treatment?				
XT 694		XRP62	oo <sub>I</sub> El	FC6193

XRP6258		XT 694   0 2
FOLLOW-UP 14	Country No. Centre No. Subj	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no:	AE form no: [9][4]-[0][4] AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: L L L L L L L L L L L L L L L L L L L
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes No D
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0 1 2 3 4 5 5	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🔲 No 🗖	Yes No No
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL	Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes
Investigator's name, date of repo	ort and signature: Monitoring rep	resentative's name, date of receipt:

 $\ensuremath{^*}$  Is there a reasonable possibility that the AE was caused by study treatment?

XT 694 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subjection	Tot No.   XT 694 03
Follow-up 14	V 94	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: [9][4]-[0][5] AE ref. no: [][-[][-	AE form no:  9 4 - 0 6  AE ref. no:   -
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LLL LLLL LLLL LLLL LLLL LLLLL LLLLL LLLL	1 Date of start: LL LL Lyear 2 (do not complete the remaining items in the column) 3 Date of start: LL
3. GRADE (1 - 4)	1	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No D	Yes No 🗆
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes  No	Yes No No
7. <b>QUTCOME</b> 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year  4 Specify sequelae:	1 Date: LL LLL year  4 Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA	Yes No No C - Date event became serious:	Yes No No C

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 694 , XRP6258 , EFC6193

day month year

Life-threatening . . . . . . . . . . . . . . . . .

Requiring/prolonging hospitalization  $\dots$ 

Persistent/significant disability/incapacity . .  $\Box$ 

Other medically important event  $\dots$ 

Congenital anomaly/birth defect . . . . . . . .

IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY

Investigator's name, date of report and signature:

**FORM** 

Monitoring representative's name, date of receipt:

- Tick below all criteria that apply:

Requiring/prolonging hospitalization . . . . .

Persistent/significant disability/incapacity ...

Congenital anomaly/birth defect . . . . . . . .

Other medically important event ......

XRP6258 EFC6193	Country No. Centre No. Subje	XT 694 04				
Follow-up 14	V 94	See Page 62				
ADVERSE EV	ENT FORM	O.1_AE_1				
1.	AE form no: [9] 4]-[0 [7]	AE form no: [9]4]-[0]8]				
Adverse Event Diagnosis	AE ref. no:	AE ref. no:				
2. STATUS OF AE	1 □ Date of start: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	1 Date of start:				
2= Ongoing from previous period without change	2 (do not complete the remaining items in the column)	2 (do not complete the remaining items in the column)				
3= Ongoing with change	3 🗖	3 🗖				
3. GRADE (1 - 4)	1 2 3 4	1 🗆 2 🗔 3 🗔 4 🗔				
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes No D				
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted				
	0 1 2 3 4 5	0 1 2 3 4 5				
6. CORRECTIVE TREATMENT/THERAPY	Yes	Yes No 🗆				
7. OUTCOME 1= Recovered	1 🗖 🕽 Date: 🔟 🔟 🖂 Ullum Jear	1 Date: UUUUUUUU				
4= Recovered with sequelae	4 🗆 🕽 Specify sequelae:	4 D Specify sequelae:				
2= Recovering	2 🗖	2 🗖				
3= Not recovered	3 ☐ 5 ☐ Date of death: ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐	3 □ 5 □ Date of death: □□ □□□□ □□□□				
5= Fatal (complete the death report form) 6= Unknown	5	day month year				
8. Seriousness	Yes 🔲 No 🗖	Yes No 🗆				
CRITERIA	- Date event became serious:	- Date event became serious:				
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick below all criteria that apply:	Tick below all criteria that apply:				
	Resulting in death	Resulting in death				
	Life-threatening	Life-threatening				
	Persistent/significant disability/incapacity	Persistent/significant disability/incapacity				
	Congenital anomaly/birth defect	Congenital anomaly/birth defect				
Investigator's name, date of repo	Other medically important event	Other medically important event				
investigator s name, date of repr	or and signature.	eschiative s hame, date of feceipt.				
* Is there a reasonable	* Is there a reasonable possibility that the AE was caused by study treatment?					

XT 694 XRP6258 EFC6193

XRP6258			][ хт	694	0[5]
FOLLOW-UP 14	V 94	tre No. Subje	ct No.	Page	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>94</b> AE ref. no: <b>1</b>	- <mark> 0  9 </mark>  -		form no:	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change		nonth year ng items in the column)	1	art:	year
3. GRADE (1 - 4)	1 2 2 3	4 🗆	1 🗆 🗀	2 🔲 3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 📮	Yes	□ No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and red 0	duced / 5= Interrupted		ermanently discontinued / 2= [ / 4= Delayed and reduced / 5: 2  3  4 [	= Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🗖	Yes	□ No	
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)			2	e: LL LLL I day month cify sequelae:	year
6= Unknown		month year	6	day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes ☐ - Date event be □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □		Yes	No - Date event became so  Like and the solution of the soluti	year
Investigator's name, date of repo	Resulting in death  Life-threatening  Requiring/prolonging hospitaliz  Persistent/significant disability/  Congenital anomaly/birth defed  Other medically important eve	tation	Life-threaten Requiring/pr Persistent/sig Congenital a Other medic	death  ing  rolonging hospitalization gnificant disability/incapacit anomaly/birth defect cally important event  ame, date of receipt:	
* Is there a reasonable possibility that the AE was caused by study treatment?					

XT 694 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No.	Subjec	XT	694 Page	06
FOLLOW-UP 14	v 94		See Page 6	2	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: [9][4]-[1][1] AE ref. no: []-[]		AE form AE ref. no	no:   <b>9  4 - 1  2</b> o:    -	
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: LL LL LL L L L L L L L L L L L L L L	· I	1  Date of start: 2  (do not completed)	day month te the remaining items i	,
3. GRADE (1 - 4)	1 2 3 3	4 🔲	1 🔲 2 🖵	3 🗖	4 🔲
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No		Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delay 3= Dose reduced / 4= Delayed and reduced / 5= Interest   0		3= Dose reduced / 4=	ently discontinued / 2= [ Delayed and reduced / 5:  3	= Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖 No 🛚		Yes 🗖	No	
7. OUTCOME  1 = Recovered  4 = Recovered with sequelae  2 = Recovering  3 = Not recovered  5 = Fatal (complete the death report form)	Date: LIL LIL LIL  4 D Specify sequelae:  2 D  3 D  Date of death: LIL LIL LIL  day month	year	2	day month coquelae:	year year
6= Unknown	6 🗆		6 🗖		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes □ No □  - Date event became serio  □ □ □ □ □ □ □ □ □  day month year  - Tick below all criteria the		⇒ IF YES	No ate event became so ILI LILI LIL lay month ick below all criteria	year
	Resulting in death		Resulting in death		
Investigator's name, date of rep	ort and signature: Monitc	⊦ oring repre	sentative's name,	date of receipt:	

XT 694 , XRP6258 , EFC6193

		_			
XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	229 Page
FOLLOW-UP 15	V 95		Date of visit:	ay/	month year
_	0070				See Page 12
FOLLOW-UP 15	See Page 278				O.FOLLOWUP_2
<b>Subject condition</b> (tick "✓"	one box only	·):			
☐ Alive					
☐ Lost to follow-up					
☐ Dead (complete Death f	orm)				
Progression					
Has the subject had diseas	e progression?	(tick "✓" one	box only)		
☐ Unknown					
☐ Previously reported pro	ogression				
□ No *					
☐ Yes **					

- If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- If YES, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

XRP6258 NO 229 EFC6193 sanofi aventis

XRP6258 EFC6193	Country No.	Centre No. Subject No. Page
Follow-up 15	V 95	See Page 279

### POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

	None		l Unknown
--	------	--	-----------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			۵
2.			
3.			٥
4.			
5.			
6.			٥
7.			
8.			
9.			
10.			٥

NO 230 XRP6258 EFC6193			. ■ 21 May 2009		ofi aventis	_
	NO	230		XRP6258	EFC6193	

XRP6258 EFC6193	Country No.	Centre No. Subject I	NO.	231 Page	
Follow-up 15	V 95	See Page 26	1		

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

Loca	ation:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.0	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	232 Page	
FOLLOW-UP 15	V 95	See	Page 55			

## **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	L.I.I.I.I.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L.L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□ Not Done			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		∟∟∟ mm	
8		□□ □□□ □□□□□ □ Not Done			
9		□□□□□□□□□□□□□□□□ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done			
12	L. L. L.	□□ □□□ □□□□□ □ Not Done			
13		□□□□□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 232 XRP6258 EFC6193

XRP6258 EFC6193			\	IO 233	
EFC0193	Country No.	Centre No.	Subject No.	Page	
FOLLOW-UP 15	V 95	See Pag	ge 53		

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.		
2		LJLL . LJL
3.		
4.	L	
5.		
6.		
7.		

NO 233 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cent	tre No. Subje	Tct No.	695 Page	01
FOLLOW-UP 15	V 95   [		See Page	62	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>1915</b> AE ref. no: <b>11</b>	- <u> 0   1  </u> 	AE fori AE ref.	m no: [ <b>9</b> ][ <b>5</b> ]- <b>0</b> ][ <b>2</b> ] no: []-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change	2 (do not complete the remaining	onth year  g items in the column)		day month  lete the remaining items in  es, e:	year the column)
3= Ongoing with change  3. GRADE (1 - 4)	1	onth year	1 2 2	3 🗖	4 🗖
RELATIONSHIP TO STUDY TREATMENT*     ACTION TAKEN WITH     STUDY TREATMENT	Yes    0= None / 1= Permanently discontinuer 3= Dose reduced / 4= Delayed and red  0			No  anently discontinued / 2= Delayed and reduced / 5= 1 2 3 4 4	Interrupted
<ul><li>6. CORRECTIVE TREATMENT/THERAPY</li><li>7. OUTCOME</li><li>1= Recovered</li><li>4= Recovered with sequelae</li></ul>	Yes  Date: LLL Ll day n  Specify sequelae:	No 🔲	Yes  1  Date: 4  Specify	No No day month sequelae:	JULIU year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	nonth year	2	th: LLL LLLL L day month	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event be  The Yes - Date event be  Aday month  Tick below all	No Came serious:	⇒ IF YES {	Date event became ser	JLJ LJ /ear
	Resulting in death  Life-threatening  Requiring/prolonging hospitaliz  Persistent/significant disability/in  Congenital anomaly/birth defectory  Other medically important ever	ation	Resulting in dea Life-threatening Requiring/prolo Persistent/signifi Congenital anoi	nging hospitalization	0
Investigator's name, date of repo			L	e, date of receipt:	
* Is there a reasonable XT 695	possibility that the AE was caus	ed by study treatmer  XRP62		EFC6193	_

XRP6258 EFC6193 FOLLOW-UP 15	Country No. Centre No. Subject V 95	XT 695 02  ect No.   Page  See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no:	AE form no:  9 5 - 0 4  AE ref. no:   - - -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: Lay
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*  5. ACTION TAKEN WITH STUDY TREATMENT	Yes □ No □  0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted   0 □ 1 □ 2 □ 3 □ 4 □ 5 □	Yes No No O No No D No D No D No D No D No
6. Corrective Treatment/Therapy	Yes No D	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year  4 D Specify sequelae:	1 Date: LL LL LLL year  Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2 □ 3 □ 5 □ Date of death: □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM  Investigator's name, date of repo	Yes	Yes

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 695 XRP6258 EFC6193

XRP6258 EFC6193 FOLLOW-UP 15	Country No. Centre No. Subje	XT 695 03  Page  See Page 62		
ADVERSE EVI	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no: 1915-1015  AE ref. no: 1-11	AE form no: 1915-10161 AE ref. no: 11-11		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL		
3. GRADE (1 - 4)	1	1		
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes No 🗖		
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0		
6. Corrective Treatment/Therapy	Yes 🔲 No 🚨	Yes 🔲 No 🗖		
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL	1 Date: LL LLL year 4 D Specify sequelae:		
2= Recovering	2 🗖	2 🗖		
3= Not recovered				
5= Fatal (complete the death report form) 6= Unknown	5 Date of death:	5 Date of death: LL LLL year of death: Say month year		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Control No Cont	Yes No No In Figure 1. No In Figure 1. No In Figure 2. No In Figure 2. No In Figure 2. No In Figure 3. No In F		
	Resulting in death	Resulting in death		
Investigator's name, date of repo	ort and signature: Monitoring repr	esentative's name, date of receipt:		

695 XRP6258 EFC6193 XT

XRP6258 EFC6193	Country No. Centre No. Subje	XT 695 04
Follow-up 15	V 95	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
Г.		
Adverse Event Diagnosis	AE form no:	AE form no:   <b>9</b>   <b>5</b>  - <b>0</b>   <b>8</b>    AE ref. no:   -
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗆	Yes No C
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. Corrective Treatment/Therapy	Yes No D	Yes No C
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	1 Date: LL	Date: LL
8. SERIOUSNESS CRITERIA	Yes  No  - Date event became serious:	Yes  No  No  The second
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	⇒ IF YES	⇒ IF YES
	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event	Resulting in death
Investigator's name, date of repo		esentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatment	nt?

EFC6193 695 XRP6258 XT

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 695 05
FOLLOW-UP 15	V 95	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no:	AE form no: [9 5]-[1][0] AE ref. no: []-[]-
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3 D	1 Date of start: LL
3. GRADE (1 - 4)	1	1
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖	Yes No 🗅
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🔲 No 🖵	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LL year  4 Specify sequelae:	1 Date: LL LL LL year 4 Specify sequelae:
2= Recovering 3= Not recovered 5	2	2
5= Fatal (complete the death report form) 6= Unknown	day month year	day month year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION	Yes No C  - Date event became serious:  IF YES	Yes No Date event became serious:
AND THE SAE COMPLEMENTARY	day month year	day month year

- Tick below all criteria that apply: - Tick below all criteria that apply: Requiring/prolonging hospitalization . . . . .  $\Box$ Requiring/prolonging hospitalization ..... Persistent/significant disability/incapacity  $\dots$ Persistent/significant disability/incapacity . . Congenital anomaly/birth defect . . . . . . . . Congenital anomaly/birth defect . . . . . . . Other medically important event ..... Investigator's name, date of report and signature: Monitoring representative's name, date of receipt:

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 695 | XRP6258 | EFC6193

XRP6258 EFC6193	Country No. Cen	tre No.   Subje	XT	695 Page	06
FOLLOW-UP 15	v 95		See Page 62	<u>.</u>	
ADVERSE EV	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: [9]5 AE ref. no: []	- <u> 1   1  </u>  - <u>                                     </u>	AE form AE ref. no	no: [9][5]-[1][2 o: [][-[]	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		year  ng items in the column)	1  Date of start: 2  (do not comple	day month te the remaining items in	year n the column)
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖵	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖	No 🚨	Yes 🗖	No	
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and rec		3= Dose reduced / 4=	ently discontinued / 2= Delayed and reduced / 5= 2  3  4  4	Interrupted
6. CORRECTIVE TREATMENT/THERAPY	Yes 📮	No 🗖	Yes 🗖	No	
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae		nonth year	1 Date: 4 Specify se	day month equelae:	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	LILI LILILI Jear	2	1: L L day month	year
8. SERIOUSNESS CRITERIA	Yes - Date event be	No	Yes 🔲	No Date event became se	erious:
IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Tick below al  Resulting in death	ation	- T Resulting in death Life-threatening . Requiring/prolong Persistent/signific Congenital anom	day month  ick below all criteria  in  ging hospitalization  ant disability/incapacity aly/birth defect important event	0
Investigator's name, date of rep	ort and signature:	Monitoring repr	esentative's name	, date of receipt:	

XT 695 XRP6258 EFC6193

XRP6258 EFC6193				NO	234	
	Country No.	Centre No.	Subject No.		Page	
FOLLOW-UP 16	V 96		Date of visit	day /	month year	ur
	-		-		See Page 12	
<u> </u>	See Page 278	1				
FOLLOW-UP 16					O.FOLLOWUP_2	
Subject condition (tick "v	✓ one box only	y):				
☐ Alive						
☐ Lost to follow-up						
☐ Dead (complete Death	form)					
Progression						
Has the subject had disea	se progression	? (tick " <b>√</b> " one	box only)			
☐ Unknown						
☐ Previously reported p	rogression					
□ No *						
☐ Yes **						

- \* If **NO**, please complete the Tumor Measurement page, PSA, Pain Intensity Assessment forms.
- \*\* If **YES**, please complete the Tumor Measurement and Symptomatic Deterioration forms, PSA, Pain Intensity Assessment form appropriately.

NO 234 XRP6258 EFC6193

Confidential FINAL 21-May-2008 Sanofi aventis

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
FOLLOW-UP 16	V 96	See Page 279

# POST TREATMENT ANTI-CANCER DRUG THERAPY O.MED\_2

	NONE	Į		Unknown
--	------	---	--	---------

Drug/Regimen/Agent	Start Date	STOP DATE	ONGOING
	Day Month Year	Day Month Year	
1.			٥
2.			
3.			۵
4.			
5.			٥
6.			۰
7.			
8.			۵
9.			
10.			

INO	230	ARF0236	LFC0193
NO	235	XRP6258	EFC6193

XRP6258 EFC6193	Country No.	Centre No.   Subject No.   Page
Follow-up 16	V 96	See Page 26

PSA LABH\_1

DATE OF SAMPLING day month year	TEST	<b>V</b> ALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

NO 236 XRP6258 EFC6193

Location:						
01	Skin	12	Liver	22	Mediastinum	
02	Muscle/Soft Tissue	13	Stomach	23	Uterus	
03	Bone	14	Pancreas	24	Abdomen	
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract	
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis	
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum	
07	Head/Neck	17	Bladder	28	Testis	
80	Esophagus	18	Prostate	29	Thorax	
09	Breast	19	Cervix	29.01	Pleura	
10	Lungs	20.10	Colon	30	Other	
11.0	Regional Lymph Nodes	20.20	Rectum			
11.02	2 Distant Lymph Nodes	21	Adrenal			

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
 2 - Spiral CT
 4 - PET
 7 - Ultrasound
 8 - X-Ray
 10 - Physical Exam
 99 - Other

### \*\*\*Response of Non-Target Codes:

CR - Complete Response IR/SD - Incomplete Response/Stable Disease PD - Progressive Disease

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193		NO 237
	Country No.	Centre No. Subject No. Page
Follow-up 16	V 96	See Page 55

## **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3	LJLJ.LJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5	L. L L. L.	□□□□□□□□□□□□□□□□ Not Done			
6		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
7		□□□□□□□□□□□□□□□□ Not Done			
8		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
9		□□ □□□ □□□□□ □ Not Done			
10	LJLJ.LJ	□□ □□□□□□□□□□□□ Not Done			
11	L_  L_  . L_  L_	□□□□□□□□□□□□□□□□ Not Done			
12	L_  L	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□ □□□□□ □ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

NO 237 , XRP6258 , EFC6193

XRP6258 EFC6193				NO	238	
LI 00193	Country No.	Centre No.	Subject No.		Page	
Follow-up 16	V 96	See	Page 53			

### **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date corresponds to current visit (7 days prior to each follow-up visit)

Date (Day Month Year)	PPI	Analgesic Score
1.	Ш	
2.		
3.		
4		
5.		
7.	Ш	

NO 238 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Cent	tre No. Subje	ct No.	696 Page	01
FOLLOW-UP 16	v 96   [		See Page	62	
ADVERSE EVI	ENT FORM			O.1_AE_1	
1. Adverse Event Diagnosis	AE form no: <b>916</b> AE ref. no: <b>1</b>	- <u> 0   1  </u>   _		orm no:   <b>9   6   - 10</b>     2 ef. no:         -	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	2 (do not complete the remaining	onth year  g items in the column)		day month  mplete the remaining items  nges, nge: day month	year in the column)
3. GRADE (1 - 4)	1	onth year	1 🗖 2	3 🗖	4 🗖
RELATIONSHIP TO STUDY TREATMENT*     ACTION TAKEN WITH     STUDY TREATMENT	Yes			manently discontinued / 2= 4= Delayed and reduced / 5	= Interrupted
6. Corrective Treatment/Therapy	Yes 📮	No 🗖	Yes	□ No	
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: LL LI day n 4 Specify sequelae:	nonth year	1 Date: 4 Specif	day month fy sequelae:	
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	nonth year	2	eath:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event be  The Yes - Date event be  Aday month  Tick below all	No	Yes	No - Date event became s - Date event became s - Tick below all criteric	year
	ation	Resulting in death			
Investigator's name, date of report and signature:  Monitoring representative's name, date of receipt:					
* Is there a reasonable XT 696	possibility that the AE was caus	ed by study treatmer		EFC6193	_

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 696 02
Follow-up 16	v 96 🗆	See Page 62
ADVERSE EVI	ENT FORM	O.1_AE_1
1.  Adverse Event Diagnosis	AE form no: \( \begin{array}{c c c c c c c c c c c c c c c c c c c	AE form no: [9]6]-0]4 AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 4	1 🗆 2 🖸 3 🗖 4 🗖
Action Taken with     Study Treatment*  5. Action Taken with     Study Treatment	Yes No No On the Normal No No No No No No Normal No	Yes No No  0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted  0
6. Corrective Treatment/Therapy	Yes No D	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLL LLLL year 4 Specify sequelae:	1 Date: LL LL LL LL LA year 4 Specify sequelae:
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes ONO ONO ONE Press OF The Pr	Yes □ No □  - Date event became serious:  □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □
Investigator's name, date of repo	Resulting in death	Resulting in death

\* Is there a reasonable possibility that the AE was caused by study treatment?

XT 696 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Subje	XT 696 03
FOLLOW-UP 16	v 96   00	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [9][6]-[0][5] AE ref. no: []-[]-	AE form no: [9] 6]-[0] 6] AE ref. no: []-[]-
2. STATUS OF AE  1= New  2= Ongoing from previous period without change  3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LLLLL LLLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1	1 🗆 2 🖸 3 🗖 4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🗖 No 🗖	Yes 🗖 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗆 No 🗅	Yes No D
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date: LL	1 Date: day month year 4 Specify sequelae:
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes	Yes
Investigator's name, date of repo		esentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?

XT 696 XRP6258 EFC6193

XRP6258 EFC6193 FOLLOW-UP 16	Country No. Cer  V 96	tre No. Subje	XT XT See Page 62	696 Page	04
ADVERSE EVE	ENT FORM			O.1_AE_1	_
1.  Adverse Event  Diagnosis	AE form no: <b>916</b> AE ref. no: <b>1</b>	- <mark> 0_  7</mark>    - _	AE form AE ref. no	no: [ <b>9][6]-[0][8</b>	
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change		nonth year ng items in the column)	1 Date of start: 2 (do not comple	day month te the remaining items i	year
3. GRADE (1 - 4)	1 2 3	4 🗆	1 🔲 2 🖸	3 🗖	4 🗖
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 📮	No 📮	Yes 🗖	No	٥
5. ACTION TAKEN WITH STUDY TREATMENT	d / 2= Delayed duced / 5= Interrupted 4  5	3= Dose reduced / 4=	ently discontinued / 2= I Delayed and reduced / 5	= Interrupted	
6. CORRECTIVE TREATMENT/THERAPY	Yes 🗖	No 🗖	Yes 🔲	No	
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LLL Lday 4 Specify sequelae:	month year	1 Date: 4 Specify se	day month	year
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	Month year	2	:	year
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes - Date event be day month - Tick below al		⇒ IF YES	No late event became s JU UUU Ul Jay month ick below all criteria	year
	Resulting in death Life-threatening Requiring/prolonging hospitaliz Persistent/significant disability/i Congenital anomaly/birth defec	ration	Life-threatening . Requiring/prolong Persistent/significa Congenital anoma	ing hospitalization ant disability/incapacit aly/birth defect mportant event	
Investigator's name, date of repo	ort and signature:	Monitoring repr	esentative's name,	date of receipt:	

XRP6258 | EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 696 05		
FOLLOW-UP 16	v 96	See Page 62		
ADVERSE EVI	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no:	AE form no: [9]6]-[1]0 AE ref. no: []-[]		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay Lay month year 2 (do not complete the remaining items in the column) 3	1 Date of start: LL LLL year 2 (do not complete the remaining items in the column) 3		
3. GRADE (1 - 4)	1	1 2 3 4 4		
RELATIONSHIP TO STUDY TREATMENT*     ACTION TAKEN WITH     STUDY TREATMENT	Yes	Yes		
6. Corrective Treatment/Therapy	Yes No D	Yes 🔲 No 🗖		
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LL LLL year 4 Specify sequelae:	1 Date: U UUU Vear 4 Specify sequelae:		
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2		
8. SERIOUSNESS CRITERIA	Yes	Yes No C - Date event became serious:		
If yes, complete this section and the SAE complementary form	Tick below all criteria that apply:  Resulting in death	Tick below all criteria that apply:  Resulting in death		
		esentative's name, date of receipt:		

XT 696 XRP6258 EFC6193

XRP6258 EFC6193	Country No. Centre No. Sub	XT 696 06		
FOLLOW-UP 16	v 96	See Page 62		
ADVERSE EV	ENT FORM	O.1_AE_1		
1. Adverse Event Diagnosis	AE form no: <b>1916-111</b> AE ref. no: <b>11-11</b>	AE form no: 19161-112  AE ref. no: 11-11		
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL LLL LLL LLL LLL LLL LLL LLL L			
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4		
Action Taken with     Study Treatment*	0= None / 1= Permanently discontinued / 2= Delayed 0= None / 1= Permanently discontinue 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted   3= Dose reduced / 4= Delayed and reduced / 5= Interrupted   3= Dose reduced / 4= Delayed and reduced / 5= Interrupted   3= Dose reduced / 4= Delayed and reduced / 5= Interrupted   3= Dose reduced / 4= Delayed and reduce			
6. Corrective Treatment/Therapy	Yes No 🗖	Yes  No		
7. OUTCOME  1= Recovered  4= Recovered with sequelae  2= Recovering  3= Not recovered  5= Fatal (complete the death report form)  6= Unknown	Date:	4  Specify sequelae:		
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	SERIOUSNESS CRITERIA COMPLETE THIS SECTION HE SAE COMPLEMENTARY FORM  Yes  NO  NO  Yes  No  O  Seriousness  - Date event became serious:  O  Seriousness  - Date event became  - Date e			
Investigator's name, date of rep	Life-threatening	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event  presentative's name, date of receipt:		

XT 696 XRP6258 EFC6193

\* Is there a reasonable possibility that the AE was caused by study treatment?

FC6193	Country No.   Centre No.   Subject No.   Page
END OF STUDY	v 99
END OF STUD	Y O.ENDST_1
Date of end of study*:	day month year
Main reason for stopping	study (tick one box only):
- Completed follow-up pe	eriod
- Adverse event**	
- Death***	
- Poor compliance to pro-	otocol
- Subject lost to follow-up	p
- Other reason	<b>□</b>
If other reason, speci	ify:
, ,	checked only if the subject withdraw his consent and none
	s are present especially adverse event.
Specify:	
эреспу	
	in case of patient lost to follow-up.
* Date of last contact i  ** In case of an adverse	in case of patient lost to follow-up. e event complete the Adverse Event form. mplete the Death form.
* Date of last contact is  ** In case of an adverse  *** In case of death, con  "I, the undersigned, certif	e event complete the Adverse Event form.
* Date of last contact is  ** In case of an adverse  *** In case of death, con  "I, the undersigned, certif  To the best of my knowle	the event complete the Adverse Event form.  Implete the Death form.  If y that I have carefully examined all entries on the CRF for this subject.
* Date of last contact is  ** In case of an adverse  *** In case of death, con  "I, the undersigned, certif  To the best of my knowle	re event complete the Adverse Event form.  Implete the Death form.  If y that I have carefully examined all entries on the CRF for this subject. edge, all information is correct."  Date:

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	551 Page	01
Visit 99	V 99		Se	e Page 60	)	

# CONCOMITANT MEDICATION O.MED\_9

☐ NONE

Tick the box if no medication(s) has been taken concomitantly with study drug.

	Medication	Start Date	End Date
		Day Month Year	Day Month Year
1.		Ongoing	Ongoing
2.		Ongoing	Ongoing
3.		Ongoing	Ongoing
4.		Ongoing	Ongoing
5.		Ongoing	Ongoing
6.		Ongoing	Ongoing
7.		Ongoing	Ongoing
8.		Ongoing	Ongoing
9.		Ongoing	Ongoing
10.		Ongoing	Ongoing

XT	551	XRP6258	EFC6193
Confid	ential = FINIAL = 21 NOV 2006	san	ofi aventis

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	551 Page	02
VISIT 99	V 99		See	Page 60	0	

# CONCOMITANT MEDICATION O.MED\_9

	MEDICATION	START DATE END DATE			E		
		Day	Month	Year	Day	Month	Year
1.			□ Ongoir			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
2.			⊔⊔⊔ ∟ □ Ongoir			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
3.			□□□□□□□ □□ Ongoir			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
4.			⊔⊔⊔ ∟ □ Ongoir			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
5.			⊔∟∟ □ Ongoir			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
6.			□□□□□□□ □□□□□□□□□□□□□□□□□□□□□□□□□□□□□		□□ □□□ □□□□□ □ Ongoing		
7.			□ Ongoir		Ongoing		
8.			□□□□□□□ □□□□□□□□□□□□□□□□□□□□□□□□□□□□□			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
9.			□ Ongoir			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	
10.			□ Ongoir			□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	551 Page	
Visit 99	V 99		See	Page 60	)	

# CONCOMITANT MEDICATION O.MED\_9

	Medication	START DATE	END DATE	
		Day Month Year	Day Month Year	
1.		Ongoing	Ongoing	
2.		Ongoing	Ongoing	
3.		Ongoing	Ongoing	
4.		Ongoing	Ongoing	
5.		Ongoing	Ongoing	
6.		Ongoing	Ongoing	
7.		Ongoing	Ongoing	
8.		Ongoing	Ongoing	
9.		Ongoing	Ongoing	
10.		Ongoing	Ongoing	

				EGO	ofi aventic
_	XT	551	I	XRP6258	EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	651 Page	01
Visit 99	V 99		See	Page 24		

# **ADDITIONAL HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10 <sup>9</sup> /L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

XT 651 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	651 Page	02
Visit 99	V 99		See F	Page 24	]	

# **ADDITIONAL HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

XT 651 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	651 Page	
Visit 99	V 99		See	Page 24		

# **ADDITIONAL HEMATOLOGY**

LABH\_1

Date of sampling:			
	day	month	year

TEST	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
WBC		10°/L	
RBC		10 <sup>6</sup> /mm <sup>3</sup>	
Neutrophils		10°/L	
Eosinophils		10°/L	
Basophils		10°/L	
Monocytes		10°/L	
Lymphocytes		10°/L	
Platelets		10°/L	
Hemoglobin		g/dL	

XT 651 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	652 Page	01
Visit 99	V 99		See	Page 2	5	

# **ADDITIONAL BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

652 XRP6258 EFC6193 XT

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	652 Page	02
VISIT 99	V 99		See I	Page 25	]	

# **ADDITIONAL BIOCHEMISTRY**

LABB\_1

Date of sampling:			
	day	month	year

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

XT 652 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	652 Page	
Visit 99	V 99		See	Page 25		

## **ADDITIONAL BIOCHEMISTRY**

LABB\_1

Date of sampling:			
. 0	day	month	year

Теѕт	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Sodium		mmol/L	
Potassium		mmol/L	
SGOT (AST)		U/L	
SGPT (ALT)		U/L	
Alkaline phosphatase		U/L	
Total bilirubin		mg/dL	
BUN		mg/dL	
Creatinine		mg/dL	
Glucose		mg/dL	
Chloride		mmol/L	
Bicarbonate		mmol/L	

XT 652 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	653 Page	01
Visit 99	V 99		See Page	<mark>25</mark>	

# REPEATED TESTOSTERONE LABB\_1 Date of sampling: Labb\_1 Labb\_1

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Testosterone		ng/dL	

XT 653 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	653 Page	02
Visit 99	V 99		See Page 2	<b>5</b>	

REPEATE	D TESTOSTERONE	LABB_1
Date of sampling:	day month year	

Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Testosterone		ng/dL	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	653 Page	
Visit 99	V 99		See Page 25	5	

REPEATE	D TESTOSTERONE	LABB_1
Date of sampling:	day month year	

Test	<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
Testosterone		ng/dL	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	654 Page	01
Visit 99	V 99		See I	Page 26	7	

# **REPEATED PSA**

LABH\_1

DATE OF SAMPLING TEST  day month year		<b>VALUE</b> (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

XT 654 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	654 Page	02
Visit 99	V 99		See I	Page 26		

# **REPEATED PSA**

LABH\_1

DATE OF SAMPLING day month year	Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	T 654	
VISIT 99	V 99		See Page	<del>2</del> 26	

# **REPEATED PSA**

LABH\_1

DATE OF SAMPLING day month year	Test	VALUE (MD if not done)	Unit	IF OTHER UNIT, SPECIFY
	PSA		ng/mL	

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	661 Page		01
Visit 99	V 99		See	Page 28	]		
							$\Box$
REPEATED ECC	3					ECG_1	
• Date performed: LLLLL LLL day month year							
• ECG: Normal	A	Abnormal* 🗖					
If abnormal, specify:							

\* If clinically relevant, please report on appropriate form.

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	661 Page		02	
Visit 99	V 99		See	Page 28	]			
REPEATED ECC	REPEATED ECG_1							
• Date performed: LLL L	month	<b></b> year						
• ECG: Normal	Д	Abnormal* 🗖						
If abnormal, specify:								

<sup>\*</sup> If clinically relevant, please report on appropriate form.

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	661 Page		
Visit 99	V 99		See	Page 28	]		
REPEATED ECG							
• Date performed: L_L_L L_day	month	year					
• ECG: Normal	A	Nbnormal* 🗖					
If abnormal, specify:							

\* If clinically relevant, please report on appropriate form.

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	Г 662 <sub>Раде</sub>	01
Visit 99	V 99		See Pa	age 29	

#### REPEATED ECHOCARDIOGRAPHY ECHOCARD\_1

• 2D-Echocardiography: Normal □ Abnormal\* □

- Left ventricular ejection fraction (LVEF)

- Lower Limit Normal of LVEF

XT 662 XRP6258 EFC6193

<sup>\*</sup> If clinically relevant, please report on appropriate form.

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	662 Page	02
Visit 99	V 99		Sec	e Page 29	· · · · · · · · · · · · · · · · · · ·	

## REPEATED ECHOCARDIOGRAPHY ECHOCARD\_1

• 2D-Echocardiography: Normal  $\square$  Abnormal\*  $\square$ 

- Left ventricular ejection fraction (LVEF)

- Lower Limit Normal of LVEF

 XT
 662
 XRP6258
 EFC6193

 Confidential ■ FINAL ■ 21-NOV-2006
 sanofi aventis

<sup>\*</sup> If clinically relevant, please report on appropriate form.

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	662 Page	
Visit 99	V 99		See P	age 29	1	

## REPEATED ECHOCARDIOGRAPHY ECHOCARD\_1

• Date performed: LLLLL LLLL wonth year

• 2D-Echocardiography: Normal ☐ Abnormal\* ☐

- Left ventricular ejection fraction (LVEF)

- Lower Limit Normal of LVEF

\* If clinically relevant, please report on appropriate form.

XT 662 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	663 Page	01
Visit 99	V 99		See	Page 29	1	

## RADIONUCLIDE VENTRICULOGRAPHY

MUGA\_1

•	Date performed:			
		day	month	year

- Radionuclide Ventriculography: Normal  $\square$  Abnormal\*  $\square$
- Left ventricular ejection fraction (LVEF)
- Lower Limit Normal of LVEF
- \* If clinically relevant, please report on the Adverse Event form.

XT 663 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	663 Page	02
Visit 99	V 99		See	Page 2	9	

#### RADIONUCLIDE VENTRICULOGRAPHY

MUGA\_1

•	Radionuclide Vei	ntriculo	graphy: N	Normal $\square$	Abnormal* 🗖
		day	month	year	
•	Date performed:				

- Left ventricular ejection fraction (LVEF)
- Lower Limit Normal of LVEF
- \* If clinically relevant, please report on the Adverse Event form.

XT 663 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	663 Page	
Visit 99	V 99		See	Page 2	9	

## RADIONUCLIDE VENTRICULOGRAPHY

MUGA\_1

•	Date performed:			
	•	day	month	year

- Radionuclide Ventriculography: Normal  $\square$  Abnormal\*  $\square$
- Left ventricular ejection fraction (LVEF)
- Lower Limit Normal of LVEF
- \* If clinically relevant, please report on the Adverse Event form.

XT 663 | XRP6258 | EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	664 Page	01
Visit 99	V 99		See P	Page 53	]	

## **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date (Day Month Year)	PPI	Analgesic Score
1.	Ш	
2.		
3.		
4		
5.		
6.	Ш	
7.		

XT 664 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.		64 02
Visit 99	V 99		See Pa	nge 53	

## **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		
3.	<u></u>	
4		
5.		
6.		
7		

XT 664 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	664 Page	
Visit 99	V 99		See P	age 53	]	

## **PAIN INTENSITY ASSESSMENT**

PAINVAS1

Date (Day Month Year)	PPI	Analgesic Score
1.		
2.		
3.		
4		
5.		
6.		
7	Ш	

XT 664 , XRP6258 , EFC6193

Loca	tion:				
01	Skin	12	Liver	22	Mediastinum
02	Muscle/Soft Tissue	13	Stomach	23	Uterus
03	Bone	14	Pancreas	24	Abdomen
04	Bone Marrow	15	Kidneys	25	Gastrointestinal Tract
05	Peripheral Blood Stream	16	Ovaries	26	Pelvis
06	Brain/CNS	16.01	Fallopian Tubes	27	Peritoneum
07	Head/Neck	17	Bladder	28	Testis
80	Esophagus	18	Prostate	29	Thorax
09	Breast	19	Cervix	29.01	Pleura
10	Lungs	20.10	Colon	30	Other
11.01	Regional Lymph Nodes	20.20	Rectum		
11.02	2 Distant Lymph Nodes	21	Adrenal		

#### \*\* METHOD OF MEASUREMENT CODES:

1 - CT Scan
2 - Spiral CT
4 - PET
7 - Ultrasound
8 - X-Ray
10 - Physical Exam
99 - Other

#### \*\*\*Response of Non-Target Codes:

NL - New Lesion NE - Not Evaluable

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	665 Page	01
Visit 99	v 99		See	Page 55		

## **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.I.I.I.I.I.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
3		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4	LJLJ.LJLJ	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
5		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
6		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
7		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
8		□□ □□□ □□□□ □ Not Done		LJLJ mm	
9		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
10	L	□□□□□□□□□□□□□□□□□ Not Done		L_ L_  mm	
11		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
12	L  L	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
13		□□ □□□ □□□□□ □ Not Done			
14		□ Not Done			

XT 665 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	665 Page	02
Visit 99	V 99		See	Page 5		

## **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ Not done

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□ Not Done			
3		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
4	LJLJ.LJLJ	□□□□□□□□□□□□□□□□ Not Done			
5		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		LJLJ mm	
6		□□□□□□□□□□□□□□□□□ Not Done			
7	LJLJ.LJ	□□ □□□□□□□□□□□□□□ Not Done			
8	L.I.L.I.L.I	□□□□□□□□□□□□□□□□ Not Done		LJLJ mm	
9		□□ □□□ □□□□□ □ Not Done			
10	L.L.	□□□□□□□□□□□□□□□□□ Not Done			
11	L.I.L.I.L.I	□□□□□□□□□□□□□□□□□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13	L.L.	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
14	<u> </u>	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		mm	

XT 665 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	665 Page	
Visit 99	V 99		See Page 55		

### **TUMOR MEASUREMENTS**

O.ASSESS\_3

■ NOT DONE

LESION NUMBER	LOCATION SITE*	<b>DATE OF ASSESSMENT</b> Day Month Year	METHOD OF MEASUREMENT**	MEASUREMENT OF TARGET LESION: longest diameter	RESPONSE OF NON-TARGET LESIONS***
1	L.I.L.I.L.I	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
2		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
3		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□		L L  mm	
4	L	□□ □□□ □□□□□ □ Not Done			
5		□ Not Done			
6		□ Not Done			
7		□ Not Done			
8		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
9		□□ □□□□□□□□□□□□□ Not Done			
10	L]L].L]L]	□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			
11		□ Not Done			
12	L.I.L.I.L.I	□□ □□□ □□□□□ □ Not Done			
13		□□ □□□□□□□□□□□□□ Not Done			
14		□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□			

XT 665 XRP6258 EFC6193

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	666 Page	`
Visit 99	V 99					
SYMPTOMATIC	: DETER	RIORAT	rion		O.SYMPTO 1	
Was there symptomatic de		Yes 🗖	No 🗖			
If yes, date: ニロニニ	JLJ LJLL nth year					

NO 666 XRP6258 EFC6193

/ <u>^</u>	Country No. Centre No.	Subject No. Pag	ge		
/ISIT 99	V 99 LLL				
	NOT SUBMITT	ED	_		
PHARMACOKINETIC - BLOOD SAMPLING (SCHEDULE 1) PK_1					
NOT APPLIC	CABLE				
SAMPLE	THEORETICAL	SAMPLE DATE	SAMPLE TIM		
ID	TIME	day month year	24 hour clock		
P00	Prior to Infusion of XRP6528				
P01	30 minutes before end of infusion				
P02	5 minutes post end of Infusion				
P03	1 hour post end of infusion				
P04	6-10 hours post end of infusion		<u> </u>		
P04 P05	6-10 hours post end of infusion  24-72 hours post end of infusion				
P05	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI		LJLJ : LJL		
PHARMAC	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI	PLING (SCHEDULE 2	2) <i>PK_1</i>		
PHARMACO NOT APPLIC	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL	PLING (SCHEDULE 2	PK_1  SAMPLE TIM 24 hour clock		
PHARMACO NOT APPLIC	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME	PLING (SCHEDULE 2  SAMPLE DATE day month year	SAMPLE TIM 24 hour clock		
PHARMACO NOT APPLICE SAMPLE ID P00	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528	PLING (SCHEDULE 2  SAMPLE DATE day month year	SAMPLE TIM 24 hour clock		
PHARMACO NOT APPLICATION POO PO1	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock		
PHARMACO NOT APPLICE SAMPLE ID P00 P01 P02	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion	SAMPLE DATE day month year	2) <i>PK_1</i> SAMPLE TIM 24 hour clock  LILL: LIL  LILL: LIL  LILL: LIL  LILL: LIL		
PHARMACO NOT APPLICATION POO PO1 PO2 PO3	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion  2 hours post end of infusion	SAMPLE DATE day month year	SAMPLE TIM		

FC6193	Country No. Centre No.	Subject No.   Pat			
/ISIT	99 v 99 LLL				
	NOT SUBMITT	ED	_		
PHARMACOKINETIC - BLOOD SAMPLING (SCHEDULE 1) PK_1					
☐ Not	Applicable				
SAMPLE ID	THEORETICAL TIME	SAMPLE DATE  day month year	SAMPLE TIMI 24 hour clock		
P00	Prior to Infusion of XRP6528				
P01	30 minutes before end of infusion				
P02	5 minutes post end of Infusion				
P03	1 hour post end of infusion				
	•				
P04	6-10 hours post end of infusion				
P04	6-10 hours post end of infusion  24-168 hours post end of infusion				
	6-10 hours post end of infusion  24-168 hours post end of infusion				
P05			PK_1		
PHARN NOT	24-168 hours post end of infusion  ACOKINETIC - BLOOD SAMF  APPLICABLE  THEORETICAL	PLING (SCHEDULE 2	PK_1  SAMPLE TIMI 24 hour clock		
PHARM Not SAMPLE ID	24-168 hours post end of infusion  MACOKINETIC - BLOOD SAME  APPLICABLE  THEORETICAL  TIME	PLING (SCHEDULE 2  SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock		
PHARN Not SAMPLE ID P00	24-168 hours post end of infusion  MACOKINETIC - BLOOD SAMF  APPLICABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock		
PO5 PHARM Not SAMPLE ID P00 P01	24-168 hours post end of infusion  MACOKINETIC - BLOOD SAME  APPLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion	SAMPLE DATE day month year	SAMPLE TIME 24 hour clock  LILL: LILL  LILL: LILL		
POS PHARN NOT SAMPLE ID P00 P01 P02	24-168 hours post end of infusion  MACOKINETIC - BLOOD SAMF  APPLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion	SAMPLE DATE day month year	2) <i>PK_1</i> SAMPLE TIMI 24 hour clock		
PO5 PHARN Not SAMPLE ID P00 P01 P02 P03	24-168 hours post end of infusion  MACOKINETIC - BLOOD SAME  APPLICABLE  THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  10 minutes post end of Infusion  2 hours post end of infusion	SAMPLE DATE day month year	2) <i>PK_1</i> SAMPLE TIME 24 hour clock  LILL: LILL  LILL: LILL  LILL: LILL  LILL: LILL  LILL: LILL		

/ISIT 99	v 99   LLL				
	NOT SUBMIT	TED .	-		
PHARMACOKINETIC - BLOOD SAMPLING (SCHEDULE 3) PK_1					
NOT APPLIC			ı		
SAMPLE ID	THEORETICAL TIME	SAMPLE DATE  day month year	SAMPLE TIMI 24 hour clock		
P00	Prior to Infusion of XRP6528				
P01	30 minutes before end of infusion				
P02	20 minutes post end of Infusion				
P03	3 hours post end of infusion		<u> </u>		
			1		
P04	10-14 hours post end of infusion				
P04 P05	10-14 hours post end of infusion 24-72 hours post end of infusion				
P05	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI				
PHARMAC NOT APPLIC	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI	PLING (SCHEDULE 4	<b>L)</b> PK_1		
PHARMAC	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI		<b>L</b> ) PK_1		
PHARMACO NOT APPLIC	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL	PLING (SCHEDULE 4	SAMPLE TIMI 24 hour clock		
PHARMACO NOT APPLICATION	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME	PLING (SCHEDULE 4  SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock		
PHARMACO NOT APPLIC SAMPLE ID P00	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock		
PHARMACO NOT APPLICE SAMPLE ID P00 P01	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock  LILL: LILL  LILL: LILL		
PHARMACO NOT APPLIC SAMPLE ID P00 P01 P02	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion	SAMPLE DATE day month year	SAMPLE TIMI 24 hour clock  LILL: LILL  LILL: LILL  LILL: LILL		
PHARMACO NOT APPLICATE ID P00 P01 P02 P03	24-72 hours post end of infusion  OKINETIC - BLOOD SAMI  CABLE  THEORETICAL  TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion  4 hours post end of infusion	SAMPLE DATE day month year  LILL LILL LILL LILL LILL LILL LILL LI	SAMPLE TIME 24 hour clock  LILL: LILL  LILL: LILL  LILL: LILL		

	Country No. Centre No.		8 .01 0
Visit 99	v 99		
	NOT SUBMITT	ED	-
_	COKINETIC - BLOOD SAME	PLING (SCHEDULE :	<b>3)</b> PK_1
NOT APP		CAMBLE DATE	SAMPLE TIM
ID	THEORETICAL TIME	SAMPLE DATE day month year	24 hour clock
P00	Prior to Infusion of XRP6528		
P01	30 minutes before end of infusion		
P02	20 minutes post end of Infusion		
P03	3 hours post end of infusion		
P04	10-20 hours post end of infusion		
P05	24-168 hours post end of infusion		
		1	1
☐ NOT APP		·	
_		SAMPLE DATE day month year	SAMPLE TIM
NOT APP	PLICABLE	SAMPLE DATE	SAMPLE TIM 24 hour clock
SAMPLE ID	PLICABLE  THEORETICAL  TIME	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock
SAMPLE ID P00	THEORETICAL TIME  Prior to Infusion of XRP6528	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock
SAMPLE ID P00	THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock  LJL: LJL  LJL: LJL
SAMPLE ID P00 P01 P02	THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock  LILL: LILL  LILL: LILL  LILL: LILL
SAMPLE ID P00 P01 P02 P03	THEORETICAL TIME  Prior to Infusion of XRP6528  10 minutes before end of infusion  30 minutes post end of Infusion  4 hours post end of infusion	SAMPLE DATE day month year	SAMPLE TIM 24 hour clock  LILI: LIL  LILI: LIL  LILI: LIL  LILI: LIL  LILI: LIL

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	<b>701</b> Page	01
Visit 99	V 99					

### OTHER PROCEDURES

O.PROCEDUR\_1

	Procedure	DATE PE	RFORMED	Reason
		Day Month	Year	
1.				
2.				
3.				
4.				
5.				
6.				
7.				
8.				
9.				
10.				

XT	701	XRP6258	EFC6193
Confid	optiol ■ FINIAL ■ 21 NOV 2006	san	ofi aventis

XRP6258 EFC6193				XT	701	02
	Country No.	Centre No.	Subject No.	1	Page	,
Visit 99	V 99		Se	ee Page	511	

### **OTHER PROCEDURES**

O.PROCEDUR\_1

	Procedure	Date Performed	Reason
<u> </u>		Day Month Year	
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	XT	<b>701</b> Page	
Visit 99	V 99		See	Page 51	1	

### **OTHER PROCEDURES**

O.PROCEDUR\_1

	Procedure	Date Performed	Reason
		Day Month Year	
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			

	·	Mac rooms	ofi aventis
XT 7	· 01	XRP6258	EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	XT 699
Visit 99	v 99	See Page 62
ADVERSE EV	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: [9] 9-0 1 AE ref. no:	AE form no: [9]9]-[0]2  AE ref. no: []-[]
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: LLL LLL Lyear 2 (do not complete the remaining items in the column) 3	1 Date of start: LLL LLL year 2 (do not complete the remaining items in the column) 3
3. GRADE (1 - 4)	1 2 3 4 4	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes 🔲 No 🗖	Yes No No
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0 1 2 3 4 5 5
6. Corrective Treatment/Therapy	Yes No No	Yes No 🗆
7. OUTCOME 1 = Recovered 4 = Recovered with sequelae	1 Date: U U U Vear  4 Specify sequelae:	1 Date: LL LLL LLL LLL LLL LLL LLL LLL LLL LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown	2	2
8. SERIOUSNESS CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	Yes No Company No Comp	Yes No No In Figure 1. No In Figure 1. No In Figure 2. No In F
	Resulting in death	Resulting in death  Life-threatening  Requiring/prolonging hospitalization  Persistent/significant disability/incapacity  Congenital anomaly/birth defect  Other medically important event
Investigator's name, date of repo	ort and signature: Monitoring repr	resentative's name, date of receipt:
* Is there a reasonable	possibility that the AE was caused by study treatmer	nt?

XT 699 , XRP6258 , EFC6193

XRP6258 EFC6193	Country No.   Centre No.   Subje	Tot No.   XT 699 OF Page
Visit 99	v 99	See Page 62
ADVERSE EVE	ENT FORM	O.1_AE_1
1. Adverse Event Diagnosis	AE form no: LLL-LLL	AE form no: LLL-LLL AE ref. no: LLL-LLL
2. STATUS OF AE 1= New 2= Ongoing from previous period without change 3= Ongoing with change	1 Date of start: Lay	1 Date of start: L L L L L L L L L L L L L L L L L L L
3. GRADE (1 - 4)	1 🔲 2 🔲 3 🔲 4 🔲	1 2 3 4 4
4. RELATIONSHIP TO STUDY TREATMENT*	Yes No 🗆	Yes 🗖 No 🗖
5. ACTION TAKEN WITH STUDY TREATMENT	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0	0= None / 1= Permanently discontinued / 2= Delayed 3= Dose reduced / 4= Delayed and reduced / 5= Interrupted 0
6. CORRECTIVE TREATMENT/THERAPY	Yes No D	Yes No D
7. OUTCOME 1= Recovered 4= Recovered with sequelae	1 Date: LIL LIL year 4 Specify sequelae:	1 Date: LL
2= Recovering 3= Not recovered 5= Fatal (complete the death report form) 6= Unknown  8. SERIOUSNESS CRITERIA	2	2
CRITERIA  IF YES, COMPLETE THIS SECTION AND THE SAE COMPLEMENTARY FORM	- Date event became serious:  - Date event became serious:  - Tick below all criteria that apply:  Resulting in death	- Date event became serious:  - Date
Investigator's name, date of repo	Congenital anomaly/birth defect	Congenital anomaly/birth defect

XT 601 , XRP6258 , EFC6193

XRP6258 EFC6193	Country N	lo.   Centre No.	Subject No.	XT	631 Page	01
Visit 99	V 99					
	NO	T SUBMITTEI				
SAE CO	MPLEMENTA	RY FOR	M 1/2	O.SAEC_	1	
AE FORM NO.:	_					
	IC INFORMATION	-	ce:		DI I	
Date of birth: _	day month	year As	ian, Oriental	<b>_</b> <b>_</b> - <i>t</i> /	Black Other	
-				other, spec		
	male ☑ fe SCRIPTION OF THE SERI	_	ight: ШШШ с	vveign		кд
<b>3.</b> DATE OF STAR	RT OF EVENT: L	month year				
<b>4. STUDY TREAT</b> First administra	MENT tion of study treatment:	day month	year			
	Last Administra Before SAE	,	Last dosage Before SAE	Action taken*	New Dos (dose redu	U
XRP6258			mg/m²/cyc	le 🔲		g/m²/cycle
Mitoxantrone			mg/m²/cyc	le 🔲		g/m²/cycle
Prednisone $0 = \text{None}  1 = \text{Po}$	ermanently discontinued		mg  Dose reduced 4	= Delayed/re	educed 5 = I	g nterrupted
5. IN CASE OF H	OSPITALIZATION hospita	al report to be sent				
Date of admissi	on:	year				
<b>6.</b> IN CASE OF D	EATH Autopsy report	: Yes	(copy to be ser	nt)	No 🗖	
					_	

(RP6258 EFC6193	Country No	). [] o.   Cer	ntre No. Subject	No. XT	632 Page	0
Visit 99	V 99			NOT SU	BMITTED	)
	'					
SAE COMP	PLEMENTA	RY F	ORM 2	<b>2/2</b> o.	SAEC_1.1	
'. CORRECTIVE TR	REATMENT/THERAF	γ				
				(Releva	nt CRF page	can be faxed
. PREVIOUS AND	CONCOMITANT A	MEDICAT	IONS:			
DELEVANT MEDI	ICAL HISTORY AN		OMITANIT DISEA		nt CRF page	can be faxed
. KELEVANI MEDI	CAL HISTORY AIN	D CONC	OMITANT DISEA	ASES:		
				(Releva	nt CRF page	can be faxed
	E DISEASE					
					nown 🔲	
Is this SAE related to	o progression of the c	ancer?		☐ Unkr		П
Is this SAE related to	Lymph nodes	ancer?	Peritoneum	Unkr	Brain	
Is this SAE related to  If Yes: Local  Liver  Liver	Lymph nodes Bone		Peritoneum Lung	Unkr		
Is this SAE related to	Lymph nodes		Peritoneum Lung	Unkr		
If Yes: Local  Liver	Lymph nodes Bone		Peritoneum Lung	Unkr		

XRP6258 EFC6193	Country No.	Centre No.	XT 641	01
<b>V</b> ISIT <b>99</b>	V 99		NOT SUBMITT	ED

### SAE FOLLOW-UP FORM 0.SAEF\_1

# PROVIDE THE SPONSOR BY FAX WITH ALL ADDITIONAL INFORMATION INCLUDING AE FORM IF UPDATED

E For	:м No.: []	
1.	SERIOUS ADVERSE EVENT (diagnosis):	
2.	DATE OF THE EVALUATION: Light	month year
3.	NEW RELEVANT INFORMATION ADDEE	O TO INITIAL REPORT(S):
nvesti	gator's name, date of report and signature:	Monitoring representative's name, date of receipt:
_	YT 6/1	YRP6258 FEC6103 -

XRP6258 EFC6193		Country No. Cent	re No.   Subject No.	XT 631	02
VISIT 99	V	99			
		NOT SUBMIT	ITED		
SAE COI	MPLEME	NTARY F	ORM 1/2	O.SAEC_1	
AE FORM NO.:					
1. DEMOGRAPH			Race:	<b>」</b> Bla	alı 🗖
	day month	year	Asian, Oriental	Oth	her 🔲
	 male ☑	female 🔲	Height: LLL cr		
		HE SERIOUS ADVE			
	lementary investiga		COL LIVEIVI		
<b>3.</b> DATE OF STAI		day month	year		
<b>4.</b> STUDY TREAT	MENIT				
First administra	tion of study treat	ment:	onth year		
		ministration	Last dosage		ew Dosage
	day month	ore SAE year	Before SAE	taken* (dos	se reduced)
XRP6258	,		□□□ mg/m²/cycl	е Ц ЦЦ	mg/m²/cycle
Mitoxantrone			□□□ mg/m²/cycle	е Ц ЦЦ	☐ mg/m²/cycle
Prednisone			∟∟∟ mg		Ll mg
0 = None  1 = P	ermanently disconti	nued 2 = Delayed	3 = Dose reduced 4	= Delayed/reduced	5 = Interrupted
<b>5.</b> IN CASE OF H	OSPITALIZATION	I hospital report to be	sent		
Date of admissi	on:		1		
Date Of duffilss		nonth year	_		
<b>6.</b> IN CASE OF D	EATH Autopsy	y report:	Yes (copy to be sent	t) No 🗖	l
<u> </u>	631		XRP6258	EFC6193	
- • •				_ =: = = : = 3	

XRP6258 EFC6193	Country No	Ce	ntre No. Subject N	XT	632 Page	02
Visit 99	v 99					
	NOT	SUBM	ITTED			
SAE COM	PLEMENTA	RY F	ORM 2	<b>2/2</b> 0.9	SAEC_1.1	
7. CORRECTIVE T	REATMENT/THERAP	Y				
				(Relevai	nt CRF page	e can be faxed)
8. PREVIOUS AN	D CONCOMITANT A	<b>MEDICAT</b>	IONS:			
<b>0</b> DELEVANIT ME	NCAL LUCTORY AND	CONC	OMITANIT DISEA		nt CRF page	e can be faxed)
9. KELEVANI MEI	DICAL HISTORY ANI	CONC	OMITANT DISEA	SES:		
				(Relevai	nt CRF page	e can be faxed)
10. STATUS OF T						<u> </u>
_	to progression of the ca	ancer?		☐ Unkn		
If Yes: Local Liver	Lymph nodes Bone		Peritoneum		Brain	u
Other $\Box$	Бопе		Lung	_		
						<del></del>
	000		VDD0050		FF00400	_
XT	632		XRP6258	<u> </u>	EFC6193	<u> </u>

XRP6258 EFC6193				XT	641	02
21 00 100	Country No.	Centre No.	Subject No.		Page	
Visit 99	V 99		NO	T SUB	MITTED	

### SAE FOLLOW-UP FORM 0.SAEF\_1

## PROVIDE THE SPONSOR BY FAX WITH ALL ADDITIONAL INFORMATION INCLUDING AE FORM IF UPDATED

	INCLUDING AE FORM IF UPDATED							
AE Fo	rm No.:							
1.	SERIOUS ADVERSE EVENT (diagnosis):							
2.		month year						
3.	NEW RELEVANT INFORMATION ADDED	TO INITIAL REPORT(3).						
Inves	igator's name, date of report and signature:	Monitoring representative's name, date of receipt:						
	YT 6/1	YRP6258 FFC6103						

XRP6258 EFC6193	ı	Country No.	Centre	No.	Subject No.	l	ΚΤ	631 Page	
Visit 99		v 99							
		NOT SU	<mark>JBMIT</mark>	TED					_
SAE COI	MPLEME	ENTAR	Y FC	RM	1/	2	O.SAEC	_1	
E FORM NO.:									
	IC INFORMATION AND ADMINISTRATION AND ADMINISTRATIO			Race: Cauca Asian		☐ ☐ If oth	ner, spe	Black Othe cify:_	r $\overline{\square}$
Ü	nale <b>☑</b>	female		Heigh	t: ШШL	J cm	Weig	ht: ШШL	⊥. L⊥ kg
3. DATE OF STAF		day month		year	1				
First administra	tion of study tre	atment: day			year				
		dministration efore SAE	ar		t dosage fore SAE		Action taken*	_	Dosage reduced)
XRP6258					mg/m²,	cycle/			」 mg/m²/cycle
Mitoxantrone					mg/m²/	cycle/			□ mg/m²/cycle
Prednisone $0 = \text{None}  1 = P$	ermanently disco		L L Delayed		mg se reduced	4 =	Ll Delayed/	reduced 5	」 mg 5 = Interrupted
<b>5.</b> IN CASE OF H	OSPITALIZATIC	N hospital repo	ort to be s	sent					
Date of admissi	on: LLL L	month	year						
<b>6.</b> IN CASE OF D	<b>EATH</b> Autoբ	osy report:		Yes 🗖	(copy to be	sent)		No 🗖	
<u></u>	631			XF	RP6258		EF	C6193	

XRP6258 EFC6193	Country No	o. Cer	ntre No.	Subject No.	XT	632 Page	
Visit 99	v 99						
	NOT	SUBMI	TTED				_
SAE COMP	LEMENTA	RY F	ORM	2/2	O.S.	AEC_1.1	
7. CORRECTIVE TR	EATMENT/THERA	PΥ					
					(Relevan	nt CRF page	can be faxed)
<b>8.</b> PREVIOUS AND	CONCOMITANT A	MEDICAT	IONS:				
9. RELEVANT MEDI	CAL HISTORY AN	D CONC	OMITANI			t CRF page	e can be faxed,
	0,12,11101,0111,711,1	2 00.10		2102/1020			
					(Relevan	nt CRF page	can be faxed
<b>10. STATUS OF TH</b> Is this SAE related to	E DISEASE  o progression of the c	eancer?	Yes $\square$	No 🗖	Unkne	own 🗖	
If Yes: Local	Lymph nodes		Periton			Brain	
Liver $\Box$	Bone		Lung				
Other 🗖							
XT 6	532		, XF	RP6258	, 1	EFC6193	_
	■ FINAL ■ 21-NOV					ventis	

XRP6258 EFC6193				XT	641	
LI 00133	Country No.	Centre No.	Subject No.		Page	
Visit 99	V 99		NOT	SUBI	MITTED	

### SAE FOLLOW-UP FORM 0.SAEF\_1

## PROVIDE THE SPONSOR BY FAX WITH ALL ADDITIONAL INFORMATION INCLUDING AE FORM IF UPDATED

-	SERIOUS ADVERSE EVENT (diagnosis):							
•	DATE OF THE EVALUATION: Lay	month year						
	NEW RELEVANT INFORMATION ADDED	TO INITIAL REPORT(S):						
est	igator's name, date of report and signature:	Monitoring representative's name, date of receipt:						

XRP6258 EFC6193	Country No.	Centre No.	Subject No.	NO	999 Page					
Visit 99	V 99									
DEATH			O.DEATH_1							
Date of death: LLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLLL										
<b>Reason for death</b> (tick "✓" one box only):										
☐ Progression										
☐ Adverse event										
☐ Other	Specify:									

NO 999 XRP6258 EFC6193