Clinical trial results:
Clinical non-inferiority study between Daflon® 1000 mg, one oral suspension in a sachet per day and Daflon 500® mg, 2 tablets daily after eight weeks of treatment in patients suffering from symptomatic Chronic Venous Disease (CVD). International, multicenter, double-blind, randomized, parallel group study.

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-003559-13
Trial protocol	SI CZ ES SK
Global end of trial date	15 December 2014

Results information

Result version number	v1 (current)
This version publication date	16 April 2016
First version publication date	16 April 2016

Trial information

Trial identification

Sponsor protocol code	CL3-05682-105

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1135-8530

Notes:

Sponsors

Sponsor organisation name	Institut de Recherche Internationales Servier (I.R.I.S)
Sponsor organisation address	50 rue Carnot, Suresnes, France, 92284
Public contact	Clinical Studies Department, Institut de Recherches Internationales Servier, +33 155 72 43 66, clinicaltrials@servier.com
Scientific contact	Clinical Studies Department, Institut de Recherches Internationales Servier, +33 155 72 43 66, clinicaltrials@servier.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	15 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 December 2014
Global end of trial reached?	Yes
Global end of trial date	15 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the clinical non inferiority of efficacy between Daflon® 1000 mg (1 sachet per day) and Daflon® 500 mg (2 tablets per day), in improving lower limb discomfort assessed by a 10 cm visual analogue scale (VAS) after eight weeks of treatment in patients suffering from CVD

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice standards, ethical principles stated in the Declaration of Helsinki and applicable regulatory requirements. After the subject has ended his/her participation in the trial, the investigator provided appropriate medication and/or arranged access to appropriate care for the patient.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 2013
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	Argentina: 146
Country: Number of subjects enrolled	Brazil: 65
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Mexico: 48
Country: Number of subjects enrolled	Romania: 194
Country: Number of subjects enrolled	Russian Federation: 255
Country: Number of subjects enrolled	Czech Republic: 94
Country: Number of subjects enrolled	Slovakia: 94
Country: Number of subjects enrolled	Slovenia: 53
Country: Number of subjects enrolled	Spain: 67
Country: Number of subjects enrolled	Thailand: 47
Country: Number of subjects enrolled	Turkey: 51
Country: Number of subjects enrolled	Vietnam: 22
Worldwide total number of subjects	1139
EEA total number of subjects	502

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)	1050
From 65 to 84 years	89
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Male or female outpatient aged between 20 and 75 years old (inclusive), suffering from primary chronic venous disease, with lower limb discomfort ≥ 4 cm on the VAS scale and at least leg pain ≥ 3 cm on the VAS scale and belonging to the Clinical Etiological Anatomic Pathophysiologic (CEAP) class C0s to C4s on the most affected leg.

Period 1

Period 1 title	Double-blind treatment period (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	MPFF sachet 1000 mg o.d.

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MPFF 1000 mg sachet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral suspension in sachet
Routes of administration	Oral use

Dosage and administration details:

One sachet taken daily (in the morning) per os.

Arm title	MPFF tablet 500 mg b.i.d.

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	MPFF 500 mg tablet
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 tablets daily (one at midday and one in the evening) taken per os

Number of subjects in period 1	MPFF sachet 1000 mg o.d.	MPFF tablet 500 mg b.i.d.
Started	571	568
Completed	540	536
Not completed	31	32
Adverse event, non-fatal	6	9
Lost to follow-up	-	1

Non-medical reason	9	8
Lack of efficacy	1	-
Protocol deviation	15	14

Baseline characteristics

Reporting groups	
Reporting group title	MPFF sachet 1000 mg o.d.
Reporting group description: -	
Reporting group title	MPFF tablet 500 mg b.i.d.
Reporting group description: -	

Reporting group values	MPFF sachet 1000 mg o.d.	MPFF tablet 500 mg b.i.d.	Total
Number of subjects	571	568	1139
Age categorical Units: Subjects			
Adults (18-64 years)	534	516	1050
From 65-84 years	37	52	89
Age continuous Units: years			
arithmetic mean	45.9	46.1	
standard deviation	± 11.9	± 12.2	-
Gender categorical Units: Subjects			
Female	488	489	977
Male	83	79	162

End points

End points reporting groups

Reporting group title	MPFF sachet 1000 mg o.d.
Reporting group description: -	
Reporting group title	MPFF tablet 500 mg b.i.d.
Reporting group description: -	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

All patients of the Randomised Set having taken at least one dose of IMP and having a value at baseline and at least one post-baseline value for the lower limb discomfort assessed by a VAS scale.

Primary: Lower limb discomfort (VAS)

End point title	Lower limb discomfort (VAS)

End point description:

On the VAS scale: 0 cm = no discomfort and 10 cm = extreme discomfort

End point type	Primary

End point timeframe:

Evaluation at selection, W0, W2, W4 and W8.
The primary analysis was the change from baseline to last post-baseline value up to W8 visit

End point values	MPFF sachet 1000 mg o.d.	MPFF tablet 500 mg b.i.d.		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	568	557		
Units: cm				
arithmetic mean (standard deviation)	-3.272 (± 2.419)	-3.33 (± 2.404)		

Statistical analyses

Statistical analysis title	Non-inferiority analysis
Comparison groups	MPFF sachet 1000 mg o.d. v MPFF tablet 500 mg b.i.d.
Number of subjects included in analysis	1125
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.0001
Method	ANCOVA

Notes:

[1] - Non-inferiority limit = 1 cm. One-sided type I error rate = 0.025.
Analysis included the fixed, categorical effects of treatment and centre, as well as the continous, fixed covariate of baseline.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported all over the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	MPFF sachet 1000 mg o.d.
Reporting group description: -	
Reporting group title	MPFF tablet 500 mg b.i.d.

Reporting group description: -

Serious adverse events	MPFF sachet 1000 mg o.d.	MPFF tablet 500 mg b.i.d.	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 568 (0.35%)	3 / 568 (0.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular insufficiency			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Face oedema			

subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine adhesions			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			

subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (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: 0.1 %

Non-serious adverse events	MPFF sachet 1000 mg o.d.	MPFF tablet 500 mg b.i.d.	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	72 / 568 (12.68%)	75 / 568 (13.20%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Hypertensive crisis			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Phlebitis superficial			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			
Carpal tunnel decompression			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			

subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Genital paraesthesia			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Menstruation delayed			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 568 (0.00%)	2 / 568 (0.35%)	
occurrences (all)	0	3	
Anxiety			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Investigations			
Weight increased			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 568 (0.35%)	1 / 568 (0.18%)	
occurrences (all)	2	1	
Ligament sprain			
subjects affected / exposed	2 / 568 (0.35%)	1 / 568 (0.18%)	
occurrences (all)	2	1	
Contusion			
subjects affected / exposed	2 / 568 (0.35%)	0 / 568 (0.00%)	
occurrences (all)	2	0	
Arthropod bite			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	

Excoriation			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Road traffic accident			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Soft tissue injury			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Traumatic haematoma			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 568 (0.88%)	7 / 568 (1.23%)	
occurrences (all)	5	8	
Paraesthesia			
subjects affected / exposed	1 / 568 (0.18%)	3 / 568 (0.53%)	
occurrences (all)	1	3	
Dizziness			
subjects affected / exposed	0 / 568 (0.00%)	2 / 568 (0.35%)	
occurrences (all)	0	2	
Hypoaesthesia			
subjects affected / exposed	1 / 568 (0.18%)	1 / 568 (0.18%)	
occurrences (all)	1	1	
Somnolence			
subjects affected / exposed	0 / 568 (0.00%)	2 / 568 (0.35%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
Lymph node pain			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 568 (0.88%)	7 / 568 (1.23%)	
occurrences (all)	5	7	
Nausea			

subjects affected / exposed	7 / 568 (1.23%)	5 / 568 (0.88%)	
occurrences (all)	7	5	
Abdominal pain upper			
subjects affected / exposed	7 / 568 (1.23%)	2 / 568 (0.35%)	
occurrences (all)	7	2	
Gastritis			
subjects affected / exposed	0 / 568 (0.00%)	4 / 568 (0.70%)	
occurrences (all)	0	4	
Dyspepsia			
subjects affected / exposed	2 / 568 (0.35%)	3 / 568 (0.53%)	
occurrences (all)	2	4	
Abdominal discomfort			
subjects affected / exposed	3 / 568 (0.53%)	0 / 568 (0.00%)	
occurrences (all)	3	0	
Constipation			
subjects affected / exposed	2 / 568 (0.35%)	0 / 568 (0.00%)	
occurrences (all)	2	0	
Abdominal distension			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Colitis			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Defaecation urgency			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Epigastric discomfort			

subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Gingival bleeding			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	2	
Hyperchlorhydria			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Irritable bowel syndrome			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Hepatitis acute			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	

Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 568 (0.00%)	2 / 568 (0.35%)	
occurrences (all)	0	2	
Dermatitis allergic			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Ingrowing nail			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Pruritus generalised			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Muscle spasms			
subjects affected / exposed	5 / 568 (0.88%)	0 / 568 (0.00%)	
occurrences (all)	5	0	
Arthralgia			
subjects affected / exposed	2 / 568 (0.35%)	1 / 568 (0.18%)	
occurrences (all)	2	1	
Back pain			
subjects affected / exposed	2 / 568 (0.35%)	0 / 568 (0.00%)	
occurrences (all)	2	0	
Pain in extremity			
subjects affected / exposed	1 / 568 (0.18%)	1 / 568 (0.18%)	
occurrences (all)	2	1	
Muscle twitching			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Musculoskeletal pain			

subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Osteoarthritis			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Tenosynovitis			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Muscle contracture			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 568 (0.53%)	5 / 568 (0.88%)	
occurrences (all)	3	5	
Pharyngitis			
subjects affected / exposed	2 / 568 (0.35%)	4 / 568 (0.70%)	
occurrences (all)	2	4	
Gastroenteritis			
subjects affected / exposed	4 / 568 (0.70%)	0 / 568 (0.00%)	
occurrences (all)	4	0	
Influenza			
subjects affected / exposed	2 / 568 (0.35%)	2 / 568 (0.35%)	
occurrences (all)	2	2	
Upper respiratory tract infection			
subjects affected / exposed	3 / 568 (0.53%)	1 / 568 (0.18%)	
occurrences (all)	3	1	
Urinary tract infection			
subjects affected / exposed	2 / 568 (0.35%)	2 / 568 (0.35%)	
occurrences (all)	2	2	
Bronchitis			
subjects affected / exposed	1 / 568 (0.18%)	1 / 568 (0.18%)	
occurrences (all)	1	1	
Respiratory tract infection viral			
subjects affected / exposed	2 / 568 (0.35%)	0 / 568 (0.00%)	
occurrences (all)	2	0	

Rhinitis				
subjects affected / exposed	1 / 568 (0.18%)	1 / 568 (0.18%)		
occurrences (all)	1	1		
Sinusitis				
subjects affected / exposed	2 / 568 (0.35%)	0 / 568 (0.00%)		
occurrences (all)	2	0		
Acute tonsillitis				
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)		
occurrences (all)	1	0		
Conjunctivitis				
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)		
occurrences (all)	1	0		
Cystitis				
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)		
occurrences (all)	1	0		
Diarrhoea infectious				
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)		
occurrences (all)	0	1		
Myringitis				
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)		
occurrences (all)	1	0		
Oral herpes				
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)		
occurrences (all)	0	1		
Otitis media				
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)		
occurrences (all)	0	1		
Respiratory tract infection				
subjects affected / exposed	1 / 568 (0.18%)	0 / 568 (0.00%)		
occurrences (all)	1	0		
Soft tissue infection				
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)		
occurrences (all)	0	1		
Tinea versicolour				
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)		
occurrences (all)	0	1		

Tracheitis			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	
Viral rhinitis			
subjects affected / exposed	0 / 568 (0.00%)	1 / 568 (0.18%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 November 2013	Applicable in all centres and concerned mainly: - Deletion of urinary proteinuria test; blood biochemistry testing was maintained to ensure detection of abnormality in renal dysfunction. - Reduce to one measurement, instead of three, of sitting blood pressure, considered as reliable enough in blood pressure assessment. - Change to one month before the selection of the patient, the planned period of 3 months without compression and for non-authorized pharmacological treatment. - Deletion of the detailed mention regarding Ankle Brachial Pressure Index for assessment of peripheral arterial occlusive disease. - Clarification of the definition and wording of following non-selection criteria: "on going deep or superficial vein thrombosis" and "Evidence of cancer". - Precision regarding non-compliance (protocol deviation). - Deletion of the question 8a in CIVIQ-20 in accordance with Pr Launois (author of CIVIQ-20). Only the question 8b was taken in account for the questionnaire analysis for the study. Indeed, question 8a was restrictive to car use which was not common in all countries.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported