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
Arm title	ABH001 application plus wound care dressings

Arm description:

ABH001 applications topically every 4 weeks (±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

Arm title	Control wound treatment

Arm description:

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

Number of subjects in period 1	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:	
ABH001 applications topically every 4 weeks (±1 week) with protocol-specified dressings until wound healed or up to 44 weeks	
Reporting group title	Control wound treatment
Reporting group description:	
Control wound care with protocol-specified dressings every 4 weeks (±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.[1]
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[2]	0[3]		
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 occurrences (all)	1 / 12 (8.33%) 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 ± 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: