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# Oral Utidelone Capsule, a First-in-Class Solid Microtubule Stabilizer, in Advanced Breast Cancer: A First-in-Human Phase I-II Trial

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**Article**

**Keywords:**

**Posted Date:** November 2nd, 2026

**DOI:** https://doi.org/10.21203/rs.3.rs-11347488/v1

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**Additional Declarations:**
There is **NO** Competing Interest.

Tables 1 to 3 are available in the supplementary files section

**Oral Utidelone Capsule, a First-in-Class Solid Microtubule Stabilizer, in Advanced Breast Cancer: A First-in-Human Phase I-II Trial**

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**ABSTRACT**

**Purpose**: Chemotherapy options for advanced breast cancer (ABC), which are usually given intravenously, may have suboptimal tolerability and convenience for long-term disease management. This first-in-human phase I-II study evaluated the efficacy, safety and pharmacokinetic (PK) profile of utidelone capsule (UTD2), the first oral solid microtubule stabilizer and an oral formulation of the approved microtubule inhibitor utidelone injection (UTD1), as monotherapy and in combination with capecitabine in ABC.

**Patients and Methods**: This multicenter trial (NCT05700084) had three parts. In Part 1, dose-escalation of UTD2 in patients with advanced solid tumors was done to establish the maximum tolerated dose (MTD). Part 2 used a crossover design to compare PK profiles of UTD2 and UTD1 in patients with advanced solid tumors. In Part 3 patients with ABC received UTD2 plus capecitabine.

Primary endpoints included the MTD of UTD2 and the objective response rate (ORR) of UTD2 plus capecitabine. Secondary endpoints included PK parameters, progression-free survival (PFS), disease control rate (DCR), and safety.

**Results**: Between August 30, 2023 and May 9, 2025, 82 patients were enrolled. All 10 evaluable patients who received UTD2 monotherapy had ABC; the confirmed ORR was 20.0% and DCR was 70.0%. In the 44 evaluable patients treated with all-oral UTD2 plus capecitabine, the confirmed ORR was 52.3% (95% CI, 36.7–67.5), median PFS was 8.3 months (95% CI, 5.4–10.6) and DCR was 88.6% (95% CI, 75.4–96.2). No dose-limiting toxicities were observed. The absolute oral bioavailability of UTD2 was 31.8%. Grade ≥3 neutropenia occurred in 12% of patients and grade ≥3 peripheral neuropathy in 2%.

**Conclusion**: UTD2 showed promising antitumor efficacy and was well-tolerated. UTD2 plus capecitabine provided clinical benefit in patients with ABC, offering an alternative to intravenous formulations of microtubule stabilizer.

## INTRODUCTION

Breast cancer remains the most prevalent malignant tumor and the leading cause of cancer-related mortality in women globally. GLOBOCAN 2024 epidemiological data indicate that breast cancer accounts for 694,000 cancer deaths annually, constituting approximately 16.9% of all cancer-related deaths in women.[1] For patients with metastatic breast cancer, the median overall survival (OS) across all molecular subtypes is 25 months, with a prognosis of only 11 months for patients with triple-negative breast cancer (TNBC).[2] Most patients with advanced breast cancer (ABC) receive anthracycline- and taxane-based regimens in the adjuvant or neoadjuvant setting. Prior taxane exposure frequently induces multidrug resistance, compromising the efficacy of taxane re-treatment in the metastatic setting.[3] Following taxane failure, available chemotherapy options include eribulin,[4] vinorelbine,[5] gemcitabine,[6] capecitabine[7] and utidelone (UTD1).[8,9] However, most of the chemotherapy options are injected intravenously, which subsequently brings the pretreatment for preventing solvent allergies and the infusion reactions.

Utidelone is a genetically engineered epothilone analog and a non-taxane tubulin inhibitor that exerts antitumor activity by promoting tubulin polymerization, blocking microtubule depolymerization, and inducing mitotic arrest and apoptosis (unpublished data, R Qiu and colleagues). A pivotal phase III trial established the clinical benefit of intravenous UTD1 plus capecitabine versus capecitabine alone in patients with ABC who had progressed on anthracyclines or taxanes. In that study, the combination

regimen significantly improved median progression-free survival (PFS; 7.72 vs 4.76 months; hazard ratio [HR]=0.65, P=0.0007), objective response rate (ORR; 39.6% vs 28.1%), and median overall survival (OS; 20.9 vs 15.7 months; HR=0.69, P=0.0032).[8,9] Notably, UTD1 is the only chemotherapeutic agent approved in the past 20 years that has demonstrated concurrent PFS and OS benefits in patients previously treated with anthracyclines or taxanes. Based on these data, UTD1 was approved in China in 2021 for use in combination with capecitabine in patients with recurrent or metastatic breast cancer who had received prior anthracycline or taxane therapy.

Despite the proven clinical efficacy of intravenous UTD1, its long-term clinical use is hindered by its formulation. Like other common chemotherapy, UTD1 requires premedication to prevent hypersensitivity reactions due to the properties of its solvent, Cremophor EL (CrEL).[10] This also adds extra burden of hospitalization for patients. The development of utidelone capsule (UTD2) addresses these limitations. Unlike taxanes, utidelone is not a substrate for P-glycoprotein, conferring an inherent advantage for oral delivery.[11] Compared with injectable UTD1, the oral formulation eliminates the need for five consecutive days of inpatient infusion, routine anti-allergic prophylaxis, and the associated risks of infusion-related reactions and pain. Oral formulation is expected shown to improve patient adherence, have a more favorable safety profile and enhanced convenience for long-term disease management, and reduce healthcare costs compared with intravenous formulations.[12,13,8,9] This first-in-human open-label phase I-II study (NCT05700084) was conducted in 10 sites in China and was designed to investigate the safety, efficacy, and pharmacokinetic (PK) profiles of UTD2 as a single agent and in combination with capecitabine.

The rationale for combining UTD2 with capecitabine is supported by three complementary considerations. First, microtubule stabilizers and antimetabolites act on distinct phases of the cell cycle, providing a mechanistic basis for synergistic activity. Second, both agents are orally bioavailable, enabling a truly all-oral regimen that eliminates infusion-related burden. Third, their toxicity profiles are non-overlapping—UTD2's principal toxicity is manageable diarrhea without significant myelosuppression, while capecitabine's dose-limiting toxicity is hand-foot syndrome—supporting the feasibility of combination dosing.

## METHODS

The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol and amendments were approved by the Ethics Committee of the

National Cancer Center / Cancer Hospital, Chinese Academy of Medical Sciences. All patients provided written informed consent prior to enrollment.

**Patient population**

Part 1 and Part 2 of this study enrolled patients aged 18–65 years with advanced solid tumors who had progressed after standard therapy. Eligible patients for Part 3 were aged 18–70 years, had ABC and had received ≤4 prior lines of chemotherapy, including at least one prior anthracycline- or taxane-based treatment, Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0–1, measurable disease per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1),[14] and a life expectancy ≥12 weeks. Full inclusion and exclusion criteria can be found in the full study protocol (Supplementary materials).

**Study treatment**

Part 1 (Phase I) was a dose-escalation study in which patients received UTD2 monotherapy. Dose escalation followed a modified Fibonacci design, with cohorts receiving 50 mg/m²/day for 5 days, 75 mg/m²/day for 5 days, and 75 mg/m²/day for 7 days, in 21-day cycles to establish the maximum tolerated dose (MTD).

Part 2 was a PK comparison and food effect study. The patients received UTD1 (by intravenous infusion) and UTD2 (oral administration as a capsule; fasting or fed) in a crossover design. Fasting conditions were defined as fasting for 2 hours before and 2 hours after administration of the study drugs. Fed conditions were defined as study drug administration occurring 30–35 minutes after the start of the high-fat meal, with a 2-hour fasting period following drug administration.

For Part 3 (Phase II), the UTD2 plus capecitabine expansion study. Patients received UTD2 60 mg/m²/day on Days 1–5 (fasting) plus capecitabine 1000 mg/m² twice daily on Days 1–14, in 21-day cycles. Treatment continued until disease progression, intolerable toxicity, or patient withdrawal. Dose reductions and interruptions due to adverse events (AEs) were predefined in the protocol (Supplementary materials).

**Endpoints**

The primary endpoints were the MTD of UTD2 (Part 1) and the ORR (proportion of evaluable patients who achieved a best overall response of complete response (CR) or partial response (PR) from enrollment to disease progression) of UTD2 combined with capecitabine in advanced metastatic breast

cancer (Part 3). Secondary endpoints included absolute oral bioavailability of UTD2, progression-free survival (PFS; time from treatment initiation to first documented disease progression per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)[14]or death from any cause, whichever occurred first), disease control rate (DCR; percentage of patients with CR, PR, or stable disease (SD)), duration of response (DoR; time from the first documented date of CR or PR until the date of documented disease progression or death from any cause, for patients achieving confirmed CR or PR), safety and PK parameters. Tumor responses were assessed by investigator per RECIST v1.1[14] and AEs were graded according to NCI Common Terminology Criteria for Adverse Events version 5.0.[15]

**Pharmacokinetic evaluation**

Blood samples was taken pre and post dose in all parts of the study. In Part 3, intensive blood sampling was also done in 12 patients, pre-dose and at 11 timepoints post-dose in cycle 1 days 1-5. In addition, urine and feces were sampled during Part 2 of the study. For details, please see the full study protocol (Supplementary materials).

PK evaluation endpoints included peak plasma concentration ($C_{max}$; maximum observed plasma drug concentration after dosing), time to peak plasma concentration ($T_{max}$; time from drug administration to occurrence of $C_{max}$), $AUC_{0-t}$ (area under the plasma concentration-time curve from time zero to the time of the last quantifiable plasma concentration) $AUC_{inf}$ (area under the plasma concentration-time curve extrapolated from the last quantifiable concentration to infinity) and ($t_{1/2}$; time required for plasma drug concentration to decrease by 50% during the terminal elimination phase), and absolute oral bioavailability. Absolute oral bioavailability was calculated as $F=(\text{mean } AUC_{UTD2}\times Dose_{UTD1})/(\text{mean } AUC_{UTD1}\times Dose_{UTD2})$.

**Statistical Analysis**

This trial had no formal statistical power calculation. The main prespecified analysis populations included: the full-analysis set (FAS; all participants receiving ≥1 study-drug dose, analyzed per intention-to-treat principle); the per-protocol set (PPS; efficacy population with ≥2 treatment cycles, RECIST 1.1-measurable baseline lesions, evaluable post-dose efficacy data, and no major protocol deviations impacting efficacy assessment); and the safety set (SS; all participants with ≥1 drug exposure and available post-dose safety data, analyzed by actual treatment received.

Descriptive statistics summarized baseline, safety, PK and efficacy data. Non-compartmental PK analyses were performed using Phoenix WinNonLin and general statistical analyses were conducted in SAS. AEs were coded with MedDRA. ORR and DCR were reported with point estimates and 95% confidence intervals (CI). Time-to-event endpoints, including PFS and DoR, were estimated using via the Kaplan-Meier method with survival curves generated.

## Results

### Patients

A total of 82 patients were enrolled between August 30, 2023 and May 9, 2025.

In Part 1, all the patients that were enrolled across the three dose cohorts (n=12) were female and had stage IV ABC. The median age was 50.5 years (range, 38–64) (Supplementary Appendix Table S1). Liver and lung metastasis were each present in 50% of patients, brain metastases were observed in 8.3%, and 91.7% had ≥2 metastatic lesions. Most patients (58.3%) had received ≥3 prior lines of systemic anticancer therapy, and all had prior exposure to taxanes or anthracyclines. In the modified Fibonacci dosing escalation design, two patients received UTD2 50 mg/m²/day for 5 days, seven patients 75 mg/m²/day for 5 days, and three patients 75 mg/m²/day for 7 days.

Part 2 enrolled 20 patients with advanced solid tumors (3 male and 17 female), with a median age of 51.5 years (range, 27–65). The tumor types were breast cancer (n=16), pancreatic cancer (n=2), colorectal cancer (n=1), and renal cell carcinoma (n=1).

Part 3 enrolled 50 patients with ABC (49 female and 1 male), all of whom had received prior taxane or anthracycline treatment (Table 1; Appendix Figure S1). The median number of prior treatment lines for advanced disease was 2 (range, 0–6). Visceral metastases were present in 43 patients (86.0%), and 42 patients (84.0%) had two or more metastatic sites. Hormone receptor (HR)-positive/human epidermal growth factor receptor-2 (HER2)-negative was the predominant subtype (36 patients, 72.0%), followed by HR-negative/HER2-negative (12 patients, 24.0%), and HR-positive/HER2-positive (1 patient, 2.0%).

### Efficacy

By the data cutoff date of October 8, 2025, 10 of the 12 patients in Part 1 were evaluable per protocol. One confirmed PR was observed in the 50 mg/m²/day for 5 days cohort and one in the 75 mg/m²/day for 7 days cohort; one unconfirmed PR occurred in the 75 mg/m²/day for 5 days cohort (Appendix Figure S2). The confirmed ORR was 20.0%, the unconfirmed ORR was 30.0%, and the DCR was 70.0%. Results from the FAS showed consistent efficacy trends and are presented in the Appendix Table S2.

In Part 3, 44 of the 50 patients were evaluable per protocol. Twenty-seven patients achieved a PR, with

23 confirmed PRs (Figure 1). The confirmed ORR was 52.3% (95% CI, 36.7–67.5), the DCR was 88.6% (95% CI, 75.4–96.2), the median PFS was 8.3 months (95% CI, 5.4–10.6) (Figure 2), and the median DoR was 7.6 months (95% CI, 4.2–not estimable [NE]). At data cutoff, 16 patients remained on treatment, and the median number of treatment cycles was 9. Results from the FAS showed consistent efficacy trends and are presented in the Appendix Table S3.

Ad-hoc subgroup analyses of Part 3 by molecular subtype showed benefit regardless of HR status (Table 2). In the HR-positive/HER2-negative subgroup (n=33), the confirmed ORR was 54.6% (95% CI, 36.4–71.9), in the TNBC subgroup (n=10), it was 50.0% (95% CI, 18.7–81.3). The one patient with HR-positive HER2-positive disease had SD. In all the key subgroups, such as the population with ≥2 metastatic sites, visceral metastases or who had received ≥3 prior lines of treatment, consistent clinical benefit were obtained. In patients who had received ≥3 prior lines of treatment (n=18), the confirmed ORR was 50.0% (95% CI, 26.0–74.0), median PFS was 8.3 months (95% CI, 6.0–NE), and median DoR was 7.7 months (95% CI, 3.4–NE).

**Safety**

No dose-limiting toxicities (DLTs) were reported in Part 1; therefore, no MTD was identified in this study. However, AEs observed in the 75 mg/m²/day for 7 days cohort included one case of grade 3 diarrhea (lasting <24 hours after optimal management) and two cases of grade 3 asthenia (which resolved within 7 days). Following discussion by the Safety Monitoring Committee, the 75 mg/m²/day for 5 days schedule was recommended for further UTD2 monotherapy development. A reduced dose of 60 mg/m²/day for 5 days was selected as the recommended dose for UTD2 in combination with capecitabine.

In Part 1, UTD2 monotherapy demonstrated a favorable safety profile across a treatment duration ranging from 2 to 15 cycles (Appendix Table S4). Most treatment- emergent adverse events (TEAEs) were grade 1–2.

In Part 3, patients were treated with UTD2 plus capecitabine, and the median number of treatment cycles was 9. All 50 patients experienced at least one TEAE; 27 patients (54.0%) had grade ≥3 TEAEs (Table 3). Diarrhea was the most common AE and was generally well controlled with symptomatic treatment. Hematologic toxicity was mild, with a grade ≥3 neutropenia incidence of 12.0%. No grade ≥3 liver or renal function abnormalities were observed. Peripheral neuropathy was infrequent, with

one patient (2.0%) experiencing grade 3 (no grade 4). Palmar-plantar erythrodysesthesia (PPE) was also rare, with one patient (2.0%) experiencing a grade 3 AE. Two patients (4.0%) discontinued UTD2 due to AEs, while three patients (6.0%) discontinued capecitabine due to AEs. No treatment-related deaths occurred.

**Pharmacokinetics**

In Part 2, oral UTD2 was rapidly absorbed, with a median time to peak plasma concentration of approximately 1.3 hours (Appendix Table S5). Plasma concentrations declined thereafter, dropping below 10% of peak levels within 24 hours, with a mean terminal elimination half-life of 7.2 hours. In the sensitivity analysis, the geometric mean $AUC_{0-\infty}$ of 30 mg/m² intravenous UTD1 was 2974.8 h*ng/mL, and that of 60 mg/m² oral UTD2 was 1870.5 h*ng/mL. The absolute bioavailability (F) was 31.8% (Supplementary Appendix Table S6).

A high-fat meal reduced the $C_{max}$, $AUC_{0-t}$ and $AUC_{inf}$ of oral UTD2 to 35.0%, 91.6% and 73.8%, respectively, of that achieved under fasting conditions. These data support fasting administration of UTD2 (Appendix Table S7).

Utidelone is predominantly eliminated as metabolites. Approximately 7% of the administered utidelone capsule dose was excreted as its metabolite seco-UTD via feces (approximately 99%) or urine (approximately 1%).

The PK parameters of UTD2 when combined with capecitabine were comparable to UTD2 monotherapy, indicating that there was no clinically meaningful drug–drug interaction with capecitabine (Figure 3, Appendix Figure S3 and Appendix Table S5 and S8).

**Discussion**

UTD2, developed through formulation optimization of its intravenous counterpart, UTD1, represents a therapeutic advance as, to the best of our knowledge, UTD2 is the first solid oral microtubule stabilizer to enter clinical development for solid tumors. The oral regimen eliminates the need for five consecutive days of inpatient infusion and routine anti-allergic pretreatment, thereby reducing infusion-related discomfort and hypersensitivity risks. These attributes collectively enhance treatment convenience, improve adherence, facilitate long-term disease management, and reduce the overall economic burden for patients with ABC.

UTD2 monotherapy showed promising efficacy in solid tumors, and the combination of UTD2 with capecitabine recapitulated the clinical benefits observed with UTD1 combined with capecitabine in ABC.[8,9] In this trial, the all-oral UTD2 plus capecitabine combination achieved a confirmed ORR of 52.3%, a median PFS of 8.3 months, and a DCR of 88.6%. In the pivotal phase III trial of UTD1 in ABC, the ORR was 39.6%, the median PFS was 7.7 months, and the DCR was 85.2%.[8,9] The population in this trial shared similar characteristics with the phase III trial of UTD1, as both enrolled patients with ABC previously treated with taxane- or anthracycline-based regimens and having a similar proportion of visceral metastases. However, substantial shifts in the standard-of-care landscape for ABC occurred between the two studies. Virtually no patients in the UTD1 phase III trial had received prior CDK4/6 inhibitors or antibody–drug conjugates (ADCs). By contrast, 70.0% of patients in the present phase II portion (Part 3) had prior exposure to CDK4/6 inhibitors, and 50.0% had received ADC therapy. Although comparison with historical data requires caution, UTD2 demonstrated efficacy that compared favorably with that of UTD1 despite including a more heavily pretreated patient population. Efficacy in this phase II trial was consistent across clinically relevant subgroups, including HR-positive/HER2-negative disease, TNBC, visceral metastases, and multiple prior lines of therapy, highlighting the broad clinical applicability of this all-oral regimen.

The therapeutic landscape of ABC continues to evolve, and ADCs have emerged as vital therapeutic options. Phase III clinical trials of ADCs have demonstrated that ADCs yield significant clinical benefits compared with conventional chemotherapy control regimens. In patients with HR-positive/HER2-negative ABC, sacituzumab govitecan yielded a median PFS of 5.5 months and an ORR of 21%, compared with 4.0 months and 14% for physician's choice chemotherapy (eribulin, vinorelbine, capecitabine, or gemcitabine). [16] In the same subtype, datopotamab deruxtecan demonstrated a median PFS of 6.9 months and an ORR of 36.4%, versus 4.9 months and 22.9% with physician's choice chemotherapy (eribulin, vinorelbine, capecitabine, or gemcitabine).[17] For HER2-low ABC, trastuzumab deruxtecan (T-DXd) was associated with a median PFS of 9.9 months and an ORR of 52.3%, compared with 5.1 months and 16.3% for physician's choice chemotherapy (capecitabine, eribulin, gemcitabine, paclitaxel, or nab-paclitaxel).[18] In TNBC, sacituzumab govitecan provided a median PFS of 6.7 months and an ORR of 45.4%, whereas physician's choice chemotherapy (eribulin, vinorelbine, capecitabine, or gemcitabine) resulted in a median PFS of 2.5 months and an ORR of 12.0%.[19] Nevertheless, ADCs have notable clinical limitations. Similar to conventional chemotherapy, ADCs require routine premedication and cannot avoid the clinical burden

of intravenous infusion, accompanied by substantial toxicities, including a high incidence of grade ≥3 hematologic adverse events and a potential risk of fatal interstitial lung disease.[20,21,22,23] Against this backdrop, the all-oral regimen of UTD2 plus capecitabine serves as a promising alternative. In the HR-positive/HER2-negative population of the trial, this regimen achieved an ORR of 54.6% and a median PFS of 10.4 months. Among patients with TNBC, UTD2 plus capecitabine produced an ORR of 50.0% and median PFS of 4.3 months.

Safety remains a critical consideration in heavily pretreated patients. The UTD2-based regimen exhibited a favorable tolerability profile. In the development of reformulated taxane agents, the incidence of peripheral neuropathy remains a key endpoint of interest. In phase 3 trials of nab-paclitaxel, the rate of grade ≥3 peripheral neuropathy ranged from 8% to 10%,[24,25] whereas phase 3 studies of oral paclitaxel reported grade ≥3 peripheral neuropathy incidence of 1.8% to 2.3%.[26,27] Grade ≥3 peripheral neurotoxicity was 2.0% for UTD2 combined with capecitabineand 25.1% for UTD1 in the pivotal phase III trial.[8,9] UTD2 maintains the low hematotoxicity profile of UTD1. The incidence of grade ≥3 neutropenia was only 12.0%, which is similar to the 11.6% observed in the UTD1 phase III trial.[8,9] By comparison, grade ≥3 neutropenia rates reported for conventional chemotherapies and ADCs are often 45–60%.[6,28,29,30,31] Diarrhea was the most frequent AE. The possible influencing factor may include the higher drug concentration in the gastrointestinal tract of the oral formulation. Nevertheless, it was generally manageable with dose modifications and supportive care. No treatment-related deaths or severe interstitial lung disease were observed, underscoring the favorable safety profile of this all-oral regimen. Consistent with the favorable safety profile of UTD2, the mean number of treatment cycles of UTD2 plus capecitabine in this trial was 9, whereas that for UTD1 plus capecitabine in the phase III study was 6.[8,9] Together, these data suggest that long-term use of UTD2 plus capecitabine is possible.

PK analyses confirmed oral absorption of UTD2, with an absolute bioavailability of 31.8%, which is higher than that reported for oral paclitaxel (approximately 23%).[32] Following oral administration of UTD2 capsules, similar to intravenous UTD1, utidelone undergoes extensive metabolism. Only a small fraction of the drug is excreted unchanged in urine and feces, with the majority eliminated in the form of metabolites. The major metabolites of UTD2 are identical to those of UTD1, and no new metabolic characteristics have been observed.[33] Coadministration with capecitabine did not alter the PK profile of UTD2, indicating no clinically significant drug–drug interactions. These findings support the feasibility of long-term oral administration and are consistent with the observed clinical activity.

In conclusion, UTD2 is, to the best of our knowledge, the first solid oral microtubule stabilizer to enter clinical development for solid tumors, offering a novel, convenient, and well-tolerated therapeutic option for patients with ABC. The all-oral UTD2 plus capecitabine regimen demonstrates promising antitumor activity, a favorable safety profile with minimal hematologic and neurologic toxicity, and consistent efficacy across clinically relevant subgroups. Further evaluation in the ongoing phase III trial comparing UTD2 plus capecitabine with UTD1 plus capecitabine (NCT07684456) will help define the role of this regimen in the treatment landscape of ABC.

**Data Availability**

On request, and subject to certain criteria, conditions, and exceptions, Beijing Biostar Pharmaceuticals Co., Ltd. will provide access to individual deidentified participant data from applicable Beijing Biostar Pharmaceuticals-sponsored studies. Qualified scientific and medical researchers with appropriate competencies who are engaged in novel scientific research may submit are quest for participant-level data with a research proposal for Beijing Biostar Pharmaceuticals review. Research teams must include a biostatistician and sign a Data Sharing Agreement prior to receiving access to clinical trial data. Beijing Biostar Pharmaceuticals shares data only when permitted by applicable data privacy and security laws and regulations, shares when it is feasible to do so without compromising the privacy of the study participants, and other considerations. Data requests may be submitted to contact@biostar-pharma.com. Estimated time to response is 3 months. The study protocol is available in Supplementary. Source data are provided with this paper.

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**Acknowledgements**

We would like to thank all patients and their families for their participation. We also thank our colleagues for their support, dedication, and contributions to the completion of this study.

**Author contributions**

Binghe Xu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Binghe Xu and Tao Sun contributed equally to this work, and they share the co-first authorship.

Conceptualization: Binghe Xu, Li Tang. Recruited and/or treated patients: Binghe Xu, Tao Sun, Yanxia Shi, Pin Zhang, Jin Yang, Huihui Li, Yanxia Zhao, Zhenchuan Song, Jinsong Lu, Zefei Jiang, Huangming Hong. Collection and assembly of data：Binghe Xu, Tao Sun. Data analysis and its interpretation, project administration and supervision: Binghe Xu. Writing—original draft: Binghe Xu. All authors reviewed and approved the final manuscript.

**Funding**

This study was supported by Fundamental and Interdisciplinary Disciplines Breakthrough Plan of the Ministry of Education of China（JYB2025XDXM609）, CAMS Innovation Fund for Medical Sciences (2026-I2M-SXZX13-04), Noncommunicable Chronic Diseases-National Science and Technology Major Project (2025ZD0552504)， and National High Level Hospital Clinical Research Funding (2025-LYZX-D-A02).

**Competing interests**

Li Tang, Lin Li and Jin Guan are employees of Beijing Biostar Pharmaceuticals Co., Ltd. Binghe Xu has served as advisor or consultant for Novartis and AstraZeneca. The remaining authors declare no competing interests.

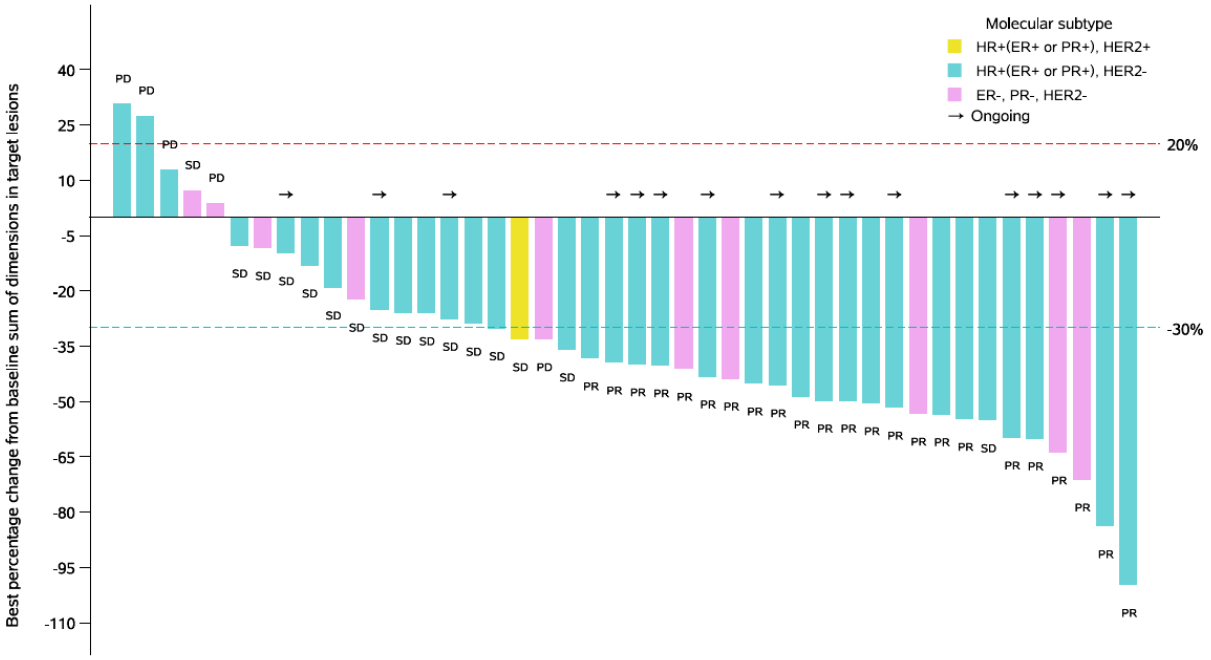



**Figure 1 Best percentage change from baseline sum of dimensions in target lesions in Part 3 (UTD2 plus capecitabine in patients with ABC)**

Each bar represents an individual patient. Bars extending upward indicate increase in tumor dimensions, whereas bars extending downward indicate a decrease in tumor dimensions. Horizontal dashed reference lines denote a 30% reduction and a 20% increase in target-lesion sum of diameters. Tumor response status (partial response [PR, defined as confirmed PR], stable disease [SD, meet the minimum duration], progressive disease[PD]) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)and molecular subtype are annotated for each patient. Ongoing treatment status is marked with an arrow.

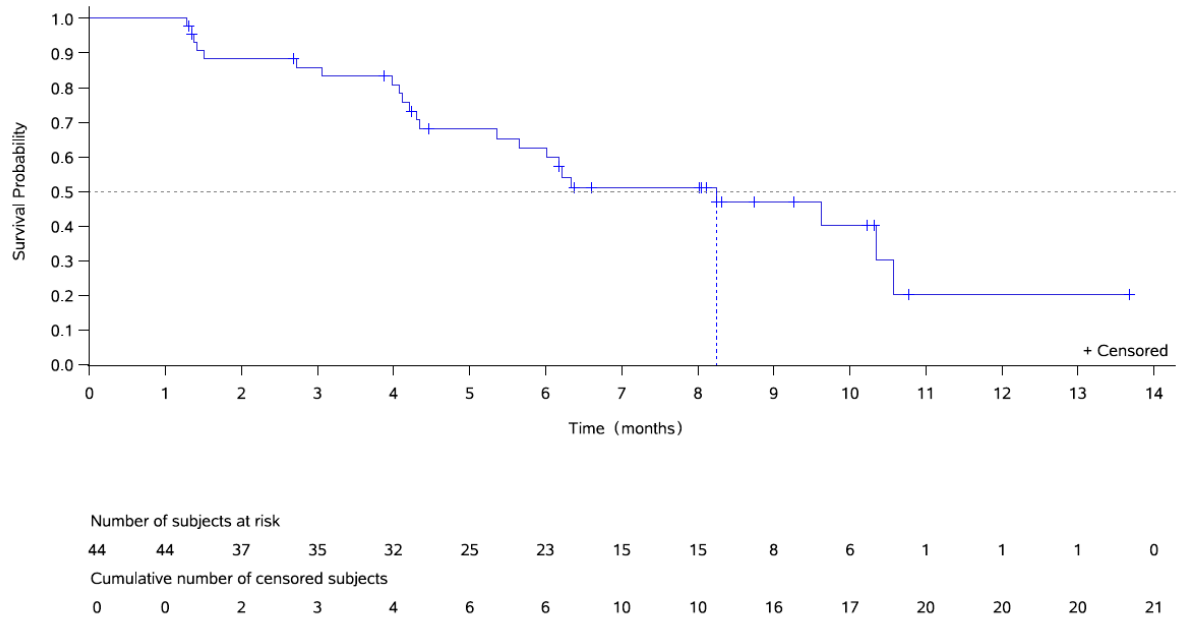



**Figure 2 Kaplan-Meier estimate of progression free survival in Part 3 (UTD2 plus capecitabine in patients with ABC)**

Progression-free survival was defined as the time from treatment initiation to first documented disease progression per RECIST v1.1 or death from any cause, whichever occurred first. Censored observations are indicated by tick marks (+). The median PFS is marked by vertical dotted line. The number of patients at risk is shown below the survival curve.

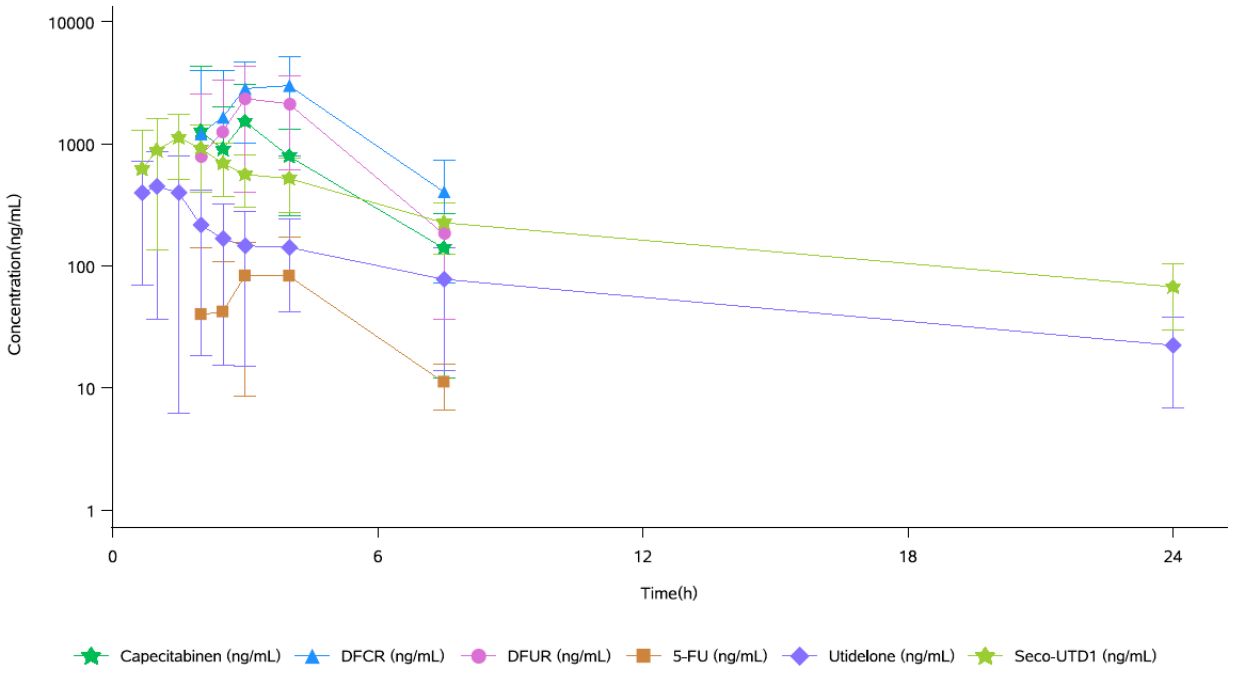



**Figure 3. Plasma Concentration-Time Curve of Utidelone and Capecitabine Following Single Dosing (Part 3, UTD2 plus capecitabine in patients with ABC)**

Error bars denote standard deviation. The x-axis shows time in hours post-dose; y-axis shows plasma concentration (ng/mL) on a semi-logarithmic scale. Abbreviations: DFCR, 5-deoxy-5-fluorocytidine; DFUR, 5-deoxy-5-fluorouridine; 5-FU, 5-fluorouracil; Seco-UTD1, seco-utidelone metabolite.

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