Clinical trial results:
Single-arm study to assess a potential effect of anti-IL-17 (Secukinumab) in the treatment of pyoderma gangrenosum

Summary

EudraCT number	2015-000762-65
Trial protocol	DE
Global end of trial date	19 September 2019

Results information

Result version number	v1 (current)
This version publication date	02 October 2020
First version publication date	02 October 2020

Trial information

Trial identification

Sponsor protocol code	CAIN457ADE01T

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02733094
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Technische Universität München, Fakultät für Medizin
Sponsor organisation address	Ismaninger Str. 22, München, Germany, 81675
Public contact	Studienzentrum Dermatologie, Department of Dermatology and Allergy Technische Universität München , +49 894140 3579, kilian.eyerich@tum.de
Scientific contact	Studienzentrum Dermatologie, Department of Dermatology and Allergy Technische Universität München , +49 894140 3579, kilian.eyerich@tum.de

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	02 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 September 2019
Global end of trial reached?	Yes
Global end of trial date	19 September 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy and tolerability of secukinumab in patients with pyoderma gangrenosum after 16 week treatment with 300 mg s.c. secukinumab.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance the ethical principles of Good Clinical Practice (GCP).
Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision.
The study was regularly monitored by the Sponsor and all investigators connected to the study were GCP trained.

Background therapy:

None applied

Evidence for comparator:

n.a.

Actual start date of recruitment	30 May 2016
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	Germany: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	7

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in Germany single-centre between 30.05.2016 (first Patient recruited) and 19.09.2019 (last patient completed).

Pre-assignment

Screening details:

Patients must have all screening evaluations performed prior to the first dose of study drug and must meet all inclusion and none of the exclusion criteria. The patients must be thoroughly informed about all aspects of the study, all evaluations as required per protocol and all regulatory requirements for informed consent.

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:

This is a single-arm not blinded study.

Arms

Arm title	CAIN trial

Arm description:

Single arm study to assess a potential effect of anti IL 17 (Secukinumab) in the treatment of pyoderma gangrenosum.

Arm type	Experimental
Investigational medicinal product name	Cosentyx
Investigational medicinal product code	ATC L04AC10
Other name	Secukinumab
Pharmaceutical forms	Solution and suspension for suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg secukinumab per week 1-4 and subsequently each 4 weeks subcutaneuously over a study period of 16 weeks; follow up until week 40.
300 mg secukinumab per week 1-4 and subsequently each 2 weeks subcutaneuously over a study period of 32 weeks; follow up until week 40. (Amendment)

Number of subjects in period 1	CAIN trial
Started	8
Completed	2
Not completed	6
Consent withdrawn by subject	3
Adverse event, non-fatal	2
Deterioration of pre-existing health condition	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
Adults (18-64 years)	7	7	
From 65-84 years	1	1	
Age continuous Units: years			
median	45.3		
full range (min-max)	22 to 70	-	
Gender categorical Units: Subjects			
Female	5	5	
Male	3	3	
Previous treatment for PG			
Number of patients receiving treatment for pyoderma gangrenosum prior to inclusion in the study			
Units: Subjects			
previous treatment	8	8	
no previous treatment	0	0	
Time between first diagnosis and study begin			
Duration (in months) between first diagnosis of pyoderma gangrenosum and study begin.			
Units: months			
arithmetic mean	32.3		
standard deviation	± 41.7	-	

Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients included in the study except one, who withdrew before receiving study medication.

Reporting group values	ITT		
Number of subjects	7		
Age categorical Units: Subjects			
Adults (18-64 years)	6		
From 65-84 years	1		
Age continuous Units: years			
median	39		
full range (min-max)	22 to 70		

Gender categorical Units: Subjects			
Female	4		
Male	3		
Previous treatment for PG			
Number of patients receiving treatment for pyoderma gangrenosum prior to inclusion in the study			
Units: Subjects			
previous treatment	7		
no previous treatment	0		
Time between first diagnosis and study begin			
Duration (in months) between first diagnosis of pyoderma gangrenosum and study begin.			
Units: months			
arithmetic mean	33		
standard deviation	± 42		

End points

End points reporting groups

Reporting group title	CAIN trial

Reporting group description:

Single arm study to assess a potential effect of anti IL 17 (Secukinumab) in the treatment of pyoderma gangrenosum.

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients included in the study except one, who withdrew before receiving study medication.

Primary: Change in PGA

End point title	Change in PGA[1]

End point description:

Change in PGA at week 16 as compared to baseline.
Grade 0: Total resolution of ulcer(s) with no signs of active PG
Grade 1: Almost completely healed uncer(s) with only minimal signs of active PG
Grade 2: Evidence of ulcer healing which involves at least 50% of ulcer/ulcer margin
Grade 3: Evidence of ulcer healing which involves less than 50% of ulcer/ulcer margin
Grade 4: No evicence of ulcer healing

End point type	Primary

End point timeframe:

16 weeks from baseline

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: Only descriptive statistics were planned for this single arm study.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Patients				
Grade 0	0			
Grade 1	0			
Grade 2	2			
Grade 3	1			
Grade 4	1			
Missing	3			

Statistical analyses

No statistical analyses for this end point

Primary: Change in PGA (LOCF)

End point title	Change in PGA (LOCF)[2]

End point description:

Sensitivity analysis of the primary endpoint using LOCF imputation for the three missing values at week 16.

End point type	Primary

End point timeframe:

16 wochen from baseline

Notes:

[2] - 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: Only descriptive statistics were planned for this single arm study.

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Patients				
Grade 0	0			
Grade 1	0			
Grade 2	4			
Grade 3	1			
Grade 4	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in surface area of PG at week 16

End point title	Change in surface area of PG at week 16

End point description:

Change in surface area of PG lesions at week 16 as compared to week 0.

End point type	Secondary

End point timeframe:

At week 16

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: mm²				
arithmetic mean (standard deviation)	-22.76 (± 1010.61)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in QoL

End point title	Change in QoL

End point description:

Change in patient's quality of life from week 0 to week 16.

End point type	Secondary

End point timeframe:

16 weeks

End point values	ITT			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: points				
arithmetic mean (standard deviation)	-5.25 (± 7.25)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were documented in the timeframe from signed informed consent till the end of the follow-up period (week 40).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Overall study

Reporting group description:

The safety set consisted of all patients who entered the trial and was used for conducting all safety analyses.

Serious adverse events	Overall study		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pyoderma			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Overall study		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)		

Nervous system disorders			
Dysaesthesia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Gastrointestinal disorders			
Aphthous ulcer			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Pain of skin			
subjects affected / exposed	4 / 8 (50.00%)		
occurrences (all)	4		
Pruritus	Additional description: Pruritus generalised		
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Skin ulcer			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Infections and infestations			
Ulcer			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Acarodermatitis			
subjects affected / exposed	3 / 8 (37.50%)		
occurrences (all)	3		
Urinary tract infection			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Viral upper respiratory tract infection			

subjects affected / exposed occurrences (all)	3 / 8 (37.50%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 May 2017	After weekly administration of lnvestigational Medicinal Product (IMP) until week 4 (five injections), IMP tobe administered for 32 weeks every two weeks (14 injections) [instead of administration for 16 weeks every four weeks (3 injections)], secondary endpoints (and physician's global assessment (Grade 0 - 4) of the target lesion) should also be assessed at week 32; follow-up (FU).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported