A Single-center, Randomized, Open-label Phase Ic/IIb Clinical Study to Evaluate the Efficacy and Safety of Multiple Doses of TNP-2198 Capsules + Rabeprazole Sodium Enteric-coated Tablets + Amoxicillin Capsules, Multiple Doses of TNP-2198 Capsules + Rabeprazole Sodium Enteric-coated Tablets Compared with Multiple Doses of Rabeprazole Sodium Enteric-Coated Tablets + Amoxicillin Capsules in Participants with Positive Helicobacter Pylori Infection

Protocol Synopsis

Protocol No.: TNP-2198-06

Approval Date; 20 January 2022

Protocol Synopsis

Study Title	A Single-center, Randomized, Open-label Phase Ic/IIb Clinical Study to Evaluate the Efficacy and Safety of Multiple Doses of TNP-2198 Capsules + Rabeprazole Sodium Enteric-coated Tablets + Amoxicillin Capsules, Multiple Doses of TNP-2198 Capsules + Rabeprazole Sodium Enteric-coated Tablets Compared with Multiple Doses of Rabeprazole Sodium Enteric-Coated Tablets + Amoxicillin Capsules in Participants with Positive Helicobacter Pylori Infection
Study Objectives	**Primary Objectives:** 1 To evaluate the helicobacter pylori eradication effect of multiple doses of TNP-2198 capsules, rabeprazole sodium enteric-coated tablets and amoxicillin capsules in participants with positive H. pylori infection; 2 To evaluate the helicobacter pylori eradication effect of multiple doses of TNP-2198 capsules and rabeprazole sodium enteric-coated tablets in participants with positive H. pylori infection. **Secondary Objectives:** 1 To evaluate the safety and tolerability of multiple doses of TNP-2198 capsules, rabeprazole sodium enteric-coated tablets, and amoxicillin capsules in participant with positive H. pylori infection; 2 To evaluate the safety and tolerability of multiple doses of TNP-2198 capsules and rabeprazole sodium enteric-coated tablets in participant with positive H. pylori infection; 3 To evaluate the pharmacokinetic characteristics of TNP-2198 (including major metabolites), rabeprazole, and amoxicillin.
Study Endpoints	**Primary Study Endpoint** H. pylori eradication rate (confirmed by ^{14}C UBT) on Days 28 to 34 after the last dose. **Secondary Study Endpoints** 1 The negative rate of ^{14}C UBT on Day 8 after the first dose; 2 The negative rate of ^{14}C UBT on Day 16 after the first dose; 3 Safety endpoints: Incidence of adverse events (AE) during the study, correlation with the investigational medicinal product and severity, laboratory tests, vital signs, ECG, physical examination, etc.; 4 Pharmacokinetic endpoints: Pharmacokinetic parameters of TNP-2198, rabeprazole, amoxicillin in each group of consecutive administrations.
Protocol No.	TNP-2198-PO-06
Sponsor	TenNor Therapeutics
Clinical Trial Notification No.	CXHL1800160/161
Study Facility	Phase I Drug Clinical Study Center of the First Hospital of Jilin University, Department of Gastroenterology of the First Hospital of Jilin University
Study Phase	Phase Ic/IIb

Investigational Products

TNP-2198 capsules
- Manufacturer: WuXi STA (Shanghai) Co., Ltd. (entrusted)
- Strength: 100 mg
- Storage Condition: Preserve in tightly closed containers, protected from light and stored at ambient temperature (10-30 °C)

Rabeprazole Sodium Enteric-coated Tablets
- Manufacturer: Eisai China lnc.
- Drug Approval No.: GuoYaoZhunZi H20090090
- Strength: 20 mg
- Storage Condition: Preserve in tightly closed containers, protected from light and stored below 25 °C

Amoxicillin Capsules
- Manufacturer: Zhuhai United Laboratories (Zhongshan) Co., Ltd.
- Drug approval No.: GuoYaoZhunZi H44021351
- Strength: 0.5 g
- Storage conditions: to be determined

Study Design

Study participant: 80 participants positive for H. pylori infection.

The purpose is to evaluate the efficacy, safety and tolerability, and pharmacokinetic characteristics of multiple-dose treatment with TNP-2198 capsules, rabeprazole sodium enteric-coated tablets and amoxicillin capsules, and TNP-2198 capsules and rabeprazole sodium enteric-coated tablets compared with continuous administration of rabeprazole sodium enteric-coated tablets and amoxicillin capsules.

In this study, a total of 4 test groups and 1 control group are set, 80 participants are planned to be enrolled and randomly assigned in a ratio of 2:2:1:1:2:

Study grouping		Dosing regimen	Frequency of administration and course of treatment	Number of participants
Test group	Group A	TNP-2198 capsules 400 mg, rabeprazole sodium enteric-coated tablets 20 mg, amoxicillin capsules 1 g	BID × 14 days	20
	Group B	TNP-2198 capsules 600 mg, rabeprazole sodium enteric-coated tablets 20 mg, amoxicillin capsules 1 g	BID × 14 days	20
	Group C	TNP-2198 capsules 600 mg, rabeprazole sodium enteric-coated tablets 20 mg	TID × 14 days	10
	Group D	TNP-2198 capsules 600 mg, rabeprazole sodium enteric-coated tablets 20 mg, amoxicillin capsules 1 g	TID × 7 days	10
Control group		Rabeprazole sodium enteric-coated tablets 20 mg, amoxicillin capsules 1 g	BID × 14 days	20

Eligible participants will be admitted to the clinical study center 1 day before dosing (D-1).

Study procedures of Group A, Group B, Group C and Control Group (administration for 14 consecutive days):

	The participants take the investigational product every day on Days 1 to 14 (D1-D14) aand take the last dose of the investigational product in the morning of Day 15 (D15) according to the dosage regimen of each group. Pharmacokinetic blood samples will be collected at the time points scheduled in the protocol during the study, and safety and tolerability evaluation, and ^{14}C UBT will be conducted. All participants are discharged from the study center after safety and tolerability evaluation and PK blood collection are completed on Day 17 (D17), and return to the study center for follow-up visit on Days 44 to 50 (D44-D50). Adverse events and laboratory test abnormalities are followed until complete response or return to baseline or steady state, safety and tolerability assessments are performed, and ^{14}C UBT is performed to evaluate the effect of Hp eradication. **Study procedures of Group D (administration for 7 consecutive days):** The investigational product is administered daily on study Days 1 to 7 (D1-D7), and the last dose of the investigational product is administered as specified in the dosage regimen in the morning of Day 8 (D8). Pharmacokinetic blood samples will be collected at the time points scheduled in the protocol during the study, and safety and tolerability evaluation, and ^{14}C UBT will be conducted. All participants are discharged from the study center after safety and tolerability evaluation and PK blood collection are completed on Day 10 (D10), and return to the study center for follow-up visit on Days 37 to 43 (D37-D43). Adverse events and laboratory test abnormalities are followed until complete response or return to baseline or steady state, safety and tolerability assessments are performed, and ^{14}C UBT is performed to evaluate the effect of Hp eradication.
Screening Examination Items and Time	I.e., D-14-D-2. After the participants sign the informed consent form, collect and record their demographic information (including sex, ethnicity, age, weight, height, and calculate BMI), medical history, operation history, smoking history, reproductive status, alcohol history/diet, prior medication, etc. And conduct physical examination, record of vital signs (blood pressure, pulse rate, respiratory rate and body temperature), clinical laboratory tests (blood routine, blood biochemistry, urine routine and coagulation function), infectious disease screening (hepatitis B two half and half, hepatitis C antibody, HIV antigen/antibody, treponema pallidum antibody [rapid plasma reagin RPR test is required for those with positive treponema pallidum antibody]), serum pregnancy test (only for female participants), 12-lead electrocardiogram, chest plain X-ray, abdominal Dopler ultrasound (digestive system + urinary system) and ^{14}C UBT. Note: Test results of hepatitis B two half and half, hepatitis C antibody, HIV antigen/antibody and treponema pallidum antibody are acceptable within 3 months before screening; The test results of chest plain X-ray are acceptable within 1 year before screening; The test results of abdominal Dopler ultrasound are acceptable within 1 month prior to screening.
Admission (Baseline) Examination Items and Time	I.e., D-1. Participants will be admitted to the clinical study center one day before dosing, medical and surgical history will be collected, physical examination will be performed, vital signs will be recorded, and the following tests will be performed: blood routine, urine routine, blood biochemistry, coagulation function, serum pregnancy test (only for female participants), urine drug screen (morphine, marijuana), alcohol breath test, ECG, and ^{14}C UBT. Laboratory tests, except serum pregnancy test, are conducted within 7 days of baseline. The inclusion and exclusion criteria are checked again. Randomization numbers are assigned to enrolled participants.
Hospitalization/Dosing Period	1) Group A, Group B, Group C and Control Group

<table>
<tr><td></td><td>The hospitalization/administration period is from D1 to D17. According to the dosage regimen, the investigational product is orally administered on time every day for 14 consecutive days, and the last dose of the investigational product is administered in the morning of D15. Physical examination, vital signs, blood routine, urine routine, blood biochemistry, coagulation function, ECG, ^{14}C UBT and other tests will be performed during hospitalization, and PK blood samples will be collected at the time points specified in the protocol. After all tests (serum pregnancy test is required only for female participants) and PK blood collection are completed on D17, the participants can be discharged from the study center.

2) Group D
The hospitalization/administration period is from D1 to D10. According to the dosage regimen, the investigational product is orally administered on time every day for 7 consecutive days, and the last dose of investigational product is administered in the morning of D8. Physical examination, vital signs, blood routine, urine routine, blood biochemistry, coagulation function, ECG, ^{14}C UBT and other tests will be performed during hospitalization, and PK blood samples will be collected at the time points specified in the protocol. Participants can be discharged from the study center on D10 after completion of all tests (serum pregnancy test for female participants only) and PK blood sampling.</td></tr>
<tr><td>Follow-up Period</td><td>Participants in Group A, Group B, Group C and Control Group will return to the study center for follow-up visit from D44 to D50. Participants in Group D will return to the study center for follow-up visit from D37 to D43. Adverse events and laboratory test abnormalities are followed until complete response or return to baseline or steady state, safety and tolerability assessments are performed, and ^{14}C UBT is performed to evaluate the effect of Hp eradication.</td></tr>
<tr><td>Dosing Regimen</td><td>Group A, Group B and Control Group:
Two doses per day, breakfast and dinner should be eaten within 30 minutes prior to dosing, and oral administration should be given after meals. All investigational products should be taken after meals for 14 consecutive days. On Day 15, participants will have breakfast within 30 minutes prior to dosing, and the last dose will be taken after completion of meals. Each participant will take 29 doses of investigational products.

Group C, Group D:
Three doses per day, 8 hours apart. Group C is administered for 14 consecutive days, with the last dose on the morning of Day 15, and each participant receives 43 doses of investigational product; Group D is administered for 7 consecutive days, with the last dose on the morning of Day 8, and each participant receives 22 doses of investigational product.
The drug name, dose and course of treatment in each group are shown in the following table:
<table>
<tr><th colspan="2" rowspan="2">Study grouping</th><th rowspan="2">Frequency of administration</th><th colspan="3">Number of capsules/tablets per dose</th><th rowspan="2">Dosing course (days)</th></tr>
<tr><th>TNP-2198 capsules (100 mg/capsule)</th><th>Rabeprazole Sodium Enteric-coated Tablets (20 mg/tablet)</th><th>Amoxicillin Capsules (0.5 g/capsule)</th></tr>
<tr><td rowspan="4">Test group</td><td>Group A</td><td>BID</td><td>4</td><td>1</td><td>2</td><td>14</td></tr>
<tr><td>Group B</td><td>BID</td><td>6</td><td>1</td><td>2</td><td>14</td></tr>
<tr><td>Group C</td><td>TID</td><td>6</td><td>1</td><td>-</td><td>14</td></tr>
<tr><td>Group D</td><td>TID</td><td>6</td><td>1</td><td>2</td><td>7</td></tr>
<tr><td colspan="2">Control group</td><td>BID</td><td>-</td><td>1</td><td>2</td><td>14</td></tr>
</table></td></tr>
</table>

Inclusion Criteria	Participants must meet all of the following criteria to be enrolled: 1 Voluntary signing of the Informed Consent Form (ICF); 2 Age 18-65 years (inclusive), male or female; 3 Health status: participants do not have history of clinically significant cardiovascular, liver, kidney, digestive tract, nervous system, respiratory system, mental disorder and metabolic disorder; 4 Physical examination and vital signs are normal or abnormal but not clinically significant as judged by the investigator; 5 Clinical laboratory test results are within normal range or abnormal but not clinically significant as judged by the investigator; 6 Those whose ^{14}C urea breath test (^{14}C UBT) results are positive. 7 Participants must agree to have no pregnancy plan and voluntarily take effective contraceptive measures during the study and for at least 6 months after last dose administration; 8 Willing to follow and be able to complete all study procedures.
Exclusion Criteria	Participants were not to be enrolled if they met any of the following exclusion criteria: 1 History of helicobacter pylori eradication therapy (including participation in other clinical studys for helicobacter pylori eradication); 2 Those who smoked more than 5 cigarettes per day in the 3 months prior to screening; 3 Those who are allergic to the investigational product or or its excipients, or participants with allergic constitution (multiple drug and food allergies); 4 Those who have a history of drug and/or alcohol abuse (average weekly consumption of ≥ 14 units of alcohol: 1 unit = 285 mL of beer, or 25 mL of spirits, or 100 mL of wine); 5 Those who have blood donation or massive blood loss (> 450 mL) within 3 months prior to screening; 6 Those who have taken any drug that changes the activity of liver enzyme within 28 days prior to screening; 7 Those who have taken any prescription drugs, over-the-counter drugs, any vitamin products, or herbal remedies within 14 days prior to screening; 8 Those who have taken special diet (including pitaya, mango, grapefruit, etc.) or have had strenuous exercise within 2 weeks prior to screening, or other factors affecting drug absorption, distribution, metabolism, excretion, etc.; 9 Those who have had a major change in diet or exercise habits recently; 10 Those who have taken the other study drug or participated in the other clinical study that have not been finished within 1 month prior to administration of the investigational products; 11 Those who have a history of dysphagia or any gastrointestinal disease affecting drug absorption; 12 Those who have any disease that increases the risk of bleeding, such as hemorrhoids, acute gastritis or gastric and duodenal ulcers; 13 Those who have abnormal ECG with clinical significance; 14 Female participants who are in lactation or have a positive result in serum pregnancy test at screening or during the course of the study; 15 Those with symptoms of cardiovascular, digestive, respiratory, urinary, neurological, hematological, immunological, endocrine system or tumor, and mental illness or with past medical history that has not been cured; 16 The following diseases (including but not limited to gastrointestinal, renal, hepatic, neurologic, hematologic, endocrine, oncologic, pulmonary, immunologic, psychiatric or cardiovascular and cerebrovascular diseases) with clinically significant abnormalities in clinical laboratory tests or other clinical findings;

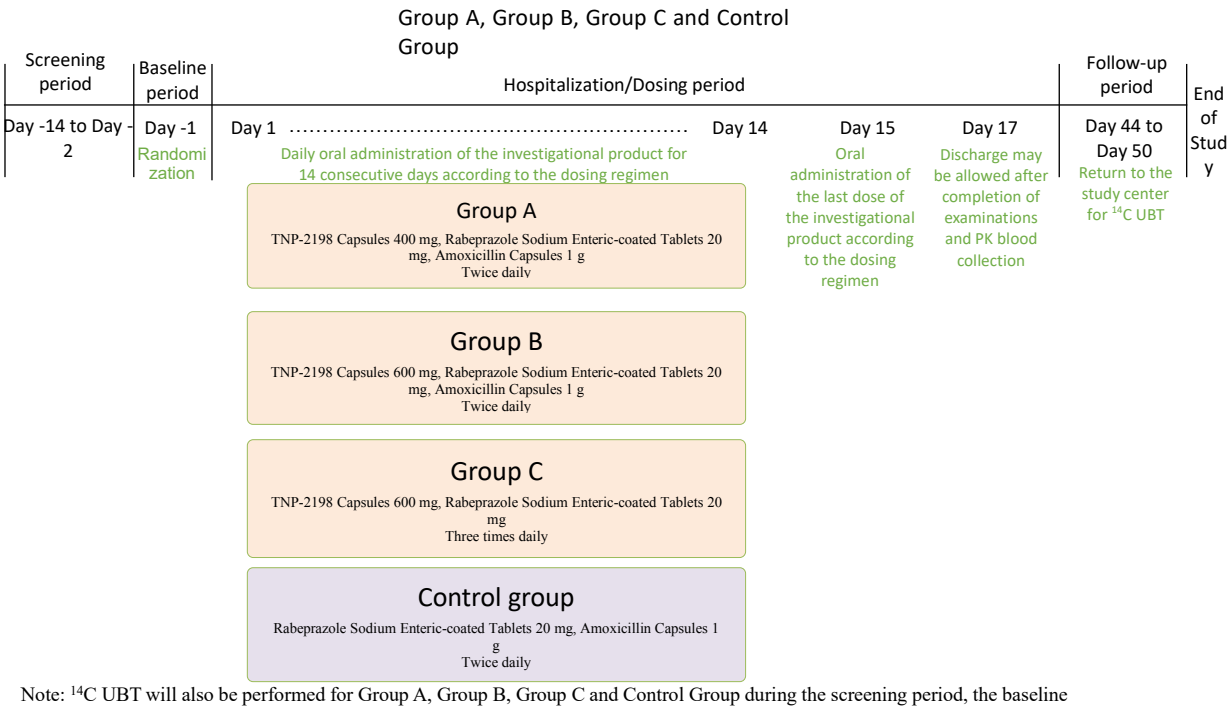
	17 Viral hepatitis (including hepatitis B and C), HIV antibody, treponema pallidum antibody positive (those with positive treponema pallidum antibody need additional RPR test); 18 Acute illness or concomitant medication from the time of signing the informed consent form to the time before administration of investigational product; 19 Consumption of chocolate, any caffeine-containing or xanthine-rich food or beverages within 48 hours prior to administration of the investigational product; 20 Those who have taken any alcohol-containing products within 48 hours prior to administration of the investigational product; 21 Those with a positive result in urine drug screening or a history of drug abuse or drug use within the past 5 years; 22 Other conditions considered by the investigator unsuitable for participation in the study.
Safety and Tolerability Judgement Criteria	CTCAE 5.0 criteria are used.
Safety and Tolerability Evaluation	All participants are observed for any adverse events occurring during the clinical study, and their clinical manifestations, severity, onset time, end time, treatment measures and outcome are recorded, and their correlation with the investigational product shall be determined. Safety and tolerability evaluation mainly includes adverse events (AE), physical examination, vital signs (blood pressure, pulse rate, respiratory rate and body temperature), clinical laboratory tests (hematology, urinalysis, blood biochemistry, coagulation function) and ECG.
Concomitant Medications	All non-investigational products taken by the participant from the time of signing the informed consent form through the last study visit are considered concomitant medications, and information regarding the medication will be recorded on the CRF, including the drug name (trade name and generic name), start date, dose, mode of administration, reason for use, and stop date. Use of concomitant medications should be minimized during the study. However, if these medications are beneficial to the participant and necessary, and are not likely to interfere with the study, they may be administered at the discretion of the investigator.
Prohibited Medications	Any prescribed drugs or over-the-counter drugs, including vitamins, minerals, nutritional supplements, herbal remedies, etc., are not allowed within 2 weeks prior to screening and during the study, except for drugs used to treat adverse events.
Pharmacokinetics Sample Collection	PK collection time points: PK blood samples will be collected at the following time points. 1) Blood sampling time points in Group A, Group B and Control Group: • Day 1: within 30 Minutes Pre-dose, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 9, 10, 11, 12 Hours Post-Dose (Prior to the Second Dose of the Day); • Days 3, 5, 7, 9, 11, 13, and 14: within 30 minutes prior to dosing; • Day 15: Within 30 Minutes Pre-dose, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 9, 10, 11, 12, 24 Hours (Day 16) and 48 Hours (Day 17) Post-dose. 2) Blood sampling time points in Group C: • Day 1: within 30 minutes before dosing, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8 hours after dosing (prior to the second dose of the day); • Days 3, 5, 7, 9, 11, 13, 14: within 30 minutes prior to dosing;

	• Day 15: Within 30 Minutes Pre-dose, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 9, 10, 11, 12, 24 Hours (Day 16) and 48 Hours (Day 17) Post-dose. 3) Blood sampling time points in Group D: • Day 1: within 30 minutes before dosing, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8 hours after dosing (prior to the second dose of the day); • Days 3, 5, 7: within 30 minutes prior to dosing; • Day 8: Within 30 Minutes Pre-dose, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 9, 10, 11, 12, 24 Hours (Day 9) and 48 Hours (Day 10) Post-dose. PK blood sample processing method: Whole blood is collected in vacutainers containing anticoagulant, 4 mL per tube, and plasma is obtained by centrifugation after completion of whole blood collection, and the plasma samples are divided into two aliquots and stored in a -80 ℃ refrigerator, one for pharmacokinetics analysis and the other as a backup. The process from sample collection to -80 ℃ refrigerator storage needs to be completed within 1 hour. Refer to the Laboratory Operation Manual for specific operation requirements.
Pharmacokinetic Parameters	First dose PK parameters include at least: • Time to peak concentration (T_{max}) • Peak concentration (C_{max}) • Elimination half-life ($t_{1/2}$) • Area under the plasma concentration-time curve from the first dose extrapolated to infinity ($AUC_{0-\infty}$) • Area under the plasma concentration-time curve from the first dose to the dosing interval (AUC_{0-tau}) ■ Groups A, B, Control: dosing interval is 12 hours ■ Groups C, D: dosing interval is 8 hours • Apparent volume of distribution (V_d/F) • Apparent clearance (CL/F) Last dose PK parameters include at least: • Time to peak ($T_{max,ss}$) • Maximum plasma concentration at steady state ($C_{max,ss}$) • Minimum plasma concentration at steady state ($C_{min,ss}$) • Mean plasma concentration at steady state（$C_{avg,ss}$) • Elimination half-life ($t_{1/2,ss}$) • Area under the plasma concentration-time curve from the last dose to the last measurable concentration time point ($AUC_{0-last,\ ss}$) • Area under the plasma concentration-time curve from the last dose to the dosing interval ($AUC_{0-tau,ss}$) ■ Groups A, B, Control: dosing interval is 12 hours ■ Groups C, D: dosing interval is 8 hours • Area under the plasma concentration-time curve from the last dose extrapolated to infinity ($AUC_{0-\infty,\ ss}$) • Apparent volume of distribution at steady state (V/F_{ss}) • Apparent clearance (CL/F_{ss}) • Accumulation Index (R_{ac}) ■ Groups A, B, C, Control: $AUC_{0-tau,ss}$ on Day 15/AUC_{0-tau} on Day 1 ■ Group D: $AUC_{0-tau,ss}$ on Day 8/AUC_{0-tau} on Day 1 • Fluctuation index (DF): Percent fluctuation at steady state = $100 \times (C_{max,ss} - C_{min,ss})/C_{avg,ss}$

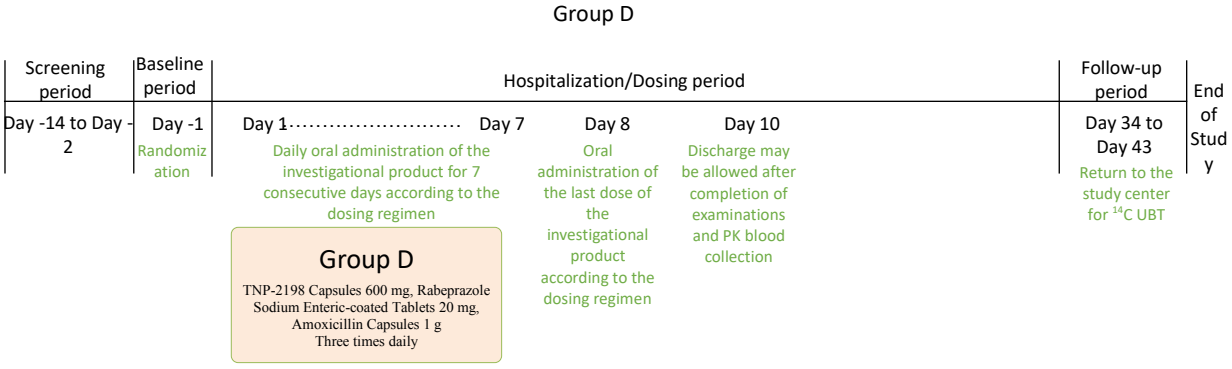
	Note: The apparent volume of distribution (Vd/F) and apparent clearance (CL/F) are not applicable to the analysis of pharmacokinetic parameters of the main metabolites.
Evaluation of Helicobacter Pylori Eradication	Group A, Group B, Group C and Control Group: The ^{14}C UBT are performed on participants under fasting conditions before breakfast at screening (D-14 to D-2), baseline (D-1), day 8 (D8), day 16 (D16) and day 44 to 50 (D44 to D50) to evaluate the effect of H. pylori eradication in each group. Group D: The ^{14}C UBT will be performed on participants under fasting conditions before breakfast at screening (D-14 to D-2), baseline (D-1), Day 8 (D8) and Day 37 to 43 (D37 to D43) to evaluate the effect of H. pylori eradication.
Statistical Analysis	Definition of Statistical Analysis Set: • Full Analysis Set (FAS): Refers to the participant of all randomized participants who have taken the investigational product at least once; • Modified Intent-to-Treat Analysis Set (mITT): Refers to all randomized participants who have ^{14}C UBT performed on Day 28 to 34 after the last dose of the study; • Per Protocol Set (PP): Refers to participants without major protocol violation: participants who are randomized and receive more than 80% (inclusive) of the expected total amount of investigational product, and undergo ^{14}C UBT on Day 28 to 34 after the last dose of the study; • Safety Analysis Set (SS): refers to the participant participant who entered the study and used the investigational product at least once; • Pharmacokinetic Concentration Analysis Set (PKCS): refers to all enrolled participants who have used the investigational product and have at least one observed PK concentration data; • Pharmacokinetic Parameter Analysis Set (PKPS): refers to all enrolled participants who have used the investigational product and have at least one observed PK parameter data. **Demographic Analysis:** Demographic analyses are based on the Full Analysis Set (FAS). Descriptive statistics will be performed for all demographics (age, gender, weight, height, BMI, ethnicity, etc.) and baseline characteristics, taking the last valid measurement data before the administration of the investigational product as the baseline. **Analysis of Helicobacter pylori eradication effect:** The eradication effect will be analyzed descriptively by frequency (percentage) according to four ^{14}C UBT results (negative or positive) at baseline, Day 8, Day 16, and Day 44 to 50 of follow-up in Group A, Group B, Group C and the Control Group, and three ^{14}C UBT results (negative or positive) at baseline, Day 8, and Day 37 to 43 of follow-up in Group D, based on the full analysis set (FAS). And make inter-group comparison, which shall focus on comparison between the test group and the control group, supplemented by the comparison among the test groups. Inter-group comparison of percentages will adopt Fisher's exact test. H. pylori eradication rate is defined as the proportion of participants with negative ^{14}C UBT results from Day 28 to Day 34 after the last dose of the study. At the same time, the H. pylori eradication rate of each group will be calculated in the mITT analysis set and the PP analysis set, and the sensitivity analysis will be performed. There are no clear statistical hypotheses in this study and all statistical tests are exploratory test with a two-sided 5% nominal significance level. The statistical analysis method and plan are detailed in the statistical analysis plan.

	Safety Analysis: The analysis of safety and tolerability are mainly based on descriptive statistics. AEs, treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), drug-related AEs and AEs leading to withdrawal from the study are summarized. The number, frequency and incidence of all adverse events will be tabulated and summarized by different groups, system organ class and preferred term. The number, frequency and incidence of adverse events of each grade will be tabulated according to CTCAE grade by different groups. The number, frequency and incidence of AEs in each group will be tabulated by system organ class and preferred term according to severity and relevancy to the investigational product. The number, frequency and incidence of common adverse events in each group will be tabulated and described by system organ class and preferred term. Laboratory test results that were normal before the test but abnormal after treatment are described by group. The mean, standard deviation, median, minimum and maximum values of vital signs (blood pressure, respiration, pulse and body temperature) and laboratory indicators before and after administration are calculated respectively by different groups. If necessary, paired t test or non-parametric test can be used for comparison before and after administration. SAE and suspected unexpected serious adverse reactions (SUSARs) are presented separately. **Pharmacokinetic Analysis:** Non-compartmental pharmacokinetic parameters are estimated and analyzed for plasma concentration data using Phoenix WinNolin software, PK concentration data are analyzed using PKCS, and main pharmacokinetic parameters are calculated using PKPS data. Participants with serious deviations from the study protocol should be excluded from the pharmacokinetic analysis. The results of the analysis of the main pharmacokinetic parameters are summarized by groups using sample size, arithmetic mean, standard deviation, coefficient of variation, median, minimum, maximum and geometric mean and geometric coefficient of variation. Main pharmacokinetic parameters include: PK parameters of the first dose, such as T_{max}, C_{max}, $t_{1/2}$, $AUC_{0-\infty}$, AUC_{0-tau}, Vd/F, CL/F, etc.; PK parameters of the last dose, including $T_{max,ss}$, $C_{max,ss}$, $C_{min,ss}$, $C_{avg,ss}$, $t_{1/2,ss}$, $AUC_{0-last,ss}$, $AUC_{0-tau,ss}$, $AUC_{0-\infty,ss}$, V/F_{ss}, CL/F_{ss}, Rac, DF, etc.

Study Design



Note: ^{14}C UBT will also be performed for Group A, Group B, Group C and Control Group during the screening period, the baseline period, and on Day 8 and Day 16 during the hospitalization/dosing period.



Note: ^{14}C UBT will also be performed for Group D during the screening period, the baseline period, and on Day 8 during the hospitalization/dosing period.

Schedule of Activities for Group A, Group B, Group C and Control Group

Study Procedures		Screening period	Baseline period	Hospitalization/Dosing period																Follow-up period
		D-14～D-2	D-1	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15	D16	D17	D44～D50
Screening	Signing of ICF	X																			
	Demographics	X																			
	Medical and surgical history	X	X																		
	Concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Chest plain X-ray[1]	X																			
	Abdominal Dopler ultrasound[2]	X																			
	Infectious disease screening[3]	X																			
	Breath alcohol test		X																		
	Urine drug screening[4]		X																		
	Serum pregnancy test[5]	X	X																	X	
	Verification of inclusion and exclusion criteria	X	X																		
Enrollment	Admission		X																		
	Randomization		X																		
Study treatment administration	Dosing[6]			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			

Study Procedures		Screening period	Baseline period	Hospitalization/Dosing period																Follow-up period
		D-14～D-2	D-1	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15	D16	D17	D44～D50
Safety and tolerability assessment	Clinical laboratory tests[7]	X	X		X		X		X		X		X		X		X			X	
	Physical examination[8]	X	X				X		X		X				X					X	
	12-lead ECG[9]	X	X	X														X		X	
	Vital signs[10]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
	Recording of adverse events			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PK sample collection	Blood sample[11]			X		X		X		X		X		X		X	X	X	X	X	
Hp eradication assessment	^{14}C UBT[12]	X	X								X								X		X
End of study	Discharge[13]																			X	
	Follow-up, study completion[14]																				X

1 Results of chest plain X-ray within 1 year prior to screening are acceptable.

2 Abdominal Dopler ultrasound includes digestive system and urinary system, and the results within 1 month prior to screening are acceptable.

3 Infectious disease screening includes hepatitis B serologic test, hepatitis C antibody, HIV antigen/antibody, and treponema pallidum antibody tests (an additional rapid plasma regain (RPR) test is required in patients positive for treponema pallidum antibody), and the test results within 3 months prior to screening are acceptable.

4 Urine drug screening (morphine, and marijuana) is performed at baseline (Day -1).

5 The serum pregnancy test is performed only for female participants during the screening period (Day -14 to Day -2) and the baseline period (Day -1) and on Day 17.

6 Oral administration is started on Day 1 for 14 consecutive days, during which

a) Group A, Group B and Control Group each are given two oral doses each day, with breakfast and dinner within 30 min prior to dosing; the last dose of investigational product is given after breakfast on Day 15, with a total of 29 doses of the investigational product;

b) Group C is given three oral doses each day at an interval of 8 h, and the last dose of investigational product is given in the morning on Day 15, with a total of 43 doses of the investigational product.

7 Clinical laboratory tests include hematology, urinalysis, blood biochemistry and coagulation function, which are carried out during the screening period (Day -14 to Day -2), and the baseline period (Day -1), and before the first dose each on Day 2, Day 4, Day 6, Day 8, Day 10, Day 12 and Day 14 and on Day 17 (48 h after dosing on Day 15). The test results obtained within 7 days of the screening period are acceptable for the baseline period, and no additional examination is required.

8 Physical examinations include skin, mucosa, lymph nodes, head, neck, chest, abdomen, and spine/limbs, which are carried out during the screening period (Day -14 to Day -2), and the baseline period (Day -1), and on Day 4, Day 6, Day 8, Day 12 and Day 17.

9 The 12-lead ECG examination is performed during the screening period (Day -14 to Day -2), and the baseline period (Day -1), 2 h after the first dose on Day 1, within 60 min before dosing on Day 15 and 2 h and 48 h (Day 17) after the dosing.

10 Vital sign tests include blood pressure, pulse, body temperature and respiration, which are carried out during the screening period (Day -14 to Day -2), and the baseline period (Day -1), within 60 min before the first dose on Day 1 and 0.5, 2, 4, 8 and 12 h after the dosing, within 60 min before the first dose each from Day 2 to Day 14, within 60 min before dosing on Day 15 and 0.5, 2, 4, 8, 12, 24 h (Day 16) and 48 h (Day 17) after the dosing.

11 PK blood collection time:

a) Group A, Group B, and Control Group: within 30 min before dosing on Day 1 and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 9, 10, 11 and 12 h (before the second dose on the day) after the dosing, within 30 min before dosing each on Day 3, Day 5, Day 7, Day 9, Day 11, Day 13 and Day 14, within 30 min before dosing on Day 15 and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 9, 10, 11, 12, 24 h (Day 16) and 48 h (Day 17) after the dosing.

b) Group C: within 30 min before dosing on Day 1 and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7 and 8 h after the dosing, within 30 min before dosing each on Day 3, Day 5, Day 7, Day 9, Day 11, Day 13 and Day 14, within 30 min before dosing on Day 15 and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 9, 10, 11, 12, 24 h (Day 16) and 48 h (Day 17) after the dosing.

12 Participants are required to undergo the ^{14}C UBT in the fasting state before breakfast during the screening period (Day -14 to Day -2), and the baseline period (Day -1), on Day 8 and Day 16 and during the follow-up period (Day 44 to Day 50).

13 After all examinations and PK blood collection are completed on Day 17, participants may be discharged from the study center.

14 Participants are required to return to the study center for follow-up visits from Day 44 to Day 50. Adverse events and laboratory abnormalities are followed up until the complete response or the return to baseline levels, the assessment of safety and tolerability is performed, and ^{14}C UBT is performed to evaluate the effect of Hp eradication.

Schedule of Activities for Group D

Study Procedures		Screening period	Baseline period	Hospitalization/Dosing period										Follow-up
		D-14～D-2	D-1	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D37～D43
Screening	Signing of ICF	X												
	Demographics	X												
	Medical and surgical history	X	X											
	Concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X	X
	Chest plain X-ray[1]	X												
	Abdominal Dopler ultrasound[2]	X												
	Infectious disease screening[3]	X												
	Breath alcohol test		X											
	Urine drug screening[4]		X											
	Serum pregnancy test[5]	X	X										X	
	Verification of inclusion and exclusion criteria	X	X											
Enrollment	Admission		X											
	Randomization		X											
Study treatment administration	Dosing[6]			X	X	X	X	X	X	X	X			
Safety and tolerability assessment	Clinical laboratory tests[7]	X	X		X		X		X		X		X	
	Physical examination[8]	X	X				X		X		X		X	
	12-lead ECG[9]	X	X	X							X		X	
	Vital signs[10]	X	X	X	X	X	X	X	X	X	X	X	X	

Study Procedures		Screening period	Baseline period	Hospitalization/Dosing period										Follow-up
		D-14～D-2	D-1	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D37～D43
	Recording of adverse events			X	X	X	X	X	X	X	X	X	X	X
PK sample collection	Blood sample[11]			X		X		X		X	X	X	X	
Hp eradication assessment	^{14}C UBT[12]	X	X								X			X
End of study	Discharge[13]												X	
	Follow-up, study completion[14]													X

1 Results of chest plain X-ray within 1 year prior to screening are acceptable.
2 Abdominal Dopler ultrasound includes digestive system and urinary system, and the results within 1 month prior to screening are acceptable.
3 Infectious disease screening includes hepatitis B serologic test, hepatitis C antibody, HIV antigen/antibody, and treponema pallidum antibody tests (an additional rapid plasma regain (RPR) test is required in patients positive for treponema pallidum antibody), and the test results within 3 months prior to screening are acceptable.
4 Urine drug screening (morphine, and marijuana) is performed at baseline (Day -1).
5 The serum pregnancy test is performed only for female participants during the screening period (Day -14 to Day -2) and the baseline period (Day -1) and on Day 10.
6 Starting from Day 1, three oral doses are given each day for 7 consecutive days, at an interval of 8 h. The last dose is given in the morning of Day 8, and each participant receives 22 doses of the investigational product.
7 Clinical laboratory tests include hematology, urinalysis, blood biochemistry and coagulation function, which are carried out during the screening period (Day -14 to Day -2), and the baseline period (Day -1), before the first dose each on Day 2, Day 4 and Day 6, before the first dose on Day 8 and on Day 10 (48 h after dosing on Day 8). The test results obtained within 7 days of the screening period are acceptable for the baseline period, and no additional examination is required.
8 Physical examinations include skin, mucosa, lymph nodes, head, neck, chest, abdomen, and spine/limbs, which are carried out during the screening period (Day -14 to Day -2), and the baseline period (Day -1), and on Day 4, Day 6, Day 8 and Day 10.
9 The 12-lead ECG examination is performed during the screening period (Day -14 to Day -2), and the baseline period (Day -1), 2 h after the first dose on Day 1, within 60 min before dosing on Day 8 and 2 h and 48 h (Day 10) after the dosing.
10 Vital sign tests include blood pressure, pulse, body temperature and respiration, which are carried out during the screening period (Day -14 to Day -2), and the baseline period (Day -1), within 60 min before the first dose on Day 1 and 0.5, 2, 4, 8 and 12 h after the dosing, within 60 min before the first dose each from Day 2 to Day 7, within 60 min before dosing on Day 8 and 0.5, 2, 4, 8, 12, 24 h (Day 9) and 48 h (Day 10) after the dosing.
11 PK blood collection time: within 30 min before dosing on Day 1 and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7 and 8 h (before the second dose on the day) after the dosing, within 30 min before dosing each on Day 3, Day 5 and Day 7, within 30 min before dosing on Day 8 and 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 9, 10, 11, 12, 24 h (Day 9) and 48 h (Day 10) after the dosing.
12 Participants are required to undergo the ^{14}C UBT in the fasting state before breakfast during the screening period (Day -14 to Day -2), and the baseline period (Day -1), on Day 8 and during the follow-up period (Day 37 to Day 43).
13 After all examinations and PK blood collection are completed on Day 10, participants may be discharged from the study center.

14 Participants are required to return to the study center for follow-up visits from Day 37 to Day 43. Adverse events and laboratory abnormalities are followed up until the complete response or the return to baseline levels, the assessment of safety and tolerability is performed, and ^{14}C UBT is performed to evaluate the effect of Hp eradication.