Utidelone Plus Bevacizumab for the Treatment of HER2-positive Breast Cancer Brain Metastases (U-BOMB-HER): A Multicenter, Single-arm Phase II study

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Abstract

- While novel HER2-targeted agents (including TKIs and ADCs) have demonstrated intracranial activity in HER2 positive (HER2+) metastatic breast cancer (MBC) with active brain metastases (BM), effective management of TKI- and/or ADC-refractory disease remains an ongoing clinical challenge.
- Building on preclinical evidence of utidelone's superior blood-brain barrier penetration and bevacizumab's established anti-edema effects, we conducted this phase II study (NCT05357417) to evaluate the efficacy and safety of utidelone plus bevacizumab in HER2+ BM patients progressed after transtuzumab and TKI treatment.
- The results of HER2-negative cohort (U-BOMB study) have been published [Yan M, et al, JAMA Oncol, 2025 Jun 26].

Methods and Materials

- This multicenter, two-cohort, single-arm phase II trial (NCT05357417) enrolled breast cancer patients ≥18 years old with untreated brain metastases or intracranial disease progression following local radiotherapy. The overall study design is shown in Figure 1.

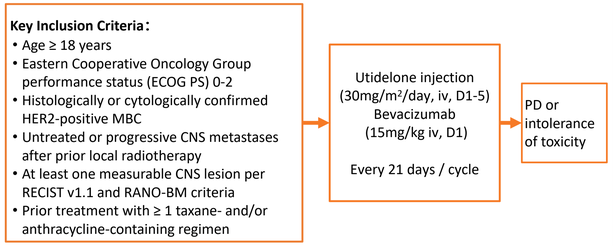


Figure 1. Study design

- Patients received utidelone (30 mg/m² IV on days 1-5) plus bevacizumab (15 mg/kg IV on day 1) every 3 weeks until disease progression or intolerance.
- The primary endpoint was central nervous system(CNS) objective response rate (CNS-ORR) as assessed by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1). The secondary endpoints included CNS disease control rate (CNS-DCR), progression-free survival (PFS), CNS-PFS, overall survival (OS) and safety.

Efficacy Results

- From May 2022 to April 2025, 50 patients were enrolled and evaluable. The baseline characteristics are shown in Table 1-2.
- The CNS-ORR was 54.0% (27/50), with a disease control rate of 92.0% (46/50). The details are shown in Figure 2-5.

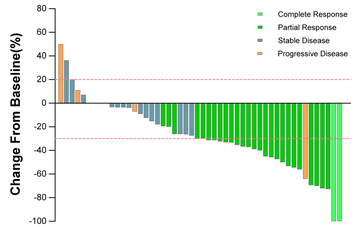


Figure 2. Waterfall plot showing changes in the target lesion(s)

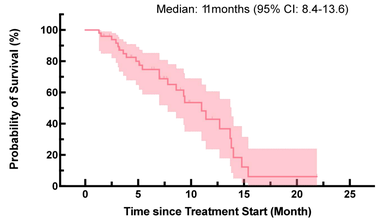


Figure 3. Kaplan-Meier curve of CNS-PFS

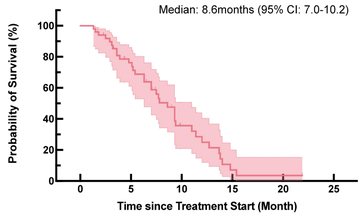


Figure 4. Kaplan-Meier curve of PFS

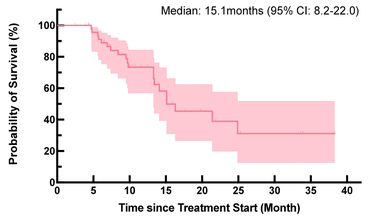


Figure 5. Kaplan-Meier curve of OS

Table 1. Baseline characteristics（N=50）

Age (years), median (min, max)	51 (32, 68)
Duration from breast cancer diagnosis to brain metastasis (months) , median (min, max)	52 (4, 65)
Prior line of therapy, median (min, max)	3 (1, 9)
ECOG performance status	
0	1 (2%)
1	48 (96%)
2	1 (2%)
Prior ADC exposed	26 (52%)
Prior intra-cranial radiotherapy exposed	22 (44%)
Number of intracranial lesions	
1	14 (28%)
2	10 (20%)
3	26 (52%)

Table 2. Sites of Metastasis（N=50）

Meninges	2(4%)
Lymph node	26(52%)
Bone	21(42%)
Lung	22(44%)
Liver	19(38%)
Pleural effusion	2(4%)
Pleura	2(4%)
Chest wall	3(6%)
Subcutaneous soft tissue	2(4%)
Dura mater	2(4%)
Breast	8(16%)
Left breast skin	1(2%)

Safety Results

- Most adverse events were mild to moderate in severity (Grade 1 or 2) and were considered manageable and reversible. No treatment-related deaths were reported.
- The details are shown in Table 3.

Table 3. Treatment-related adverse events（N=50）

	Grade1-2	Grade3-4
Peripheral neuropathy	45(90%)	3(6%)
Elevated AST/ALT	26(52%)	-
Elevated creatinine	7(14%)	-
Decreased white blood cell count	25(50%)	4(8%)
Decreased neutrophil count	17(34%)	8(16%)
Anemia	20(40%)	1(2%)
Decreased platelet count	11(22%)	2(4%)
Hypertension	15(30%)	6(12%)
Hypokalemia	8(16%)	-
Hypocalcemia	4(8%)	-
Proteinuria	19(38%)	-
Elevated GGT	-	1(2%)
Blurred vision	1(2%)	-
Hypoproteinemia	2(4%)	-
Nausea	4(8%)	-
Vomiting	1(2%)	-
Diarrhea	2(4%)	-
Constipation	3(6%)	-
Dizziness	4(8%)	-
Headache	1(2%)	-
Hyperbilirubinemia	3(6%)	-
Alopecia	1(2%)	-
Low back pain	1(2%)	-
Hoarseness	1(2%)	-
Oral infection	2(4%)	-
Allergic conjunctivitis	1(2%)	-
Hyponatremia	1(2%)	-
Fatigue	3(6%)	-

Conclusions

- Utidelone plus bevacizumab demonstrates clinically meaningful CNS activity, along with a manageable safety profile, in HER2-positive breast cancer patients with brain metastases refractory to trastuzumab and TKI.

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