

**Clinical trial results:****Efficacy and Safety of oral Alitretinoin (Toctino®) in the Treatment of Patients with Cutaneous Lupus Erythematosus: A Multicentre, Open-Label, Prospective Pilot Study****Summary**

EudraCT number	2010-024131-16
Trial protocol	DE
Global end of trial date	30 April 2014

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information**Trial identification**

Sponsor protocol code	UKM10_0019
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Münster
Sponsor organisation address	Albert-Schweitzer-Campus 1, Münster, Germany, 48149
Public contact	Prof. Dr. Annegret Kuhn, Universitätsklinikum Münster , kuhnan@uni-muenster.de
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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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 May 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 May 2013
Global end of trial reached?	Yes
Global end of trial date	30 April 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the therapeutic effect of alitretinoin (Toctino®) in the treatment of Cutaneous Lupus Erythematosus (CLE) with respect to proportion of responders based on the Revised Cutaneous Lupus Disease Area and Severity Index (RCLASI) activity score for skin lesions at baseline and after 24 weeks of treatment or at the latest assessment for patients who withdrew prematurely (Last Observation Carried Forward, LOCF).

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and the ICH Guidelines in Good Clinical Practice. The study was not started before the competent ethics committee had given a favorable opinion. Written informed consent was obtained from all patients and the study was only conducted as approved by the Ethics committee and the competent authority. Amendments were only implemented after approval.

Background therapy:

Throughout the trial, daily use of sunscreen (sun protection factor, SPF \geq 50) was recommended to all patients. The management of CLE could involve the use of topical medications, such as topical steroids, or systemic rescue medications, such as antimalarials.

Evidence for comparator: -

Actual start date of recruitment	08 December 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 7
Worldwide total number of subjects	7
EEA total number of subjects	7

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)	0
Adults (18-64 years)	6
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from 2 dermatology clinics in Germany. The recruitment period was from December 2011 to April 2013.

Pre-assignment

Screening details:

7 patients with a clinically and histologically confirmed diagnosis of CLE refractory to topical corticosteroids were included in the study.

Pre-assignment period milestones

Number of subjects started	7
Number of subjects completed	5

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Consent withdrawn by subject: 1
Reason: Number of subjects	Patient did not meet the inclusion criteria: 1

Period 1

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

Arms

Arm title	Alitretinoin
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Arm description:

Patients who received study treatment with alitretinoin (Toctino®).

Arm type	Experimental
Investigational medicinal product name	Toctino®
Investigational medicinal product code	
Other name	Alitretinoin
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details:

Patients were treated for 24 weeks with alitretinoin (Toctino®). Study treatment started with 30 mg alitretinoin per day. The daily dose was reduced to 10 mg alitretinoin if adverse reactions such as hyperlipidemia or severe headaches occurred.

Number of subjects in period 1^[1]	Alitretinoin
Started	5
Completed	2
Not completed	3
Non-Compliance	1
Adverse event, non-fatal	1

Lack of efficacy	1
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Notes:

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

Justification: 7 patients were enrolled in the study and assessed for eligibility. Because one patient did not meet the inclusion criteria and one patient withdrew consent before start of treatment, only 5 patients entered the baseline period.

Baseline characteristics

Reporting groups

Reporting group title	Treatment period
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Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	5	5	
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)	4	4	
From 65-84 years	1	1	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	1	1	

End points

End points reporting groups

Reporting group title	Alitretinoin
Reporting group description:	Patients who received study treatment with alitretinoin (Toctino®).
Subject analysis set title	Visit (Baseline)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	Examination visit before starting alitretinoin treatment.
Subject analysis set title	Visit (last)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	Last examination visit of patients treated with alitretinoin.

Primary: RCLASI activity score for skin lesions

End point title	RCLASI activity score for skin lesions ^[1]
End point description:	Efficacy of alitretinoin on disease severity as evaluated by RCLASI activity score for skin lesions.
End point type	Primary
End point timeframe:	Week 0, 2, 4, 8, 12, 16, 20, 24 and 28

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: The study was terminated prematurely. Since not enough patients were included, no statistical analysis of the results was performed.

End point values	Visit (Baseline)	Visit (last)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	4		
Units: Activity score				
arithmetic mean (standard deviation)	12.8 (± 4.1)	10.3 (± 4.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: RCLASI activity score total

End point title	RCLASI activity score total
End point description:	Efficacy of alitretinoin on disease severity as evaluated by total RCLASI activity score.
End point type	Secondary
End point timeframe:	Week 0, 2, 4, 8, 12, 16, 20, 24 and 28

End point values	Visit (Baseline)	Visit (last)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	4		
Units: Activity score				
arithmetic mean (standard deviation)	12.8 (± 4.1)	11.3 (± 4.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: RCLASI damage score total

End point title	RCLASI damage score total
End point description:	Efficacy of alitretinoin on disease severity as evaluated by total RCLASI damage score.
End point type	Secondary
End point timeframe:	Week 0, 2, 4, 8, 12, 16, 20, 24 and 28

End point values	Visit (Baseline)	Visit (last)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	4		
Units: Activity score				
arithmetic mean (standard deviation)	2.0 (± 2.0)	2.3 (± 1.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS score for itch

End point title	VAS score for itch
End point description:	Efficacy of alitretinoin on disease severity as evaluated by patient assessment score VAS (Visual Analogue Scale) for itch.
End point type	Secondary
End point timeframe:	Week 0, 2, 4, 8, 12, 16, 20, 24 and 28

End point values	Visit (Baseline)	Visit (last)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	3		
Units: VAS score				
arithmetic mean (standard deviation)	3.5 (\pm 2.2)	2.2 (\pm 3.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: VAS score for pain

End point title	VAS score for pain
End point description:	Efficacy of alitretinoin on disease severity as evaluated by patient assessment score VAS for pain.
End point type	Secondary
End point timeframe:	Week 0, 2, 4, 8, 12, 16, 20, 24 and 28

End point values	Visit (Baseline)	Visit (last)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	5	3		
Units: VAS score				
arithmetic mean (standard deviation)	0 (\pm 0)	1.8 (\pm 3.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: PAGI Score

End point title	PAGI Score
End point description:	Efficacy of alitretinoin on disease severity as evaluated by patient assessment score PAGI (Patient Assessment of Global Improvement).
End point type	Secondary
End point timeframe:	Week 0, 2, 4, 8, 12, 16, 20, 24 and 28

End point values	Visit (Baseline)	Visit (last)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	4	3		
Units: PAGI score				
arithmetic mean (standard deviation)	0 (\pm 0.8)	0 (\pm 1.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from the time of informed consent until the final study visit.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Safety group
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Reporting group description:

Patients who received at least one dose of alitretinoin (Toctino®).

Serious adverse events	Safety group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychotic disorder			
subjects affected / exposed	1 / 5 (20.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety group		
Total subjects affected by non-serious adverse events subjects affected / exposed	3 / 5 (60.00%)		
Vascular disorders Flushing subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Nervous system disorders Head discomfort subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1 1 / 5 (20.00%) 1		
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Gastrointestinal disorders Diarrhoea haemorrhagic subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		
Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 May 2013	<ul style="list-style-type: none">- Exclusion criteria were amended. Patients with hereditary myopathy in patient and family history as well as patients with known rhabdomyolysis in patient history (e.g. muscular-toxic complications in association with statin and fibrate therapy) should not participate in the study.- In patients with clinical suspicion of myalgia and/ or myopathia, creatine kinase should be determined. If the level was significantly increased, the patient should be excluded from the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
11 April 2013	Only 7 patients could be enrolled in the study within 18 months and it was not expected that more patients or even all 30 patients would be recruited in the near future. Therefore, recruitment of patients was interrupted on April 11, 2013, and on April 30, 2014, the study was officially terminated.	-

Notes:

Limitations and caveats

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

The study was terminated prematurely because only 7 patients could be enrolled in the study (only 5 patients started study treatment).

Notes: