Clinical trial results:
A randomized, multi-centre, observer-blind, controlled exploratory study to assess efficacy and safety of new topical formulations (MC2-01) in patients with plaque psoriasis

Summary

EudraCT number	2013-005003-14
Trial protocol	DE
Global end of trial date	01 September 2015

Results information

Result version number	v1 (current)
This version publication date	05 June 2021
First version publication date	05 June 2021

Trial information

Trial identification

Sponsor protocol code	MC2-01-C1 (Pro_MC2-01_13_Biotek)

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	MC2 Therapeutics Ltd.
Sponsor organisation address	C/O Agern Allé 24-26, Hørsholm, Denmark, 2970
Public contact	Senior Project Manager, Clinical Operations, MC2 Therapeutics Ltd., 45 20157033, isa@mc2therapeutics.com
Scientific contact	Senior Project Manager, Clinical Operations, MC2 Therapeutics Ltd., 45 20157033, isa@mc2therapeutics.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	01 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2015
Global end of trial reached?	Yes
Global end of trial date	01 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To investigate the efficacy of MC2-01 (calcipotriol + BDP) compared to MC2-01 (calcipotriol) and to MC2-01 (vehicle control) in the treatment of stable plaque psoriasis assessed by Total Clinical Score (TCS).

- To investigate the efficacy of MC2-01 (calcipotriol + BDP) compared to MC2-01 (BDP) and to the marketed reference products Daivobet® Ointment and Daivobet® Gel in the treatment of stable plaque psoriasis assessed by TCS.

- To evaluate the safety of the IPs by means of the occurrence of SAEs/AEs.

Protection of trial subjects:

The investigator performed a physical examination at Screening Visit and at the End of Study Visit. Vital signs (pulse rate, blood pressure and body temperature) were measured at Screening Visit and at the End of Study Visit.
Any findings of clinical relevance at Screening Visit were to be documented as concomitant disease. Any changes of clinical relevance compared to the Screening Visit examination were documented as AEs.

The general non-clinical safety (pharmacology, pharmacokinetics and toxicology) of the two single active ingredients as well as of the fixed-dose combination in MC2-01, was evaluated with reference to the safety information contained in the Summary of Product Characteristics (SmPC) for the two marketed reference products Daivobet® Ointment and Daivobet® Gel.
The investigator took appropriate diagnostic and therapeutic measures to minimize the risk for the patient. Where appropriate, he/she took diagnostic measures to collect evidence for clarification of the relationship between the SAE and the IP. Furthermore, the risk was minimized by the care and expertise of conduction. All assessments were only be conducted by qualified medical personnel and no further precautionary measures were taken.

Background therapy: -

Evidence for comparator:

The 2 comparator products were both approved topical ointment or gel containing calcipotriol/betamethasone.

Actual start date of recruitment	08 May 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	Germany: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	27
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

It was planned that 1 study site located in Germany should randomize 33 evaluable patients, however due to very slow recruitment 1 additional site was integrated.
All subjects approached for the study was selected from an internal database of potential candidates at the clinic or during general appointments in the clinic.

Pre-assignment

Screening details:

A signed informed consent form was obtained prior to performing any study related activities.

Screening visit could take place up to 14 days prior to the baseline visit, or the 2 visits could be conducted together in case all inclusion and exclusion criteria were assessable.

Period 1

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

Blinding implementation details:

This trial was an observer-blinded trial. The investigator, responsible for the clinical rating process (observer), had to be blinded throughout the trial. The site staff, responsible for the application of IPs as well as the subjects were non-blinded.
To ensure that the investigator remained blinded throughout the study, the test areas were covered with gauze by the non-blinded site staff and IPs were wiped off by the non-blinded site staff before study assessments.

Arms

Arm title	Test sites

Arm description:

Each patient received repeatedly applications with 6 products:
- MC2-01 (calcipotriol + betamethasone dipropionate (BDP)) cream
- MC2-01 (calcipotriol) cream
- MC2-01 (betamethasone dipropionate) (BDP) cream
- MC2-01 (vehicle)
- Daivobet (Calcipotriol/betamethasone dipropionate) ointment
- Daivobet (Calcipotriol/betamethasone dipropionate) cream

Arm type	Experimental
Investigational medicinal product name	MC2-01 (calcipotriol + BDP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

MC2-01 cream contained calcipotriol (50µg/g) + Betamethasone (betamethasone dipropionate (BDP) (0.5 mg/g).
The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 1,4 cm diameter, 6 days a week over a period of 28 days, in total 24 applications. After application of IPs a non-occlusive gauze was fixed using a breathable film dressing.

Investigational medicinal product name	MC2-01 (calcipotriol)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

MC2-01 cream contained calcipotriol (50µg/g).
The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 1,4 cm diameter, 6 days a week over a period of 28 days, in total 24 applications.
After application of IPs a non-occlusive gauze was fixed using a breathable film dressing.

Investigational medicinal product name	MC2-01 (BDP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

MC2-01 cream contained Betamethasone (betamethasone dipropionate (BDP) (0.5 mg/g).
The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 1,4 cm diameter, 6 days a week over a period of 28 days, in total 24 applications.
After application of IPs a non-occlusive gauze was fixed using a breathable film dressing.

Investigational medicinal product name	MC2-01 vehicle
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

MC2-01 vehicle does not contain any active ingredient.
The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 1,4 cm diameter, 6 days a week over a period of 28 days, in total 24 applications.
After application of IPs a non-occlusive gauze was fixed using a breathable film dressing.

Investigational medicinal product name	Daivobet® Ointment
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Daivobet® Ointment contained calcipotriol (50µg/g) + Betamethasone (betamethasone dipropionate (BDP) (0.5 mg/g).
The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 1,4 cm diameter, 6 days a week over a period of 28 days, in total 24 applications.
After application of IPs a non-occlusive gauze was fixed using a breathable film dressing.

Investigational medicinal product name	Daivobet® Gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

Daivobet® Gel contained calcipotriol (50µg/g) + Betamethasone (betamethasone dipropionate (BDP) (0.5 mg/g).
The dose regimen was 50 µl repeatedly topical (cutaneous to the skin) applications to a predefined test site with an area of 1,4 cm diameter, 6 days a week over a period of 28 days, in total 24 applications.
After application of IPs a non-occlusive gauze was fixed using a breathable film dressing.

Number of subjects in period 1	Test sites
Started	33
Completed	29
Not completed	4
Consent withdrawn by subject	2
Physician decision	1
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Test sites
Reporting group description:	
Each patient received repeatedly applications with 6 products: - MC2-01 (calcipotriol + betamethasone dipropionate (BDP)) cream - MC2-01 (calcipotriol) cream - MC2-01 (betamethasone dipropionate) (BDP) cream - MC2-01 (vehicle) - Daivobet (Calcipotriol/betamethasone dipropionate) ointment - Daivobet (Calcipotriol/betamethasone dipropionate) cream	

Reporting group values	Test sites	Total	
Number of subjects	33	33	
Age categorical Units: Subjects			
Adults (18-64 years)	27	27	
From 65-84 years	6	6	
Gender categorical Units: Subjects			
Female	10	10	
Male	23	23	

End points

End points reporting groups

Reporting group title	Test sites

Reporting group description:

Each patient received repeatedly applications with 6 products:
- MC2-01 (calcipotriol + betamethasone dipropionate (BDP)) cream
- MC2-01 (calcipotriol) cream
- MC2-01 (betamethasone dipropionate) (BDP) cream
- MC2-01 (vehicle)
- Daivobet (Calcipotriol/betamethasone dipropionate) ointment
- Daivobet (Calcipotriol/betamethasone dipropionate) cream

Subject analysis set title	MC2-01 (calcipotriol + betamethasone dipropionate (BDP)) cream
Subject analysis set type	Full analysis

Subject analysis set description:

32 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

Subject analysis set title	MC2-01 (calcipotriol) cream
Subject analysis set type	Full analysis

Subject analysis set description:

32 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

Subject analysis set title	MC2-01 (betamethasone dipropionate) (BDP) cream
Subject analysis set type	Full analysis

Subject analysis set description:

32 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

Subject analysis set title	MC2-01 (vehicle)
Subject analysis set type	Full analysis

Subject analysis set description:

32 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

Subject analysis set title	Daivobet (Calcipotriol/betamethasone dipropionate) ointment
Subject analysis set type	Full analysis

Subject analysis set description:

32 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

Subject analysis set title	Daivobet (Calcipotriol/betamethasone dipropionate) cream
Subject analysis set type	Full analysis

Subject analysis set description:

32 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

Primary: TCS score

End point title	TCS score

End point description:

End point type	Primary

End point timeframe:

32 randomized subjects were included in the Full Analysis Set and analyzed for absolute change in Total Clinical score (TCS) from baseline of End of Trial.

End point values	MC2-01 (calcipotriol + betamethasone dipropionate (BDP)) cream	MC2-01 (calcipotriol) cream	MC2-01 (betamethasone dipropionate) (BDP) cream	MC2-01 (vehicle)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32	32	32	32
Units: Score				
arithmetic mean (standard deviation)	-5.1 (± 1.8)	-3.5 (± 2.4)	-5.5 (± 1.5)	-2.1 (± 2.3)

End point values	Daivobet (Calcipotriol/betamethasone dipropionate) ointment	Daivobet (Calcipotriol/betamethasone dipropionate) cream		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	32	32		
Units: Score				
arithmetic mean (standard deviation)	-5.6 (± 1.5)	-5.0 (± 2.0)		

Statistical analyses

Statistical analysis title	Absolute change in TCS

Statistical analysis description:

The primary endpoint is the absolute change in Total Clinical Score (TCS) of clinical signs (intensity of erythema, scaling and infiltration) from baseline to End of Study (EOS) was analyzed using a two-way ANOVA with subjects and treatments as factors. Treatment differences will be tested using Tukey's honestly significant difference method for correcting p-values. Ninety five percent (95%) confidence interval of differences between treatments will be calculated.

Comparison groups	MC2-01 (calcipotriol + betamethasone dipropionate (BDP)) cream v MC2-01 (calcipotriol) cream v MC2-01 (betamethasone dipropionate) (BDP) cream v MC2-01 (vehicle) v Daivobet (Calcipotriol/betamethasone dipropionate) ointment v Daivobet (Calcipotriol/betamethasone dipropionate) cream
Number of subjects included in analysis	192
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.05
Method	ANOVA
Confidence interval	
level	95 %
sides	2-sided

Notes:

[1] - 32 subject were each treated with different treatments at 6 individual test sites, which add up to 192 test sites in total

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected/assessed from the time the informed consent form was signed. AEs assessed to reasonably possibly related to the trial medication had to be followed until it was resolved or until the medical condition of the subject was stable.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	Test sites

Reporting group description:

Each patient received repeatedly applications with 6 products:
- MC2-01 (calcipotriol + betamethasone dipropionate (BDP)) cream
- MC2-01 (calcipotriol) cream
- MC2-01 (betamethasone dipropionate) (BDP) cream
- MC2-01 (vehicle)
- Daivobet (Calcipotriol/betamethasone dipropionate) ointment
- Daivobet (Calcipotriol/betamethasone dipropionate) cream

Serious adverse events	Test sites		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 33 (3.03%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Musculoskeletal and connective tissue disorders			
Psoriatic arthropathy	Additional description: 1 AE of "psoriatic arthropathy " was reported with "worsening of psoriatic arthropathy" 3 days later. The "worsening of psoriasis arthritis" led to hospitalization of the patient and was reported as SAE.		
subjects affected / exposed	1 / 33 (3.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Test sites		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 33 (24.24%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Basal cell carcinoma subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Injury, poisoning and procedural complications Ligament sprain subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	3 / 33 (9.09%) 3		
Eye disorders Blepharitis subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Psoriatic arthropathy subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2 1 / 33 (3.03%) 2		
Infections and infestations Gastrointestinal infection subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Tonsillitis subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1 1 / 33 (3.03%) 1 1 / 33 (3.03%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 March 2014	Although stability data certified that the IPs were stable for more than 6 month, no in-use stability data of the test products and the vehicle had been made available prior to study start. Requested by the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM).
10 June 2014	With Amendment 2 to CSP the usage and storage conditions for the test products were further specified: Following amendment 2 to CSP the period of possible usage of opened test product containers was extended to 28 days if stored in a refrigerator at 2-8°C.
25 June 2014	In amendment 3 to CSP (resulting in version 2.0 of the CSP, dated 25 Jun 2014) the number of study sites was increased from one to two study sites. Therefore, the title of the study was changed as the study was no longer a mono-center study. Since this amendment was planned to recruit N=20 subjects per site and accordingly the randomization numbers 1-30 were allocated to site 01 and the randomization numbers 31-60 to site 02. Finally, the recruitment period was extended from 2 to 4 months and overall study duration was extended from 3.5 to 5.5 months.
24 September 2014	The distance of test areas to plaque outline was reduced from 1.5 cm to 0.5 cm in order to allow inclusion of patients with smaller plaques.
13 November 2014	The data set for the primary efficacy analysis was changed from PPS to FAS and the data set for the sensitivity analysis was changed from FAS to PPS. Furthermore an interim analysis was added after study completion of 28 patients with the aim to re-determine the sample size necessary for the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported