STATISTICAL ANALYSIS PLAN

Protocol Title:	**A Randomized, Double-blind, Placebo-controlled Study to Assess the Safety, Pharmacokinetics and Efficacy of MAU868 for the Treatment of BK Viremia in Kidney Transplant Recipients**
Protocol Number:	MAU868-201
Protocol Version/Date:	Version 2.0, 15 April 2020
Investigational Product:	MAU868
Phase:	2
Sponsor:	Amplyx Pharmaceuticals, Inc. 12730 High Bluff Drive, Suite 160 San Diego, CA 92130 United States
SAP Version/Date:	Version 1.0, 27 May 2021

SIGNATURE PAGE

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This Statistical Analysis Plan is prepared by:

Sixiu Xiao — *Electronically signed by: Sixiu Xiao Reason: Approved Date: May 27, 2021 17:53 EDT* — 27-May-2021

Sixiu Xiao
Project Statistician
Medpace, Inc.

We, the undersigned, have reviewed and approved this Statistical Analysis Plan:

Signature		**Date**
Mei Chen	*Electronically signed by: Mei Chen Reason: Approved Date: May 27, 2021 18:13 EDT*	27-May-2021
Mei Chen, PhD Vice-President, Biostatistics Medpace, Inc.		
Herve Mommeja-Marin	*Electronically signed by: Herve Mommeja-Marin Reason: Approved Date: May 27, 2021 18:15 EDT*	27-May-2021
Herve Mommeja-Marin, MD Vice President, Medical Department Medpace, Inc.		
MHodg	*Electronically signed by: michael hodges Reason: Approved Date: May 27, 2021 15:49 PDT*	27-May-2021
Michael R. Hodges, MD Chief Medical Officer Amplyx Pharmaceutical, Inc.		

TABLE OF CONTENTS

LIST OF ABBREVIATIONS

Abbreviation	Definition
ADA	Antidrug antibody
AE	Adverse event
ALP	Alkaline phosphatase
ALT	Alanine transaminase
ANOVA	Analysis of variance
AST	Aspartate aminotransferase
ATC	Anatomical therapeutic chemical
BKV	BK virus
CI	Confidence interval
CSR	Clinical study report
DNA	Deoxyribonucleic acid
DSMB	Data and safety monitoring board
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
eGFR	Estimated glomerular filtration rate
I/E	Inclusion and exclusion
INR	International normalized ratio
ITT	Intent-to-Treat
IV	Intravenous
IWRS	Interactive Web Response System
KDPI	Kidney donor profile index
LLN	Lower limit of normal
LLOQ	Lower limit of quantification
LOCF	Last observation carried forward
LOD	Limit of detection
LS	Least squares
MedDRA	Medical dictionary for regulatory activities
MITT	Modified Intent-to-Treat
PCR	Polymerase chain reaction
PK	Pharmacokinetic(s)
SAE	Serious adverse event
SAP	Statistical analysis plan
SE	Standard error
SSRC	Sponsor study review committee
TEAE	Treatment-emergent adverse event
ULN	Upper limit of normal
WHO	World Health Organization

1 INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to provide a description of the statistical methods to be implemented for the analysis of data from the study with protocol number MAU868-201. The SAP will be finalized prior to database lock. Any deviations from the SAP after database lock will be documented in the final Clinical Study Report (CSR).

2 STUDY OVERVIEW

2.1 Study Objectives

2.1.1 Primary Objective

The primary objective of this study is to assess the safety and tolerability of MAU868.

2.1.2 Secondary Objectives

The secondary objectives of this study are to:

- Assess the impact of MAU868 on BK viremia and BK viremia related outcomes i.e., BK virus nephropathy, graft function and acute rejection among renal transplant recipients with BK viremia; and
- Assess the pharmacokinetics of MAU868.

2.2 Study Design

2.2.1 Overview

This is a randomized, placebo-controlled, double-blinded, proof-of-concept study in kidney transplant recipients. Up to 36 subjects with BK viremia will participate in 1 of 3 sequential cohorts. Each cohort will randomize approximately 12 subjects (8 MAU868 and 4 placebo).

The study will consist of a screening period, a 12-week treatment period and a 24-week follow up period.

Protocol-specific procedures should not be performed until the patient has consented to participation in the study. However, assessments and procedures performed as part of standard of care prior to informed consent, including determination of BK viral load in plasma may be used to qualify a patient for the study. Once qualifying BK viremia has been confirmed, subjects should be randomized as soon as possible and no more than 10 days after the sample documenting the viremia was collected.

During the treatment period, subjects will receive MAU868 or placebo approximately every 28 days (every 4 weeks) for 12 weeks (4 doses total). Urine and blood will be monitored for BKV DNA by polymerase chain reaction (PCR) weekly for the first 6 weeks after initiation of treatment. For the remainder of the treatment period, urine and blood must be collected for BKV DNA by PCR at least every other week. However, the Investigator may also request testing more frequently (i.e., weekly) than mandated by the protocol after the first 6 weeks of treatment and when clinically indicated. During the study, BKV DNA by PCR will be tested at the central laboratory. Pharmacokinetics (PK), viral resistance, and anti-drug antibodies (ADA) will also be monitored. Subjects should continue study drug until the last scheduled dose, regardless of changes in plasma

BK viral load, use of rescue therapy, and/or need for change in immunosuppressive regimen for any reason.

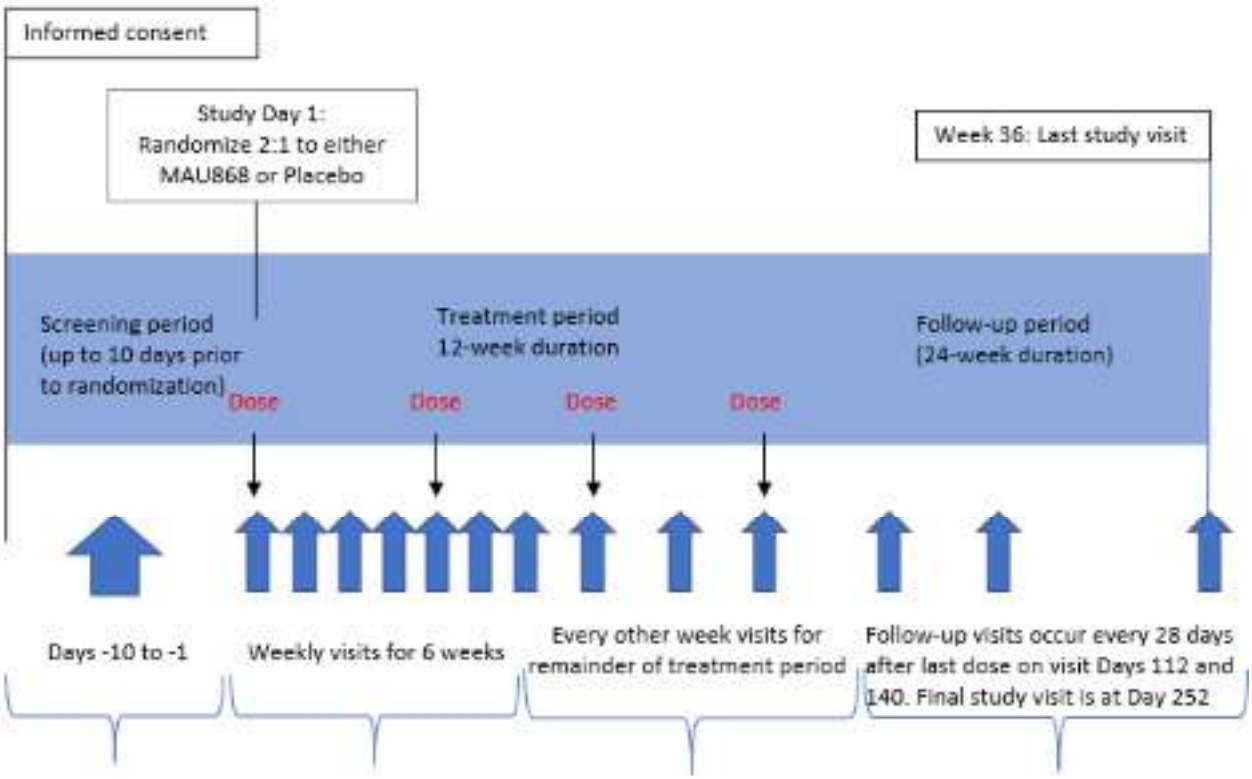
During the 24-week follow-up period, 3 follow-up visits will be scheduled. At each visit, urine and blood samples for BKV DNA and samples for PK will be collected. Investigators may collect samples for BKV DNA more often as clinically indicated. During the follow-up period, BKV DNA by PCR will be tested at the central laboratory.

Routine post-transplantation care is to be guided by the Investigator's discretion and site standard of care. This includes decisions to change the immunosuppressive regimen for a subject for any reason except for changes in immunosuppression in response to BK viremia. In order to treat BK viremia, prior to randomization, (i.e., prior to screening, during the screening period and at the Baseline Visit) Investigators are permitted to decrease or alter immunosuppressive therapy at their discretion and/or per standard of care at their site. However, in the first 4 weeks after randomization, Investigators should refrain from additional changes in immunosuppressive regimen in response to BKV unless the viral load has increased by >1 log and the Investigator determines that a change is in the best interest of the subject. Use of other antiviral agents including cidofovir and leflunomide as well as IVIG are not permitted during the first 4 weeks of therapy and are strongly discouraged thereafter.

Use of fluoroquinolones for reasons other than treatment of BKV is permitted.

Between screening and the last visit, subjects will attend a total of 14 planned visits. Unscheduled visits are permitted at the Investigator's discretion.

A schematic representing the study's design is included below.



2.2.2 Randomization and Blinding

Study participants will be randomly assigned to their treatments. Two participants will be assigned to receive treatment with MAU868 for each participant assigned to receive treatment with placebo (2:1 randomization). Randomization will occur via an Interactive Web Response System (IWRS). The Investigator or delegate will contact the IWRS after confirming that a potential study participant is eligible. The IWRS will assign a randomization number that will be used to link the subject to a treatment arm.

The randomization number is only used to identify which treatment study participants have been assigned to receive. The number assigned to a subject at screening remains the unique identifier for the subject throughout the study. The randomization numbers will be generated using procedures that ensure that treatment assignment is unbiased and concealed from the Sponsor, subjects, and Investigator staff.

This is a subject, Investigator, and Sponsor-blinded study. Subjects and Investigators will remain blinded to study treatment arm (MAU868 or placebo) throughout the study.

Drug product will be supplied in bulk, so an unblinded pharmacist, or appropriately designated study site staff who is independent of the study team, will be required in order to maintain the blind. This unblinded associate at the site will be notified by the IWRS that a subject is randomized and to which treatment arm, which will then enable and instruct them to prepare the study drug.

2.2.3 Breaking the Blind

Blinding is critical to the integrity of this clinical study. However, in the event of a medical emergency or pregnancy in an individual subject, in which knowledge of the investigational product is critical to the subject's management, the Investigator should contact the Medical Monitor to review the situation prior to breaking the blind.

Before breaking the blind of an individual subject's treatment, the Investigator should have determined that the information is necessary (i.e., that it will alter the subject's immediate management). In many cases, particularly when the emergency is clearly not investigational product related, the problem may be properly managed by assuming that the subject is receiving active product without the need for unblinding.

When the Investigator contacts the system to break a treatment code for a subject, he/she must provide the requested subject identifying information and confirm the necessity to break the treatment code for the subject. The Investigator will then receive details of the investigational drug treatment for the specified subject via the IWRS. The system will automatically inform the study monitor for the site and the Study Team that the code has been broken.

It is the Investigator's responsibility to ensure that there is a dependable procedure in place to allow access to the IWRS /code break at any time in case of emergency.

An assessment will be done by the appropriate site personnel and Sponsor after an emergency unblinding to assess whether or not study drug should be discontinued for a given subject.

In cases of accidental unblinding, contact the Medical Monitor and ensure every attempt to preserve the blind is made.

2.2.4 Study Drug

Study drug is administered only at clinical sites. All clinical sites must have the appropriate equipment and trained personnel needed to effectively manage hypersensitivity reactions including anaphylaxis and infusion reactions.

A brief description of study drug administration is listed below.

Cohort 1 MAU868 Arm:

- MAU868 1350 mg IV over at least 60 minutes approximately every 28 days for a total of 4 doses.

Cohort 2 MAU868 Arm:

- MAU868 6750 mg IV over at least 180 minutes on Study Day 1, then 1350 mg IV over at least 60 minutes for subsequent doses approximately every 28 days for a total of 4 doses.

Cohort 3 MAU868 Arm:

- MAU868 6750 mg IV over at least 180 minutes approximately every 28 days for a total of 4 doses.

Placebo

- Cohort 1: Placebo (D5W) will be administered as an IV infusion over at least 60 minutes approximately every 28 days for a total of 4 doses.
- Cohort 2: Placebo (D5W) will be administered as an IV infusion over at least 180 minutes on Day 1 and then over 60 minutes approximately every 28 days for a total of 4 infusions.
- Cohort 3: Placebo (D5W) will be administered as an IV infusion over at least 180 minutes approximately every 28 days for a total of 4 infusions.
- Placebo is prepared as a standard 250 mL volume of intravenous fluid.

All infusions will be followed by at least a 25 mL D5W flush to run at the same infusion rate as the dose of study drug.

Dose adjustments and interruptions of study drug are not permitted. Interruptions of individual infusions, however, are permitted in the event venous access becomes compromised or a subject is not tolerating the infusion. The details of any interruption of an infusion, including the reason(s), the timing, and the resumption and completion of the infusion if applicable, must be recorded in the source documents and the eCRF.

For subjects who may require a hemodialysis, plasmapheresis, or immunoadsorption treatment, it shall be assumed that the study drug has been removed. A blood sample for PK analysis should be collected prior to and following these treatments. In the event that a subject requires hemodialysis, plasmapheresis, or immunoadsorption treatments; if <15 days since last MAU868/placebo treatment another dose will be given as soon as possible, and the next scheduled monthly dose skipped. Regular dosing will occur the following month. If the last dose was 15 days or greater no interim dose will be administered, and the regular monthly schedule will be followed. No subject will receive more than 4 doses. Subjects anticipated to require hemodialysis, plasmapheresis or immunoadsorption treatment at the time of randomization should not be randomized.

2.2.5 Study Assessments

Table 1 illustrates the visit schedule and procedures of the study to be conducted at each visit.

TABLE 1: SCHEDULE OF EVENTS

	Pre-treatment[1,7]	Treatment Period[2] (12 weeks)										Follow-up Period[3] (24 weeks)		
Visit Name	**Screening**	**Baseline**	**Tx1**	**Tx2**	**Tx3**	**Tx4**	**Tx5**	**Tx6**	**Tx7**	**Tx8**	**Tx9**	**FU1**	**FU2**	**FU3/ET**
Study Weeks		**0**	**1**	**2**	**3**	**4**	**5**	**6**	**8**	**10**	**12**	**16**	**20**	**36**
Study Days	**-10 to -1**	**1[4]**	**7**	**14**	**21**	**28**	**35**	**42**	**56**	**70**	**84**	**112**	**140**	**252**
Informed consent	X													
I/E criteria	X	X												
Medical history	X													
KDPI[5]	X													
Prior and concomitant medications[6]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Demography	X													
Randomization[7]		X												
Dose administration[4,8]		X				X			X		X			
Urine for BKV PCR and resistance testing[9]		X[10]	X	X	X	X	X	X	X	X	X	X	X	X
Plasma for BKV PCR and resistance testing[11]	X	X[10]	X	X	X	X	X	X	X	X	X	X	X	X
PK sample[12,]		X[13]	X	X	X	X[14]			X[14]		X[13]	X	X	X
Anti-drug antibodies[10]		X[10]				X			X		X	X	X	X
Anti-donor antibodies[15]														
Pregnancy test[16]	X					X			X		X			X
Vital signs[17]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body height	X													
Body weight	X	X				X			X		X			X
Physical examination	X										X			X
ECG (12-lead)[18]		X									X			X

	Pre-treatment[1,7]	Treatment Period[2] (12 weeks)										Follow-up Period[3] (24 weeks)		
Visit Name	**Screening**	**Baseline**	**Tx1**	**Tx2**	**Tx3**	**Tx4**	**Tx5**	**Tx6**	**Tx7**	**Tx8**	**Tx9**	**FU1**	**FU2**	**FU3/ET**
Study Weeks		**0**	**1**	**2**	**3**	**4**	**5**	**6**	**8**	**10**	**12**	**16**	**20**	**36**
Study Days	**-10 to -1**	**1[4]**	**7**	**14**	**21**	**28**	**35**	**42**	**56**	**70**	**84**	**112**	**140**	**252**
Blood and urine for safety[19]		X[10]		X		X			X		X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X	X	X	X	X	X

BKV BK virus; PCR polymerase chain reaction; PK pharmacokinetic; ECG electrocardiogram

1. Protocol specific procedures should not be performed until the subject has consented to participation in the study. However, assessments and procedures performed as part of standard of care prior to informed consent, including determination of BK viral load in plasma may be used to qualify a subject for the study.
2. During the treatment period, subjects should be seen approximately every 7 days (+/-3 days) during the first 6 weeks and approximately every 14 days (+/-5 days) for the duration of treatment. Subjects may be seen more often at the Investigator's discretion. Visit dates are determined from the Baseline Visit.
3. During the follow-up period, if the subject cannot be seen on the precise protocol-defined study day, the acceptable visit window is +/10 days.
4. Study Day 1 is the calendar day on which the first dose of study drug is administered. Subsequent study days are based on calendar days.
5. The information necessary for determining the KDPI includes *donor* age, height, weight, ethnicity, history of hypertension, history of diabetes mellitus, cause of death, serum creatinine, hepatitis C serostatus, and whether donation occurred after circulatory death.
6. Record any and all immunosuppressive medication from induction to randomization as well as any other medications taken during the 10 days prior to randomization.
7. Randomization should occur as soon as possible after confirmation of qualifying viremia but not more than 10 days after the qualifying sample was collected. Dosing of study drug should occur as soon as possible after randomization.
8. In the event that a subject requires hemodialysis, plasmapheresis, or immunoadsorption treatments; if <15 days since last MAU868/placebo treatment another dose will be given as soon as possible, and the next scheduled monthly dose skipped. Regular dosing will occur the following month. If the last dose was 15 days or greater no interim dose will be administered and the regular monthly scheduled will be followed. No subject will receive more than 4 doses.
9. A sufficient amount of urine should be collected at each assessment to accommodate three tests; one for BKV DNA PCR, one for possible genotypic resistance testing and a back up sample. Refer to the study's Laboratory Manual for volume requirements.
10. On Study Day 1 collect samples for BKV PCR, antidrug antibodies, and safety labs prior to administration of first dose of MAU868. Refer to the study's Laboratory Manual for collection requirements.
11. After screening, plasma samples should be collected and sent to the central laboratory at each assessment for BKV DNA PCR, possible genotypic resistance testing and a backup sample. During screening, only BKV PCR is required and may be performed by the laboratory used by the site for usual clinical care, or sent to the central lab for testing. Refer to the study's Laboratory Manual for volume requirements.
12. In the event subject undergoes hemodialysis, plasmapheresis, or immunoadsorption treatment, a PK sample should be collected prior to and following the respective treatment.

13. Three PK samples should be collected on Study Day 1 (first dose administration) and Study Day 84 (last dose administration) : within approximately 30 minutes prior to the start of the infusion, within approximately 30 minutes following the end of the infusion and between approximately 3-6 hours after the end of infusion.
14. On Study days 28 and 56 (2^{nd} and 3^{rd} dose administrations), two PK samples should be collected: within 30 minutes prior to the start of infusion and within 30 minutes following the end of infusion.
15. Any anti-donor antibodies collected by the site should be recorded in the eCRF, but collection is not mandatory.
16. Only for females of child-bearing potential. A negative urine or serum pregnancy test performed locally within 96 hours prior to Study Day 1 (Baseline). Local urine dipstick or serum pregnancy testing should be performed before infusions #2 on Day 28, #3 on Day 56 and #4 on Day 84.
17. Vital signs (temperature, blood pressure, heart rate, respiratory rate and oxygen saturation) should be obtained at each visit if the visit is in person. If the visit is not in person vital signs are not required. On drug infusion days, vitals should be taken within 30 minutes before starting the infusion, and then approximately every 30 minutes (+/- 10 minutes) after the start of the infusion until at least 2 hours after completing the infusion.
18. ECGs should be performed prior to dose administration on Study Day 1 and after dose administration on Study Day 84 and on Day 252 (or at the Early Termination Visit)
19. Blood and urine for safety should be collected and sent to the central laboratory. Laboratory tests used in for the management and monitoring of the subject per standard practice may be performed at the local laboratory at the Investigator's discretion.

3 SAMPLE SIZE DETERMINATION

This study will randomize approximately 36 subjects (12 per cohort) to MAU868 and placebo in a 2:1 ratio (24 MAU868 and 12 placebo; 8 MAU868 and 4 placebo per cohort). This study is not powered to an efficacy endpoint. The number of subjects chosen will provide data useful in determining proof of concept.

4 DATA SAFETY MONITORING BOARD (DSMB)

An independent DSMB will review cumulative unblinded safety data as outlined in the DSMB charter. The DSMB will advise the Sponsor on the continuing safety of the study patients and those yet to be recruited to the study, as well as the continuing validity and scientific merit of the study. At any time, the DSMB may temporarily suspend enrollment until any significant safety concerns are resolved or terminate the study to ensure patient safety, if in the opinion of the DSMB, further dosing would pose an inappropriate safety risk.

5 SPONSOR STUDY REVIEW COMMITTEE (SSRC)

The SSRC includes a Sponsor medical representative, the Medical Monitor and a selected site Principal Investigator acting as the SSRC Chair. Approximately 12 weeks after the 9th subject in Cohort 1 has been randomized, blinded safety data will be reviewed by the SSRC to determine progression from Cohort 1 to Cohort 2. Cohort 3 will not be opened for screening and enrollment until an evaluation of unblinded safety, efficacy and pharmacokinetics findings from both Cohorts 1 and 2 through the 12-week treatment period has been completed by the SSRC.

The SSRC may recommend enrolling more than 12 subjects into a cohort (Cohort 1, 2, and/or 3) to allow adequate data collection for assessment of cohort progression and/or study objectives. Expansion of a given cohort, if needed, will not affect the size of subsequent cohort(s).

In addition, a first interim analysis on unblinded safety and tolerability data, efficacy data will be reviewed by the SSRC once all 12 subjects in Cohort 1 have completed the treatment period. Unless a significant safety issue related to administration of MAU868 has been identified, the conclusions will have no impact on Cohort 2 or the study's design.

Following completion of the 12-week treatment periods for Cohorts 1 and 2, a second interim analysis on cumulative unblinded data from both cohorts will be reviewed for safety and tolerability, efficacy and PK. Based on the SSRC's safety, efficacy and PK conclusions for Cohorts 1 and 2, the dosing regimen for Cohort 3 may be adjusted in dosage and/or duration; however, the dosage and duration for Cohort 3 will not exceed the dose already specified in the protocol.

6 STUDY ENDPOINTS

6.1.1 Safety Endpoints

Safety endpoints include physical examinations, vital signs, clinical safety laboratory parameters, 12-lead ECGs, and adverse events.

6.1.2 Efficacy Endpoints

The efficacy endpoints are the following:

- Time (weeks) to decrease of BKV plasma viral load by 1 log;
- Time (weeks) to first decrease of BKV plasma viral load to <LLOQ;
- Time (weeks) to first decrease of BKV plasma viral load to <LOD;
- Proportion of subjects with ≥1 log decrease of BKV plasma viral load by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks;
- Proportion of subjects with decrease BKV plasma viral load to <LLOQ by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks;
- Proportion of subjects with decrease BKV plasma viral load to <LOD by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks;
- Rate of decrease in BKV plasma viral load over time by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks;
- Change in eGFR from baseline to week 12, baseline to week 16 and from baseline to week 36;
- Proportion of subjects with BKV nephropathy at week 12, week 16 and 36;
- Proportion of subjects with graft failure at week 12, week 16 and 36;
- Proportion of subjects with acute rejection at week 12, week 16 and 36 ; and
- Proportion of subjects who have died at week 12, week 16 and 36.

6.1.3 Exploratory Endpoints

The exploratory endpoints include the following:

- Presence of anti-drug antibodies (ADA);
- Presence of genotypic resistance. Genotype resistance data will be described in a separate report;
- Association between BKV genotype and outcome; and
- Viral kinetics of BKV in plasma and urine including rate of decrease in BKV urine viral load over time by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks.

6.1.4 Pharmacokinetic Endpoints

The pharmacokinetic endpoints include the following:

- MAU868 serum concentrations and the pharmacokinetic parameters estimated from them.

7 STATISTICAL METHODOLOGY

7.1 General Considerations

7.1.1 Analysis Day

Analysis day will be calculated from the date of first dose of study drug. The day of the first dose of study drug will be Day 1, and the day immediately before Day 1 will be Day -1. There will be no Day 0.

7.1.2 Analysis Visits

Scheduled visits will be assigned to analysis visits as recorded on the CRF.

7.1.3 Definition of Baseline

Baseline is defined as the last measurement prior to the first dose of study drug.

7.1.4 Summary of Statistics

Summary statistics will be presented by treatment group. The placebo subjects from the cohorts will be combined. For continuous variables, the number of observations (n), mean, standard deviation, median, minimum, and maximum will be provided. For categorical variables, the frequency and percentage in each category will be displayed.

For summary statistics, the mean and median will be displayed to one decimal place greater than the original value and the measure of variability (e.g. standard deviation) will be displayed to two decimal places greater than the original value.

All efficacy analyses will be conducted using two-sided tests at the alpha=0.05 level of significance, with no adjustment for multiplicity.

7.1.5 Handling of Dropouts and Missing Data

For Viracor/Eurofins BK viral load test results in both plasma and urine, the non-numerical results will be imputed as below in the analysis:

- ‘Detected:<39 copies/mL’ will be imputed as ‘38 copies/mL’ for plasma;
- ‘Detected:<61 copies/mL’ will be imputed as ‘60 copies/mL’ for urine;
- ‘Not Detected’ will be imputed as ‘25 copies/ mL’; and
- ‘>1.00E+10 copies/ mL’ will be imputed as ‘$10^{\wedge 10}$ +1 copies/ mL’.

If there are multiple BK viral load test results for a single timepoint from both initial and back-up samples, the result from the back-up sample will be used in the analysis. If there are exceptions that require a different rule, it will be documented separately for the scenarios.

For Viracor/Eurofins BK viral load test results in both plasma and urine, missing data at each scheduled post-baseline visit will be imputed using the last post-baseline observation carried forward (LOCF) in the analysis.

Subjects who dropped out or had missing data will be included in the denominator for safety and efficacy analyses as described in Section 7.2.

In cases of missing or incomplete dates (e.g. Adverse event [AE] and concomitant medications), the missing component(s) will be assumed as the most conservative value possible. For example, AEs with missing start dates, but with stop dates either overlapping into the treatment period or missing, will be counted as treatment-emergent, taking the worst-case approach. When partial dates are present in the data, both a partial start date and/or a partial stop date will be evaluated to determine whether it can be conclusively established that the AE started prior to the start of study drug or ended prior to the start of study drug. If the above cannot be conclusively established based on the partial and/or present dates, then the AE will be considered as treatment-emergent. Actual data values as they appear in the original eCRF will be presented in the data listings.

Missing values for other variables will not be imputed and only observed values will be used in data analyses and summaries.

7.2 Analysis Populations

7.2.1 Intent-to-Treat (ITT) Population

The ITT Population includes all randomized subjects in the study.

7.2.2 Modified Intent-to-Treat (MITT) Population

The MITT Population includes subjects who had the disease under study (had renal transplant within the year with a graft that is currently functioning and have met the BK viremia protocol entry criteria [baseline BK PCR plasma viral load test result $\geq 10^3$ based on central laboratory data]), received at least 1 dose of study drug and have at least 1 post-baseline plasma BK viral load result available.

7.2.3 Safety Population

The Safety Population includes all subjects who received at least 1 dose of study drug.

7.2.4 Pharmacokinetic (PK) Population

The PK Population includes all subjects with at least 1 post-baseline PK sample available. A separate PK analysis plan will outline PK analyses.

7.3 Subject Data and Study Conduct

7.3.1 Subject Disposition

Subject disposition will be summarized by treatment group and in total for the ITT and MITT Populations. The following subject disposition categories will be included in the summary:

- Subjects who received study drug;
- Subjects who did not receive study drug;
- Subjects who completed the study drug;
- Subjects who did not complete the study drug (and reason);
- Subjects who did not complete the study drug due to the impacts of the COVID-19 pandemic;
- Subjects who completed the study;
- Subjects who did not complete the study (and reason); and
- Subjects who did not complete the study due to the impacts of the Covid-19 pandemic.

For subjects who did not complete study drug and subjects who did not complete study, a summary will be provided by reason of discontinuation. In addition, the total number of subjects for each defined analysis population will be tabulated.

Subject disposition will also be listed by treatment and subject.

7.3.2 Protocol Deviations

The number of subjects with at least one reportable protocol deviation, and the number of patients with at least one reportable deviation in each deviation category defined in the study protocol deviation plan will be presented by treatment group and in total based on the ITT and MITT Populations. In addition, the protocol deviations related to COVID-19 pandemic will be categorized and summarized separately.

Protocol deviations will also be listed by treatment and subject.

7.3.3 Demographic and Baseline Characteristics

The following demographic and baseline characteristics will be summarized:

- Age (years) and age categories (<65 years vs. ≥65 years);
- Sex;
- Race;
- Ethnicity
- Height (cm);
- Weight (kg);
- Body mass index (BMI) (kg/m^2) ;
- eGFR based on the CK-EPI equation ($mL/min/1.73m^2$) and eGFR categories (<15, 15-<30, 30-<60, 60-<90, and >=90);
- Living donor (Yes vs. No);
- Pre-existing BKV nephropathy (Yes);

  Note: Pre-existing BKV nephropathy can be identified based on the following CRF data:

  - Medical history using the preferred term 'Polyomavirus-associated nephropathy'; and
  - Clinical outcome assessments indicating subjects developed or possibly developed BKV associated nephropathy at Baseline visit.
- Time from kidney transplant (days);

  Time from kidney transplant (days) is calculated as the first dose date of study drug - date of kidney transplant;
- Baseline plasma viral load (copies/mL);
- Duration of BK viremia

  Duration of BK viremia (days) is calculated as the first dose date of study drug - date of first reported BK plasma positive PCR

  Note: the first reported BK plasma positive PCR is based on CRF data of Historical BKV Blood Sample Results and the quantitative result in copies/mL $\geq 10^3$.
- BKV genotype

Demographic and Baseline characteristics will be summarized with descriptive statistics or counts and percentages of subjects as appropriate for the ITT, MITT, and Safety Populations. Other parameters of Kidney donor profile index (KDPI) will be listed.

7.3.4 Medical History

Medical history will be coded to system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA, Version 22.1). Counts and percentages of subjects with medical history by system organ class and preferred term will be summarized by treatment based on the ITT, MITT and Safety Populations.

All medical history will be listed by treatment and subject.

7.3.5 Concomitant Medications

Prior and Concomitant medications will be coded to anatomical therapeutic chemical (ATC) class and preferred term using the World Health Organization (WHO) Drug Dictionary (September 2019G B3).

Prior medications are medications used before the first dose of study drug. Concomitant medications are medications that were taken on or after first dose of study drug. Any medications used before first dose of study drug and continued will be counted as both prior and concomitant medications.

The number and percentages of patients who receive the following prior and concomitant medications will be summarized by ATC class and preferred term based on ITT, MITT, and Safety Populations:

- Prior medications;
- Concomitant medications;
- Prior immunosuppressive agents with dose decreased or discontinued due to BKV;
- Concomitant immunosuppressive agents with dose decreased or discontinued due to BKV;
- Prior immunosuppressive agents with clinically significant decrease in dose or discontinuation;
- Concomitant immunosuppressive agents with clinically significant decrease in dose or discontinuation.

All prior and concomitant medications will be listed by treatment and subjects.

Any clinically significant (based on blinded review of medical monitor) decrease in dose or discontinuation of prior or concomitant immunosuppressive medication will be described regardless of whether the reason was due to BKV or not.

7.3.6 Study Drug Exposure

All study drug will be administered by IV infusion. Days of exposure to study drug will be calculated as the last dose date of study drug – first dose date of study drug + 1. The days of exposure to study drug will be summarized based on the Safety and MITT Populations with

descriptive statistics and with counts and percentages of subjects with exposure in the following categories:

- ≤28 days
- >28 to ≤56 days
- >56 to ≤84 days
- >84 days

Total number of doses received will be summarized based on the Safety and MITT Populations with counts and percentages of subjects in the following categories: 1, 2, 3, and 4 doses.

7.4 Safety Assessment

Safety data will be summarized based on the Safety Population.

7.4.1 Adverse Events (AEs)

AEs will be captured from the date of informed consent through study completion. All AEs will be coded to system organ class and preferred term using the MedDRA, Version 22.1. Treatment-emergent adverse events (TEAEs) are defined as AEs that start on or after the administration of study drug.

An overview of AEs will be provided including counts and percentages of subjects (and event counts) with the following:

- Any AEs;
- Any infusion reactions;
- Any TEAEs (overall and by maximum severity);
- Any study drug-related TEAEs (overall and by maximum severity);
- Any TEAEs leading to discontinuation of study drug;
- Any TEAEs leading to discontinuation of the study;
- Any serious AEs (SAEs) (overall and by maximum severity);
- Any treatment-emergent SAEs (TESAEs);
- Any study drug-related treatment-emergent SAEs (TESAEs);
- Any death.

The number and percentage of subjects who experienced at least one TEAE will be presented by system organ class and preferred term. Drug-related TEAEs, study drug withdrawals due to TEAEs, study discontinuation due to TEAEs, and all SAEs will be summarized in the same manner.

Summaries will be provided by worst grade for the number and percentage of subjects with TEAEs and for subjects with drug-related TEAEs by system organ class and preferred term.

Although a subject may have two or more TEAEs, the subject is counted only once within a system organ class and preferred term category. The same subject may contribute to two or more preferred terms in the same system organ class category.

A list of patients who have SAEs, a list of patients who discontinue from study drug due to TEAEs, and a list of death due to AEs will be provided. All adverse events will be listed.

7.4.2 Clinical Laboratory Tests

Central laboratory test results (chemistry, hematology, coagulation, and urinalysis) at each scheduled visit and change from baseline will be summarized with descriptive statistics. See Appendix A for a complete list of clinical laboratory analytes.

Shift tables from baseline to each scheduled post-baseline visit will be provided for selected chemistry parameters (ALT, AST, ALP, Total Bilirubin, Creatinine, Creatinine Kinase, Sodium, Potassium, Bicarbonate, Calcium, and Phosphorus) and hematology parameters (Hematocrit, Hemoglobin, Platelets, White blood cell count and differential). For chemistry parameters, the following categories will be used: < the lower limit of normal (LLN), normal, >ULN to ≤2×ULN, >2×ULN to ≤3×ULN, >3×ULN to ≤5×ULN, >5×ULN, and missing. For hematology parameters, the following categories will be used: low, normal, high, and missing.

The number and percentage of patients with the following potentially clinically significant abnormal liver function tests at any post-baseline visit will be summarized:

- ALT ≥3×ULN
- ALT ≥5×ULN
- ALT ≥10×ULN
- AST ≥3×ULN
- AST ≥5×ULN
- AST ≥10×ULN
- ALT or AST ≥3×ULN
- Total Bilirubin >1.5×ULN
- Total Bilirubin >2×ULN
- ALT or AST ≥3×ULN and Total Bilirubin >1.5×ULN
- ALT or AST ≥3×ULN and Total Bilirubin >2×ULN
- Potential Hy's Law cases: ALT or AST ≥3×ULN and Total Bilirubin >2×ULN, and ALP ≤ 2×ULN

A listing of subjects with any post-baseline clinically significant abnormal liver function tests will be presented.

All clinical laboratory data will be listed. Values outside the normal ranges will be flagged.

7.4.3 Vital Signs

Descriptive statistics will be provided for vital sign data (systolic and diastolic blood pressure, heart rate, respiratory rate, body temperature, and oxygen saturation) presented as both actual values and changes from baseline for each scheduled visit.

The number and percentage of patients with the following potentially clinically significant abnormal vital signs at any post-baseline visit will be summarized:

- SBP ≥180 mmHg and Increase ≥20 mmHg from Baseline
- SBP ≤90 mmHg and Decrease ≥20 mmHg from Baseline or SBP decrease >40 mmHg from baseline
- DBP ≥150 mmHg and Increase ≥15 mmHg from Baseline
- DBP ≤50 mm Hg and Decrease ≥15 mm Hg from Baseline
- HR ≥120 bpm and Increase ≥15 bpm from Baseline
- HR ≤50 bpm and Decrease ≥15 bpm from Baseline

A listing of all vital signs will be provided by treatment and subject.

7.4.4 Electrocardiograms

Descriptive statistics will be provided by treatment for 12-lead ECG interval data (Heart rate, PR interval, QRS duration, QT interval, and RR interval) and changes from baseline for each scheduled visit. The ECG overall interpretation categories (Normal, Abnormal not clinically significant, and Abnormal clinically significant) will be summarized by visit.

All ECG measurements and the overall interpretation will be listed by treatment and subject.

7.4.5 Physical Examinations

Physical examination data will be listed by treatment and subject.

7.4.6 Other Safety Assessments

Other safety assessments not summarized in the sections above will be listed by treatment and subject.

7.5 Efficacy Assessment

The efficacy analysis will be performed based on the MITT Population and will be repeated on the ITT Population.

In efficacy analyses, pairwise contrasts comparing each of the three active groups to the combined placebo group will be tested. Efficacy analyses will be conducted using two sided tests at the alpha=0.05 level of significance, with no adjustment for multiplicity.

7.5.1 Efficacy Endpoints

7.5.1.1 Time (weeks) to First Decrease of BKV Plasma Viral Load by 1 Log

Time (weeks) to first decrease of BKV plasma viral load by >1 log is defined as the number of days from first dose date of study drug to the first decrease of BKV plasma viral load during the study by 1 log from baseline plus 1, then divided by 7.

Subjects who did not have a decrease of BKV plasma viral load by >1 log at any post-baseline visits, discontinued from the study, or died will be considered censored. For the censored subjects, the last assessment date will be used as the date of censoring.

The number and percentage of subjects with a decrease of BKV plasma viral load by 1 log during the study and subjects who are censored will be tabulated. Time to first decrease of BKV plasma viral load by 1 log will be summarized using descriptive statistics.

The median time to first decrease of BKV plasma viral load by 1 log and associated 95% confidence interval (CI) will be estimated for each treatment group using the Kaplan-Meier method. The estimate of the hazard ratio for the treatment comparison between each treatment dose group and the combined placebo group along with the 95% CI will be calculated using a Cox proportional hazard model with treatment (four levels) as a factor. The log-rank p-value for the treatment comparison will be presented as well.

Time (weeks) to first decrease of BKV plasma viral load by >1 log will also be summarized by baseline BKV genotype.

7.5.1.2 Time (weeks) to First Decrease of BKV Plasma Viral Load to <LLOQ

The lower limit of quantitation (LLOQ) of BKV plasma viral load is 39 copies/mL BK virus DNA detected <LLOQ will be reported as 'Detected:<39 copies/mL' in data.

Time (weeks) to first decrease of BKV plasma viral load to <LLOQ is defined as the number of days from first dose date of study drug to the first decrease of BKV plasma viral load to <LLOQ during the study plus 1, then divided by 7.

Subjects who did not have a decrease of BKV plasma viral load to <LLOQ at any post-baseline visits, discontinued from the study, or died will be considered censored. For the censored subjects, the last assessment date will be used as the date of censoring.

The number and percentage of subjects with a decrease of BKV plasma viral load to <LLOQ during the study and subjects who are censored will be tabulated. Time to first decrease of BKV plasma viral load to <LLOQ will be summarized using descriptive statistics.

The median time to first decrease of BKV plasma viral load to <LLOQ and associated 95% CI will be estimated for each treatment group using the Kaplan-Meier method. The estimate of the hazard ratio for the treatment comparison between each treatment dose group and the combined placebo group along with the 95% CI will be calculated using a Cox proportional hazard model with treatment (four levels) as a factor. The log-rank p-value for the treatment comparison will be presented as well.

Time (weeks) to first decrease of BKV plasma viral load to <LLOQ will also be summarized by baseline BKV genotype.

7.5.1.3 Time (weeks) to First Decrease of BKV Plasma Viral Load to <LOD

The limit of detection (LOD) of BKV plasma viral load is 26 copies/mL. BK virus DNA detected <LOD will be reported as 'Not Detected' in data.

Time (weeks) to first decrease of BKV plasma viral load to <LOD is defined as the number of days from first dose date of study drug to the first decrease of BKV plasma viral load to <LOD during the study plus 1, then divided by 7.

Time (weeks) to first decrease of BKV plasma viral load to <LOD will be analyzed in the same manner as Time (weeks) to first decrease of BKV plasma viral load to <LLOQ.

7.5.1.4 Proportion of Subjects with ≥1 log Decrease of BKV Plasma Viral Load by Visit

The number and percentage of subjects with ≥1 log decrease of BKV plasma viral load by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks will be tabulated. The last observation by the specified timepoint will be used to identify '≥1 log decrease of BKV plasma viral load'.

The proportion of subjects with ≥1 log decrease of BKV plasma viral load by the specified visit will be analyzed using a logistic regression model with treatment (four levels) as a factor. For the treatment comparison between each treatment dose group and combined placebo group, the estimated odds ratio, 95% CI, and p-value will be presented.

In addition, the pairwise treatment comparisons in the proportion will be made using Fisher's Exact Test. The treatment difference estimates, the exact 95% CI, and p-values from Fisher's Exact Test will be presented.

The proportion of subjects with ≥1 log decrease of BKV plasma viral load by the specified visit will also be summarized by baseline BKV genotype.

7.5.1.5 Proportion of Subjects with Decrease of BKV Plasma Viral Load to <LLOQ by Visit

The number and percentage of subjects with decrease of BKV plasma viral load to <LLOQ by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks will be tabulated. The last observation by the specified timepoint will be used to identify 'decrease of BKV plasma viral load to <LLOQ'.

The proportion of subjects with decrease of BKV plasma viral load to <LLOQ by the specified visit will be analyzed using a logistic regression model with treatment (four levels) as a factor. For the treatment comparison between each treatment dose group and combined placebo group, the estimated odds ratio, 95% CI, and p-value will be presented.

In addition, the pairwise treatment comparisons in the proportion will be made using Fisher's Exact Test. The treatment difference estimates, the exact 95% CI, and p-values from Fisher's Exact Test will be presented.

The proportion of subjects with decrease of BKV plasma viral load to <LLOQ by the specified visit will also be summarized by baseline BKV genotype.

7.5.1.6 Proportion of Subjects with Decrease of BKV Plasma Viral Load to <LOD by Visit

The number and percentage of subjects with decrease of BKV plasma viral load to <LOD by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks will be tabulated. The last observation by the specified timepoint will be used to identify 'decrease of BKV plasma viral load to <LOD'.

The proportion of subjects with decrease of BKV plasma viral load to <LOD by visit will be analyzed in the same manner as the proportion of subjects with decrease of BKV plasma viral load to <LLOQ by visit.

7.5.1.7 Rate of Decrease in BKV Plasma Viral Load by Visit

Rate of decrease in BKV plasma viral load is calculated using the following formula:

Rate of decrease = Change from baseline (copies/mL) / time (weeks) between baseline and post-baseline.

The BKV plasma viral load at 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks with LOCF, change from baseline and rate of decrease will be summarized with descriptive statistics.

Treatment difference in the rate of decrease between each treatment dose group and combined placebo group will be assessed at the specified visit with LOCF using an ANOVA model with treatment (four levels) as a factor. The least squares (LS) mean, SE, 95% CI, and p-value will be obtained from the model estimates. The normality of the residuals from the ANOVA model will be assessed using the Shapiro-Wilk statistic and graphical examination. If data shows significant deviation from normality, the Wilcoxon rank sum test will be applied if necessary.

In addition, the pairwise treatment differences will be analysed using the two-sample t test. The p-value from each t test will be presented.

7.5.1.8 Change in eGFR from Baseline to Week 12, Week 16 and Week 36

eGFR is calculated using the CK-EPI equation. The eGFR at Week 12, Week 16 and Week 36 with LOCF, change from baseline will be summarized with descriptive statistics.

Treatment difference in the eGFR change from baseline between each treatment dose group and combined placebo group will be assessed at Week 12, Week 16 and Week 36 with LOCF using an ANOVA model with treatment (four levels) as a factor. The LS mean, SE, 95% CI, and p-value will be obtained from the model estimates. The normality of the residuals from the ANOVA model will be assessed using the Shapiro-Wilk statistic and graphical examination. If data shows significant deviation from normality, the Wilcoxon rank sum test will be applied if necessary.

In addition, the pairwise treatment differences will be analysed using the two-sample t test. The p-value from t test will be presented.

7.5.1.9 Proportion of Subjects with BKV Nephropathy by Week 12, Week 16 and Week 36

The number and percentage of subjects with BKV nephropathy by Week 12, Week 16 and Week 36 based on renal biopsy, clinical diagnosis or other method of diagnosis as reported in the eCRF

will be tabulated and summarized by whether BKV nephropathy was confirmed by biopsy or diagnosed clinically in the absence of biopsy results. All instances of biopsies demonstrating BKV nephropathy will be reported in the CSR, however cases of biopsy-proven BKV nephropathy in patients with no pre-study biopsy, stable or improvement serum creatinine and improving BKV plasma viral loads will be excluded from the summary to avoid counting patients who most likely had BKV nephropathy prior to study entry. Exclusion of these patients from the summary will be based on the opinion of the SSRC and documented.

The method of diagnosis during the study reported in eCRF will be summarized at an overall post-baseline visit. If the subjects have different methods of diagnosis reported at different post-baseline visits, the same subject will be counted in the different methods of diagnosis.

The proportion of subjects with BKV nephropathy by Week 12, Week 16 and Week 36 will be analyzed using a logistic regression model with treatment (four levels) as a factor. For the treatment comparison between each treatment dose group and combined placebo group, the estimated odds ratio, 95% CI, and p-value will be presented.

In addition, the pairwise treatment comparisons in the proportion will be made using Fisher's Exact Test. The treatment difference estimates, the exact 95% CI, and p-values from Fisher's Exact Test will be presented.

7.5.1.10 Proportion of Subjects with Graft Failure by Week 12, Week 16 and Week 36

The number and percentage of subjects with graft failure (i.e., permanent requirement for renal replacement therapy) by Week 12, Week 16 and Week 36 will be tabulated.

The proportion of subjects with graft failure by Week 12, Week 16 and Week 36 will be analyzed using a logistic regression model with treatment (four levels) as a factor. For the treatment comparison between each treatment dose group and combined placebo group, the estimated odds ratio, 95% CI, and p-value will be presented.

In addition, the pairwise treatment comparisons in the proportion will be made using Fisher's Exact Test. The treatment difference estimates, the exact 95% CI, and p-values from Fisher's Exact Test will be presented.

7.5.1.11 Proportion of Subjects with Acute Rejection by Week 12, Week 16 and Week 36

The number and percentage of subjects with acute rejection (based on kidney biopsy results and 2017 Banff Kidney Meeting Report) by Week 12, Week 16 and Week 36 will be tabulated.

The proportion of subjects with acute rejection by Week 12, Week 16 and Week 36 will be analyzed using a logistic regression model with treatment (four levels) as a factor. For the treatment comparison between each treatment dose group and combined placebo group, the estimated odds ratio, 95% CI, and p-value will be presented.

In addition, the pairwise treatment comparisons in the proportion will be made using Fisher's Exact Test. The treatment difference estimates, the exact 95% CI, and p-values from Fisher's Exact Test will be presented.

7.5.1.12 Mortality Rate/Survival by Week 12, Week 16 and Week 36

Time (weeks) to death is defined as the number of days from first dose date of study drug to the date of death during the study plus 1, then divided by 7.

Subjects who are alive by Week 12, Week 16 and Week 36, not known to die, or lost to follow-up will be censored on the last date the subject is known to be alive.

The number and percentage of subjects who died by Week 12, Week 16 and Week 36 and subjects who are censored will be tabulated. Time (weeks) to death will be summarized using descriptive statistics.

The median time to death by Week 12, Week 16 and Week 36 and associated 95% CI will be estimated for each treatment group using the Kaplan-Meier method. The estimate of the hazard ratio for the treatment comparison between each treatment dose group and the combined placebo group along with the 95% CI will be calculated using a Cox proportional hazard model with treatment (four levels) as a factor. The log-rank p-value for the treatment comparison will be presented as well.

7.5.2 Exploratory Endpoints

7.5.2.1 Proportion of Subjects with Presence of Anti-Drug Antibodies (ADA) at Any Time during the Study

The number and percentage of subjects with presence of anti-drug antibodies (ADA) at any post-baseline visits during the study will be summarized descriptively.

All ADA data will be listed by treatment and subject.

7.5.2.2 Presence of genotypic resistance

The presence of genotypic resistance and association between genotypic resistance and outcome will be an exploratory endpoint described in a separate report.

7.5.2.3 Viral Kinetics of BKV in Plasma and Urine

The BKV plasma and urine viral load, change from baseline and rate of decrease over time by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks will be summarized with descriptive statistics. Missing data at each scheduled post-baseline visit will be imputed using the LOCF approach. The corresponding line plots of the plasma and urine BKV viral load over time will be presented by treatment group and study visit.

All plasma and urine BKV viral load data will be listed by treatment and subject.

7.5.3 Other Efficacy Data

All other efficacy data will be listed by treatment and subject.

7.6 Pharmacokinetic Assessment

All pharmacokinetic analyses will be performed by another vendor and described in a standalone PK analysis plan.

The PK of MAU868 will be assessed by fitting a compartmental model to each subject's full set of data, i.e. data collected over the full course of treatment. The specific model will be determined from the data and will be parameterized in terms of clearance(s) and volume(s) of distribution. Additional parameters such as area under the curve and distribution and/or elimination half-lives will also be estimated. Relationships between PK parameters and subject covariates such as age, gender, weight, etc., will be examined as appropriate.

8 INTERIM ANALYSIS

8.1 First Interim Analysis

Following completion of the 12-week treatment period of Cohort 1, unblinded safety and tolerability data (adverse events, clinical laboratories, vitals/physical exams and ECGs), efficacy data (BKV viral load in the plasma) and PK (MAU868 plasma levels) will be provided in the form of individual subject case data packages and reviewed by the SSRC. The treatment assignment in Cohort 1 will be unblinded; however, these data will not include associated subject or site identifiers. The objectives of this interim analysis/this data review are to evaluate whether four doses MAU868 1350 mg IV administered every 28 days for a total of 4 doses demonstrate:

- safety and tolerability signals compared to placebo
- a decrease in BK plasma viral load compared to placebo
- predicted MAU868 plasma levels

The conclusions from this first interim analysis will be used by the Sponsor to evaluate the safety and efficacy of MAU868 early-on in this first-in-patient study. Unless a significant safety issue related to administration of MAU868 has been identified, the conclusions will have no impact on Cohort 2 or the study's design.

For the first interim analysis, unblinded programmed patient profiles will be provided.

8.2 Second Interim Analysis

Following completion of the 12-week treatment periods for Cohorts 1 and 2, cumulative unblinded programmed data from both cohorts will be reviewed for safety and tolerability (adverse events, clinical laboratories, vitals/physical exams and ECGs), efficacy (BKV viral load in the plasma) and PK (MAU868 plasma levels). The objectives of this second interim analysis are to evaluate whether four doses MAU868 1350 mg IV administered every 28 days for a total of 4 doses or MAU868 6750 mg IV administered as a first dose followed by 3 more doses of MAU868 1350 mg IV administered every 28 days demonstrate:

- safety and tolerability signals compared to placebo
- a decrease in viral load compared to placebo

- predicted MAU868 plasma levels

Based on the SSRC's assessment of safety and tolerability and the sponsor assessment of the safety and tolerability, efficacy and PK conclusions for Cohorts 1 and 2, the dosing regimen for Cohort 3 may be adjusted in dosage and/or duration; however, the dosage and duration for Cohort 3 will not exceed the dose already specified in the protocol. Cohort 3 will not be opened for screening and enrollment this evaluation has been completed.

For the second interim analysis, cumulative unblinded programmed patient profiles will be provided. In addition, the programmed statistical tables and listings for Cohorts 1 and 2 will be presented.

8.2.1 Cohorts 1 & 2: Safety and Tolerability

Physical examinations, vital signs, clinical safety laboratory parameters, concomitant procedures and medications, and adverse events will be assessed by the SSRC via programmed statistical tables and listings for both Cohorts 1 and 2.

8.2.2 Cohorts 1 & 2: Response to Study Treatment

The following efficacy endpoints are included in the second interim analysis and will be assessed by the SSRC for subjects in Cohorts 1 and 2. The analysis will be performed based on the MITT Population and will be repeated on the ITT Population.

- Time (weeks) to decrease of BKV plasma viral load by 1 log;
- Time (weeks) to first decrease of BKV plasma viral load to <LLOQ ;
- Proportion of subjects with ≥1 log decrease of BKV plasma viral load by 1 week, 2 weeks, 4 weeks, 8 weeks, and 12 weeks;
- Proportion of subjects with decrease of BKV plasma viral load to <LLOQ by 1 week, 2 weeks, 4 weeks, 8 weeks, and 12 weeks;
- Rate of decrease in BKV plasma viral load by 1 week, 2 weeks, 4 weeks, 8 weeks, and 12 weeks;
- Change in eGFR from baseline to week 12;
- Proportion of subjects with BKV nephropathy through week 12;
- Proportion of subjects with graft failure through week 12;
- Proportion of subjects with acute rejection through week 12;
- Proportion of subjects who have died through week 12.

In the efficacy analyses, pairwise contrasts comparing each of the two active groups to the combined placebo group will be tested. The treatment groups will be 3 levels (i.e. Cohort 1 active group, Cohort 2 active group and combined placebo group). The analyses will be conducted using two sided tests at the alpha=0.05 level of significance, with no adjustment for multiplicity.

The efficacy endpoints above for the second interim analysis will be summarized and analyzed in the same manner as described in Section 7.5.1 with the exception that Cohort 3 subjects will not be included in the interim analysis.

8.2.3 Pharmacokinetics Cohort 1 and 2

MAU868 serum concentrations through Week 16 will be evaluated by the SSRC for both Cohorts 1 and 2. The pharmacokinetic analyses will be performed by another vendor and described in a standalone PK analysis plan.

9 CHANGES FROM PROTOCOL-SPECIFIED STATISTICAL ANALYSES

The following changes are made in the SAP compared to the description in the protocol as clarification:

- Changed the MITT Population definition 'subjects who received at least 1 dose of study drug and has at least 1 post-baseline plasma BK viral load result available' to be 'subjects who had the disease under study (had renal transplant within the year with a graft that is currently functioning and have met the BK viremia protocol entry criteria [baseline BK PCR plasma viral load test result ≥103 based on central laboratory data]), received at least 1 dose of study drug and have at least 1 post-baseline plasma BK viral load result available.'.

- Added the following efficacy endpoints:
  - Time (weeks) to first decrease of BKV plasma viral load to <LOD;
  - Proportion of subjects with decrease BKV plasma viral load to <LOD by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks.
- Added 'Week 16' in the following efficacy endpoints:
  - Proportion of subjects with ≥1 log decrease of BKV plasma viral load by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks and 36 weeks;
  - Proportion of subjects with decrease BKV plasma viral load to <LLOQ by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks and 36 weeks;
  - Proportion of subjects with decrease BKV plasma viral load to <LOD by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks and 36 weeks;
  - Rate of decrease in BKV plasma viral load over time by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks and 36 weeks;
  - Change in eGFR from baseline to week 12 and from baseline to week 36;
- Added 'Week 12, Week 16, and Week 36' in the following efficacy endpoints:
  - Proportion of subjects with BKV nephropathy;
  - Proportion of subjects with graft failure during the study;
  - Proportion of subjects with acute rejection during the study; and
  - Mortality rate during the study.
- Added 'rate of decrease in BKV plasma and urine viral load over time by 1 week, 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 36 weeks' in the exploratory endpoints.

- Added presence of genotype and genotypic resistance and association with outcome in the exploratory endpoints, which will be described in a separate report.

10 PROGRAMMING SPECIFICATIONS

Analyses will be performed using SAS® version 9.3 or higher. All available data will be presented in subject data listings which will be sorted by subject and visit date as applicable. Detailed Programming Specifications will be provided in a separate document.

Appendix A: Clinical Safety Laboratory Analytes

Standard Safety Chemistry Panel

Alanine aminotransferase	Albumin
Alkaline phosphatase	Amylase
Aspartate aminotransferase	Bicarbonate
Blood urea nitrogen	Calcium
Chloride	Creatine kinase
Creatinine	Estimated glomerular filtration rate
Gamma-glutamyl transferase	Glucose
Inorganic phosphorus	Lactate dehydrogenase
Lipase	Potassium
Sodium	Bilirubin (total, direct, and indirect)
Total protein	Uric acid

Hematology

Hematocrit	Hemoglobin
Platelets	Red blood cell count
White blood cell count and differential [1]	

1. Manual microscopic review is performed only if white blood cell count and/or differential values are out of reference range.

Coagulation

Prothrombin time	International normalized ratio (INR)
Activated Partial Thromboplastin Time (aPTT)	

Urinalysis

Bilirubin	Blood
Glucose	Ketones
Leukocyte esterase	Microscopy [1]
Nitrite	pH
Protein	Specific gravity
Urobilinogen	

2. Microscopy is performed only as needed based on positive dipstick test results.

Other Tests

Urine or serum pregnancy test [1]	

1. Women of childbearing potential only.