Clinical trial results:
A Multicenter, Open-label, Non-comparative Study of Modigraf® (Tacrolimus Granules) to Evaluate the Pharmacokinetics and Long-term Safety and Efficacy in De Novo Pediatric Allograft Liver and Kidney Transplantation Recipients

Summary

EudraCT number	2022-002350-68
Trial protocol	Outside EU/EEA
Global end of trial date	06 March 2024

Results information

Result version number	v1 (current)
This version publication date	14 September 2024
First version publication date	14 September 2024

Trial information

Trial identification

Sponsor protocol code	F506-CL-0405

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05152628
WHO universal trial number (UTN)	-
Other trial identifiers	Chinese Clinical Trial Registry: CTR20212678

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma China, Inc.
Sponsor organisation address	No.3 Jia 6 Road 10, Shenyang City, China,
Public contact	Clinical Trial Transparency, Astellas Pharma China, Inc., +86 (0)10-85216666, astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Trial Transparency, Astellas Pharma China, Inc., +86 (0)10-85216666, astellas.resultsdisclosure@astellas.com

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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 March 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to determine the pharmacokinetics of tacrolimus following oral administration of Modigraf, after the first oral dose and at steady state in pediatric participants undergoing de novo allograft liver or kidney transplantation.

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of Protected Health Information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 January 2022
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 55
Worldwide total number of subjects	55
EEA total number of subjects	0

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)	14
Children (2-11 years)	30
Adolescents (12-17 years)	11
Adults (18-64 years)	0

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Chinese pediatric participants who had de novo allograft liver or kidney transplantation were enrolled in the study.

Pre-assignment

Screening details:

Participants who met all inclusion criteria and none of the exclusion criteria were enrolled in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Liver transplant

Arm description:

Pediatric participants who underwent de novo allograft liver transplantation received initial daily dose of 0.2 milligram per kilogram (mg/kg) of body weight oral suspension of tacrolimus granules post-operatively for 12 months.

Arm type	Experimental
Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	
Other name	Modigraf
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Participants received oral suspension of tacrolimus granules.

Arm title	Kidney transplant

Arm description:

Pediatric participants who underwent de novo allograft kidney transplantation received initial daily dose of 0.2 mg/kg of body weight oral suspension of tacrolimus granules post-operatively for 12 months.

Arm type	Experimental
Investigational medicinal product name	Tacrolimus
Investigational medicinal product code	
Other name	Modigraf
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Participants received oral suspension of tacrolimus granules.

Number of subjects in period 1	Liver transplant	Kidney transplant
Started	41	14
Completed	33	8
Not completed	8	6
Adverse event, serious fatal	1	-
Consent withdrawn by subject	-	2
Adverse event, non-fatal	5	4
Medicine not sent due to city lockdown	1	-
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Liver transplant
Reporting group description:	
Pediatric participants who underwent de novo allograft liver transplantation received initial daily dose of 0.2 milligram per kilogram (mg/kg) of body weight oral suspension of tacrolimus granules post-operatively for 12 months.	
Reporting group title	Kidney transplant
Reporting group description:	
Pediatric participants who underwent de novo allograft kidney transplantation received initial daily dose of 0.2 mg/kg of body weight oral suspension of tacrolimus granules post-operatively for 12 months.	

Reporting group values	Liver transplant	Kidney transplant	Total
Number of subjects	41	14	55
Age Categorical Units: participants			
Infants and toddlers (28 days-23 months)	14	0	14
Children (2-11 years)	24	6	30
Adolescents (12-17 years)	3	8	11
Gender Categorical Units: participants			
Female	23	3	26
Male	18	11	29
Race Units: Subjects			
Asian	41	14	55

End points

End points reporting groups

Reporting group title	Liver transplant
Reporting group description:	
Pediatric participants who underwent de novo allograft liver transplantation received initial daily dose of 0.2 milligram per kilogram (mg/kg) of body weight oral suspension of tacrolimus granules post-operatively for 12 months.	
Reporting group title	Kidney transplant
Reporting group description:	
Pediatric participants who underwent de novo allograft kidney transplantation received initial daily dose of 0.2 mg/kg of body weight oral suspension of tacrolimus granules post-operatively for 12 months.	

Primary: PK of tacrolimus granules in Whole Blood: AUCtau on Day 7

End point title	PK of tacrolimus granules in Whole Blood: AUCtau on Day 7[1]
End point description:	
AUCtau was recorded from the PK blood samples collected. EPKS population with available data were reported.	
End point type	Primary
End point timeframe:	
Predose, 0.5, 1, 2, 8, 12 hr post dose on day 7	

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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	11		
Units: h*ng/mL				
arithmetic mean (standard deviation)	104 (± 40.0)	121 (± 41.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Pharmacokinetic (PK) of tacrolimus granules in Whole Blood: Area under the curve (AUCtau) on Day 1

End point title	Pharmacokinetic (PK) of tacrolimus granules in Whole Blood: Area under the curve (AUCtau) on Day 1[2]
End point description:	
AUCtau was recorded from the PK blood samples collected. The Extended Pharmacokinetic Set (EPKS) consisted of all participants from the Safety Analysis Set (SAF) population for whom sufficient plasma concentration data was available to facilitate derivation of at least one pharmacokinetic parameter. SAF population consisted of all participants who took at least one dose of study drug. EPKS population with available data were reported.	
End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hours (hr) post dose on day 1

Notes:

[2] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	13		
Units: hour*nanograms per milliliter (h*ng/mL)				
arithmetic mean (standard deviation)	124 (± 72.1)	107 (± 40.9)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Cmax on Day 7

End point title	PK of tacrolimus granules in Whole Blood: Cmax on Day 7[3]

End point description:

Cmax was recorded from the PK blood samples collected. Cmax is maximum concentration observed in an observation period. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 7

Notes:

[3] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	12		
Units: ng/mL				
arithmetic mean (standard deviation)	16.1 (± 8.52)	24.6 (± 8.72)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Maximum Concentration (Cmax) on Day 1

End point title	PK of tacrolimus granules in Whole Blood: Maximum Concentration (Cmax) on Day 1[4]

End point description:

Cmax was recorded from the PK blood samples collected. Cmax is maximum concentration observed in

an observation period. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 1

Notes:

[4] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	13		
Units: ng/mL				
arithmetic mean (standard deviation)	16.9 (± 9.72)	19.2 (± 7.43)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Time of Maximum Concentration (Tmax) on Day 1

End point title	PK of tacrolimus granules in Whole Blood: Time of Maximum Concentration (Tmax) on Day 1[5]

End point description:

Tmax was recorded from the PK blood samples collected. Tmax is time of maximum concentration in an observation period. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 1

Notes:

[5] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	13		
Units: hr				
median (full range (min-max))	1.97 (0.533 to 8.10)	1.97 (0.467 to 2.03)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Tmax on Day 7

End point title	PK of tacrolimus granules in Whole Blood: Tmax on Day 7[6]

End point description:

Tmax was recorded from the PK blood samples collected. Tmax is time of maximum concentration in an observation period. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 7

Notes:

[6] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	12		
Units: hr				
median (full range (min-max))	1.93 (0.433 to 7.87)	0.983 (0.433 to 2.00)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Trough blood concentration (Ctrough) on Day 1

End point title	PK of tacrolimus granules in Whole Blood: Trough blood concentration (Ctrough) on Day 1[7]

End point description:

Ctrough was recorded from the PK blood samples collected. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Pre-dose on day 1

Notes:

[7] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	13		
Units: ng/mL				
arithmetic mean (standard deviation)	6.95 (± 5.30)	4.03 (± 2.17)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Ctrough on Day 7

End point title	PK of tacrolimus granules in Whole Blood: Ctrough on Day 7[8]

End point description:

Ctrough was recorded from the PK blood samples collected. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Pre-dose on day 7

Notes:

[8] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	12		
Units: ng/mL				
arithmetic mean (standard deviation)	5.25 (± 2.00)	5.16 (± 2.19)		

Statistical analyses

No statistical analyses for this end point

Primary: Correlation between Ctrough and AUCtau of tacrolimus granules in Whole Blood on Day 1

End point title	Correlation between Ctrough and AUCtau of tacrolimus granules in Whole Blood on Day 1[9]

End point description:

The correlation between Ctrough and AUCtau was assessed by Pearson’s coefficient at each sample time by visit. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 1

Notes:

[9] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	13		
Units: Pearson Correlation Coefficient				
number (not applicable)	0.90	0.83		

Statistical analyses

No statistical analyses for this end point

Primary: Correlation between Ctrough and AUCtau of tacrolimus granules in Whole Blood on Day 7

End point title	Correlation between Ctrough and AUCtau of tacrolimus granules in Whole Blood on Day 7[10]

End point description:

The correlation between Ctrough and AUCtau was assessed by Pearson's coefficient at each sample time by visit. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 7

Notes:

[10] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	11		
Units: Pearson Correlation Coefficient				
number (not applicable)	0.83	0.90		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Dose-normalized AUCtau on Day 1

End point title	PK of tacrolimus granules in Whole Blood: Dose-normalized AUCtau on Day 1[11]

End point description:

Dose-normalized AUCtau was AUCtau normalized with the dose just prior to blood sampling. Dose-normalized AUCtau was calculated as AUCtau/dose. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 1

Notes:

[11] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	13		
Units: h*ng/mL/mg				
arithmetic mean (standard deviation)	83.5 (± 46.6)	29.7 (± 14.9)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Dose-normalized AUCtau on Day 7

End point title	PK of tacrolimus granules in Whole Blood: Dose-normalized AUCtau on Day 7[12]

End point description:

Dose-normalized AUCtau was AUCtau normalized with the dose just prior to blood sampling. Dose-normalized AUCtau was calculated as AUCtau/dose. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 7

Notes:

[12] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	11		
Units: h*ng/mL/mg				
arithmetic mean (standard deviation)	129 (± 78.9)	32.1 (± 15.0)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Dose-normalized Ctrough on Day 1

End point title	PK of tacrolimus granules in Whole Blood: Dose-normalized Ctrough on Day 1[13]

End point description:

Ctrough normalized with the dose just prior to blood sampling. Dose-normalized Ctrough was calculated as Ctrough/dose. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 1

Notes:

[13] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	13		
Units: ng/mL/mg				
arithmetic mean (standard deviation)	4.30 (± 2.82)	1.09 (± 0.687)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Dose-normalized Cmax on Day 7

End point title	PK of tacrolimus granules in Whole Blood: Dose-normalized Cmax on Day 7[14]

End point description:

Dose-normalized Cmax was Cmax normalized with the dose just prior to blood sampling. Dose-normalized Cmax was calculated as Cmax/dose. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 7

Notes:

[14] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	12		
Units: ng/mL/mg				
arithmetic mean (standard deviation)	19.4 (± 12.6)	6.91 (± 3.44)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Dose-normalized Cmax at Day 1

End point title	PK of tacrolimus granules in Whole Blood: Dose-normalized Cmax at Day 1[15]

End point description:

Dose-normalized Cmax was Cmax normalized with the dose just prior to blood sampling. Dose-normalized Cmax was calculated as Cmax/dose. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 1

Notes:

[15] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	13		
Units: ng/mL/mg				
arithmetic mean (standard deviation)	12.1 (± 7.50)	5.59 (± 2.97)		

Statistical analyses

No statistical analyses for this end point

Primary: PK of tacrolimus granules in Whole Blood: Dose-normalized Ctrough on Day 7

End point title	PK of tacrolimus granules in Whole Blood: Dose-normalized Ctrough on Day 7[16]

End point description:

Ctrough normalized with the dose just prior to blood sampling. Dose-normalized Ctrough was calculated as Ctrough/dose. EPKS population with available data were reported.

End point type	Primary

End point timeframe:

Predose, 0.5, 1, 2, 8, 12 hr post dose on day 7

Notes:

[16] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	12		
Units: ng/mL/mg				
arithmetic mean (standard deviation)	6.52 (± 3.79)	1.49 (± 0.946)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Acute Rejection (AR)

End point title	Percentage of Participants With Acute Rejection (AR)[17]

End point description:

AR is an immune response against the donor graft that causes tissue impairment and potential failure. The criteria for rejection was performed by the local histopathologist following the "Histological Grading of Liver Biopsies for Rejection", the "Banff diagnostic categories for renal allograft biopsies". The Full Analysis Set (FAS) consisted of all participants who took at least one dose of study drug.

End point type	Primary

End point timeframe:

From first dose to month 12

Notes:

[17] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	14		
Units: Percentage of participants				
number (confidence interval 95%)	17.1 (7.2 to 32.1)	0 (0.0 to 23.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Biopsy-Proven Acute Rejections (BPAR)

End point title	Percentage of Participants With Biopsy-Proven Acute Rejections (BPAR)[18]

End point description:

AR is an immune response against the donor graft that causes tissue impairment and potential failure. The criteria for rejection was performed by the local histopathologist following the "Histological Grading of Liver Biopsies for Rejection", the "Banff diagnostic categories for renal allograft biopsies". A BPAR episode was defined as any AR episode confirmed by biopsy. FAS population.

End point type	Primary

End point timeframe:

From first dose to month 12

Notes:

[18] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	14		
Units: Percentage of participants				
number (confidence interval 95%)	9.8 (2.7 to 23.1)	0 (0.0 to 23.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Clinically Suspected Rejection

End point title	Percentage of Participants With Clinically Suspected

End point description:

AR is an immune response against the donor graft that causes tissue impairment and potential failure. The criteria for rejection was performed by the local histopathologist following the "Histological Grading

of Liver Biopsies for Rejection", the "Banff diagnostic categories for renal allograft biopsies". An AR was clinically suspected in participants who experienced an increase in serum creatinine, after the exclusion of other causes of graft dysfunction (generally with biopsy). FAS population.

End point type	Primary

End point timeframe:

From first dose to month 12

Notes:

[19] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	14		
Units: Percentage of participants				
number (confidence interval 95%)	7.3 (1.5 to 19.9)	0 (0.0 to 23.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants who Died

End point title	Number of Participants who Died[20]

End point description:

Number of participant who died was recorded during 12 months' post-transplant; any cause of death was taken into account. FAS population.

End point type	Primary

End point timeframe:

From first dose to month 12

Notes:

[20] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	14		
Units: participants				
number (not applicable)				
Death by Acute liver failure	1	0		
Kidney tumor worsened; died of respiratory failure	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Graft Failure

End point title	Number of Participants with Graft Failure[21]

End point description:

Graft failure was defined as graft dysfunction, including re-transplantation, graft loss or death, during the study period. A graft dysfunction to permanent dialysis in kidney transplantation was also considered as graft failure. FAS population.

End point type	Primary

End point timeframe:

From first dose to month 12

Notes:

[21] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	14		
Units: participants				
number (not applicable)	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Dose Adjustments Throughout the Study Period

End point title	Number of Dose Adjustments Throughout the Study Period[22]

End point description:

The dose adjustments required for the organ transplant were reported. SAF population.

End point type	Primary

End point timeframe:

From first dose to month 12

Notes:

[22] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	14		
Units: dose adjustments				
arithmetic mean (standard deviation)	9.0 (± 5.0)	13.8 (± 5.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Treatment Emergent Adverse Events (AEs)

End point title	Number of Participants with Treatment Emergent Adverse Events (AEs)[23]

End point description:

An AE is defined as any untoward medical occurrence in a participant given a study drug not necessarily linked to this treatment. An AE can be any unfavorable and unintended sign (e.g., abnormal laboratory finding; abnormal laboratory test result or other safety assessment, symptom, or disease temporally associated with the use of study drug whether or not considered related to the study drug. Treatment emergent adverse event (TEAE) is defined as AE observed after administering the study drug. SAF population.

End point type	Primary

End point timeframe:

From first dose to month 12

Notes:

[23] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	14		
Units: participants				
number (not applicable)	36	14		

Statistical analyses

No statistical analyses for this end point

Primary: Whole Blood Trough Levels of Tacrolimus

End point title	Whole Blood Trough Levels of Tacrolimus[24]

End point description:

Tacrolimus whole blood trough levels were routinely monitored from whole blood samples, using a local assay method, for example EMITÒ or Liquid-Chromatography-Mass-Spectrometry-Mass-Spectrometry (LC-MS-MS) in the local laboratories. Mean trough levels of tacrolimus from day 1 through month 12 has been reported. SAF population.

End point type	Primary

End point timeframe:

From day 1 through month 12 (predose)

Notes:

[24] - 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: Per protocol, statistical analysis was not planned for this endpoint.

End point values	Liver transplant	Kidney transplant		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	14		
Units: ng/mL				
arithmetic mean (standard deviation)	7.80 (± 2.21)	8.13 (± 1.45)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose to month 12	
Adverse event reporting additional description:	
SAF population	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	v26.0

Reporting groups	
Reporting group title	Kidney Transplant
Reporting group description:	
Pediatric participants who underwent de novo allograft kidney transplantation received initial daily dose of 0.2 mg/kg of body weight oral suspension of tacrolimus granules post-operatively for 12 months.	
Reporting group title	Liver Transplant
Reporting group description:	
Pediatric participants who underwent de novo allograft liver transplantation received initial daily dose of 0.2 mg/kg of body weight oral suspension of tacrolimus granules post-operatively for 12 months.	

Serious adverse events	Kidney Transplant	Liver Transplant	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 14 (64.29%)	16 / 41 (39.02%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Investigations			
Glucose urine present			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Post transplant lymphoproliferative disorder			

subjects affected / exposed	1 / 14 (7.14%)	3 / 41 (7.32%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Injury, poisoning and procedural complications			
Complications of transplanted kidney			
subjects affected / exposed	3 / 14 (21.43%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Embolism arterial			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphorrhoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Biliary fistula			
subjects affected / exposed	0 / 14 (0.00%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein stenosis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic artery embolism			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus hepatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis adenovirus			

subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	3 / 41 (7.32%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 14 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	2 / 41 (4.88%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Kidney Transplant	Liver Transplant	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	33 / 41 (80.49%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Post transplant lymphoproliferative disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Jugular vein thrombosis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Lymphorrhoea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Puncture site haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	3 / 14 (21.43%)	14 / 41 (34.15%)	
occurrences (all)	6	22	
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 14 (7.14%)	7 / 41 (17.07%)	
occurrences (all)	1	9	

Epistaxis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Psychiatric disorders			
Mood altered			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Enuresis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Investigations			
BK polyomavirus test positive			
subjects affected / exposed	3 / 14 (21.43%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Bacterial test positive			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Blood urea increased			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	4	0	
Blood urine present			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Carbon dioxide combining power decreased			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Fungal test positive			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Glucose urine present			

subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	4	0	
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Lymphocyte count increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Neutrophil count increased			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Platelet count increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Protein urine present			
subjects affected / exposed	6 / 14 (42.86%)	0 / 41 (0.00%)	
occurrences (all)	7	0	
Red blood cells urine positive			
subjects affected / exposed	4 / 14 (28.57%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
SARS-CoV-2 test positive			
subjects affected / exposed	2 / 14 (14.29%)	15 / 41 (36.59%)	
occurrences (all)	2	17	
Transaminases increased			
subjects affected / exposed	5 / 14 (35.71%)	0 / 41 (0.00%)	
occurrences (all)	10	0	
Urinary occult blood positive			
subjects affected / exposed	5 / 14 (35.71%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
Urine leukocyte esterase positive			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
White blood cell count increased			

subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Arteriovenous fistula occlusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Complications of transplanted kidney			
subjects affected / exposed	5 / 14 (35.71%)	0 / 41 (0.00%)	
occurrences (all)	7	0	
Delayed graft function			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Ectopic atrial rhythm			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Right atrial enlargement			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Granulocytopenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Agranulocytosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	

Leukopenia			
subjects affected / exposed	5 / 14 (35.71%)	0 / 41 (0.00%)	
occurrences (all)	8	0	
Lymphopenia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
Neutropenia			
subjects affected / exposed	3 / 14 (21.43%)	0 / 41 (0.00%)	
occurrences (all)	8	0	
Splenomegaly			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 14 (0.00%)	4 / 41 (9.76%)	
occurrences (all)	0	4	
Aphthous ulcer			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Abdominal pain			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Abdominal discomfort			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	9 / 14 (64.29%)	11 / 41 (26.83%)	
occurrences (all)	18	26	
Nausea			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Vomiting			

subjects affected / exposed	4 / 14 (28.57%)	4 / 41 (9.76%)	
occurrences (all)	4	4	
Constipation			
subjects affected / exposed	3 / 14 (21.43%)	2 / 41 (4.88%)	
occurrences (all)	4	4	
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Hepatic steatosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Hepatic function abnormal			
subjects affected / exposed	2 / 14 (14.29%)	10 / 41 (24.39%)	
occurrences (all)	2	13	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Dermatitis			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Eczema			
subjects affected / exposed	0 / 14 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	3	
Prurigo			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Albuminuria			

subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	4 / 14 (28.57%)	0 / 41 (0.00%)	
occurrences (all)	4	0	
Upper respiratory tract infection			
subjects affected / exposed	5 / 14 (35.71%)	13 / 41 (31.71%)	
occurrences (all)	10	18	
Respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	3 / 41 (7.32%)	
occurrences (all)	1	4	
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	4	
Mycoplasma infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 41 (2.44%)	
occurrences (all)	1	1	
Folliculitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Febrile infection			
subjects affected / exposed	0 / 14 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	5	
Epstein-Barr virus infection			
subjects affected / exposed	0 / 14 (0.00%)	22 / 41 (53.66%)	
occurrences (all)	0	25	
Cytomegalovirus infection			
subjects affected / exposed	4 / 14 (28.57%)	11 / 41 (26.83%)	
occurrences (all)	4	17	

Cytomegalovirus hepatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Bacterial infection			
subjects affected / exposed	0 / 14 (0.00%)	3 / 41 (7.32%)	
occurrences (all)	0	3	
Anal abscess			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	3 / 14 (21.43%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
Alkalosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Hypercalcaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
Hypercholesterolaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Hyperphosphataemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Hyperglycaemia			
subjects affected / exposed	4 / 14 (28.57%)	0 / 41 (0.00%)	
occurrences (all)	8	0	
Hyperkalaemia			
subjects affected / exposed	5 / 14 (35.71%)	0 / 41 (0.00%)	
occurrences (all)	16	0	
Hyperlipidaemia			

subjects affected / exposed	10 / 14 (71.43%)	0 / 41 (0.00%)	
occurrences (all)	17	0	
Hypo HDL cholesterolaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			
subjects affected / exposed	11 / 14 (78.57%)	0 / 41 (0.00%)	
occurrences (all)	22	0	
Hypertriglyceridaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Hypokalaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Hypomagnesaemia			
subjects affected / exposed	7 / 14 (50.00%)	1 / 41 (2.44%)	
occurrences (all)	9	1	
Hypocalcaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Hypochloraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Metabolic acidosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
Hyponatraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Hypophosphataemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 41 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2020	The study design was updated to ensure participants can continue Modigraf treatment before commercial drug available in China, these participants will continue treatment on study for 12 months. The safety and efficacy evaluation will be continued. A pooled analysis of F506-CL-0405 and F506-CL-0406 is planned to have efficacy and safety data of about 100 participants for analyses. An inclusion criterion was added as advised by authority. The exclusion criteria were updated based on the advice from Key Opinion Leaders (KOLs). The proportion of bilateral kidney transplantation was very small, and there was higher risk of post-operative complications. Same for the participants with a low body weight and severe primary diseases. The initial daily dose was updated as advised by KOLs. The safety endpoints were added as the study was aiming to accumulate safety and efficacy data from the very first Chinese pediatric patients who receive Modigraf. Flow chart and Schedule of assessments and consistency was maintained throughout the protocol as the study was extended to 12 months. Other administrative changes were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported