



## Clinical trial results:

### The ONE Study: A Unified Approach to Evaluating Cellular Immunotherapy in Solid Organ Transplantation – Natural regulatory T-cells (nTregs) Trial.

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2013-001294-24  |
| Trial protocol           | DE              |
| Global end of trial date | 18 January 2019 |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 24 June 2021  |
| First version publication date    | 24 June 2021  |
| Summary attachment (see zip file) | Final Study Report Summary for PEI / BfArM (2019-02-01 OneStudy-PEI_Rev final.pdf)<br>Paper BMJ 2020 (bmj.m3734.full.pdf) |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | ONEnTreg13 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02371434 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Charité - Universitätsmedizin Berlin  |
| Sponsor organisation address | Augustenburger Platz 1, Berlin, Germany, 13353  |
| Public contact               | Principal Investigator, Charité - Universitätsmedizin Berlin, +49 30450653 490, petra.reinke@charite.de |
| Scientific contact           | Principal Investigator, Charité - Universitätsmedizin Berlin, +49 30450653 490, petra.reinke@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                       | 18 January 2019 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 18 January 2019 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 18 January 2019 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

The ONE Study aims to explore the feasibility, safety and efficacy of regulatory cell therapies as adjunct immunosuppressive treatments in the context of living-donor renal transplantation. The objective of The ONE Study nTregs Trial is to determine whether administration of nTregs to the recipients of living-donor kidney transplants combined with standard triple immunosuppressive therapy (Prednisolone, Mycophenolate Mofetil and Tacrolimus) is safe and able to polarise the immunological response of the recipient away from graft rejection and towards graft acceptance, allowing a reduction in the doses of pharmacological maintenance immunosuppression.

Protection of trial subjects:

Risk Assessment: The clinical trials in The ONE Study have been designed to reduce the level of foreseeable risk, wherever this is possible. The medical context for The ONE Study has been chosen to minimize the level of risk involved in the Cell Therapy Trials. Living-donor renal transplantation has been selected to provide a relatively low-risk transplant cohort. Patients assigned to undergo kidney transplantation are generally in a stable state prior to transplantation, offering the safest possible context for testing an immunosuppressive agent in solid organ transplantation. The clinical assessment within the ONE Study is performed according to the KDIGO Clinical Practice Guideline and covers all tests recommended there. However, in order to ensure that data collected within this study will be comparable between all patients included, some tests are set to fixed follow-up visits. In addition to the recommended standard assessment, extensive immunomonitoring will be performed within a sub-project called "Immune Monitoring" (IM). Biomarkers collected within the IM Subproject are tailored to monitor the recipient's immune status before and after transplantation. Identical data were collected from the patients included in the reference group (The ONE Study Reference Group). These data are now employed as reference values. Thereby the patient will be closely monitored and potential risks might be identified. Therefore, patient's safety might be increased. In addition to the IM, protocol biopsies are planned as a safety measure. Control biopsies will be performed as follows: • Visit 3 (2 weeks post-Tx) Signs of early subclinical rejection (Optional) • Visit 6 (12 weeks post-Tx) To guide steroid withdrawal (Optional) • Visit 8 (36 weeks post-Tx) To guide MMF withdrawal (Mandatory) • Visit 10 (60 weeks post-Tx) Graft status at the final trial visit (Optional). The decision on optional protocol biopsy is upon the responsible clinician.

Background therapy: -

Evidence for comparator: -

|   |   |
|---|---|
| Actual start date of recruitment                          | 09 March 2015   |
| Long term follow-up planned                               | Yes   |
| Long term follow-up rationale                             | Safety, Efficacy, Ethical reason, Scientific research |
| Long term follow-up duration                              | 5 Years   |
| Independent data monitoring committee (IDMC) involvement? | Yes   |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 17 |
|--------------------------------------|-------------|

|                                    |    |
|------------------------------------|----|
| Worldwide total number of subjects | 17 |
| EEA total number of subjects       | 17 |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| 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)                      | 17 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

February 2015 - October 2016; Germany; Charité Universitätsmedizin Berlin

### Pre-assignment

Screening details:

Living-donor renal transplantation has been selected based on scientific and practical grounds. Patients who require kidney transplantation are considered low-risk transplant recipients. Additionally, the absence of major comorbidities are essential. Live donations allows timely preparation of the cell product.

### Period 1

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

### Arms

|  |                                       |
|--|---------------------------------------|
| Arm title                              | experimental arm                      |
| Arm description: -                     |                                       |
| Arm type                               | Experimental                          |
| Investigational medicinal product name | nTreg                                 |
| Investigational medicinal product code |                                       |
| Other name                             |                                       |
| Pharmaceutical forms                   | Concentrate for solution for infusion |
| Routes of administration               | Intravenous use                       |

Dosage and administration details:

nTreg cells will be infused in an escalating dose of  $0.5 \times 10^6$ ,  $1 \times 10^6$ , and  $3 \times 10^6$  cells/kg body weight in cohorts of three patients each. The product is administered by slow peripheral venous infusion on Day +7 ( $\pm 2$

| Number of subjects in period 1 | experimental arm |
|--------------------------------|------------------|
| Started                        | 17               |
| Completed                      | 11               |
| Not completed                  | 6                |
| Physician decision             | 6                |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                                | overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 17            | 17    |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero  | 0             | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0             | 0     |  |
| Children (2-11 years)                                 | 0             | 0     |  |
| Adolescents (12-17 years)                             | 0             | 0     |  |
| Adults (18-64 years)                                  | 17            | 17    |  |
| From 65-84 years                                      | 0             | 0     |  |
| 85 years and over                                     | 0             | 0     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female  | 6             | 6     |  |
| Male  | 11            | 11    |  |

## End points

### End points reporting groups

|                                |                  |
|--------------------------------|------------------|
| Reporting group title          | experimental arm |
| Reporting group description: - |                  |

### Primary: safety

|                        |                       |
|------------------------|-----------------------|
| End point title        | safety <sup>[1]</sup> |
| End point description: |                       |

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Primary clinical endpoint: incidence of biopsy-confirmed acute rejection (BCAR) within 60 weeks of Transplantation; Primary safety endpoint (nTreg cell Administration): Oversuppression of immune system assessed by incidence of neoplasia & infections

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: It was a Phase I/IIa first-in-human trial with a classical 3+3 design; no statistics are possible

| End point values            | experimental arm |  |  |  |
|-----------------------------|------------------|--|--|--|
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 11               |  |  |  |
| Units: number of events     |                  |  |  |  |
| number (not applicable)     |                  |  |  |  |
| safety                      | 11               |  |  |  |
| efficacy                    | 11               |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

For each subject, AEs should be reported from the time of first study-specific procedure until the final trial visit, or until premature discontinuation of patient participation (whichever occurs sooner).

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 18.0   |

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| <b>Serious adverse events</b>                     | overall trial   |  |  |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 4 / 11 (36.36%) |  |  |
| number of deaths (all causes)                     | 0               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |
| Surgical and medical procedures                   |                 |  |  |
| dislocation of transplant kidney                  |                 |  |  |
| subjects affected / exposed                       | 1 / 11 (9.09%)  |  |  |
| occurrences causally related to treatment / all   | 0 / 1           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |
| Immune system disorders                           |                 |  |  |
| Rejection   |                 |  |  |
| subjects affected / exposed                       | 3 / 11 (27.27%) |  |  |
| occurrences causally related to treatment / all   | 0 / 3           |  |  |
| deaths causally related to treatment / all        | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | overall trial   |  |  |
|---|-----------------|--|--|
| Total subjects affected by non-serious adverse events |                 |  |  |
| subjects affected / exposed                           | 7 / 11 (63.64%) |  |  |
| Vascular disorders                                    |                 |  |  |

|   |                      |  |  |
|---|----------------------|--|--|
| thrombosis dialysis shunt<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 11 (9.09%)<br>1  |  |  |
| Renal and urinary disorders<br>increased creatinine<br>subjects affected / exposed<br>occurrences (all) | 5 / 11 (45.45%)<br>5 |  |  |
| proteinuria<br>subjects affected / exposed<br>occurrences (all)   | 1 / 11 (9.09%)<br>1  |  |  |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### 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.

|                |
|----------------|
| not applicable |
|----------------|

Notes: