Clinical trial results:
Anti-donor alloreactivity-guided CNI minimization versus unguided standard triple therapy in living-donor kidney transplantation

Summary

EudraCT number	2015-002465-28
Trial protocol	DE
Global end of trial date	05 February 2021

Results information

Result version number	v2 (current)
This version publication date	07 July 2022
First version publication date	18 June 2022
Version creation reason	• Changes to summary attachments Dear Sir or Madam, we would like to exchange the summary report or remove it (ICANMINI Final Study report), as it contains data that should not be published. we would provide them with a new report. Thank you very much!
Summary attachment (see zip file)	ICANMINISummary (ICANMINISummary220531.pdf)

Trial information

Trial identification

Sponsor protocol code	ICANMINI

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LMU Klinikum - Koordinationszentrum Chirurgische Studien - AVT-KliniK
Sponsor organisation address	Marchioninistr. 15, Munich, Germany, 81377
Public contact	KCS Chirurgie, Klinik für Allgemeine-, Viszeral-, und Transplantationschirurgie, Klinikum der Universität München, +49 894400-0, michael.eder@med.uni-muenchen.de
Scientific contact	KCS Chirurgie, Klinik für Allgemeine-, Viszeral-, und Transplantationschirurgie, Klinikum der Universität München, 9440076573 894400-0, michael.eder@med.uni-muenchen.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	31 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 February 2021
Global end of trial reached?	Yes
Global end of trial date	05 February 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of an anti-donor alloreactivity guided CNI minimization on the evolution of renal function

Protection of trial subjects:

In principle, the Safety population should include all patients who had taken at least one dose of the study medication. Yet, patients not treated, not treated for certain or patients with no observation after first intake of study medication were excluded from the safety evaluation. Excluding patients with no observation after the first intake from the safety population serves the purpose of consumer protection, as their exclusion leads to higher percentages of adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 May 2016
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: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

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)	35
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Due to difficulties in study conduct and recruitment, further enhanced by the pandemic situation with COVIUD-19, it was decided to stop recruitment prematurely on 20-APR-2020. Already included patients remained in the follow up until their regular 12 months visit. The study end then occurred with the last patient last visit (LPLV) on 05-FEB-2021.

Pre-assignment

Screening details:

Between 23-May-2016(First Patient First Visit: Pat # 001) and 14-JAN-2020 (Last Patient First Visit: Pat. # 035) a total of 35 patients were included into the study (Table 4).
The first 28 Patients were recruited under the contract with Astellas and the last patient (pat. #28) included 26-Feb-2019 within this contract. Pat 29 (included 19-Mar-2019

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Reference

Arm description:

Unguided standard triple therapy with prolonged-release tacrolimus, EC mycophenolic acid (720 mg b.i.d.) and steroids.
Tacrolimus target trough levels 8-12 ng/ml 0-w4, 8-12 ng/ml w5-w12; 6-8 ng/ml w13-m12

Arm type	unguided
Investigational medicinal product name	tacrolimus
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops
Routes of administration	Oral use

Dosage and administration details:

Tacrolimus target trough levels 8-12 ng/ml 0-w4, 6-8 ng/ml w5-w12; 4-6 ng/ml w13-m12

Arm title	Investigational

Arm description:

Anti-donor alloreactivity-guided CNI minimization with prolonged-release tacrolimus, EC mycophenolic acid (720 mg b.i.d.) and steroids.
Tacrolimus target trough levels 8-12 ng/ml 0-w4, 6-8 ng/ml w5-w12; 4-6 ng/ml w13-m12

Arm type	guided

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Reference	Investigational
Started	14	21
Completed	14	21

Baseline characteristics

Reporting groups	
Reporting group title	Reference
Reporting group description:	
Unguided standard triple therapy with prolonged-release tacrolimus, EC mycophenolic acid (720 mg b.i.d.) and steroids. Tacrolimus target trough levels 8-12 ng/ml 0-w4, 8-12 ng/ml w5-w12; 6-8 ng/ml w13-m12	
Reporting group title	Investigational
Reporting group description:	
Anti-donor alloreactivity-guided CNI minimization with prolonged-release tacrolimus, EC mycophenolic acid (720 mg b.i.d.) and steroids. Tacrolimus target trough levels 8-12 ng/ml 0-w4, 6-8 ng/ml w5-w12; 4-6 ng/ml w13-m12	

Reporting group values	Reference	Investigational	Total
Number of subjects	14	21	35
Age categorical			
Male or female subjects ≥ 18 years of age. Subjects must be recipients of a primary renal transplant from a living unrelated, living related non-human leukocyte antigen identical donor			
Units: Subjects			
only Adults	14	21	35
Gender categorical Units: Subjects			
Female	3	11	14
Male	11	10	21

End points

End points reporting groups

Reporting group title	Reference

Reporting group description:

Unguided standard triple therapy with prolonged-release tacrolimus, EC mycophenolic acid (720 mg b.i.d.) and steroids.
Tacrolimus target trough levels 8-12 ng/ml 0-w4, 8-12 ng/ml w5-w12; 6-8 ng/ml w13-m12

Reporting group title	Investigational

Reporting group description:

Anti-donor alloreactivity-guided CNI minimization with prolonged-release tacrolimus, EC mycophenolic acid (720 mg b.i.d.) and steroids.
Tacrolimus target trough levels 8-12 ng/ml 0-w4, 6-8 ng/ml w5-w12; 4-6 ng/ml w13-m12

Primary: Primary Endpoint

End point title	Primary Endpoint

End point description:

eGFR (MDRD-4) [ml/min/1.73 m2]
IM (immune monitored)
UC (unguided control)
N
21
14
Mean ± SD
52.6±16.9
60.7±12.7
Median (Q1-Q3)
53.9 (43.1-60.4)
58.5 (50.2-66.0)
P=0.1524 (Wilcoxon rank sum test)

End point type	Primary

End point timeframe:

The primary endpoint was defined as eGFR calculated according to the 4 variable MDRD formula at 12 months after transplantation. The result shows a numerically lower eGFR in the immune monitored group but no statistically significant difference. The resul

End point values	Reference	Investigational		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14[1]	21[2]		
Units: 35				
eGFR	14	21		

Notes:

[1] - 60,7

[2] - 52

Statistical analyses

Statistical analysis title	Primary Efficacy Criterion

Statistical analysis description:

Among various measures of renal function, the MDRD-4 formula has been selected for the primary endpoint. The parameter to be tested will therefore be the eGFR calculated by the MDRD-4 formula at

12 months after transplantation.
The 4-variable MDRD formula estimates GFR using the four variables: serum creatinine, age, ethnicity, and gender (Version 2000 [10]):
eGFR12M (ml/min/1.73 m2) = 186 * Serum Creatinine (mg/dl)-1.154
* age-0.203
* [1.210 if black]
* [0.742 if female]
(Creatinine level

Comparison groups	Reference v Investigational
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.05 [4]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Cox proportional hazard
Point estimate	95
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	95
Variability estimate	Standard deviation
Dispersion value	0.8881

Notes:

[3] - The statistical analysis was planned after completion of the trial, which is when all patients had completed their follow up phase. This final analysis therefore includes all efficacy and safety data until end of study.
Statistical analysis is based on the final statistical analysis plan, dated 07-FEB-2022 which is available in the appendix.
If p values are calculated in the area of explorative analysis, they should be presented explicitly without referring to hypotheses or a significance leve

[4] - The confirmatory analysis is based on the ITT population. A detailed analysis plan is given in the Study Protocol amendment 1, dated MMM DD, YYYY and elaborated with the final statistical analysis plan dated 30-JAN-2019.
The primary analysis had bee

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First Patient First Visit: 23-May-2016
Last Patient Last Visit: 05-Feb-2021

Adverse event reporting additional description:

A qualified physician associated with the study will be available to assess clinical signs and symptoms that may be indicative of an adverse event. All physical examination findings, vital sign abnormalities, and clinical laboratory abnormalities will be captured as AEs when deemed medically significant by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	unguided
Reporting group description: -	
Reporting group title	IM group

Reporting group description: -

Serious adverse events	unguided	IM group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	unguided	IM group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 11 (27.27%)	8 / 12 (66.67%)	
Blood and lymphatic system disorders			
After bleeding	Additional description: Injury, poisoning and procedural complications 1 18 After bleeding 11/04/18 1 3-Severe Not related to study drug Post procedural haemorrhage UC		
subjects affected / exposed[1]	3 / 3 (100.00%)	8 / 8 (100.00%)	
occurrences (all)	65	146	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: NA

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

None reported