

Neo-Adjuvant Lapatinib and/or Trastuzumab Treatment Optimisation

### CASE REPORT FORM

Protocol number BIG 1-06 / EGF 106903

Amended survival follow-up from Protocol Amendment 4 Approval

Centre No.			
Subject No.			

Protocol number BIG 1-06 / EGF106903 Centre No. Page 205 Subject No. **Patient status** During a standard of care visit ■ Not Done Date of patient's status evaluation (phone call or standard of care visit) Are there any changes from last patient status?  $\square$  No  $\longrightarrow$  Please sign and date at the bottom of the page ☐ Yes → Specify below and sign and date at the bottom of the page Changes Recurrence of disease (complete the next page "Event and radiological examinations") ☐ Second primary malignancy or contralateral breast cancer (complete the next page "Event and radiological examinations") ☐ Death (complete the "Death" section below) ☐ Lost to follow-up → Date of last contact (or date L study consent withdrawn) □ Patient withdrew study consent (For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive. The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.) Death Every effort should be made to exercise diligence Date of death in reporting the complete date of death. Overall survival is an important study endpoint. Primary cause of death (check one) Breast cancer progression Malignant disease other than breast cancer Other, specify: **Signature** All data entered in this case report form have been entered under my authority and to the best of my knowledge are accurate and complete. Investigator's signature \_\_\_ (A medically qualified sub-investigator is allowed to sign the CRF if he/she is listed on the form FDA 1572) Date

Type of event code	Description	Type of ever
	Local Recurrence	
1a	Breast surgical scar	3a
1b	Ipsilateral breast	
1c	Ipsilateral anterior chest wall	3b
1d	Skin or soft tissue within local area	3c
	Regional Recurrence	3d
2a	Ipsilateral axillary	3e
2b	Infraclavicular	3f
2c	Internal mammary	
2d	Skin or soft tissue within the regional area	4a

Type of event code   Description	Description
	Distant Recurrence
За	Skin or lymph nodes other than specified for local/regional recurrence
3b	Bone
3c	Lung
3d	Liver
3e	Pleural effusion
3f	Other distant site (description to be provided)
	Central nervous system
4a	Brain metastasis
4b	Meningitis carcinomatosa
5	Contralateral breast cancer
6	Second primary malignancy (description to be provided)

\*\* Method of evaluation: C = clinical; R = radiological (please report the radiological test in the second section of facing page).

\*\*\* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

Anatomical site	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CL	Colon
CR	Colorectal
SO	CNS (brain)
CW	Chest
CX	Cervix
EO	Esophagus/Oesophagus

Anatomical site	Description
NH	Head and neck
HT	Heart
소	Kidney
97	Lung
N	Lymph nodes
ΓΛ	Liver
00	Oral cavity
10	Other
۸٥	Ovary
PA	Pleura
PM	Peritoneum

Anatomical site	Description
PR	Prostate
PS	Pancreas
ΡV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
TE	Testicle
WB	Whole body

Subject No.

Centre No.

# Amended survival FU from Protocol Amendment 4 Approval Event and Radiological examinations

Page 206

Histology type

Biopsy date

		Biopsy No Yes		
	on of event.	Method of E evaluation** N C R		
	For all events, please complete "Type of event code". For "Other distant site" or "Second Primary malignancy", please provide description of event.	Recurrence date M (dd/mmm/yyyy) eva		
2	For all events, please complete "Type of event code". For "Other distant site" or "Second Primary malignanc	Description of event		
	For all events, plea For "Other distant s	Type of event*		

: abnormalities?				
Are there any <u>clinically significant</u> abnormalities? (Please report a short description)	」☐ No ☐ Yes —> Specify	J ☐ No ☐ Yes —➤ Specify	J ☐ No ☐ Yes —➤ Specify ————	☐ No Specify ————
r Date of test (dd/mmm/yyyy)				-
Side (L o R or Both				
Anatomical site****				
ype of radiological Anatomical Side (L or sxamination*** Site*** R or Both)	]	]	$\exists$	]

Study: Neo-ALTTO Amended survival FU from Protocol Amendment 4 Approval - Final version 2 (20SEP2016)

rotocol number BIG 1-06 / EGF106903
Centre No. Subject No. Page 207
atient status  Patient was last contacted:
DD MMM YYYY
Are there any changes from last patient status?  ☐ No → Please sign and date at the bottom of the page ☐ Yes → Specify below and sign and date at the bottom of the page
Changes  ☐ Recurrence of disease (complete the next page "Event and radiological examinations")
<ul> <li>□ Second primary malignancy or contralateral breast cancer (complete the next page "Event and radiological examinations")</li> </ul>
□ Death (complete the "Death" section below)
□ Lost to follow-up
☐ Patient withdrew study consent ☐ Date of last contact (or date ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
(For patients "Lost to Follow-up", the date of last contact should be the last date the patient was known to be alive. The last date the patient was known to be alive could either be the same as the previous reported visit date or any date between the previous visit and this one.)
Death
Date of death  DD MMM YYYY  Every effort should be made to exercise diligence in reporting the complete date of death. Overall survival is an important study endpoint.
Primary cause of death (check one)
☐ Breast cancer progression
Malignant disease other than breast cancer
Other, specify:
Signature All data entered in this case report form have been entered under my authority and to the best of my knowledge are accurate and complete.
Investigator's signature (A medically qualified sub-investigator is allowed to sign the CRF if he/she is
Date DD MMM YYYY

Type of event code	Description	Type of ever
	Local Recurrence	
1a	Breast surgical scar	3a
1b	Ipsilateral breast	
1c	Ipsilateral anterior chest wall	3b
1d	Skin or soft tissue within local area	3c
	Regional Recurrence	3d
2a	Ipsilateral axillary	3e
2b	Infraclavicular	3f
2c	Internal mammary	
2d	Skin or soft tissue within the regional area	4a

Type of event code   Description	Description
	Distant Recurrence
За	Skin or lymph nodes other than specified for local/regional recurrence
3b	Bone
3c	Lung
3d	Liver
3e	Pleural effusion
3f	Other distant site (description to be provided)
	Central nervous system
4a	Brain metastasis
4b	Meningitis carcinomatosa
5	Contralateral breast cancer
6	Second primary malignancy (description to be provided)

\*\* Method of evaluation: C = clinical; R = radiological (please report the radiological test in the second section of facing page).

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Anatomical site	Description
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CR	Colorectal
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CX	Cervix
EO	Esophagus/Oesophagus

Anatomical site	Description
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97	Lung
N	Lymph nodes
ΓΛ	Liver
00	Oral cavity
10	Other
۸٥	Ovary
PA	Pleura
PM	Peritoneum

Anatomical site	Description
PR	Prostate
PS	Pancreas
ΡV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
TE	Testicle
WB	Whole body

Subject No.

Centre No.

# Amended survival FU from Protocol Amendment 4 Approval Event and Radiological examinations

Page 208

	of event.
	escription
	For all events, please complete "Type of event code". For "Other distant site" or "Second Primary malignancy", please provide description of event.
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	For all events, please complete "Type of event code". For "Other distant site" or "Second Primary malignand

Type of event*	Description of event	iion nt	Recurrence date (dd/mmm/yyyy)	Method of evaluation** C R	Biopsy No Yes	Biopsy date	Histology type
lype of radiological Anatomical sxamination***		Side (L or R or Both)	Date of test (dd/mmm/yyyy)	Are there (Please re	Are there any <u>clinically significant</u> abnormalities? (Please report a short description)	<u>ıt</u> abnormalities?	
]	]		-	l Ses □ Xes	→ Specify		
			- - - - - - -	⊢ No □ Yes □	→ Specify		
]	]			l S C C	→ Specify		
]				l ⊗ □ √es □	□ No □ Yes —➤ Specify ————		
		75.17	Study: Neo-Al TTO Amended survival ETI from Protocol Amendment 4 Approval - Final version 2 (20SED2016)	FII from Drot	Amendment 4 Approx	.val - Final version 2 (	SOSEDS016)

Protocol number	er BIG 1-06 / EGF106903	
Centre N	lo. Subject No.	Page 209
	2 0	
Patient status		
	contacted:   Via a phone call	
	☐ During a standard of care visit	
	☐ Not Done	
Date of patient's	status evaluation (phone call or standard of care visit)	DD MMM YYYY
Are there any cha	anges from last patient status?	
	□ No → Please sign and date at the b	· -
Changes	☐ Yes → Specify below and sign and d	late at the bottom of the page
Changes  Recurrence of	of disease (complete the next page "Event and radiolog	gical examinations")
☐ Second prima	ary malignancy or contralateral breast cancer (completexaminations")	•
_	plete the "Death" section below)	
☐ Lost to follow	/	
	Propresent Date of last contact (or date study consent withdrawn)	DD MMM YYYY
be alive. The last	st to Follow-up", the date of last contact should be the t date the patient was known to be alive could either be date between the previous visit and this one.)	
Death		
Date of death	in reporting th	hould be made to exercise diligence be complete date of death. Overall important study endpoint.
Primary cause of	of death (check one)	
	☐ Breast cancer progression	
	Malignant disease other than breast cancer	
	Other, specify:	
	I in this case report form have been entered under my are accurate and complete.	authority and to the best of
Investigator's si		medically qualified sub-investigator allowed to sign the CRF if he/she is
Date		ed on the form FDA 1572)

Type of event code	Description	Type of ever
	Local Recurrence	
1a	Breast surgical scar	3a
1b	Ipsilateral breast	
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	Regional Recurrence	3d
2a	Ipsilateral axillary	3e
2b	Infraclavicular	3f
2c	Internal mammary	
2d	Skin or soft tissue within the regional area	4a

Type of event code   Description	Description
	Distant Recurrence
За	Skin or lymph nodes other than specified for local/regional recurrence
3b	Bone
3c	Lung
3d	Liver
3e	Pleural effusion
3f	Other distant site (description to be provided)
	Central nervous system
4a	Brain metastasis
4b	Meningitis carcinomatosa
5	Contralateral breast cancer
6	Second primary malignancy (description to be provided)

\*\* Method of evaluation: C = clinical; R = radiological (please report the radiological test in the second section of facing page).

\*\*\* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

Anatomical site	Description
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NH	Head and neck
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۸٥	Ovary
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Anatomical site	Description
PR	Prostate
PS	Pancreas
ΡV	Pelvis
RC	Rectum
SH	Stomach
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SK	Skin
SP	Spleen
TD	Thyroid
TE	Testicle
WB	Whole body

# Amended survival FU from Protocol Amendment 4 Approval Event and Radiological examinations

Page 210

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For all events, please complete "Type of event code"	events. please co	events. pleas	

Subject No.

Centre No.

Type of event*	Description of event	tion nt	Recurrence date (dd/mmm/yyyy)	Method of evaluation**	Biopsy Biopsy date No Yes	te Histology type
Type of radiological Anatomical examination***		Side (L or R or Both)	Date of test (dd/mmm/yyyy)	<b>Are there a</b> (Please repo	Are there an <u>y clinically significant</u> abnormalities? (Please report a short description)	rmalities?
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			- - - - - - -	No □ No □ Yes □	► Specify	
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		Study:	Study: Neo-ALTTO Amended survival FU from Protocol Amendment 4 Approval - Final version 2 (20SEP2016)	FU from Protoc	ol Amendment 4 Approval - Fir	al version 2 (20SEP2016)

Protocol number BIG 1-06 / EGF106903
Centre No. Subject No. Page 21
20
Patient status  Patient was last contacted:   During a standard of care visit  Not Done
Date of patient's status evaluation (phone call or standard of care visit)  DD MMM YYYY
Are there any changes from last patient status?  ☐ No → Please sign and date at the bottom of the page ☐ Yes → Specify below and sign and date at the bottom of the page
Changes
<ul> <li>☐ Recurrence of disease (complete the next page "Event and radiological examinations")</li> <li>☐ Second primary malignancy or contralateral breast cancer (complete the next page "Event and</li> </ul>
radiological examinations")
Death (complete the "Death" section below)
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Death Charles to be used to experience diligense
Date of death  DD MMM YYYY  Every effort should be made to exercise diligence in reporting the complete date of death. Overall survival is an important study endpoint.
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Malignant disease other than breast cancer
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Investigator's signature (A medically qualified sub-investigator is allowed to sign the CRF if he/she is
Date DD MMM YYYY

Type of event code   Description	Description	Type of ever
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	Regional Recurrence	3d
2a	Ipsilateral axillary	3e
2b	Infraclavicular	3f
2c	Internal mammary	
2d	Skin or soft tissue within the regional area	<b>4</b> a
	,	-

Type of event code   Description	Description
	Distant Recurrence
3a	Skin or lymph nodes other than specified for local/regional
3b	Bone
3c	Lung
3d	Liver
3e	Pleural effusion
3f	Other distant site (description to be provided)
	Central nervous system
4a	Brain metastasis
4b	Meningitis carcinomatosa
5	Contralateral breast cancer
9	Second primary malignancy (description to be provided)

\*\* Method of evaluation: C = clinical; R = radiological (please report the radiological test in the second section of facing page).

\*\*\* BS=Bone scan (scintigraphy); C=CT scan; E=Endoscopy; L=Lymphangiogram; M=MRI; MA=Mammography; NS=Nuclear scan; PC=PET/CT Scan; PT=PET scan; TU=Transvaginal ultrasound; UL=Ultrasound (echography); XR=X-ray

	Description
AB	Abdomen/abdominal wall
AD	Adrenals
BE	Bone
BR	Bladder
BT	Breast
CF	Colon
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SO	CNS (brain)
CW	Chest
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Anatomical site	Description
NH	Head and neck
HT	Heart
소	Kidney
97	Lung
N	Lymph nodes
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۸٥	Ovary
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Anatomical site	Description
PR	Prostate
PS	Pancreas
ΡV	Pelvis
RC	Rectum
SH	Stomach
SI	Small intestine
SK	Skin
SP	Spleen
TD	Thyroid
TE	Testicle
WB	Whole body

Subject No.

Centre No.

# Amended survival FU from Protocol Amendment 4 Approval Event and Radiological examinations

Page 212

	or all events, please complete "Type of event code". For "Other distant site" or "Second Primary malignancy", please provide description of event.
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	or all events, please complete "Type of event code" or "Other distant site" or "Second Primary malignan
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Type of event*	Description of event	otion ent	Recurrence date (dd/mmm/yyyy)	Method of evaluation**	Biopsy No Yes	Biopsy date	Histology type
Type of radiological Anatomical examination***	Anatomical site****	Side (L or R or Both)	Date of test (dd/mmm/yyyy)	Are there a (Please rep	Are there any <u>clinically significant</u> abnormalities? (Please report a short description)	<u>:ant</u> abnormalities? م)	
			-	SS C	→ Specify		
			- - - - - - -	% % □ □	► Specify		
]			-	Ses — √Ses — √S	➤ Specify		
]				% % 	→ Specify		
		Study:	Neo-ALTTO Amended survival FU from Protocol Amendment 4 Approval - Final version 2 (20SEP2016)	FU from Protoc	col Amendment 4 App	roval - Final version 2	(20SEP2016)

Protocol number BIG 1-06 / EGF106903	
Centre No. Subject No.	Page 213
Patient status  Patient was last contacted: ☐ Via a phone call ☐ During a standard of care visit ☐ Not Done	
Date of patient's status evaluation (phone call or standard of care v	risit) DD MMM YYYY
Are there any changes from last patient status?  ☐ No → Please sign and date at to Yes → Specify below and sign a	
Changes  ☐ Recurrence of disease (complete the next page "Event and rac	tiological examinations")
Second primary malignancy or contralateral breast cancer (conradiological examinations")	,
☐ Death (complete the "Death" section below)	
☐ Lost to follow-up	
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(For patients "Lost to Follow-up", the date of last contact should be be alive. The last date the patient was known to be alive could eith visit date or any date between the previous visit and this one.)	
Death	
Date of death in reporting	ort should be made to exercise diligence ng the complete date of death. Overall is an important study endpoint.
Primary cause of death (check one)	
☐ Breast cancer progression	
Malignant disease other than breast cancer	
Other, specify:	
Signature All data entered in this case report form have been entered under my knowledge are accurate and complete.	
Investigator's signature	(A medically qualified sub-investigator is allowed to sign the CRF if he/she is
Date DD MMM YYYY	listed on the form FDA 1572)

Type of event code   Description	Description	Type of ever
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	,	-

Type of event code   Description	Description
	Distant Recurrence
3a	Skin or lymph nodes other than specified for local/regional
3b	Bone
3c	Lung
3d	Liver
3e	Pleural effusion
3f	Other distant site (description to be provided)
	Central nervous system
4a	Brain metastasis
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SP	Spleen
TD	Thyroid
TE	Testicle
WB	Whole body

Subject No.

Centre No.

### Amended survival FU from Protocol Amendment 4 Approval Event and Radiological examinations

Page 214

Histology type

Are there any clinically significant abnormalities? (Please report a short description)	Are there any (Please report	Date of test (dd/mmm/yyyy)	Type of radiological Anatomical Side (L or examination*** site**** R or Both)	Type of radiological examination***
				]
Biopsy Biopsy date No Yes	Method of evaluation** N	Recurrence date (dd/mmm/yyyy)	Description of event	Type of event*
	otion of event.	For all events, please complete "Type of event code". For "Other distant site" or "Second Primary malignancy", please provide description of event.	For all events, please complete "Type of event code". For "Other distant site" or "Second Primary malignan	For all events, plea For "Other distant s
			2 0	

☐ No ☐ Yes —➤ Specify □ No □ Yes —> Specify □ No □ Yes —➤ Specify □ No □ Yes → Specify

Study: Neo-ALTTO Amended survival FU from Protocol Amendment 4 Approval - Final version 2 (20SEP2016)

### Amended survival FU from Protocol Amendment 4 Approval

Informed consent Protocol number BIG 1-06 / EGF106903 Centre No. Subject No. Page 215 Did the patient sign the Main Informed Consent version nb \_\_\_\_ corresponding to Protocol Amendment 4? □ No ☐ Yes → Specify date of consent below Date Main Informed Consent was signed? Did the patient sign the PGx Informed Consent version nb \_\_\_\_\_ corresponding to Protocol Amendment 4? ☐ No ☐ Yes → Specify date of consent below Date PGx Informed Consent was signed? All data entered in this case report form have been entered under my authority and to the best of my knowledge are accurate and complete. (A medically qualified sub-investigator Investigator's signature \_\_\_\_\_ is allowed to sign the CRF if he/she is listed on the form FDA 1572) Date