



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
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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Patients were withdrawn if medically necessary according to investigator.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
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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 \pm 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 response) at end of chemotherapy visit (Visit 16/Day 127+7)

End point title	Overall response rate (partial and complete response) 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 \pm 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Docecal
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Reporting group description:

Patients randomized to receive Docecal.

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

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

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

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

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

Thrombocytosis subjects affected / exposed occurrences (all)	2 / 98 (2.04%) 4	1 / 100 (1.00%) 2	
Eye disorders			
Eyelid oedema subjects affected / exposed occurrences (all)	2 / 98 (2.04%) 2	1 / 100 (1.00%) 1	
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	3 / 100 (3.00%) 3	
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	30 / 98 (30.61%) 79	17 / 100 (17.00%) 43	
Diarrhoea subjects affected / exposed occurrences (all)	20 / 98 (20.41%) 29	25 / 100 (25.00%) 35	
Stomatitis subjects affected / exposed occurrences (all)	13 / 98 (13.27%) 24	21 / 100 (21.00%) 43	
Vomiting subjects affected / exposed occurrences (all)	9 / 98 (9.18%) 10	2 / 100 (2.00%) 4	
Dry mouth subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 5	7 / 100 (7.00%) 10	
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	3 / 100 (3.00%) 5	
Abdominal pain subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	2 / 100 (2.00%) 3	
Hepatobiliary disorders			
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 4	2 / 100 (2.00%) 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	
Onychoclasia			
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 occurrences (all)	1 / 98 (1.02%) 1	2 / 100 (2.00%) 2	
Pain in extremity subjects affected / exposed occurrences (all)	2 / 98 (2.04%) 2	0 / 100 (0.00%) 0	
Infections and infestations			
Respiratory tract infection subjects affected / exposed occurrences (all)	4 / 98 (4.08%) 4	3 / 100 (3.00%) 3	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 3	2 / 100 (2.00%) 2	
Erysipelas subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	3 / 100 (3.00%) 3	
Metabolism and nutrition disorders			
Hyperglycaemia subjects affected / exposed occurrences (all)	12 / 98 (12.24%) 31	34 / 100 (34.00%) 92	
Decreased appetite subjects affected / exposed occurrences (all)	12 / 98 (12.24%) 46	15 / 100 (15.00%) 46	
Hypoproteinaemia subjects affected / exposed occurrences (all)	4 / 98 (4.08%) 7	4 / 100 (4.00%) 8	
Fluid retention subjects affected / exposed occurrences (all)	4 / 98 (4.08%) 5	3 / 100 (3.00%) 4	
Hypoalbuminaemia subjects affected / exposed occurrences (all)	2 / 98 (2.04%) 3	3 / 100 (3.00%) 6	
Hypocalcaemia subjects affected / exposed occurrences (all)	3 / 98 (3.06%) 5	2 / 100 (2.00%) 2	
Type 2 diabetes mellitus			

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