# Phase I/II Clinical Study on Tolerability and Bioavailability of Utidelone Capsule in Patients with Advanced Solid Tumors

BG02-2101

## Statistical Analysis Plan

## Final Analysis of Part III

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# 1. Introduction

This statistical analysis plan has been prepared for the Phase I/II clinical trial of "Utedron Capsulesin Patients with Advanced Solid Tumors" (Protocol No.: BG02-2101) conducted by Chengdu Huahao Zhongtian Pharmaceutical Co., Ltd. and Beijing Huahao Zhongtian Biopharmaceutical Co., Ltd., and provides a detailed description of the statistical analysis content and methods for Part III of the study.

This statistical analysisplan wasprepared based on the study protocol version 4.0 dated January 22, 2024, and the case report form (CRF) version 5.0 dated September 14, 2024.

The data cutoff date for the statistical analysis in this study is December 1, 2025.

# 2. Experiment Overview

## 2.1. Overall Design

This study is a Phase I/II clinical trial. The study design was conducted in strict accordance with the relevant requirements of regulatory documents issued by the NMPA, including the "Good Clinical Practice for Drug Clinical Trials" [1], the "Guiding Principles for the Management of Phase I Clinical Trials of Drugs (Trial)" [2], and the "Technical Guidance Principles for Clinical Pharmacokinetic Studies of Chemical Drugs" [3], to evaluate the tolerability, safety, pharmacokinetic profile, and efficacy of Utedron capsules in patients with advanced solid tumors.

Part 3: Expanded Trial of Uterodron Capsules in Combination with Capecitabine:

UtedronCapsules:60mg/m²/day, administered once daily on an empty stomach, for 5 consecutive days from Day 1 to Day 5; a treatment cycle lasts 21 days. The dose and administration schedule may be adjusted according to the dosage determined by the Safety Monitoring Committee (SMC) based on the safety and efficacy data obtained in Parts 1 and 2.

Capecitabine: 1000mg/m², twice daily (total daily doseof 2000 mg/m²),administered once in the morning and once in the evening, orally within 30 minutes after meals. Administer continuously from day 1 to day 14, with each treatment cycle lasting 21 days.

## 2.2. Randomization and Blinding

Part 3: Expanded Trial of Uterodron Capsules in Combination with Capecitabine:

Randomization is not performed. During screening, subjects are identified by a screening number, formatted as S + trial number +center number + a three-digit Arabic numeral. Center numbers are assigned sequentially from 1 to 99 according to the order in which centers were selected, with the Part 3 trial number set to 3; for

example, S31001…S399001. Eligible subjects are assigned enrollment numbers in ascending order based on their screening numbers. Enrollment numbers are structured as trial number + center number + a three-digit Arabic numeral, with center numbers assigned sequentially from 1 to 99. For instance, the enrollment numbers for Center 1 range from 31001 to 31002, while those for Center 99 range from 399001 to 399002, and so on.

This trial is an open-label study. Investigators, project managers, monitors, bioanalytical assay personnel, and data management and statistical analysis staff will all be unblinded.

## 2.3. Administration of medication

**Part 3: Expanded Trial of Utedron Capsules in Combination with Capecitabine**

During thefirst three dosing cycles (C1–C3), subjects began breakfast approximately 30 minutes after administration of ublituximab capsules. Within 30 minutes post-meal, they orally took capecitabine tablets (on days when intensive pharmacokinetic sampling was conducted, capecitabine was administered only after the 1-hour blood-draw time following dosing). Subjects meticulously recorded meal times, medication times, and sampling times, with minute-level precision.

Dose calculations are based on body surface area (BSA) during the subject screening period. BSA is calculated using the DuBois formula: BSA ($m^2$) = 0.0061 × height (cm)+ 0.0128 × weight (kg) − 0.1529. Unless body weight changes by more than 10% from baseline, dose adjustments will not be made in subsequent cycles based on weight. Depending on capsule strength, the original and adjusted doses of Utedron capsules are rounded, and the corresponding dosage allocation is specified in the study protocol.

The investigational drug may be dose-adjusted in accordance with the protocol, based on the subject's adverse reactions; see Section 6.5, Dose Adjustment. Subjects shall continue treatment until disease progression, the occurrence of intolerable adverse events, voluntary withdrawal, or as determined by the investigator to warrant discontinuation. In the event of a missed dose, the time at which the dose was originally scheduled to be taken and the reason for the omission must be documented in detail, and subsequent doses should be administered according to the protocol-specified schedule without dose again or adjustment of the dosing interval.

## 3. Trial Objective and Endpoint

| Main purpose | Primary endpoint |
|---|---|
| To evaluate the safety and tolerability of utidelone capsules in patients with advanced solid tumors, and to determine the maximum tolerated dose and dose-limiting toxicities. | MaximumTolerated Dose (MTD), Dose-Limiting Toxicity (DLT) |
| Evaluation of the objective response rate (ORR) of utidelone capsules in combination with capecitabine for patients with advanced metastatic breast cancer. | Objective response rate (ORR) was assessed according to RECIST 1.1 criteria. |
| **Secondary objective** | **Secondary endpoint** |
| Evaluation of the absolute bioavailability of Utedron capsules relative to Utedron injection. | F |
| Evaluation of the pharmacokinetic characteristics of Utedron capsules in patients with advanced solid tumors | ● $C_{max}$,$T_{max}$,$AU_{C0-}$t, $A_{UCi}$nf,$\lambda z_{,t}$1/2,$C_L$, Vd, etc.;<br>● $C_{max,ss}$,$AU_{C0-t,s}$s, $A_{UCinf,}$ss, $A_{UC0-\tau,}$ss, $A_{UC_\%Ext}$ra$_p$,$\lambda_{Z,T}$1/2$_Z$,CLs$_s$/F,$V_{z/F,C}$mi$_{n,ss,}$Cav,ss, and others. |
| Preliminary evaluation of the efficacy and safety of Utedron capsules in patients with advanced solid tumors. | ● Efficacyassessment criteria (RECIST1.1 objective response evaluation standard): objective response rate (ORR);<br>● Safety assessment endpoints: vitalsigns, physical examination, laboratory tests, electrocardiogram, ECOG performance status, adverse events, and serious adverse events. |
| Recommendation of the dosing regimen and administration schedule for subsequent clinical trials | RP2D |
| To evaluate the efficacy, safety, and pharmacokinetic profile of utidelone capsules in combination with capecitabine for patients with advanced metastatic breast cancer. | ● Progression-free survival (PFS): assessed according to RECIST 1.1 criteria;<br>● Disease Control Rate (DCR): assessed according to RECIST 1.1 criteria;<br>● Duration of Response (DoR): assessed according to RECIST 1.1 criteria; |

| | |
|---|---|
| | ● Safety endpoints: vital signs, physical examination, laboratory tests,ECOG performance status, adverse events (AEs), and serious adverse events (SAEs), among others. Adverse events were graded according to the NCI-CTCAE v5.0 criteria. |

## 4. Analysis Set

**Full Analysis Set (FAS):** The FAS comprises all subjects who were enrolled and received at least one dose of the investigational medicinal product. In accordance with the intention-to-treat principle, analyses are performed based on the treatment assigned to each subject at the time of enrollment.

**Per-Protocol Set (PPS):** This is the efficacy analysis set, comprising all subjects who were enrolled, received at least two cycles of the investigational medicinal product, had measurable lesions according to RECIST 1.1 at baseline, and provided at least one post-dose efficacy assessment, while excluding those with significant protocol deviations that could affect the primary efficacy endpoints. Analyses are performed based on the actual treatment received.

**Safety Set (SS):** All subjects who have received at least one dose of the investigational product and for whom safety data are available following administration of the investigational product. Safety analyses are conducted based on the actual treatment received.

**Blood Pharmacokinetics Concentration Set (BPKCS):** All subjects who were enrolled and received at least one dose of the investigational drug, and who had at least one valid post-dose plasma concentration measurement during the study. Situations that may preclude inclusion in the pharmacokinetic analysis include: a) factors present during the study that could significantly affect PK concentration measurements; b) pre-dose concentrations exceeding 5% of the Cmax. Analyses are conducted based on the actual treatment received.

**Pharmacokinetics Parameter Set (PKPS):** All subjects who were enrolled and received at least one dose of the investigational medicinal product, with at least one valid PK parameter during the study period. Situations that may be excluded from pharmacokinetic parameter analysis include: a)violations of the protocol's dosing requirements, such as incorrect blood-sampling times, concomitant use of prohibited medications, or ingestion of foods not specified in the protocol, which could affect PK parameter outcomes or render parameters unestimable; b) pre-dose concentrations exceeding 5% of Cmax; c) loss of three or more consecutive samples in either the absorption or elimination phase, or inability to report such data [if the

absorption phase is adequately characterized, absorption-related parameters—such as Cmax and Tmax—will be calculated]; d) the first post-dose sample being Cmax, with no early-time samples (5–15 minutes post-dose) collected; e) extremely low concentrations (AUC0-t less than 5% of the geometric mean AUC0-t observed in other subjects receiving the same dose); f) vomiting occurring within twice the median Tmax after administration of the investigational medicinal product; g) errors in sample handling, transport, or storage between sample collection and completion of bioanalytical testing that compromise the accuracy of bioanalytical results. Analyses shall be conducted based on the actual treatment received.

Tolerabilitywill be assessed using the DLTS, safety will be evaluated using the SS, and efficacy will be analyzed using both the FAS and PPS; pharmacokinetic analyses will employ the corresponding datasets. Compliance and baseline characteristics will be analyzed using the FAS.

## 5. Statistical analysis methods

### 5.1. Overall Considerations in Statistics

Pharmacokinetic parameters were estimated using the Phoenix WinNonLin software (Certara, Princeton, NJ, USA, version 8.3.5) with a non-compartmental model. Statistical and other analyses were performed using SAS software (version 9.4 or later).

For measurement data, statistical descriptions are provided using counts, means, standard deviations, medians, minimum values, and maximum values; for categorical or ordinal data, statistical descriptions are presented as counts and percentages. “–” is used to indicate inapplicability; “NE” is used when a statistic cannot be estimated.

All analyses are based on observed data, without imputation; outliers are handled according to the methods agreed upon during the data review meeting.

The number of decimal places retained follows the rules below:

| Statistic | Number of decimal places to retain |
|---|---|
| The number of observed values and the number of missing values | Integer |
| Individual Safety/Efficacy Data | Consistent with EDC data |
| Individual PK concentration data | Maintain consistency with the maximum number of decimal places in the external PK concentration data. |
| Individual PK parameter data | Retain 2 decimal places |
| Median, mean, geometric mean, standard deviation | One digit more than the maximum number of decimal places in the individual data. |
| %CV,%$CV_b$ | Retain 1 decimal place |

| | |
|---|---|
| Minimum value, maximum value | Maintain consistency with the maximum number of decimal places in individual data. |
| Percentage | Retain 2 decimal places |
| 95% CI | Retain the same number of decimal places as the point estimate. |
| P-value | Retain 4 decimal places |

When the P-valueis less than0.0001, it will be reported as "<0.0001"; when the P-value is greater than 0.9999, it will be reported as ">0.9999".

Except for P-values, all results are reported to a maximum of four decimal places.

Part 3Study: Asingle cohort, the ublituximab capsules plus capecitabine group.

## 5.2. Data processing method

### 5.2.1.Early dropout and missing data

**Imputation of Missing Dates in AE**

Themissing datesfor AEs are imputed as follows: this imputation is used solely for AE classification; when generating the AE-related data list, the original unimputed dates remain displayed.

- The AE start date is missing.
  1) If the year and month are known and the year-month is earlier than the date of the first administration of the investigational drug, the last day of the known month shall be used for imputation.
  2) If the year and month are known and match the year and monthofthe first administration of the investigational drug, then set the AE onset date to the date of the first administration of the investigational drug (where "date" refers to "month day").
  3) If the year and month are known and the year-month is later than the date of the first administration of the investigational drug, the first day of the known month shall be used for imputation.
  4) If only the year is known anditprecedes the year of the first administration of the investigational drug, "December 31" shall be used for imputation.
  5) If only the year is known and the year equals the year ofthefirst administration of the investigational drug, then set the AE's onset date to the date of the first administration of the investigational drug (where "date" refers to "month day").
  6) If only the year is known anditislater than the year of the first administration of the investigational drug, "January 1" shall be used for imputation.
  7) If the year, month, and day are all missing, use the date of the first administration of the investigational drug as the corresponding start date.
  8) All other cases are considered missing.
- The AE end date is missing.

If the outcome is classified as “recovered with no sequelae,” “recovered with sequelae,” “improved,” or “worsened,” it shall be coded according to the following rules:

1) If the year and month are known, fill in using the last day of the known month.

2) If only the yearis known, use “December 31” as the placeholder.

3) If the date on which the shortfall is filled occurs after the dates listed below, the shortfall shall be filled in accordance with the following rules:

a. If the subject remains in the study and the imputed date is later than the data cut-off date, imputation shall be performed using the cut-off date.

b. If a subject completes the study or withdraws early, and the imputed date is later than any of the dates listed below, the imputation shall be based on the earliest of those dates:

-28 days after the last dose

-Date of initiation of new anticancer therapy

-Study completion date

-Date of death

4) If the start date of the filled-in period is later than the end date, the end date shall be taken as the corresponding start date.

5) All other cases are considered missing.

If the outcome is “death,” it shall be filled in accordance with the following rules:

1) Ifthedate of death is known, it shall be used to impute the missing data.

2) Ifthe date of death is unknown, impute the last known day of survival.

If the outcomeis classified as “persistent” or “unknown,” the AE end date is considered missing.

**Imputation of missing dates for prior/combined medications**

Themissing dates forprior/combined medications are imputed as follows: the imputation of missing dates for prior/combined medications is intended solely for the purpose of categorizing such medications; when generating the list of data related to prior/combined medications, the unimputed dates will still be displayed.

- Previous/Concomitant medication start dates are missing.

1) If the year and month are known, fill in using the first day of the known month.

2) Ifonly the yearis known, use “January 1” as the placeholder.

3) If the year, month, and day are all missing, do not fill them in.

4) All other cases are considered missing.

- Previous/Concomitant medication end dates are missing.

If “No” is selected for the continuity question, the following rules will be applied to impute the missing values:

1) If the year and month are known, fill in using the last day of the known month.

2) If only the yearis known, use “December 31” as the placeholder.

3) If the completion date of the imputation is later than the subject’s study end date or the data cut-off date, the imputation shall be performed according to the following rules:

a. If the subject remains in the study, imputation is performed using the data cut-off date for this analysis.

b. If the subject has completed the study or withdrawn from the study early, imputation shall be performed using the earliest of the following dates:

-28 days after the last dose;

-Study completion date;

-Date of death;

-Data cut-off date.

4) If the start date of the filled-in period is later than the end date, the end date shall be taken as the corresponding start date.

5) All other cases are considered missing.

If “Yes” is selected for the continuation status, the end date is treated as missing.

**Filling in missing dates for non-pharmacological treatments**

Fill inmissing dates by referring to the “Previous/Concomitant Medication Date Missing” rule.

**Filling in the missing dates for new anti-tumor therapies**

The missing dates for the new anti-tumor treatment are imputed as follows: this imputation applies only to the censoring date for efficacy; when generating the list of new anti-tumor treatment–related data, the unimputed dates remain displayed.

- The end date for the new anticancer treatment is missing.

1) If the year and monthare known, fill in using the last day of the known month.

2) If the year andday are known, use “December” to fill in the missing information.

3) Ifonly the yearis known, use “December 31” as the placeholder.

4) If the year, month, and day are all missing, do not fill them in.

5) All other cases are considered missing.

6) If the completion date of the imputation is later than the subject’s study end date or the data cut-off date, the imputation shall be performed according to the following rules:

a. If the subject remains in the study, imputation is performed using the data cut-off date for this analysis.

b. If the subject has completed the study or withdrawn from the study early, impute using the earliest of the following dates:

-Study completion date;

-Date of death;

-Data cut-off date.

- The startdate of the new anticancer treatment is missing (the new anticancer end date mentioned in the following rules will only be considered if the imputed end date is not null. For subjects whose treatment had not yet ended as of the data cut-off date, the last dose date below will be replaced by the data cut-off date);

1) If the year and month are known, use the following rules to fill in.

a. If year equals year{min[max(Progression Date +1, Last Drug Administration Date+1), New Antitumor Treatment End Date]}, and month is less than month{min[max(Progression Date + 1, Last Drug Administration Date + 1), New Antitumor Treatment End Date]}, then the last day of that month shall be used for imputation;

b. If year equals year{min[max(Progression Date +1, Last Drug Administration Date+1), New Antitumor Treatment End Date]}, and month equals month{min[max(Progression Date + 1, Last Drug Administration Date + 1), New Antitumor Treatment End Date]}, then fill in using the earliest of the following dates:

-max(Progression Date +1, Last Drug Administration Date + 1)

-Date of completion of the new anticancer treatment

c. If the year equals year{min[max(Progression Date +1,LastDrug Administration Date+1), New AntitumorTreatment End Date]}, and the month is greater than month{min[max(Progression Date + 1, Last Drug Administration Date + 1), New Antitumor Treatment End Date]}, then fill in with “Day 1”;

d. If the age is less than year{min[max(Progression Date + 1, Last Drug Administration Date + 1), New Antitumor Treatment End Date]}, then impute with the last day of the non-missing year and month.

e. If the age is greater than year{min[max(Progression Date + 1, Last Drug Administration Date + 1), New Antitumor Treatment End Date]}, then fill in with “Day 1”;

2) If the year is known but the month and day are missing, or if the year and day are known but the month is missing, then fill in the missing values according to the following rules:

a. Ifthe age is less thanyear{min[max(Progression Date +1, Last Drug Administration Date + 1), New Antitumor Treatment End Date]}, then fill in with “December 31”;

b. If age equals year{min[max(Progression Date +1, Last Drug Administration Date + 1), New Antitumor Treatment End Date]}, then impute using the earliest of the following dates:

-max(Progression Date +1, Last Drug Administration Date + 1)

-Date of completion of the new anticancer treatment

c. If the age is greaterthan year{min[max(ProgressionDate + 1, Last Drug Administration Date + 1), New Antitumor Treatment End Date]}, then impute "January 1."

3) If the year,month, and day are all missing, the earliest of the following dates shall be used to fill in the missing values:

-max(Progression Date +1,Last Drug Administration Date + 1)

-Date of completion of the new anticancer treatment

**5.2.2.Derivation of laboratory test results**

If the resultis">xxx"or"≥xxx", the numeric value following ">" or "≥" will be included in the analysis.

If the resultis"<xxx"or"≤xxx", the numeric value following "<" or "≤" will be extracted for analysis.

If the result is non-numeric—e.g., "not detected" or "below the limit of quantification"—it will be treated as 0 in the analysis.

**5.2.3.Baseline Definition**

The baseline is defined as the last non-missing value prior to the first dose.

**5.2.4.Unscheduled visit**

When conducting summary analyses by visit, unscheduled visits areexcluded; however, whengenerating clinical-significance cross-tabulations, unscheduled visits are included to assess the worst-case scenario following dosing—defined as the most severe clinical-significance outcome, with "abnormal with clinical significance" being more serious than "abnormal without clinical significance," and "abnormal without clinical significance" being more serious than "normal."

**5.3. Subject Distribution Analysis**

Provides the number of subjectscategorizedasscreened, screened but ineligible, screened and eligible,screened and eligible but not enrolled/randomized, and enrolled/randomized. Summarized by treatment group, it reports the number and percentage of subjects in each category—administered, completed treatment, reason for study termination, and under study follow-up (subjects who have completed treatment but the study remains ongoing)—as well as the number and percentage of subjects included in each analysis set. Percentages are based on the number of subjects enrolled/randomized.

A list ofdata that do not meet the inclusion/exclusion criteria will be provided.

BasedonFAS, summarized by treatment group, protocol deviation categories were summarized and analyzed to provide number of cases, number of cases, and percentage.

### 5.4. Analysis of demographic data and baseline characteristics

Basedon FAS, summaries were performed by treatment group.

Provide descriptive primary statistical indicators ofdemographic characteristics. The measurement data include age, height, weight, and body mass index, and provide the number of cases, mean, standard deviation, median, minimum, and maximum values. Categorized data by gender, age group, ethnicity, marital status, etc., providing the number and percentage of subjects in each category.

Solid tumor history, providing primary site ofadvanced solid tumor,current tumorclinical stage, and initial tumor stage (stage I, II, IIIA,IIIB, IIIC, III, IVA,IVB, IVC, IV, others)Whether there are currently any metastases (none,bone metastasis, brain metastasis, liver metastasis, visceral metastasis, lymph node metastasis, lung metastasis,other metastases), the number of metastatic sites (≥2, <2), molecular classification (ER+PR-HER2+, ER-PR-HER2-, unknown, etc.), and the number and percentage of subjects in each category with baseline ECOG score. For the first tumor clinical stage selected other, other stages will be listed (both UN and UK are listed as unknown, both stages IIA and IIA are listed as stage IIA, both stages IIB and IIB are listed as stage IIB, other lists the stage description entered in the EDC). For molecular typing, the most recent one shall prevail, that is, the results of metastatic lesions shall prevail, and the results of non-metastatic lesions shall prevail. Subjects with ER+ or PR+ were summarized as HR+, and the remaining categories were presented as ER/PR/HER2 according to the EDC inclusion category.

Past anti-tumor (solid tumor) drug treatment history, providing the classification of drug treatment history (chemotherapy, molecular targeted therapy, immunotherapy, biological therapy, traditional Chinese medicine treatment, endocrine therapy, previous CDK4/6 inhibitor treatment, others), whether paclitaxel or anthracycline treatment has been received, the highest number of previous treatment lines (neoadjuvant therapy, adjuvant therapy, first-line, second-line, third-line, fourth-line, fifth-line, sixth-line) and its median and extreme value.

In the past, the highest number of treatment lines inthe third line did not include the second and first lines, and the same applies to the number of other lines. Maintenance therapy counts as adjuvant therapy. The number of neoadjuvant therapy and adjuvant therapy lines was included in the median (minimum to maximum) summary according to the 0-line treatment. The number of treatment lines is ranked from low to high as follows: neoadjuvant therapy < adjuvant therapy (including maintenance therapy) < first-line

treatment for metastatic disease < second-line treatment for metastatic disease < third-line treatment for metastatic disease < fourth-line treatment for metastatic disease < fifth-line treatment for metastatic disease < sixth-line treatment for metastatic disease. Advanced <3-line treatment includes subjects with the highest number of lines of neoadjuvant treatment, adjuvant treatment (including maintenance treatment), first-line treatment for metastatic disease, and second-line treatment for metastatic disease, and advanced ≥3-line treatment includes subjects with the highest number of lines of third-line treatment for metastatic disease, fourth-line treatment for metastatic disease, fifth-line treatment for metastatic disease, and sixth-line treatment for metastatic disease.

The previous highest number of chemotherapy lines was summarized with reference to the above rules.

In the endocrine therapy category, records with ATC2 coding for endocrine therapy were screened. Records with ATC2 coding for endocrine therapy were not counted repeatedly in other categories. In the previous CDK4/6 inhibitor therapy classification, ATC4 was screened as a cyclin-dependent kinase (CDK) inhibitor. Other categories, chemotherapy, molecular targeted therapy, etc. must also include this record.

Having previouslyreceived taxoid drugs, ATC4 was screened for taxanes; Having previously received anthracyclines, screening ATC4 codes for anthracyclines and related drugs.

Provide the number and percentage of subjects with a history of prior anti-tumor (solid tumor) surgery, prior anti-tumor (solid tumor) non-drug therapy, prior surgery (excluding solid tumor of the study disease), history of hepatitis B/hepatitis C/HIV/syphilis infection, history of allergy, history of alcohol abuse, history of drug abuse.

Provide the number and percentage of subjects for each category of smoking history.

Medicalhistory provides the number and percentage of subjects in each category by SOC and PT.

Pregnancy tests, infectious disease tests, HIV antibody tests only provide a list of data.

### 5.5. Extent of exposure and compliance

Number of cases, mean, standard deviation, median, minimum, and maximum for treatment duration are provided by treatment group based on SS.

Basedon FAS, the number and percentage of subjects for the planned total dose, actual total dose, and medication compliance categories (<80%, 80%-120%, >120%) are provided.

Total planned dose (mg) =added to the planned dose (mg) ordered by the physician for each cycle, i.e., added tothe number of pills plannedto be taken daily on the study drug dosing page * drug strength; Actual total dose (mg) = accumulated actual dose (mg) for each cycle, i.e., accumulated actual number of pills taken

daily on the study drug dosing page * drug strength; Medication compliance (%) = actual total dose (mg)/planned total dose (mg)*100.

Total exposuredose (mg/m2)= actual total dose administered (mg) / baseline body surface area (m2)

### 5.6. Prior/Concomitant Medications, Prior/Concomitant Non-Drug Therapy

Previous and concomitant medications were coded using the Chinese version of WHO-Drug.

Priormedication/non-drug therapy isdefined as medication/non-drugtherapy that has been completed prior tothe first dose of study drug; Concomitant medication/non-drug therapy was defined as a drug/non-drug therapy that was initiated or is still being used after the first dose of study drug. If the start or end date of treatment or medication is incomplete and it cannot be determined whether it is a concomitant medication/non-drug treatment, it is considered a concomitant medication/non-drug treatment.

BasedonFAS,thenumber and percentage ofsubjectswith prior medication were provided by treatment group and summarized by ATC classification grades 2 and 4; Number and percentage of subjects with prior non-drug therapy provided.

Basedon SS,thenumber and percentage ofsubjectswith concomitant medications were provided by treatment group and summarized by ATC classification grades 2 and 4; Number and percentage of subjects with concomitant non-drug therapy provided.

### 5.7. Efficacy analysis

Basedon FASand PPS, summaries were performed by treatment group. Confirmed efficacy results and unconfirmed efficacy results are output simultaneously.

1month = 30.4375 days. The conversion result retains two decimal places.

Efficacy Evaluation Indicators:

Subjects must have measurable tumor lesionsat baseline, and the efficacy criteria are divided into complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD), and incomplete response/non-progressive disease (non-CR/non-PD) according to RECIST 1.1 criteria. The best overall efficacy was the first CR or PR or SD. Subjects whose best confirmed overall efficacy was first assessed as CR, PR were required to confirm after at least 4 weeks (28 days), and best efficacy was the best recorded efficacy from the start of the first dose to progression or initiation of new anti-tumor therapy. Efficacy evaluations after PD and after initiation of new anti-tumor therapy were not considered in deriving the best efficacy. The confirmation rules are as follows:

| First overall efficacy | Next overall efficacy | Bestconfirmed overall efficacy | |
|---|---|---|---|
| CR | CR | CR | |
| CR | PR* | MeetSD minimum time limit: SD | Does not meet the minimum SD time limit: PD |
| CR | SD | Meetthe minimum SD deadline: SD | Does not meet the minimum SD time limit: PD |
| CR | PD | Meetthe minimum SD deadline: SD | Does not meet the minimum SD time limit: PD |
| CR | NE | Meetthe minimum SD deadline: SD | Does not meet the minimum SD time limit: PD |
| PR | CR | PR | |
| PR | Public Relations | PR | |
| PR | SD | SD | |
| PR | PD | Meetthe minimum SD deadline: SD | Does not meet the minimum SD time limit: PD |
| Public Relations | NE | Meetthe minimum SD deadline: SD | Does not meet the minimum SD time limit: NE |
| NE | NE | NE | |

*Even if the efficacyassessment at the nexttime point afterCR meets the criteria for PR, it still indicates disease progression following CR; therefore, the efficacy assessment at the subsequent time point can only be classified as CR or PD. The optimal overall response depends on the interval between the date of CR and the date of first drug administration.

To classifythe best overall responseas SD, theminimum duration requirement must be met, with a minimum interval of 6 weeks from the first dose (accounting for a 7-day visit window, totaling 35 days). If the confirmed assessment time falls short of this minimum interval, the originally assigned SD classification should be revised to NE.

For subjects without baseline target lesions, whenassessing the bestoverall response, a responsecategory of PR is not applicable. Otherwise, the table remains valid if SD is replaced with “non-CR/non-PD.” To be classified as non-CR/non-PD, the minimum duration requirement must be met: at least 6 weeks must elapse since the first dose (accounting for a 7-day visit window, corresponding to 35 days).

If there is an NE between twoCRs or two PRs, or ifthere isan NE or SD between two PRs,the best response can still be considered a confirmed CR or PR as long as the interval between the two CRs or PRs meets the requirement of at least 4 weeks (28 days).

If a subject has only one post-baselineefficacy assessment,and that assessment is CR/PR/SD or non-CR/non-PD, with an interval of less than 6 weeks (accounting for a 7-day visit window, i.e., 35 days) between the assessment date and the first dose administration date, or if all post-baseline efficacy assessments are NE, then the subject’s best response is NE.

If a subject has no post-baseline efficacy assessment, the subject’s best response is recorded as “not evaluable.”

If a subject hasone efficacyassessment classified as PD, then the subject’s best overall response is PD.

• Objective Response Rate (ORR): Theproportion of subjects achieving confirmed best overall response of complete response (CR) or partial response (PR), as assessed according to RECIST 1.1 criteria.

• Disease Control Rate (DCR): The proportion of patients achieving a best response of CR, PR, or SD, as assessed according to RECIST 1.1 criteria, relative to the total number of patients.

Thenumber and percentageof subjects in each category (CR, PR, SD, PD) were reported according to tumor response group; ORR and DCR were described using frequencies and percentages, with 95% confidence intervals calculated.

• Progression-free survival (PFS): As assessed according to RECIST 1.1 criteria,it is defined as the time from enrollment to the first radiologic evidence of disease progression or death from any cause. If, at the study's cut-off date, the subject has neither experienced progressive disease nor died, or if they have already initiated another anticancer therapy, the last efficacy-assessment visit prior to the cut-off date or the start date of the alternative anticancer treatment—whichever occurs first—will be used as the censoring time. The median PFS will be estimated using the Kaplan–Meier method, and a survival curve will be plotted.

• Duration of Response (DoR): Assessed according to RECIST 1.1 criteria, defined as the timefrom the first documented achievement of complete response (CR) or partial response (PR)—whichever occurs first—to the occurrence of progressive disease (PD) or death. The duration of response is calculated only for patients whose best response was CR or PR. The median DoR is estimated using the Kaplan–Meier method, and a survival curve is plotted.

Time to response: the timefrom the first dose of ublituximab tothe date of confirmed complete response (CR) or partial response (PR), whichever occurs first. Time to response is described descriptively only for patients whose best response was CR or PR; no survival curve analysis is performed. The date of confirmed CR or PR is defined as the date of the last imaging assessment corresponding to the respective evaluation.

**Table 5-1 Censoring Rules**

| Therapeutic efficacy indicators | Data situation | Censoring date |
|---|---|---|
| PFS, time to onset of response | Randomized/No tumor assessment after enrollment | Randomization/Enrollment Date |
| PFS,DOR | Alive and without tumor disease progression as of the cutoff date. | Date of the last imaging assessment |
| PFS,DOR | Tumor disease progression or death occurs after two or more consecutive imaging assessments are missing. | Date of the last imaging assessment without progression prior to the first consecutive missing |

| Therapeutic efficacy indicators | Data situation | Censoring date |
|---|---|---|
| | | assessment. |
| PFS,DOR | Underwent other anti-tumor therapies prior to tumor disease progression or death. | Date of the last imaging assessment prior to initiation of other anticancer therapies |
| Time to onset of relief | Alive as of the cutoff date, not receiving any other anticancer therapy, and not achieving CR or PR. | Date of the last imaging assessment |
| Time to onset of relief | Other antitumor therapies were administered up to the cutoff date, and neither CR nor PR was achieved. | Date of the last imaging assessment prior to other antitumor therapies |
| Time to onset of relief | Death, with nootherantitumor treatment administered and without achieving CR or PR. | Date of death |

Subgroupanalyses were conducted for ORR, DOR, and PFS, including the following subgroups:

- Number of metastatic sites (<2, ≥2)
- Whether there is visceral metastasis (yes, no)
- Previous lines of therapy (<3, ≥3)
- Molecularsubtyping(e.g., ER+, PR−, HER2+ etc.)

## 5.8. Pharmacokinetic analysis

Key PK data-point definitions: For concentrations below the lower limit of quantification (BLQ), BLQ values observed prior to reaching Cmax will be assigned a value of “0”; BLQ valuesobserved after Cmax will be marked as “missing.” When conducting pharmacokinetic concentration summary analyses, the planned sampling times shall be used for analysis regardless of whether the actual sampling times deviate from the protocol. If a blood-sampling time point is subject to a protocol deviation and that deviation has a substantial impact on the concentration results, the corresponding data shall not be included in the concentration summary analysis. For the calculation of pharmacokinetic parameters, all calculations shall be based on the actual time of sample collection relative to the first administration of the study drug in that cycle. If a sampling time point is scheduled before dosing but the sample is collected prior to dosing, the actual collection time shall be defined as 0; if a sampling time point is scheduled before dosing but the sample is not collected before dosing, pharmacokinetic parameter calculations shall still be performed using the actual time of sample collection relative to the first administration of the study drug in that cycle.

Pooled analysis by treatment group.

Drug Concentration (c)–Time (t)Data Analysis: Based on BPKCS, for each group, the plasma concentrations of utidelone or capecitabine at each time point, as well as those of the major metabolite (at leastone), are reported, along with the number of subjects (N), arithmetic mean, standard deviation (SD), coefficient of variation (CV), minimum value (Min), median, maximum value (Max), geometric mean (Geo_Mean), and geometric coefficient of variation (CV%-GM). Linear and semi-logarithmic plots are used to depict individual drug concentration–time profiles and the population-averaged drug concentration–time curve.

Pharmacokinetic parameteranalysis: Based on PKPS, summarizedby treatment group, with the number of cases (N), arithmetic mean, standard deviation (SD), coefficient of variation (CV), minimum value (Min), median, maximum value (Max), geometric mean (Geo_Mean), and geometric coefficient of variation (CV%-GM) provided.

At theC1D1 samplingtime point for S33009, 1.5hours after administration of capecitabineandits metabolites, blood was not collected as required—first administering utidelone 1.5 hours prior to then taking the capecitabine tablet—resulting in a significant impact on the PK analysis. Consequently, data from this time point were excluded from the PK concentration analysis of capecitabine and its metabolites, and PK parameters for capecitabine and its metabolites were calculated based on the actual blood-collection times relative to the capecitabine dosing time at C1D1.

Seven subjects (S33001, S33003, S33005, S34001, S34002, S38001, and S38005) had their first post-dose sample at the timeof Cmax, and no early-time samples (within 5–15 minutes after dosing) were collected. The corresponding PK data for the respective analytes in the relevant period were excluded to conduct a sensitivity analysis (summary analysis of PK concentrations and parameters).

In11 cases (S33001, S33003, S33005, S33009, S34001, S34002, S34003, S38001, S38002, S38004, and S38006), fewer than three quantifiable data points were available for the elimination phase. Accordingly, the PK parameters associated with λz for the respective analytes will not be reported.

### 5.9. Safety Analysis

Based on the SS, analyses were conducted by treatment group.

#### 5.9.1.Adverse event

Adverse events werecoded using MedDRA terminology. For the pooledanalysis, only adverse events occurring from the first dose of the study drug through 28 days after the last dose were included. Adverse

events that occurred prior to the first dose of the study drug or more than 28 days after the last dose were excluded from the pooled analysis and are presented in a separate list.

Summary of the number ofoccurrences, cases, and percentagesforAEs:all adverse events; Grade 3 or higher adverse events; investigational medicinal product–related adverse events (classifiedas "definitelyrelated," "probablyrelated," or "uncertain" in relation to the study treatment); Grade 3 or higher investigational medicinal product–related adverse events; adverse events leading to a reduction in the study treatment dose; adverse events resulting in temporary discontinuation of the study drug; adverse events leading to permanent discontinuation of the study drug; serious adverse events; serious adverse events related to the investigational medicinal product; adverse events leading to withdrawal from the study; adverse events resulting in death; and serious adverse events related to the investigational medicinal product that resulted in death. For each of these AE categories, data are summarized by System Organ Class (SOC) and Preferred Term (PT), with the number of occurrences, cases, and percentages reported for each subject. Adverse events and investigational medicinal product–related adverse events are further stratified by System Organ Class (SOC), Preferred Term (PT), and severity, with the number of occurrences, cases, and percentages provided for each subject. In addition, a tabular list of the corresponding data for each AE category is included.

When summarizing adverse events, forthe same subject, if an AE meets all of the following criteria, it is considered to be part of the same AEGRPID:

- Same asAEDECOD
- Theend date of the preceding AE equalsthe start date of the subsequent AE, or the end date of the preceding AE is later than the start date of the subsequent AE.
- Theprevious AE did not have an outcome of "recovery without sequelae" or "recovery with sequelae."

If a combined AE is recorded in multiple split records, with both dose-reduction and discontinuation entries, it will be counted as one case in each relevant category. Other AE classification and aggregation rules follow a similar approach.

When summarizingtables related to toxicity grades, for each AEDECOD, the count of cases will be based on the AE with the highest toxicity grade among different AEGRPID values; for all AEGRPID values under the same AEDECOD, cases will be counted across all toxicity grades.

When selecting the toxicity grade for AEGRPID, the highest toxicity grade among all split records that meet the aggregation criteria shall be adopted as the toxicity grade for AEGRPID.

### 5.9.2. Death

For reported deaths, provide the number and percentage of subjects in each cause-of-death category, stratified by deaths occurring during the treatment period and during the follow-up period.

Deaths occurring during the treatment period: the date of death is on or before 28 days after the last dose.

Deaths occurring during the follow-up period: the date of death was later than the last dose administration date plus 28 days.

### 5.9.3. Vital signs

Provide the number of cases, mean, standard deviation, median, minimum, and maximum for each visit's vital signs (body weight, body surface area, body temperature, respiration rate, pulse, seated systolic blood pressure, and seated diastolic blood pressure), along with the corresponding changes from baseline; present cross-tabulations comparing baseline values with post-dose values (under worst-case scenarios) for clinical significance assessment; and furnish a summary table of newly observed clinically significant laboratory findings.

Change from baseline = Visit value − Baseline value

The summary of newlydetected abnormalities with clinical significance includes: records where the baseline was normal or abnormal but deemed non-clinically significant, or not assessed; and records where abnormalities observed after baseline were found to be clinically significant.

### 5.9.4. Physical examination

The physical examination provides a cross-tabulation of baseline and post-administration (based on the worst-case scenario) clinical significance assessments, as well as a summary table of newly detected abnormalities with clinical relevance.

The summary of newlydetected abnormalities with clinical significance includes: records where the baseline was normal or abnormal but deemed non-clinically significant, or not assessed; and records where abnormalities observed after the baseline were found to be clinically significant.

### 5.9.5. Laboratory tests

Laboratory tests (complete blood count, urinalysis, and serumbiochemistry) are presented as cross-tabulations comparing baseline values with post-dose results, with clinical significance assessed on a worst-case basis. A summary table of newly observed abnormalities deemed clinically significant is also

provided. Stool routine examination and fecal occult blood testing are off-protocol studies with no baseline data; only a list is reported.

Change from baseline = Visit value − Baseline value

The summary of newlydetected abnormalities with clinical significance includes: records where the baseline was normal or abnormal but deemed non-clinically significant, or not assessed; and records where abnormalities observed after the baseline were found to be clinically significant.

**5.9.6.12-lead electrocardiogram**

Provide the number of cases, mean, standard deviation, median, minimum, and maximum for each visit's 12-lead electrocardiogram results (heart rate, PR interval, QRS duration, QT interval, QTcB interval, and QTcF interval), along with the corresponding changes from baseline; present cross-tabulations for determining clinical significance between baseline and post-dose visits (using the worst-case scenario); and furnish a summary table of newly observed clinically significant abnormalities.

Change from baseline = Visit value − Baseline value

The summary of newlydetected abnormalities with clinical significance includes: records where the baseline was normal or abnormal but deemed non-clinically significant, or not assessed; and records where abnormalities observed after the baseline were found to be clinically significant.

**5.9.7.ECOGperformance status**

A cross-tabulation of ECOG performance status scores at baseline and at the post-dose visit (under the worst-case scenario) is provided.

## 6. Interim Analysis

No interim analysis was planned for this trial.

## 7. Changes tothe plan analysis of the proposal

None.

## 8. References

[1]. Wen-Zhao Zhong, Qun Wang, Wei-Min Mao, et al. Gefitinib versus vinorelbine plus cisplatin as adjuvant treatment for stage II–IIIA (N1–N2) EGFR-mutant NSCLC (ADJUVANT/CTONG1104): a randomised, open-label, phase 3 study. Lancet Oncol 2018; 19: 139–48.

[2].Dongsheng Yue, Shidong Xu, Qun Wang, et al. Erlotinib versus vinorelbine plus cisplatin as adjuvant therapy in Chinese patients with stage IIIA EGFR mutation-positive non-

small-cell lung cancer (EVAN): a randomised, open-label, phase 2 trial. Lancet Respir Med 2018;6: 863–73.

[3]. Y-iLong Wu, Masahiro Tsuboi, Jie He, et al. Osimertinib in Resected EGFR-Mutated Non–Small-Cell Lung Cancer. The New England Journal of Medicine 2020; 383(18):1711-1723.