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ORIGINAL RESEARCH

Pharmacokinetics, Relative Bioavailability, and Safety of the SHR0302 Oral Solution and Tablets: A Single-Center, Randomized, Open-Label, Crossover (Two-Formulation, Two-Period) Phase I Trial in Healthy Chinese Volunteers

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Purpose: This study investigates the pharmacokinetic characteristics and relative bioavailability of SHR0302 oral solution and tablets in healthy Chinese male volunteers.

Patients and Methods: This single-center, randomized, open-label, crossover (two-formulation, two-period) phase I study enrolled 16 healthy male volunteers. Participants were randomized 1:1 to receive single dose 8mg of either the SHR0302 oral solution or the SHR0302 tablet. Blood samples were collected according to the protocol requirements, and SHR0302 plasma concentrations were analyzed using Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS). Pharmacokinetic parameters were calculated using a non-compartmental analysis in Phoenix WinNonlin (version 8.3). Data processing and analysis of pharmacokinetic characteristics and relative bioavailability were conducted using SAS software (version 9.4). Safety was assessed through treatment-emergent adverse events (TEAEs), vital signs, physical examinations, 12-lead electrocardiograms, and laboratory tests.

Results: All 16 enrolled subjects completed the study. The geometric mean ratio (90% confidence interval) for C_{max} of SHR0302 oral solution versus tablets was 1.04 (0.998, 1.09), and the geometric mean ratios (90% confidence intervals) for AUC_{0-t} and AUC_{0-inf} were both 1.04 (1.02, 1.06). These results fell entirely within the bioequivalence range of 80% to 125%. Among the 16 subjects, 5 (31.3%) experienced a total of 6 TEAEs, all of which were mild in severity. No serious adverse events were reported.

Conclusion: In healthy Chinese male volunteers, the bioavailability of the SHR0302 oral solution was comparable to that of the SHR0302 tablet. The drug was safe and well tolerated following a single dose.

Keywords: pharmacokinetics research, comparative bioavailability, different dosage forms, healthy Chinese male subjects

Introduction

Graft-versus-host disease (GVHD) is a clinicopathological syndrome caused by donor-derived lymphocytes attacking the recipient's organs during the immune reconstitution phase following allogeneic hematopoietic stem cell transplantation (allo-HSCT). It is the most common complication and a leading cause of death in allo-HSCT. The National Institutes of Health (NIH) classifies GVHD into acute and chronic forms based on clinical manifestations.[1] The incidence of GVHD ranges from approximately 50% to 60%, depending on various factors, such as age, HLA matching, conditioning regimens, prophylactic treatments, concomitant infections, and the type of stem cell source.[2] The incidence of moderate-to-severe acute GVHD is 13%–47%,[3] while chronic GVHD occurs in 30–70% of cases.[4]

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JAK family proteins (JAK1, JAK2, JAK3, TYK2) and their downstream effectors, signal transducers, and activators of transcription (STAT) are crucial in the pathogenesis of GVHD.[2] The JAK/STAT signaling pathway is essential for T lymphocyte activation, differentiation, and survival, as well as the production of cytokines and chemokines, which mediate the multi-layered immune response in GVHD. Studies have shown that JAK1 and JAK2 inhibitors can successfully block immune cell receptors such as INF-γB and IL-6R, reduce effector T cell proliferation and proinflammatory cytokine responses,[5] downregulate INF-γB signaling and CXC chemokine receptor 3 (CXCR3) expression, and inhibit T cell migration to GVHD target organs.[6] Additionally, JAK inhibitors downregulate antigen-presenting cell activation, major histocompatibility complex expression, co-stimulatory signals, and CD4+Th cell function and prevent effector lymphocytes from migrating to target tissues. JAK1/2 selective inhibitors suppress INF-γ and IL-6 signaling while preserving the IL-2-JAK3-STAT5 pathway, thereby preserving the function of Treg cells.[2]

SHR0302 tablet (SHR0302) is JAK1-selective inhibitors developed by Jiangsu Hengrui Medicine Co., Ltd. and Shanghai Hengrui Medicine Co., Ltd. (hereinafter referred to as Hengrui).[7] It received initial clinical trial approval as a Class 1.1 chemical drug from the National Medical Products Administration (NMPA) in 2015. SHR0302 has a molecular formula of $C_{18}H_{22}N_8O_2S{\cdot}H_2SO_4$, a molecular weight of 512.56, and the chemical name (3aR,5s,6aS)-N-(3-methoxy-1,2,4-thiadiazol-5-yl)-5-(methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino)hexahydrocyclopenta[c]pyrrole-2(1H)-carboxamide hydrogen sulfate. The selective inhibitor targeting JAK1 can block the JAK/STAT pathway in a targeted manner and reduce drug-related adverse reactions, achieving good clinical efficacy. Due to the potential for GVHD to affect the oral cavity and digestive tract, causing dysphagia in patients, and considering that pediatric and elderly patients also commonly experience swallowing difficulties, an oral solution formulation offers a more suitable alternative. Consequently, a new formulation, SHR0302 oral solution, has been developed based on SHR0302 tablet and is intended to be used to apply for GVHD indications. The oral solution formulation aims to improve medication adherence, offering significant application prospects particularly for children or individuals with GVHD affecting the oral cavity. Therefore, a bioavailability study is required to characterize the pharmacokinetics (PK) on SHR0302 oral solution and determine the dosage regimen.

Materials and Methods

Study Design and Population

This study was conducted at Beijing Hospital, China, between May and October 2023. The study protocol was approved by the Ethics Committee of Beijing Hospital (approval number 2023BJYYEC-033-02), and all volunteers provided written informed consent. The trial was registered on Clinicaltrials.gov (NCT05856058) and Chinadrugtrials.org.cn (CTR20231363).

Healthy Chinese male subjects aged 18–45 years, weighing ≥50 kg, and with a body mass index (BMI) between 19 and 26 kg/m^2 were recruited. The inclusion and exclusion criteria are detailed in the supplementary materials.

According to the Technical Guidelines for Human Bioavailability and Bioequivalence Studies of Innovative Drugs[8] and the Technical Guidelines for Human Bioequivalence Studies of Generic Chemical Drugs Using Pharmacokinetic Parameters as Endpoint Evaluation Indicators[9] issued by the Center for Drug Evaluation of the National Medical Products Administration, bioavailability (BA) studies are commonly used to assess changes in formulations during drug development. BA studies can also provide pharmacokinetic (PK) information for revised formulations. Following these guidelines, this study employed a two-formulation, two-period crossover design to evaluate the relative bioavailability of a single dose of SHR0302 oral solution versus tablets.

The study consisted of four phases: screening, baseline, dosing observation, and follow-up. A total of 16 healthy Chinese male volunteers were enrolled, with 8 subjects in group 1 (tablets to oral solution) and 8 in group 2 (oral solution to tablets).

Following baseline examinations, subjects underwent reassessment against inclusion and exclusion criteria. Eligible participants were admitted to the clinical research center and randomly assigned to Group 1 or Group 2 in a 1:1 ratio. In cycle 1, subjects in Group 1 received a single 8 mg dose of SHR0302 tablets after fasting, while those in Group 2 received 8 mg of SHR0302 oral solution (20 mL) under fasting conditions. In cycle 2, the treatments were

crossed: Group 1 received the oral solution, and Group 2 received the tablets, both administered after an overnight fast. All subjects consumed a light dinner the night before each administration and fasted for >10 hours (water permitted).

In the first cycle, subjects in group 1 took 8mg SHR0302 tablet in the morning on the day of administration. The drug was required to be swallowed without chewing and taken with about 240 mL of warm water. The subjects were fasted for 10 hours before administration, no water intake 1 hour before and after administration, and were fasted for 4 hours after administration. In the second cycle, the subjects followed the same medication protocol as the group 2 subjects in the first cycle.

In the first cycle, subjects in group 2 took 20 mL of SHR0302 oral solution in the morning of the day of administration and then took it with about 220 mL of warm water. They were required to fast for 10 hours before administration, no water intake 1 hour before and after administration, and were fasted for 4 hours after administration. In the second cycle, the subjects follows the same medication protocol as the group 1 subjects in the first cycle.

Blood Sample Collection

Venous blood was collected within 1 h before administration of each period and 0.25 h, 0.5 h, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h, 8 h, 10 h, 12 h, 24 h, 48 h, and 72 h after administration.

Fifteen blood samples were collected per period, comprising one pre-dose and fourteen post-dose samples. About 4 mL of venous blood was collected each time into a K_2EDTA anticoagulant vacuum blood collection tube, which was gently inverted 5–8 times to fully mix the blood and anticoagulant.

Within 1 hour after collection, the blood samples were centrifuged at room temperature or 2–8°C (set temperature 4°C) and 2000g±100g for 10 minutes to fully separate the plasma and obtain the clarified upper plasma. The centrifuged plasma samples were transferred to −60 to −90°C ultra-low temperature for long-term storage within 1 hour or temporarily stored in a refrigerator at −20°C (−12 to −28°C) or below −20°C, followed by transfer to −60 to −90°C ultra-low temperature for long-term storage within 24 hours.

Determination Method and Sample Treatment

Detection Condition

In this study, the validated LC-MS/MS method was used to detect SHR0302 in human K2EDTA plasma. Method validation and sample analysis were commissioned by Shanghai Fangda Bio-Technology Co., LTD.

Chromatographic conditions: Chromatographic column: Phenomenex, model Synergi 4μm Polar-RP 80A C18, specification 2.0×50 mm, column temperature: 40°C, automatic injector temperature: 5°C, mobile phase A: aqueous solution containing 0.1% formic acid and 5mM ammonium acetate, mobile phase B: 100% methanol. Needle washing solvent: methanol/acetonitrile/water/formic acid mixed solution: 40/40/20/0.1 (volume ratio). Injection volume: 10 μL, flow rate: 1.0 mL/min, initial mobile phase B component: 40%, running time: 3.5 minutes.

Mass spectrum conditions: Instrument model: Sciex API 4000, Ion source: TurboIonSpray®, ionization mode: positive ion, scanning mode: multiple reaction monitoring (MRM), ion spray voltage (IS) 5000, ion source temperature 500, collision-induced dissociation (CAD) 10, curtain gas (CUR) 25, spray gas/auxiliary gas (Gas1/2) 55; MRM ion pairs: SHR0302, m/z 415.1→m/z 258.2, cluster removal voltage (DP) 38, collision energy (CE) 23, collision unit exit potential (CXP) 15. SHR143181(IS) m/z 398.2→m/z 258.2, cluster removal voltage (DP) 46, collision energy (CE) 21, collision cell exit potential (CXP) 11.

Methodological Verification Results

In this study, the validated LC-MS/MS method was used to detect the concentration of SHR0302 in human K_2EDTA plasma. SHR0302 had a good linear relationship with a peak area in the range of 1–1000ng/mL, and the lower limit of quantification (LLOQ) was 1 ng/mL. The precision and accuracy of the method were calculated based on the results of the quality control samples. The intra-lot relative standard deviation [% coefficient of variation (CV)] of SHR0302 quality control samples for each concentration level (except LLOQ) was ≤5.5%, and the inter-lot relative standard deviation (%CV) was ≤4.4%. For each concentration level (except LLOQ) of SHR0302 quality control sample, the in-lot accuracy (deviation %) ranged from −3.7% to 4.9%, and the inter-lot accuracy (deviation %) ranged from −2.5% to

2.2%. The relative standard deviation (%CV) of the LLOQ concentration level of SHR0302 quality control sample was ≤8.3% within the lot, and the relative standard deviation (%CV) between the lot was ≤6.2%. The LLOQ concentration level of SHR0302 quality control sample had an intra-lot accuracy (deviation %) in the range of −4.2–5.1% and an inter-lot accuracy (deviation %) of 0.6%. The precision and accuracy of the quality control samples within and between batches met the acceptance criteria for biological samples. The results of methodology verification showed that SHR0302 plasma samples were stable at room temperature for 21 hours, at −70 °C for 5 freezing/thawing cycles, at −20 °C for 294 days, and at −70°C for 937 days. The selectivity, accuracy, precision, matrix effect, recovery rate, residual effect, dilution reliability, stability, and other indicators of the method met the accepted criteria and can be used to determine the concentration of SHR0302 in human K_2EDTA plasma.[10–12]

Endpoints and Assessments

The main study objective was to evaluate the relative bioavailability of SHR0302 oral solution and tablets in healthy subjects.

The main PK parameters were C_{max}, $AUC_{0\text{-}t}$, and $AUC_{0\text{-}inf}$; other PK parameters were T_{max}, $t_{1/2}$, $C_{L/F}$, and $V_{z/F}$. The WinNonlin (version 8.3) noncompartmental model was used to estimate and analyze the PK parameters.[13] The mixed-effects model was used to analyze the main PK parameters (C_{max}, $AUC_{0\text{-}t}$, $AUC_{0\text{-}inf}$) after natural logarithm transformation. In the model, drug preparation (oral solution and tablets), administration sequence, and cycle were used as fixed effects, and subjects were used as random effects. The least-squares mean difference and its 90% confidence interval (CI) between different preparations were estimated by the model, and then the antilogarithm was taken to obtain the estimation of the least-squares geometric mean ratio and 90% CI of the corresponding PK parameters.

The secondary study objective was to evaluate the safety and tolerability of a single dose of SHR0302 oral solution and tablets.

Safety evaluation included the assessment of adverse events, vital signs, physical examination, 12-lead electrocardiogram, and laboratory tests. Treatment-emergent adverse events (TEAEs) were defined as any untoward medical event occurring in subjects after taking the study drug.[14] They were monitored throughout the study and coded using the ICH International Medical Dictionary for Research Use (MedDRA Dictionary, v26.0).

Statistical Analysis

All statistical analyses were performed using SAS9.4 (SAS Institute, Inc., Cary, NC, USA) software. Continuous variables are presented as mean (standard deviation, SD). Categorical variables are summarized as frequency counts (n) and percentages (%). Group differences in categorical variable distributions are presented in frequency tables. For pharmacokinetic (PK) parameters (e.g. drug concentrations, PK indices), geometric mean and geometric CV, were reported when log-normality was confirmed. These metrics provide a more accurate representation of central tendency and dispersion for skewed distributions. Inferential statistical tests for bioequivalence and the significance level ($\alpha = 0.05$, two-tailed) will be detailed in the reporting of group comparisons.

Results

Demographics and Baseline Characteristics

A total of 16 subjects were enrolled in this study, and all of them completed the entire trial. All subjects were male, of whom 14 were Han, 1 was Mongolian, and 1 was Manchu. The mean age (standard deviation) of the enrolled subjects was 27.9 years (4.15 years); the mean weight (standard deviation) was 66.3 kg (6.93 kg), mean height (standard deviation) was 170.8 cm (4.92 cm), and mean BMI (standard deviation) was 22.7 kg/m^2 (1.77 kg/m^2) (see Table 1).

Pharmacokinetics

After a single oral dose of the SHR0302 oral solution (8 mg) and SHR0302 tablets (8 mg) in healthy subjects, the geometric means of SHR0302 C_{max} in plasma were 619 and 593 ng/mL, respectively; the geometric means of $AUC_{0\text{-}t}$ were 4750 and 4570 h*ng/mL, respectively; and the geometric means of $AUC_{0\text{-}inf}$ were 4770 and 4600 h*ng/mL,

Table 1 Demographic Characteristics

Characteristics	Group 1 (Tablets to Oral Solution) (N=8)	Group 2 (Oral Solution to Tablets) (N=8)	Total (N=16)
Age (years)			
N	8	8	16
Mean (SD)	27.1 (4.82)	28.8 (3.49)	27.9 (4.15)
Median	26.5	29.5	28
Min, Max	22:35	23:33	22:35
Sex, n (%)			
Male	8 (100%)	8 (100%)	16 (100%)
Female	0	0	0
Total	8	8	16
Ethnicity [n (%)]			
Han	7 (87.5%)	7 (87.5%)	14 (87.5%)
Rest	1 (12.5%)	1 (12.5%)	2 (12.5%)
Total	8	8	16
Height (cm)			
N	8	8	16
Mean (SD)	169.88 (5.276)	171.75 (4.683)	170.81 (4.916)
Median	170.5	171	171
Min, Max	162.0: 176.0	166.0: 180.0	162.0: 180.0
Weight (kg)			
N	8	8	16
Mean (SD)	65.03 (7.564)	67.51 (6.493)	66.27 (6.930)
Median	66.85	65.7	65.7
Min, Max	52.4: 74.3	59.6: 79.0	52.4: 79.0
BMI (kg/m^2)			
N	8	8	16
Mean (SD)	22.48 (1.904)	22.87 (1.735)	22.68 (1.771)
Median	22.9	22.85	22.85
Min, Max	20.0: 24.5	20.6: 25.0	20.0: 25.0

Notes: Data are presented as the number of observations, mean (standard deviation), and median (minimum, maximum), except for sex and nation, which are presented as n (%) for each category. Baseline is defined as the last nonmissing measurement before the first dose of any study medication.

Abbreviations: BMI, body mass index; N, number of subjects in the population/cohort; n, number of subjects with valid observations; %, percentage of subjects with valid observations (n/Nx100).

respectively. The relative bioavailability between SHR0302 oral solution and SHR0302 tablets was calculated using $AUC_{0\text{-}t}$. Compared with SHR0302 tablet, the relative bioavailability mean (standard deviation) of the SHR0302 oral solution was 103.8% (4.63%; Figures 1, 2 and Tables 2, 3).

Bioequivalence Evaluation

The SAS PROCMIXED mixed-effects model was used for analysis, in which medication, treatment sequence, and treatment cycle were used as fixed effects and subjects were used as random effects to participate in model fitting. For SHR0302 in plasma, the geometric mean ratio of C_{max} and its 90% CI of the SHR0302 oral solution and SHR0302 tablet were 1.04 (0.998, 1.09); those of $AUC_{0\text{-}t}$ were 1.04 (1.02, 1.06); and those of $AUC_{0\text{-}inf}$ were 1.04 (1.02, 1.06). These ratios and 90% CI values were all within the range of 80–125%. Compared with SHR0302 tablets, the mean (standard deviation) relative bioavailability of the SHR0302 oral solution was 103.8% (4.63%).

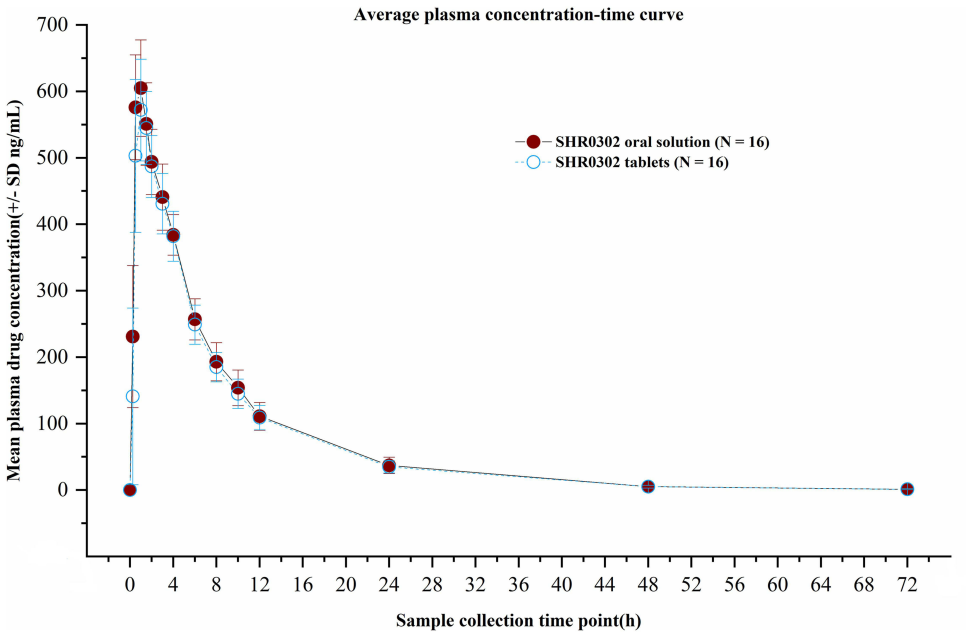

Figure 1 Average plasma concentration-time curve of SHR0302 in different preparations.

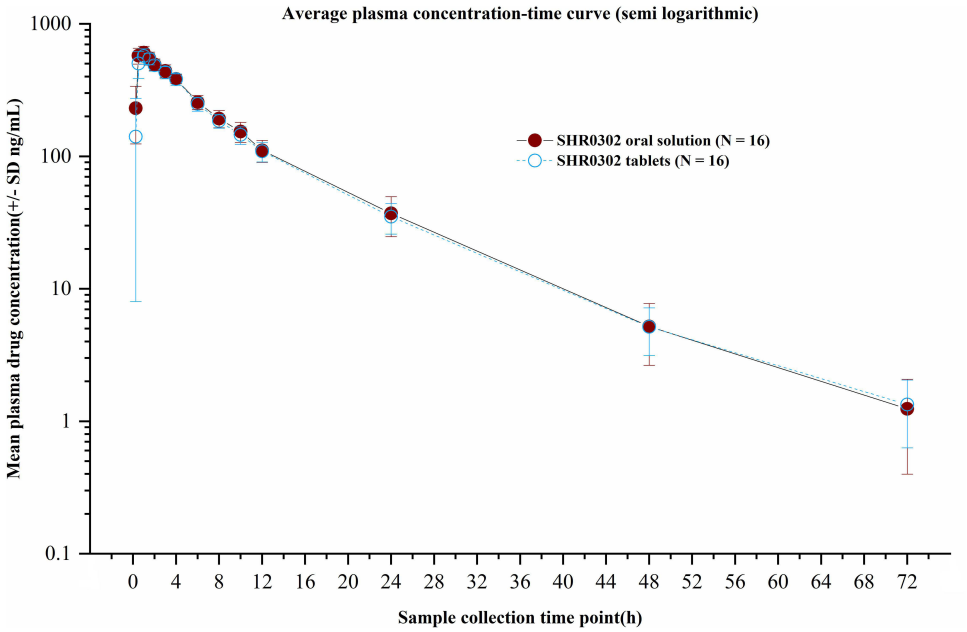

Figure 2 Average concentration-time curves of SHR0302 in plasma from different preparations (semi-logarithmic).

Safety Assessment

During the study, 6 adverse events (TEAEs) occurring later than during treatment were reported in 5 of the 16 subjects, with a TEAE incidence rate of 31.3% (5/16).

During the SHR0302 oral solution administration phase, a total of 4 subjects (4/16, 25%) experienced 5 TEAEs: increased blood levels of alanine aminotransferase (2/16, 12.5%), increased blood levels of aspartate aminotransferase (1/16, 6.3%), increased blood triglycerides (1/16, 6.3%), and increased blood bilirubin (1/16, 6.3%).

During the SHR0302 tablet administration phase, 1 subject (1/16, 6.3%) experienced 1 TEAE of increased blood uric acid (1/16, 6.3%). All TEAEs were assessed as drug-related, mild in severity, and resolved without sequelae (Table 4).

Table 2 Summary of PK Parameters of SHR0302 in Different Formulations in the Plasma of Healthy Male Subjects in China

Parameter	SHR0302 Oral Solution (N=16)	SHR0302 Tablets (N=16)
AUC_{0-t} (h*ng/mL)	4750 (14.0)	4570 (12.2)
AUC_{0-inf} (h*ng/mL)	4770 (14.0)	4600 (12.2)
C_{max} (ng/mL)	619 (10.9)	593 (10.6)
$C_{L/F}$ (L/h)	1.68 (14.0)	1.74 (12.2)
T_{max} (h)	1.00 (0.50:1.50)	1.00 (0.50:1.50)
$t_{1/2}$ (h)	8.41 (17.4)	8.81 (16.9)
$V_{z/F}$ (L)	20.3 (12.9)	22.1 (15.6)
AUC_%Extrap (%)	0.556 (41.9)	0.546 (36.9)

Notes: Except for T_{max}, which is expressed in the form of median (minimum value: maximum value), the data in other tables are expressed in the form of geometric mean (geometric CV %).

Abbreviations: AUC_{0-t}, area under the concentration-time curve in the sampling matrix from zero (before dosing) to the last quantifiable concentration at time "t" (ng*h/mL); AUC_{0-inf}, area under the concentration-time curve in the sampling matrix from zero to infinity (ng*h/mL); AUC_%Extrap: residual area or extrapolated area as a percentage of the total AUC; C_{max}, maximum plasma concentration (ng/mL); $C_{L/F}$, apparent systemic clearance after extravascular administration (L/h); CV, coefficient of variation; T_{max}, time of maximum concentration (h); $t_{1/2}$, terminal elimination half-life (h); $V_{z/F}$, apparent volume of distribution (L).

Table 3 Comparison of PK Parameters of SHR0302 in Different Formulations

Parameter	SHR0302 Oral Solution (N=16)	SHR0302Tablets (N=16)
C_{max} (ng/mL)		
Geometric mean(GM)	619	593
Within-subject coefficient of variation (WSCV) (%)	7.3	-
GMR (90% CI)	1.04 (0.998, 1.09)	-
AUC_{0-t} (h*ng/mL)		
Geometric mean(GM)	4750	4570
Within-subject CV (WSCV) (%)	3.21	-
GMR (90% CI)	1.04 (1.02, 1.06)	-
AUC_{0-inf} (h*ng/mL)		
Geometric mean (GM)	4770	4600
Within-subject CV (WSCV) (%)	3.2	-
GMR (90% CI)	1.04 (1.02, 1.06)	-

Abbreviations: AUC_{0-t}, area under the concentration-time curve in the sampling matrix from zero (before dosing) to the last quantifiable concentration at time "t" (ng*h/mL); AUC_{0-inf}, area under the concentration-time curve in the sampling matrix from zero to infinity (ng*h/mL); C_{max}, maximum plasma concentration (ng/mL); CV, coefficient of variation.

Discussion

Globally, the proportion of pediatric patients receiving allogeneic hematopoietic stem cell transplantation does not exceed 30%.[15–17] Despite the selection of highly HLA-matched donors, chronic GVHD still occurs in approximately 50% of children receiving allogeneic hematopoietic stem cell transplantation.[18] Considering children or other patients who find it difficult to swallow tablets, which may affect their medication adherence, the SHR0302 oral solution was developed based on SHR0302 tablet. SHR0302 is a selective inhibitor of JAK1 that blocks the JAK/STAT pathway by targeting JAK1 and is intended to be applied for the indication of GVHD.[2] Therefore, a bioavailability study was necessary to obtain the PK parameters of the SHR0302 oral solution to determine the dosage regimen.

This study adopted a single-center, randomized, open-label, crossover (two-formulation, two-period) design to compare the relative bioavailability of the SHR0302 oral solution and tablet in healthy male subjects. According to

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Table 4 Summary of Adverse Events During Treatment in Chinese Healthy Subjects

Classification of System Organs Preferred Term	SHR0302 Oral Solution (N=16)		SHR0302 Tablets (N=16)		Total (N=16)	
	Number of subjects (%)	Cases	Number of subjects (%)	Cases	Number of subjects (%)	Cases
Any TEAE	4 (25.0%)	5	1 (6.3%)	1	5 (31.3%)	6
Various inspection	4 (25.0%)	5	1 (6.3%)	1	5 (31.3%)	6
Alanine aminotransferase was elevated	2 (12.5%)	2	0	0	2 (12.5%)	2
Aspartate aminotransferase increased	1 (6.3%)	1	0	0	1 (6.3%)	1
Elevated blood bilirubin	1 (6.3%)	1	0	0	1 (6.3%)	1
Elevated blood triglycerides	1 (6.3%)	1	0	0	1 (6.3%)	1
Hyperuricemia	0	0	1 (6.3%)	1	1 (6.3%)	1

Notes: Adverse Event Coding Dictionary, MedDRA26.0; N, the number of persons in different formulations who belong to the safety analysis set.
Abbreviations: PT, Preferred Term; SOC, System Organ Classification; TEAE, adverse events that occur during treatment.

the study protocol, 16 eligible adult healthy subjects were enrolled and randomly divided into two groups, with all completing the medication as scheduled.

After the administration of the SHR0302 oral solution on an empty stomach, the maximum plasma concentration was reached within 1.00 h (range: 0.50–1.50 h), and the elimination half-life was approximately 8.41 h (range: 7.4–9.5 h). Following the administration of SHR0302 tablets under the same conditions, the highest plasma concentration was also reached within 1.00 h (range: 0.50–1.50 h), with an elimination half-life of approximately 8.81 h (range: 7.9–9.7 h). For SHR0302 in plasma, the geometric mean ratios of C_{max}, AUC_{0-t}, and AUC_{0-o} for the oral solution compared with the tablets, along with their 90% CIs, were all within the range of 80–125%. Compared with SHR0302 tablets, the mean (± standard deviation) relative bioavailability of the oral solution was 103.8% (± 4.63%), indicating that the bioavailability of the oral solution was comparable to that of the tablets. In vitro pharmaceutical dissolution studies of SHR0302 tablets showed that they dissolved rapidly at both pH 1.2 and pH 6.8, with a dissolution rate >85% within 15 min. Consequently, the PK curves of the SHR0302 tablets and oral solution were nearly identical.

Among the 16 subjects who received the drug, a total of 5 subjects (31.3%) experienced 6 TEAEs, all of which were mild in severity. No serious adverse events, adverse events leading to withdrawal, or deaths were reported. This indicates that both the SHR0302 oral solution and tablet were safe and well tolerated after a single dose in healthy subjects. The study results demonstrated that the 20 mL SHR0302 oral solution (containing 8 mg SHR0302) exhibited comparable bioavailability and safety profiles to the 8 mg reference tablet. This solution formulation shows significant promise for enhancing medication adherence in dysphagic patients, indicating substantial clinical utility.

Conclusion

The bioavailability of the SHR0302 oral solution was found to be comparable to that of SHR0302 tablets. Both formulations were demonstrated to be safe and well-tolerated following a single dose administration in healthy volunteers.

Data Sharing Statement

All data generated or analyzed during this study were included in the published article. Further inquiries about the datasets can be directed to the corresponding author on reasonable request. Any information we share will be deidentified.

Ethics Approval

The study was approved by the Ethics Committee of Beijing Hospital. All subjects provided written informed consent. This study was conducted in accordance with consensus ethics principles derived from international ethics guidelines,

including the Declaration of Helsinki and the International Council for Harmonisation guidelines for Good Clinical Practice, as well as all applicable laws, rules, and regulations.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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