



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 be recorded 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, comparable age (+/- 10Y), transplant. 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 of mTORi 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 | Belatacept |
| 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 of mTORi 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 of mTORi 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.. Ateriosklerose) | | | |
| 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 ateriosklerosos | | | |
| 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 aterosklerosos | | | |
| 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 | | | |
| Skin and subcutaneous tissue disorders | subjects affected / exposed | 0 / 10 (0.00%) | | |
| | occurrences causally related to treatment / all | 0 / 0 | | |
| | deaths causally related to treatment / all | 0 / 0 | | |
| | erysipiel | | | |
| | 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 | | | |
| Musculoskeletal and connective tissue disorders | subjects affected / exposed | 1 / 10 (10.00%) | | |
| | occurrences causally related to treatment / all | 0 / 1 | | |
| | deaths causally related to treatment / all | 0 / 0 | | |
| | 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 occurrences (all) | 0 / 11 (0.00%) 0 | 0 / 10 (0.00%) 0 | 1 / 9 (11.11%) 1 |
| Vascular disorders arterial hypertension (Worsening) subjects affected / exposed occurrences (all) Edema subjects affected / exposed occurrences (all) | 0 / 11 (0.00%) 0 1 / 11 (9.09%) 2 | 1 / 10 (10.00%) 1 5 / 10 (50.00%) 7 | 1 / 9 (11.11%) 1 0 / 9 (0.00%) 0 |
| Surgical and medical procedures Verrucas on foot subjects affected / exposed occurrences (all) | 1 / 11 (9.09%) 1 | 0 / 10 (0.00%) 0 | 0 / 9 (0.00%) 0 |
| General disorders and administration site conditions common cold subjects affected / exposed occurrences (all) cough subjects affected / exposed occurrences (all) dizziness subjects affected / exposed occurrences (all) nausea subjects affected / exposed occurrences (all) night sweat subjects affected / exposed occurrences (all) | 4 / 11 (36.36%) 4 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0 | 2 / 10 (20.00%) 3 1 / 10 (10.00%) 1 1 / 10 (10.00%) 0 0 / 10 (0.00%) 0 0 / 10 (0.00%) 0 | 2 / 9 (22.22%) 2 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 0 / 9 (0.00%) 0 |
| Reproductive system and breast disorders | | | |

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

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

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

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

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