Clinical trial results:
Safety and efficacy of Abatacept in patients with treatment-resistant sarcoidosis

Summary

EudraCT number	2016-003360-39
Trial protocol	DE
Global end of trial date	15 February 2021

Results information

Result version number	v1 (current)
This version publication date	03 June 2022
First version publication date	03 June 2022

Trial information

Trial identification

Sponsor protocol code	P001382

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS00011660: Deutsches Register Klinischer Studien

Notes:

Sponsors

Sponsor organisation name	Medical Center - University of Freiburg
Sponsor organisation address	Hugstetter Straße 55, Freiburg, Germany, 79106
Public contact	Leiter der Klinischen Prüfung, Universitätsklinikum Freiburg, +49 761270 37060, joachim.mueller-quernheim@uniklinik-freiburg.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	31 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2021
Global end of trial reached?	Yes
Global end of trial date	15 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety of Abatacept in patients with treatment-resistant sarcoidosis, measured as number of infectious complications during treatment period.

Protection of trial subjects:

A Data Monitoring Committee (DMC) was established to review safety data of part I of the study in order to monitor overall patient safety and to give a recommendation regarding the frequency of study visits for patients in part II of the study. A patient was able to withdraw from the study at any time, at his or her own request, for any reason (specified or unspecified) and without penalty or loss of benefits to which the patient is otherwise entitled.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 February 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	23
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Part I: included 6 patients monitored for therapy-associated complications. A Data Monitoring Committee decided on the frequency of study visits for part II patients based on safety data from part I patients. 1st meeting after visit 1(week 6) of last Patient part I. Part II study: another 24 patients: focus on efficacy and safety.

Period 1

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

Arms

Arm title	Abatacept
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	Orencia
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Proprietary name: Orencia, Name of substance: Abatacept, Manufacturer: Bristol-Myers Squibb, Strength: 125 mg/syringe, Dose: 1x125 mg weekly, Dosage Form: Solution for injection: pre-filled syringe with a passive needle safety guard

Number of subjects in period 1	Abatacept
Started	30
Completed	24
Not completed	6
Adverse event, serious fatal	1
Disease progression	1
Wish of patient	2
Stay in hospital due to ureterolithiasis	1
Lost contact	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	30	30	
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)	23	23	
From 65-84 years	7	7	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	9	9	
Male	21	21	

End points

End points reporting groups

Reporting group title	Abatacept

Reporting group description: -

Primary: Severe infections

End point title	Severe infections[1]

End point description:

End point type	Primary

End point timeframe:

During observation period

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: Single-arm trial. The primary analysis was performed in terms of an annual incidence rate, calculated as the number of infectious complications related to the duration of observation, both measures cumulated for all patients.

End point values	Abatacept			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Number of severe infections	1			

Statistical analyses

No statistical analyses for this end point

Primary: Severe infections

End point title	Severe infections[2]

End point description:

End point type	Primary

End point timeframe:

During observation period

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: Single-arm trial. The primary analysis was performed in terms of an annual incidence rate, calculated as the number of infectious complications related to the duration of observation, both measures cumulated for all patients.

End point values	Abatacept			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Incidence rate				
number (confidence interval 95%)	0.0352 (0.0009 to 0.1959)			

Statistical analyses

No statistical analyses for this end point

Secondary: Non-severe infections

End point title	Non-severe infections

End point description:

Number of patients who experienced non-severe infections under abatacept treatment.

End point type	Secondary

End point timeframe:

During observation period

End point values	Abatacept			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Number of patients				
0 infections	8			
1 infection	10			
2 infections	5			
3 infections	5			
4 infections	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Complete study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22

Reporting groups	
Reporting group title	Abatacept
Reporting group description:	
Abatacept 125 mg	

Serious adverse events	Abatacept		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 30 (20.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural fever			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ventricular fibrillation			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Trigeminal nerve disorder			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Ureterolithiasis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Abatacept		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 30 (100.00%)		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hot flush			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Surgical and medical procedures			
Inguinal hernia repair			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Fatigue			

subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Oedema peripheral			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Dyspnoea exertional			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Pharyngeal erythema			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Rales			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			

Animal scratch			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hand fracture			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Infusion related reaction			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Limb injury			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Rib fracture			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Cardiac disorders			
Cardiovascular disorder			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Diastolic dysfunction			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Paraesthesia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Syncope			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Erythema of eyelid			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Aerophagia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Faeces soft			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Melaena			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Oral mucosal erythema			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hand dermatitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Arthropathy			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Costochondritis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Osteoarthritis			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Osteoporotic fracture			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Tenosynovitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	7		
Cystitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	7		
Oral candidiasis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	2		
Oral herpes			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Periodontitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Pulpitis dental			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		

Respiratory tract infection			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	5		
Scarlet fever			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	10		
Urinary tract infection			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2017	Amendment was done to adapt the total amount of blood taken for laboratory testing, and to harmonize the protocol and the patient informed consent form (PIC) in this regard.
17 December 2018	Amendment was done primarily to clarify two inclusion criteria. With regard to pre-existing immunosuppressive treatment (inclusion criterion no. 5), it was specified that patients with (exactly) 5 mg prednisolone equivalent per day can also be included ("greater than" was replaced by "greater than or equal"), and that in case of additional immunosuppressive therapy, patients can be included irrespective of steroid dose. In inclusion criterion no. 6, the KSQ module was specified, as there is no total or generic KSQ score. Furthermore, disease progression was added as criterion for premature termination.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/32551397