Clinical trial results:
A multi-country, multicenter, randomized, open-label, parallel group study to assess the efficacy and safety of Docecal compared with Taxotere®

Summary

EudraCT number	2012-005161-12
Trial protocol	LV
Global end of trial date	11 January 2018

Results information

Result version number	v1 (current)
This version publication date	04 August 2019
First version publication date	04 August 2019

Trial information

Trial identification

Sponsor protocol code	OAS-12DOC-BIO

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Oasmia Pharmaceutical AB
Sponsor organisation address	Vallongatan 1, Uppsala, Sweden, SE-752 28
Public contact	Oasmia Pharmaceutical AB , Oasmia Pharmaceutical AB , info@oasmia.com
Scientific contact	Head of Clinical Development, Oasmia Pharmaceutical AB , nina.heldring@oasmia.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	17 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2018
Global end of trial reached?	Yes
Global end of trial date	11 January 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to demonstrate that Docecal is not inferior to Taxotere®, measured as overall response rate (ORR).

Protection of trial subjects:

An independent medical monitor reviewed safety data during the study.
Laboratory measurements (haematology and clinical chemistry), vital signs and physical examination were assessed to monitor safety of patients.
Patients were withdrawn if medically necessary according to investigator.

Background therapy: -

Evidence for comparator:

Taxotere is a well known anticancer treatment that has been approved on the market for breast cancer for several decades. Both Taxotere and the test drug contain the same active molecule and the only difference between the formulations are the excipients.

Actual start date of recruitment	11 March 2016
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	Russian Federation: 120
Country: Number of subjects enrolled	Ukraine: 80
Worldwide total number of subjects	200
EEA total number of subjects	0

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)	163

From 65 to 84 years	37
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening was performed maximum 21 days before first dose. Criteria included female with adenocarcinoma of breast who had failed anthracycline treatment, age ≥18 years, ECOG ≤2 . 15 of 217 screened patients did not meet inclusion/exclusion criteria and 2 patients withdraw their consent before randomization.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Docecal

Arm description:

Patients randomized to receive Docecal.

Arm type	Experimental
Investigational medicinal product name	Docecal
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docecal was administered as 1-hour intravenous infusion at a dose of 100 mg/m2 docetaxel every 21 days for a total of 6 cycles. The dose was calculated based on body surface area. The powder was reconstituted to a concentration of 0.5 mg/ml using NaCl solution before infusion. No dexamethasone premedication was required, unless hypersensitivity reactions or fluid retention occurred during the study.

Arm title	Taxotere

Arm description:

Patients randomized to receive Taxotere.

Arm type	Active comparator
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:

Taxotere was administered as 1-hour intravenous infusion at a dose of 100 mg/m2 docetaxel every 21 days for a total of 6 cycles. The dose was calculated based on body surface area. The powder was reconstituted according to Taxotere´s SmPC before infusion. Dexamethasone premedication was given at a dose of 16 mg/day (8 mg twice per day) for 3 days starting 1 day prior docetaxel administration.

Number of subjects in period 1	Docecal	Taxotere
Started	100	100
Completed	79	80
Not completed	21	20
Adverse event, serious fatal	-	2
Consent withdrawn by subject	1	2
Physician decision	4	2
Other illness that prevents further treatment	1	-
Adverse event, non-fatal	2	3
Death	1	1
Inability to follow treatment schedule	1	-
Patient´s condition	2	-
Lost to follow-up	-	2
Lack of efficacy	9	8

Baseline characteristics

Reporting groups	
Reporting group title	Docecal
Reporting group description:	
Patients randomized to receive Docecal.	
Reporting group title	Taxotere
Reporting group description:	
Patients randomized to receive Taxotere.	

Reporting group values	Docecal	Taxotere	Total
Number of subjects	100	100	200
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)	82	81	163
From 65-84 years	18	19	37
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	54.9	56.2	
standard deviation	± 10.2	± 8.3	-
Gender categorical Units: Subjects			
Female	100	100	200
Male	0	0	0
Body surface area Units: m2			
arithmetic mean	1.76	1.80	
standard deviation	± 0.18	± 0.15	-

End points

End points reporting groups

Reporting group title	Docecal
Reporting group description:	
Patients randomized to receive Docecal.	
Reporting group title	Taxotere
Reporting group description:	
Patients randomized to receive Taxotere.	

Primary: Overall response rate (partial and complete response) after 6 cycles of chemotherapy

End point title	Overall response rate (partial and complete response) after 6 cycles of chemotherapy
End point description:	
Overall response rate (partial and complete response) after 6 cycles of chemotherapy, based on the assessments of the Independent Imaging Review Facility according to RECIST 1.1 criteria (2009).	
End point type	Primary
End point timeframe:	
CT/MR scans were performed at baseline (within 28 days prior to the start of treatment) and every 9 weeks ± 3 days after the date of randomization	

End point values	Docecal	Taxotere		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: patients				
Complete response	1	3		
Partial response	30	42		
Stable disease	53	42		
Disease progression	9	9		
Not evaluable	7	4		

Statistical analyses

Statistical analysis title	Non-inferiority testing
Statistical analysis description:	
The primary endpoint was analyzed by a non-inferiority test using the Farrington-Manning method. The criterion for non-inferiority at final analysis is considered to have been met if the lower limit of the 1-sided 97.36% confidence interval for the difference in ORR between groups (test drug – reference drug) is above the predefined non-inferiority margin -23%.	
Comparison groups	Docecal v Taxotere

Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in ORR (Docecal-Taxotere)
Point estimate	-14
Confidence interval	
level	Other: 97.36 %
sides	1-sided
lower limit	-27

Post-hoc: Overall response rate (partial and complete repsonse) at end of chemotherapy visit (Visit 16/Day 127+7)

End point title	Overall response rate (partial and complete repsonse) at end of chemotherapy visit (Visit 16/Day 127+7)

End point description:

Overall response rate (partial and complete response) at the end of chemotherapy visit (Visit 16/Day 127+7) based on the assessments of the Independent Imaging Review Facility

End point type	Post-hoc

End point timeframe:

CT/MR scans were performed at baseline (within 28 days prior to the start of treatment) and every 9 weeks ± 3 days after the date of randomization

End point values	Docecal	Taxotere		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	100		
Units: patients				
Complete response	1	2		
Partial response	26	33		
Stable disease	30	28		
Disease progression	19	14		
Neither complete response nor progressive disease	2	2		
Not evaluable	1	1		
Missing (no tumour assessment at visit 16)	21	20		

Statistical analyses

Statistical analysis title	Non-inferiority testing

Statistical analysis description:

Non-inferiority test using the Farrington-Manning method. The criterion for non-inferiority at final analysis is considered to have been met if the lower limit of the 1-sided 97.36% confidence interval for the difference in ORR between groups (test drug – reference drug) is above the predefined non-inferiority margin -23%.

Comparison groups	Docecal v Taxotere

Number of subjects included in analysis	200
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	Difference in ORR (Docecal-Taxotere)
Point estimate	-8
Confidence interval	
level	Other: 97.36 %
sides	1-sided
lower limit	-20.4

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Reporting period started on the first day of protocol therapy and ended when the patient left the study, whether prematurely or at the end of study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Docecal

Reporting group description:

Patients randomized to receive Docecal.

Reporting group title	Taxotere

Reporting group description:

Patients randomized to receive Taxotere.

Serious adverse events	Docecal	Taxotere	
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 98 (58.16%)	87 / 100 (87.00%)	
number of deaths (all causes)	1	3	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour haemorrhage			
subjects affected / exposed	1 / 98 (1.02%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery insufficiency			
subjects affected / exposed	0 / 98 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Central pain syndrome			
subjects affected / exposed	1 / 98 (1.02%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	1 / 98 (1.02%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	51 / 98 (52.04%)	83 / 100 (83.00%)	
occurrences causally related to treatment / all	151 / 151	256 / 256	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	15 / 98 (15.31%)	27 / 100 (27.00%)	
occurrences causally related to treatment / all	27 / 27	43 / 43	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	14 / 98 (14.29%)	23 / 100 (23.00%)	
occurrences causally related to treatment / all	15 / 15	24 / 24	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 98 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 98 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 98 (0.00%)	1 / 100 (1.00%)	
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			
Asthma			
subjects affected / exposed	1 / 98 (1.02%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 98 (1.02%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 98 (2.04%)	0 / 100 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess soft tissue			
subjects affected / exposed	0 / 98 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 98 (0.00%)	1 / 100 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Docecal	Taxotere	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	98 / 98 (100.00%)	100 / 100 (100.00%)	
Vascular disorders			
Phlebitis			
subjects affected / exposed	11 / 98 (11.22%)	0 / 100 (0.00%)	
occurrences (all)	12	0	
Phlebitis superficial			

subjects affected / exposed	4 / 98 (4.08%)	0 / 100 (0.00%)	
occurrences (all)	5	0	
Hypertension			
subjects affected / exposed	1 / 98 (1.02%)	2 / 100 (2.00%)	
occurrences (all)	2	2	
Thrombophlebitis			
subjects affected / exposed	2 / 98 (2.04%)	1 / 100 (1.00%)	
occurrences (all)	7	1	
Lymphostasis			
subjects affected / exposed	2 / 98 (2.04%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Vascular pain			
subjects affected / exposed	2 / 98 (2.04%)	0 / 100 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	44 / 98 (44.90%)	50 / 100 (50.00%)	
occurrences (all)	91	89	
Oedema peripheral			
subjects affected / exposed	28 / 98 (28.57%)	18 / 100 (18.00%)	
occurrences (all)	37	21	
Face oedema			
subjects affected / exposed	21 / 98 (21.43%)	21 / 100 (21.00%)	
occurrences (all)	23	25	
Fatigue			
subjects affected / exposed	11 / 98 (11.22%)	16 / 100 (16.00%)	
occurrences (all)	22	36	
Pyrexia			
subjects affected / exposed	4 / 98 (4.08%)	12 / 100 (12.00%)	
occurrences (all)	5	12	
Injection site phlebitis			
subjects affected / exposed	13 / 98 (13.27%)	0 / 100 (0.00%)	
occurrences (all)	43	0	
Injection site thrombosis			

subjects affected / exposed	9 / 98 (9.18%)	0 / 100 (0.00%)	
occurrences (all)	20	0	
Injection site erythema			
subjects affected / exposed	6 / 98 (6.12%)	0 / 100 (0.00%)	
occurrences (all)	7	0	
Peripheral swelling			
subjects affected / exposed	1 / 98 (1.02%)	4 / 100 (4.00%)	
occurrences (all)	1	4	
Oedema			
subjects affected / exposed	2 / 98 (2.04%)	2 / 100 (2.00%)	
occurrences (all)	2	2	
Hyperthermia			
subjects affected / exposed	3 / 98 (3.06%)	0 / 100 (0.00%)	
occurrences (all)	5	0	
Localised oedema			
subjects affected / exposed	1 / 98 (1.02%)	2 / 100 (2.00%)	
occurrences (all)	1	3	
Influenza like illness			
subjects affected / exposed	2 / 98 (2.04%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Injection site discolouration			
subjects affected / exposed	2 / 98 (2.04%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Injection site pain			
subjects affected / exposed	2 / 98 (2.04%)	0 / 100 (0.00%)	
occurrences (all)	6	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 98 (0.00%)	4 / 100 (4.00%)	
occurrences (all)	0	4	
Hydrothorax			
subjects affected / exposed	4 / 98 (4.08%)	0 / 100 (0.00%)	
occurrences (all)	4	0	
Cough			

subjects affected / exposed	0 / 98 (0.00%)	3 / 100 (3.00%)	
occurrences (all)	0	4	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	25 / 98 (25.51%)	28 / 100 (28.00%)	
occurrences (all)	39	42	
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 98 (21.43%)	27 / 100 (27.00%)	
occurrences (all)	33	35	
Blood bilirubin increased			
subjects affected / exposed	5 / 98 (5.10%)	13 / 100 (13.00%)	
occurrences (all)	8	20	
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 98 (5.10%)	10 / 100 (10.00%)	
occurrences (all)	7	17	
Blood chloride increased			
subjects affected / exposed	2 / 98 (2.04%)	12 / 100 (12.00%)	
occurrences (all)	5	13	
Blood sodium decreased			
subjects affected / exposed	3 / 98 (3.06%)	8 / 100 (8.00%)	
occurrences (all)	10	11	
Blood calcium decreased			
subjects affected / exposed	2 / 98 (2.04%)	6 / 100 (6.00%)	
occurrences (all)	4	8	
Blood magnesium increased			
subjects affected / exposed	1 / 98 (1.02%)	6 / 100 (6.00%)	
occurrences (all)	1	8	
Blood magnesium decreased			
subjects affected / exposed	3 / 98 (3.06%)	2 / 100 (2.00%)	
occurrences (all)	7	3	
Blood uric acid increased			
subjects affected / exposed	1 / 98 (1.02%)	4 / 100 (4.00%)	
occurrences (all)	1	5	
Blood creatine increased			

subjects affected / exposed	2 / 98 (2.04%)	2 / 100 (2.00%)	
occurrences (all)	2	3	
Electrocardiogram abnormal			
subjects affected / exposed	1 / 98 (1.02%)	3 / 100 (3.00%)	
occurrences (all)	1	3	
Blood urea increased			
subjects affected / exposed	2 / 98 (2.04%)	1 / 100 (1.00%)	
occurrences (all)	2	2	
Electrocardiogram repolarisation abnormality			
subjects affected / exposed	0 / 98 (0.00%)	3 / 100 (3.00%)	
occurrences (all)	0	3	
Weight increased			
subjects affected / exposed	2 / 98 (2.04%)	1 / 100 (1.00%)	
occurrences (all)	2	1	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	3 / 98 (3.06%)	3 / 100 (3.00%)	
occurrences (all)	3	3	
Pericardial effusion			
subjects affected / exposed	2 / 98 (2.04%)	1 / 100 (1.00%)	
occurrences (all)	2	1	
Defect conduction intraventricular			
subjects affected / exposed	0 / 98 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	11 / 98 (11.22%)	25 / 100 (25.00%)	
occurrences (all)	11	26	
Dysgeusia			
subjects affected / exposed	8 / 98 (8.16%)	11 / 100 (11.00%)	
occurrences (all)	13	22	
Hypoaesthesia			
subjects affected / exposed	4 / 98 (4.08%)	7 / 100 (7.00%)	
occurrences (all)	7	7	
Headache			

subjects affected / exposed	3 / 98 (3.06%)	2 / 100 (2.00%)	
occurrences (all)	3	3	
Neuropathy peripheral			
subjects affected / exposed	3 / 98 (3.06%)	3 / 100 (3.00%)	
occurrences (all)	3	3	
Polyneuropathy			
subjects affected / exposed	1 / 98 (1.02%)	5 / 100 (5.00%)	
occurrences (all)	1	6	
Hypogeusia			
subjects affected / exposed	1 / 98 (1.02%)	2 / 100 (2.00%)	
occurrences (all)	1	4	
Somnolence			
subjects affected / exposed	0 / 98 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Syncope			
subjects affected / exposed	0 / 98 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	76 / 98 (77.55%)	85 / 100 (85.00%)	
occurrences (all)	241	219	
Leukopenia			
subjects affected / exposed	77 / 98 (78.57%)	93 / 100 (93.00%)	
occurrences (all)	299	374	
Anaemia			
subjects affected / exposed	34 / 98 (34.69%)	35 / 100 (35.00%)	
occurrences (all)	69	62	
Febrile neutropenia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 100 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	13 / 98 (13.27%)	10 / 100 (10.00%)	
occurrences (all)	23	19	
Hypoglobulinaemia			
subjects affected / exposed	2 / 98 (2.04%)	5 / 100 (5.00%)	
occurrences (all)	6	9	

Thrombocytosis			
subjects affected / exposed	2 / 98 (2.04%)	1 / 100 (1.00%)	
occurrences (all)	4	2	
Eye disorders			
Eyelid oedema			
subjects affected / exposed	2 / 98 (2.04%)	1 / 100 (1.00%)	
occurrences (all)	2	1	
Lacrimation increased			
subjects affected / exposed	0 / 98 (0.00%)	3 / 100 (3.00%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	30 / 98 (30.61%)	17 / 100 (17.00%)	
occurrences (all)	79	43	
Diarrhoea			
subjects affected / exposed	20 / 98 (20.41%)	25 / 100 (25.00%)	
occurrences (all)	29	35	
Stomatitis			
subjects affected / exposed	13 / 98 (13.27%)	21 / 100 (21.00%)	
occurrences (all)	24	43	
Vomiting			
subjects affected / exposed	9 / 98 (9.18%)	2 / 100 (2.00%)	
occurrences (all)	10	4	
Dry mouth			
subjects affected / exposed	3 / 98 (3.06%)	7 / 100 (7.00%)	
occurrences (all)	5	10	
Abdominal pain upper			
subjects affected / exposed	0 / 98 (0.00%)	3 / 100 (3.00%)	
occurrences (all)	0	5	
Abdominal pain			
subjects affected / exposed	0 / 98 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	3	
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	3 / 98 (3.06%)	2 / 100 (2.00%)	
occurrences (all)	4	2	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	39 / 98 (39.80%)	60 / 100 (60.00%)	
occurrences (all)	44	71	
Erythema			
subjects affected / exposed	2 / 98 (2.04%)	10 / 100 (10.00%)	
occurrences (all)	3	16	
Nail discolouration			
subjects affected / exposed	4 / 98 (4.08%)	7 / 100 (7.00%)	
occurrences (all)	4	8	
Nail disorder			
subjects affected / exposed	0 / 98 (0.00%)	4 / 100 (4.00%)	
occurrences (all)	0	4	
Pruritus			
subjects affected / exposed	3 / 98 (3.06%)	0 / 100 (0.00%)	
occurrences (all)	3	0	
Dermatitis allergic			
subjects affected / exposed	0 / 98 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Erythema multiforme			
subjects affected / exposed	0 / 98 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Onychoclasis			
subjects affected / exposed	0 / 98 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	0 / 98 (0.00%)	2 / 100 (2.00%)	
occurrences (all)	0	2	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 98 (7.14%)	11 / 100 (11.00%)	
occurrences (all)	22	33	
Bone pain			
subjects affected / exposed	2 / 98 (2.04%)	4 / 100 (4.00%)	
occurrences (all)	7	6	
Myalgia			

subjects affected / exposed	1 / 98 (1.02%)	2 / 100 (2.00%)	
occurrences (all)	1	2	
Pain in extremity			
subjects affected / exposed	2 / 98 (2.04%)	0 / 100 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	4 / 98 (4.08%)	3 / 100 (3.00%)	
occurrences (all)	4	3	
Upper respiratory tract infection			
subjects affected / exposed	3 / 98 (3.06%)	2 / 100 (2.00%)	
occurrences (all)	3	2	
Erysipelas			
subjects affected / exposed	0 / 98 (0.00%)	3 / 100 (3.00%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	12 / 98 (12.24%)	34 / 100 (34.00%)	
occurrences (all)	31	92	
Decreased appetite			
subjects affected / exposed	12 / 98 (12.24%)	15 / 100 (15.00%)	
occurrences (all)	46	46	
Hypoproteinaemia			
subjects affected / exposed	4 / 98 (4.08%)	4 / 100 (4.00%)	
occurrences (all)	7	8	
Fluid retention			
subjects affected / exposed	4 / 98 (4.08%)	3 / 100 (3.00%)	
occurrences (all)	5	4	
Hypoalbuminaemia			
subjects affected / exposed	2 / 98 (2.04%)	3 / 100 (3.00%)	
occurrences (all)	3	6	
Hypocalcaemia			
subjects affected / exposed	3 / 98 (3.06%)	2 / 100 (2.00%)	
occurrences (all)	5	2	
Type 2 diabetes mellitus			

subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	2 / 100 (2.00%) 2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 December 2015	The objective of Protocol amendment was to clarify an inclusion criterion, to correct the description of the main and interim analyses and safety data reporting. A new drug strength of Docecal was added (100 mg/vial). The possibility of primary prophylaxis with G-CSF to individual patients was also added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported