



## Clinical trial results:

### A Multicenter, Prospective, Randomized, Open-label, Intra-patient Controlled Study of the Efficacy and Safety of ABH001 for the Treatment of Stalled Chronic Cutaneous Wounds Associated with Generalized Epidermolysis Bullosa

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2012-001815-21   |
| Trial protocol           | ES DE AT PT      |
| Global end of trial date | 18 November 2013 |

#### Results information

|                                |                   |
|--------------------------------|-------------------|
| Result version number          | v1 (current)      |
| This version publication date  | 21 September 2019 |
| First version publication date | 21 September 2019 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | EB01-ABH001 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |                        |
|------------------------------------|------------------------|
| ISRCTN number                      | -                      |
| ClinicalTrials.gov id (NCT number) | NCT01749306            |
| WHO universal trial number (UTN)   | -                      |
| Other trial identifiers            | ABH_EB-001: ABH_EB-001 |

Notes:

##### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Organogenesis (Transferred from Shire to Organogenesis)                                    |
| Sponsor organisation address | 85 Dan Road, Canton, United States, MA 02021   |
| Public contact               | Compliance, Organogenesis (Transferred from Shire to Organogenesis), Compliance@organo.com |
| Scientific contact           | Compliance, Organogenesis (Transferred from Shire to Organogenesis), Compliance@organo.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? | Yes |

Notes:

## Results analysis stage

|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 18 November 2013 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 18 November 2013 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

The main objective is to evaluate the efficacy of ABH001 in initiating healing of selected cutaneous, clinically non-infected 'stalled' wounds in Epidermolysis Bullosa (EB) subjects by comparing the maximum percent reduction in wound surface area from Baseline (Week 0) to Week 24 between ABH001-treated wounds and Control-treated wounds in the Intent-to-Treat population.

Protection of trial subjects:

The study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 01 December 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 | Spain: 5         |
| Country: Number of subjects enrolled | United States: 7 |
| Worldwide total number of subjects   | 12               |
| EEA total number of subjects         | 5                |

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)                     | 6 |
| Adolescents (12-17 years)                 | 4 |
| Adults (18-64 years)                      | 2 |
| From 65 to 84 years                       | 0 |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Twelve unique subjects were enrolled into the Observation period of the study.

### Period 1

|                              |                                   |
|------------------------------|-----------------------------------|
| Period 1 title               | Treatment Period (overall period) |
| Is this the baseline period? | Yes                               |
| Allocation method            | Randomised - controlled           |
| Blinding used                | Not blinded                       |

### Arms

|                              |  |
|------------------------------|--|
| Are arms mutually exclusive? | No   |
| <b>Arm title</b>             | ABH001 application plus wound care dressings |

Arm description:

ABH001 applications topically every 4 weeks ( $\pm 1$  week) with protocol-specified dressings until wound healed or up to 44 weeks

|  |  |
|--|--|
| Arm type                               | Experimental                                 |
| Investigational medicinal product name | ABH001 application plus wound care dressings |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Cutaneous patch                              |
| Routes of administration               | Cutaneous use                                |

Dosage and administration details:

ABH001 application plus wound care dressings

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Control wound treatment |
|------------------|-------------------------|

Arm description:

Control wound care with protocol-specified dressings every 4 weeks ( $\pm 1$  week) up to 20 weeks with optional cross-over to ABH001 for additional 24 weeks

|  |                         |
|--|-------------------------|
| Arm type                               | Control wound treatment |
| Investigational medicinal product name | Control wound treatment |
| Investigational medicinal product code |                         |
| Other name                             |                         |
| Pharmaceutical forms                   | Cutaneous patch         |
| Routes of administration               | Cutaneous use           |

Dosage and administration details:

Control wound care with protocol-specified dressings every 4 weeks ( $\pm 1$  week) up to 20 weeks with optional cross-over to ABH001 for additional 24 weeks

| <b>Number of subjects in period 1</b> | ABH001 application plus wound care dressings | Control wound treatment |
|---------------------------------------|--|-------------------------|
| Started                               | 12   | 12                      |
| Completed                             | 0  | 0                       |
| Not completed                         | 12   | 12                      |
| Screen Failure                        | 10   | 10                      |

|                  |   |   |
|------------------|---|---|
| Not Randomized   | 1 | 1 |
| Study Terminated | 1 | 1 |

## Baseline characteristics

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Treatment Period |
|-----------------------|------------------|

|                              |
|------------------------------|
| Reporting group description: |
|------------------------------|

|                  |
|------------------|
| Treatment Period |
|------------------|

| Reporting group values | Treatment Period | Total |  |
|------------------------|------------------|-------|--|
| Number of subjects     | 12               | 12    |  |
| Age categorical        |                  |       |  |
| Units: Subjects        |                  |       |  |

|                    |         |   |  |
|--------------------|---------|---|--|
| Age continuous     |         |   |  |
| Units: years       |         |   |  |
| arithmetic mean    | 12.8    |   |  |
| standard deviation | ± 9.825 | - |  |
| Gender categorical |         |   |  |
| Units:             |         |   |  |
| Male               | 9       | 9 |  |
| Female             | 3       | 3 |  |

## End points

### End points reporting groups

|  |  |
|--|--|
| Reporting group title  | ABH001 application plus wound care dressings |
| Reporting group description:<br>ABH001 applications topically every 4 weeks ( $\pm 1$ week) with protocol-specified dressings until wound healed or up to 44 weeks                           |  |
| Reporting group title  | Control wound treatment                      |
| Reporting group description:<br>Control wound care with protocol-specified dressings every 4 weeks ( $\pm 1$ week) up to 20 weeks with optional cross-over to ABH001 for additional 24 weeks |  |

### Primary: Reduction in wound surface area in ABH001-treated versus control-treated wounds.

|                        |   |
|------------------------|---|
| End point title        | Reduction in wound surface area in ABH001-treated versus control-treated wounds. <sup>[1]</sup> |
| End point description: |   |
| End point type         | Primary   |
| End point timeframe:   | 24 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: Study was terminated (NOT due to safety concerns). The product Dermagraft was sold to Organogenesis (announcement dated 17 Jan 2014: <https://www.shire.com/en/newsroom/2014/january/shire-executes-agreement> ).

| End point values                     | ABH001 application plus wound care dressings | Control wound treatment |  |  |
|--------------------------------------|--|-------------------------|--|--|
| Subject group type                   | Reporting group                              | Reporting group         |  |  |
| Number of subjects analysed          | 0 <sup>[2]</sup>                             | 0 <sup>[3]</sup>        |  |  |
| Units: Percent                       |  |                         |  |  |
| arithmetic mean (standard deviation) | ()   | ()                      |  |  |

#### Notes:

[2] - Study was terminated (NOT due to safety concerns).

[3] - Study was terminated (NOT due to safety concerns).

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Week 48

Adverse event reporting additional description:

Study was terminated (NOT due to safety concerns). The product Dermagraft was sold to Organogenesis (announcement dated 17 Jan 2014: <https://www.shire.com/en/newsroom/2014/january/shire-executes-agreement> ).

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

### Reporting groups

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

Reporting group description:

Adverse events which occurred during the study

| Serious adverse events                            | Overall Trial  |  |  |
|---|----------------|--|--|
| Total subjects affected by serious adverse events |                |  |  |
| subjects affected / exposed                       | 0 / 12 (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                            | Overall Trial   |  |  |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 2 / 12 (16.67%) |  |  |
| Injury, poisoning and procedural complications        |                 |  |  |
| Wound pain  |                 |  |  |
| subjects affected / exposed                           | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                                     | 2               |  |  |
| General disorders and administration site conditions  |                 |  |  |
| Fever   |                 |  |  |
| subjects affected / exposed                           | 1 / 12 (8.33%)  |  |  |
| occurrences (all)                                     | 1               |  |  |
| Gastrointestinal disorders                            |                 |  |  |



|                             |                |  |  |
|-----------------------------|----------------|--|--|
| Diarrhea                    |                |  |  |
| subjects affected / exposed | 1 / 12 (8.33%) |  |  |
| occurrences (all)           | 1              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 09 January 2013 | Re-ordering of secondary objectives and secondary efficacy endpoints. Clarification of safety secondary objective and endpoint to include the capture of subject Adverse Events as well as study wound (added) Adverse Events. Clarification of use of topical antimicrobial dressings and treatment and reformatting of pre-treatment bio-burden reduction components. Follow-up telephone contact time window changed. Addition of monthly follow-up phone contacts between Day 7 and Day 11 after each treatment. Added that in the event that a subject early terminates participation prior to Week 48, the subject or legal guardian/caregiver will be given the option to be contacted by the site through regular follow-up phone contacts post study termination. Addition of Study Completer Part A and Study Completer Part B definitions. Addition of pre-configured (on loan from Sponsor) digital image equipment. Clarification that ClinRO and CGIC are the same reported outcome (Clinician Global Impression of Change). The Intent-to-treat population and Per-protocol populations to include only subjects 3 years or older at the time of enrollment. The statistical considerations were updated for the clinical trial. Wound Care and Dressings: Addition that the lot number for each protocol specified wound care dressing dispensed will be captured on the applicable accountability log. Female Subjects: A definition of what constitutes a Female Of Child Bearing Potential (FOCP) has been added. Screening Period (Week -10): Only medications the subject is currently taking at the time of screening and information regarding exclusionary concomitant medications will be captured during the Screening Period. Subject Stopping Rules have been added. Planned Interim Analysis and Data Monitoring Committee: Steps for blinded sample size-re-estimation have been added. |
| 24 May 2013     | Addition of procedure to report SAE information to Shire Medical Monitor in addition to Shire Pharmacovigilance and Risk Management (PVRM). Screening Period changed to begin at Week -6. Visit numbers altered to adjust to the screening period change beginning at Week -6. Screening visit window of $\pm 1$ week added for Week -2. Clarification of the Central Reviewer role and the process to be followed between Week -6 and Week -2 for selection of wounds to receive bioburden pre-treatment reduction. Age of wound duration increased from 4 to 8 weeks. Wound selection criteria changed. Mepilex Lite foam dressing added to protocol specified dressings. Randomization of selected wound procedures (using an IWRS system) added regarding storage of randomization codes and breaking the study blind procedures. Wording was added to clarify that during the post treatment phone contacts, sites will also inquire about compliance with wound dressing change and bathing restrictions during the first 7-11 days post treatment. Inclusion criteria altered to allow the wound location to extend over the joint area if the joint area is immobilized or splinted. Addition of inclusion in another Shire Sponsored study pending Investigator assessment that participation does not interfere with any treatment aspect of the EB01-ABH001 study. Adverse and Serious Adverse Events Assessment: Wording was added for suspension of the application of ABH001 on an affected subject pending an immediate safety review by the Sponsor or designated service provider. Clarification for monthly follow-up phone contacts after early termination to occur according to weeks (4 weeks = 1 month).   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study was terminated (NOT due to safety concerns). The product Dermagraft was sold to Organogenesis (announcement dated 17 Jan 2014: <https://www.shire.com/en/newsroom/2014/january/shire-executes-agreement> ).

Notes: