Clinical trial results:
A randomized, placebo-controlled, double-blind study to scrutinize the efficacy of Secukinumab in patients with moderate to severe atopic dermatitis

Summary

EudraCT number	2016-005181-57
Trial protocol	DE
Global end of trial date	04 May 2020

Results information

Result version number	v1 (current)
This version publication date	27 August 2021
First version publication date	27 August 2021

Trial information

Trial identification

Sponsor protocol code	GWT12395-2017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03568136
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GWT-TUD GmbH
Sponsor organisation address	Freiberger Str. 33, Dresden, Germany, 01067
Public contact	Medical Consulting, GWT-TUD GmbH, +49 35125933172, carmen.weigt@gwtonline.de
Scientific contact	Medical Consulting, GWT-TUD GmbH, +49 35125933172, carmen.weigt@gwtonline.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	04 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 May 2020
Global end of trial reached?	Yes
Global end of trial date	04 May 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate and demonstrate the efficacy of secukinumab in patients with atopic dermatitis based on the reduction of the eczema score EASI 50 at week 4 (visit 4).

Protection of trial subjects:

The conduct of this study was in compliance with the Good Clinical Practice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also be carried out in keeping with applicable local law(s) and regulation(s).
In this study, no invasive investigations (e.g. biopsies) were planned. The skin condition was investigated at all study visits and blood samples were investigated which did, however, not implied a risk for the study patients. The risk to subjects in this trial was minimized by compliance with the eligibility criteria and close clinical monitoring.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 September 2018
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: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	20
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Clinical conduct of the study was between 05 Sep 2018 (date of first informed consent) and 04 May 2020. 32 patients were screened at 5 study sites. 22 patients completed screening and were randomized to one of the two treatment groups, 16 in Arm A and 6 in Arm B. The study was prematurely ended by the sponsor because of poor recruitment.

Pre-assignment

Screening details:

During the screening period eligibility of the patients was confirmed. Eligible patients were randomized 2:1 to treatment Arm A or B at Day -7 (+2 to -15) during the randomization visit.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

Patients were allocated in a ratio of 2:1 to Arm A or Arm B. All patients were randomized during the baseline visit using a central block randomization process based at the sponsor's randomization office. The study site requesting randomization of a patient sent a randomization form containing site ID, patient screening number and confirmation of eligibility to the sponsor. In return, the site received the randomization form containing the randomization number (Patient ID) by fax or email.

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Patients in treatment Arm A received 300 mg Secukinumab administered as 2 subcutaneous (SC) injections of 150 mg at baseline Day 1 (Visit 0) and Week 1 (Visit 1), Week 2 (Visit 2), Week 3 (Visit 3), Week 4 (Visit 4), Week 8 (Visit 8), Week 12 (Visit 9) and injections with placebo (2 SC injections) at Week 5 (Visit 5), 6 (Visit 6), 7 (Visit 7) and 16 (Visit 10). Follow-up visits were performed at Week 20 (Visit 11) and 24 (Visit 12).

Arm type	Experimental
Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
Other name	Cosentyx®
Pharmaceutical forms	Solution for infusion in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Secukinumab (Cosentyx®) was used according to the local SmPC. The study dose was 300 mg of Secukinumab by SC injection with initial dosing at baseline (Day 1, Visit 0) and Week 1 (Visit 1), 2 (Visit 2) and 3 (Visit 3), followed by monthly maintenance dosing starting at Week 4. Each 300 mg dose was given as two SC injections of 150 mg.

Arm title	Arm B

Arm description:

Patients in treatment Arm B received placebo until Week 3 (Visit 3) and then switched to Secukinumab as 2 SC injections of 150 mg at Week 4 (Visit 4) and Weeks 5, 6, 7, 8, 12 and 16 (Visits 5 to 10). Follow-up visits were performed at Week 20 (Visit 11) and 24 (Visit 12).

Arm type	Experimental

Investigational medicinal product name	Secukinumab
Investigational medicinal product code	
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Number of subjects in period 1	Arm A	Arm B
Started	16	6
Completed	7	2
Not completed	9	4
Consent withdrawn by subject	8	3
Adverse event, non-fatal	1	-
Lost to follow-up	-	1

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	22	22	
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)	20	20	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	38.8		
standard deviation	± 18.3	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	13	13	

End points

End points reporting groups

Reporting group title	Arm A

Reporting group description:

Patients in treatment Arm A received 300 mg Secukinumab administered as 2 subcutaneous (SC) injections of 150 mg at baseline Day 1 (Visit 0) and Week 1 (Visit 1), Week 2 (Visit 2), Week 3 (Visit 3), Week 4 (Visit 4), Week 8 (Visit 8), Week 12 (Visit 9) and injections with placebo (2 SC injections) at Week 5 (Visit 5), 6 (Visit 6), 7 (Visit 7) and 16 (Visit 10). Follow-up visits were performed at Week 20 (Visit 11) and 24 (Visit 12).

Reporting group title	Arm B

Reporting group description:

Patients in treatment Arm B received placebo until Week 3 (Visit 3) and then switched to Secukinumab as 2 SC injections of 150 mg at Week 4 (Visit 4) and Weeks 5, 6, 7, 8, 12 and 16 (Visits 5 to 10). Follow-up visits were performed at Week 20 (Visit 11) and 24 (Visit 12).

Primary: Reduction of EASI

End point title	Reduction of EASI

End point description:

The primary objective of this study was to investigate and demonstrate the efficacy of Secukinumab in patients with AD based on the reduction of the eczema score EASI 50 at week 4.

End point type	Primary

End point timeframe:

at week 4 (Visit 4)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	5		
Units: Proportion of patients				
median (standard deviation)	18.00 (± 20.33)	15.60 (± 16.68)		

Statistical analyses

Statistical analysis title	Comparison of treatment groups

Statistical analysis description:

The hypothesis H0 : p1 = p2 was tested against the alternative hypothesis: H1: p1 ≠ p2, where p1 is the proportion of patients in the Secukinumab treated group with a reduction of EASI by at least 50% (EASI 50) at week 4 in comparison to baseline and p2 is the EASI 50 in the placebo arm. The hypothesis was tested by Fisher's exact test (with Yates correction). The $\chi 2$-test originally planned in the study protocol could not be performed due to the reduced sample size.

Comparison groups	Arm A v Arm B

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 1
Method	Fisher exact

Notes:

[1] - The hypothesis was tested by Fisher's exact test (with Yates correction). The $\chi 2$-test originally planned in the study protocol could not be performed due to the reduced sample size.

Secondary: Reduction of EASI at baseline and EoT

End point title	Reduction of EASI at baseline and EoT

End point description:

To compare the proportion of patients with a reduction of the eczema score EASI 50 at baseline and at end of treatment.

End point type	Secondary

End point timeframe:

Day 1 (Visit 0), EoT (study Arm A, Visit 9; study Arm B, Visit 10)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16[2]	6[3]		
Units: Proportion of patients				
median (standard deviation)				
Day 1	22.80 (± 12.05)	24.65 (± 15.00)		
EoT	16.00 (± 17.46)	6.60 (± 3.25)		

Notes:

[2] - Subjects analysed EoT: 7

[3] - Subjects analysed EoT: 3

Statistical analyses

No statistical analyses for this end point

Secondary: Change in SCORAD by 50%

End point title	Change in SCORAD by 50%

End point description:

End point type	Secondary

End point timeframe:

Day 1 (Visit 0), week 4 (Visit 4) EoT (study Arm A, Visit 9; study Arm B Visit 10)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: Proportion of patients				
arithmetic mean (standard deviation)				
Day 1	64.12 (± 12.45)	67.56 (± 14.58)		
Week 4	56.01 (± 23.65)	49.30 (± 20.42)		
EoT	50.93 (± 20.70)	31.37 (± 6.66)		

Statistical analyses

No statistical analyses for this end point

Secondary: IGA score of “clear" or "almost clear”

End point title	IGA score of “clear" or "almost clear”

End point description:

To compare the proportion of patients who achieve a score of "clear-0" or "almost clear-1" in the static IGA score at EoT as compared to baseline.

End point type	Secondary

End point timeframe:

EoT (Study Arm A, Visit 9; Study Arm B, Visit 10)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: Proportion of patients				
number (not applicable)				
Yes	0	1		
No	16	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Increase in DLQI by 30%

End point title	Increase in DLQI by 30%

End point description:

End point type	Secondary

End point timeframe:

Day 1 (Visit 0), week 4 (Visit 4), EoT (study Arm A, Visit 9; study Arm B, Visit 10)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: Proportion of patients				
arithmetic mean (standard deviation)				
Day 1	11.5 (± 7.9)	12.2 (± 4.7)		
Week 4	8.5 (± 6.3)	10.4 (± 5.0)		
EoT	7.7 (± 5.8)	5.7 (± 2.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Biomarker CCL17 and CCL22

End point title	Biomarker CCL17 and CCL22

End point description:

End point type	Secondary

End point timeframe:
at week 4 (Visit 4)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	4		
Units: Serum concentration				
median (standard deviation)				
CCL17	139 (± 373)	168 (± 65)		
CCL22	1418 (± 3193)	2524 (± 2333)		

Statistical analyses

No statistical analyses for this end point

Secondary: Missing days at work

End point title	Missing days at work

End point description:

End point type	Secondary

End point timeframe:
at week 4 (Visit 4)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	3		
Units: Sum of missing days				
arithmetic mean (standard deviation)	1.4 (± 3.1)	0.0 (± 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Consumption of topical corticosteroid drug

End point title	Consumption of topical corticosteroid drug

End point description:

End point type	Secondary

End point timeframe:
at week 4 (Visit 4)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	6		
Units: gram(s)				
arithmetic mean (standard deviation)				
With Imputation	0.25 (± 36.87)	3.38 (± 34.90)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The observation phase for AEs started with signing the informed consent form and ended 28 days after the last intake of study drug, unless the investigator suspected a delayed adverse reaction to the study drug.

Adverse event reporting additional description:

For this trial, only treatment-emergent AEs were documented. All AEs starting or worsening after first study drug administration up to 30 days after last study drug administration were considered as treatment-emergent.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 22 (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	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 22 (81.82%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acanthoma			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			

Rhinitis allergic subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Investigations Blood glucose increased subjects affected / exposed occurrences (all) Urine protein/creatinine ratio subjects affected / exposed occurrences (all) Urine analysis abnormal subjects affected / exposed occurrences (all) Hepatic enzyme increased subjects affected / exposed occurrences (all) Diagnostic procedure subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1 1 / 22 (4.55%) 1 1 / 22 (4.55%) 1 1 / 22 (4.55%) 1 1 / 22 (4.55%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all) Muscle strain subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1 1 / 22 (4.55%) 1		
Cardiac disorders Sinus bradycardia subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 1 / 22 (4.55%) 1		
Blood and lymphatic system disorders			

Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Lymphadenopathy subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	3 / 22 (13.64%) 5		
Vomiting subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Gastritis subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Flatulence subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Skin and subcutaneous tissue disorders Nasopharyngitis subjects affected / exposed occurrences (all)	13 / 22 (59.09%) 23		
Eczema subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Dermatitis atopic subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 2		
Urticaria subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2		
Acne subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1		
Neurodermatitis			

subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Pain of skin			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	6		
Musculoskeletal pain			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Pain in extremity			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Infections and infestations			
Gastrointestinal infection			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Otitis externa			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Abscess			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Diverticulitis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Urinary tract infection			

subjects affected / exposed	3 / 22 (13.64%)		
occurrences (all)	3		
Tonsillitis			
subjects affected / exposed	2 / 22 (9.09%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	1 / 22 (4.55%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2018	Protocol Version 3.0, dated 16 Nov 2018 • Extension of exclusion criteria • Adjustment of time windows for screening and randomization • Documentation of adverse events between initial screening failure and re-screening not necessary • No fasting before blood collection necessary
27 August 2019	Protocol Version 4.0, dated 24 Jul 2019 • Implementation of telephone visits at V1 to V3 and V5 to V7 instead of visits at trial site • Implementation of patient diary at home on the days of telephone visits

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.

Study was prematurely terminated because of a delayed recruitment which did not suggest completion in a reasonable time frame. Due to the explorative character of the study inclusion of less subjects was deemed to have no impact on the study outcome.

Notes: