Clinical trial results:
Safety and Efficacy of abatacept (s.c.) in patients with CTLA4 insufficiency or LRBA deficiency

Summary

EudraCT number	2019-000972-40
Trial protocol	DE
Global end of trial date	28 June 2023

Results information

Result version number	v1 (current)
This version publication date	02 January 2025
First version publication date	02 January 2025

Trial information

Trial identification

Sponsor protocol code	IM101-774

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS: DRKS00017736

Notes:

Sponsors

Sponsor organisation name	Medical Center - University of Freiburg
Sponsor organisation address	Breisacher Str. 115, Freiburg, Germany, 79106
Public contact	Coordinating Investigator: Bodo Grimbacher, Medical Center - University of Freiburg, +49 761270-77731, bodo.grimbacher@uniklinik-freiburg.de
Scientific contact	Coordinating Investigator Bodo Grimbacher, Medical Center - University of Freiburg, +49 761270-77731, bodo.grimbacher@uniklinik-freiburg.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	08 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 June 2023
Global end of trial reached?	Yes
Global end of trial date	28 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

to assess the safety of abatacept for patients with cytotoxic T-lymphocyte-associated protein 4 (CTLA4) insufficiency or lipopolysaccharide-responsive and beige-like anchor protein (LRBA) deficiency

Protection of trial subjects:

The investigator was responsible for ensuring that the study was performed in accordance with the ethical principles of the Declaration of Helsinki as well as with the national laws and guidelines for the clinical testing of drugs. Before enrolment in the clinical trial, the patient was informed that participation in the clinical trial is voluntary and that he/she may withdraw from the clinical trial at any time without having to give reasons and without penalty or loss of benefits to which the patient is otherwise entitled.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 July 2020
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: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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	1
85 years and over	0

Subject disposition

Recruitment
Recruitment details: -

Pre-assignment
Screening details: -

Pre-assignment period milestones	
Number of subjects started	24
Number of subjects completed	20

Pre-assignment subject non-completion reasons	
Reason: Number of subjects	Not meeting inclusion criteria: 3
Reason: Number of subjects	Other reasons: 1

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

Blinding implementation details:

ABACHAI is a phase IIa prospective, non-randomized, open-label, single arm multi-center trial.

Arms	
Arm title	Abatacept

Arm description:

All patients were treated with abatacept 125 mg once a week as a subcutaneous injection.

Arm type	Experimental
Investigational medicinal product name	Abatacept
Investigational medicinal product code	
Other name	Orencia
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Solution for injection

Dosage and administration details:

Strength: 125 mg/1 ml syringe

Dose: 1x 125 mg/1 ml syringe weekly

Number of subjects in period 1[1]	Abatacept
Started	20
Completed	20

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: Overall, 24 patients gave their informed consent for study participation. From these, 4 patients were screening failures, i.e. did not met the inclusion/exclusion criteria and were not treated with the study medication. For the other 20 patients, treatment with abatacept as part of the study was approved. Of those, 16 patients completed the study per protocol.

Baseline characteristics

Reporting groups

Reporting group title	Overall

Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	20	20	
Age categorical Units: Subjects			
Adults (18-64 years)	19	19	
From 65-84 years	1	1	
Age continuous Units: years			
median	37		
full range (min-max)	19 to 70	-	
Gender categorical Units: Subjects			
Female	14	14	
Male	6	6	

Subject analysis sets

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) includes all 20 patients who were treated with at least one dose of abatacept

Reporting group values	Full analysis set (FAS)		
Number of subjects	20		
Age categorical Units: Subjects			
Adults (18-64 years)	19		
From 65-84 years	1		
Age continuous Units: years			
median	37		
full range (min-max)	19 to 70		
Gender categorical Units: Subjects			
Female	14		
Male	6		

End points

End points reporting groups

Reporting group title	Abatacept

Reporting group description:

All patients were treated with abatacept 125 mg once a week as a subcutaneous injection.

Subject analysis set title	Full analysis set (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

The full analysis set (FAS) includes all 20 patients who were treated with at least one dose of abatacept

Primary: Number of episodes of failed infection control under therapy with abatacept during the trial period of one year

End point title	Number of episodes of failed infection control under therapy with abatacept during the trial period of one year[1]

End point description:

Number of episodes of failed infection control under therapy with abatacept during the trial period of one year. An episode of failed infection control was defined as a severe infection, defined as

a. Infections requiring hospitalization, OR

b. Infectious requiring intravenous antibiotic, anti-fungal or anti-viral treatment, OR/AND

c. EBV reactivation (≥ 5.000 IU/ml) or CMV viral load ≥ 1.000 IU/ml.

End point type	Primary

End point timeframe:

During the trial period of one year.

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 number of episodes of failed infection control during the trial period of one year is calculated as an annual incidence rate, and is presented with
a two-sided 95% CI.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of episodes				
Number of severe infections during trial period	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of severe infections

End point title	Number of severe infections

End point description:

Defined as i.e. requiring hospitalization, or an infection requiring i.v. antibiotic, i.v. anti-fungal, or i.v.

anti-viral treatment.

End point type	Secondary

End point timeframe:

the year preceding 1st abatacept application

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of severe infections	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of episodes of failed infection control exceeding 3 months under therapy

End point title	Number of episodes of failed infection control exceeding 3 months under therapy

End point description:

Number of episodes of failed infection control exceeding 3 months under therapy with abatacept during the trial period of one year. These were as defined above (primary endpoint), with three exceptions:

o primary viral infections which were controlled within 0 to 3 months.

o hospitalizations which were conducted solely for preventive reasons

o i.v. antibiotic, or i.v. anti-fungal, or i.v. anti-viral treatments which were conducted solely for preventive reasons

End point type	Secondary

End point timeframe:

Exceeding 3 months under therapy with abatacept during the trial period of one year.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Number of episodes	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Characterization of severe infections

End point title	Characterization of severe infections

End point description:

Characterization (incl. type of pathogen and involved organ system) of severe infections (defined as: an infection requiring hospitalization OR an infection requiring i.v. antibiotic, or i.v. anti-fungal, or i.v. anti-viral treatment).

End point type	Secondary

End point timeframe:

During abatacept trial treatment period.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Characterization				
SARS-CoV-2 infection	3			
Exacerbated COPD due to infection, DD Covid 19	1			
Exacerbation of COPD due to infection	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Event free Survival

End point title	Event free Survival

End point description:

Results of the Kaplan-Meier analysis

End point type	Secondary

End point timeframe:

Calculated as time from start of treatment with abatacept as trial medication until death from any cause or treatment failure (premature termination of abatacept treatment for any reason).

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Rates				
number (confidence interval 95%)				
Month 3	100 (100 to 100)			
Month 6	95 (69.5 to 99.3)			
Month 12	80 (55.1 to 92)			

Month 15	80 (55.1 to 92)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Results of the Kaplan-Meier analysis

End point type	Secondary

End point timeframe:

Defined as time from start of abatacept treatment as trial medication (i.e. after trial registration) until death from any cause.

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Rates				
number (confidence interval 95%)				
Month 3	100 (100 to 100)			
Month 6	100 (100 to 100)			
Month 12	94.4 (66.6 to 99.2)			
Month 15	94.4 (66.6 to 99.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment failure

End point title	Treatment failure

End point description:

Defined as any premature termination of treatment for any reason.

End point type	Secondary

End point timeframe:

during study

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Rate				
number (confidence interval 95%)	20 (5.73 to 43.66)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulative steroid dose

End point title	Cumulative steroid dose

End point description:

14 (70.0%) of the 20 FAS patients were treated with steroids during the observation period as well as during abatacept/study drug application.

End point type	Secondary

End point timeframe:

During observation period and during abatacept application

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20[2]			
Units: Cumulative dose [mg]				
arithmetic mean (standard deviation)				
Cumulative dose during observation period	3720 (± 2049)			
Cumulative dose during abatacept application	2805 (± 1312)			

Notes:

[2] - Number of patients with at least one steroid application: 14

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of live measured by SF36

End point title	Quality of live measured by SF36

End point description:

End point type	Secondary

End point timeframe:

Difference month 12 to screening

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: Points				
arithmetic mean (standard deviation)				
Physical function index	1.35 (± 18.66)			
Role-physical index	6.25 (± 45.18)			
Role-emotional functioning	-12.5 (± 50.0)			
Social functioning index	13.3 (± 30.4)			
Mental health index	2.27 (± 19.9)			
Pain	1.50 (± 31.6)			
Vitality	3.44 (± 21.5)			
General health perception	5.60 (± 22.75)			
Physical component summary	2.26 (± 11.54)			
Mental component summary	1.07 (± 11.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Improvement Scale (CGI-I) at month 6

End point title	Clinical Global Impression-Improvement Scale (CGI-I) at month 6

End point description:

The CGI-I is a 7 point scale that requires the physician to assess how much the patient’s illness has improved or worsened relative to a baseline state at the beginning of the intervention and is rated from ‘complete improvement’ to ‘worse than baseline’.

End point type	Secondary

End point timeframe:

Change from the beginning of the intervention to Month 6

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20[3]			
Units: Number of patients				
Complete improvement	1			
Excellent improvement	1			
Marked improvement	0			
Moderate improvement	6			
Minimal improvement	4			

No change	5			
Worse	1			

Notes:

[3] - Number of patients valid: 18

Statistical analyses

No statistical analyses for this end point

Secondary: CHAI-Morbidity Score

End point title	CHAI-Morbidity Score

End point description:

Assessment ranged from 0 points (none) over 1 point (mild) and 2 points (moderate) to 3 points (severe).

End point type	Secondary

End point timeframe:

Difference month 12 to screening

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20			
Units: CHAI score points				
arithmetic mean (standard deviation)				
Lung	0.25 (± 1.14)			
Gut	-0.18 (± 1.59)			
Cytopenia	-0.12 (± 0.33)			
CNS	0 (± 0)			
Immune system	-2.41 (± 3.18)			
Lymphoproliferation	-0.88 (± 1.69)			
Skin	0.06 (± 1.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Improvement Scale (CGI-I) at month 12

End point title	Clinical Global Impression-Improvement Scale (CGI-I) at month 12

End point description:

End point type	Secondary

End point timeframe:

Change from the beginning of the intervention to Month 12

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20[4]			
Units: Number of patients				
Complete improvement	0			
Excellent improvement	2			
Marked improvement	3			
Moderate improvement	4			
Minimal improvement	1			
No change	6			
Worse	1			

Notes:

[4] - Number of patients valid: 17

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression-Improvement Scale (CGI-I) at month 15

End point title	Clinical Global Impression-Improvement Scale (CGI-I) at month 15

End point description:

According to CTP the visit at month 15 (follow-up visit) was performed as onsite visit only in case of termination of abatacept treatment after 12 months trial treatment (n=7)

End point type	Secondary

End point timeframe:

Change from the beginning of the intervention to Month 15

End point values	Full analysis set (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	20[5]			
Units: Number of patients				
Complete improvement	0			
Excellent improvement	1			
Marked improvement	0			
Moderate improvement	0			
Minimal improvement	0			
No change	4			
Worse	2			

Notes:

[5] - Number of patients valid: 7

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:	
125 mg abatacept s.c. once weekly	

Serious adverse events	Abatacept		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 20 (45.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Tremor			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Renal tubular acidosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Primary adrenal insufficiency			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Peritonitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
COVID-19			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 20 (5.00%)		
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	19 / 20 (95.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin papilloma			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Surgical and medical procedures			

COVID-19 immunisation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	3		
Injection site paraesthesia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Puncture site pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Genital tract inflammation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Throat irritation			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Tonsillar hypertrophy			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Blood potassium decreased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Haemoglobin decreased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Intraocular pressure increased			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	11 / 20 (55.00%)		
occurrences (all)	50		

Hyperaesthesia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Migraine			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Lymphadenopathy			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Monoclonal B-cell lymphocytosis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eye inflammation			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Abdominal pain upper			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Cheilitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Constipation			

subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Abdominal pain lower			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Noninfective gingivitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Cholestasis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Alopecia			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Dermatitis psoriasiform			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Hidradenitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Petechiae			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 20 (25.00%)		
occurrences (all)	6		
Arthritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Back pain			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Muscle tightness			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Neck pain			

subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Osteoarthritis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Bronchitis			
subjects affected / exposed	3 / 20 (15.00%)		
occurrences (all)	3		
COVID-19			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	3		
Clostridium difficile infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Coronavirus infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Folliculitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Gastrointestinal viral infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Genital herpes			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	3		

Herpes zoster			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Hordeolum			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	2 / 20 (10.00%)		
occurrences (all)	2		
Oesophageal candidiasis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	4		
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	1		
Viral infection			
subjects affected / exposed	1 / 20 (5.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2020	Implemented changes during initial approval process according to CA requirements: • In section 4.3, page 34 the wording of the exclusion criterion No. 21 has been adapted according to the CTFG paper, section 4.1 „Birth control methods which may be considered as highly effective". The methods „vasectomised partner " and „sexual abstinence" seem not feasible to us in this clinical trial. The request to use appropriate contraceptive measures at least up to 14 weeks after the last dose of abatacept has been included in section 4.3. • In section 4.3, page 35 the definition according to the CTFG paper has been included. In section 19, page 74 the CTFG paper has been added to the list of references. In the complete Clinical Trial Protocol the wording „women in reproductive age" has been replaced by „women of child bearing potential". • In section 1.4, page 27 we have added further information based on unpublished data of patients with CTLA4 insufficiency treated with abatacept on local compassionate use programs.
21 April 2020	• In the synopsis, page 14 as well as in section 4.3, page 35 the exclusion criteria 8 and 9 have been changed to an overall exclusion criterion no. 8: any malignancies within the last 4 years. • In section 13.5.5, page 68 the term "treatment failure rate" was precised: defined as the number of treatment failures divided by the number of patients receiving abatacept • In section 15.3, page 70 the patients´ agreement during the informed consent procedure to "codified ("pseudonymised") transmission to the members of the GAIN network" was deleted.

19 October 2020	- Change of LKP - elongation of screening period - Corrected: abdominal lymph nodes are measured by ultrasonography not by palpation. - Bodyplethysmography is performed for all patients during screening period to evaluate the inclusion criteria for lung involvement (in V 2.0 only for patients with lung involvement). During course of study the examination is performed only for patients with lung involvement. - Borg Dyspnoe Scala is performed for all patients (in V 2.0 only for patients with lung involvement) to check possible changes of lung function during course of study. - Completion of patient questionnaires SF36, SGRQ, IBDQ is shifted from screening to baseline visit, because this is the time point directly before application of first trial medication. - Assessment based on NANO Scale is performed for all patients during screening period to evaluate possible neurological impairment (in V 2.0 only for patients with CNS involvement). During course of study the examination is performed only for patients with CNS involvement. - Examination of skin is performed for all patients during all onsite visits to evaluate possible skin involvement (in V 2.0 only for patients with skin involvement). - Incorrect unit - Elongation of period between stopping rituximab therapy and inclusion into trial adapted according to half-life period of rituximab. - The exclusion criterion No 5 was splitted - Definition of a lag period between stopping prophylactic CMV treatment and inclusion into the trial - Decision for treatment with abatacept already was done before inclusion into the trial.
23 July 2021	- change of LKP - Adaptation to current trial status - The secondary endpoints for patients with involvement of immune system do not reflect the parameters used in the CHAI-Morbidity-Score for the Immune System. The endpoints have been adapted accordingly. - Implementation of further secondary endpoints (safety). - Inclusion criteria do not reflect the parameters used in the CHAI-Morbidity-Score for the Immune System. The inclusion criteria have been adapted accordingly. - Adaption of exclusion criteria - Addition of mandatory concomitant medication - Adaption of secondary endpoints

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/36262801