Clinical trial results:
Effect of calcium dobesilate in early stages of diabetic retinopathy

Summary

EudraCT number	2017-000250-19
Trial protocol	ES
Global end of trial date	24 November 2020

Results information

Result version number	v1 (current)
This version publication date	09 June 2022
First version publication date	09 June 2022

Trial information

Trial identification

Sponsor protocol code	CADODIAME

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez-Soriano, Fundació Hospital Universitari Vall d'Hebron - Institut de Recersa (VHIR), 34 934894172, joaquin.lopez.soriano@vhir.org
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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	24 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 November 2020
Global end of trial reached?	Yes
Global end of trial date	24 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether Doxium® is able to prevent or reduce thickening of the retina.

Protection of trial subjects:

Treatment was interrupted if any contraindication was observed, or if laboratory analyses were abnormal, according to clinicians criterion. No other measures were required for the treatment

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 October 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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

Subject disposition

Recruitment

Recruitment details:

235 patients were recruited in 3 hospitals from Catalonia

Pre-assignment

Screening details:

65 patients met the requirements. Finally, 61 were selected, and 60 engaged in the study. Inclusion criteria were Type2 diabetes, subclinical macular edema, ETDRS 20-47, diabetes diagnosed for more than 5 years, 49-75 years of age, HbA1c ≥ 6.5% and ≤ 9.5% at 6 months previous to the screening

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dobesilate

Arm description: -

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

Dosage and administration details:

2 tablets in the morning (2x500 mg) and 2 at night (2x500 mg), orally (total daily dose: 2000 mg)

Arm title	Placebo

Arm description: -

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

Dosage and administration details:

Oral daily, same conditions as treatment

Number of subjects in period 1	Dobesilate	Placebo
Started	30	30
Completed	29	22
Not completed	1	8
Adverse event, non-fatal	1	8

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	60	60	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	65.43		
full range (min-max)	49 to 80	-	
Gender categorical Units: Subjects			
Female	22	22	
Male	38	38	

End points

End points reporting groups	
Reporting group title	Dobesilate
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Retinal thickness	
End point title	Retinal thickness
End point description: Difference in retinal thickness from initial visit to 12 months visit, assessed by SD-OCT	
End point type	Primary
End point timeframe: 12 months	

End point values	Dobesilate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	24		
Units: micrometer(s)				
arithmetic mean (standard deviation)	1 (± 24)	4 (± 24)		

Statistical analyses

Statistical analysis title	Retinal thickness
Comparison groups	Placebo v Dobesilate
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7092
Method	t-test, 2-sided

Secondary: Visual acuity	
End point title	Visual acuity
End point description: ETDRS scale	
End point type	Secondary
End point timeframe: 12 months	

End point values	Dobesilate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	24		
Units: number				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

Statistical analysis title	Visual acuity
Comparison groups	Dobesilate v Placebo
Number of subjects included in analysis	50
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9783
Method	t-test, 2-sided

Secondary: Change in EDTRS

End point title	Change in EDTRS

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Dobesilate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	30		
Units: subjects	25	24		

Statistical analyses

Statistical analysis title	EDTRS
Comparison groups	Dobesilate v Placebo

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1706
Method	Wilcoxon (Mann-Whitney)

Secondary: Retinal volume

End point title	Retinal volume

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Dobesilate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: cubic milimeters				
arithmetic mean (standard deviation)	0 (± 0)	0 (± 0)		

Statistical analyses

Statistical analysis title	Retinal volume
Comparison groups	Dobesilate v Placebo
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.6366
Method	t-test, 2-sided

Secondary: Ganglionar layer

End point title	Ganglionar layer

End point description:

Difference in ganglionar layer thickness between 12 months and first visit

End point type	Secondary

End point timeframe:

12 months

End point values	Dobesilate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: micrometer(s)				
arithmetic mean (standard deviation)	-3 (± 21)	-2 (± 13)		

Statistical analyses

Statistical analysis title	Ganglionar layer
Comparison groups	Dobesilate v Placebo
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.7603
Method	t-test, 2-sided

Secondary: Nervous fiber layer

End point title	Nervous fiber layer

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Dobesilate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	18		
Units: micrometer(s)				
arithmetic mean (standard deviation)	0 (± 2)	2 (± 8)		

Statistical analyses

Statistical analysis title	Nervous fiber layer
Comparison groups	Dobesilate v Placebo
Number of subjects included in analysis	38
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.33
Method	t-test, 2-sided

Secondary: Foveal area

End point title	Foveal area

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Dobesilate	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	21		
Units: square millimeter				
arithmetic mean (standard error)	0 (± 2)	0 (± 0)		

Statistical analyses

Statistical analysis title	Foveolar area
Comparison groups	Dobesilate v Placebo
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2898
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
12 months	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	Dobesilate
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Dobesilate	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 30 (20.00%)	4 / 30 (13.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Aspiration pleural cavity			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Penile discomfort			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dobesilate	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 30 (90.00%)	25 / 30 (83.33%)	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cutaneous T-cell lymphoma			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Lipoma			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Hypertension			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Lymphoedema			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Venous thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Thrombophlebitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Gastric polypectomy			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Tumour excision			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	

Breast capsulotomy			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Polypectomy			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Tooth extraction			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Lens capsulotomy			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Swelling			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Condition aggravated			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Gait disturbance			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Influenza like illness			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Chest discomfort			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Polyp			

subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Inflammation			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 30 (13.33%)	4 / 30 (13.33%)	
occurrences (all)	4	4	
Dyspnoea			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Hiccups			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Pleural disorder			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Orthopnoea			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Pharyngeal erythema			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Pharyngeal oedema			

subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Dysphonia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Psychiatric disorders			
Restlessness			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Investigations			
Weight loss			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Cystitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Fracture			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Wound			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Arthropod bite			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Cardiac disorders			

Cardiac failure			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Atrioventricular block first degree			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Tachycardia paroxysmal			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hypertensive cardiomyopathy			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Sinus tachycardia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Nerve compression			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Vascular headache			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Cerebral ischaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Diabetic neuropathy			

subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Radiculopathy			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Carotid artery thrombosis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Optic neuritis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Iridocyclitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Macular oedema			
subjects affected / exposed	1 / 30 (3.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Conjunctival haemorrhage			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Eye inflammation			

subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Gastric erosive			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Haemorrhoids			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Anal incontinence			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Odynophagia			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Lip pain			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	

Diarrhoea			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatic mass			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Liver disorder			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Intertrigo			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Lipodystrophy acquired			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Diabetic nephropathy			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Albuminuria			

subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Bladder spasm			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Renal failure			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Renal colic			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Microalbuminuria			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Renal impairment			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Endocrine disorders			
Adrenal atrophy			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Pharyngitis			
subjects affected / exposed	2 / 30 (6.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Gingivitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Nasopharyngitis			

subjects affected / exposed	2 / 30 (6.67%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
Viral infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Respiratory tract infection viral			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Syphilis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	0 / 30 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Renal cyst infection			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Onychomycosis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hypercholesterolaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Diabetes mellitus			
subjects affected / exposed	1 / 30 (3.33%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
Hypoglycaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	

Hypokalaemia subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	0 / 30 (0.00%) 0	
Dyslipidaemia subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	1 / 30 (3.33%) 1	

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