Study of Tacrolimus vs Mycophenolate Mofetil in Pediatric Patients with Frequently Relapsing or Steroid-dependent Nephrotic Syndrome: a Prospective, Randomized, Multicenter, Open-label, and Parallel-arm Study on Efficacy and Safety (the STAMP study)

Statistical Analysis Plan

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Study title	Study of Tacrolimus vs Mycophenolate Mofetil in Pediatric Patients with Frequently Relapsing or Steroid-dependent Nephrotic Syndrome: a Prospective, Randomized, Multicenter, Open-label, and Parallel-arm Study on Efficacy and Safety
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I have read this plan and confirm that it accurately describes the implementation plan for the statistical analysis of the study.

SAP prepared by (signature): _____

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CONTENTS

1. Abbreviations

Abbreviations	Description
ALT	Alanine aminotransferase
ALB	Albumin
AUC	Area under curve
ACEi	Angiotensin converting enzyme inhibitor
ARB	Angiotensin II receptor blocker
AE	Adverse event
ANCOVA	Analysis of covariance
BID	Bis in die
CMV	Cytomegalovirus
CsA	Cyclosporin A
CR	Complete remission
CSR	Clinical Study Report
CRF	Case Report Form
CMH	Cochran's and Mantel-Haenszel
DAE	Drug adverse event
EB	Epstein-Barr
EBV-DNA	Epstein-Barr virus deoxyribonucleic acid
eGFR	Glomerular filtration rate
eCRF	Electronic Case Report Form
FAS	Full analysis set
FR	Frequent relapse
FDA	Food and Drug Administration
FK506	Tacrolimus
FK-BP-12	Tacrolimus binding protein-12
FK-BP-52	Tacrolimus binding protein-52

FK506-FKBP	Tacrolimus - tacrolimus binding protein
FRNS	Frequently relapsing nephrotic syndrome
GCP	Good Clinical Practice
g	Gram
GTP	Guanine nucleotide
HBV	Hepatitis B virus
HbsAg	Hepatitis B surface antigen
HbeAg	Hepatitis B E antigen
HbcAb	Hepatitis B core antigen
HCV	Hepatitis C virus
hr	Hour
ITT	Intentionality
LSMEAN	Least squares mean
LC-MS	Liquid chromatography-mass spectrometry
MMF	Mycophenolate mofetil
MPA	Mycophenolic acid
MPA-d3	Mycophenolic acid-d3
MPA-AUC	Mycophenolic acid - Area under curve
MI	Myocardial infarction
mg	Milligram
NR	No remission
PP	Per-protocol
PR	Partial remission
PML	Progressive multifocal leukoencephalopathy
PRCA	Pure red cell aplasia
PPS	Per-protocol set
SAS 9.4	STATISTICAL ANALYSIS SYSTEM Version 9.4
SD	Steroid-dependent

SDNS	Steroid-dependent nephrotic syndrome
SRNS	Steroid-resistant nephrotic syndrome
SCV	Site close-out visit
SAE	Serious adverse event
SOP	Standard Operation Procedures
SS	Safety set
Scr	Serum creatinine
TBiL	Total bilirubin
TIMP-1	Tissue inhibitor of metalloproteinase-1
TIA	Transient ischemic attack
WHO	World Health Organization
WBDC	Web-based data collection
α	Inspection level
β	Power of test
δ	Cut-off value

2. Study title

Study of Tacrolimus vs Mycophenolate Mofetil in Pediatric Patients with Frequently Relapsing or Steroid-dependent Nephrotic Syndrome: a Prospective, Randomized, Multicenter, Open-label, and Parallel-arm Study on Efficacy and Safety

3. Study objectives and endpoints

3.1 To evaluate the efficacy of the test drugs on the frequently relapsing or steroid-dependent nephrotic syndrome in pediatric patients

Efficacy outcomes:

Primary observation outcomes: 1-year relapse-free survival

Secondary observation outcomes: Renal function; cumulative steroid dosage; blood pressure;

height; weight; blood lipids; hemoglobin; serum albumin; urinary protein/creatinine (morning urine); 24hr urinary protein quantification (applicable to subjects > 3 years old); frequency of relapses; the time of the first relapse after enrollment; relapse-free survival in the first six months after enrollment; adverse reactions;

3.2 To assess the safety outcomes of test drugs

Changes of vital signs (respiration and heart rate), routine blood and urine tests, liver function, renal function, blood glucose, ECG, chest X-ray, and observation of clinically reported adverse events and adverse reactions.

4. Study design

4.1. Design overview

This trial is a prospective, randomized, multicenter, open-label, parallel-arm clinical study, using the Logrank method to compare the difference of 1-year relapse free survival between the two groups. Enrollment was completed by 12 sites using competitive enrollment. The whole observation period is 1 year for this trial. Eligible patients who sign the informed consent form will be randomly divided into FK506 Group or MMF Group at the ratio of 1:1. Both groups follow the "clinical trial flow chart" in operation.

4.2. Design principle and case allocation

4.2.1 Difference analysis

In this research, Logrank method is used to compare the difference of 1-year relapse-free survival between the two groups.

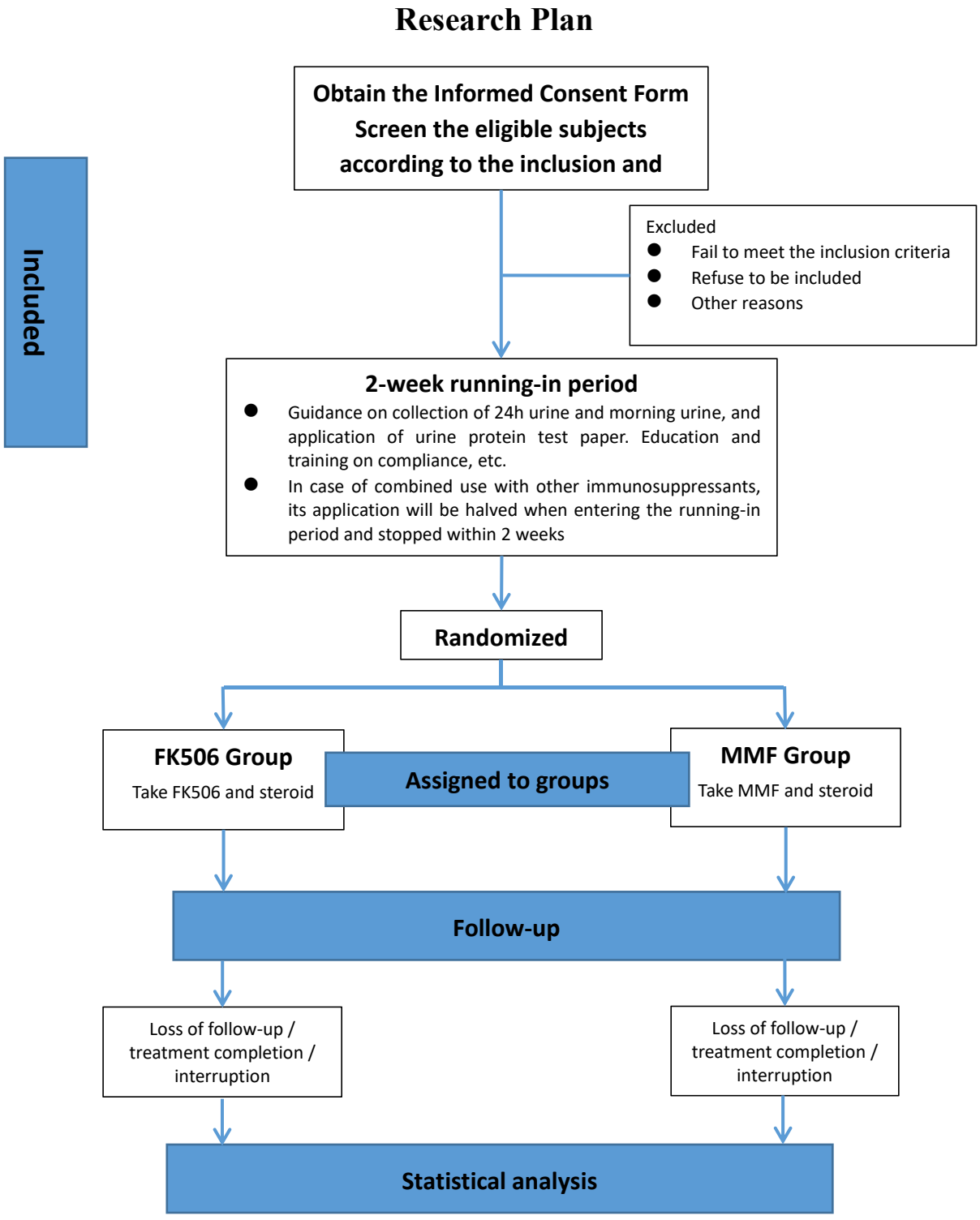
Eligible patients will be randomly divided into FK506 Group or MMF Group at the ratio of 1:1. The random codes are generated by the computer and the random envelopes are made according to these random codes. Grouping information is attached in each envelope. Each code is provided with a corresponding random envelope, and the random numbers are given to the subjects from small to large according to the time sequence when the subjects meet the inclusion criteria. The

corresponding random envelopes can only be opened when grouping. Any random number falling off midway after use cannot be used again.

4.2.2 Determination of the number of cases

It is estimated that 1-year relapse-free survival is 0.56 in MMF Group, and 0.70 in FK506 Group. The enrollment time of this research is expected to be 2 years, and the total time of this research is 3 years, with a test level $\alpha = 0.05$, and a power of test $1-\beta = 80\%$. It is estimated to have 114 patients in MMF group and 115 patients in FK506 group, with a total of 229 patients. With the consideration of 15% loss of follow-up, a total of 270 patients are needed, including 135 patients in each group.

4.3. Research plan



4.4. Clinical trial flow chart

Clinical trial flow chart

Items	Screening and enrollment period		Treatment and follow-up period							
	Screen (V0)	Visit 1 (V1)	Visit 2 (V2)	Visit 3 (V3)	Visit 4 (V4)	Visit 5 (V5)	Visit 6 (V6)	Visit 7 (V7)	Visit 8 (V8)	Visit 9 (V9)
Follow-up week	Day -30 - 0	Included	Day 7	Day 28	Day 56	Day 112	Day 168	Day 224	Day 280	Day 364
Sign the informed consent gorm	√									
Inclusion/exclusion criteria		√								

Stop the original immunosuppressants after 2 weeks	$	$								
Randomized		√								
General data	√									
Medical history (course of disease, frequency of relapses in 1 year and 6 months before enrollment, steroid dosage)	√									
Vital signs	√	√	√	√	√	√	√	√	√	√
Height and weight	√	√	√	√	√	√	√	√	√	√
Physical examination	√	◎	√	√	√	√	√	√	√	√
Blood routine examination	√	◎	√	√	√	√	√	√	√	√
Urine routine examination	√	◎	√	√	√	√	√	√	√	√

Fasting blood glucose	√		√	√	√	√	√	√	√	√
Serum liver function	√	◎	√	√	√	√	√	√	√	√
Blood lipid	√	◎	√	√	√	√	√	√	√	√
Serum renal function	√	◎	√	√	√	√	√	√	√	√
Blood EBV-DNA, and CMV antibody	√									√
24hr urinary protein (>3 years old)	√	◎	√	√	√	√	√	√	√	√
Urinary protein / creatinine	√	◎	√	√	√	√	√	√	√	√
eGFR	√	◎	√	√	√	√	√	√	√	√
Tacrolimus concentration in plasma			√	√	√	√	√	√		√
Mycophenolic acid concentration in plasma			√				√			

Chest X-ray	√									√
ECG	√									√
Markers of hepatitis B and hepatitis C virus	√									
Examination of Mycobacterium tuberculosis and fungi	√									
Biological samples of blood and urine	√						√			√
Drug distribution and measurement		√	√	√	√	√	√	√	√	√
Guidance on the administration of test drug		√	√	√	√	√	√	√	√	√
Clinical efficacy (relapse or no)			√	√	√	√	√	√	√	√

Concomitant medication	√	√	√	√	√	√	√	√	√	√
Adverse event			√	√	√	√	√	√	√	√
Record case report form	√	√	√	√	√	√	√	√	√	√

Remarks:

1. Liver function: ALT, TBiL, ALB; Renal function: creatinine, blood Blood urea nitrogen, uric acid, Cystatin C;
2. Blood lipids: Triglycerides, cholesterol; Urinary protein / creatinine: morning urine; Markers of hepatitis B and hepatitis C virus: HBsAg, HBeAg, HBcAb, HCV;
3. Mycobacterium tuberculosis examination: T-sport; Fungal examination: fungal G test or other; Estimated glomerular filtration rate: eGFR = K × height (cm) / serum creatinine (mg/dL) (see Appendix);
4. Visit time window: ±3 days for visit 2, and ±7 days for other visits;
5. $ Items are applicable to the pediatric patients with combined use of other immunosuppressants before enrollment; ◎ Items are optional, depending on the judgment and decision of the investigators;
6. This research accepts the examination data from our hospital within 2 weeks before the screening period, and no repeated test is needed.

4.5. Selection of cases

4.5.1. Inclusion criteria

Only those who meet all the conditions listed in this column can be considered for inclusion in this research:

(1) Steroid-sensitive nephrotic syndrome with frequent relapse (FRNS) or steroid dependence (SDNS).

(2) Age: 2-18 years old.

(3) Normal renal function: eGFR ≥90 mL/min/1.73m^2.

(4) At the time of enrollment, urinary protein <1+ or urinary protein/creatinine <0.2g/g (<20 mg/mmol) in the morning for 3 consecutive days or more.

(5) No use of tacrolimus, mycophenolate mofetil, cyclosporine A, rituximab or cyclophosphamide within 2 years before enrollment.

4.5.2. Exclusion criteria

Anyone with one of the following conditions cannot be included in this research:

(1) Steroid-resistant nephrotic syndrome (SRNS).

(2) Family history of nephrotic syndrome, chronic glomerulonephritis or uremia.

(3) Leukopenia (leukocyte ≤3.0*10^9/L).

(4) Moderate and severe anemia (hemoglobin <9.0 g/dL).

(5) Thrombocytopenia (platelet count <100*10^{12}/L).

(6) Those with positive HBV serological indexes (HBsAg or/and HBeAg or/and HBcAb), positive HCV or abnormal liver function (ALT or total bilirubin exceeding 2 times or more of the upper limit, with a continuous increase for 2 weeks).

(7) There are chronic active infections such as Epstein-Barrvirus, cytomegalovirus or Mycobacterium tuberculosis, and the usage of steroids and immunosuppressive agents may aggravate the state of an illness.

(8) Secondary nephrotic syndrome (such as purpura nephritis ,lupus nephritis,etc).

(9) Those who with hematological or endocrine system diseases as well as serious organs illness such as heart, liver or kidney.

(10) Other autoimmune diseases or primary immunodeficiency or tumors.

(11) Those who was known be sensitized to tacrolimus, mycophenolate mofetil, glucocorticoids or any ingredient of the above drugs.

(12) Those who have participated in other clinical trials within three months before enrollment.

(13) Those who was not suitable for participating this study judged by investigator.

4.5.3. Elimination criteria

- Those who fail to take the test drugs as required, with a compliance <80% or >120%.
- Those who cannot cooperate well or complete the follow-up as planned, and those who change the drug dose at will.

4.5.4. Withdrawal criteria

Patients are free to withdraw from the trial at any time without any reason.

Patients must withdraw from this research in the following conditions:

(1) Withdrawal of the Informed Consent Form.

(2) Violation of the inclusion criteria or compliance with the exclusion criteria.

(3) No administration of the test drug according to the Protocol for 14 consecutive days due to various reasons.

(4) For two consecutive times, the measured value of SCr with an interval of at least 4 weeks has increased more than twice the baseline, and eGFR < 60mL/min.1.73m^2.

(5) The target concentration of tacrolimus or mycophenolate mofetil can not be reached after dose adjustment for one month.

(6) ALT or total bilirubin levels reach more than 2 times of the upper limit after medication, with a continuous increase for 2 weeks; if ALT or total bilirubin levels still rise to more than 2 times of the

upper limit after 2 weeks of liver protection drug treatment, stop the test drug. In case of no recovery after 2 weeks of drug withdrawal, the patient shall withdraw from the test.

(7) Occurrence of unknown adverse events of unacceptable nature, severity and/or duration, or occurrence of known unacceptable adverse events or the occurrence frequency exceeding expectations.

(8) The clinical events or safety-affecting events result in withdrawal from the clinical trial, and the investigators believe that such subjects shall withdraw from the trial.

(9) If pregnancy occurs during treatment, withdraw from the trial.

(10) Unauthorized use of drugs prohibited by this research.

4.5.5. Drop-out and treament

4.5.5.1 Definition of drop-out

All patients who have completed the Informed Consent Form and screened to be enrolled in the trial have the right to withdraw at any time. Whenever and for whatever reason, subjects who fail to complete the observation period specified in the Protocol are considered as drop-out cases, including the following situations:

- The subject has serious adverse events and the clinician believes that he/she should withdraw from the clinical trial;
- The subject shows aggravated condition or has other symptoms affecting the trial observation during the trial, and the clinician believes that he/she should withdraw from the clinical trial;
- Important deviations occur in the implementation of clinical trial protocol, such as poor compliance, which would cause difficulty in evaluating the drug effect;
- The subject is unwilling to continue the clinical trial and asks to withdraw from the clinical trial, or loss of follow-up has occurred although no request to withdraw from the trial is proposed.

4.5.5.2 Treatment of drop-out cases

The investigators shall contact the drop-off subjects by means of visiting, making an appointment for follow-up, calling, letter and so on, to ask the reasons, record the last medication time and complete

the evaluation Items that can be completed. For the cases withdrawing from the trial due to allergy or other adverse reactions and ineffective treatment, the investigators shall take corresponding treatment measures according to the actual situation of the subjects. The investigators shall properly keep the relevant test data of the drop-off cases, not only for filing, but also for full analysis and statistics.

4.5.6. Relevant definitions in inclusion and exclusion criteria

Steroid-sensitive nephrotic syndrome (SSNS): Complete remission after 4 weeks of prednisone or prednisolone at standard dose [2mg/kg.d or 60mg/m^2. d].

Steroid-resistant nephrotic syndrome (SRNS): Lack of complete remission at 4 weeks of therapy with daily prednisone or prednisolone at standard dose [2mg/kg.d or 60mg/m^2. d].

Steroid-dependent nephrotic syndrome (SDNS): Two consecutive relapses during therapy with prednisone or prednisolone (either at full dose or during tapering) or within 15 days of prednisone or prednisolone discontinuation

Frequently relapsing nephrotic syndrome (FRNS): ≥2 relapses per 6 months within 6months of disease onset or 24 relapses per 12 months in any subsequent 12-month period.

Secondary nephrotic syndrome: It refers to the nephrotic syndrome with clear causes. Secondary nephrotic syndrome can be caused by autoimmune diseases (such as systemic lupus erythematosus), diabetes, infections (such as bacteria and hepatitis B virus), circulatory system diseases, drug poisoning, etc.

5. Test drugs and their allocation

5.1. Drug name and specifications

(1) Tacrolimus capsules (trade name: Saifukai®， capsules, 1.0 mg/capsule, 0.5 mg/capsule); Storage conditions: Keep away from sunlight, and store in a dry place below 25°C after sealing.

(2) Mycophenolate mofetil dispersible tablets (trade name: Saikeping®, tablets, 250 mg/tablet); Storage conditions: Store under 30°C and keep away from sunlight.

(3) Storage conditions of prednisone tablets (tablets, 5 mg/tablet): Keep away from sunlight, and store at room temperature after sealing.

[Prednisone tablets can be replaced by other glucocorticoids during the test, but the dose shall have the same therapeutic effect, for example prednisone 5 mg = prednisolone 5 mg, prednisone 5 mg = methylprednisolone 4mg, etc.]

5.2. Administration method, dose, route and course of treatment

5.2.1. Initial administration protocol

FK506 dose: 0.05-0.10mg/kg/day，BID

Maintained concentration: In the induction period (the first six months after treatment) (visit 2, 3, 4, 5 and 6), the trough plasma concentration of tacrolimus is 5 - 10 ng/mL;

In the maintenance period, drug dose is gradually reduced when the patient's condition is stable:

In the last six months after administration (visit 7, 8, and 9), the trough concentration **is <5 ng/mL**

MMF dose: 20-30 mg/kg/day, BID

Plasma concentration (AUC) [Formula: MPA-AUC =7.75+(6.49*C0)+(0.76*C0.5)+(2.43*C2)]

Maintained concentration: In the induction period (the first six months after treatment) (visit 2, 3, 4, 5 and 6)

MPA-AUC=30 - 50 μg.h/mL

In the maintenance period, drug dose is gradually reduced when the patient's condition is stable:

In the last six months after administration (visit 7, 8, and 9), MPA-AUC≤40 μg.h/mL

Prednisone dose: The initial dose is 1.0-1.5 mg/kg every other day or 0.5-0.75 mg/kg every day. The dose shall be reduced after 4 weeks by 0.25 mg/kg (qd alt) or 0.125 mg/kg (every day) every 2-4 weeks. If the condition is stable, continue to reduce to 5mg (body surface area > 1 m^2) and 2.5mg (body surface area < 1 m^2) qd alt. Maintain at such doses until this research is completed.

5.2.2. Treatment of relapses

If the disease is complicated with infection in the relapse for the pediatric patients, anti-infection treatment can be given first. After infection control, if the disease still shows relapse, the prednisone

dose shall be restored to 1.0-1.5 mg/kg per day, with a maximum dose ≤60mg; If there is no infection at the time of relapse in the pediatric patients, the prednisone dose should be restored to 1.0-1.5 mg/kg per day directly, with a maximum dose ≤60mg. 5-7 days after the urine protein turns into negative results, the prednisone dose is reduced by 1.0-1.5 mg/kg every other day or 0.5-0.75mg/kg per day × 4 weeks. Then the dose is reduced as per the above steroid reduction method, while the dose of MMF or FK506 remains unchanged.

5.2.3. Dose adjustment of tacrolimus (FK506)

5.2.3.1 Adjust the dose according to the trough plasma concentration of tacrolimus. If the trough plasma concentration cannot meet the target concentration, it can be increased by adding Wuzhi capsules, ketoconazole, Hexin Shuang or cimetidine. If the trough plasma concentration of tacrolimus is >10 ng/mL, the dose of tacrolimus shall be reduced, and the trough concentration shall be rechecked after one week to adjust the target concentration. After treatment, the increase of SCr ≥ 30% of the basic value and eGFR < 60mL/min.1.73m^2 (excluding non-drug factors) shall prompt tacrolimus dose reduction by 50%. If the concentration still fails to reach the target after tacrolimus dose adjustment for one month, the subject shall withdraw from the trial.

5.2.3.2 If the trough plasma concentration of tacrolimus in visit 7 is ≥ 5 ng/mL, the dose of tacrolimus needs to be reduced by 20%-30%, and the trough concentration shall be rechecked in visit 8. If the trough concentration of tacrolimus is still ≥ 5 ng/mL in visit 8, it is necessary to continue to reduce the dose of tacrolimus by 20%-30%, and recheck this concentration in visit 9.

5.2.4. Dose adjustment of mycophenolate mofetil (MMF)

5.2.4.1 Adjust the dose according to the plasma concentration of mycophenolic acid. If MPA-AUC fails to meet the target, increase the oral dose of mycophenolate mofetil, but the maximum dose shall not exceed 1.0g each time, BID. Recheck MPA-AUC after 1 week and adjust the drug administration to meet the target concentration. If the patient has blood neutrophils less than 1300 per μL or total leukocytes less than 3000 per μL, diarrhea or severe infection, the dose of mycophenolate mofetil needs to be reduced by 25%. If the side effect persists, it shall be adjusted to half of the original dose. If the case of mycophenolate mofetil dose adjustment, the plasma concentration shall be measured according to the judgment of the investigators. If the concentration still fails to reach the target after

mycophenolate mofetil dose adjustment for one month, the subject shall withdraw from the trial.

5.2.4.2 If MPA-AUC is ≥ 40 ng/mL in visit 6, the dose of mycophenolate mofetil needs to be reduced by 20%-30%. After that, retest is no longer required.

5.3. concomitant medication

- Statins are allowed for use during this research, which can be increased or decreased according to the blood lipid status.
- Various anticoagulant drugs are allowed for use during this research.
- Immunosuppressants other than the test drug are prohibited for use.
- Plasma exchange and biological agents are prohibited for treatment.
- IVIG can be used during this research, but the reason needs to be recorded.
- When hypertension occurs during treatment, angiotensin converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB) cannot be used, but dihydropyridine calcium antagonists, β-receptor blocker, diuretic and/or α-receptor blocker can be used for control, with a target blood pressure of: <120/80 mmHg.
- Liver protection drugs are allowed for use during this research.
- If blood glucose rises during treatment, the blood glucose shall be actively controlled with hypoglycemic drugs.
- Various Chinese herbal medicines are prohibited for the treatment of kidney diseases during this research.
- The investigators shall ask the subjects to bring all the drugs they are taking at the time of follow-up, so as to check the concomitant medication for the subjects. For the other drugs or treatments that must be continued for the complicated diseases, the drug name (or other treatment name), dosage, times of use and time must be recorded on the Clinical Study Report for analysis and reporting during summary.

5.4. Medication adherence

The medication adherence is calculated as follows, and shall be ranging from 80% to 120%:

$$\text{adherence} = \frac{\text{actual administration}}{\text{planned administration}} \times 100\%$$

6. Evaluation of efficacy and safety

6.1. Primary efficacy outcomes

1-year relapse-free survival

6.2. Efficacy evaluation

6.2.1. Primary observation outcomes: 1-year relapse-free survival

6.2.2. Secondary observation outcomes:

(1) Frequency of relapses; the time of the first relapse after enrollment; relapse-free survival in the first six months after enrollment;

(2) Renal function: Serum creatinine and glomerular filtration rate (eGFR, see Appendix 1 for the calculation method)

(3) Cumulative steroid dosage: The total amount of steroids taken during this research and the total amount of steroids in the first half of the year

(4) Others: Blood pressure (see Appendix 2 for details), height, weight, blood lipid, hemoglobin, blood albumin, urinary protein/creatinine (morning urine), etc.

(5) Adverse reaction

(6) 24hr urinary protein quantification (applicable to subjects > 3 years old)

6.2.3. Efficacy criteria

Complete remission (CR): Completely normal in blood biochemistry test and urine examination;

Partial remission (PR): Urinary protein positive < (+++);

No remission (NR): Urinary protein positive ≥ (+++).

6.2.4. Relapse criteria

For 3 consecutive days, morning urinary protein changes from negative to (+++) or (++++), or 24hr urinary protein quantification ≥ 50 mg/kg, or urinary protein/creatinine (mg/mg) ≥2.0.

6.3. Safety evaluation

Changes of vital signs: Respiration and heart rate.

Various indexes in laboratory examination: Blood and urine routine examination, liver function, renal function, ECG, chest X-ray examination.

Clinically reported adverse events and adverse reactions.

7. Statistical analysis

7.1. Analysis data set

Full analysis set (FAS): It refers to the set of eligible cases and drop-off cases. The cases are required to have evaluation data after at least one treatment, but excluding the eliminated cases. Per-protocol set (PPS): It refers to the set of cases that meet the inclusion criteria, do not meet the exclusion criteria and complete the treatment plan, that is, the analysis of cases that meet the trial protocol, have good compliance and complete the specified content in CRF (PP analysis).

Safety set (SS): It refers to the actual data with safety index records after receipt of at least one treatment. The missed safety values shall not be carried forward. It includes some eliminated cases that can be evaluated, such as those whose age exceeds the inclusion criteria, but excludes those whose safety judgment cannot be made due to the use of banned drugs. For the incidence of adverse reactions, the number of cases in the safety set is used as the denominator.

7.2. General considerations of date analyses

7.2.1. General Statistical methods

SAS 9.4 software is adopted for Statistical analysis. Two-sided test is adopted for all Statistical tests. If the P value is less than 0.05, the tested difference will be considered “Statistically significant” (unless otherwise specified).

Descriptive analysis: Sort out and summarize a large number of data obtained from the survey to find out the internal law of these data - centralized trend and decentralized trend. Single factor analysis is mainly carried out with the help of statistics represented by various data, such as mean and percentage.

7.2.2. Statistical inference method

- The description of quantitative indicators includes the calculation of the mean, standard deviation, median, minimum value, maximum value, lower quartile (Q1), upper quartile (Q3), as well as the number and percentage of various types of classification indicators.

- In the comparison of the general conditions between the two groups, appropriate methods shall be adopted for analysis according to the type of indicators. The group t-test or Wilcoxon rank sum test is used for the comparison of quantitative data between two groups; Chi-square test or exact probability method is used for classification data; Wilcoxon rank sum test or CMH test is used for hierarchical data.

- The report is mainly expressed in tables: The tables are self-evident, that is, they have table titles, table notes and number of cases.

8. Data handling conventions

Data conversion:

Age (years) = (date of signing of informed consent form - date of birth + 1) / 365.25, rounded down.

Drug-related definitions are: definitely related, probably related, and possibly related.

Missing date: Since it is survival analysis data, it does not need to be filled. Missing text-type data is displayed as "" in the list. Numeric data is missing from the list with "." to display. If the data is recorded as "not applicable"/"NA" and "unable to assess"/"NK", the data will be displayed as raw records when described in the inventory, and processed as missing data for Statistical analysis.

Outlier: In general, all assay results will be used for Statistical analysis. If there is a clear outlier caused by special reasons and affects the Statistical analysis, it is missing and marked in the

Statistical analysis results / report.

8.1. Content of Statistical analysis

8.1.1. Basic value equilibrium analysis

The demographic characteristics, general conditions and baseline conditions (basic value indicators) of the two groups are analyzed to measure the comparability of the two groups. Group t-test or Wilcoxon rank sum test is used for measurement data; Wilcoxon rank sum test is used for classification or grade data; χ^2 test or Fisher test is used for classification data.

8.1.2. Effectiveness analysis

All effectiveness analysis/global indicators will be based on ITT principles, and FAS is adopted, for only the adjudicated endpoint events. The investigators are required to report all the potential endpoint events in eCRF.

8.1.3. Primary efficacy analysis

Logrank test is used for the analysis of relapse-free survival rate which is then used as a covariate for stratification by Sites. HR and its 95% confidence interval (CI) are calculated with Cox proportional hazard model to estimate the efficacy, the confidence interval is applied to verify the superiority of the experimental group and the control group, with a cut-off value of 1 (risk ratio). The model incorporates the same covariate as the Logrank test for fitting, and the definition method of covariates is also the same as that in the Logrank test. The Kaplan-Meier curve of relapse-free survival is drawn by treatment groups. The 1-year relapse-free survival rate and its confidence interval are then calculated.

Calculation rules for the main efficacy indicators:

- If relapse occurred within 9 visits (within 364±7 days) or unscheduled visits within 365 days of randomization, defined as the occurrence of endpoint events. Time of relapse = date of relapse - Random date + 1, calculated by days.
- If the visit stipulated in the protocol was not completed within 9 visits (within 364±7 days) due to loss of follow-up midway or withdrawal or other reasons, it is defined as censoring. Time of

censoring = date of withdrawal - random date + 1, calculated by days.

- If the visit stipulated in the protocol was not completed within 9 visits (within 364±7 days) due to death in the trial, it is defined as censoring. Time of censoring = Death date - random date + 1, calculated by days.
- If the visit stipulated in the protocol was completed and there is no relapse within 9 visits (within 364±7 days), it is defined as censoring. Time of censoring = date of visit 9 (within 364±7 days) - random date + 1, calculated by days.

8.1.4. Secondary efficacy analysis

Secondary outcomes (renal function; cumulative steroid dosage; blood pressure; height; body weight; blood lipids; hemoglobin; serum albumin; urinary protein/creatinine (morning urine); 24hr urinary protein quantification (applicable to subjects > 3 years old); frequency of relapses; the time of the first relapse after enrollment; relapse-free rate in the first six months after enrollment) are described and compared with use of the above general Statistical methods, and the adverse reactions are analyzed by descriptive analysis.

8.1.5. Other analysis

(1) Case distribution: Different data sets in each group, case distribution in each Site, comparison of total drop-off rate, detailed list of termination reasons, and descriptive analysis.

(2) Compliance analysis: Compare whether the two groups of patients take the test drugs on time and in quantity, whether they take the drugs and foods prohibited in the Protocol, and conduct the same descriptive analysis as well as χ^2 test or Fisher test for analysis.

(3) The incidence of drug withdrawal or drug change due to adverse reactions in the clinical trial shall be analyzed with χ^2 test or Fisher test. The efficacy in the long-term follow-up after the trial is evaluated by descriptive analysis and χ^2 test or Fisher test.

8.1.6. Safety analysis

Safety analysis mainly adopts safety set. All adverse events are coded by MedDRA 20.0 to describe the total number and incidence of adverse events (including serious adverse events), and the

frequency table is used to describe the frequency, severity of each adverse event and its relationship with the treatment. Adverse events relevant (related, probably related, and possibly relayed) to this research treatment are described and listed separately. Other safety indicators will also be described and summarized. The laboratory changes with clinical significance will be counted as AE.

9. Statistical analysis results

9.1. Research overview

Table 1. Distribution of subjects at each site (All enrolled subjects)

Research Site	Group	No. of subjects enrolled	No. of subjects drop-out	Drop-out rate	No. of subjects eliminated	Elimination rate	No. of subjects completed
Site 1	Experimental group						
	Control group						
	Total						
Site 2	Experimental group						
	Control group						
	Total						
…							
Total	Experimental group						
	Control group						
	Total						

Note: 1. The Site name is not displayed in following table, only the site number. Same below. 2. No. of subjects completed = No. of subjects enrolled - No. of subjects drop-out. Elimination refers to subjects who complete the trial, but were not included in the PPS. Subjects who withdrew due to the endpoint event were considered to have completed the trial. 3. Drop-out rate = No. of subjects drop-out / No. of subjects enrolled; Elimination rate = No. of subjects eliminated / No. of subjects enrolled.

Table 2. Distribution of subjects at each site

	PPS			FAS			SS		
Site	Experimental group	Control group	Total	Experimental group	Control group	Total	Experimental group	Control group	Total
Site 1									
Site 2									
Total									

Table 3. Trial completion and distribution of analysis data set (All enrolled subjects)

Items	Indicator	Experimental group	Control group	Total
No. of subjects enrolled	Yes			
	No			
Complete 1 week follow-up	Yes			
	No			
Complete 4 week follow-up	Yes			
	No			
Complete 8 week follow-up	Yes			
	No			
Complete 16 week follow-up	Yes			
	No			
Complete 24 week follow-up	Yes			
	No			
Complete 32 week follow-up	Yes			
	No			
Complete 40 week follow-up	Yes			
	No			
Complete 52 week follow-up	Yes			
	No			
Trial completion	Yes			

Items	Indicator	Experimental group	Control group	Total
	No			
Treatment discontinuation reason	Subject voluntarily withdrew prematurely			
	Decision by the investigator			
	Poor compliance that decided by the investigator			
	Meet the exclusion criteria, or did not meet the inclusion criteria			
	Refusal to continue trial participation			
	Lack of efficacy			
	Adverse events			
	Lost to follow-up			
	Death			
	Other			
FAS				
PPS				
SS				

Note: Follow-up time (years) = (last visit date - random date + 1) / 365.25. Complete 1 week follow-up: follow-up duration ≥ 1 week, and so on.

9.2. Demographic characteristics (FAS)

Table 4. Baseline demographics

Items	Indicator	Experimental group	Control group	Total
Age (years)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Gender	male n (%)			

Items	Indicator	Experimental group	Control group	Total
	Female n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Ethnicity	Han n (%)			
	Others n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Source of disease	Outpatient n (%)			
	Ward n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 5. Baseline vital signs

Items	Indicator	Experimental group	Control group	Total
Height (cm)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Weight (kg)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			

Items	Indicator	Experimental group	Control group	Total
	Min, Max			
	Statistics			
	P-value			
BMI (kg/m^2)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Temperature (℃)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Systolic blood pressure (mmHg)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Diastolic blood pressure (mmHg)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			

Items	Indicator	Experimental group	Control group	Total
	Min, Max			
	Statistics			
	P-value			
Heart rate (times/min)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Respiratory rate (times/minute)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			

Table 6. Family history and personal history

Items	Indicator	Experimental group	Control group	Total
Family history	No n (%)			
	Yes n (%)			
	Total (Missing)			
	Statistics			
	P-value			
History of drug allergy	No n (%)			
	Yes n (%)			
	Total (Missing)			

Items	Indicator	Experimental group	Control group	Total
	Statistics			
	P-value			
History of surgery	No n (%)			
	Yes n (%)			
	Total (Missing)			
	Statistics			
	P-value			
History of pet ownership	No n (%)			
	Yes n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Number of gestation	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Number of parturition	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Birth weight (kg)	N (Missing)			
	Mean (SD)			

Items	Indicator	Experimental group	Control group	Total
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
History of dystocia	No n (%)			
	Yes n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Feeding	Mixed feeding n (%)			
	Single feeding n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Partial eclipse	No n (%)			
	Yes n (%)			
	Total (Missing)			
	Statistics			
	P-value			
History of growth and development	Normal n (%)			
	Abnormal n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Vaccination history	No n (%)			
	Yes n (%)			
	Total (Missing)			

Items	Indicator	Experimental group	Control group	Total
	Statistics			
	P-value			

Table 7. History of other diseases, concomitant medications and nephrotic syndrome

Items	Indicator	Experimental group	Control group	Total
History of other diseases and concomitant medications	No n (%)			
	Yes n (%)			
	Total (Missing)			
	Statistics			
	P-value			
History of nephrotic syndrome (years)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
History of nephrotic syndrome (Number of relapses in the past 1 year)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
History of nephrotic syndrome (Number of relapses in the past 6 months)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			

Items	Indicator	Experimental group	Control group	Total
	Min, Max			
	Statistics			
	P-value			

Note: History of other diseases and concomitant medications: history of diseases other than the nephrotic syndrome, such as pneumonia, cardiovascular, diabetes, purpura and enuresis, etc.

Table 8. Visual palpation of physical examination Items

Items	Indicator	Experimental group	Control group	Total
Heart	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Superficial lymph node	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Skin and sclera	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Thyroid gland	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value
Limbs and spine	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value
Lung, abdomen and back	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value
Nervous system	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value
Other	Normal n (%)

	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 9. Diagnostic consultation of physical examination Items

Items	Indicator	Experimental group	Control group	Total
Defecation	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Fever/dizziness/vertigo	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Dry mouth and eyes	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			

	P-value
Gastrointestinal digestion	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value
Myalgia/muscle weakness	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value
Arthralgia/arthritis	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value
Dry/itchy skin	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value

Other	Normal n (%)
	Abnormal but not clinically significant n (%)
	Abnormal and clinically significant n (%)
	Not tested n (%)
	Total (Missing)
	Statistics
	P-value

9.3. Baseline examinations (FAS)

Table 10. DNA/antibody tests

Items	Indicator	Experimental group	Control group	Total
Blood EBV-DNA	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Blood CMV antibody	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
IgM	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			

	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
IgG	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 11. Hepatitis virus

Items	Indicator	Experimental group	Control group	Total
HBs-Ag	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Anti-HCV	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 12. Examination of mycobacterium tuberculosis and fungi

Items	Indicator	Experimental group	Control group	Total
Mycobacterium tuberculosis test	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Fungal examination	Fungal G test n (%)			
	Fungal other n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Fungal examination result	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 13. Urine test

Items	Indicator	Experimental group	Control group	Total
24hr urine protein (>3 years old)	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			

	Statistics			
	P-value			
Urine protein/serum creatinine	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 14. Glomerular filtration rate

Items	Indicator	Experimental group	Control group	Total
Examine or not	No n (%)			
	Yes n (%)			
	Total (Missing)			
	Statistics			
	P-value			
eGFR	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 15. Retained biological samples of blood and urine

Items	Indicator	Experimental group	Control group	Total
Retained biological samples of blood and urine	No n (%)			
	Yes n (%)			

	Total (Missing)			
	Statistics			
	P-value			

Table 16. Chest X-ray

Items	Indicator	Experimental group	Control group	Total
Result	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 17. ECG examinations

Items	Indicator	Experimental group	Control group	Total
Result	Normal n (%)			
	Abnormal but not clinically significant n (%)			
	Abnormal and clinically significant n (%)			
	Not tested n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 18. Primary diagnosis

Items	Indicator	Experimental group	Control group	Total
Primary diagnosis	Steroid-sensitive nephrotic syndrome (SSNS) n (%)			
	Steroid-resistant nephrotic syndrome (SRNS) n (%)			
	Secondary nephrotic syndrome n (%)			

	Steroid-dependent nephrotic syndrome (SDNS) n (%)
	Frequently relapsing nephrotic syndrome (FRNS) n (%)
	Other nephrotic syndrome n (%)
	Total (Missing)
	Statistics
	P-value

9.4. Efficacy analysis (FAS/PPS)

9.4.1. Primary efficacy indicators: 1-year relapse-free survival rate

Table 19. 1-year relapse-free survival analysis

		FAS		PPS	
Items	Indicator	Experimental group	Control group	Experimental group	Control group
1-year recurrence time (days)	N (Missing)				
	Endpoint event (%)				
	Censoring (%)				
	Median survival time				
	95%CI				
	Q1, Q3				
	Log-rank test				
	P-value				
Cox regression analysis	Hazard Ratio				
	95%CI				
	Wald chi-square				
	P-value				

Note: The independent variables of Cox regression analysis are group and Site. Same below.

Figure 1. 1-year relapse-free survival analysis chart (FAS)

Figure 2. 1-year relapse-free survival analysis chart (PPS)

9.4.2. Secondary efficacy indicators

9.4.2.1. The first relapse survival analysis after enrollment

Table 20. The time of the first relapse after enrollment

		FAS		PPS	
Items	Indicator	Experimental group	Control group	Experimental group	Control group
The time of the first relapse after enrollment (days)	N (Missing)				
	Mean (SD)				
	Median				
	Q1, Q3				
	Min, Max				
	95%CI				
	P-value				

Note: The time of first relapse after enrollment (days) = Date of first relapse after enrollment - Random date + 1.

Table 21. The first relapse survival analysis after enrollment

		FAS		PPS	
Items	Indicator	Experimental group	Control group	Experimental group	Control group
The time of the first relapse after enrollment (days)	N (Missing)				
	Endpoint event (%)(%)				
	Censoring (%)				
	Median survival time				
	95%CI				
	Q1, Q3				
	Log-rank test				
Cox regression analysis	Hazard Ratio				
	95%CI				
	Wald Chi-square				
	P-value				

9.4.2.2. **6-month relapse-free survival analysis after enrollment**

Table 22. 6-month relapse-free survival analysis after enrollment

		FAS		PPS	
Items	Indicator	Experimental group	Control group	Experimental group	Control group
6-month recurrence time (days)	N (Missing)				
	Endpoint event (%)(%)				
	Censoring (%)				
	Median survival time				
	95%CI				
	Q1, Q3				
	Log-rank test				
Cox regression analysis	Hazard Ratio				
	95%CI				
	Wald Chi-square				
	P-value				

Figure 3. 6-month relapse-free survival analysis chart (FAS)

Figure 4. 6-month relapse-free survival analysis chart (PPS)

9.4.2.3. **Serum renal function**

Table 23. Changes in eGFR relative to baseline at each visit

		FAS			PPS		
Items	Indicator	Experimental group	Control group	Total	Experimental group	Control group	Total
Baseline	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Between-group comparison in baseline	Statistics						
	P-value						
Visit 2/Day 7±3	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Between-group comparison in Visit 2/Day 7±3	Statistics						
	P-value						
Change in Visit 2/Day 7±3 from baseline	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Pre- and post-treatment comparison of intra-group	Statistical method						
	Statistics						
	P-value						
Comparison of changes between groups pre- and post-treatment	Statistics						
	P-value						
Visit 4/Day 56±7	N (Missing)						
	Mean (SD)						

		FAS			PPS		
Items	Indicator	Experimental group	Control group	Total	Experimental group	Control group	Total
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Between-group comparison in Visit 4/Day 56±7	Statistics						
	P-value						
Change in Visit 4/Day 56±7 from baseline	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Pre- and post-treatment comparison of intra-group	Statistical method						
	Statistics						
	P-value						
Comparison of changes between groups pre- and post-treatment	Statistics						
	P-value						
Visit 5/Day 112±7	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Between-group comparison in Visit 5/Day 112±7	Statistics						
	P-value						
Change in Visit 5/Day 112±7 from baseline	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						

		FAS			PPS		
Items	Indicator	Experimental group	Control group	Total	Experimental group	Control group	Total
Pre- and post-treatment comparison of intra-group	Statistical method						
	Statistics						
	P-value						
Comparison of changes between groups pre- and post-treatment	Statistics						
	P-value						
Visit 6/Day 168±7	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Between-group comparison in Visit 6/Day 168±7	Statistics						
	P-value						
Change in Visit 6/Day 168±7 from baseline	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Pre- and post-treatment comparison of intra-group	Statistical method						
	Statistics						
	P-value						
Comparison of changes between groups pre- and post-treatment	Statistics						
	P-value						
Visit 7/Day 224±7	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Between-group comparison in Visit 7/Day 224±7	Statistics						

		FAS			PPS		
Items	Indicator	Experimental group	Control group	Total	Experimental group	Control group	Total
	P-value						
Change in Visit 7/Day 224±7 from baseline	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Pre- and post-treatment comparison of intra-group	Statistical method						
	Statistics						
	P-value						
Comparison of changes between groups pre- and post-treatment	Statistics						
	P-value						
Visit 8/Day 280±7	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Between-group comparison in Visit 8/Day 280±7	Statistics						
	P-value						
Change in Visit 8/Day 280±7 from baseline	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Pre- and post-treatment comparison of intra-group	Statistical method						
	Statistics						
	P-value						
Comparison of changes between groups pre- and post-treatment	Statistics						
	P-value						

		FAS			PPS		
Items	Indicator	Experimental group	Control group	Total	Experimental group	Control group	Total
Visit 9/Day 364±7	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Between-group comparison in Visit 9/Day 364±7	Statistics						
	P-value						
Change in Visit 9/Day 364±7 from baseline	N (Missing)						
	Mean (SD)						
	Median						
	Q1, Q3						
	Min, Max						
	95%CI						
Pre- and post-treatment comparison of intra-group	Statistical method						
	Statistics						
	P-value						
Comparison of changes between groups pre- and post-treatment	Statistics						
	P-value						

Figure 5. Quantitative variables of eGFR at each visit

Table 24. Change in Scr from baseline at each visit

Ibid. Same below.

Figure 6. Quantitative variables of Scr at each visit

Table 25. Change in serum uric acid from baseline at each visit

Figure 7. Quantitative variables of serum uric acid at each visit

Table 26. Change in blood urea nitrogen from baseline at each visit

Figure 8. Quantitative variables of blood urea nitrogen at each visit

Table 27. Change in serum cystatin C from baseline at each visit

Figure 9. Quantitative variables of serum cystatin C at each visit

9.4.2.4. **Cumulative steroid dosage**

Table 28. Total amount of steroids taken during the study

Items	Indicator	Experimental group	Control group	Total
Total amount of steroids taken during the study	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			

Table 29. Total amount of steroids taken during 6 months after enrollment

Items	Indicator	Experimental group	Control group	Total
Total amount of steroids taken during 6 months after enrollment	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			

Items	Indicator	Experimental group	Control group	Total
	Statistics			
	P-value			

9.4.2.5. Vital signs

Table 30. Change in systolic blood pressure from baseline at each visit

Table 31. Change in diastolic blood pressure from baseline at each visit

Table 32. Change in height from baseline at each visit

Table 33. Change in weight from baseline at each visit

Table 34. Height percentile

Items	Indicator	Experimental group	Control group	Total
Baseline	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Visit 5/Day 112±7	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Visit 9/Day 364±7	N (Missing)			
	Mean (SD)			
	Median			

Items	Indicator	Experimental group	Control group	Total
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			

Note: Data from the external file “XX”.

9.4.2.6. **Blood lipid**

Table 35. Change in triglyceride from baseline at each visit

Table 36. Change in total cholesterol from baseline at each visit

9.4.2.7. **Haemoglobin and albumin (ALB)**

Table 37. Change in haemoglobin from baseline at each visit

Table 38. Change in ALB from baseline at each visit

9.4.2.8. **Urine test**

Table 39. Change in 24hr urine protein (>3 years old) from baseline at each visit

Table 40. Change in urine protein/creatinine (morning urine) from baseline at each visit

9.4.2.9. **Serum liver function and fasting blood glucose**

Table 41. Change in glutamyl transpeptidase (GT) from baseline at each visit

Table 42. Change in alanine aminotransferase (ALT) from baseline at each visit

Table 43. Change in aspartate aminotransferase (AST) from baseline at each visit

Table 44. Change in lactate dehydrogenase from baseline at each visit

Table 45. Change in total bilirubin from baseline at each visit

Table 46. Change in direct bilirubin from baseline at each visit

Table 47. Change in alkaline phosphatase from baseline at each visit

Table 48. Change in total protein from baseline at each visit

Table 49. Change in globulin from baseline at each visit

Table 50. Change in fasting blood glucosefrom baseline at each visit

9.4.2.10. Blood routine examination

Table 51. Change in leukocyte count (WBC) from baseline at each visit

Table 52. Change in erythrocyte count (RBC) from baseline at each visit

Table 53. Change in platelet count (PLT) from baseline at each visit

Table 54. Change in lymphocyte percentage (LY) from baseline at each visit

9.4.2.11. Urine routine examination

Table 55. Change in leukocyte from baseline at each visit

Table 56. Change in erythrocyte from baseline at each visit

Table 57. Change in pH from baseline at each visit

Table 58. Change in urine protein from baseline at each visit

9.4.2.12. Plasma concentration

Table 59. Change in tacrolimus concentration in plasma from baseline at each visit

Table 60. Change in mycophenolic acid concentration in plasma from baseline at each visit

9.4.3. Disease remission

Table 61. Disease remission at each visit

Items	Indicator	Experimental group	Control group	Total
Visit 1/Day 0	Complete remission (CR) n (%)			
	Partial remission (PR) n (%)			
	Non remission (NR) n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Visit 2/Day 7±3	Complete remission (CR) n (%)			

	Partial remission (PR) n (%)
	Non remission (NR) n (%)
	Total (Missing)
	Statistics
	P-value

…

9.5. Safety analysis (SS)

9.5.1. Adverse event (AE)

Table 62. Between-group comparison of AE

Items	Experimental group			Control group			P-value
	No. of AEs	No. of subjects	Percentage	No. of AEs	No. of subjects	Percentage	
AE							
AE of severe severity							
Drug-related AE							
Serious adverse event (SAE)							
Drug-related SAE							
Drop-out due to AE							
Drop-out due to SAE							

Note 1: The definitions related to drugs are “definitely related”, “probably related”, “possibly related”, “unlikely related” and “not related”.

Note 2: The data of SAE that cause the drop-out came from the external file “XX”.

Table 63. characteristics of AE in each group

Items		Experimental group			Control group			P-value
		No. of AEs	No. of subjects	Incidence	No. of AEs	No. of subjects	Incidence	
Relationship with study drug	Definitely related							
	Probably related							

Items		Experimental group			Control group			P-value
		No. of AEs	No. of subjects	Incidence	No. of AEs	No. of subjects	Incidence	
	Possibly related							
	Unlikely related							
	Not related							
Outcome	Recovered/resolved							
	Recovered/resolved with sequelae							
	Not recovered							
	Recovering/resolving							
	Death							
	Unknown							

Table 64. Between-group comparison of SAE

Items	Experimental group (n=XX)			Control group (n=XX)			Total (n=XX)			P-value
	No. of AEs	No. of subjects	Incidence (%)	No. of AEs	No. of subjects	Incidence (%)	No. of AEs	No. of subjects	Incidence (%)	
Results in death										
Requires hospitalization										
Prolongs hospitalization										
Disability										
Dysfunction										
Congenital malformation										
Life threatening										
Other										

Table 65. Summary of AE base on SOC and PT coding

Indicator	Experimental group (n=XX)			Control group (n=XX)			Total (n=XX)			P-value
	No. of AEs	No. of subjects	Incidence (%)	No. of AEs	No. of subjects	Incidence (%)	No. of AEs	No. of subjects	Incidence (%)	
AE										

Indicator	Experimental group (n=XX)			Control group (n=XX)			Total (n=XX)			
	No. of AEs	No. of subjects	Incidence (%)	No. of AEs	No. of subjects	Incidence (%)	No. of AEs	No. of subjects	Incidence (%)	P-value
SOC1										
PT1										
PT2										
…										
SOC2										
PT1										
PT2										
…										

Table 66. Summary of adverse reactions base on SOC and PT coding

Indicator	Experimental group (n=XX)			Control group (n=XX)			Total (n=XX)			
	No. of AEs	No. of subjects	Incidence (%)	No. of AEs	No. of subjects	Incidence (%)	No. of AEs	No. of subjects	Incidence (%)	P-value
Adverse event										
SOC1										
PT1										
PT2										
…										
SOC2										
PT1										
PT2										
…										

9.5.2. Vital signs

Table 67. Change in heart rate from baseline at each visit

Items	Indicator	Experimental group	Control group	Total
Baseline	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Between-group comparison in baseline	Statistics			
	P-value			
Visit 2/Day 7±3	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Between-group comparison in Visit 2/Day 7±3	Statistics			
	P-value			
Change in Visit 2/Day 7±3 from baseline	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Pre- and post-treatment comparison of intra-group	Statistical method			
	Statistics			
	P-value			
Comparison of changes between groups pre- and post-treatment	Statistics			
	P-value			
Visit 4/Day 56±7	N (Missing)			
	Mean (SD)			

Items	Indicator	Experimental group	Control group	Total
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Between-group comparison in Visit 4/Day 56±7	Statistics			
	P-value			
Change in Visit 4/Day 56±7 from baseline	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Pre- and post-treatment comparison of intra-group	Statistical method			
	Statistics			
	P-value			
Comparison of changes between groups pre- and post-treatment	Statistics			
	P-value			
Visit 5/Day 112±7	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Between-group comparison in Visit 5/Day 112±7	Statistics			
	P-value			
Change in Visit 5/Day 112±7 from baseline	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Pre- and post-treatment comparison of intra-group	Statistical method			

Items	Indicator	Experimental group	Control group	Total
	Statistics			
	P-value			
Comparison of changes between groups pre- and post-treatment	Statistics			
	P-value			
Visit 6/Day 168±7	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Between-group comparison in Visit 6/Day 168±7	Statistics			
	P-value			
Change in Visit 6/Day 168±7 from baseline	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Pre- and post-treatment comparison of intra-group	Statistical method			
	Statistics			
	P-value			
Comparison of changes between groups pre- and post-treatment	Statistics			
	P-value			
Visit 7/Day 224±7	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Between-group comparison in Visit 7/Day 224±7	Statistics			
	P-value			
Change in Visit 7/Day 224±7 from baseline	N (Missing)			

Items	Indicator	Experimental group	Control group	Total
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Pre- and post-treatment comparison of intra-group	Statistical method			
	Statistics			
	P-value			
Comparison of changes between groups pre- and post-treatment	Statistics			
	P-value			
Visit 8/Day 280±7	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Between-group comparison in Visit 8/Day 280±7	Statistics			
	P-value			
Change in Visit 8/Day 280±7 from baseline	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Pre- and post-treatment comparison of intra-group	Statistical method			
	Statistics			
	P-value			
Comparison of changes between groups pre- and post-treatment	Statistics			
	P-value			
Visit 9/Day 364±7	N (Missing)			
	Mean (SD)			
	Median			

Items	Indicator	Experimental group	Control group	Total
	Q1, Q3			
	Min, Max			
	95%CI			
Between-group comparison in Visit 9/Day 364±7	Statistics			
	P-value			
Change in Visit 9/Day 364±7 from baseline	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	95%CI			
Pre- and post-treatment comparison of intra-group	Statistical method			
	Statistics			
	P-value			
Comparison of changes between groups pre- and post-treatment	Statistics			
	P-value			

Table 68. Change in respiratory rate from baseline at each visit

Ibid.

9.5.3. Blood routine examination

Table 69. Summary of blood routine examination-Leukocyte count (WBC)

Items	Indicator	Experimental group	Control group	Total
Visit 1/Day 0	Within the normal range n (%)			
	Below the normal range n (%)			
	Higher than the normal range n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Visit 9/Day 364±7	Within the normal range n (%)
	Below the normal range n (%)
	Higher than the normal range n (%)
	Total (Missing)
	Statistics
	P-value

Table 70. Summary of blood routine examination-Lymphocyte percentage (LY)

Items	Indicator	Experimental group	Control group	Total
Visit 1/Day 0	Within the normal range n (%)			
	Below the normal range n (%)			
	Higher than the normal range n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Visit 9/Day 364±7	Within the normal range n (%)			
	Below the normal range n (%)			
	Higher than the normal range n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 71. Shift-table of blood routine examination results before and after treatment-Leukocyte count (WBC)

		Day 364±7 after treatment					
Group	Before treatment	Normal	Abnormal but not clinically significant	Abnormal and clinically significant	Not tested	Missing	Total
Experimental group	Normal						
	Abnormal but not clinically significant						
	Abnormal and clinically significant						
	Not tested						

	Missing	
	Total	
Control group	Normal	
	Abnormal but not clinically significant	
	Abnormal and clinically significant	
	Not tested	
	Missing	
	Total	

Table 72. Shift-table of blood routine examination results before and after treatment-Erythrocyte count (RBC)
Ibid. Same below.

Table 73. Shift-table of blood routine examination results before and after treatment-Haemoglobin (Hb)

Table 74. Shift-table of blood routine examination results before and after treatment-Platelet count (PLT)

Table 75. Shift-table of blood routine examination results before and after treatment-Lymphocyte percentage (LY)

9.5.4. Urine routine examination

Table 76. Shift-table of urine routine examination results before and after treatment-Leukocyte
Table 77. Shift-table of urine routine examination results before and after treatment-Erythrocyte
Table 78. Shift-table of urine routine examination results before and after treatment-pH
Table 79. Shift-table of urine routine examination results before and after treatment-Urine protein
Table 80. Shift-table of urine routine examination results before and after treatment-Color
Table 81. Shift-table of urine routine examination results before and after treatment-Definition

9.5.5. Serum biochemistry

9.5.6. DNA/antibody test

9.5.7. Urine test

9.5.8. Glomerular filtration rate

Table 104. Shift-table of eGFR results before and after treatment-eGFR

9.5.9. Chest X-ray

Table 105. Shift-table of chest X-ray results before and after treatment

9.5.10. ECG

Table 106. Shift-table of ECG examination results before and after treatment

9.5.11. Concomitant medication and medication adherence

Table 107. Concomitant medication

Items	Indicator	Experimental group	Control group	Total
Concomitant medication	No n (%)			
	Yes n (%)			
	Total (Missing)			
	Statistics			
	P-value			

Table 108. Medication adherence

Items	Indicator	Experimental group	Control group	Total
Adherence to tacrolimus capsules/mycophenolate mofetil dispersible tablets (%)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Adherence to tacrolimus capsules/mycophenolate mofetil dispersible tablets	Excellent (80-120%) n (%)			
	Poor (<80% or >120%) n (%)			
	Total (Missing)			
	Statistics			
	P-value			
Adherence to steroids (%)	N (Missing)			
	Mean (SD)			
	Median			
	Q1, Q3			
	Min, Max			
	Statistics			
	P-value			
Adherence to steroids	Excellent (80-120%) n (%)			
	Poor (<80% or >120%) n (%)			
	Total (Missing)			
	Statistics			
	P-value			

10. Attachments

Table 109. List of subjects drop-out (All randomized subjects)

Site	Subject code	Random number	Group	Drop-out	Trial completion	Termination date	Treatment discontinuation reason	FAS	PPS	SS	Reason for not be included in the PPS

Table 110. List of subjects exclusions (All randomized subjects)

Site	Subject code	Random number	Group	Exclusion	Trial completion	Termination date	Treatment discontinuation reason	FAS	PPS	SS	Reason for not be included in the PPS

Table 111. List of protocol deviations (All randomize subjects)

Note: Analysis based on external file "XX".

Table 112. List of demographic characteristics (FAS)

Site	Subject code	Random number	Group	Date of birth	Age (years)	Gender	Ethnicity	Other ethnicity	Source of disease	Height (cm)	Weight (kg)	BMI (kg/m^2)

Table 113. List of family history and personal history (FAS)

Site	Subject code	Random number	Group	Family history	History of drug allergy	History of surgery	History of pet ownership	Number of gestation	Number of parturition	Birth weight (kg)	History of dystocia	Feeding history	Partial eclipse	History of growth and development	Vaccination history

Table 114. List of history of other diseases and concomitant medications (FAS)

Site	Subject code	Random number	Group	Disease name	Start date	End date	Disease persists or not	Drug name	Drug dosage form	Dosage	Frequency	Still on medication or not

Table 115. List of history of nephrotic syndrome (FAS)

Site	Subject code	Random number	Group	Onset date	Diagnosis date	Course of disease	No. of relapses in the past 1 year	No. of relapses in the past 6 months	Time to recurrence	Negative conversion time of urine protein

Table 116. List of treatment history for nephrotic syndrome (FAS)

Site	Subject code	Random number	Group	Drug name	Drug dosage form	Dosage	Frequency of medication	Start medication date	Stop medication date	Still on medication or not

Table 117. List of disease relapse (urine protein) situations (FAS)

Site	Subject code	Random number	Group	Visit	Relapse or not	Serial number	Relapse start date	Relapse end date	Description of relapse

Table 118. List of primary efficacy indicator (1-year relapse-free) situations (FAS/PPS)

Site	Subject code	Random number	Group	Relapse or not	Relapse start date	Relapse end date	Random date	Analyze date	Endpoint event

Table 119. List of secondary efficacy indicator (first relapse after enrollment) situations (FAS/PPS)

Site	Subject code	Random number	Group	Relapse or not	Relapse start date	Relapse end date	Random date	Analyze date	Endpoint event

Table 120. List of secondary efficacy indicator (6-month relapse-free) situations (FAS/PPS)

Site	Subject code	Random number	Group	Relapse or not	Relapse start date	Relapse end date	Random date	Analyze date	Endpoint event

Table 121. List of blood routine examination results that were normal before treatment and abnormal after treatment (SS)

Site	Subject code	Random number	Group	Examination items	Visit	Baseline result	Baseline unit	Baseline clinical judgment	Visit result	Visit unit	Visit clinical judgment

Table 122. List of urine routine examination results that were normal before treatment and abnormal after treatment (SS)

Site	Subject code	Random number	Group	Examination items	Visit	Baseline result	Baseline unit	Baseline clinical judgment	Visit result	Visit unit	Visit clinical judgment

Table 123. List of serum biochemistry results that were normal before treatment and abnormal after treatment (SS)

Site	Subject code	Random number	Group	Examination items	Visit	Baseline result	Baseline unit	Baseline clinical judgment	Visit result	Visit unit	Visit clinical judgment

Table 124. List of urine test results that were normal before treatment and abnormal after treatment (SS)

Site	Subject code	Random number	Group	Examination items	Visit	Baseline result	Baseline unit	Baseline clinical judgment	Visit result	Visit unit	Visit clinical judgment

Table 125. List of eGFR results that were normal before treatment and abnormal after treatment (SS)

Site	Subject code	Random number	Group	Visit	Baseline result	Baseline clinical judgment	Visit result	Visit clinical judgment

Table 126. List of chest X-ray results that were normal before treatment and abnormal after treatment (SS)

Site	Subject code	Random number	Group	Visit	Baseline result	Baseline clinical judgment	Visit result	Visit clinical judgment	Description of abnormal

Table 127. List of ECG examination results that were normal before treatment and abnormal after treatment (SS)

Site	Subject code	Random number	Group	Visit	Baseline result	Baseline clinical judgment	Visit result	Visit clinical judgment	Description of abnormal

Table 128. List of AE (SS)

Site	Subject code	Random number	Group	AE ID	Description of AE	Severity	Start date	Treatment or not	AE ended or not	End date	Treatment	Relationships with drug	Measures taken on study drug

Table 129. List of AE-continued (SS)

Site	Subject code	Random number	Group	AE ID	Description of AE	AE outcomes	Recovery/cure date	Details of sequelae	Death date	SAE or not	Cause withdraw or not

Table 130. List of SAE (SS)

Site	Subject code	Random number	Group	SAE ID	Type of SAE	Report date	Description of SAE	SAE situations	Death date	Severity	Onset Date	SAE outcomes	Relationships with drug

Table 131. List of SAE-continued (SS)

Site	Subject code	Random number	Group	SAE ID	Type of SAE	Report time	Description of SAE	Measures taken on study drug	Reported SAE situation	Details of SAE cccurrence and treatment

Table 132. List of concomitant medication (SS)

Site	Subject code	Random number	Group	CM ID	China approved drug names	Administration route	Single dose	Unit	Frequency	Purpose of medication	Dosing start date	Still in use	Dosing end date