



## Clinical trial results:

### Open, Blindly Evaluated, Prospective, Controlled, Randomised, Multicentre Phase III Clinical Trial to Compare Intra-individually the Efficacy and Tolerance of Oleogel-S10 versus Standard of Care in Accelerating the Healing of Grade 2a Partial-Thickness Burn Wounds Summary

EudraCT number	2012-000362-38
Trial protocol	DE SE GB
Global end of trial date	04 July 2014

#### Results information

Result version number	v1 (current)
This version publication date	20 June 2016
First version publication date	14 August 2015

#### Trial information

##### Trial identification

Sponsor protocol code	BBW-11
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01657292
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Birken AG
Sponsor organisation address	Streiflingsweg 11, Niefern-Oeschelbronn, Germany, 75223
Public contact	Head of pharmaceutical development, Birken AG, T.Zahn@birken.eu
Scientific contact	Head of pharmaceutical development, Birken AG, T.Zahn@birken.eu

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	07 April 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 July 2014
Global end of trial reached?	Yes
Global end of trial date	04 July 2014
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:

To compare intra-individually the efficacy and tolerance of Oleogel-S10 with fatty gauze as wound dressing versus standard of care (defined as Octenilin wound gel) with fatty gauze as wound dressing in accelerating the healing of Grade 2a burns.

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Protection of trial subjects:

The study was conducted in compliance with the study protocol, ethical principles originating in or derived from the Declaration of Helsinki, ethics committee informed consent regulations, and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines. In addition, all national and local regulatory requirements were followed. Insurance coverage for all participating subjects was guaranteed according to applicable legal requirements. Before undergoing any study-specific procedures, subjects were informed about the nature, scope, and possible consequences of the study. The investigator was responsible for obtaining a subject's written informed consent to participate in the study.

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Background therapy:

Fatty gauze wound dressing.

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Evidence for comparator:

Octenilin wound gel, an antiseptic octenidine formulated as hydrogel, was used as reference because it represents a standard of care for treating patients with burn injuries.

Actual start date of recruitment	31 August 2012
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	Sweden: 3
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	Germany: 31
Country: Number of subjects enrolled	Switzerland: 4
Worldwide total number of subjects	66
EEA total number of subjects	62

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	60
From 65 to 84 years	6
85 years and over	0

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## Subject disposition

### Recruitment

Recruitment details:

Study participants were enrolled from 31-Aug-2012 to 10-Jul-2013, in 10 clinical centres in 4 countries: Germany (4 centres), Uk (3 centres), Sweden (2 centres), and Switzerland (1 centre).

### Pre-assignment

Screening details:

During screening the following was performed: check for inclusion/exclusion criteria, concomitant medication, pregnancy, demographics, medical history and signing informed consent form. 66 subjects were screened of which 5 violated eligibility criteria and thus 61 subjects were treated.

### Pre-assignment period milestones

Number of subjects started	66
Number of subjects completed	61

### Pre-assignment subject non-completion reasons

Reason: Number of subjects	Violation of eligibility criteria: 4
Reason: Number of subjects	Language and social reasons: 1

### Period 1

Period 1 title	Treatment period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Assessor <sup>[1]</sup>

Blinding implementation details:

Treatments were intra-individually compared. Either 2 halves of 1 wound or 2 wounds of similar size and depth were used per subject. Treatment was assigned using a tamper-proof randomisation method. Treatment was open to study subjects and investigators, but assessment of efficacy was primarily based on blinded photo evaluation. Special care was taken to ensure blinding i.e. all markings were removed.

### Arms

Are arms mutually exclusive?	No
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<b>Arm title</b>	Oleogel-S10
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Arm description:

A suitable study wound was divided into 2 halves of equal size or 2 separate wounds of similar size and depth were used for evaluation. One randomly assigned wound or wound half was treated with Oleogel-S10 ointment and covered with fatty gauze.

Arm type	Experimental
Investigational medicinal product name	Oleogel-S10
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Ointment
Routes of administration	Topical use

Dosage and administration details:

1 cm of ointment string Oleogel-S10 (approximately 100 mg) per cm<sup>2</sup> of wound (i.e. approximately 1 mm thick), applied at every wound dressing change (latest every second day).

<b>Arm title</b>	Octenilin
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Arm description:

The other wound or wound half was treated with Octenilin wound gel and covered with fatty gauze.

Arm type	Active comparator
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Investigational medicinal product name	Octenilin wound gel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gel
Routes of administration	Topical use

Dosage and administration details:

Administered at each wound dressing change (latest every second day).

Notes:

[1] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Treatment was open to study subjects and investigators, but assessment of efficacy was primarily based on blinded photo evaluation.

<b>Number of subjects in period 1</b>	Oleogel-S10	Octenilin
Started	61	61
Completed	51	51
Not completed	10	10
Consent withdrawn by subject	2	2
Adverse event, non-fatal	6	6
Violation of eligibility criteria	1	1
Change of therapy	1	1

## Baseline characteristics

### Reporting groups<sup>[1]</sup>

Reporting group title	Treatment period
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Reporting group description: -

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: Of the 66 subjects enrolled only wounds of 61 subjects were randomised and treated.

Baseline characteristics are provided for these 61 subjects included in the safety and efficacy analyses.

Reporting group values	Treatment period	Total	
Number of subjects	61	61	
Age categorical			
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)	0	0	
Adults (18-64 years)	55	55	
From 65-84 years	6	6	
85 years and over	0	0	
Age continuous			
Units: years			
median	41		
full range (min-max)	18 to 79	-	
Gender categorical			
Units: Subjects			
Female	19	19	
Male	42	42	

## End points

### End points reporting groups

Reporting group title	Oleogel-S10
Reporting group description: A suitable study wound was divided into 2 halves of equal size or 2 separate wounds of similar size and depth were used for evaluation. One randomly assigned wound or wound half was treated with Oleogel-S10 ointment and covered with fatty gauze.	
Reporting group title	Octenilin
Reporting group description: The other wound or wound half was treated with Octenilin wound gel and covered with fatty gauze.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT analysis set included all subjects who were treated at least once, i.e. who received any dose of Oleogel-S10 or Octenilin wound gel. If the application of any study medication was not certain, the subjects was included in the ITT analysis set. Patients whose wound halves were not treated with the intended (i.e. randomised) treatment regimen were excluded from the ITT analysis set.	

### **Primary: Percentage of patients with earlier healing (at least 95% epithelialisation) of the wound half treated with Oleogel-S10 compared to standard of care (Octenilin wound gel), as evaluated by the majority decision of 3 independent, blinded experts**

End point title	Percentage of patients with earlier healing (at least 95% epithelialisation) of the wound half treated with Oleogel-S10 compared to standard of care (Octenilin wound gel), as evaluated by the majority decision of 3 independent, blinded experts
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#### End point description:

The blinded experts indicated for each subject whether the wounds or wound halves showed differences in time to wound closure (at least 95% epithelialisation) and, if such a difference was observed, which wound half healed faster. The majority decision of the 3 readers was used for evaluation.

End point type	Primary
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#### End point timeframe:

Photo acquired at every wound dressing change (at least every second day until full wound closure was achieved. At maximum Day 21 if wound closure was not achieved before).

End point values	Oleogel-S10	Octenilin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	57	57		
Units: Wounds				
Wounds with difference in healing	35	35		
Wounds with earlier healing	30	5		

## Statistical analyses

<b>Statistical analysis title</b>	Primary analysis
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Statistical analysis description:

The following hypotheses were tested:  $H_0: s_0 \leq 0.5$  and  $H_1: s_0 > 0.5$  (with  $s_0$ =rate of superiority of Oleogel-S10) using a 1-sided, exact binomial test with a significance level of 0.025. A total of 57 subjects were included in the analysis (intra-individual comparison). Earlier healing was shown for Oleogel-S10 treated vs Octenilin treated wound halves in 30 subjects (85.7%). Earlier healing of the Octenilin treated vs the Oleogel-S10 treated wound halves was observed in 5 subjects (14.3%).

Comparison groups	Oleogel-S10 v Octenilin
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[1]</sup>
Method	Exact binomial test

Notes:

[1] - Based on 1-sided, exact binomial test evaluating the rate of superiority of Oleogel-S10 being  $>0.5$ . The analysis is based only on the 35 subjects for whom a difference in healing was noted.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 0 (start of treatment) till end of treatment (Day 21 or earlier if full wound closure was achieved earlier, or later, if the investigator decided to change medication and/or treatment due to unsatisfying wound closure after Day 21).

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

### Reporting groups

Reporting group title	Safety analysis set
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Reporting group description:

The SAF included all subjects who were treated at least once, i.e. who received any dose of Oleogel-S10 or Octenilin wound gel.

<b>Serious adverse events</b>	Safety analysis set		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 61 (13.11%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tonsil cancer			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Wound necrosis			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			

subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Infections and infestations</b>			
Soft tissue infection			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	Safety analysis set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 61 (21.31%)		
<b>Injury, poisoning and procedural complications</b>			
Inflammation of wound			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
Wound complication			
subjects affected / exposed	2 / 61 (3.28%)		
occurrences (all)	3		
<b>Nervous system disorders</b>			
Headache			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
<b>General disorders and administration site conditions</b>			
Pain			
subjects affected / exposed	1 / 61 (1.64%)		
occurrences (all)	1		
<b>Gastrointestinal disorders</b>			

Nausea subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1		
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1		
Skin and subcutaneous tissue disorders Pain of skin subjects affected / exposed occurrences (all)  Pruritus subjects affected / exposed occurrences (all)  Purpura subjects affected / exposed occurrences (all)  Rash pruritic subjects affected / exposed occurrences (all)	3 / 61 (4.92%) 4  3 / 61 (4.92%) 3  1 / 61 (1.64%) 1  1 / 61 (1.64%) 1		
Infections and infestations Cystitis subjects affected / exposed occurrences (all)  Urinary tract infection subjects affected / exposed occurrences (all)  Wound infection subjects affected / exposed occurrences (all)	1 / 61 (1.64%) 1  1 / 61 (1.64%) 1  2 / 61 (3.28%) 2		

## **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