Clinical trial results:
A Randomized, Double-Blind Pharmacokinetic Study Of PF 05280014 Plus Taxotere® And Carboplatin Versus Herceptin® Plus Taxotere® And Carboplatin For The Neoadjuvant Treatment Of Patients With Operable HER2 Positive Breast Cancer.

Summary

EudraCT number	2013-004679-11
Trial protocol	IT SK CZ HU PL
Global end of trial date	09 March 2016

Results information

Result version number	v1 (current)
This version publication date	16 March 2017
First version publication date	16 March 2017

Trial information

Trial identification

Sponsor protocol code	B3271004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer, Inc.
Sponsor organisation address	235 East 42nd Street, New York, United States, NY 10017
Public contact	Pfizer CT.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer CT.gov Call Center, Pfizer, Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 January 2017

Is this the analysis of the primary completion data?	Yes
Primary completion date	09 March 2016
Global end of trial reached?	Yes
Global end of trial date	09 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the percentage of participants with steady state (Cycle 5) trough plasma concentration (Ctrough) >20 µg/mL for PF 05280014 versus trastuzumab-EU in patients with operable HER2-positive breast cancer who received study therapy together with Taxotere and carboplatin in the neoadjuvant setting.

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation Good Clinical Practice Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial participants.
A signed and dated informed consent was required before any screening procedures were done, with the exception of radiographic tumor assessments (which were performed as part of routine procedures within 6 weeks prior to randomization and in accordance with protocol method/documentation requirements).
Appropriate documentation indicating that these radiographic tumor assessments were performed as standard of care were available in the patient's source notes. The investigators explained the nature, purpose, and risks of the study to each participant. Each participant was informed that she could withdraw from the study at any time and for any reason. Each participant was given sufficient time to consider the implications of the study before deciding whether to participate.

Background therapy:

Taxotere was administered every 3 weeks on Day 1 of each cycle. The starting dose of Taxotere was 75 mg/m2 administered IV over 60 minutes. Carboplatin was administered every 3 weeks on Day 1 of each cycle.

Evidence for comparator: -

Actual start date of recruitment	23 September 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 4
Country: Number of subjects enrolled	Ukraine: 40
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Belarus: 2
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Hungary: 17
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Poland: 25
Country: Number of subjects enrolled	Russian Federation: 117
Country: Number of subjects enrolled	Serbia: 1
Worldwide total number of subjects	225
EEA total number of subjects	62

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	183
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was initiated at 67 sites in 10 countries (across Europe and the United States [US]), of which 21 sites had no enrollment activity.
Advertisements approved by ethics committees and investigator databases may be used as recruitment procedures. All advertisements must have been approved by the study Sponsor prior to use.

Pre-assignment

Screening details:

Informed consent must have been obtained before any study specific procedures were performed (with the exception of certain imaging assessments if meeting the protocol specified criteria); however, it may be obtained more than 28 days before randomization.

Period 1

Period 1 title	Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	PF-05280014

Arm description:

Participants received a loading dose of 8 mg/kg of PF-05280014 on Cycle 1 Day 1. Subsequent infusions followed every 3 weeks with a dose of 6 mg/kg. Taxotere 75 mg/m2 and carboplatin area under the concentration versus time curve (AUC) 6 were administered on Day 1 of each cycle.

Arm type	Experimental
Investigational medicinal product name	PF-05280014
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The first administration of PF-05280014 on Day 1, Cycle 1 was a loading dose of 8 mg/kg infused over 90 minutes. The duration of infusion could be lengthened according to local standard of care or tolerability. Subsequent infusions followed every 3 weeks (ie, cycled every 21 days) with a dose of 6 mg/kg administered over 30 to 90 minutes depending on tolerability. In the absence of objective disease progression or prohibitive toxicity, patients received PF-05280014 for 6 cycles.

Arm title	Trastuzumab-EU

Arm description:

Participants received a loading dose of 8 mg/kg of trastuzumab-EU on Cycle 1 Day 1. Subsequent infusions followed every 3 weeks with a dose of 6 mg/kg. Taxotere 75 mg/m2 and carboplatin AUC 6 were administered on Day 1 of each cycle.

Arm type	Active comparator
Investigational medicinal product name	Trastuzumab-EU
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The first administration of trastuzumab-EU on Day 1, Cycle 1 was a loading dose of 8 mg/kg infused over 90 minutes. The duration of infusion could be lengthened according to local standard of care or tolerability. Subsequent infusions followed every 3 weeks (ie, cycled every 21 days) with a dose of 6

mg/kg administered over 30 to 90 minutes depending on tolerability. In the absence of objective disease progression or prohibitive toxicity, patients received trastuzumab-EU for 6 cycles.

Number of subjects in period 1	PF-05280014	Trastuzumab-EU
Started	113	112
Completed	109	106
Not completed	4	6
NotSpecified	2	1
Participant refused further follow-up	1	-
Adverse event, serious fatal	1	-
Related adverse event, not serious	-	2
Related adverse event, serious non-fatal	-	1
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	PF-05280014
Reporting group description:	
Participants received a loading dose of 8 mg/kg of PF-05280014 on Cycle 1 Day 1. Subsequent infusions followed every 3 weeks with a dose of 6 mg/kg. Taxotere 75 mg/m2 and carboplatin area under the concentration versus time curve (AUC) 6 were administered on Day 1 of each cycle.	
Reporting group title	Trastuzumab-EU
Reporting group description:	
Participants received a loading dose of 8 mg/kg of trastuzumab-EU on Cycle 1 Day 1. Subsequent infusions followed every 3 weeks with a dose of 6 mg/kg. Taxotere 75 mg/m2 and carboplatin AUC 6 were administered on Day 1 of each cycle.	

Reporting group values	PF-05280014	Trastuzumab-EU	Total
Number of subjects	113	112	225
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	88	95	183
From 65-84 years	25	17	42
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	54.2	51.2	
standard deviation	± 11.7	± 12.7	-
Gender Categorical Units: Subjects			
Female	113	112	225

End points

End points reporting groups

Reporting group title	PF-05280014
Reporting group description:	
Participants received a loading dose of 8 mg/kg of PF-05280014 on Cycle 1 Day 1. Subsequent infusions followed every 3 weeks with a dose of 6 mg/kg. Taxotere 75 mg/m2 and carboplatin area under the concentration versus time curve (AUC) 6 were administered on Day 1 of each cycle.	
Reporting group title	Trastuzumab-EU
Reporting group description:	
Participants received a loading dose of 8 mg/kg of trastuzumab-EU on Cycle 1 Day 1. Subsequent infusions followed every 3 weeks with a dose of 6 mg/kg. Taxotere 75 mg/m2 and carboplatin AUC 6 were administered on Day 1 of each cycle.	

Primary: Percentage of Participants with Steady State Drug Concentration Ctrough (Cycle 6 pre-dose) >20 µg/mL at Cycle 5.

End point title	Percentage of Participants with Steady State Drug Concentration Ctrough (Cycle 6 pre-dose) >20 µg/mL at Cycle 5.
End point description:	
The percentage of participants with Cycle 5 Ctrough (Cycle 6 pre-dose) >20 µg/mL in each treatment group, the denominator being the number of participants in the per protocol population for each treatment group.	
End point type	Primary
End point timeframe:	
Cycle 5	

End point values	PF-05280014	Trastuzumab-EU		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	89		
Units: Percentage of participants				
number (confidence interval 95%)	92.1 (85 to 96.5)	93.3 (85.9 to 97.5)		

Statistical analyses

Statistical analysis title	Estimated difference (stratified)
Statistical analysis description:	
Stratified estimated difference between PF-05280014 and Trastuzuamb-EU.	
Comparison groups	PF-05280014 v Trastuzumab-EU
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	

Parameter estimate	Mean difference (final values)
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.02
upper limit	6.49
Variability estimate	Standard error of the mean
Dispersion value	3.7

Statistical analysis title	Estimated difference (unstratified)
Statistical analysis description:	
Unstratified estimated difference between PF-05280014 and Trastuzuamb-EU.	
Comparison groups	PF-05280014 v Trastuzumab-EU
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.59
upper limit	6.23
Variability estimate	Standard error of the mean
Dispersion value	3.78

Secondary: Mean Predose Trastuzumab-Pfizer and Trastuzumab-EU Concentrations at Cycles 1 through 6.

End point title	Mean Predose Trastuzumab-Pfizer and Trastuzumab-EU Concentrations at Cycles 1 through 6.
End point description:	
Samples of blood were taken pre-dose on Cycles 1, 2, 4, 5, and 6, and at 1 hour post dose on Cycles 1 and 5 for pharmacokinetic evaluation.	
End point type	Secondary
End point timeframe:	
Cycles 1 through 6	

End point values	PF-05280014	Trastuzumab-EU		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	89		
Units: µg/mL				
arithmetic mean (standard deviation)				

Cycle 1/Day 1 0 hours N= 101, 88	2.313 (± 17.949)	1.318 (± 12.366)		
Cycle 1/Day 1 1 hour N= 97, 80	160.4 (± 57.329)	164.8 (± 47.033)		
Cycle 2/Day 21 0 hours N= 99, 88	24.29 (± 13.796)	27.2 (± 10.65)		
Cycle 4/Day 63 0 hours N= 98, 89	33.43 (± 14.488)	37.33 (± 15.629)		
Cycle 5/Day 84 0 hours N= 101, 87	35.01 (± 15.571)	40.44 (± 26.765)		
Cycle 5/Day 84 1 hour N= 90, 80	137 (± 37.748)	138.8 (± 37.417)		
Cycle 6/Day 105 0 hours N= 101, 89	37.77 (± 17.523)	40.1 (± 16.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pathologic Complete Response (pCR) Defined as the Absence of Invasive Neoplastic Cells in the Breast and Lymph Nodes.

End point title	Pathologic Complete Response (pCR) Defined as the Absence of Invasive Neoplastic Cells in the Breast and Lymph Nodes.

End point description:

Following surgery after treatment completion, tumors were assessed as Complete Pathological Response, Partial Pathological Response, or No Pathological Response.

End point type	Secondary

End point timeframe:

Cycle 6/End of treatment

End point values	PF-05280014	Trastuzumab-EU		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	86		
Units: Percentage of participants				
number (confidence interval 95%)	47 (36.9 to 57.2)	50 (39 to 61)		

Statistical analyses

Statistical analysis title	Estimated difference (stratified)

Statistical analysis description:

Stratified estimated difference between PF-05280014 and Trastuzuamb-EU.

Comparison groups	PF-05280014 v Trastuzumab-EU
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	

Parameter estimate	Mean difference (final values)
Point estimate	-2.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.58
upper limit	10.96
Variability estimate	Standard error of the mean
Dispersion value	7.03

Statistical analysis title	Estimated difference (unstratified)
Statistical analysis description:	
Unstratified estimated difference between PF-05280014 and Trastuzuamb-EU.	
Comparison groups	PF-05280014 v Trastuzumab-EU
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.4
upper limit	11.4
Variability estimate	Standard error of the mean
Dispersion value	7.35

Secondary: Objective Response Rate (ORR) Defined as the Percentage of Participants having Complete or Partial Response at End of Treatment, Based on Radiographic Assessments of the Tumor.

End point title	Objective Response Rate (ORR) Defined as the Percentage of Participants having Complete or Partial Response at End of Treatment, Based on Radiographic Assessments of the Tumor.
End point description:	
ORR was defined as Complete Response (CR), Partial Response (PR), Stable (SD), Progressive Disease (PD) or Indeterminate (IND). ORR was the percentage of participants who had CR or PR at Cycle 6/End of treatment.	
End point type	Secondary
End point timeframe:	
Cycle 6/End of treatment	

End point values	PF-05280014	Trastuzumab-EU		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	101	89		
Units: Percentage of participants				
number (confidence interval 95%)	88.1 (80.2 to 93.7)	82 (72.5 to 89.4)		

Statistical analyses

Statistical analysis title	Estimated difference (stratified)
Statistical analysis description: Stratified estimated difference between PF-05280014 and Trastuzuamb-EU.	
Comparison groups	PF-05280014 v Trastuzumab-EU
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	5.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.01
upper limit	15.94
Variability estimate	Standard error of the mean
Dispersion value	5.09

Statistical analysis title	Estimated difference (unstratified)
Statistical analysis description: Unstratified estimated difference between PF-05280014 and Trastuzuamb-EU.	
Comparison groups	PF-05280014 v Trastuzumab-EU
Number of subjects included in analysis	190
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Mean difference (final values)
Point estimate	6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.08
upper limit	16.27
Variability estimate	Standard error of the mean
Dispersion value	5.19

Secondary: Incidence of Anti-trastuzumab Antibodies (ADAs) at Cycles 1 through 6.

End point title	Incidence of Anti-trastuzumab Antibodies (ADAs) at Cycles 1 through 6.

End point description:

The number of participants with positive (titer >=1.00) pre-dose ADA samples, participants counted towards the total if for at least one sample, the ADA was positive.

End point type	Secondary

End point timeframe:

Cycles 1 through 6

End point values	PF-05280014	Trastuzumab-EU		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	112		
Units: Number of participants				
Cycle 1 (n=113,112)	0	1		
Cycle 2 (n=111,112)	0	0		
Cycle 4 (n=108,109)	0	0		
Cycle 6 (n=108,108)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Neutralizing Antibodies (NAb) at Cycles 1 through 6.

End point title	Incidence of Neutralizing Antibodies (NAb) at Cycles 1 through 6.

End point description:

The number of participants with positive (NAb response >=1.48) pre-dose NAb samples, participants counted towards the total if for at least one sample, the NAb was positive.

End point type	Secondary

End point timeframe:

Cycles 1 through 6

End point values	PF-05280014	Trastuzumab-EU		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	112		
Units: Number of participants				
Cycle 1 (n=113,112)	0	0		
Cycle 2 (n=110,112)	0	0		
Cycle 4 (n=108,110)	0	0		
Cycle 6 (n=108,108)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events were captured from the beginning of the study drug treatment up to 6 months after the last dose. Treatment emergent adverse events were captured from the beginning of the study drug treatment up to 50 days after the last dose.

Adverse event reporting additional description:

Treatment emergent adverse events were defined as any adverse event that occurred or any preexisting adverse event that worsened within the reporting time frame.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	PF-05280014

Reporting group description:

Participants received a loading dose of 8 mg/kg of PF-05280014 on Cycle 1 Day 1. Subsequent infusions followed every 3 weeks with a dose of 6 mg/kg. Taxotere 75 mg/m2 and carboplatin AUC 6 were administered on Day 1 of each cycle.

Reporting group title	Trastuzumab-EU

Reporting group description:

Participants received a loading dose of 8 mg/kg of trastuzumab-EU on Cycle 1 Day 1. Subsequent infusions followed every 3 weeks with a dose of 6 mg/kg. Taxotere 75 mg/m2 and carboplatin AUC 6 were administered on Day 1 of each cycle.

Serious adverse events	PF-05280014	Trastuzumab-EU	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 113 (6.19%)	6 / 112 (5.36%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	0 / 113 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 113 (0.88%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Febrile neutropenia			
subjects affected / exposed	1 / 113 (0.88%)	2 / 112 (1.79%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 113 (0.88%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 113 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 113 (0.88%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Gastrointestinal disorders			
Proctitis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 113 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 113 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related sepsis			
subjects affected / exposed	1 / 113 (0.88%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 113 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site abscess			
subjects affected / exposed	1 / 113 (0.88%)	0 / 112 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	0 / 113 (0.00%)	1 / 112 (0.89%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	PF-05280014	Trastuzumab-EU	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	106 / 113 (93.81%)	106 / 112 (94.64%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 113 (6.19%)	10 / 112 (8.93%)	
occurrences (all)	10	14	
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 113 (2.65%)	7 / 112 (6.25%)	
occurrences (all)	4	9	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	56 / 113 (49.56%)	51 / 112 (45.54%)	
occurrences (all)	114	112	
Leukopenia			
subjects affected / exposed	16 / 113 (14.16%)	25 / 112 (22.32%)	
occurrences (all)	59	95	
Neutropenia			
subjects affected / exposed	37 / 113 (32.74%)	41 / 112 (36.61%)	

occurrences (all)	112	139	
Thrombocytopenia			
subjects affected / exposed	16 / 113 (14.16%)	19 / 112 (16.96%)	
occurrences (all)	30	24	
Febrile neutropenia			
subjects affected / exposed	3 / 113 (2.65%)	6 / 112 (5.36%)	
occurrences (all)	4	6	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	7 / 113 (6.19%)	4 / 112 (3.57%)	
occurrences (all)	7	4	
Dysgeusia			
subjects affected / exposed	4 / 113 (3.54%)	6 / 112 (5.36%)	
occurrences (all)	8	12	
Neuropathy peripheral			
subjects affected / exposed	6 / 113 (5.31%)	4 / 112 (3.57%)	
occurrences (all)	7	4	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	36 / 113 (31.86%)	23 / 112 (20.54%)	
occurrences (all)	68	46	
Fatigue			
subjects affected / exposed	15 / 113 (13.27%)	19 / 112 (16.96%)	
occurrences (all)	38	34	
Pyrexia			
subjects affected / exposed	6 / 113 (5.31%)	5 / 112 (4.46%)	
occurrences (all)	9	11	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	16 / 113 (14.16%)	19 / 112 (16.96%)	
occurrences (all)	23	33	
Nausea			
subjects affected / exposed	38 / 113 (33.63%)	34 / 112 (30.36%)	
occurrences (all)	72	75	
Vomiting			
subjects affected / exposed	7 / 113 (6.19%)	10 / 112 (8.93%)	

occurrences (all)	10	16	

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	72 / 113 (63.72%)	69 / 112 (61.61%)	
occurrences (all)	88	81	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	16 / 113 (14.16%)	8 / 112 (7.14%)	
occurrences (all)	23	13	
Bone pain			
subjects affected / exposed	13 / 113 (11.50%)	5 / 112 (4.46%)	
occurrences (all)	22	13	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	13 / 113 (11.50%)	9 / 112 (8.04%)	
occurrences (all)	16	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 October 2014	Amendment 1 was implemented as a result of feedback from the E-DMC and Study B3271002 protocol Amendment 2, as well as Pfizer SOP updates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

It was decided that the secondary study objective to explore the relationship between drug exposure and pCR for PF-05280014 versus trastuzumab-EU would not be analyzed.

Notes: