NOVARTIS

Clinical Trial Results Website

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Iscalimab

Trial Indication(s)

Kidney Transplantation

Protocol Number

CCFZ533A2201

Protocol Title

A partially-blinded, active-controlled, multicenter, randomized study evaluating efficacy, safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) of an anti-CD40 monoclonal antibody, CFZ533, in de novo and maintenance kidney transplant recipients (CIRRUS I)

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase II

Study Start/End Dates

Study Start Date: November 28, 2018 (Actual)
Primary Completion Date: October 29, 2021 (Actual)
Study Completion Date: October 29, 2021 (Actual)

Reason for Termination (If applicable)

Study stopped due to lack of efficacy.

Study Design/Methodology

Study CCFZ533A2201 was a randomized, active-controlled, partially-blinded for the initial 12 months of treatment, multicenter, dose range finding study to evaluate the efficacy, safety, tolerability, PK and PD of CFZ533 in 2 different cohorts: adult *de novo* kidney transplant recipients and maintenance kidney transplant population (6-24 months post-transplant). Randomized patients in both cohorts were to remain on CFZ533 treatment until the planned Month 59.5 visit and undergo Study Completion evaluations at the Month 60 visit. However, the study was terminated prematurely after the interim analysis.

The interim analysis was performed on N=213 in Cohort 1 and N=65 in Cohort 2 who completed Month 12 or discontinued the study early.

Centers

74 centers in 20 countries: Australia(3), Norway(1), Sweden(2), France(8), Netherlands(3), Czech Republic(1), United States(15), United Kingdom(3), Germany(8), Spain(6), Belgium(1), Hungary(2), Japan(9), Argentina(3), Italy(2), Brazil(3), Korea, Republic of(1), Latvia(1), Switzerland(1), Canada(1)

Objectives:

Primary Objectives:

Cohort 1:

To demonstrate that CFZ533 600 mg and/or 300 mg bi-weekly (Q2W) subcutaneous (SC) are non-inferior to a Tacrolimus (TAC)-based regimen with respect to the proportion of patients who experience composite efficacy failure event (biopsy proven acute rejection (BPAR), graft loss, or death) over 12 months post-transplantation

Cohort 2:

To demonstrate that CFZ533 450 mg bi-weekly (Q2W) subcutaneous (SC) is non-inferior to a TAC-based regimen with respect to the proportion of patients who experience composite efficacy failure event (biopsy proven acute rejection (BPAR), graft loss, or death) over 12 months post-conversion

Secondary Objectives:

Cohort 1:

- To demonstrate that CFZ533 600 mg and/or 300 mg Q2W SC are superior to a TAC-based regimen with respect to the mean estimated Glomerular Filtration Rate (eGFR) over 12 months post-transplantation.
- To assess the safety and tolerability of CFZ533 regimens compared to a TAC based regimen.
- To assess the pharmacokinetics of CFZ533 and explore the dose exposure relationship during the 60 months treatment period.
- To assess the immunogenicity of CFZ533 during the 60 months treatment period.

Cohort 2:

- To demonstrate that CFZ533 450 mg Q2W SC is superior to a TAC based regimen with respect to the mean change in eGFR from baseline to 12 months post-conversion.
- To assess the safety and tolerability of CFZ533 regimen compared to a TAC-based regimen.
- To assess the pharmacokinetics of CFZ533 during the 60 months treatment period and explore the dose-exposure relationship (together with PK data from Cohort 1).=
- To evaluate the immunogenicity of CFZ533 during the 60 months treatment period.

Test Product (s), Dose(s), and Mode(s) of Administration

CFZ533 300 mg, 450 mg and 600 mg was first administered intravenously and subcutaneously thereafter.
Tacrolimus oral - 0.2 - 0.3 mg/kg/day, Tacrolimus, IV - 0.05 - 0.1 mg/kg/day, Mycophenolate mofetil, oral - 2g/day or mycophenolate mofetil, IV - 2g/day were also administered.
Placebo 1 mL solution taken subcutaneously and was used for blinding of the CFZ533 300 mg dose only.

Statistical Methods

The number of composite (BPAR, graft loss, death) events was assumed to follow a Poisson distribution. The pre-defined success criteria were considered to be a composite rate difference between at least one of the CFZ533 arms and the control group of less than a non-inferiority (NI) margin of 20% in the *de novo* cohort (Cohort 1) and 12% in the maintenance cohort (Cohort 2), with a posterior
probability greater than 90%. Posterior mean composite rates for each treatment arm and the difference in mean response rates between treatments were presented together with 95% credible intervals (CIs).

Study Population: Key Inclusion/Exclusion Criteria

Inclusion Criteria:
Key inclusion criteria for both cohorts
• Written informed consent obtained before any assessment.
• Male or female patient ≥ 18 years old.
• Up to date vaccination as per local immunization schedules.

Key inclusion criteria specific to Cohort 1:
• Recipients of a primary kidney transplant from a brain-dead donor, living unrelated or non-human leukocyte antigen (HLA) identical living related donors.
• Recipients of a kidney with a cold ischemia time < 24 hours.

Key inclusion criteria specific to Cohort 2:
• Recipients of a primary graft received 6 to 24 months prior enrollment, on a regimen containing TAC+MMF/ Enteric-coated mycophenolate sodium (EC-MPS)±corticosteroids (CS).
• Patients with an actual eGFR according to Modification of Diet in Renal Disease (MDRD-4) ≥ 45 mL/min/1.73m2.

Exclusion Criteria:
Key exclusion criteria for both cohorts

• Recipient who tests positive for anti-HIV, HBsAg or anti-HCV (without proof of sustained viral response (SVR12) after anti-HCV treatment) within 28 days prior to baseline visit.
• Recipient who tests negative for Epstein Barr virus (EBV) within 28 days prior to baseline visit.
• Evidence of advanced liver disease (Child-Pugh C), or any sign of liver decompensation.
• Patient with severe systemic infections, current or within the two weeks prior to randomization.
• History of malignancy of any organ system, treated or untreated, within the past 5 years, regardless of whether there is evidence of local recurrence or metastases, with the exception of localized excised non-melanomatous skin lesions.
• Patients who weighed less than 30 kg or more than 180 kg.

Key exclusion criteria specific to Cohort 1:
• Multi-organ transplant recipients, including en bloc and dual kidney transplantation, or prior kidney transplant
• Recipients of an organ from a donor after cardiac death.
• Recipient of an organ from an HLA identical living related donor.
• ABO incompatible or complement-dependent lymphocytotoxic crossmatch positive transplant (isolated positive B cell crossmatches were not an exclusion criterion).
• Recipients of kidneys from donors who were older than >65 years.
• Recipients of kidneys from donors with terminal serum creatinine > 2 mg/dL.
• Patients at high immunological risk for rejection as determined for assessment of anti-donor reactivity:
• high panel reactive antibodies> 20% or
• Presence of pre-formed DSA. Results 12 weeks prior to enrollment were acceptable if no blood transfusion or abortion occurred during this period.
• Recipient of a kidney from a donor who tests positive for HIV, HBsAg or HCV.

Key exclusion criteria to Cohort 2
• Recipients of a kidney re-transplant.
• Recipient of a multi-organ transplant, including en bloc and dual kidney transplantation.
• DSA within 12 weeks prior enrollment.
• eGFR decline ≥10.0 mL/min within 12 weeks prior enrollment.

- Ongoing rejection or rejection that required treatment within 12 weeks prior enrollment.
- Severe humoral and/or cellular rejection (BANFF ≥ IIb) within 12 weeks before enrollment.
- Proteinuria > 1 g/day or UPCR >1.2 mg/mg at time of enrollment

Participant Flow Table

Overall Study

	Arm 1/Cohort 1 (De Novo Cohort): CFZ533 600 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 2/Cohort 1 (De Novo Cohort): CFZ533 300 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 3/Cohort 1 (De Novo Cohort): Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids	Arm 1/Cohort 2 (Maintenance Cohort): CFZ533 450 mg + MMF ± Corticosteroids	Arm 2/Cohort 2 (Maintenance Cohort): TAC + MMF ± Corticosteroids	Total
Arm/Group Description	Eligible patients were randomized to CFZ533 600 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and	Eligible patients were randomized to CFZ533 300 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and	Patients randomized to the TAC control arm were initiated on a TAC-based regimen with MMF and corticosteroids.	Eligible patients who were 6 to 24 months post renal transplantation and were on a stable regimen containing TAC+MMF/Enteric-coated mycophenolate sodium (EC-MPS)±CS were randomized to CFZ533 450 mg sc Q2W. On Day 1, patients randomized to Arm 1 were administered the 1st dose of CFZ533 at 30 mg/kg IV, concomitantly with MMF/EC-MPS and 50% of the current TAC dose. At Day 15,	Patients received TAC-based regimen throughout the study.	

	corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 600 mg sc (2 injections of 2 mL CFZ533 at 150 mg/mL) Q2W, up to a planned Month 59.5 visit.	corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 300 mg sc (1 injection of 2 mL CFZ533 at 150 mg/mL, and 1 injection of 2 mL of the generic placebo) sc, Q2W, up to a planned Month 59.5 visit.		CFZ533 was administered sc 450 mg (1 injection of 2 mL & 1 injection of 1 mL CFZ533 at 150 mg/mL) concomitantly with MMF/EC-MPS, and TAC reduced by a further 50%. By Day 29, patients were fully tapered off their TAC. Subsequent doses of 450 mg sc Q2W, were administered in combination with MMF/EC-MPS with or without corticosteroids, up to Month 59.5 visit.		
Started	108	109	74	70	42	403
Full Analysis Set	108	109	74	70	42	403
Pharmacokinetics Analysis Set	110	109	0	70	0	289
Completed	0	0	0	0	0	0
Not Completed	108	109	74	70	42	403
Unsatisfactory therapeutic effect	5	2	1	0	0	8
Adverse Event	8	19	3	6	0	36
Death	9	1	2	1	2	15
Lost to Follow-up	0	0	1	0	0	1

Patient not continuing after Month12	12	9	11	3	2	37
Physician Decision	0	0	0	0	1	1
Study terminated by Sponsor	71	73	53	60	33	290
Subject decision	3	5	3	0	4	15

Baseline Characteristics

	Arm 1/Cohort 1 (De Novo Cohort): CFZ533 600 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 2/Cohort 1 (De Novo Cohort): CFZ533 300 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 3/Cohort 1 (De Novo Cohort): Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids	Arm 1/Cohort 2 (Maintenance Cohort): CFZ533 450 mg + MMF ± Corticosteroids	Arm 2/Cohort 2 (Maintenance Cohort): TAC + MMF ± Corticosteroids	Total
Arm/Group Description	Eligible patients were randomized to CFZ533 600 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the	Eligible patients were randomized to CFZ533 300 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the	Patients randomized to the TAC control arm were initiated on a TAC-based regimen with MMF and corticosteroids.	Eligible patients who were 6 to 24 months post renal transplantation and were on a stable regimen containing TAC+MMF/Enteric-coated mycophenolate sodium (EC-MPS)±CS were randomized to CFZ533 450 mg sc Q2W. On Day 1, patients randomized to Arm 1 were administered the 1st dose of CFZ533 at	Patients received TAC-based regimen throughout the study.	

	infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 600 mg sc (2 injections of 2 mL CFZ533 at 150 mg/mL) Q2W, up to a planned Month 59.5 visit.	infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 300 mg sc (1 injection of 2 mL CFZ533 at 150 mg/mL, and 1 injection of 2 mL of the generic placebo) sc, Q2W, up to a planned Month 59.5 visit.		30 mg/kg IV, concomitantly with MMF/EC-MPS and 50% of the current TAC dose. At Day 15, CFZ533 was administered sc 450 mg (1 injection of 2 mL & 1 injection of 1 mL CFZ533 at 150 mg/mL) concomitantly with MMF/EC-MPS, and TAC reduced by a further 50%. By Day 29, patients were fully tapered off their TAC. Subsequent doses of 450 mg sc Q2W, were administered in combination with MMF/EC-MPS with or without corticosteroids, up to Month 59.5 visit.		
Number of Participants [units: participants]	108	109	74	70	42	403
Age, Customized (units: Participants) Analysis Population Type: Participants						
< 60 years	86	79	54	53	32	304
>= 60 6years	22	30	20	17	10	99
Sex: Female, Male (units: Participants)						

Analysis Population Type: Participants Count of Participants (Not Applicable)						
Female	34	32	14	18	14	112
Male	74	77	60	52	28	291
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants						
White	84	86	59	47	32	308
Black or African American	14	6	6	3	4	33
Asian: Indian	2	0	0	1	0	3
Asian: Japanese	4	12	3	12	4	35
Asian: Korean	1	0	0	3	0	4
Asian: Other	0	1	2	1	1	5
American Indian or Alaskan Native	0	0	1	0	0	1
Multiple	3	4	3	2	1	13
Other - Unknown	0	0	0	1	0	1

Primary Outcome Result(s)

Percentage of participants with composite efficacy failure event (Biopsy Proven Acute Rejection (BPAR), Graft Loss or Death) over 12 months post-transplantation (Cohort 1)

Description	The composite efficacy failure event is defined as any of the following: (1) biopsy-proven acute rejection (BPAR) or (2) graft loss or (3) death. BPAR (BANFF ≥ 1A) is based on the central and adjudicated assessments. Graft loss is defined as when the allograft was presumed lost on the day the participant started dialysis and was not able to subsequently be removed from dialysis or re-transplanted. If the participant underwent allograft nephrectomy prior to start of permanent dialysis, the day of the nephrectomy was day of graft loss.
Time Frame	12 Months

	Arm 1/Cohort 1 (De Novo Cohort): CFZ533 600 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 2/Cohort 1 (De Novo Cohort): CFZ533 300 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 3/Cohort 1 (De Novo Cohort): Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids
Arm/Group Description	Eligible patients were randomized to CFZ533 600 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 600 mg sc (2 injections of 2 mL CFZ533 at 150 mg/mL) Q2W, up to a planned Month 59.5 visit.	Eligible patients were randomized to CFZ533 300 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 300 mg sc (1 injection of 2 mL CFZ533 at 150 mg/mL, and 1 injection of 2 mL of the generic placebo) sc, Q2W, up to a planned Month 59.5 visit.	Patients randomized to the TAC control arm were initiated on a TAC-based regimen with MMF and corticosteroids.
Number of Participants Analyzed [units: participants]	66	70	41
Percentage of participants with composite efficacy failure event (Biopsy Proven Acute Rejection (BPAR), Graft Loss or Death) over 12 months post-transplantation (Cohort 1) (units: Percentage of participants)			
	60.6	38.6	22.0

Statistical Analysis

Groups	Arm 1/Cohort 1 (De Novo Cohort): CFZ533 600 mg + Mycophenolate Mofetil (MMF) + Corticosteroids, Arm 3/Cohort 1 (De Novo Cohort): Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids	
Non-Inferiority/Equivalence Test	Non-Inferiority	The non-inferiority (NI) margin was set at 20%.
Other Rate Difference	15.80	
95 % Confidence Interval 2-Sided	3.86 to 27.74	

Statistical Analysis

Groups	Arm 2/Cohort 1 (De Novo Cohort): CFZ533 300 mg + Mycophenolate Mofetil (MMF) + Corticosteroids, Arm 3/Cohort 1 (De Novo Cohort): Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids	
Non-Inferiority/Equivalence Test	Non-Inferiority	The non-inferiority (NI) margin was set at 20%.
Other Rate Difference	5.61	
95 % Confidence Interval 2-Sided	-5.67 to 16.90	

Percentage of participants with composite efficacy failure event (BPAR, Graft Loss or Death) over 12 months post-conversion (Cohort 2)

Description	The composite efficacy failure event is defined as any of the following: (1) biopsy-proven acute rejection (BPAR) or (2) graft loss or (3) death. BPAR (BANFF ≥ 1A) is based on the central and adjudicated assessments. Graft loss is defined as when the allograft was presumed lost on the day the participant started dialysis and was not able to subsequently be removed from dialysis or re-transplanted. If the participant underwent allograft nephrectomy prior to start of permanent dialysis, the day of the nephrectomy was day of graft loss.
Time Frame	12 Months

	Arm 1/Cohort 2 (Maintenance Cohort): CFZ533 450 mg + MMF ± Corticosteroids	Arm 2/Cohort 2 (Maintenance Cohort): TAC + MMF ± Corticosteroids
Arm/Group Description	Eligible patients who were 6 to 24 months post renal transplantation and were on a stable regimen containing TAC+MMF/Enteric-coated mycophenolate sodium (EC-MPS)±CS were randomized to CFZ533 450 mg sc Q2W. On Day 1, patients randomized to Arm 1 were administered the 1st dose of CFZ533 at 30 mg/kg IV, concomitantly with MMF/EC-MPS and 50% of the current TAC dose. At Day 15, CFZ533 was administered sc 450 mg (1 injection of 2 mL & 1 injection of 1 mL CFZ533 at 150 mg/mL) concomitantly with MMF/EC-MPS, and TAC reduced by a further 50%. By Day 29, patients were fully tapered off their TAC. Subsequent doses of 450 mg sc Q2W, were administered in combination with MMF/EC-MPS with or without corticosteroids, up to Month 59.5 visit.	Patients received TAC-based regimen throughout the study.
Number of Participants Analyzed [units: participants]	34	18
Percentage of participants with composite efficacy failure event (BPAR, Graft Loss or Death) over 12 months post-conversion (Cohort 2) (units: Percentage of participants)		
	14.7	11.1

Statistical Analysis

Groups	Arm 1/Cohort 2 (Maintenance Cohort): CFZ533 450 mg + MMF ± Corticosteroids	
Non-Inferiority/Equivalence Test	Non-Inferiority	The non-inferiority (NI) margin was set at 20%.
Other Rate Difference	-1.43	

95 % Confidence Interval 2-Sided	-14.24 to 11.39

Secondary Outcome Result(s)

Cohort 1: Mean estimated Glomerular Filtration Rate (eGFR) ((MDRD4) at 12 months post-transplantation

Description	In the de novo population (Cohort 1), the mean eGFR at Month 12 post-transplantation was the endpoint of interest. Estimated GFR using central laboratory serum creatinine values was calculated using the MDRD4 formula.
Time Frame	12 months

	Arm 1/Cohort 1 (De Novo Cohort): CFZ533 600 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 2/Cohort 1 (De Novo Cohort): CFZ533 300 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 3/Cohort 1 (De Novo Cohort): Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids
Arm/Group Description	Eligible patients were randomized to CFZ533 600 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 600 mg sc (2 injections	Eligible patients were randomized to CFZ533 300 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 300 mg sc (1 injection of	Patients randomized to the TAC control arm were initiated on a TAC-based regimen with MMF and corticosteroids.

	of 2 mL CFZ533 at 150 mg/mL) Q2W, up to a planned Month 59.5 visit.	2 mL CFZ533 at 150 mg/mL, and 1 injection of 2 mL of the generic placebo) sc, Q2W, up to a planned Month 59.5 visit.	
Number of Participants Analyzed [units: participants]	58	58	51
Cohort 1: Mean estimated Glomerular Filtration Rate (eGFR) ((MDRD4) at 12 months post-transplantation (units: mL/min/1.73m^2)	**Mean ± Standard Error**	**Mean ± Standard Error**	**Mean ± Standard Error**
	58.83 ± 1.971	60.63 ± 1.976	54.12 ± 2.101

Statistical Analysis

Groups	Arm 1/Cohort 1 (De Novo Cohort): CFZ533 600 mg + Mycophenolate Mofetil (MMF) + Corticosteroids, Arm 3/Cohort 1 (De Novo Cohort): Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids	
P Value	0.103	
Method	ANOVA	the ANOVA model adjusted by treatment group, donor category and induction therapy
Other mean difference	4.71	
Standard Deviation	2.873	
95 % Confidence Interval 2-Sided	-0.96 to 10.38	

Statistical Analysis

Groups	Arm 2/Cohort 1 (De Novo Cohort): CFZ533 300 mg + Mycophenolate Mofetil (MMF) + Corticosteroids, Arm 3/Cohort 1 (De Novo Cohort):	

	Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids	
P Value	0.025	
Method	ANOVA	the ANOVA model adjusted by treatment group, donor category and induction therapy
Other mean difference	6.51	
Standard Error of the mean	2.875	
95 % Confidence Interval 2-Sided	0.83 to 12.18	

Cohort 2: Mean change in estimated Glomerular Filtration Rate (eGFR) ((MDRD4) at 12 months post-conversion

Description	In the maintenance population (Cohort 2), a baseline kidney function and the mean change from baseline at Month 12 post-conversion of eGFR was the endpoint of interest. Estimated GFR using central laboratory serum creatinine values was calculated using the MDRD4 formula.
Time Frame	12 months

	Arm 1/Cohort 2 (Maintenance Cohort): CFZ533 450 mg + MMF ± Corticosteroids	Arm 2/Cohort 2 (Maintenance Cohort): TAC + MMF ± Corticosteroids
Arm/Group Description	Eligible patients who were 6 to 24 months post renal transplantation and were on a stable regimen containing TAC+MMF/Enteric-coated mycophenolate sodium (EC-MPS)±CS were randomized to CFZ533 450 mg sc Q2W. On Day 1, patients randomized to Arm 1 were administered the 1st dose of CFZ533 at 30 mg/kg IV, concomitantly with MMF/EC-MPS and 50% of the current TAC dose. At Day 15, CFZ533 was administered sc 450 mg (1 injection of 2 mL & 1 injection of 1 mL CFZ533 at 150 mg/mL) concomitantly with MMF/EC-MPS, and TAC reduced by a further 50%. By	Patients received TAC-based regimen throughout the study.

	Day 29, patients were fully tapered off their TAC. Subsequent doses of 450 mg sc Q2W, were administered in combination with MMF/EC-MPS with or without corticosteroids, up to Month 59.5 visit.	
Number of Participants Analyzed [units: participants]	39	27
Cohort 2: Mean change in estimated Glomerular Filtration Rate (eGFR) ((MDRD4) at 12 months post-conversion (units: mL/min/1.73m^2)	**Mean ± Standard Error**	**Mean ± Standard Error**
	4.30 ± 1.722	1.42 ± 1.866

Statistical Analysis

Groups	Arm 1/Cohort 2 (Maintenance Cohort): CFZ533 450 mg + MMF ± Corticosteroids, Arm 2/Cohort 2 (Maintenance Cohort): TAC + MMF ± Corticosteroids	
P Value	0.153	
Method	ANOVA	ANCOVA model adjusted by baseline, treatment group, corticosteroid use, time since transplant
Other mean change difference	2.88	
Standard Error of the mean	1.987	
95 % Confidence Interval 2-Sided	-1.10 to 6.85	

Free CFZ533 plasma concentrations over time (Cohort 1)

Description	Pharmacokinetics were determined for free CFZ533 plasma concentrations during the treatment period.
Time Frame	Day 1-Pre-Dose to Month 30-Pre-Dose

	Arm 1/Cohort 1 (De Novo Cohort): CFZ533 600 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 2/Cohort 1 (De Novo Cohort): CFZ533 300 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 3/Cohort 1 (De Novo Cohort): Control/Standard of Care: Tacrolimus (TAC) + MMF + Corticosteroids
Arm/Group Description	Eligible patients were randomized to CFZ533 600 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 600 mg sc (2 injections of 2 mL CFZ533 at 150 mg/mL) Q2W, up to a planned Month 59.5 visit.	Eligible patients were randomized to CFZ533 300 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice. A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 300 mg sc (1 injection of 2 mL CFZ533 at 150 mg/mL, and 1 injection of 2 mL of the generic placebo) sc, Q2W, up to a planned Month 59.5 visit.	Patients screened to the TAC control arm were initiated on a TAC-based regimen with MMF and corticosteroids.
Number of Participants Analyzed [units: participants]	110	109	0
Free CFZ533 plasma concentrations over time (Cohort 1) (units: µg/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Day 1 Pre-dose (n = 96, 94, 0)	0.00 ± 0.000	0.00 ± 0.000	
Day 1 post-dose (n = 106, 106, 0)	471.20 ± 222.169	441.67 ± 246.474	
Day 5 pre-dose (n = 95, 97, 0)	231.93 ± 102.947	205.16 ± 77.632	

Day 5 post-dose (n = 98, 99, 0)	502.48 ± 211.592	502.32 ± 186.159
Day 15 pre-dose (n = 104, 98, 0)	251.17 ± 92.466	242.99 ± 83.780
Day 29 pre-dose (n = 98, 95, 0)	197.47 ± 74.937	187.38 ± 79.884
Month 1.5 pre-dose (n = 93, 93, 0)	172.84 ± 67.444	122.80 ± 38.604
Month 2 pre-dose (n = 89, 90, 0)	155.68 ± 64.661	102.52 ± 33.798
Month 2.5 pre-dose (n = 86, 88, 0)	151.81 ± 58.367	85.21 ± 34.835
Month 3 pre-dose (n = 84, 83, 0)	147.62 ± 51.971	86.16 ± 35.463
Month 4 pre-dose (n = 81, 72, 0)	159.58 ± 70.382	68.72 ± 27.269
Month 6 pre-dose (n = 69, 77, 0)	161.21 ± 63.195	73.27 ± 35.126
Month 8 pre-dose (n = 60, 64, 0)	151.34 ± 52.778	71.92 ± 33.683
Month 10 pre-dose (n = 56, 58, 0)	141.18 ± 46.999	62.55 ± 31.199
Moth 12 pre-dose (n = 51, 55, 0)	148.71 ± 62.106	56.81 ± 30.717
Month 15 pre-dose(n = 36, 40, 0)	149.86 ± 58.888	48.37 ± 20.604
Month 18 pre-dose (n = 43, 37, 0)	122.24 ± 54.056	49.68 ± 31.768
Month 21 pre-dose (n = 40, 32, 0)	132.51 ± 65.146	59.96 ± 36.583
Month 24 pre-dose (n = 36, 33, 0)	139.55 ± 53.177	60.96 ± 31.988
Month 30 pre-dose (n = 11, 12, 0)	140.80 ± 47.339	56.63 ± 23.195

Free CFZ533 plasma concentrations over time (Cohort 2)

Description	Pharmacokinetics were determined for free CFZ533 plasma concentrations during the treatment period.
Time Frame	Day 1-Pre-Dose to Month 30-Pre-Dose

	Arm 1/Cohort 2 (Maintenance Cohort): CFZ533 450 mg + MMF ± Corticosteroids	Arm 2/Cohort 2 (Maintenance Cohort): TAC + MMF ± Corticosteroids
Arm/Group Description	Eligible patients who were 6 to 24 months post renal transplantation and were on a stable regimen containing TAC+MMF/Enteric-coated mycophenolate sodium (EC-MPS)±CS were randomized to CFZ533 450 mg sc Q2W. On Day 1, patients randomized to Arm 1 were administered the 1st dose of CFZ533 at 30 mg/kg IV, concomitantly with MMF/EC-MPS and 50% of the current TAC dose. At Day 15, CFZ533 was administered sc 450 mg (1 injection of 2 mL & 1 injection of 1 mL CFZ533 at 150 mg/mL) concomitantly with MMF/EC-MPS, and TAC reduced by a further 50%. By Day 29, patients were fully tapered off their TAC. Subsequent doses of 450 mg sc Q2W, were administered in combination with MMF/EC-MPS with or without corticosteroids, up to Month 59.5 visit.	Patients received TAC-based regimen throughout the study.
Number of Participants Analyzed [units: participants]	70	0
Free CFZ533 plasma concentrations over time (Cohort 2) (units: µg/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Day 1 Pre-dose (n = 67, 0)	0.00 ± 0.000	
Day 1 post-dose (n = 68, 0)	681.59 ± 698.086	
Day 15 pre-dose (n = 67, 0)	181.81 ± 72.297	
Day 29 pre-dose (n = 65, 0)	147.56 ± 43.749	
Month 1.5 pre-dose (n = 65, 0)	127.55 ± 39.794	
Month 2 pre-dose (n = 61, 0)	121.81 ± 44.801	
Month 2.5 pre-dose (n = 66, 0)	114.53 ± 44.759	
Month 3 pre-dose (n = 63, 0)	104.40 ± 42.563	
Month 4 pre-dose (n = 62, 0)	108.61 ± 51.790	

Month 6 pre-dose (n = 56, 0)	112.14 ± 46.932
Month 8 pre-dose (n = 51, 0)	118.08 ± 42.868
Month 10 pre-dose (n = 41, 0)	106.98 ± 53.798
Moth 12 pre-dose (n = 37, 0)	111.05 ± 54.629
Month 15 pre-dose(n = 25, 0)	104.11 ± 67.744
Month 18 pre-dose (n = 24, 0)	115.59 ± 66.227
Month 21 pre-dose (n = 24, 0)	116.89 ± 53.953
Month 24 pre-dose (n = 18, 0)	111.03 ± 39.901
Month 30 pre-dose (n = 3, 0)	132.97 ± 65.132

Semi-quantiative analysis of anti-CFZ533 antibodes in plasma (CFZ533 treated patients only) (Cohort 1)

Description The presence of anti-CFZ533 antibodies was assessed using screening and confirmatory assays.

Time Frame 24 Months

	Arm 1/Cohort 1 (De Novo Cohort): CFZ533 600 mg + Mycophenolate Mofetil (MMF) + Corticosteroids	Arm 2/Cohort 1 (De Novo Cohort): CFZ533 300 mg + Mycophenolate Mofetil (MMF) + Corticosteroids
Arm/Group Description	Eligible patients were randomized to CFZ533 600 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice.	Eligible patients were randomized to CFZ533 300 mg sc bi-weekly (Q2W) + Mycophenolate Mofetil (MMF) + Corticosteroids. Patients randomized to CFZ533 arms were administered the first dose of CFZ533 at 30 mg/kg IV pre- or intra-operatively (Day 1) with completion of the infusion within one hour of unclamping and prior graft revascularization, in combination with MMF and corticosteroids. MMF and corticosteroids might be initiated prior to surgery according to local practice.

	A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 600 mg sc (2 injections of 2 mL CFZ533 at 150 mg/mL) Q2W, up to a planned Month 59.5 visit.	A second IV dose of CFZ533 at 15 mg/kg was infused at Day 5 post-transplant. Subsequent doses starting at Day 15: 300 mg sc (1 injection of 2 mL CFZ533 at 150 mg/mL, and 1 injection of 2 mL of the generic placebo) sc, Q2W, up to a planned Month 59.5 visit.
Number of Participants Analyzed [units: participants]	110	109
Semi-quantiative analysis of anti-CFZ533 antibodes in plasma (CFZ533 treated patients only) (Cohort 1) (units: Participants)		
Subject with an on-study result	109	108
Binding antibody positive at any time	2	0
Subject with a result at baseline	104	101
Binding antibody positive at or before baseline	0	0
Subject with a post-baseline result	102	103
Binding antibody positive post-baseline with a positive result at baseline	0	0
Binding antibody positive post-baseline with a negative result at baseline	2	0

Semi-quantiative analysis of anti-CFZ533 antibodes in plasma (CFZ533 treated patients only) (Cohort 2)

Description The presence of anti-CFZ533 antibodies was assessed using screening and confirmatory assays.

Time Frame 24 Months

	Arm 1/Cohort 2 (Maintenance Cohort): CFZ533 450 mg + MMF ± Corticosteroids
Arm/Group Description	Eligible patients who were 6 to 24 months post renal transplantation and were on a stable regimen containing TAC+MMF/Enteric-coated mycophenolate sodium (EC-MPS)±CS were randomized to CFZ533 450 mg sc Q2W. On Day 1, patients randomized to Arm 1 were administered the 1st dose of CFZ533

	at 30 mg/kg IV, concomitantly with MMF/EC-MPS and 50% of the current TAC dose. At Day 15, CFZ533 was administered sc 450 mg (1 injection of 2 mL & 1 injection of 1 mL CFZ533 at 150 mg/mL) concomitantly with MMF/EC-MPS, and TAC reduced by a further 50%. By Day 29, patients were fully tapered off their TAC. Subsequent doses of 450 mg sc Q2W, were administered in combination with MMF/EC-MPS with or without corticosteroids, up to Month 59.5 visit.
Number of Participants Analyzed [units: participants]	70
Semi-quantiative analysis of anti-CFZ533 antibodes in plasma (CFZ533 treated patients only) (Cohort 2) (units: Participants)	
Subject with an on-study result	70
Binding antibody positive at any time	0
Subject with a result at baseline	68
Binding antibody positive at or before baseline	0
Subject with a post-baseline result	69
Binding antibody positive post-baseline with a positive result at baseline	0
Binding antibody positive post-baseline with a negative or no result at baseline	0

Safety Results

All-Cause Mortality

De Novo Cohort: CFZ533 600 mg + MMF + CS on-treatment	De Novo Cohort: CFZ533 600 mg + MMF + CS follow-up	De Novo Cohort: CFZ533 300 mg + MMF + CS on-treatment	De Novo Cohort: CFZ533 300 mg + MMF + CS follow-up	De Novo Cohort: TAC + MMF + CS on-treatment	De Novo Cohort: TAC + MMF + CS follow-up period N = 73	Maintenance Cohort: CFZ533 450 mg + MMF +/- CS on-treatment	Maintenance Cohort: CFZ533 450 mg + MMF +/- CS follow-up	Maintenance Cohort: TAC + MMF +/- CS on-treatment period N = 42	Maintenance Cohort: TAC + MMF +/- CS follow-up period N = 42

	period N = 108	period N = 108	period N = 109	period N = 109	period N = 73		period N = 70	period N = 70		
Arm/Group Description	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From 1st dose to last dose of TAC	From day 1 after last dose of TAC till completion of the 12 weeks safety follow up. Note: patients may have switched to Standard of care.	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From 1st dose to last dose of TAC	From day 1 after last dose of TAC till completion of the 12 weeks safety follow up. Note: patients may have switched to Standard of care.
Total Number Affected	2	5	0	1	1	0	0	1	1	1
Total Number At Risk	108	108	109	109	73	73	70	70	42	42

Serious Adverse Events by System Organ Class

	De Novo Cohort: CFZ533 600 mg + MMF + CS on-treatment period N = 108	**De Novo Cohort: CFZ533 600 mg + MMF + CS follow-up period N = 108**	**De Novo Cohort: CFZ533 300 mg + MMF + CS on-treatment period N = 109**	**De Novo Cohort: CFZ533 300 mg + MMF + CS follow-up period N = 109**	**De Novo Cohort: TAC + MMF + CS on-treatment period N = 73**	**De Novo Cohort: TAC + MMF + CS follow-up period N = 73**	**Maintenance Cohort: CFZ533 450 mg + MMF +/- CS on-treatment period N = 70**	**Maintenance Cohort: CFZ533 450 mg + MMF +/- CS follow-up period N = 70**	**Maintenance Cohort: TAC + MMF +/- CS on-treatment period N = 42**	**Maintenance Cohort: TAC + MMF +/- CS follow-up period N = 42**

Arm/Group Description	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From 1st dose to last dose of TAC	From day 1 after last dose of TAC till completion of the 12 weeks safety follow up. Note: patients may have switched to Standard of care.	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From 1st dose to last dose of TAC	From day 1 after last dose of TAC till completion of the 12 weeks safety follow up. Note: patients may have switched to Standard of care.
Total # Affected by any Serious Adverse Event	71	18	76	19	39	3	25	4	11	1
Total # at Risk by any Serious Adverse Event	108	108	109	109	73	73	70	70	42	42
Blood and lymphatic system disorders										
Anaemia	2 (1.85%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bicytopenia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
Eosinophilia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Febrile neutropenia	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Leukopenia	1 (0.93%)	0 (0.00%)	4 (3.67%)	1 (0.92%)	1 (1.37%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Lymphadenopathy mediastinal	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphopenia	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutropenia	2 (1.85%)	0 (0.00%)	1 (0.92%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pancytopenia	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac disorders										
Acute coronary syndrome	2 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Acute myocardial infarction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Angina pectoris	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Angina unstable	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Atrial fibrillation	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardiac failure	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cardio-respiratory arrest	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myocardial infarction	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Myocardial ischaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
Endocrine disorders										
Adrenal insufficiency	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Goitre	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperaldosteronism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperparathyroidism	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperparathyroidism secondary	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Eye disorders										
Photophobia	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Retinal detachment	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Uveitis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal disorders										
Abdominal pain	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Abdominal pain upper	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ascites	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Colitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diarrhoea	1 (0.93%)	0 (0.00%)	2 (1.83%)	1 (0.92%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Enteritis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Food poisoning	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ileus	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Inguinal hernia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Large intestine perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mesenteric panniculitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
Pancreatitis acute	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Small intestinal obstruction	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Stomatitis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vomiting	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
General disorders and administration site conditions										
Asthenia	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chest pain	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chills	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Fatigue	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
General physical health deterioration	0 (0.00%)	0 (0.00%)	2 (1.83%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Hernia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyperthermia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Inflammation	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Malaise	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyrexia	4 (3.70%)	0 (0.00%)	5 (4.59%)	3 (2.75%)	1 (1.37%)	0 (0.00%)	4 (5.71%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hepatobiliary disorders										
Hepatic cytolysis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
Immune system disorders										
Anti-neutrophil cytoplasmic antibody positive vasculitis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemophagocytic lymphohistiocytosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
Transplant rejection	16 (14.81%)	0 (0.00%)	10 (9.17%)	1 (0.92%)	6 (8.22%)	0 (0.00%)	2 (2.86%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infections and infestations										
Adenovirus infection	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bacteraemia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

BK virus infection	1 (0.93%)	1 (0.93%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchitis	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Bronchopulmonary aspergillosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Campylobacter gastroenteritis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Campylobacter infection	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Candida infection	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cellulitis	1 (0.93%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cerebral toxoplasmosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Clostridium difficile colitis	0 (0.00%)	1 (0.93%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Clostridium difficile infection	0 (0.00%)	0 (0.00%)	1 (0.92%)	1 (0.92%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
COVID-19	5 (4.63%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	3 (4.11%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	2 (4.76%)	0 (0.00%)
COVID-19 pneumonia	1 (0.93%)	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cryptococcal meningoencephalitis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cytomegalovirus chorioretinitis	1 (0.93%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cytomegalovirus colitis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Cytomegalovirus gastritis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cytomegalovirus hepatitis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cytomegalovirus infection	16 (14.81%)	2 (1.85%)	11 (10.09%)	3 (2.75%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Cytomegalovirus infection reactivation	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Device related infection	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diarrhoea infectious	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diverticulitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Escherichia sepsis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastroenteritis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Gastroenteritis viral	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gastrointestinal infection	0 (0.00%)	2 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
H1N1 influenza	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Herpes zoster	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infected lymphocele	0 (0.00%)	1 (0.93%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infection	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)

Influenza	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Leishmaniasis	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Localised infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Necrotising fasciitis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ophthalmic herpes zoster	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Oral candidiasis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Parotitis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Parvovirus B19 infection	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumocystis jirovecii infection	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumocystis jirovecii pneumonia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia	3 (2.78%)	1 (0.93%)	0 (0.00%)	1 (0.92%)	1 (1.37%)	1 (1.37%)	0 (0.00%)	2 (2.86%)	2 (4.76%)	0 (0.00%)
Pneumonia legionella	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pneumonia viral	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Polyomavirus-associated nephropathy	0 (0.00%)	2 (1.85%)	5 (4.59%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Postoperative wound infection	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Prostatitis Escherichia coli	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pseudomonas infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pyelonephritis	2 (1.85%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	2 (2.86%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Pyelonephritis acute	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal abscess	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory tract infection	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rhinitis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Sepsis	2 (1.85%)	1 (0.93%)	1 (0.92%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Septic shock	1 (0.93%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Staphylococcal bacteraemia	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Suspected COVID-19	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Toxoplasmosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tuberculosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Upper respiratory tract infection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary tract infection	5 (4.63%)	1 (0.93%)	6 (5.50%)	0 (0.00%)	6 (8.22%)	0 (0.00%)	5 (7.14%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Urinary tract infection bacterial	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Urinary tract infection enterococcal	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urosepsis	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Wound infection	2 (1.85%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Injury, poisoning and procedural complications										
Arteriovenous fistula thrombosis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Clavicle fracture	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Complications of transplanted kidney	1 (0.93%)	1 (0.93%)	3 (2.75%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Delayed graft function	6 (5.56%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Graft complication	2 (1.85%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Graft ischaemia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Graft loss	2 (1.85%)	0 (0.00%)	3 (2.75%)	2 (1.83%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
Hip fracture	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nerve injury	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Post procedural haematoma	2 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Postoperative lymphocele	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Postoperative wound complication	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Procedural shock	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Road traffic accident	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Transplant dysfunction	4 (3.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Wound dehiscence	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Investigations										
Blood creatine increased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood creatinine increased	4 (3.70%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Blood glucose increased	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Clostridium test positive	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Troponin increased	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Weight decreased	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders										
Diabetes mellitus	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Diabetic complication	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Diabetic ketoacidosis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypercalcaemia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypercreatininaemia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypervolaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypocalcaemia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoglycaemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hyponatraemia	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders										
Arthritis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Myalgia	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain in extremity	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)										
Basal cell carcinoma	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Metastases to lung	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)
Ovarian adenoma	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Parathyroid tumour benign	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Squamous cell carcinoma	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (4.76%)	0 (0.00%)
Nervous system disorders										
Anosmia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cerebrovascular accident	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Guillain-Barre syndrome	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Headache	0 (0.00%)	0 (0.00%)	1 (0.92%)	1 (0.92%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertensive encephalopathy	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Intensive care unit acquired weakness	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ischaemic neuropathy	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Mononeuropathy multiplex	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Posterior reversible encephalopathy syndrome	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Quadrantanopia	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Radiculitis brachial	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Seizure	2 (1.85%)	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Subarachnoid haemorrhage	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Syncope	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
Product issues										
Device dislocation	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Psychiatric disorders										
Anxiety	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal and urinary disorders										
Acute kidney injury	3 (2.78%)	3 (2.78%)	4 (3.67%)	1 (0.92%)	7 (9.59%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Calculus urinary	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dysuria	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Glomerulonephritis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematuria	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hydronephrosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Perinephric collection	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal artery stenosis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal cyst	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal cyst haemorrhage	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Renal impairment	2 (1.85%)	0 (0.00%)	1 (0.92%)	1 (0.92%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal infarct	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal ischaemia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal tubular necrosis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Renal vein thrombosis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Subcapsular renal haematoma	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Tubulointerstitial nephritis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Ureteric stenosis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urethral obstruction	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary fistula	2 (1.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary incontinence	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Urinary retention	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Urinary tract disorder	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Reproductive system and breast disorders										
Acquired hydrocele	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Prostatitis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders										
Acute pulmonary oedema	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Chronic obstructive pulmonary disease	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cough	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyspnoea	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypoxia	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)
Pulmonary embolism	2 (1.85%)	0 (0.00%)	3 (2.75%)	1 (0.92%)	1 (1.37%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Skin and subcutaneous tissue disorders										
Diabetic foot	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Stasis dermatitis	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders										
Arterial stenosis	0 (0.00%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Arterial thrombosis	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Arteriosclerosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Deep vein thrombosis	1 (0.93%)	0 (0.00%)	1 (0.92%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haematoma	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypotension	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Iliac artery stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Infarction	0 (0.00%)	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphocele	1 (0.93%)	2 (1.85%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Peripheral artery stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Shock	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Shock haemorrhagic	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Subclavian artery stenosis	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Varicose ulceration	1 (0.93%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Venous thrombosis	0 (0.00%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Other Adverse Events by System Organ Class

	De Novo Cohort: CFZ533 600 mg + MMF + CS on-treatment period N = 108	De Novo Cohort: CFZ533 600 mg + MMF + CS follow-up period N = 108	De Novo Cohort: CFZ533 300 mg + MMF + CS on-treatment period N = 109	De Novo Cohort: CFZ533 300 mg + MMF + CS follow-up period N = 109	De Novo Cohort: TAC + MMF + CS on-treatment period N = 73	De Novo Cohort: TAC + MMF + CS follow-up period N = 73	Maintenance Cohort: CFZ533 450 mg + MMF +/- CS on-treatment period N = 70	Maintenance Cohort: CFZ533 450 mg + MMF +/- CS follow-up period N = 70	Maintenance Cohort: TAC + MMF +/- CS on-treatment period N = 42	Maintenance Cohort: TAC + MMF +/- CS follow-up period N = 42
Arm/Group Description	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From 1st dose to last dose of TAC	From day 1 after last dose of TAC till completion of the 12 weeks safety follow up. Note: patients may have switched to Standard of care.	From first dose up to 14 days after last dose of CFZ533	From day 15 after last CFZ533 dose till completion of the 14 weeks safety follow up. Note: patients may have switched to Standard of care.	From 1st dose to last dose of TAC	From day 1 after last dose of TAC till completion of the 12 weeks safety follow up. Note: patients may have switched to Standard of care.
Total # Affected by any Other Adverse Event	105	20	102	19	67	4	54	4	26	0

Total # at Risk by any Other Adverse Event	108	108	109	109	73	73	70	70	42	42
Blood and lymphatic system disorders										
Anaemia	36 (33.33 %)	0 (0.00%)	23 (21.10 %)	1 (0.92%)	12 (16.44 %)	2 (2.74%)	4 (5.71%)	1 (1.43%)	3 (7.14%)	0 (0.00%)
Leukocytosis	6 (5.56%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	3 (4.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Leukopenia	31 (28.70 %)	4 (3.70%)	31 (28.44 %)	4 (3.67%)	16 (21.92 %)	1 (1.37%)	9 (12.86%)	2 (2.86%)	1 (2.38%)	0 (0.00%)
Lymphopenia	14 (12.96 %)	1 (0.93%)	16 (14.68 %)	1 (0.92%)	5 (6.85%)	0 (0.00%)	3 (4.29%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Neutropenia	9 (8.33%)	0 (0.00%)	13 (11.93 %)	2 (1.83%)	2 (2.74%)	0 (0.00%)	7 (10.00%)	1 (1.43%)	1 (2.38%)	0 (0.00%)
Polycythaemia	2 (1.85%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Gastrointestinal disorders										
Abdominal pain	8 (7.41%)	1 (0.93%)	10 (9.17%)	2 (1.83%)	5 (6.85%)	1 (1.37%)	4 (5.71%)	1 (1.43%)	3 (7.14%)	0 (0.00%)
Abdominal pain upper	3 (2.78%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	6 (8.22%)	0 (0.00%)	4 (5.71%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Constipation	30 (27.78 %)	2 (1.85%)	21 (19.27 %)	1 (0.92%)	12 (16.44 %)	0 (0.00%)	3 (4.29%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Diarrhoea	19 (17.59 %)	5 (4.63%)	25 (22.94 %)	4 (3.67%)	20 (27.40 %)	0 (0.00%)	11 (15.71%)	1 (1.43%)	4 (9.52%)	0 (0.00%)
Dyspepsia	4 (3.70%)	1 (0.93%)	2 (1.83%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Haemorrhoids	6 (5.56%)	0 (0.00%)	5 (4.59%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nausea	13 (12.04 %)	1 (0.93%)	13 (11.93 %)	1 (0.92%)	11 (15.07 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	4 (9.52%)	0 (0.00%)
Vomiting	12 (11.11 %)	0 (0.00%)	10 (9.17%)	1 (0.92%)	7 (9.59%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	3 (7.14%)	0 (0.00%)

General disorders and administration site conditions										
Asthenia	2 (1.85%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	4 (5.71%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Fatigue	10 (9.26%)	0 (0.00%)	4 (3.67%)	1 (0.92%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Oedema peripheral	21 (19.44 %)	3 (2.78%)	13 (11.93 %)	1 (0.92%)	7 (9.59%)	0 (0.00%)	4 (5.71%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Pyrexia	20 (18.52 %)	3 (2.78%)	17 (15.60 %)	3 (2.75%)	4 (5.48%)	0 (0.00%)	7 (10.00%)	2 (2.86%)	4 (9.52%)	0 (0.00%)
Infections and infestations										
BK virus infection	13 (12.04 %)	1 (0.93%)	11 (10.09 %)	0 (0.00%)	9 (12.33%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Bronchitis	7 (6.48%)	0 (0.00%)	4 (3.67%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
COVID-19	9 (8.33%)	0 (0.00%)	6 (5.50%)	3 (2.75%)	7 (9.59%)	0 (0.00%)	2 (2.86%)	0 (0.00%)	4 (9.52%)	0 (0.00%)
Cytomegalovirus infection	15 (13.89 %)	3 (2.78%)	8 (7.34%)	1 (0.92%)	8 (10.96%)	0 (0.00%)	2 (2.86%)	1 (1.43%)	1 (2.38%)	0 (0.00%)
Gastroenteritis	3 (2.78%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	3 (4.11%)	0 (0.00%)	4 (5.71%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Herpes zoster	4 (3.70%)	1 (0.93%)	2 (1.83%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	3 (4.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Nasopharyngitis	8 (7.41%)	1 (0.93%)	6 (5.50%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	5 (7.14%)	0 (0.00%)	2 (4.76%)	0 (0.00%)
Oral herpes	7 (6.48%)	1 (0.93%)	1 (0.92%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	4 (5.71%)	0 (0.00%)	2 (4.76%)	0 (0.00%)
Upper respiratory tract infection	8 (7.41%)	1 (0.93%)	6 (5.50%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	2 (2.86%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Urinary tract infection	19 (17.59 %)	3 (2.78%)	27 (24.77 %)	2 (1.83%)	17 (23.29 %)	1 (1.37%)	5 (7.14%)	0 (0.00%)	2 (4.76%)	0 (0.00%)
Injury, poisoning and procedural complications										
Delayed graft function	7 (6.48%)	0 (0.00%)	8 (7.34%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Procedural pain	13 (12.04 %)	0 (0.00%)	19 (17.43 %)	0 (0.00%)	4 (5.48%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Transplant dysfunction	8 (7.41%)	0 (0.00%)	4 (3.67%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Investigations										
Blood creatinine increased	4 (3.70%)	0 (0.00%)	6 (5.50%)	1 (0.92%)	5 (6.85%)	0 (0.00%)	3 (4.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Cytomegalovirus test positive	1 (0.93%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphocyte count decreased	10 (9.26%)	0 (0.00%)	5 (4.59%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	3 (4.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Neutrophil count decreased	13 (12.04 %)	0 (0.00%)	5 (4.59%)	1 (0.92%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
SARS-CoV-2 test negative	1 (0.93%)	0 (0.00%)	6 (5.50%)	0 (0.00%)	3 (4.11%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolism and nutrition disorders										
Acidosis	6 (5.56%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Dyslipidaemia	1 (0.93%)	0 (0.00%)	4 (3.67%)	0 (0.00%)	5 (6.85%)	0 (0.00%)	2 (2.86%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Gout	1 (0.93%)	0 (0.00%)	1 (0.92%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypercalcaemia	5 (4.63%)	0 (0.00%)	7 (6.42%)	0 (0.00%)	2 (2.74%)	1 (1.37%)	1 (1.43%)	0 (0.00%)	2 (4.76%)	0 (0.00%)
Hyperglycaemia	12 (11.11 %)	4 (3.70%)	16 (14.68 %)	0 (0.00%)	17 (23.29 %)	0 (0.00%)	1 (1.43%)	2 (2.86%)	1 (2.38%)	0 (0.00%)
Hyperkalaemia	18 (16.67 %)	1 (0.93%)	8 (7.34%)	0 (0.00%)	18 (24.66 %)	0 (0.00%)	1 (1.43%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Hypervolaemia	6 (5.56%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypocalcaemia	5 (4.63%)	0 (0.00%)	7 (6.42%)	0 (0.00%)	10 (13.70 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Hypokalaemia	21 (19.44 %)	3 (2.78%)	13 (11.93 %)	0 (0.00%)	3 (4.11%)	0 (0.00%)	1 (1.43%)	1 (1.43%)	1 (2.38%)	0 (0.00%)

Hypomagnesaemia	7 (6.48%)	3 (2.78%)	3 (2.75%)	1 (0.92%)	4 (5.48%)	0 (0.00%)	0 (0.00%)	1 (1.43%)	1 (2.38%)	0 (0.00%)
Hypophosphataemia	12 (11.11 %)	1 (0.93%)	14 (12.84 %)	1 (0.92%)	7 (9.59%)	0 (0.00%)	3 (4.29%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypovolaemia	4 (3.70%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Iron deficiency	1 (0.93%)	0 (0.00%)	7 (6.42%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Metabolic acidosis	5 (4.63%)	0 (0.00%)	7 (6.42%)	1 (0.92%)	6 (8.22%)	1 (1.37%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Steroid diabetes	9 (8.33%)	0 (0.00%)	7 (6.42%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vitamin D deficiency	6 (5.56%)	1 (0.93%)	2 (1.83%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Musculoskeletal and connective tissue disorders										
Arthralgia	6 (5.56%)	0 (0.00%)	6 (5.50%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	3 (4.29%)	0 (0.00%)	3 (7.14%)	0 (0.00%)
Back pain	5 (4.63%)	2 (1.85%)	2 (1.83%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	3 (4.29%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Groin pain	1 (0.93%)	1 (0.93%)	1 (0.92%)	0 (0.00%)	5 (6.85%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Pain in extremity	3 (2.78%)	0 (0.00%)	1 (0.92%)	2 (1.83%)	2 (2.74%)	0 (0.00%)	2 (2.86%)	0 (0.00%)	3 (7.14%)	0 (0.00%)
Nervous system disorders										
Dizziness	3 (2.78%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	3 (7.14%)	0 (0.00%)
Headache	15 (13.89 %)	1 (0.93%)	11 (10.09 %)	0 (0.00%)	8 (10.96%)	1 (1.37%)	6 (8.57%)	1 (1.43%)	4 (9.52%)	0 (0.00%)
Tremor	2 (1.85%)	0 (0.00%)	5 (4.59%)	3 (2.75%)	11 (15.07 %)	0 (0.00%)	0 (0.00%)	0 (0.00%)	3 (7.14%)	0 (0.00%)
Psychiatric disorders										
Insomnia	9 (8.33%)	0 (0.00%)	8 (7.34%)	0 (0.00%)	7 (9.59%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	3 (7.14%)	0 (0.00%)
Renal and urinary disorders										

Dysuria	3 (2.78%)	1 (0.93%)	11 (10.09 %)	0 (0.00%)	8 (10.96%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Haematuria	5 (4.63%)	0 (0.00%)	7 (6.42%)	1 (0.92%)	5 (6.85%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Perinephric collection	1 (0.93%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Proteinuria	6 (5.56%)	1 (0.93%)	7 (6.42%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	6 (8.57%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Renal impairment	3 (2.78%)	1 (0.93%)	6 (5.50%)	0 (0.00%)	2 (2.74%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Respiratory, thoracic and mediastinal disorders										
Cough	11 (10.19 %)	1 (0.93%)	7 (6.42%)	1 (0.92%)	2 (2.74%)	0 (0.00%)	6 (8.57%)	0 (0.00%)	2 (4.76%)	0 (0.00%)
Dyspnoea	9 (8.33%)	0 (0.00%)	5 (4.59%)	1 (0.92%)	5 (6.85%)	0 (0.00%)	1 (1.43%)	1 (1.43%)	2 (4.76%)	0 (0.00%)
Oropharyngeal pain	10 (9.26%)	2 (1.85%)	5 (4.59%)	1 (0.92%)	2 (2.74%)	0 (0.00%)	2 (2.86%)	0 (0.00%)	4 (9.52%)	0 (0.00%)
Skin and subcutaneous tissue disorders										
Alopecia	6 (5.56%)	0 (0.00%)	1 (0.92%)	1 (0.92%)	1 (1.37%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Rash	6 (5.56%)	0 (0.00%)	2 (1.83%)	0 (0.00%)	1 (1.37%)	0 (0.00%)	2 (2.86%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Vascular disorders										
Haematoma	1 (0.93%)	0 (0.00%)	3 (2.75%)	0 (0.00%)	4 (5.48%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Hypertension	36 (33.33 %)	1 (0.93%)	29 (26.61 %)	0 (0.00%)	15 (20.55 %)	1 (1.37%)	12 (17.14%)	0 (0.00%)	1 (2.38%)	0 (0.00%)
Hypotension	12 (11.11 %)	2 (1.85%)	5 (4.59%)	0 (0.00%)	5 (6.85%)	0 (0.00%)	1 (1.43%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Lymphocele	4 (3.70%)	0 (0.00%)	7 (6.42%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)

Conclusion:

The results of the study demonstrated that CFZ533 based regimen was numerically less efficacious than a TAC based regimen for treatment of kidney transplant patients. No new safety signals were observed for CFZ533 in the study.

Date of Clinical Trial Report

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