



## Clinical trial results:

### An International, Multicenter, Open-label, Long Term Extension Study Evaluating the Safety of Diacerein 1% Ointment Topical Formulation in Subjects with Epidermolysis Bullosa Simplex (EBS)

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-003757-41 |
| Trial protocol           | GB AT NL DE FR |
| Global end of trial date | 17 April 2020  |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 17 October 2020 |
| First version publication date | 17 October 2020 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | CCP-020-302 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |              |
|------------------------------------|--------------|
| ISRCTN number                      | -            |
| ClinicalTrials.gov id (NCT number) | NCT03389308  |
| 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:

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**Results analysis stage**

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|                                                      |               |
|------------------------------------------------------|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 08 July 2020  |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 17 April 2020 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 17 April 2020 |
| Was the trial ended prematurely?                     | No            |

Notes:

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**General information about the trial**

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Main objective of the trial:

The primary objective of this study is to evaluate the long-term safety and tolerability of Diacerein 1% Ointment in subjects with EBS that were previously enrolled in studies CCP-020-301 or CCP-020-101.

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 International Council for Harmonisation (ICH)/Good Clinical Practice (GCP), applicable regulatory requirements, and the Castle Creek Policy on Bioethics.

Background therapy:

-

Evidence for comparator:

-

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 15 November 2017 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Netherlands: 3    |
| Country: Number of subjects enrolled | United Kingdom: 7 |
| Country: Number of subjects enrolled | Austria: 1        |
| Country: Number of subjects enrolled | France: 9         |
| Country: Number of subjects enrolled | Germany: 2        |
| Country: Number of subjects enrolled | Australia: 2      |
| Country: Number of subjects enrolled | Israel: 5         |
| Country: Number of subjects enrolled | United States: 22 |
| Worldwide total number of subjects   | 51                |
| EEA total number of subjects         | 22                |

Notes:

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**Subjects enrolled per age group**

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|                                           |   |
|-------------------------------------------|---|
| 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)                    | 33 |
| Adolescents (12-17 years)                | 7  |
| Adults (18-64 years)                     | 11 |
| From 65 to 84 years                      | 0  |
| 85 years and over                        | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Subjects with EBS that were previously enrolled in studies CCP-020-301 or CCP-020-101 were recruited.

### Pre-assignment

Screening details:

At baseline, EBS subjects who participated in the CCP-020-301 double-blind safety and efficacy study or participated in the CCP-020-101 pharmacokinetic study (feeder studies) and who met all of the inclusion/exclusion criteria were eligible to enroll and complete up to 2 treatment cycles of diacerein 1% ointment in this study.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Trial (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Non-randomised - controlled    |
| Blinding used                | Not blinded                    |

### Arms

|           |            |
|-----------|------------|
| Arm title | Open Label |
|-----------|------------|

Arm description:

Each treatment cycle consisted of 8 weeks on treatment (once-daily, at-home study drug applications) followed by 8 weeks off treatment (only Investigator-approved, bland, non-medicated emollient/moisturizer, routine cleansing products, and sunscreens were allowed off treatment), with a maximum of 2 treatment cycles allowed for up to 52 weeks.

|                                        |              |
|----------------------------------------|--------------|
| 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 treatment period of each cycle, subjects/caregivers applied a thin layer of the assigned study drug, sufficient to cover the subject's EBS lesions and approximately  $\frac{3}{4}$  inch (2 cm) of surrounding uninvolved skin, and gently rubbed in the study drug. Subjects/caregivers applied the assigned study drug to all EBS lesions, including any new EBS lesions that developed (up to 30% BSA), once daily, every evening until the lesions resolved, for 8 weeks.

| Number of subjects in period 1 | Open Label |
|--------------------------------|------------|
| Started                        | 51         |
| Completed                      | 39         |
| Not completed                  | 12         |
| Consent withdrawn by subject   | 5          |
| Adverse event, non-fatal       | 2          |
| Sponsor request                | 2          |
| Lost to follow-up              | 3          |



## Baseline characteristics

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### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | Overall Trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values    | Overall Trial | Total |  |
|---------------------------|---------------|-------|--|
| Number of subjects        | 51            | 51    |  |
| Age categorical           |               |       |  |
| Units: Subjects           |               |       |  |
| Children (2-11 years)     | 33            | 33    |  |
| Adolescents (12-17 years) | 7             | 7     |  |
| Adults (18-64 years)      | 11            | 11    |  |
| From 65-84 years          | 0             | 0     |  |
| 85 years and over         | 0             | 0     |  |
| Gender categorical        |               |       |  |
| Units: Subjects           |               |       |  |
| Female                    | 26            | 26    |  |
| Male                      | 25            | 25    |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                          |            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                    | Open Label |
| Reporting group description:<br>Each treatment cycle consisted of 8 weeks on treatment (once-daily, at-home study drug applications) followed by 8 weeks off treatment (only Investigator-approved, bland, non-medicated emollient/moisturizer, routine cleansing products, and sunscreens were allowed off treatment), with a maximum of 2 treatment cycles allowed for up to 52 weeks. |            |

### Primary: Treatment-Emergent Adverse Events

|                                                                                                           |                                                  |
|-----------------------------------------------------------------------------------------------------------|--------------------------------------------------|
| End point title                                                                                           | Treatment-Emergent Adverse Events <sup>[1]</sup> |
| End point description:<br>Number and percentage of participants with any treatment-emergent adverse event |                                                  |
| End point type                                                                                            | Primary                                          |
| End point timeframe:<br>Up to 52 weeks                                                                    |                                                  |

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: The primary objective of this safety study was to describe treatment-emergent adverse events.

|                                   |                 |  |  |  |
|-----------------------------------|-----------------|--|--|--|
| <b>End point values</b>           | Open Label      |  |  |  |
| Subject group type                | Reporting group |  |  |  |
| Number of subjects analysed       | 51              |  |  |  |
| Units: Count of Participants      |                 |  |  |  |
| Treatment-Emergent Adverse Events | 40              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 52 weeks

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | All study participants |
|-----------------------|------------------------|

Reporting group description:

Safety population

| Serious adverse events                            | All study participants |  |  |
|---------------------------------------------------|------------------------|--|--|
| Total subjects affected by serious adverse events |                        |  |  |
| subjects affected / exposed                       | 0 / 51 (0.00%)         |  |  |
| number of deaths (all causes)                     | 0                      |  |  |
| number of deaths resulting from adverse events    | 0                      |  |  |

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

| Non-serious adverse events                            | All study participants |  |  |
|-------------------------------------------------------|------------------------|--|--|
| Total subjects affected by non-serious adverse events |                        |  |  |
| subjects affected / exposed                           | 21 / 51 (41.18%)       |  |  |
| General disorders and administration site conditions  |                        |  |  |
| Pyrexia                                               |                        |  |  |
| subjects affected / exposed                           | 4 / 51 (7.84%)         |  |  |
| occurrences (all)                                     | 4                      |  |  |
| Respiratory, thoracic and mediastinal disorders       |                        |  |  |
| Cough                                                 |                        |  |  |
| subjects affected / exposed                           | 4 / 51 (7.84%)         |  |  |
| occurrences (all)                                     | 5                      |  |  |
| Skin and subcutaneous tissue disorders                |                        |  |  |
| Pruritus                                              |                        |  |  |



|                                                  |                     |  |  |
|--------------------------------------------------|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all) | 4 / 51 (7.84%)<br>6 |  |  |
| Infections and infestations                      |                     |  |  |
| Nasopharyngitis                                  |                     |  |  |
| subjects affected / exposed                      | 7 / 51 (13.73%)     |  |  |
| occurrences (all)                                | 10                  |  |  |
| Skin infection                                   |                     |  |  |
| subjects affected / exposed                      | 5 / 51 (9.80%)      |  |  |
| occurrences (all)                                | 9                   |  |  |
| Ear infection                                    |                     |  |  |
| subjects affected / exposed                      | 3 / 51 (5.88%)      |  |  |
| occurrences (all)                                | 3                   |  |  |
| Gastroenteritis viral                            |                     |  |  |
| subjects affected / exposed                      | 3 / 51 (5.88%)      |  |  |
| occurrences (all)                                | 3                   |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported