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) 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:

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)	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 x 106, 1 x 106, and 3 x 106 cells/kg body weight in cohorts of three patients each. The product is administered by slow peripheral venous infusion on Day +7 (±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 (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)	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[1]

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: -

Serious adverse events	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 %

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

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

not applicable

Notes: