Clinical trial results:
A Long-term, Open-label, Non-comparative Study to Evaluate the Safety and Efficacy of a Modigraf® based Immunosuppression Regimen in De Novo Pediatric Allograft Liver and Kidney Transplantation Recipients

Summary

EudraCT number	2022-002351-19
Trial protocol	Outside EU/EEA
Global end of trial date	14 March 2024

Results information

Result version number	v1 (current)
This version publication date	25 September 2024
First version publication date	25 September 2024

Trial information

Trial identification

Sponsor protocol code	F506-CL-0406

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05153915
WHO universal trial number (UTN)	-
Other trial identifiers	Chinese Clinical Trial Registry: CTR20212679

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma China, Inc.
Sponsor organisation address	No.3 Jia 6 Road 10, Shenyang City, China,
Public contact	Astellas Pharma China, Inc., Clinical Trial Transparency, +86 (0)10-85216666, astellas.resultsdisclosure@astellas.com
Scientific contact	Astellas Pharma China, Inc., Clinical Trial Transparency, +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	14 March 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 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 observe the safety and efficacy of Modigraf in de novo pediatric allograft liver and kidney transplantation recipients.

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	30 December 2021
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: 56
Worldwide total number of subjects	56
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)	13
Children (2-11 years)	22
Adolescents (12-17 years)	21
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 0.15 to 0.3 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 0.15 to 0.3 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	20	36
Safety Analysis (SAF)	20	35
Completed	18	28
Not completed	2	8
Consent withdrawn by subject	1	3
Adverse event, non-fatal	1	4
Enrolled, but not treated	-	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 0.15 to 0.3 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 0.15 to 0.3 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	20	36	56
Age Categorical Units: participants			
Infants and toddlers (28 days-23 months)	13	0	13
Children (2-11 years)	6	16	22
Adolescents (12-17 years)	1	20	21
Gender Categorical Units: participants			
Female	8	12	20
Male	12	24	36
Race Units: Subjects			
Asian	20	36	56

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 0.15 to 0.3 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 0.15 to 0.3 mg/kg of body weight oral suspension of tacrolimus granules post-operatively for 12 months.	

Primary: Percentage of Participants With Acute Rejection (AR)

End point title	Percentage of Participants With Acute Rejection (AR)[1]
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:

[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	20	35		
Units: Percentage of participants				
number (confidence interval 95%)	20.0 (5.7 to 43.7)	5.7 (0.7 to 19.2)		

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)[2]
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:

[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	20	35		
Units: Percentage of participants				
number (confidence interval 95%)	15.0 (3.2 to 37.9)	2.9 (0.1 to 14.9)		

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:

[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	20	35		
Units: Percentage of participants				
number (confidence interval 95%)	5.0 (0.1 to 24.9)	2.9 (0.1 to 14.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants who Died

End point title	Number of Participants who Died[4]

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:

[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	20	35		
Units: Participants				
number (not applicable)	0	0		

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[5]

End point description:

The dose adjustments required for the organ transplant were reported. The Safety Analysis Set (SAF) consisted of all participants who took at least one dose of study drug. SAF population with available data were reported.

End point type	Primary

End point timeframe:

From first dose to month 12

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	19	33		
Units: dose adjustments				
arithmetic mean (standard deviation)	11.6 (± 5.2)	13.3 (± 5.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participant with Graft Failure

End point title	Number of Participant with Graft Failure[6]

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 with available data were reported.

End point type	Primary

End point timeframe:

From first dose to month 12

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	20	35		
Units: Participants				
number (not applicable)	0	2		

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)[7]

End point description:

An AE is defined as any untoward medical occurrence in a participant given an 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:

[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	20	35		
Units: Participants				
number (not applicable)	18	35		

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[8]

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 month 1 through month 12 has been reported. SAF population.

End point type	Primary

End point timeframe:

From month 1 through month 12 (predose)

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	20	35		
Units: nanograms per milliliter (ng/mL)				
arithmetic mean (standard deviation)	7.09 (± 2.28)	8.26 (± 1.47)		

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 0.15 to 0.3 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 0.15 to 0.3 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	19 / 35 (54.29%)	10 / 20 (50.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Donor specific antibody present			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (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	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Delayed graft function			

subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complications of transplanted kidney			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complications of transplant surgery			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (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			
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Impaired healing			

subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingivitis ulcerative			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 35 (0.00%)	2 / 20 (10.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venoocclusive liver disease			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Renal vein thrombosis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery thrombosis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proteinuria			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoporosis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (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 / 35 (0.00%)	1 / 20 (5.00%)	
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	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory tract infection			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 35 (2.86%)	4 / 20 (20.00%)	
occurrences causally related to treatment / all	0 / 1	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (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 / 35 (0.00%)	3 / 20 (15.00%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	2 / 35 (5.71%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 35 (2.86%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
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	35 / 35 (100.00%)	17 / 20 (85.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Post transplant lymphoproliferative disorder			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 35 (8.57%)	7 / 20 (35.00%)	
occurrences (all)	4	19	
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pneumothorax			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hypocapnia			

subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Atelectasis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Investigations			
BK polyomavirus test positive			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	5	0	
Blood albumin decreased			
subjects affected / exposed	1 / 35 (2.86%)	1 / 20 (5.00%)	
occurrences (all)	2	2	
Blood bilirubin increased			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Blood urea increased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Hepatic enzyme increased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Lymphocyte count decreased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	7	0	
Lymphocyte count increased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Mycoplasma test positive			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	5	0	

Neutrophil count increased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Platelet count decreased			
subjects affected / exposed	3 / 35 (8.57%)	1 / 20 (5.00%)	
occurrences (all)	5	1	
Procalcitonin increased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Protein urine present			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	4	0	
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 35 (2.86%)	4 / 20 (20.00%)	
occurrences (all)	1	4	
Transaminases increased			
subjects affected / exposed	5 / 35 (14.29%)	0 / 20 (0.00%)	
occurrences (all)	6	0	
Urine leukocyte esterase positive			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	6	0	
White blood cell count decreased			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	7	0	
White blood cell count increased			
subjects affected / exposed	1 / 35 (2.86%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			

Hypoglobulinaemia			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Anaemia			
subjects affected / exposed	4 / 35 (11.43%)	5 / 20 (25.00%)	
occurrences (all)	4	6	
Thrombocytopenia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Neutropenia			
subjects affected / exposed	5 / 35 (14.29%)	0 / 20 (0.00%)	
occurrences (all)	5	0	
Leukopenia			
subjects affected / exposed	14 / 35 (40.00%)	0 / 20 (0.00%)	
occurrences (all)	21	0	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 35 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Abdominal pain			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Constipation			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	7 / 35 (20.00%)	5 / 20 (25.00%)	
occurrences (all)	8	6	
Vomiting			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	6	0	
Mouth ulceration			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Intestinal obstruction			

subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Hepatobiliary disorders			
Liver injury			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Hepatobiliary disease			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hepatic function abnormal			
subjects affected / exposed	2 / 35 (5.71%)	4 / 20 (20.00%)	
occurrences (all)	2	8	
Hepatic artery thrombosis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Dermatitis allergic			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Eczema asteatotic			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	4 / 35 (11.43%)	0 / 20 (0.00%)	
occurrences (all)	4	0	
Proteinuria			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	4	0	
Endocrine disorders			

Hyperparathyroidism			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Bacterial infection			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
BK virus infection			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 35 (2.86%)	7 / 20 (35.00%)	
occurrences (all)	1	9	
Epstein-Barr virus infection			
subjects affected / exposed	1 / 35 (2.86%)	10 / 20 (50.00%)	
occurrences (all)	1	16	
Exanthema subitum			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	2 / 35 (5.71%)	2 / 20 (10.00%)	
occurrences (all)	3	2	
Pneumonia			
subjects affected / exposed	1 / 35 (2.86%)	4 / 20 (20.00%)	
occurrences (all)	1	4	
Post procedural infection			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Sinusitis			

subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Tonsillitis			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	7 / 35 (20.00%)	2 / 20 (10.00%)	
occurrences (all)	12	3	
Urinary tract infection			
subjects affected / exposed	14 / 35 (40.00%)	0 / 20 (0.00%)	
occurrences (all)	14	0	
Metabolism and nutrition disorders			
Hypoproteinaemia			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	5	0	
Hypophosphataemia			
subjects affected / exposed	5 / 35 (14.29%)	0 / 20 (0.00%)	
occurrences (all)	8	0	
Hyponatraemia			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Hypomagnesaemia			
subjects affected / exposed	6 / 35 (17.14%)	1 / 20 (5.00%)	
occurrences (all)	7	1	
Hypokalaemia			
subjects affected / exposed	10 / 35 (28.57%)	0 / 20 (0.00%)	
occurrences (all)	10	0	
Hypoglycaemia			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Hypochloraemia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Hypocalcaemia			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	3	0	

Hyperuricaemia			
subjects affected / exposed	19 / 35 (54.29%)	0 / 20 (0.00%)	
occurrences (all)	31	0	
Hypertriglyceridaemia			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Hyperphosphataemia			
subjects affected / exposed	6 / 35 (17.14%)	0 / 20 (0.00%)	
occurrences (all)	13	0	
Hyperlipidaemia			
subjects affected / exposed	16 / 35 (45.71%)	0 / 20 (0.00%)	
occurrences (all)	19	0	
Hyperkalaemia			
subjects affected / exposed	10 / 35 (28.57%)	0 / 20 (0.00%)	
occurrences (all)	20	0	
Hypercalcaemia			
subjects affected / exposed	3 / 35 (8.57%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Hyperglycaemia			
subjects affected / exposed	8 / 35 (22.86%)	0 / 20 (0.00%)	
occurrences (all)	10	0	
Vitamin D deficiency			
subjects affected / exposed	2 / 35 (5.71%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Metabolic acidosis			
subjects affected / exposed	8 / 35 (22.86%)	0 / 20 (0.00%)	
occurrences (all)	10	0	
Lactose intolerance			
subjects affected / exposed	0 / 35 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 December 2020	The sample size was reduced for acceptable precision. 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 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. Other administrative changes were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported