Clinical trial results:
Biomarkers Of The Humoral Immune Response After Conversion To Belatacept In Comparison To Conventional Immunosuppressive Therapy In Renal Transplant Patients

Summary

EudraCT number	2012-005652-42
Trial protocol	DE
Global end of trial date	10 March 2016

Results information

Result version number	v1 (current)
This version publication date	06 November 2022
First version publication date	06 November 2022

Trial information

Trial identification

Sponsor protocol code	IM103-319

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité - Universitätsmedizin Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Clinical Trial informations, Charité Universitätsmedizin Berlin, 0049 030614086, klemens.budde@charite.de
Scientific contact	Clinical Trial informations, Charité Universitätsmedizin Berlin, 0049 030614086, klemens.budde@charite.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	11 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 March 2016
Global end of trial reached?	Yes
Global end of trial date	10 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine cellular and transcriptional Biomarker candidates of the humoral and cellular immune system that elucidate the effect of Nulojix in preventing DSA formation after conversion in comparison to a CNI- or mTORi-based therapy in renal transplant recipients.

Protection of trial subjects:

Routine haematology, biochemistry, renal transokabt function, urine analyses and vital signs will becorded according the visit schedule. In addition, physical examination, an electrocardiogram and medical history will be recorded at study entry

Background therapy:

Regulatory T-cells (Tregs) are considered to play a crucial role in maintaining control of immune response following renal transplantation (Tx). So far, only limited data are available from prospective controlled trials on the time course and frequency of Tregs after conversion from either Calcineurin inhibitors (CNIs) or mammalian target of Rapamycin inhibitors (mTORi) to Belatacept, a co-stimulatory blocker of CD80/86. The aim of this study was to evaluate the influence of belatacept on T-cell subsets with focus on Tregs after withdrawal from CNI or mTORi.

Evidence for comparator:

Belatacept, cytotoxic T lymphocyte-associated protein 4 (CTLA-4)-Ig (Nulojix®) is the first clinically relevant co-stimulation blocker, and is a high-affinity chimeric fusion protein that binds to CD80/CD86 on (Antigen-presenting cells) APC . One of the best- characterized costimulatory reactions is between CD28/CTLA-4 on T cells and CD80/CD86 on APC. The interaction between CD28 and CD80/CD86 leads to T-cell activation. Because of its non-renal toxicities, belatacept provides a benefit in preserving renal function by avoiding calcineurin inhibitors and a better cardiovascular risk profile.

Actual start date of recruitment	11 November 2013
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: 41
Worldwide total number of subjects	41
EEA total number of subjects	41

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)	32
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at one study centers in Germany, between 2013/11/11 (first patient first visit) and 2016/03/10 (last patient last visit).

Pre-assignment

Screening details:

Renal transplant recipients, whose received renal allograft at least 3 months were screened. Patients, who have signs of CNI- or mTORi- related toxicity or intolerance were included. One matched control patient was identified and investigated for each renal transplant patient. e.g. gender, comparabel age (+/- 10Y), tranplant. durat. (+/-5Y)

Period 1

Period 1 title	overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

open design of trial with parallel groups

Arms

Are arms mutually exclusive?	Yes
Arm title	CNI conversion

Arm description:

Patients on a CNI-based therapy for more than 3 months, who have signs of CNI- related toxicity or intolerance and are converted due to clinical indication to a CNI-free immunosuppression with Belatacept. Patients received belatacept 5 mg/kg on baseline (day 0), week 2 (day 14), week 4 (day 28), week 6 (day 42), and week 8 (day 56), and then every 4 weeks thereafter until completion of the trial. In addition, immunosuppressive co-medication of steroids and Mycophenolate was continued unchanged in all study patients.

Arm type	Experimental
Investigational medicinal product name	Belatacept
Investigational medicinal product code	
Other name	NULOJIX
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

A dose of 5 mg/kg NULOJIX, administered every 2 weeks for the first 8 weeks, followed by the same dose every 4 weeks thereafter.
In addition, immunosuppressive co-medication of steroids and Mycophenolate was continued unchanged in all study patients.

Investigational medicinal product name	Prograf
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

0.5 mg, 1 mg, 5 mg

Investigational medicinal product name	Sandimmun Optoral
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use

Dosage and administration details: 10 mg, 25 mg, 50 mg, 100 mg	
Investigational medicinal product name	Advagraf
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: 0.5 mg, 1 mg, 3mg, 5mg	
Arm title	mTORi conversion
Arm description: Patients on a mTORi-based therapy for more than 3 months, who have signs ofmTORi related toxicity or intolerance and are converted due to clinical indication to a mTORi-free immunosuppression with Belatacept. Patients received belatacept 5 mg/kg on baseline (day 0), week 2 (day 14), week 4 (day 28), week 6 (day 42), and week 8 (day 56), and then every 4 weeks thereafter until completion of the trial. In addition, immunosuppressive co-medication of steroids and Mycophenolate was continued unchanged in all study patients.	
Arm type	Experimental
Investigational medicinal product name	Belatacep
Investigational medicinal product code	
Other name	NULOJIX
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: A dose of 5 mg/kg NULOJIX, administered every 2 weeks for the first 8 weeks, followed by the same dose every 4 weeks thereafter. In addition, immunosuppressive co-medication of steroids and Mycophenolate was continued unchanged in all study patients.	
Investigational medicinal product name	Certican
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 0.1 mg, 0.25 mg, 0.5 mg, 0.75 mg, 1 mg	
Arm title	CNI control
Arm description: matched-control patients who remain on their current immunosuppression regimen.	
Arm type	Active comparator
Investigational medicinal product name	Prograf
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: 0.5 mg, 1 mg, 5 mg	
Investigational medicinal product name	Sandimmun Optoral
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, soft
Routes of administration	Oral use
Dosage and administration details: 10 mg, 25 mg, 50 mg, 100 mg	

Investigational medicinal product name	Advagraf
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:
0.5 mg, 1 mg, 3mg, 5mg

Arm title	mTORi control

Arm description:
matched-control patients who remain on their current immunosuppression regimen.

Arm type	Active comparator
Investigational medicinal product name	Certican
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
0.1 mg, 0.25 mg, 0.5 mg, 0.75 mg, 1 mg

Number of subjects in period 1	CNI conversion	mTORi conversion	CNI control
Started	11	11	10
Completed	10	9	9
Not completed	1	2	1
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	-	1	-
Adverse event, non-fatal	1	-	1

Number of subjects in period 1	mTORi control
Started	9
Completed	9
Not completed	0
Adverse event, serious fatal	-
Consent withdrawn by subject	-
Adverse event, non-fatal	-

Baseline characteristics

Reporting groups	
Reporting group title	CNI conversion
Reporting group description:	
Patients on a CNI-based therapy for more than 3 months, who have signs of CNI- related toxicity or intolerance and are converted due to clinical indication to a CNI-free immunosuppression with Belatacept. Patients received belatacept 5 mg/kg on baseline (day 0), week 2 (day 14), week 4 (day 28), week 6 (day 42), and week 8 (day 56), and then every 4 weeks thereafter until completion of the trial. In addition, immunosuppressive co-medication of steroids and Mycophenolate was continued unchanged in all study patients.	
Reporting group title	mTORi conversion
Reporting group description:	
Patients on a mTORi-based therapy for more than 3 months, who have signs ofmTORi related toxicity or intolerance and are converted due to clinical indication to a mTORi-free immunosuppression with Belatacept. Patients received belatacept 5 mg/kg on baseline (day 0), week 2 (day 14), week 4 (day 28), week 6 (day 42), and week 8 (day 56), and then every 4 weeks thereafter until completion of the trial. In addition, immunosuppressive co-medication of steroids and Mycophenolate was continued unchanged in all study patients.	
Reporting group title	CNI control
Reporting group description:	
matched-control patients who remain on their current immunosuppression regimen.	
Reporting group title	mTORi control
Reporting group description:	
matched-control patients who remain on their current immunosuppression regimen.	

Reporting group values	CNI conversion	mTORi conversion	CNI control
Number of subjects	11	11	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	9	8	8
From 65-84 years	2	3	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	1	5	1
Male	10	6	9
underlying disease Units: Subjects			
Chronic Glomerulonephritis	3	2	5
Diabetes-Adult type	2	1	0
Polycystic	3	2	1
Hypertensive Nephropathy	0	0	1
Hemolytic Uremic Syndrome	0	1	0

Pyelonephritis	0	1	0
IgA Nephropathy	0	1	1
Reflux Nephropathy	0	1	0
Alport Syndrome	0	0	1
Interstitial Nephritis	0	0	0
Immune Complex Nephritis	0	0	0
Other	3	2	1
Age at conservation			
Units: years			
arithmetic mean	53.83	55.49	50.79
standard deviation	± 13.14	± 13.88	± 12.84
Time after transplant			
Units: years			
arithmetic mean	6.53	10.15	7.82
standard deviation	± 5.75	± 4.06	± 5.07
Creatinine			
Units: mg/dl			
arithmetic mean	2.68	1.68	1.99
standard deviation	± 0.75	± 0.48	± 0.35
Proteinuria			
Units: mg/l			
arithmetic mean	155.5	268.9	193.0
standard deviation	± 104.6	± 280.2	± 180.1

Reporting group values	mTORi control	Total	
Number of subjects	9	41	
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)	7	32	
From 65-84 years	2	9	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	5	12	
Male	4	29	
underlying disease			
Units: Subjects			
Chronic Glomerulonephritis	3	13	
Diabetes-Adult type	0	3	
Polycystic	1	7	
Hypertensive Nephropathy	0	1	
Hemolytic Uremic Syndrome	0	1	
Pyelonephritis	0	1	
IgA Nephropathy	0	2	

Reflux Nephropathy	1	2	
Alport Syndrome	0	1	
Interstitial Nephritis	1	1	
Immune Complex Nephritis	1	1	
Other	2	8	
Age at conservation			
Units: years			
arithmetic mean	57.58		
standard deviation	± 14.06	-	
Time after transplant			
Units: years			
arithmetic mean	10.33		
standard deviation	± 4.69	-	
Creatinine			
Units: mg/dl			
arithmetic mean	1.11		
standard deviation	± 0.29	-	
Proteinuria			
Units: mg/l			
arithmetic mean	118.2		
standard deviation	± 57.7	-	

End points

End points reporting groups

Reporting group title	CNI conversion
Reporting group description:	
Patients on a CNI-based therapy for more than 3 months, who have signs of CNI- related toxicity or intolerance and are converted due to clinical indication to a CNI-free immunosuppression with Belatacept. Patients received belatacept 5 mg/kg on baseline (day 0), week 2 (day 14), week 4 (day 28), week 6 (day 42), and week 8 (day 56), and then every 4 weeks thereafter until completion of the trial. In addition, immunosuppressive co-medication of steroids and Mycophenolate was continued unchanged in all study patients.	
Reporting group title	mTORi conversion
Reporting group description:	
Patients on a mTORi-based therapy for more than 3 months, who have signs ofmTORi related toxicity or intolerance and are converted due to clinical indication to a mTORi-free immunosuppression with Belatacept. Patients received belatacept 5 mg/kg on baseline (day 0), week 2 (day 14), week 4 (day 28), week 6 (day 42), and week 8 (day 56), and then every 4 weeks thereafter until completion of the trial. In addition, immunosuppressive co-medication of steroids and Mycophenolate was continued unchanged in all study patients.	
Reporting group title	CNI control
Reporting group description:	
matched-control patients who remain on their current immunosuppression regimen.	
Reporting group title	mTORi control
Reporting group description:	
matched-control patients who remain on their current immunosuppression regimen.	
Subject analysis set title	Baseline
Subject analysis set type	Safety analysis
Subject analysis set description:	
Comparison between baseline and monthly changes	

Primary: Change of plasma cell levels

End point title	Change of plasma cell levels
End point description:	
We analysed CD4+ T cell frequency and absolute numbers by TBNK Kit (BD Bioscience). We found no significant changes in CD4+ T cell frequency after CNI (Figure 4A) or mTORi (Figure 4B) conversion to belatacept compared to BL at M1 (CNI: p=0.799, mTORi: p=0.646), M3 (CNI: p=0.477, mTORi: p=0.859), M6 (CNI: p=0.333, mTORi: p=0.678) and compared to the matched- CNI or mTORi control group. No differences were observed after conversion to belatacept at M3 (p=0.314) and M6 (p=0.859) comparing to pre-conversion or matched CNI control. The CD4+ absolute numbers were not significantly different after conversion to belatacept from mTORi-treated (Figure 4D) at M1, 3, 6 compared to pre-conversion and the matched mTORi controls	
End point type	Primary
End point timeframe:	
from baseline to 6 months	

End point values	CNI conversion	mTORi conversion	CNI control	mTORi control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	11	10	9
Units: µl				
arithmetic mean (standard deviation)				
1 months	577.42 (± 260.61)	0 (± 0)	0 (± 0)	0 (± 0)

End point values	Baseline			
Subject group type	Subject analysis set			
Number of subjects analysed	10			
Units: µl				
arithmetic mean (standard deviation)				
1 months	740.11 (± 319.87)			

Attachments (see zip file)	Frequency and absolute numbers of CD4+ T cells/Frequency

Statistical analyses

Statistical analysis title	Change of the plasma cells levels
Comparison groups	CNI conversion v Baseline
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: change of biomarkers of the humoral and cellular immune system: T-Helper (Th1 and Th2

End point title	change of biomarkers of the humoral and cellular immune system: T-Helper (Th1 and Th2

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	CNI conversion	mTORi conversion	CNI control	mTORi control
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	11	10	9
Units: Cell/µl				
arithmetic mean (full range (min-max))				
Baseline	70 (17 to 105)	50 (25 to 58)	264 (228 to 723)	236 (137 to 519)
Month 12	25 (10 to 88)	29 (15 to 31)	299 (200 to 529)	153 (61 to 241)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: overall trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups	
Reporting group title	CNI_control-group
Reporting group description: CNI_control patients were matched by identical baseline immunosuppression, age (+/- 10 years), gender, renal function (+/- 1.5mg/dl creatinine) and time post-transplant (+/- 10 years) Controls were investigated at 3 time points over a 6-month period with a careful documentation of clinical follow-up.	
Reporting group title	CNI-to-belatacept
Reporting group description: Renal transplantation patients were converted because of clinical reasons in context of CNI-related toxicity or intolerance with a clinical indication of conversion to CNI-free therapy with belatacept.	
Reporting group title	mTORi_control group
Reporting group description: mTORi_control patients were matched by identical baseline immunosuppression, age (+/- 10 years), gender, renal function (+/- 1.5mg/dl creatinine) and time post-transplant (+/- 10 years) Controls were investigated at 3 time points over a 6-month period with a careful documentation of clinical follow-up.	
Reporting group title	mTORi-to-belatacept
Reporting group description: Renal transplantation patients were converted because of clinical reasons in context of mTORi-related toxicity or intolerance with a clinical indication of conversion to mTORi-free therapy with belatacept.	

Serious adverse events	CNI_control-group	CNI-to-belatacept	mTORi_control group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	6 / 10 (60.00%)	6 / 9 (66.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoma of kidney			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
middle hand bone fracture			

subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fracture wrist. Re			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Claudicatio re			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAVK (periphere Arterien.. Aterioslerose)			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronay aterioslerosos			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
edema			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	3 / 9 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aneurysma spurium (re femoral)			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

myocardinfarct and death			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
syncope			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
virale panureitis, left			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
gastroenteritis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bloody stool			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
constipation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
erysipel			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
acute renal failure			

subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
akute TX failure			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
detcorntion of graft function			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
blockade brachialis re.	Additional description: (suspicion)		
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia (atypical)			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal infect			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VHF			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UTI			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Phlegmone Dig II (re hand)			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
acute gout attack			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	mTORi-to-belatacept		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoma of kidney			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
middle hand bone fracture			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
fracture wrist. Re			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Claudicatio re			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
PAVK (periphere Arterien.. Ateriosklerose)			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronay ateriosklerosos			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
edema			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Aneurysma spurium (re femoral)			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
myocardinfarct and death			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
syncope			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
virale panureitis, left			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
gastroenteritis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
bloody stool			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
constipation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
erysipel			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
acute renal failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
akute TX failure			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
detcorntion of graft function			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
blockade brachialis re.	Additional description: (suspicion)		

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia (atypical)			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
gastrointestinal infect			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VHF			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
UTI			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Phlegmone Dig II (re hand)			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
acute gout attack			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	CNI_control-group	CNI-to-belatacept	mTORi_control group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 11 (81.82%)	10 / 10 (100.00%)	6 / 9 (66.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamos cellcarcinom in situ			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Vascular disorders			
arterial hypertension (Worsening)			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Edema			
subjects affected / exposed	1 / 11 (9.09%)	5 / 10 (50.00%)	0 / 9 (0.00%)
occurrences (all)	2	7	0
Surgical and medical procedures			
Verrucas on foot			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
common cold			
subjects affected / exposed	4 / 11 (36.36%)	2 / 10 (20.00%)	2 / 9 (22.22%)
occurrences (all)	4	3	2
cough			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
dizziness			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
nausea			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
night sweat			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			

swelling of testicle (left) Hoden			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
respiartory infection, upper airway			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Investigations			
Vit D deficiency			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GGT increase			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
lack of Vit B1			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PSA increasing (suspected)			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
thrombopenia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
weight increase			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
wound (footpad)			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
VHF			

subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
lumbago			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
hyperuricemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
hypocalcemia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
PAVK			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
sudden deafness			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
tinitus, left			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
conjunctivitis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
hyosphagma eye left			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
cataract			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Diarrhoe			
subjects affected / exposed	1 / 11 (9.09%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
abdominal pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
bloody stool			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
stomach pain			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
excanthem			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
exzision nävus			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Itching			
subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
pyoderma face skin			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
acne dermatitis (worsening)			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
acne pustulara			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Alopezia			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
hair loss			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
aggravation proteinuria			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
back pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
heel spurs			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
neck pain			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
aphthae, Oral blood blister			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	1 / 11 (9.09%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
bursitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
denditis left underleg			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
herpes infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Herpes lapiales			

subjects affected / exposed	0 / 11 (0.00%)	2 / 10 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Laryngitis			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Polyposis nasi			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
sinusitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
suspicion of tendonitis left			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
swollen/pain ankle			
subjects affected / exposed	2 / 11 (18.18%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
UTI			
subjects affected / exposed	1 / 11 (9.09%)	2 / 10 (20.00%)	2 / 9 (22.22%)
occurrences (all)	1	3	2
oral trush			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
sore throat			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
swollen left forearm			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
tooth disease			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperkalimie			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

metabolic acidose			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
azidosis			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
hypophosphatemia	Additional description: (<0.5 mmol/l)		
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

Non-serious adverse events	mTORi-to-belatacept		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamos cellcarcinom in situ			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vascular disorders			
arterial hypertension (Worsening)			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Edema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Verrucas on foot			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
common cold			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
cough			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
dizziness			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
nausea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
night sweat			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Reproductive system and breast disorders			
swelling of testicle (left) Hoden			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
respiartory infection, upper airway			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Investigations			
Vit D deficiency			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
GGT increase			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
lack of Vit B1			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
PSA increasing (suspected)			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
thrombopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
weight increase			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
wound (footpad)			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Cardiac disorders			
VHF			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
lumbago			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
hyperuricemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
hypocalcemia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
PAVK			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Ear and labyrinth disorders			
sudden deafness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
tinitus, left			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Eye disorders			

conjunctivitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
hyosphagma eye left subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
cataract subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Gastrointestinal disorders Diarrhoe subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
abdominal pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
bloody stool subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
stomach pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1		
Skin and subcutaneous tissue disorders excanthem subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
exzision nävus subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Itching subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
pyoderma face skin subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
acne dermatitis (worsening)			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
acne pustulara			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Alopezia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
hair loss			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
aggravation proteinuria			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
back pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
heel spurs			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
neck pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infections and infestations			
aphthae, Oral blood blister			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
bursitis			

subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	2			
denditis left underleg				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
herpes infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
Herpes lapiales				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Laryngitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
Polyposis nasi				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
sinusitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
suspicion of tendonitis left				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
swollen/pain ankle				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences (all)	0			
UTI				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences (all)	3			
oral trush				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
sore throat				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences (all)	1			
swollen left forearm				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
tooth disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperkalimie			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
metabolic acidose			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
azidosis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
hypophosphatemia	Additional description: (<0.5 mmol/l)		
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

-limited data available in the literature to date
-data would have to be validated with higher numbers of patients (for power calculation)
-extention with analyses of cytokine production or proliferation capacity of different cell types

Notes: