Clinical trial results:
A randomized phase III trial of erlotinib versus docetaxel in patients with advanced squamous cell non-small cell lung cancer who failed first line platinum based doublet chemotherapy stratified by VeriStrat Good vs VeriStrat Poor

Summary

EudraCT number	2012-001896-35
Trial protocol	BE HU IE AT ES NL DE IT DK GB GR
Global end of trial date	31 December 2015

Results information

Result version number	v1 (current)
This version publication date	07 February 2020
First version publication date	07 February 2020
Summary attachment (see zip file)	Publibation_Peters et al_J Thorac Oncol_2017_DOI: 10.1016/j.jtho.2016.12.017 (ETOP_EMPHASIS Peters et al JTO

Trial information

Trial identification

Sponsor protocol code	ETOP3-12

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01652469
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	European Thoracic Oncology Platform (ETOP)
Sponsor organisation address	Effingerstrasse 40, Bern, Switzerland, 3008
Public contact	ETOP Coordinating Office, ETOP , +41 31 511 94 00, emphasis@etop-eu.org
Scientific contact	ETOP Coordinating Office, ETOP , +41 31 511 94 00, emphasis@etop-eu.org

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	31 December 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 December 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Explore the predictive ability of VeriStrat signature, by testing for interaction between treatment arms (Arm A: erlotinib vs Arm B: docetaxel) and VeriStrat status (Good vs Poor) using progression free survival as outcome.

Protection of trial subjects:

Trial subjects are closely monitored during the entire duration of the trial by the participating investigators. For safety purposes any adverse events occurred from enrolment of a trial subject until 30 days after treatment discontinuation need to be reported.
In case of adverse events and treatment-related toxicities management guidance have been provided in the study protocol to treat trial subjects in adequately manner.
Precautions and warnings about the use of the study drug are provided in the trial subject information sheet to ensure that study drug is correctly used in order to avoid unnecessary adverse reactions and in addition to ensure that in case of an adverse event the study patient contacts the investigator for appropriate measures.
The safety and efficacy of the trial treatment have been regularly reviewed by the ETOP IDMC (independent data monitoring committee) at their semi-annual meetings to safeguard the interest and safety of the patients in the trial and to ensure the scientific integrity of the trial. Additionally, the risk/benefit ratio have been regularly evaluated by the ETOP Steering Committee on a semi-annual basis.
Technical and organisational controls (including physical, electronic and managerial measures) are in place to protect personal data and integrity of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 September 2012
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	Netherlands: 13
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Hungary: 1
Country: Number of subjects enrolled	Ireland: 7
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Switzerland: 14
Country: Number of subjects enrolled	Israel: 2

Worldwide total number of subjects	80
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)	27
From 65 to 84 years	53
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled to the ETOP/3-12 EMPHASIS trial on 14.01.2013. On 31.01.2014 accrual was closed due to a low accrual rate (81 patients enrolled). As of 31.12.2018 follow-up was ended.

Pre-assignment

Screening details:

One patient, who shouldn't have been included (exclusion criteria), was enrolled in the database by mistake. In the database patient's status couldn't be changed from "Enrolled" to "Ineligible", thus this patient was considered enrolled, but was not included in the efficacy cohort.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Erlotinib

Arm description:

Erlotinib in standard dose. Until progression (clinical or radiological) or unacceptable toxicity.
Erlotinib: Erlotinib 150 mg/day p.o. continuously with 21 days cycle.

Arm type	Experimental
Investigational medicinal product name	Tarceva
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Erlotinib is started at a fixed oral dose of 150 mg per day.
Tablets should be taken at a fixed time each day and at least 1 hour before, or 2 hours after the ingestion of food.
No routine premedication (e.g. to prevent skin toxicity) is recommended for erlotinib.
Systemic or local tetracyclines, systemic or local corticosteroids and loperamide in case of diarrhea are strongly recommended if significant toxicity occurs.
Smokers have reduced plasma levels and should be counseled for smoking reduction or cessation, the dose of 150 mg must never be increased.
In case of relevant toxicity, dose reductions are recommended to improve the tolerance.

Arm title	Docetaxel

Arm description:

Docetaxel in standard dose. Until progression (clinical or radiological) or unacceptable toxicity.
Docetaxel: Docetaxel 75 mg/m2 as an IV infusion every 21 days.

Arm type	Experimental
Investigational medicinal product name	Taxotere
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All patients should be premedicated with oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg BID) for 3 days starting 1 day prior to docetaxel administration in order to reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions.

In case of relevant toxicity, dose reductions are recommended to improve the tolerance.

Number of subjects in period 1	Erlotinib	Docetaxel
Started	38	42
Completed	37	36
Not completed	1	6
Withdrawal by Subject	1	4
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Erlotinib
Reporting group description:	
Erlotinib in standard dose. Until progression (clinical or radiological) or unacceptable toxicity. Erlotinib: Erlotinib 150 mg/day p.o. continuously with 21 days cycle.	
Reporting group title	Docetaxel
Reporting group description:	
Docetaxel in standard dose. Until progression (clinical or radiological) or unacceptable toxicity. Docetaxel: Docetaxel 75 mg/m2 as an IV infusion every 21 days.	

Reporting group values	Erlotinib	Docetaxel	Total
Number of subjects	38	42	80
Age categorical			
Age as continuous characteristic only			
Units: Subjects			
Age continuous			
Units: years			
median	66.7	70.1	
full range (min-max)	44.4 to 81.9	53.3 to 84.0	-
Gender categorical			
Units: Subjects			
Female	7	7	14
Male	31	35	66
Smoking history			
Units: Subjects			
Current	16	12	28
Former (>100 cigarettes & >12 months smoke-free)	20	28	48
Never	2	2	4
ECOG performance status			
PS 0:Fully active, able to carry on all pre-disease performance without restriction. PS 1:Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work. PS 2:Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours. PS 3:Capable of only limited self-care, confined to bed or chair more than 50% of waking hours. PS 4:Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.			
Units: Subjects			
PS 0	12	15	27
PS 1	24	22	46
PS 2	2	5	7
VeriStrat status			
Units: Subjects			
Good	28	30	58
Poor	10	12	22

End points

End points reporting groups

Reporting group title	Erlotinib
Reporting group description:	
Erlotinib in standard dose. Until progression (clinical or radiological) or unacceptable toxicity. Erlotinib: Erlotinib 150 mg/day p.o. continuously with 21 days cycle.	
Reporting group title	Docetaxel
Reporting group description:	
Docetaxel in standard dose. Until progression (clinical or radiological) or unacceptable toxicity. Docetaxel: Docetaxel 75 mg/m2 as an IV infusion every 21 days.	

Primary: Progression-free Survival

End point title	Progression-free Survival
End point description:	
Time from the date of randomization until documented progression or death without documented progression. Assessment of Progressive Disease (PD) based on Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1). Target lesions:At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progression). Non-target lesions:Unequivocal progression of existing non-target lesions. (Note: the appearance of one or more new lesions is also considered progression). To achieve 'unequivocal progression', there must be an overall level of substantial worsening in non-target disease such that, even in presence of SD or PR in target disease, the overall tumor burden has increased sufficiently.	
End point type	Primary
End point timeframe:	
The combined run in period, treatment and follow-up for PFS is expected to extend the study duration to a total of 24 months.	

End point values	Erlotinib	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	42		
Units: months				
median (confidence interval 95%)	1.6 (1.3 to 3.8)	3.0 (1.9 to 4.2)		

Statistical analyses

Statistical analysis title	PFS by treatment, stratified by VeriStrat status
Comparison groups	Erlotinib v Docetaxel

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.32
Method	Stratified Logrank by Veristrat status

Notes:

[1] - Explore differential activity of treatment effect on PFS in the two VeriStrat groups by testing for interaction between treatment arms (Arm A: erlotinib vs Arm B: docetaxel) and VeriStrat status (Good vs Poor).

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Defined as time from the date of randomization until death from any cause.

End point type	Secondary

End point timeframe:

All patients will be followed for survival status every 12 weeks up to 24 months after the last patient is randomized.

End point values	Erlotinib	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	42		
Units: months				
median (confidence interval 95%)	7.1 (4.4 to 10.6)	7.1 (5.3 to 8.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response

End point title	Objective Response

End point description:

Objective response is defined as best overall response (CR or PR) across all assessment time-points according to RECIST Criteria 1.1 during the period from randomization to termination of trial treatment.

End point type	Secondary

End point timeframe:

Same as primary outcome: 24 months.

End point values	Erlotinib	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	42		
Units: paticipants				
Partial Response	4	6		
Stable Disease	15	18		
Progressive Disease	17	14		
Non-Evaluable	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control

End point title	Disease Control

End point description:

Disease control is defined as achieving objective response or stable disease for at least 6 weeks.

End point type	Secondary

End point timeframe:

Same as primary outcome: 24 months.

End point values	Erlotinib	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	42		
Units: participants				
Disease Control	19	24		
No Disease Control	19	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Toxicities of treatment

End point title	Toxicities of treatment

End point description:

Adverse events classified according to NCI CTCAE version 4.

End point type	Secondary

End point timeframe:

Same as primary outcome: 24 months.

End point values	Erlotinib	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	38	41[2]		
Units: paticipants				
Experienced AE/SAE	36	39		
No AE/SAE	2	2		
Experienced SAE	7	19		

Notes:

[2] - One patient never started treatment.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study medication (Erlotinib or Docetaxel) until 30 days after the final dose, regardless of whether it is considered related to a medication.

Adverse event reporting additional description:

One patient from the Docetaxel arm never started treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	NCI CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Erlotinib

Reporting group description:

Erlotinib in standard dose. Until progression (clinical or radiological) or unacceptable toxicity.
Erlotinib: Erlotinib 150 mg/day p.o. continuously with 21 days cycle.

Reporting group title	Docetaxel

Reporting group description:

Docetaxel in standard dose. Until progression (clinical or radiological) or unacceptable toxicity.
Docetaxel: Docetaxel 75 mg/m2 as an IV infusion every 21 days.

Serious adverse events	Erlotinib	Docetaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 38 (18.42%)	19 / 41 (46.34%)	
number of deaths (all causes)	29	29	
number of deaths resulting from adverse events	7	3	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 38 (2.63%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 38 (2.63%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial flutter			

subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 38 (0.00%)	6 / 41 (14.63%)	
occurrences causally related to treatment / all	0 / 0	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death NOS			
subjects affected / exposed	3 / 38 (7.89%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Fatigue			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jejunal perforation			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vomiting			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary hemorrhage			
subjects affected / exposed	2 / 38 (5.26%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Dyspnea			
subjects affected / exposed	1 / 38 (2.63%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory failure			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnea			
subjects affected / exposed	1 / 38 (2.63%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal and urinary disorders			
Other			
subjects affected / exposed	1 / 38 (2.63%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 38 (2.63%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lung infection			
subjects affected / exposed	2 / 38 (5.26%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial infection			
subjects affected / exposed	2 / 38 (5.26%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	
Other			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	0 / 38 (0.00%)	1 / 41 (2.44%)	
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: 3 %

Non-serious adverse events	Erlotinib	Docetaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 38 (94.74%)	39 / 41 (95.12%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumor pain			
subjects affected / exposed	3 / 38 (7.89%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 38 (2.63%)	4 / 41 (9.76%)	
occurrences (all)	1	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	11 / 38 (28.95%)	24 / 41 (58.54%)	
occurrences (all)	11	24	
Pain			
subjects affected / exposed	4 / 38 (10.53%)	7 / 41 (17.07%)	
occurrences (all)	4	7	
Fever			
subjects affected / exposed	4 / 38 (10.53%)	3 / 41 (7.32%)	
occurrences (all)	4	3	
Edema limbs			
subjects affected / exposed	1 / 38 (2.63%)	4 / 41 (9.76%)	
occurrences (all)	1	4	
Flu-like symptoms			
subjects affected / exposed	2 / 38 (5.26%)	3 / 41 (7.32%)	
occurrences (all)	2	3	
Death NOS			

subjects affected / exposed	3 / 38 (7.89%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	16 / 38 (42.11%)	13 / 41 (31.71%)	
occurrences (all)	16	13	
Cough			
subjects affected / exposed	10 / 38 (26.32%)	14 / 41 (34.15%)	
occurrences (all)	10	14	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	2 / 38 (5.26%)	12 / 41 (29.27%)	
occurrences (all)	2	12	
Aspartate aminotransferase increase			
subjects affected / exposed	3 / 38 (7.89%)	1 / 41 (2.44%)	
occurrences (all)	3	1	
Creatinine increase			
subjects affected / exposed	2 / 38 (5.26%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 38 (7.89%)	4 / 41 (9.76%)	
occurrences (all)	3	4	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 38 (0.00%)	4 / 41 (9.76%)	
occurrences (all)	0	4	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 38 (5.26%)	2 / 41 (4.88%)	
occurrences (all)	2	2	
Eye disorders			
Conjuctivitis			
subjects affected / exposed	3 / 38 (7.89%)	1 / 41 (2.44%)	
occurrences (all)	3	1	
Gastrointestinal disorders			

Diarrhea			
subjects affected / exposed	10 / 38 (26.32%)	11 / 41 (26.83%)	
occurrences (all)	10	11	
Mucositis oral			
subjects affected / exposed	5 / 38 (13.16%)	9 / 41 (21.95%)	
occurrences (all)	5	9	
Nausea			
subjects affected / exposed	4 / 38 (10.53%)	10 / 41 (24.39%)	
occurrences (all)	4	10	
Vomiting			
subjects affected / exposed	3 / 38 (7.89%)	3 / 41 (7.32%)	
occurrences (all)	3	3	
Abdominal pain			
subjects affected / exposed	2 / 38 (5.26%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Constipation			
subjects affected / exposed	1 / 38 (2.63%)	3 / 41 (7.32%)	
occurrences (all)	1	3	
Dysphagia			
subjects affected / exposed	1 / 38 (2.63%)	2 / 41 (4.88%)	
occurrences (all)	1	2	
Other			
subjects affected / exposed	2 / 38 (5.26%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Oral dysesthesia			
subjects affected / exposed	2 / 38 (5.26%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	27 / 38 (71.05%)	1 / 41 (2.44%)	
occurrences (all)	27	1	
Alopecia			
subjects affected / exposed	1 / 38 (2.63%)	11 / 41 (26.83%)	
occurrences (all)	1	11	
Dry skin			

subjects affected / exposed	8 / 38 (21.05%)	1 / 41 (2.44%)	
occurrences (all)	8	1	
Nail discoloration			
subjects affected / exposed	0 / 38 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	3	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	2 / 38 (5.26%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Infections and infestations			
Lung infection			
subjects affected / exposed	2 / 38 (5.26%)	2 / 41 (4.88%)	
occurrences (all)	2	2	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	7 / 38 (18.42%)	8 / 41 (19.51%)	
occurrences (all)	7	8	

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

None reported