

**Clinical trial results:****A Multi-center Study to Evaluate the Pharmacokinetics of Diacerein and Rhein and the Safety of Diacerein after Maximum Use, Topical Administration of CCP-020 (Diacerein 1% ointment) to Patients with Epidermolysis Bullosa (EB)****Summary**

EudraCT number	2018-000439-29
Trial protocol	GB NL
Global end of trial date	14 February 2019

Results information

Result version number	v1 (current)
This version publication date	06 February 2021
First version publication date	06 February 2021

Trial information**Trial identification**

Sponsor protocol code	CCP-020-101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03472287
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 131,384

Notes:

Sponsors

Sponsor organisation name	Castle Creek Pharmaceuticals, LLC
Sponsor organisation address	233 Mt. Airy Road, Basking Ridge, United States, 07920
Public contact	Dr. Mary Spellman, Castle Creek Pharmaceuticals, LLC., 001 8622860400, mspellman@castlecreekpharma.com
Scientific contact	Dr. Mary Spellman, Castle Creek Pharmaceuticals, LLC., 001 8622860400, mspellman@castlecreekpharma.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	04 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 February 2019
Global end of trial reached?	Yes
Global end of trial date	14 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to characterize the single-dose and steady-state pharmacokinetics (PK) of diacerein and its active metabolite, rhein, after topical application of CCP-020 (diacerein 1% ointment) under maximum use conditions in adult, adolescent and in infants/children with EB.

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with the applicable International Council for Harmonisation (ICH)/Good Clinical Practice (GCP) regulatory requirements

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 April 2018
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	United States: 11
Worldwide total number of subjects	11
EEA total number of subjects	0

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)	3
Adolescents (12-17 years)	2
Adults (18-64 years)	6
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited in the United States by clinical study centers, following site initiation times but no earlier than April 2018.

Pre-assignment

Screening details:

Subjects were screened for inclusion and exclusion criteria at Visit 1. Subjects must have had a documented genetic mutation consistent with EB or via a blood or saliva genetic assessment as part of the study.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
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Arm title	Cohort 1 (Adolescents, Adults)
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Arm description:

Adolescent and adult subjects with EB (aged 12 years and older) received diacerein 1% ointment daily for 10 days.

Arm type	Experimental
Investigational medicinal product name	Diacerein
Investigational medicinal product code	CCP-020
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

During the 10-day treatment period, study drug was administered once daily to the defined application area(s). The subject/caregiver or study staff applied a sufficient quantity of study drug to cover EB lesions and uninvolved skin within the application area(s) with a thin layer and gently rubbed it in.

Arm title	Cohort 2 (Children)
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Arm description:

Children with EB (ages 4 to 11 years, inclusive) received diacerein 1% ointment daily for 10 days.

Arm type	Experimental
Investigational medicinal product name	Diacerein
Investigational medicinal product code	CCP-020
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

During the 10-day treatment period, study drug was administered once daily to the defined application area(s). The subject/caregiver or study staff applied a sufficient quantity of study drug to cover EB lesions and uninvolved skin within the application area(s) with a thin layer and gently rubbed it in.

Number of subjects in period 1	Cohort 1 (Adolescents, Adults)	Cohort 2 (Children)
Started	8	3
Completed	8	3

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1 (Adolescents, Adults)
Reporting group description: Adolescent and adult subjects with EB (aged 12 years and older) received diacerein 1% ointment daily for 10 days.	
Reporting group title	Cohort 2 (Children)
Reporting group description: Children with EB (ages 4 to 11 years, inclusive) received diacerein 1% ointment daily for 10 days.	

Reporting group values	Cohort 1 (Adolescents, Adults)	Cohort 2 (Children)	Total
Number of subjects	8	3	11
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Age at time of consent			
Units: years			
arithmetic mean	26.5	8.3	
standard deviation	± 11.74	± 1.53	-
Gender categorical			
Units: Subjects			
Female	5	1	6
Male	3	2	5
EB Classification			
Major sub-type of EB per genetic diagnoses			
Units: Subjects			
epidermolysis bullosa simplex (EBS)	4	3	7
dystrophic epidermolysis bullosa (DEB)	4	0	4
junctional epidermolysis bullosa (JEB)	0	0	0

End points

End points reporting groups

Reporting group title	Cohort 1 (Adolescents, Adults)
Reporting group description: Adolescent and adult subjects with EB (aged 12 years and older) received diacerein 1% ointment daily for 10 days.	
Reporting group title	Cohort 2 (Children)
Reporting group description: Children with EB (ages 4 to 11 years, inclusive) received diacerein 1% ointment daily for 10 days.	

Primary: Detectable Plasma Concentrations of Diacerein and Rhein

End point title	Detectable Plasma Concentrations of Diacerein and Rhein ^[1]
End point description: Bioanalytical analyses were performed to determine concentrations levels of diacerein and rhein in plasma using validated bioanalytical methods. For Cohort 1, blood samples were taken at pre-dose and 0.5, 1, 2, 3, 4, 6, and 8 hours post-dose. For Cohort 2, blood samples were taken at pre-dose and 1, 2, 4, 6, and 8 hours post-dose. Trough PK samples were collected on any 2 available days from Days 3 through 9 for Cohort 1 only. Summary statistics for each scheduled time were only reported if at least 50% of subjects had quantifiable concentrations.	
End point type	Primary
End point timeframe: Days 1-10, at select time points per protocol.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed for the descriptive exposure data.

End point values	Cohort 1 (Adolescents, Adults)	Cohort 2 (Children)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	3		
Units: Count of Participants				
Rhein below the limit of quantification - EBS	3	2		
Rhein below the limit of quantification - DEB	0	0		
Rhein above the limit of quantification - EBS	1	1		
Rhein above the limit of quantification - DEB	4	0		
Diacerein below the limit of quantification - EBS	4	3		
Diacerein below the limit of quantification - DEB	4	0		
Diacerein above the limit of quantification - EBS	0	0		
Diacerein above the limit of quantification - DEB	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline to 30 days after last dose of study drug application (40 days)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.0
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Reporting groups

Reporting group title	Cohort 1 (Adolescents, Adults)
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Reporting group description:

Adolescent/adult patients with EB (aged 12 and older) received Diacerein 1% Ointment daily for 10 days

Reporting group title	Cohort 2 (Children)
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Reporting group description:

Children with EB (aged 4 to 11 years, inclusive) received Diacerein 1% Ointment daily for 10 days.

Serious adverse events	Cohort 1 (Adolescents, Adults)	Cohort 2 (Children)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Cohort 1 (Adolescents, Adults)	Cohort 2 (Children)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 3 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported