



Clinical trial results:

A RANDOMISED, DOUBLE-BLIND, PARALLEL-GROUP, MULTICENTRE, PHASE II STUDY TO EVALUATE THE SAFETY AND PHARMACOLOGICAL ACTIVITY OF THE COMBINATION OF VANDETANIB (100 OR 300 MG/DAILY OR PLACEBO) WITH FULVESTRANT (LOADING DOSE), IN POSTMENOPAUSAL ADVANCED BREAST CANCER PATIENTS.

Summary

EudraCT number	2008-000579-12
Trial protocol	IT
Global end of trial date	28 September 2013

Results information

Result version number	v1 (current)
This version publication date	01 February 2017
First version publication date	05 August 2015

Trial information

Trial identification

Sponsor protocol code	D4200L00009
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00752986
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical Dept AstraZeneca
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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	25 July 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 September 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the event-free survival (EFS) defined as the time from randomisation to progression, death without progression, loss to follow up, whichever occurred first.

End-point Efficacy: event-free survival (EFS)

The secondary objectives of the study are to assess:

- Success rate at 6 months
- Objective tumor Response rates (complete response, CR and partial response, PR) according to RECIST criteria (Therasse P et al 2000)
- Time To Progression
- Progression Free Survival
- Overall Survival
- Safety and tolerability of vandetanib / Placebo in combination with fulvestrant

Efficacy- Safety main objective of Trial

Protection of trial subjects:

Pain relief medication

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 41
Worldwide total number of subjects	41
EEA total number of subjects	41

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)	23
From 65 to 84 years	18
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

the study was prematurely terminated with 41 enrolled patients and 39 randomized, out of the 135 scheduled by protocol.

A total of 8 serious adverse events have been reported in 6 patients overall. 2 patients had 2 SAEs
41 pts enrolled , 39 randomized. two patients never received the drug.

Pre-assignment

Screening details:

41 pts enrolled , 39 randomized. two patients never received the drug.

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, Monitor, Carer, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Vandetanib at the dose of 100 mg

Arm description:

vandetanib at the dose of 100 mg orally once-daily plus placebo to match vandetanib 300 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3)

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	Vandetanib
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

100mg

Arm title	Vandetanib at the dose of 300 mg
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Arm description:

vandetanib at the dose of 300 mg orally once-daily plus placebo to match vandetanib 100 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3)

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	Vandetanib
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

300mg

Arm title	Placebo to match vandetanib 100 mg and 300 mg
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Arm description:

placebo to match vandetanib 100 mg orally once-daily plus placebo to match vandetanib 300 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3).

Arm type	Experimental
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Investigational medicinal product name	Placebo
Investigational medicinal product code	Placebo
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to match vandetanib 100 mg and 300 mg

Number of subjects in period 1 ^[1]	Vandetanib at the dose of 100 mg	Vandetanib at the dose of 300 mg	Placebo to match vandetanib 100 mg and 300 mg
Started	16	12	11
Completed	11	11	9
Not completed	5	1	2
Consent withdrawn by subject	2	1	2
Protocol deviation	3	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The total number of patients enrolled is equal to 41.

Only 39 patients received the treatment.

Baseline characteristics

Reporting groups

Reporting group title	Vandetanib at the dose of 100 mg
Reporting group description:	vandetanib at the dose of 100 mg orally once-daily plus placebo to match vandetanib 300 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3)
Reporting group title	Vandetanib at the dose of 300 mg
Reporting group description:	vandetanib at the dose of 300 mg orally once-daily plus placebo to match vandetanib 100 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3)
Reporting group title	Placebo to match vandetanib 100 mg and 300 mg
Reporting group description:	placebo to match vandetanib 100 mg orally once-daily plus placebo to match vandetanib 300 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3).

Reporting group values	Vandetanib at the dose of 100 mg	Vandetanib at the dose of 300 mg	Placebo to match vandetanib 100 mg and 300 mg
Number of subjects	16	12	11
Age categorical Units: Subjects			
Adults (18-64 years)	16	12	11
Age Continuous Units: years arithmetic mean full range (min-max)	63.6 44 to 78	59.8 48 to 79	59.6 43 to 74
Gender, Male/Female			
Female			
Units: Participants			
Female	16	12	11

Reporting group values	Total		
Number of subjects	39		
Age categorical Units: Subjects			
Adults (18-64 years)	39		
Age Continuous Units: years arithmetic mean full range (min-max)	-		
Gender, Male/Female			
Female			
Units: Participants			
Female	39		

End points

End points reporting groups

Reporting group title	Vandetanib at the dose of 100 mg
Reporting group description: vandetanib at the dose of 100 mg orally once-daily plus placebo to match vandetanib 300 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3)	
Reporting group title	Vandetanib at the dose of 300 mg
Reporting group description: vandetanib at the dose of 300 mg orally once-daily plus placebo to match vandetanib 100 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3)	
Reporting group title	Placebo to match vandetanib 100 mg and 300 mg
Reporting group description: placebo to match vandetanib 100 mg orally once-daily plus placebo to match vandetanib 300 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3).	

Primary: Event Free Survival

End point title	Event Free Survival ^[1]
End point description: Success rate (patients without progression and still on treatment at 24 weeks)	
End point type	Primary
End point timeframe: Restaging (RECIST) is carried out at screening and every 3 months during the study until 1 year and than every 6 months until objective disease progression.	

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: No statistical analysis of data was performed.

End point values	Vandetanib at the dose of 100 mg	Vandetanib at the dose of 300 mg	Placebo to match vandetanib 100 mg and 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	
Units: participants				
number (not applicable)				

Notes:

[2] - No statistical analysis was performed

[3] - No statistical analysis was performed

[4] - No statistical analysis was performed

Statistical analyses

No statistical analyses for this end point

Secondary: TTPI, PFS, CR+PR, disease control(CR+PR+SD),DOR

End point title	TTPI, PFS, CR+PR, disease control(CR+PR+SD),DOR
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End point description:

End point type	Secondary
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End point timeframe:

Restaging (RECIST) is carried out at screening and every 3 months during the study until 1 year and than every 6 months until objective disease progression.

End point values	Vandetanib at the dose of 100 mg	Vandetanib at the dose of 300 mg	Placebo to match vandetanib 100 mg and 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[5]	0 ^[6]	0 ^[7]	
Units: participants				
number (not applicable)				

Notes:

[5] - no statistical analysis was made

[6] - no statistical analysis was made

[7] - no statistical analysis was made

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
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End point description:

End point type	Secondary
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End point timeframe:

Assessments for survival must be made at the 60 day follow-up visit and then every 3 months, unless the patient withdraws consent.

End point values	Vandetanib at the dose of 100 mg	Vandetanib at the dose of 300 mg	Placebo to match vandetanib 100 mg and 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[8]	0 ^[9]	0 ^[10]	
Units: participants				
number (not applicable)				

Notes:

[8] - no statistical analysis was made

[9] - no statistical analysis was made

[10] - no statistical analysis was made

Statistical analyses

No statistical analyses for this end point

Secondary: AEs,lab,vital sign and ECG changes

End point title | AEs,lab,vital sign and ECG changes

End point description:

End point type | Secondary

End point timeframe:

Continuous assessment of safety.

End point values	Vandetanib at the dose of 100 mg	Vandetanib at the dose of 300 mg	Placebo to match vandetanib 100 mg and 300 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[11]	0 ^[12]	0 ^[13]	
Units: participants				
number (not applicable)				

Notes:

[11] - no statistical analysis was made

[12] - no statistical analysis was made

[13] - no statistical analysis was made

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:
ongoing basis as per law

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	0
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Reporting groups

Reporting group title	Vandetanib at the dose of 100 mg
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Reporting group description:

vandetanib at the dose of 100 mg orally once-daily plus placebo to match vandetanib 300 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3)

Reporting group title	Placebo to match vandetanib 100 mg and 300 mg
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Reporting group description:

placebo to match vandetanib 100 mg orally once-daily plus placebo to match vandetanib 300 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3).

Reporting group title	Vandetanib at the dose of 300 mg
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Reporting group description:

vandetanib at the dose of 300 mg orally once-daily plus placebo to match vandetanib 100 mg orally once-daily plus fulvestrant LD (500 mg im. at day 1 and 250 mg at day 14, 28 and thereafter every 28th day +/- 3)

Serious adverse events	Vandetanib at the dose of 100 mg	Placebo to match vandetanib 100 mg and 300 mg	Vandetanib at the dose of 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 16 (18.75%)	1 / 11 (9.09%)	2 / 12 (16.67%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
severe arthralgia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 12 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 12 (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
Gastrointestinal disorders			

gastroenteritis.			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 12 (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
grade 3 diarrhoea			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 12 (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			
grade 3 erythema			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
diabetes complication			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Musculoskeletal and connective tissue disorders			
right iliac fracture			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Vandetanib at the dose of 100 mg	Placebo to match vandetanib 100 mg and 300 mg	Vandetanib at the dose of 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 16 (75.00%)	6 / 11 (54.55%)	11 / 12 (91.67%)
General disorders and administration site conditions			
RECTAL BLEEDING			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
HEMORRHOIDS			

subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
TOOTH ACHE			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	3 / 12 (25.00%)
occurrences (all)	2	0	3
VOMITING			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	2
INSOMNIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	0	3
HEADACHE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
ANOREXIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
ASTHENIA			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
FEVER			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	2 / 12 (16.67%)
occurrences (all)	2	0	2
ONYCHOPATY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
WEIGHT LOSS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
LOSS OF APPETITE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
SWEATING			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
ARTHRALGIA subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
FATIGUE subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 2	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Respiratory, thoracic and mediastinal disorders THORACIC PAIN subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
PAIN RIGHT THORAX subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
BRONCHITIS subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Psychiatric disorders ANXIETY subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
ANXIOUS-DEPRESSIVE SYNDROME subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
Cardiac disorders HYPERTENSION subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3	0 / 11 (0.00%) 0	2 / 12 (16.67%) 4
TACHICARDY subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
FLUSHING subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Nervous system disorders			

NEUROPATHY (ARMS) subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
Blood and lymphatic system disorders			
AST ELEVATION subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
ANAEMIA subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 3	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
NEUTROPENIA subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
LEUKOPENIA subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
HYPERCALCEMIA subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
HYPERTRANSAMINASEMIA subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1	2 / 12 (16.67%) 5
PIASTRINOPENIA subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 3
TRANSAMINASE INCREASE subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
HYPERPOTASSEMIA subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Ear and labyrinth disorders			
DIZZINESS subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
VERTIGO			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Eye disorders LEFT EYE PAIN subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
EYE ANGIOEDEMA subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Gastrointestinal disorders RIGHT HYPOCHONDRIUM PAIN subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0
DIARRHEA subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 3	0 / 11 (0.00%) 0	7 / 12 (58.33%) 14
Hepatobiliary disorders HEPATIC TOXICITY subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
Skin and subcutaneous tissue disorders RASH subjects affected / exposed occurrences (all)	3 / 16 (18.75%) 6	0 / 11 (0.00%) 0	6 / 12 (50.00%) 11
HYPERPIGMENTATION subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	1 / 12 (8.33%) 1
ERYTHEMA subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	2 / 12 (16.67%) 5
SCALP ERITHEMA subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1	0 / 11 (0.00%) 0	0 / 12 (0.00%) 0
Renal and urinary disorders PROTEINURIA subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 11 (9.09%) 1	0 / 12 (0.00%) 0

CYSTITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
HAEMORRHAGIC CYSTITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
BONE PAIN			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	3 / 12 (25.00%)
occurrences (all)	0	1	4
JOINT PAIN			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
RIB FRACTURE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
LUMBAR PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
MUSCOLOSKELETICAL PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
MUCOSITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
STOMATITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
UMBILICAL MYCOSES			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0

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