Clinical trial results:
MULTICENTRE, OPEN-LABEL, UNCONTROLLED, PIVOTAL CLINICAL TRIAL TO CONFIRM THE EFFICACY AND SAFETY OF AUTOLOGOUS FIBRINCULTURED EPIDERMAL GRAFTS CONTAINING EPIDERMAL STEM CELLS GENETICALLY MODIFIED FOR RESTORATION OF EPIDERMIS IN PATIENTS WITH JUNCTIONAL EPIDERMOLYSIS BULLOSA (HOLOGENE 5)

Summary

EudraCT number	2018-000261-36
Trial protocol	FR IT
Global end of trial date	12 March 2024

Results information

Result version number	v1 (current)
This version publication date	17 April 2026
First version publication date	17 April 2026

Trial information

Trial identification

Sponsor protocol code	HTA-HG5-02

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Holostem s.r.l.
Sponsor organisation address	via Glauco Gottardi 100, Modena, Italy, 41125
Public contact	Fania Ferrari, Holostem s.r.l., +39 059.2058064, f.ferrari.consultant@holostem.com
Scientific contact	Dr Roana Hasanaj , Holostem s.r.l., +39 344.2795064 , r.hasanaj.consultant@holostem.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-003137-PIP01-21
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	02 March 2026
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 March 2024
Global end of trial reached?	Yes
Global end of trial date	12 March 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of Hologene 5 at 12 months follow-up as percentage of success based on the following assessments:
• clinical performance as % of re-epithelisation in the absence of blisters measured by Investigator through imitoWound imaging application;
• functional evaluation based on laboratory analyses and mechanical assessment;
• Patient Reported Outcome (PRO) based on participants' improvement perception on the transplanted areas.

Protection of trial subjects:

After Hologene 5 transplantation, the participants received post-transplantation treatments with antibiotics, corticosteroids, immunosuppressants and/or immune-modulator agents, either systemic or topical, if considered appropriate by the Investigator, in consultation with the Sponsor Medical Expert, based on specific laboratory results and the participant's tolerability.

All medications administered during and after the transplantation procedure and during the immobilisation (if any) were reported in the eCRF.

Permitted Concomitant Medications
• Systemic and topical preservative-free corticosteroids, in case of persistent skin inflammation, based on Investigator's judgment, after completion of the by-protocol post- transplantation treatment period;
• Systemic and topical antibiotic treatment to be administered after biopsy and based on investigator's judgment;
• Immunosuppressants and/or immune-modulator agents, either systemic or topical are allowed;
• Gastroprotective treatment with proton-pump inhibitors (i.e. omeprazole);
• Additional topical or systemic treatments for skin disorders and any other therapy not interfering with the study evaluation parameters in the Investigator's judgment. All topical concomitant treatments have to be administered in a preservative-free preparation (e.g. Benzalkonium chloride, as well as other quaternary ammonium compounds, is cytotoxic), according to local pharmacopeia.

Background therapy:

See above

Evidence for comparator:

No comparator was used.

Actual start date of recruitment	15 July 2022
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	Italy: 2
Worldwide total number of subjects	2
EEA total number of subjects	2

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)	1
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was finally approved in Italy on 30 May 2022 and the study was initiated in one clinical site. The first participant was enrolled on 15 July 2022. The last participant concluded the study on 12 March 2024.
The study was finally approved in France on 21 July 2022, but it never initiated in the planned clinical site.

Pre-assignment

Screening details:

Signature of the informed consent/assent;
Inclusion/exclusion criteria verification;
AEs check and collection start after informed consent/assent;
Participant's demographic data;
Medical history, including previous/concomitant diseases and/or medications;
Verification of the certified molecular diagnosis with identified mutations.

Period 1

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

Blinding implementation details:

Not applicable

Arms

Arm title	Study treatment arm

Arm description:

Hologene 5 was an autologous cultured epidermal graft containing epidermal stem cells genetically modified with gamma-retroviral (RV) vector carrying LAMB3 cDNA. Eligible participants underwent a skin biopsy from the undamaged skin (area with no frequent blisters). After receipt of the specimen at the Sponsor's manufacturing facility, epidermal cells were isolated, cultivated, transduced, frozen and used, after thawing. The study treatment included one or more applications of Hologene 5 through a dedicated surgical preparation of the wound bed. For each application, one or more grafts for each equivalent skin surface (144 cm2) was transplanted according to the area width and to the number of wounds to be treated. The size/area of epidermal graft was adapted to the surface of affected area to treat.
Each graft contained from 20.000.000 to 30.000.000 viable autologous human epidermal cells, of which at least 50% of clonogenic cells were transduced.

Arm type	Experimental
Investigational medicinal product name	Hologene 5
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Matrix for implantation matrix
Routes of administration	Implantation

Dosage and administration details:

The participant was treated with different grafts of Hologene 5. Each batch of product contained up to 15 grafts of Hologene 5 to cover the selected skin surface. Each batch preparation of study product was intended as a single treatment. In case of failure of the first treatment or in order to treat new lesions, the treatment could be repeated according to the Investigator's assessment, in consultation with the Sponsor Medical Expert..
Study treatment was applied by an appropriately qualified surgeon in hospital under standard sterile operating room conditions. Both the biopsy and the surgery for study product application were planned in advance with the Sponsor in order to permit the manufacturer to receive and process the biopsy and prepare the grafts.

Number of subjects in period 1	Study treatment arm
Started	2
Completed	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	2	2	
Age categorical			
Male and female patients between 6-month and 65-year old were planned to be enrolled. Participant 1 was a 31-year old Caucasian man. Participant 2 was a 12-year old Mulatto boy.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	1	1	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	0	0	
Male	2	2	

End points

End points reporting groups

Reporting group title	Study treatment arm

Reporting group description:

Hologene 5 was an autologous cultured epidermal graft containing epidermal stem cells genetically modified with gamma-retroviral (RV) vector carrying LAMB3 cDNA. Eligible participants underwent a skin biopsy from the undamaged skin (area with no frequent blisters). After receipt of the specimen at the Sponsor's manufacturing facility, epidermal cells were isolated, cultivated, transduced, frozen and used, after thawing. The study treatment included one or more applications of Hologene 5 through a dedicated surgical preparation of the wound bed. For each application, one or more grafts for each equivalent skin surface (144 cm2) was transplanted according to the area width and to the number of wounds to be treated. The size/area of epidermal graft was adapted to the surface of affected area to treat.
Each graft contained from 20.000.000 to 30.000.000 viable autologous human epidermal cells, of which at least 50% of clonogenic cells were transduced.

Primary: Percentage of transplantation scored as success at the 12-month follow-up based on the definition of success using the 2-step rule

End point title	Percentage of transplantation scored as success at the 12-month follow-up based on the definition of success using the 2-step rule[1]

End point description:

End point type	Primary

End point timeframe:

12-month follow-up

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 analysis was performed. The study was interrupted prematurely and only descriptive results were presented.
No statistical analysis was performed. The study was interrupted prematurely and only descriptive results were presented.

End point values	Study treatment arm			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: 100				

Notes:

[2] - The primary endpoint could not be evaluated in any subject.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

12-month follow-up

Adverse event reporting additional description:

AEs were assessed throughout the study.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28.0

Reporting groups

Reporting group title	Safety set

Reporting group description:

all enrolled participants undergoing the skin biopsy

Serious adverse events	Safety set		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (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	Safety set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No serious adverse events were reported during the study. No frequency of non-serious adverse events was calculated for this study. Just a listing of adverse events was presented. No statistical evaluation performed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 February 2024	Final Version 5.0 (Appendix 16.1.1) was issued to implement the major change in the Sponsor's and IMP manufacturer's denomination from Holostem Terapie Avanzate s.r.l. to Holostem s.r.l. This protocol version was also harmonised towards CTR 536/2014.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
12 March 2024	LSLV was 12MAR24. Afterwards, no other patients were enrolled in the study and the premature study termination was officially notified on 22NOV24, which was considered the date of study closure. The study was prematurely terminated due to changes in the product development clinical program. Furthermore, the Sponsor considered the option of closing prematurely the study due to the fact that only one clinical site was opened and that the recruitment of eligible patients had become more and more difficult.	-

Notes:

Limitations and caveats

None reported