Clinical trial results:
A Phase 2 Multicenter, Randomized, Double-blind, Placebo-Controlled Trial to Evaluate Toreforant (JNJ-38518168) for the Treatment of Subjects with Moderate to Severe Plaque type Psoriasis

Summary

EudraCT number	2015-000277-12
Trial protocol	PL
Global end of trial date	11 March 2016

Results information

Result version number	v1 (current)
This version publication date	18 February 2017
First version publication date	18 February 2017

Trial information

Trial identification

Sponsor protocol code	38518168PSO2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02295865
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Antwerpseweg 15-17, Beerse, Belgium, B-2340
Public contact	Clinical Registry group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.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	11 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to evaluate the efficacy of JNJ-38518168 in subjects with moderate to severe plaque-type psoriasis and to assess the safety and tolerability of JNJ-38518168 in subjects with moderate to severe plaque-type psoriasis.

Protection of trial subjects:

The safety assessments included vital signs, general physical examination,adverse events (AEs), concomitant medication review, electrocardiograms (ECGs), pregnancy testing,laboratory testing, urine testing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 December 2014
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: 41
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	61
EEA total number of subjects	41

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)	55
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at Poland (5 sites) and United States (9 sites) from 14 December 2014 to 11 March 2016.

Pre-assignment

Screening details:

A total of 80 subjects were screened, of which 62 subjects were randomized at Week 0. A total of 61 subjects were treated and enrolled in the study.

Period 1

Period 1 title	Overall Study (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	Placebo

Arm description:

Subjects received 3*30 milligram(mg) placebo tablets and 1*3 mg placebo tablet orally at the same time each day upto week 12.

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

Dosage and administration details:

Subjects received oral dose of 3*30 mg tablet of placebo along with 1*3 mg tablet of placebo at the same time each day upto week 12.

Arm title	JNJ-38518168 30 milligram (mg)

Arm description:

Subjects in the JNJ-38518168 30 milligram (mg) group received 1*30 mg JNJ-38518168 tablet together with 2*30 mg placebo tablets and 1*3 mg placebo tablet at the same time each day upto week 12.

Arm type	Experimental
Investigational medicinal product name	JNJ-38518168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received oral dose of JNJ-38518168 1*30 mg tablet each day upto week 12.

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

Dosage and administration details:

Subjects received oral dose of 2*30 mg placebo and 1*3 mg placebo tablet each day upto week 12.

Arm title	JNJ-38518168 60 milligram (mg)

Arm description:

Subjects in the JNJ-38518168 60 mg group received 2*30 mg JNJ-38518168 tablets, 1*30 mg placebo tablet and 1*3 mg placebo tablet orally at the same time each day upto week 12.

Arm type	Experimental
Investigational medicinal product name	JNJ-38518168
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received oral dose of JNJ-38518168, 2*30 mg tablet each day upto week 12.

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

Dosage and administration details:

Subjects received oral dose of 1*30 mg placebo and 1*3 mg placebo tablet each day upto week 12.

Number of subjects in period 1	Placebo	JNJ-38518168 30 milligram (mg)	JNJ-38518168 60 milligram (mg)
Started	6	29	26
Completed	6	25	20
Not completed	0	4	6
Adverse event, non-fatal	-	3	-
Other	-	-	1
Pregnancy	-	-	1
Adverse event, serious non-fatal	-	-	1
Lost to follow-up	-	-	1
Lack of efficacy	-	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received 3*30 milligram(mg) placebo tablets and 1*3 mg placebo tablet orally at the same time each day upto week 12.	
Reporting group title	JNJ-38518168 30 milligram (mg)
Reporting group description:	
Subjects in the JNJ-38518168 30 milligram (mg) group received 1*30 mg JNJ-38518168 tablet together with 2*30 mg placebo tablets and 1*3 mg placebo tablet at the same time each day upto week 12.	
Reporting group title	JNJ-38518168 60 milligram (mg)
Reporting group description:	
Subjects in the JNJ-38518168 60 mg group received 2*30 mg JNJ-38518168 tablets, 1*30 mg placebo tablet and 1*3 mg placebo tablet orally at the same time each day upto week 12.	

Reporting group values	Placebo	JNJ-38518168 30 milligram (mg)	JNJ-38518168 60 milligram (mg)
Number of subjects	6	29	26
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	5	27	23
From 65 to 84 years	1	2	3
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	46.8	42.2	41.4
standard deviation	± 18.95	± 14.06	± 18.25
Title for Gender Units: subjects			
Female	0	11	5
Male	6	18	21

Reporting group values	Total		
Number of subjects	61		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	55		
From 65 to 84 years	6		
85 years and over	0		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		

Title for Gender Units: subjects			
Female	16		
Male	45		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received 3*30 milligram(mg) placebo tablets and 1*3 mg placebo tablet orally at the same time each day upto week 12.	
Reporting group title	JNJ-38518168 30 milligram (mg)
Reporting group description:	
Subjects in the JNJ-38518168 30 milligram (mg) group received 1*30 mg JNJ-38518168 tablet together with 2*30 mg placebo tablets and 1*3 mg placebo tablet at the same time each day upto week 12.	
Reporting group title	JNJ-38518168 60 milligram (mg)
Reporting group description:	
Subjects in the JNJ-38518168 60 mg group received 2*30 mg JNJ-38518168 tablets, 1*30 mg placebo tablet and 1*3 mg placebo tablet orally at the same time each day upto week 12.	

Primary: Percentage of Subjects who Achieved Psoriasis Area and Severity Index (PASI) 75 Response at Week 12

End point title	Percentage of Subjects who Achieved Psoriasis Area and Severity Index (PASI) 75 Response at Week 12
End point description:	
The PASI score is a combined assessment of lesion severity and area affected into a single score. Body is divided into 4 regions:head, arms, trunk, and legs. For each region, percent (%) area of skin involved is estimated:0=0%, 1=less than (<) 10%, 2=10 to <30%, 3=30 to <50%, 4=50 to <70%, 5=70 to <90%, 6=90 to 100%. Severity is estimated by clinical symptoms: erythema, induration, scaling; scale:0= none to 4=maximum. Final PASI=sum of severity parameters for each region*area score*weight of region (head:0.1,arms:0.2,body:0.3,legs:0.4);total possible score range: 0=no disease to 72=maximal disease. A PASI 75 response is defined as greater than or equal to (>=) 75 % improvement in PASI score from baseline.The efficacy analyses included all randomized and treated	
End point type	Primary
End point timeframe:	
Week 12	

End point values	Placebo	JNJ-38518168 30 milligram (mg)	JNJ-38518168 60 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	29	26	
Units: percentage of responders				
number (not applicable)	16.7	20.7	19.2	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Bayesian analyses with credible interval were reported.	
Comparison groups	JNJ-38518168 30 milligram (mg) v Placebo

Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	14.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	30.9

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Bayesian analyses with credible interval were reported.	
Comparison groups	Placebo v JNJ-38518168 60 milligram (mg)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	8.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	24.3

Secondary: Percentage of Subjects Who Achieved a Score of 0 or 1 on the Investigator's Global Assessment (IGA) at Week 12

End point title	Percentage of Subjects Who Achieved a Score of 0 or 1 on the Investigator's Global Assessment (IGA) at Week 12

End point description:

The IGA documents the investigator's assessment of the participants psoriasis at a given time point. Overall lesions are graded for induration, erythema, and scaling on a scale of 0 to 4 (higher score = more severe). The participant's psoriasis is assessed as 5-point scale as follows: 0=cleared, 1=minimal, 2=mild, 3=moderate, 4=severe.The efficacy analyses included all randomized and treated subjects.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	JNJ-38518168 30 milligram (mg)	JNJ-38518168 60 milligram (mg)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	29	26	
Units: percentage of responders				
number (not applicable)	16.7	20.7	19.2	

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Bayesian analyses with credible interval were reported.	
Comparison groups	Placebo v JNJ-38518168 30 milligram (mg)
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	14.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	33.2

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Bayesian analyses with credible interval were reported.	
Comparison groups	Placebo v JNJ-38518168 60 milligram (mg)
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	13.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	32.1

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Upto Week 16	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1
Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects received 3*30 milligram(mg) placebo tablets and 1*3 mg placebo tablet orally at the same time each day upto week 12.	
Reporting group title	JNJ-38518168 30 mg
Reporting group description:	
Subjects in the JNJ-38518168 30 milligram (mg) group received 1*30 mg JNJ-38518168 tablet together with 2*30 mg placebo tablets and 1*3 mg placebo tablet at the same time each day upto week 12.	
Reporting group title	JNJ-38518168 60 mg
Reporting group description:	
Subjects in the JNJ-38518168 60 mg group received 2*30 mg JNJ-38518168 tablets, 1 x 30 mg placebo tablet and 1*3 mg placebo tablet orally at the same time each day upto week 12.	

Serious adverse events	Placebo	JNJ-38518168 30 mg	JNJ-38518168 60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	JNJ-38518168 30 mg	JNJ-38518168 60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	15 / 30 (50.00%)	14 / 26 (53.85%)
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Genital Tract Inflammation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 5 (0.00%)	2 / 30 (6.67%)	1 / 26 (3.85%)
occurrences (all)	0	2	1
Oropharyngeal Pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Productive Cough			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Respiratory Tract Congestion			

subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	2 / 30 (6.67%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Sinus Congestion			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 5 (0.00%)	2 / 30 (6.67%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Blood Creatinine Increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Serum Ferritin Increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Meniscus Injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Skin Abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0

Nervous system disorders			
Headache			
subjects affected / exposed	0 / 5 (0.00%)	2 / 30 (6.67%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	1	0	1
Toothache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Skin Lesion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 30 (0.00%)	0 / 26 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			

Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 5 (20.00%)	1 / 30 (3.33%)	3 / 26 (11.54%)
occurrences (all)	1	1	4
Oral Herpes			
subjects affected / exposed	0 / 5 (0.00%)	1 / 30 (3.33%)	0 / 26 (0.00%)
occurrences (all)	0	1	0
Pulpitis Dental			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Rotavirus Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 30 (0.00%)	1 / 26 (3.85%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 September 2014	The highest dose of study agent to be tested was reduced from 90 mg once daily to 60 mg once daily based upon feedback from the FDA; Text on safety margins and adjusted values based upon the change in dose was clarified as appropriate; Screening period expanded to no more than 42 days prior to the first administration of study agent to allow more flexibility for subject screening; To ensure patient safety, a new discontinuation of treatment criterion was added. This criterion stated that all subjects whose postbaseline serum creatinine increase met toxicity Grade 3 and higher based on the Common Terminology Criteria for Adverse Events(CTCAE), version 4.0, were to be discontinued from further study treatment; To establish a baseline triglyceride value, a baseline fasting lipid panel test was added to further assess the risk of increase in triglyceride levels from baseline if needed; Corrections were made to the safety analysis section in statistical methods to summarize number and percentage of subjects by maximum CTCAE grade for each treatment group for each laboratory parameter.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported