Clinical trial results:
A Randomized, Double-Blind, Dose-Ranging, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Oral VB-201 in Patients with Moderate to Severe Plaque Psoriasis

Summary

EudraCT number	2012-002763-10
Trial protocol	DE ES
Global end of trial date	26 November 2014

Results information

Result version number	v1 (current)
This version publication date	01 December 2016
First version publication date	01 December 2016
Summary attachment (see zip file)	Synopsis for Eudract 2012-002763-10 (2012-002763-10_VB-201-079 Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	VB-201-079

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Vascular Biogenics Ltd
Sponsor organisation address	6 Jonathan Netanyahu St, Or Yehuda, Israel, 60376
Public contact	Project Manager, SCIderm GmbH, 49 040554401146, doris.greiling@sciderm.com
Scientific contact	Project Manager, SCIderm GmbH, 49 040554401146, doris.greiling@sciderm.com
Sponsor organisation name	VBL
Sponsor organisation address	6 Jonathan Netanyahu St., Or Yehuda, Israel, 60376
Public contact	Namit Sheer, Vascular Biogenics Ltd., 972 3-6346450, noalow@vblrx.com
Scientific contact	Ron Goldblum, MD, Vascular Biogenics Ltd., 972 3-6346450, noalow@vblrx.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	26 November 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 November 2014
Global end of trial reached?	Yes
Global end of trial date	26 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety Objective
To examine the safety and tolerability of up to 24 weeks' treatment with VB-201 or placebo in patients with psoriasis.

Efficacy Objective
Stage 1: To examine the effect of treatment with two different doses of VB-201 compared to placebo (initial 16 weeks) on measures of disease activity in patients with psoriasis.
Stage 2: To examine the effect of treatment with two different doses of VB-201 compared to placebo (24 weeks) on measures of disease activity in patients with psoriasis.

Exploratory Biomarker
To examine the effect of up to 24 weeks treatment with two different doses of VB-201 as compared with placebo on inflammatory related biomarkers.

Protection of trial subjects:

The protocol defined Patient Stopping Rules
The following stopping rules will be utilized in this study:
1. If a subject experiences nausea and vomiting for >24 hours, study medication should be discontinued until these symptoms resolve. After resolution of these adverse events or if an alternate explanation for these symptoms is present, the subject may resume study medication. If nausea and vomiting recur, the subject may be removed from the study, at the Investigator's discretion.
If a subject experiences worsening of his psoriasis, as demonstrated by a 50% increase in his PASI score, the subject must permanently discontinue study medication.
Furthermore, subjects who permanently discontinue study medication shall return for an Early Termination visit and subsequently for a final safety visit 4 weeks from the last dose.

Background therapy: -

Evidence for comparator:

placebo

Actual start date of recruitment	01 October 2012
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	Poland: 27
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	Germany: 122

Country: Number of subjects enrolled	Israel: 14
Worldwide total number of subjects	194
EEA total number of subjects	180

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)	189
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First subject has been included 20 Nov 2012, lPLV was 26 Nov 2014. Due to recruitment difficulties Israel has been added as addtional country

Pre-assignment

Screening details:

Subjects were screened for eligibility and, up to 28 days later, at the baseline visit, randomized to one of three treatments Groups.

Period 1

Period 1 title	Stage 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	placebo

Arm description:

placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Study drug will be supplied to the study sites as capsules in blister packs. During the initial double-blind phase of the study (Stage 1), VB-201 or placebo capsules will be administered orally twice daily at breakfast time and dinner time with food for a total of 16 weeks. Subjects randomized to the VB-201 80 mg/day (80 mg QD) treatment will receive 80 mg in the morning and placebo in the evening.

Arm title	80 mg VB-201

Arm description: -

Arm type	Experimental
Investigational medicinal product name	80 mg VB-201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Study drug will be supplied to the study sites as capsules in blister packs. During the initial double-blind phase of the study (Stage 1), VB-201 or placebo capsules will be administered orally twice daily at breakfast time and dinner time with food for a total of 16 weeks. Subjects randomized to the VB-201 80 mg/day (80 mg QD) treatment will receive 80 mg in the morning and placebo in the evening.

Arm title	160 mg VB-201

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	160 mg VB-201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Study drug will be supplied to the study sites as capsules in blister packs. During the initial double-blind phase of the study (Stage 1), VB-201 or placebo capsules will be administered orally twice daily at breakfast time and dinner time with food for a total of 16 weeks. Subjects randomized to the VB-201 80 mg/day (80 mg QD) treatment will receive 80 mg in the morning and placebo in the evening.

Number of subjects in period 1	placebo	80 mg VB-201	160 mg VB-201
Started	81	34	79
Completed	70	26	57
Not completed	11	8	22
Consent withdrawn by subject	6	1	9
Physician decision	1	1	-
Adverse event, non-fatal	1	2	4
Lost to follow-up	3	4	9

Period 2

Period 2 title	Stage 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	80 mg VB-201

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	80 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Study drug will be supplied to the study sites as capsules in blister packs. During the initial double-blind phase of the study (Stage 1), VB-201 or placebo capsules will be administered orally twice daily at breakfast time and dinner time with food for a total of 16 weeks. Subjects randomized to the VB-201 80 mg/day (80 mg QD) treatment will receive 80 mg in the morning and placebo in the evening. At Week 16 (Stage 2), all subjects on placebo will be crossed over the active drug, 160 mg (80mg BID). VB-201 will be administered orally twice daily at breakfast time and dinner time with food for an additional eight weeks.

Arm title	160 mg VB-201

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	160 mg VB-201
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Study drug will be supplied to the study sites as capsules in blister packs. During the initial double-blind phase of the study (Stage 1), VB-201 or placebo capsules will be administered orally twice daily at breakfast time and dinner time with food for a total of 16 weeks. Subjects randomized to the VB-201 80 mg/day (80 mg QD) treatment will receive 80 mg in the morning and placebo in the evening. At Week 16 (Stage 2), all subjects on placebo will be crossed over the active drug, 160 mg (80mg BID). VB-201 will be administered orally twice daily at breakfast time and dinner time with food for an additional eight weeks.

Arm title	placebo

Arm description: -	
Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Study drug will be supplied to the study sites as capsules in blister packs. During the initial double-blind phase of the study (Stage 1), VB-201 or placebo capsules will be administered orally twice daily at breakfast time and dinner time with food for a total of 16 weeks. Subjects randomized to the VB-201 80 mg/day (80 mg QD) treatment will receive 80 mg in the morning and placebo in the evening. At Week 16 (Stage 2), all subjects on placebo will be crossed over the active drug, 160 mg (80mg BID). VB-201 will be administered orally twice daily at breakfast time and dinner time with food for an additional eight weeks.

Number of subjects in period 2	80 mg VB-201	160 mg VB-201	placebo
Started	26	57	70
Completed	25	49	64
Not completed	1	8	6
Consent withdrawn by subject	1	5	4
Lost to follow-up	-	2	1
non-compliance	-	1	-
Protocol deviation	-	-	1

Baseline characteristics

End points

End points reporting groups	
Reporting group title	placebo
Reporting group description: placebo	
Reporting group title	80 mg VB-201
Reporting group description: -	
Reporting group title	160 mg VB-201
Reporting group description: -	
Reporting group title	80 mg VB-201
Reporting group description: -	
Reporting group title	160 mg VB-201
Reporting group description: -	
Reporting group title	placebo
Reporting group description: -	

Primary: Proportion of subjects in each of the VB-201 treatment groups and in the combined VB-201 treatment grozups who achieved at least 50% improvement from the baseline PASI score at week 16 and week 24 compared to placebo	
End point title	Proportion of subjects in each of the VB-201 treatment groups and in the combined VB-201 treatment grozups who achieved at least 50% improvement from the baseline PASI score at week 16 and week 24 compared to placebo
End point description:	
End point type	Primary
End point timeframe: week 16 week 24	

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	23
Units: Proportion of subjects	29	7	17	10

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	68		
Units: Proportion of subjects	19	29		

Statistical analyses

Statistical analysis title	PASI 50 responder rate
Comparison groups	placebo v 80 mg VB-201 v 160 mg VB-201 v 80 mg VB-201 v 160 mg VB-201 v placebo
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2447 [1]
Method	Chi-squared

Notes:

[1] - 0.1387 for 160 mg (Stage 1)
0.9445 for 80 mg (Stage 2)
0.7414 for 160 mg (Stage 2)

Secondary: Proportion of subjects in each of the VB-201 treatment groups who achieved at least 75% PASI improvement from the baseline at week 16 and 24 compared to placebo

End point title	Proportion of subjects in each of the VB-201 treatment groups who achieved at least 75% PASI improvement from the baseline at week 16 and 24 compared to placebo

End point description:

End point type	Secondary

End point timeframe:

week 16
week 24

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	23
Units: Responders	14	4	6	6

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	68		
Units: Responders	8	14		

Statistical analyses

Statistical analysis title	P Value global PASI 75
Comparison groups	placebo v 80 mg VB-201 v 160 mg VB-201 v 80 mg VB-201 v 160 mg VB-201 v placebo
Number of subjects included in analysis	288
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.6772 [2]
Method	Chi-squared

Notes:

[2] - 0.1264 for 160 mg (Stage 1)
0.5820 for 80 mg (Stage 2)
0.5957 for 160 mg (Stage 2)

Secondary: Mean change in the PASI score from baseline to week 16 and 24 in each of the two VB-201 treatment groups and in the combined groups compared to the mean change in the placebo group

End point title	Mean change in the PASI score from baseline to week 16 and 24 in each of the two VB-201 treatment groups and in the combined groups compared to the mean change in the placebo group

End point description:

End point type	Secondary

End point timeframe:

week 16
week 24

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	23
Units: Mean change				
geometric mean (standard deviation)	14.5 (± 2.5)	14.9 (± 3.13)	14.3 (± 2.93)	-6.1 (± 6.5)

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	68		
Units: Mean change				
geometric mean (standard deviation)	-5.3 (± 6.32)	-5.2 (± 6.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in affected Body Surface Area (BSA) from baseline to week 16 and 24 in each of the VB-201 treatment groups and in the combined VB 201 treatment groups compared to placebo

End point title	Change in affected Body Surface Area (BSA) from baseline to week 16 and 24 in each of the VB-201 treatment groups and in the combined VB 201 treatment groups compared to placebo

End point description:

End point type	Secondary

End point timeframe:

week 16
week 24

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	23
Units: Change in BSA				
arithmetic mean (standard deviation)	16.7 (± 5.25)	16.7 (± 6.85)	15.4 (± 5.59)	-5.6 (± 13.01)

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	68		
Units: Change in BSA				
arithmetic mean (standard deviation)	-3.5 (± 8.49)	-4.4 (± 7.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in PGA scorees from baseline to week 16 and 24 in each of the VB-201 treatment groups and in the combined treatment groups compared to placebo

End point title	Change in PGA scorees from baseline to week 16 and 24 in each of the VB-201 treatment groups and in the combined treatment groups compared to placebo

End point description:

End point type	Secondary

End point timeframe:

week 16
week 24

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	23
Units: Change in PGA score				
number (not applicable)	9	3	5	2

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	68		
Units: Change in PGA score				
number (not applicable)	7	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Patient Psoriasis Global Assessment scores from baseline to Week 16 and 24 in each of the Vb-201 treatment groups and in the combined treatment groups compared to placebo

End point title	Change in Patient Psoriasis Global Assessment scores from baseline to Week 16 and 24 in each of the Vb-201 treatment groups and in the combined treatment groups compared to placebo

End point description:

End point type	Secondary

End point timeframe:

week 16
week 24

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	23
Units: Change in score				
number (not applicable)	18	7	13	8

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	68		
Units: Change in score				

number (not applicable)	15	18		

Statistical analyses

No statistical analyses for this end point

Secondary: The proportion of subjects in the VB-201 80 mg/ day treatment group who achieved at least 50% improvement from the baseline PASI score at week 16 compared to placebo

End point title	The proportion of subjects in the VB-201 80 mg/ day treatment group who achieved at least 50% improvement from the baseline PASI score at week 16 compared to placebo
End point description: Stage 1	
End point type	Secondary
End point timeframe: week 16	

Statistical analyses

No statistical analyses for this end point

Secondary: Change in itching VAs from baseline to week 16 and 24 in each of the VB-201 treatment groups and in the combined groups compared to placebo

End point title	Change in itching VAs from baseline to week 16 and 24 in each of the VB-201 treatment groups and in the combined groups compared to placebo
End point description:	
End point type	Secondary
End point timeframe: week 16 week 24	

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	21
Units: Change in itching VAS				
number (not applicable)	53	48.9	49.6	-26

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	62		
Units: Change in itching VAS				
number (not applicable)	-17.9	-16.7		

Statistical analyses

Statistical analysis title	Summary Change Itching VAS
Comparison groups	placebo v 80 mg VB-201 v 160 mg VB-201 v 80 mg VB-201 v 160 mg VB-201 v placebo
Number of subjects included in analysis	275
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.3018 [3]
Method	ANCOVA

Notes:

[3] - 0.6144 for 160 mg (Stage 1)
0.1275 for 80 mg (Stage 2)
0.5595 for 160 mg (Stage 2)

Secondary: Change in Pain VAS from baseline to week 16 and 24 in each of the VB 201 treatment groups and in the combined VB-201 treatment groups compared to placebo

End point title	Change in Pain VAS from baseline to week 16 and 24 in each of the VB 201 treatment groups and in the combined VB-201 treatment groups compared to placebo

End point description:

End point type	Secondary

End point timeframe:

week 16
week 24

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	13
Units: Change in pain VAS score				
number (not applicable)	30.9	22.8	27.8	-19.2

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	46		
Units: Change in pain VAS score				
number (not applicable)	-22.6	-12.3		

Statistical analyses

Statistical analysis title	Summary of change in Pain VAS
Comparison groups	placebo v 80 mg VB-201 v 160 mg VB-201 v 80 mg VB-201 v 160 mg VB-201 v placebo
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1155 [4]
Method	ANCOVA

Notes:

[4] - 0.3494 for 160 mg (Stage 1)
0.1801 for 80 mg (Stage 2)
0.1175 for 160 mg (Stage 2)

Secondary: Change in the DLQI score from baseline to week 24 in each of the VB201 treatment group and in the combined VB-201 treatment groups compared to placebo

End point title	Change in the DLQI score from baseline to week 24 in each of the VB201 treatment group and in the combined VB-201 treatment groups compared to placebo

End point description:

Stagé 2

End point type	Secondary

End point timeframe:

24 weeks

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in itching VAS from baseline to week 16 in each of the VB-201 treatment groups and in the combined VB-201 treatment groups compared to placebo

End point title	Change in itching VAS from baseline to week 16 in each of the VB-201 treatment groups and in the combined VB-201 treatment groups compared to placebo
End point description: Stage 1	
End point type	Other pre-specified
End point timeframe: week 16	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in Pain VAS from baseline to week 16 in each of the VB 201 treatment groups and in the combined VB-201 treatment groups compared to placebo

End point title	Change in Pain VAS from baseline to week 16 in each of the VB 201 treatment groups and in the combined VB-201 treatment groups compared to placebo
End point description: Stage 1	
End point type	Other pre-specified
End point timeframe: weeks 16	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in the product PGA x BSA from baseline to week 16 and 24 in each of the VB 210 treatment groups and in the combined VB-201 treatment groups compared to placebo

End point title	Change in the product PGA x BSA from baseline to week 16 and 24 in each of the VB 210 treatment groups and in the combined VB-201 treatment groups compared to placebo

End point description:

End point type	Other pre-specified

End point timeframe:

week 16
week 24

End point values	placebo	80 mg VB-201	160 mg VB-201	80 mg VB-201
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	68	24	57	23
Units: change in the product PGA x BSA				
arithmetic mean (standard deviation)	51.4 (± 18.04)	47.2 (± 17.57)	50.1 (± 22.38)	-15.6 (± 41.92)

End point values	160 mg VB-201	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	68		
Units: change in the product PGA x BSA				
arithmetic mean (standard deviation)	-17.3 (± 27.46)	-15.8 (± 27.6)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Change in the DLQI score from baseline to week 16 in each of the VB201 treatment group and in the combined VB-201 treatment groups compared to placebo

End point title	Change in the DLQI score from baseline to week 16 in each of the VB201 treatment group and in the combined VB-201 treatment groups compared to placebo
End point description: Stage 1	
End point type	Other pre-specified
End point timeframe: week 16	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were reported from signature of Informed Consent through 28 days after the subject's last dose

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	VB 80 mg
Reporting group description: -	
Reporting group title	VB-201 160 mg
Reporting group description: -	
Reporting group title	VB 201 160 mg crossover

Reporting group description: -

Serious adverse events	Placebo	VB 80 mg	VB-201 160 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 81 (2.47%)	1 / 34 (2.94%)	1 / 79 (1.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Congenital, familial and genetic disorders			
Auricular perichondritis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 34 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 81 (1.23%)	0 / 34 (0.00%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			

subjects affected / exposed	0 / 81 (0.00%)	1 / 34 (2.94%)	0 / 79 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protusion			
subjects affected / exposed	0 / 81 (0.00%)	0 / 34 (0.00%)	1 / 79 (1.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	VB 201 160 mg crossover		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 70 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Congenital, familial and genetic disorders			
Auricular perichondritis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protusion			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	VB 80 mg	VB-201 160 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 81 (66.67%)	26 / 34 (76.47%)	61 / 79 (77.22%)
Investigations			
C-reactive protein increased			
subjects affected / exposed	2 / 81 (2.47%)	2 / 34 (5.88%)	4 / 79 (5.06%)
occurrences (all)	2	2	4
Any Event 5			
subjects affected / exposed	3 / 81 (3.70%)	1 / 34 (2.94%)	5 / 79 (6.33%)
occurrences (all)	3	1	5
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 81 (13.58%)	2 / 34 (5.88%)	13 / 79 (16.46%)
occurrences (all)	11	2	13
Any event 3			
subjects affected / exposed	3 / 81 (3.70%)	0 / 34 (0.00%)	1 / 79 (1.27%)
occurrences (all)	3	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 81 (2.47%)	4 / 34 (11.76%)	14 / 79 (17.72%)
occurrences (all)	2	4	14
Diarrhoea			
subjects affected / exposed	2 / 81 (2.47%)	1 / 34 (2.94%)	9 / 79 (11.39%)
occurrences (all)	2	1	9
Abdominal pain upper			
subjects affected / exposed	2 / 81 (2.47%)	2 / 34 (5.88%)	6 / 79 (7.59%)
occurrences (all)	2	2	6
Dyspepsia			
subjects affected / exposed	3 / 81 (3.70%)	1 / 34 (2.94%)	4 / 79 (5.06%)
occurrences (all)	3	1	4
Any event 2			

subjects affected / exposed	5 / 81 (6.17%)	3 / 34 (8.82%)	0 / 79 (0.00%)
occurrences (all)	5	3	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 81 (2.47%)	1 / 34 (2.94%)	5 / 79 (6.33%)
occurrences (all)	2	1	5
Any Event 4			
subjects affected / exposed	7 / 81 (8.64%)	1 / 34 (2.94%)	6 / 79 (7.59%)
occurrences (all)	7	1	6
Infections and infestations			
Nasopharnygitis			
subjects affected / exposed	16 / 81 (19.75%)	7 / 34 (20.59%)	15 / 79 (18.99%)
occurrences (all)	127	60	181
Urinary tract infection			
subjects affected / exposed	2 / 81 (2.47%)	2 / 34 (5.88%)	4 / 79 (5.06%)
occurrences (all)	2	2	4
Any Event			
subjects affected / exposed	10 / 81 (12.35%)	0 / 34 (0.00%)	10 / 79 (12.66%)
occurrences (all)	10	0	10

Non-serious adverse events	VB 201 160 mg crossover		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 70 (32.86%)		
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Any Event 5			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Any event 3			

subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Any event 2			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Any Event 4			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharnygitis			
subjects affected / exposed	23 / 70 (32.86%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		
Any Event			
subjects affected / exposed	0 / 70 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2012	Sub-Group (SG) Analysis VB-201 Levels - SG1: Adequate Levels was defined if lastlevel was >50% of highest Level Weight at baseline - SG2: Weight max 80 kg, SG3: Weight above 80 kg Baseline PASI, 2 analyses for SG -SG 4: PASI 10-12, SG5 PASI >12-20 Baseline PASI, 2 analyses for SG -SG6: PASI 10-14,3, SG7: PASI >14.3 Classification of AEs as TEAEs was added Modelling of week 24 Placebo Group resonse was added. PPGA (0,1) and PPGA (3-5) responder rates were to be analyzed For efficacy variable additional time Points for analysis were to be added within the Framework of scheduled visits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported