Clinical trial results:
An Open Label, Multi-centre, Extension Study to Evaluate the Long-term Safety of Zorblisa (SD-101-6.0) in Patients with Epidermolysis Bullosa

Summary

EudraCT number	2014-005679-96
Trial protocol	AT NL GB DE PL ES LT IT
Global end of trial date	03 September 2018

Results information

Result version number	v1 (current)
This version publication date	18 March 2019
First version publication date	18 March 2019

Trial information

Trial identification

Sponsor protocol code	SD-006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02670330
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Scioderm, Inc., An Amicus Therapeutics Company
Sponsor organisation address	1 Cedar Brook Drive, Cranbury, United States, NJ 08512
Public contact	Patient Advocacy, Amicus Therapeutics, Inc., Scioderm, Inc., clinicaltrials@amicusrx.com
Scientific contact	Patient Advocacy, Amicus Therapeutics, Inc., Scioderm, Inc., clinicaltrials@amicusrx.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001590-PIP01-13
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	03 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 September 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to demonstrate the long-term safety of SD-101-6.0 in subjects with simplex, recessive dystrophic and junctional non-Herlitz Epidermolysis Bullosa (EB).

Protection of trial subjects:

This study was designed and monitored in accordance with sponsor procedures, which comply with the ethical principles of Good Clinical Practice, as required by the major regulatory authorities and in accordance with the Declaration of Helsinki and its updates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 June 2015
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	Netherlands: 2
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Lithuania: 3
Country: Number of subjects enrolled	Serbia: 16
Country: Number of subjects enrolled	United States: 57
Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Israel: 4
Worldwide total number of subjects	152
EEA total number of subjects	64

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)	8
Children (2-11 years)	77
Adolescents (12-17 years)	26
Adults (18-64 years)	40
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

152 subjects with EB were enrolled, between 9 June 2015 and 3 September 2018, in this open-label, multi-centre extension study. All enrolled subjects had previously completed Study SD-005 (EudraCT number: 2014-002288-14). The planned duration of the study, as per Protocol Version 3, was up to 48 months but it was terminated early by the sponsor.

Pre-assignment

Screening details:

Analysis groups were defined based on treatment in study SD-005. 77 subjects who received placebo in SD-005 were allocated to the 'Placebo to SD-101-6.0' group and 75 subjects who received SD-101-6.0 in SD-005 were allocated to the 'SD-101-6.0 to SD-101-6.0' group. All subjects received treatment with SD-101-6.0 upon enrolling in study SD-006.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo to SD-101-6.0

Arm description:

Subjects who received placebo in Study SD-005 then went on to receive SD-101-6.0 in this open-label extension study. SD-101-6.0 was applied topically once a day to the entire body.

Arm type	Experimental
Investigational medicinal product name	SD-101-6.0
Investigational medicinal product code	
Other name	Allantoin 6% concentration, Zorblisa
Pharmaceutical forms	Cream
Routes of administration	Topical use

Dosage and administration details:

SD-101 is a white, crystalline powder that is formulated within an odourless, soft, white cream base. SD-101-6.0 cream contains allantoin, a diureide glyoxlylic acid, at a concentration of 6% and other excipients. Subjects (or their caregivers) applied the cream topically, once a day to the entire body.

Arm title	SD-101-6.0 to SD 101-6.0

Arm description:

Subjects who received SD-101-6.0 in Study SD-005 continued to receive SD-101-6.0 in this open label extension study. SD-101-6.0 was applied topically once a day to the entire body.

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Number of subjects in period 1	Placebo to SD-101-6.0	SD-101-6.0 to SD 101-6.0
Started	77	75
Completed as per Protocol Versions 1 & 2	7	5
Completed	0	0
Not completed	77	75
Consent withdrawn by subject	29	34
Adverse event, non-fatal	3	1
Study terminated by sponsor	43	36
Lost to follow-up	2	3
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo to SD-101-6.0
Reporting group description:	
Subjects who received placebo in Study SD-005 then went on to receive SD-101-6.0 in this open-label extension study. SD-101-6.0 was applied topically once a day to the entire body.	
Reporting group title	SD-101-6.0 to SD 101-6.0
Reporting group description:	
Subjects who received SD-101-6.0 in Study SD-005 continued to receive SD-101-6.0 in this open label extension study. SD-101-6.0 was applied topically once a day to the entire body.	

Reporting group values	Placebo to SD-101-6.0	SD-101-6.0 to SD 101-6.0	Total
Number of subjects	77	75	152
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	5	3	8
Children (2-11 years)	42	35	77
Adolescents (12-17 years)	10	16	26
Adults (18-64 years)	19	21	40
From 65-84 years	1	0	1
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	14.36	14.18	
standard deviation	± 13.599	± 13.381	-
Gender categorical Units: Subjects			
Female	45	28	73
Male	32	47	79
Race Units: Subjects			
White/Caucasian	63	65	128
Black or African-American	3	4	7
Asian	7	3	10
American Indian or Alaskan Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	1	1	2
Unknown	3	2	5
EB type Units: Subjects			
Simplex	7	9	16
Recessive dystrophic	56	53	109
Junctional non-Herlitz	14	13	27

End points

End points reporting groups

Reporting group title	Placebo to SD-101-6.0
Reporting group description:	
Subjects who received placebo in Study SD-005 then went on to receive SD-101-6.0 in this open-label extension study. SD-101-6.0 was applied topically once a day to the entire body.	
Reporting group title	SD-101-6.0 to SD 101-6.0
Reporting group description:	
Subjects who received SD-101-6.0 in Study SD-005 continued to receive SD-101-6.0 in this open label extension study. SD-101-6.0 was applied topically once a day to the entire body.	

Primary: Number of Subjects with Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects with Treatment Emergent Adverse Events (TEAEs)[1]
End point description:	
TEAEs were defined as adverse events that started or worsened on or after baseline visit.	
End point type	Primary
End point timeframe:	
From baseline to 30 days after last application of study drug (up to a maximum of 37 months)	

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: In accordance with the statistical analysis plan no comparison between treatment groups was performed.

End point values	Placebo to SD-101-6.0	SD-101-6.0 to SD 101-6.0		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: Subjects				
Any TEAE	58	51		
Any TEAE related to study drug	17	8		
Any fatal TEAE	0	0		
Any serious TEAE	14	11		
Any TEAE leading to discontinuation of study drug	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Body Surface Area Index (BSAI) of Lesional Skin

End point title	Change from Baseline in Body Surface Area Index (BSAI) of Lesional Skin

End point description:

Lesional skin was defined as areas that contained any of the following: blisters, erosions, ulcerations, scabbing, bullae, or eschars, as well as areas that were weeping, sloughing, oozing, crusted, or

denuded. The percentage, ranging from 0% to 100%, of affected body surface area (BSA) was recorded for each defined body region (ie, head/neck, upper limbs, trunk [includes groin], and lower limbs), multiplied by the weighting factor, then summed for all body regions to calculate the BSAI. The BSA for lesional skin was to be assessed by the same study physician on each visit for a particular subject. The mean change from baseline in BSAI was assessed every 3 months. Only subjects with data available for analysis at each time point are presented.

End point type	Secondary

End point timeframe:

From baseline to Month 30

End point values	Placebo to SD-101-6.0	SD-101-6.0 to SD 101-6.0		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Month 1 (n=71, n=70)	-0.54 (± 5.398)	-0.76 (± 4.185)		
Month 3 (n=66, n=69)	-1.21 (± 6.457)	-1.87 (± 5.999)		
Month 6 (n=60, n=64)	-1.35 (± 6.813)	-1.77 (± 6.015)		
Month 9 (n=56, n=61)	0.31 (± 10.117)	-2.48 (± 9.436)		
Month 12 (n=50, n=52)	0.44 (± 10.327)	-3.35 (± 9.566)		
Month 15 (n=29, n=35)	2.15 (± 12.546)	-1.90 (± 7.337)		
Month 18 (n=26, n=25)	-4.24 (± 8.207)	-2.46 (± 5.275)		
Month 21 (n=16, n=18)	-1.58 (± 10.442)	-3.06 (± 5.869)		
Month 24 (n=7, n=11)	-0.64 (± 5.981)	-1.63 (± 5.647)		
Month 27 (n=6, n=6)	-0.16 (± 6.514)	-1.87 (± 4.405)		
Month 30 (n=5, n=3)	3.37 (± 10.706)	-2.77 (± 5.465)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in BSAI of Total Body Wound Burden

End point title	Change from Baseline in BSAI of Total Body Wound Burden

End point description:

A wound was defined as an open area on the skin (ie, epidermal covering disrupted). Total body wound burden was calculated using BSAI; the percentage, ranging from 0% to 100%, of affected BSA was recorded for each defined body region (ie, head/neck, upper limbs, trunk [includes groin], and lower limbs), multiplied by the weighting factor, then summed for all body regions. The BSAI for total body wound burden was to be assessed by the same study physician at each visit for a particular subject. The mean change from baseline in total body wound burden was assessed every 3 months. Only subjects with data available for analysis at each time point are presented.

End point type	Secondary
End point timeframe:	
From baseline to Month 30	

End point values	Placebo to SD-101-6.0	SD-101-6.0 to SD 101-6.0		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: Percentage of BSAI				
arithmetic mean (standard deviation)				
Month 1 (n=71, n=70)	0.07 (± 4.044)	-1.75 (± 4.891)		
Month 3 (n=66, n=69)	-0.80 (± 3.001)	-1.52 (± 5.343)		
Month 6 (n=60, n=64)	-0.48 (± 3.595)	-1.54 (± 4.322)		
Month 9 (n=56, n=61)	-0.42 (± 3.586)	-1.82 (± 6.083)		
Month 12 (n=50, n=52)	-0.13 (± 3.211)	-1.38 (± 5.497)		
Month 15 (n=29, n=35)	0.26 (± 3.030)	-0.15 (± 4.511)		
Month 18 (n=26, n=25)	-1.31 (± 4.665)	-1.12 (± 3.053)		
Month 21 (n=16, n=18)	-0.28 (± 5.507)	-1.44 (± 3.150)		
Month 24 (n=7, n=11)	-0.01 (± 2.898)	-0.68 (± 3.890)		
Month 27 (n=6, n=6)	0.31 (± 3.615)	-0.43 (± 2.924)		
Month 30 (n=5, n=3)	1.69 (± 5.933)	-1.55 (± 2.883)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From baseline to 30 days after last application of study drug (up to a maximum of 37 months).	
Adverse event reporting additional description:	
The frequency threshold for reporting non-serious TEAEs is 2% in either treatment group.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Placebo to SD-101-6.0
Reporting group description:	
Subjects who received placebo in Study SD-005 then went on to receive SD-101-6.0 in this open label extension study. SD-101-6.0 was applied topically once a day to the entire body.	
Reporting group title	SD-101-6.0 to SD 101-6.0
Reporting group description:	
Subjects who received SD-101-6.0 in Study SD-005 continued to receive SD-101-6.0 in this open label extension study. SD-101-6.0 was applied topically once a day to the entire body.	

Serious adverse events	Placebo to SD-101-6.0	SD-101-6.0 to SD 101-6.0	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 77 (18.18%)	11 / 75 (14.67%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	1 / 77 (1.30%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal papillary-mucinous carcinoma of pancreas			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			

subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Intermittent explosive disorder			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Body temperature increased			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Stoma site inflammation			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural fistula			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural vomiting			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Stoma site extravasation			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital megaureter			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericarditis			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 77 (2.60%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Oesophageal stenosis			
subjects affected / exposed	2 / 77 (2.60%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 77 (1.30%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin disorder			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Staphylococcal skin infection			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	2 / 77 (2.60%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis clostridial			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implant site infection			

subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin bacterial infection			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection bacterial			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 77 (1.30%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeding intolerance			
subjects affected / exposed	0 / 77 (0.00%)	1 / 75 (1.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	1 / 77 (1.30%)	0 / 75 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Placebo to SD-101-6.0	SD-101-6.0 to SD 101-6.0	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 77 (66.23%)	44 / 75 (58.67%)	
Injury, poisoning and procedural complications			
Corneal abrasion			
subjects affected / exposed	2 / 77 (2.60%)	2 / 75 (2.67%)	
occurrences (all)	5	5	
Procedural pain			
subjects affected / exposed	0 / 77 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	5	
Wound			
subjects affected / exposed	0 / 77 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	3	
Wound complication			
subjects affected / exposed	2 / 77 (2.60%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
Congenital, familial and genetic disorders			
Epidermolysis bullosa			
subjects affected / exposed	0 / 77 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 77 (6.49%)	5 / 75 (6.67%)	
occurrences (all)	5	10	
Lymphadenopathy			
subjects affected / exposed	2 / 77 (2.60%)	1 / 75 (1.33%)	
occurrences (all)	2	1	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	10 / 77 (12.99%)	5 / 75 (6.67%)	
occurrences (all)	15	5	
Pain			
subjects affected / exposed	2 / 77 (2.60%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Systemic inflammatory response syndrome			
subjects affected / exposed	2 / 77 (2.60%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	3 / 77 (3.90%)	5 / 75 (6.67%)	
occurrences (all)	4	8	
Oesophageal stenosis			
subjects affected / exposed	4 / 77 (5.19%)	3 / 75 (4.00%)	
occurrences (all)	9	10	
Diarrhoea			
subjects affected / exposed	3 / 77 (3.90%)	2 / 75 (2.67%)	
occurrences (all)	4	3	
Vomiting			
subjects affected / exposed	3 / 77 (3.90%)	2 / 75 (2.67%)	
occurrences (all)	6	2	
Abdominal pain			
subjects affected / exposed	3 / 77 (3.90%)	1 / 75 (1.33%)	
occurrences (all)	4	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 77 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	4	
Abdominal pain upper			
subjects affected / exposed	2 / 77 (2.60%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Haematemesis			
subjects affected / exposed	2 / 77 (2.60%)	0 / 75 (0.00%)	
occurrences (all)	2	0	
Oesophageal dilatation			

subjects affected / exposed	0 / 77 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	3	
Toothache			
subjects affected / exposed	0 / 77 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 77 (3.90%)	4 / 75 (5.33%)	
occurrences (all)	5	4	
Rhinorrhoea			
subjects affected / exposed	1 / 77 (1.30%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	6 / 77 (7.79%)	3 / 75 (4.00%)	
occurrences (all)	7	3	
Skin lesion			
subjects affected / exposed	2 / 77 (2.60%)	2 / 75 (2.67%)	
occurrences (all)	2	2	
Excessive granulation tissue			
subjects affected / exposed	1 / 77 (1.30%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 77 (3.90%)	1 / 75 (1.33%)	
occurrences (all)	3	1	
Infections and infestations			
Skin infection			
subjects affected / exposed	12 / 77 (15.58%)	6 / 75 (8.00%)	
occurrences (all)	25	8	
Nasopharyngitis			
subjects affected / exposed	6 / 77 (7.79%)	10 / 75 (13.33%)	
occurrences (all)	6	13	
Upper respiratory tract infection			
subjects affected / exposed	5 / 77 (6.49%)	4 / 75 (5.33%)	
occurrences (all)	6	6	

Wound infection			
subjects affected / exposed	6 / 77 (7.79%)	3 / 75 (4.00%)	
occurrences (all)	8	7	
Skin bacterial infection			
subjects affected / exposed	4 / 77 (5.19%)	4 / 75 (5.33%)	
occurrences (all)	10	9	
Staphylococcal skin infection			
subjects affected / exposed	4 / 77 (5.19%)	4 / 75 (5.33%)	
occurrences (all)	7	7	
Wound infection bacterial			
subjects affected / exposed	5 / 77 (6.49%)	2 / 75 (2.67%)	
occurrences (all)	5	5	
Bronchitis			
subjects affected / exposed	1 / 77 (1.30%)	5 / 75 (6.67%)	
occurrences (all)	1	6	
Pharyngitis streptococcal			
subjects affected / exposed	4 / 77 (5.19%)	2 / 75 (2.67%)	
occurrences (all)	5	4	
Influenza			
subjects affected / exposed	3 / 77 (3.90%)	2 / 75 (2.67%)	
occurrences (all)	3	2	
Sinusitis			
subjects affected / exposed	1 / 77 (1.30%)	4 / 75 (5.33%)	
occurrences (all)	1	5	
Wound infection staphylococcal			
subjects affected / exposed	3 / 77 (3.90%)	2 / 75 (2.67%)	
occurrences (all)	3	9	
Wound infection pseudomonas			
subjects affected / exposed	2 / 77 (2.60%)	2 / 75 (2.67%)	
occurrences (all)	2	3	
Cellulitis			
subjects affected / exposed	0 / 77 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	5	
Eye infection			
subjects affected / exposed	1 / 77 (1.30%)	2 / 75 (2.67%)	
occurrences (all)	1	2	

Gastroenteritis			
subjects affected / exposed	3 / 77 (3.90%)	0 / 75 (0.00%)	
occurrences (all)	4	0	
Otitis media			
subjects affected / exposed	0 / 77 (0.00%)	3 / 75 (4.00%)	
occurrences (all)	0	3	
Rhinitis			
subjects affected / exposed	1 / 77 (1.30%)	2 / 75 (2.67%)	
occurrences (all)	1	2	
Urinary tract infection			
subjects affected / exposed	1 / 77 (1.30%)	2 / 75 (2.67%)	
occurrences (all)	1	6	
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 77 (2.60%)	1 / 75 (1.33%)	
occurrences (all)	3	1	
Cystitis			
subjects affected / exposed	0 / 77 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Pyoderma			
subjects affected / exposed	0 / 77 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Viral rash			
subjects affected / exposed	2 / 77 (2.60%)	0 / 75 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 December 2015	The main reason for Amendment 1 was to extend the duration of treatment with SD-101-6.0 from 360 days to 630 days (ie, 21 months).
08 November 2016	Major changes implemented with Amendment 2 included the following: • duration of treatment with SD-101-6.0 extended from 630 days to 1440 days (ie, 48 months). • enrolment estimate updated from approximately 130 patients to approximately 150 subjects to reflect the increase in enrolment in SD-005. • Adverse events (AE) follow-up period defined as 30 days after the last application of study drug treatment, with the exception of AEs that led to discontinuation of study drug, which were monitored until resolution or stabilisation.

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.

Results are presented for all study visits assessed before the early termination of the study on 4 June 2018. The maximum study duration completed by at least 1 subject was 36 months.

Notes: