Clinical trial results:
A Phase II, Double-blind, Placebo Controlled, Randomized Study to Assess the Efficacy and Safety of 2 Doses of ZD6474 (Vandetanib) in Combination With FOLFOX vs FOLFOX Alone for the Treatment of Colorectal Cancer in Patients Who Have Failed Therapy With an Irinotecan and Fluoropyrimidine Regimen

Summary

EudraCT number	2006-005022-23
Trial protocol	FR HU ES
Global end of trial date	11 November 2016

Results information

Result version number	v1 (current)
This version publication date	15 December 2017
First version publication date	15 December 2017

Trial information

Trial identification

Sponsor protocol code	D4200C00047

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00500292
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA , United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, contact-US@sanofi.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	11 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the efficacy of ZD6474 (vandetanib) in combination with oxaliplatin, leucovorin, fluorouracil (5-FU) combination regimen (FOLFOX) vs FOLFOX alone for the treatment of subjects with colorectal cancer that have failed prior treatment with irinotecan and fluoropyrimidine by assessment of disease progression.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Hungary: 27
Country: Number of subjects enrolled	Taiwan: 18
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Slovakia: 14
Worldwide total number of subjects	104
EEA total number of subjects	64

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)	74
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First subject randomised 19 March 2007, last subject randomised 11 Nov 2007, data cut off date 8 March 2008. 109 subjects were enrolled in the study.

Pre-assignment

Screening details:

109 subjects were enrolled/screened to the study but only 104 subjects were entered treatment/randomized. Completed subjects refers to ongoing study treatment at data cut-off date 8 March 2008.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Vandetanib 100 mg Plus FOLFOX

Arm description:

Vandetanib 100 mg plus FOLFOX

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	ZACTIMA™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vandetanib 100 mg tablet, once daily.

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Oxaliplatin 85 mg/m^2 IV infusion over 120 minutes.

Investigational medicinal product name	Leucovorin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin 400 mg/m^2 IV infusion over 120 minutes.

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection

Routes of administration	Intravenous use

Dosage and administration details:

5-FU 400 mg/m^2 IV bolus over 2-4 minutes and then 2400 mg/m^2 continuous IV infusion over 46 hours.

Arm title	Vandetanib 300 mg Plus FOLFOX

Arm description:

Vandetanib 300 mg plus FOLFOX

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	ZACTIMA™
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vandetanib 300 mg tablet, once daily.

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Oxaliplatin 85 mg/m^2 IV infusion over 120 minutes.

Investigational medicinal product name	Leucovorin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin 400 mg/m^2 IV infusion over 120 minutes.

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

5-FU 400 mg/m^2 IV bolus over 2-4 minutes and then 2400 mg/m^2 continuous IV infusion over 46 hours.

Arm title	Placebo Plus FOLFOX

Arm description:

Placebo plus FOLFOX

Arm type	Placebo
Investigational medicinal product name	Placebo (matched to vandetanib)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo (matched to vandetanib) tablet, once daily.

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Oxaliplatin 85 mg/m^2 IV infusion over 120 minutes.

Investigational medicinal product name	Leucovorin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Leucovorin 400 mg/m^2 IV infusion over 120 minutes.

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

5-FU 400 mg/m^2 IV bolus over 2-4 minutes and then 2400 mg/m^2 continuous IV infusion over 46 hours.

Number of subjects in period 1	Vandetanib 100 mg Plus FOLFOX	Vandetanib 300 mg Plus FOLFOX	Placebo Plus FOLFOX
Started	32	35	37
Completed	7	4	10
Not completed	25	31	27
Adverse Event	3	6	4
Other	1	1	4
Condition under investigation worsened	21	23	19
Withdrawal by Subject	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Vandetanib 100 mg Plus FOLFOX
Reporting group description:	
Vandetanib 100 mg plus FOLFOX	

Reporting group title	Vandetanib 300 mg Plus FOLFOX
Reporting group description:	
Vandetanib 300 mg plus FOLFOX	
Reporting group title	Placebo Plus FOLFOX
Reporting group description:	
Placebo plus FOLFOX	

Reporting group values	Vandetanib 100 mg Plus FOLFOX	Vandetanib 300 mg Plus FOLFOX	Placebo Plus FOLFOX
Number of subjects	32	35	37
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	57	58	59
full range (min-max)	34 to 75	37 to 71	32 to 81
Gender categorical Units: Subjects			
Female	16	11	13
Male	16	24	24

Reporting group values	Total		
Number of subjects	104		
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean			
full range (min-max)	-		
Gender categorical Units: Subjects			
Female	40		
Male	64		

End points

End points reporting groups

Reporting group title	Vandetanib 100 mg Plus FOLFOX
Reporting group description: Vandetanib 100 mg plus FOLFOX	

Reporting group title	Vandetanib 300 mg Plus FOLFOX
Reporting group description: Vandetanib 300 mg plus FOLFOX	

Reporting group title	Placebo Plus FOLFOX
Reporting group description: Placebo plus FOLFOX	

Primary: Number of Subjects With an Objective Disease Progression Event

End point title	Number of Subjects With an Objective Disease Progression Event[1]
End point description: Number of subjects with objective disease progression or death (by any cause in the absence of objective progression).	
End point type	Primary
End point timeframe: RECIST tumour assessments carried out at screening and then as per site clinical practice until objective progression. The only additional mandatory tumour assessment visit is at the point of data cut-off (5 March 2008 +/-3 days)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics were reported, inferential statistics were not planned to be reported for primary endpoint.

End point values	Vandetanib 100 mg Plus FOLFOX	Vandetanib 300 mg Plus FOLFOX	Placebo Plus FOLFOX	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	32	35	37	
Units: Subjects	23	27	24	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (up to 503 weeks) regardless of seriousness or relationship to investigational product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Vandetanib 100 mg Plus FOLFOX
Reporting group description:	
Vandetanib 100 mg plus FOLFOX	
Reporting group title	Vandetanib 300 mg Plus FOLFOX
Reporting group description:	
Vandetanib 300 mg plus FOLFOX	
Reporting group title	Placebo Plus FOLFOX
Reporting group description:	
Placebo plus FOLFOX.	

Serious adverse events	Vandetanib 100 mg Plus FOLFOX	Vandetanib 300 mg Plus FOLFOX	Placebo Plus FOLFOX
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 32 (18.75%)	10 / 35 (28.57%)	4 / 37 (10.81%)
number of deaths (all causes)	2	6	4
number of deaths resulting from adverse events	1	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma Gastric			
subjects affected / exposed	1 / 32 (3.13%)	0 / 35 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 32 (3.13%)	0 / 35 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			

subjects affected / exposed	1 / 32 (3.13%)	0 / 35 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous Thrombosis			
subjects affected / exposed	1 / 32 (3.13%)	0 / 35 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhage Intracranial			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Mucosal Inflammation			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic Reaction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal Obstruction			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	1 / 37 (2.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Female Genital Tract Fistula			
subjects affected / exposed	1 / 32 (3.13%)	0 / 35 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Toxic Epidermal Necrolysis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Device Related Infection			
subjects affected / exposed	2 / 32 (6.25%)	0 / 35 (0.00%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Abscess			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 32 (3.13%)	3 / 35 (8.57%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Staphylococcal Infection			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Sepsis			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Vandetanib 100 mg Plus FOLFOX	Vandetanib 300 mg Plus FOLFOX	Placebo Plus FOLFOX
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 32 (96.88%)	32 / 35 (91.43%)	35 / 37 (94.59%)
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 32 (40.63%)	13 / 35 (37.14%)	5 / 37 (13.51%)
occurrences (all)	13	13	8
Phlebitis			
subjects affected / exposed	2 / 32 (6.25%)	1 / 35 (2.86%)	1 / 37 (2.70%)
occurrences (all)	2	1	1
Phlebitis Superficial			
subjects affected / exposed	2 / 32 (6.25%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences (all)	2	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 32 (12.50%)	8 / 35 (22.86%)	6 / 37 (16.22%)
occurrences (all)	5	8	7
Chills			
subjects affected / exposed	1 / 32 (3.13%)	1 / 35 (2.86%)	2 / 37 (5.41%)
occurrences (all)	1	1	2
Fatigue			
subjects affected / exposed	8 / 32 (25.00%)	10 / 35 (28.57%)	15 / 37 (40.54%)
occurrences (all)	9	13	23
Oedema Peripheral			
subjects affected / exposed	1 / 32 (3.13%)	2 / 35 (5.71%)	1 / 37 (2.70%)
occurrences (all)	1	2	1
Pyrexia			
subjects affected / exposed	3 / 32 (9.38%)	5 / 35 (14.29%)	9 / 37 (24.32%)
occurrences (all)	3	6	16
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	3 / 32 (9.38%)	4 / 35 (11.43%)	5 / 37 (13.51%)
occurrences (all)	5	9	5
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	6 / 32 (18.75%)	1 / 35 (2.86%)	3 / 37 (8.11%)
occurrences (all)	6	1	3
Dyspnoea			
subjects affected / exposed	3 / 32 (9.38%)	4 / 35 (11.43%)	2 / 37 (5.41%)
occurrences (all)	3	4	2
Epistaxis			
subjects affected / exposed	2 / 32 (6.25%)	3 / 35 (8.57%)	4 / 37 (10.81%)
occurrences (all)	2	3	4
Pharyngolaryngeal Pain			
subjects affected / exposed	2 / 32 (6.25%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences (all)	2	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 32 (0.00%)	3 / 35 (8.57%)	0 / 37 (0.00%)
occurrences (all)	0	3	0
Confusional State			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Insomnia			
subjects affected / exposed	3 / 32 (9.38%)	3 / 35 (8.57%)	3 / 37 (8.11%)
occurrences (all)	3	3	3
Investigations			
Electrocardiogram Qt Prolonged			
subjects affected / exposed	1 / 32 (3.13%)	6 / 35 (17.14%)	1 / 37 (2.70%)
occurrences (all)	1	6	1
Weight Decreased			
subjects affected / exposed	3 / 32 (9.38%)	1 / 35 (2.86%)	2 / 37 (5.41%)
occurrences (all)	3	1	2
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 32 (6.25%)	2 / 35 (5.71%)	3 / 37 (8.11%)
occurrences (all)	2	2	3
Dysaesthesia			

subjects affected / exposed	1 / 32 (3.13%)	1 / 35 (2.86%)	3 / 37 (8.11%)
occurrences (all)	1	1	3
Dysgeusia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	2 / 32 (6.25%)	5 / 35 (14.29%)	2 / 37 (5.41%)
occurrences (all)	2	5	2
Lethargy			
subjects affected / exposed	2 / 32 (6.25%)	0 / 35 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	1
Paraesthesia			
subjects affected / exposed	4 / 32 (12.50%)	5 / 35 (14.29%)	3 / 37 (8.11%)
occurrences (all)	4	5	3
Peripheral Sensory Neuropathy			
subjects affected / exposed	16 / 32 (50.00%)	12 / 35 (34.29%)	18 / 37 (48.65%)
occurrences (all)	22	15	31
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	4 / 32 (12.50%)	5 / 35 (14.29%)	5 / 37 (13.51%)
occurrences (all)	4	5	8
Neutropenia			
subjects affected / exposed	13 / 32 (40.63%)	11 / 35 (31.43%)	13 / 37 (35.14%)
occurrences (all)	21	18	17
Thrombocytopenia			
subjects affected / exposed	16 / 32 (50.00%)	18 / 35 (51.43%)	13 / 37 (35.14%)
occurrences (all)	29	28	18
Eye disorders			
Vision Blurred			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	1 / 37 (2.70%)
occurrences (all)	0	2	1
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	2 / 32 (6.25%)	3 / 35 (8.57%)	2 / 37 (5.41%)
occurrences (all)	2	3	2
Abdominal Pain			

subjects affected / exposed	2 / 32 (6.25%)	3 / 35 (8.57%)	10 / 37 (27.03%)
occurrences (all)	2	3	10
Abdominal Pain Upper			
subjects affected / exposed	2 / 32 (6.25%)	1 / 35 (2.86%)	4 / 37 (10.81%)
occurrences (all)	2	1	5
Constipation			
subjects affected / exposed	6 / 32 (18.75%)	3 / 35 (8.57%)	6 / 37 (16.22%)
occurrences (all)	7	4	7
Diarrhoea			
subjects affected / exposed	16 / 32 (50.00%)	22 / 35 (62.86%)	16 / 37 (43.24%)
occurrences (all)	22	35	23
Epigastric Discomfort			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Flatulence			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Gingival Bleeding			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	13 / 32 (40.63%)	15 / 35 (42.86%)	24 / 37 (64.86%)
occurrences (all)	25	17	41
Rectal Haemorrhage			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Stomatitis			
subjects affected / exposed	8 / 32 (25.00%)	11 / 35 (31.43%)	10 / 37 (27.03%)
occurrences (all)	8	15	11
Toothache			
subjects affected / exposed	0 / 32 (0.00%)	1 / 35 (2.86%)	2 / 37 (5.41%)
occurrences (all)	0	1	2
Vomiting			
subjects affected / exposed	9 / 32 (28.13%)	5 / 35 (14.29%)	14 / 37 (37.84%)
occurrences (all)	11	6	20
Hepatobiliary disorders			

Hepatotoxicity			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	3 / 32 (9.38%)	2 / 35 (5.71%)	3 / 37 (8.11%)
occurrences (all)	3	2	3
Alopecia			
subjects affected / exposed	3 / 32 (9.38%)	1 / 35 (2.86%)	3 / 37 (8.11%)
occurrences (all)	3	1	3
Dermatitis Acneiform			
subjects affected / exposed	1 / 32 (3.13%)	5 / 35 (14.29%)	1 / 37 (2.70%)
occurrences (all)	1	5	1
Dry Skin			
subjects affected / exposed	2 / 32 (6.25%)	2 / 35 (5.71%)	1 / 37 (2.70%)
occurrences (all)	2	2	1
Hyperhidrosis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	3 / 32 (9.38%)	3 / 35 (8.57%)	1 / 37 (2.70%)
occurrences (all)	3	3	1
Photosensitivity Reaction			
subjects affected / exposed	3 / 32 (9.38%)	7 / 35 (20.00%)	1 / 37 (2.70%)
occurrences (all)	3	8	1
Pigmentation Disorder			
subjects affected / exposed	1 / 32 (3.13%)	2 / 35 (5.71%)	1 / 37 (2.70%)
occurrences (all)	1	2	1
Pruritus			
subjects affected / exposed	1 / 32 (3.13%)	2 / 35 (5.71%)	3 / 37 (8.11%)
occurrences (all)	1	2	3
Rash			

subjects affected / exposed	7 / 32 (21.88%)	7 / 35 (20.00%)	3 / 37 (8.11%)
occurrences (all)	7	7	3
Urticaria			
subjects affected / exposed	1 / 32 (3.13%)	0 / 35 (0.00%)	2 / 37 (5.41%)
occurrences (all)	1	0	2
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	1 / 37 (2.70%)
occurrences (all)	0	2	1
Haematuria			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	0 / 37 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	5 / 32 (15.63%)	4 / 35 (11.43%)	4 / 37 (10.81%)
occurrences (all)	5	4	4
Musculoskeletal Pain			
subjects affected / exposed	2 / 32 (6.25%)	0 / 35 (0.00%)	1 / 37 (2.70%)
occurrences (all)	2	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)	2 / 35 (5.71%)	1 / 37 (2.70%)
occurrences (all)	0	2	1
Nasopharyngitis			
subjects affected / exposed	4 / 32 (12.50%)	1 / 35 (2.86%)	2 / 37 (5.41%)
occurrences (all)	4	1	2
Pharyngitis			
subjects affected / exposed	2 / 32 (6.25%)	1 / 35 (2.86%)	0 / 37 (0.00%)
occurrences (all)	2	1	0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	10 / 32 (31.25%)	11 / 35 (31.43%)	9 / 37 (24.32%)
occurrences (all)	13	17	23
Decreased Appetite			
subjects affected / exposed	0 / 32 (0.00%)	0 / 35 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

Primary results are complemented by Sanofi following sponsorship transfer from Astra Zeneca to Sanofi in May 2016, only SAEs are updated per protocol.

Notes: