A Multicenter, Open-Label, Randomized, Controlled Phase III Clinical Study Comparing UTD2 Combined with Capecitabine to Capecitabine Monotherapy as Adjuvant Therapy for Triple-Negative Early Breast Cancer Patients Who Did Not Achieve Pathological Complete Response After Neoadjuvant Therapy

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Sponsor	Fudan University Shanghai Cancer Center
Investigational Product	Utidelone Capsules (UTD2)
Study ID	BG02-T2401
Study Title	A Multicenter, Open-Label, Randomized, Controlled Phase III Clinical Study Comparing UTD2 Combined with Capecitabine to Capecitabine Monotherapy as Adjuvant Therapy for Triple-Negative Early Breast Cancer Patients Who Did Not Achieve Pathological Complete Response After Neoadjuvant Therapy
Phase	Phase III
Phase III	Prof. Zhi-Min Shao
Number of Sites	Approximately 39 centers
Study Population	Triple-negative early breast cancer patients who did not achieve pCR after neoadjuvant therapy
Study Objectives	**Primary Objective** To evaluate the 3-year invasive disease-free survival (IDFS) rate of UTD2 combined with capecitabine versus capecitabine monotherapy in adjuvant therapy for triple-negative early breast cancer patients who did not achieve pCR after neoadjuvant therapy. **Secondary Objectives** - Compare IDFS rates (3-year and 5-year), overall survival (OS) rates (3-year and 5-year), and safety profiles between the two arms. **Exploratory Objectives** - Identify predictive/prognostic biomarkers using tumor/adjacent tissues, blood, and stool samples. - Investigate molecular features associated with treatment response and tumor biology.
Endpoints	**Primary Endpoint** 3-year IDFS rate **Secondary Endpoints** 5-year IDFS rate, 3-year OS rate, 5-year OS rate, safety analysis (CTCAE v5.0) **Translational Endpoints** Biomarker discovery and correlation with disease status/treatment response.

Study Design	Design: Multicenter, open-label, randomized, controlled, superiority Phase III trial. Sample Size: 440 patients (1:1 randomization: 220 in UTD2 + capecitabine arm; 220 in capecitabine monotherapy arm). Stratification Factor: Postoperative pathological lymph node status (negative vs. positive). Treatment Regimens: Experimental Arm: UTD2: 50 mg/m²/day orally on Days 1–5, repeated every 21 days for 2 years. Capecitabine: 1000 mg/m² orally twice daily on Days 1–14, repeated every 21 days for 8 cycles. Control Arm: Capecitabine: Same dose and schedule as above. Follow-up: Imaging every 6 months to assess disease recurrence.
Inclusion Criteria	1.Informed Consent and Compliance The patient has fully understood this study and voluntarily signed the informed consent form, demonstrating the ability and willingness to comply with the study protocol-defined visits, treatment plans, laboratory tests, and other study procedures. 2.Age and Gender Female patients aged 18 to 70 years old (inclusive) on the day of signing the informed consent. 3.Prior Neoadjuvant Chemotherapy without pCR Received prior neoadjuvant chemotherapy containing anthracycline or taxane agents without achieving pathological complete response (pCR). Neoadjuvant chemotherapy requirement: At least 4 completed cycles. Non-pCR definition: Residual invasive carcinoma confirmed by pathology after primary tumor resection. 4.Surgical Resection Underwent complete surgical resection (R0) with pathologically confirmed negative margins. 5.Triple-Negative Breast Cancer Confirmation

	Post-resection tumor tissue confirmed as ER-negative, PR-negative, and HER2-negative breast cancer by immunohistochemistry (IHC): ER-negative: <1% expression by IHC. PR-negative: <1% expression by IHC. HER2-negative: IHC score of 0 or 1+, or 2+ with negative in situ hybridization (ISH) results. 6.Postoperative Treatment No prior systemic anticancer therapy (excluding radiotherapy) after breast cancer surgery. 7.Performance Status ECOG performance status of 0 to 1. 8.Hematological Criteria (within 1 week prior to enrollment) Blood tests meet the following criteria (CTCAE v5.0 ≤ Grade 1, based on institutional laboratory standards): White blood cell (WBC) count ≥ 3.0 × 10^9/L. Absolute neutrophil count (ANC) ≥ 1.5 × 10^9/L. Platelet (PLT) count ≥ 100 × 10^9/L. Hemoglobin ≥ 9.0 g/dL. No administration of recombinant human granulocyte colony-stimulating factor (rhG-CSF), blood products, or erythropoietin (EPO) within 14 days prior to enrollment. 9.Biochemical Criteria (within 1 week prior to enrollment) Normal blood biochemistry (CTCAE v5.0 ≤ Grade 1, based on institutional laboratory standards): Total bilirubin (TBIL) ≤ 1.5 × upper limit of normal (ULN). Alanine aminotransferase (ALT) ≤ 1.5 × ULN. Aspartate aminotransferase (AST) ≤ 1.5 × ULN. Alkaline phosphatase (ALP) ≤ 2.5 × ULN. Creatinine clearance (Ccr) ≥ 50 mL/min. Contraception Requirements Fertile patients must agree to use highly effective contraception (hormonal, barrier methods, or abstinence) with their partners during the trial and for at least 6 months after the last dose. Premenopausal female patients must have a

	negative blood or urine pregnancy test before enrollment.
Exclusion Criteria	1.Stage IV metastatic breast cancer. 2.Bilateral breast cancer. 3.History of other malignancies within the past 5 years, except for cured basal cell carcinoma of the skin, cervical carcinoma in situ, or papillary thyroid carcinoma. 4.Radiotherapy within 2 weeks prior to the first dose of the study drug. 5.Surgery within 2 weeks prior to the first dose of the study drug. 6.Prior treatment with utidelone or capecitabine, known hypersensitivity to utidelone, capecitabine, or fluoropyrimidines, or confirmed dihydropyrimidine dehydrogenase (DPD) deficiency. 7.Prior adverse reactions to anticancer therapy have not recovered to CTCAE v5.0 Grade ≤1 (excluding toxicities deemed non-risky by the investigator, such as alopecia). 8.Gastrointestinal disorders (e.g., esophageal obstruction, pyloric obstruction, intestinal obstruction), post-gastrointestinal resection, or other factors causing dysphagia that may interfere with oral drug absorption. 9.Severe comorbidities, including significant cardiac/cerebrovascular disease, uncontrolled diabetes/hypertension, active infections, or active peptic ulcer. 10.Active hepatitis B virus (HBV) infection. 11.History of immunodeficiency (e.g., HIV-positive status, congenital/acquired immunodeficiency disorders) or organ transplantation. 12.Psychiatric disorders or poor compliance. 13.Pregnancy (positive pregnancy test) or lactation. 14.Concurrent participation in another interventional clinical study or receiving other investigational therapies. 15.Concomitant use of potent CYP3A4 inhibitors/inducers or QT-prolonging drugs within 14 days prior to the first dose or during the study. 16.Other conditions deemed unsuitable for study participation by the investigator.
Treatment Regimen	Experimental Group Utidelone Capsules (UTD2):

	Dosage: 50 mg/m²/day, administered orally once daily on Days 1–5. Cycle: 21 days per treatment cycle, for a total duration of 2 years. Capecitabine: Dosage: 1000 mg/m², administered orally twice daily on Days 1–14. Cycle: 21 days per treatment cycle, for a total of 8 cycles. Treatment Discontinuation Criteria: Study treatment will be terminated if disease recurrence or intolerable adverse events (AEs) occur during the treatment period. Control Group Capecitabine: Dosage: 1000 mg/m², administered orally twice daily on Days 1–14. Cycle: 21 days per treatment cycle, for a total of 8 cycles. Treatment Discontinuation Criteria: Study treatment will be terminated if disease recurrence or intolerable adverse events (AEs) occur during the treatment period.
Planned Enrollment	A total of 646 subjects will be enrolled, with 323 in the experimental group and 323 in the control group.
Statistical Analysis	Analysis Populations Full Analysis Set (FAS): Defined as all randomized subjects who meet the eligibility criteria based on the Intent-to-Treat (ITT) principle. Per Protocol Set (PPS): A subset of the FAS, excluding subjects with major protocol deviations that significantly impact the results. Safety Set (SS): Includes all randomized subjects who received at least one dose of the study drug. Subjects in the SS are analyzed according to the actual treatment received. Sample Size Estimation This study is a parallel-controlled superiority trial with the primary endpoint being the investigator-assessed 3-year invasive disease-free survival (IDFS) rate. Subjects are randomized 1:1 to the experimental and control groups. Assuming a 3-year IDFS rate of 72% in the control group and a hazard ratio (HR) of 0.6, a total of 122 IDFS events are required to achieve 80% power at a two-sided significance level of $\alpha = 0.05$. The calculated sample size is 418

	subjects. Accounting for an approximate 5% dropout rate, a minimum of 440 subjects (220 per group) will be enrolled. **General Statistical Principles** Statistical analyses will be performed using SAS 9.4 or later. All statistical tests will be two-sided, with 95% confidence intervals (CI). Continuous data will be summarized using counts, means, standard deviations, quartiles, minima, and maxima. Categorical data will be summarized using frequencies (percentages). **Efficacy Analysis** The primary endpoint, 3-year IDFS rate, will be analyzed using Kaplan-Meier survival curves with 95% CIs. The log-rank test will compare survival distributions between groups. Stratified Cox proportional hazards models will estimate HRs and 95% CIs, adjusting for postoperative pathological lymph node status. Both the FAS and PPS will be analyzed for the primary endpoint, with the FAS serving as the primary analysis set. Overall survival (OS) will be analyzed using the same methods as IDFS. IDFS and OS rates at different timepoints will be estimated using the Kaplan-Meier method. Continuous variables will be summarized descriptively, including mean, standard deviation, median, minimum, and maximum. **Safety Analysis** Adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and graded per NCI CTCAE v5.0. Safety analyses will focus on treatment-emergent AEs, treatment-related AEs, and serious AEs (SAEs). Summary tables will report the number and percentage of subjects experiencing each AE category.
Study Duration	Patient enrollment is expected to take approximately 24 months, with the total duration of the Phase III study estimated to be 60 months.