# Phase Ib/II Study of iza-bren (BL-B01D1), an EGFR x HER3 Bispecific Antibody-drug Conjugate, in Patients with Recurrent Metastatic Ovarian Cancer

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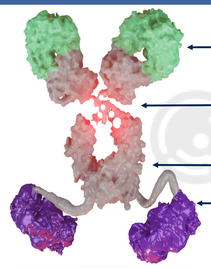
## Background




- Iza-bren (BL-B01D1) is a potential first-in-class (FIC) ADC consisting of an EGFR x HER3 bispecific antibody conjugated to a novel topoisomerase I inhibitor payload (Ed-04) via a stable tetrapeptide-based cleavable linker.
- Clinical trial information: NCT05803018 & NCT05990803.

Here the pooled safety & efficacy results from two phase Ib/II China studies evaluating iza-bren as monotherapy in patients with ovarian cancer are presented.

## Objectives

### Phase Ib Study

- To determine the recommended phase 2 dose (RP2D) of iza-bren in patients with recurrent metastatic (R/M) gynecologic cancers and other solid tumors.
- To evaluate preliminary efficacy of iza-bren in patients with R/M gynecologic cancers and other solid tumors.

### Phase II Study

- To determine the efficacy of iza-bren in patients with R/M gynecologic cancers and other solid tumors.
- To evaluate the safety and tolerability of iza-bren in patients with R/M gynecologic cancers and other solid tumors.
- To characterize the PK and immunogenicity of iza-bren.

## Methods

- Two open-label, multicenter, phase Ib/II studies evaluate the safety, efficacy, and PK profile of iza-bren as monotherapy in patients with R/M gynecologic cancers and other solid tumors.
- Patients with R/M ovarian cancer (OC) were treated with iza-bren at 2.0, 2.3, and 2.5 mg/kg on Day1 and Day 8 every 3 weeks (D1D8 Q3W).

### Study Endpoints

- **Phase Ib**
  - Primary: recommended phase 2 dose (RP2D)
  - Secondary: treatment-emergent adverse event (TEAE), objective response rate (ORR), disease control rate (DCR), duration of response (DoR), pharmacokinetics (PK), immunogenicity
- **Phase II**
  - Primary: ORR
  - Secondary: progression-free survival (PFS), DCR, DoR, TEAE, PK, immunogenicity

## Declaration of interest

- Prof. Xiaohua Wu has no conflict of interest to declare.

## Study Design

### Key Eligibility Criteria

- R/M OC and other gynecological cancers confirmed by histopathology and/or cytology
- Failed to standard therapy or without feasible standard treatment
- ECOG PS 0-1
- Measurable lesion per RECIST v1.1
- Adequate organ and marrow function

### Dosing Schedule

Iza-bren D1D8 Q3W

- 2.0 mg/kg
- 2.3 mg/kg
- 2.5 mg/kg

Note: All doses are compensated per protocol.

### Endpoints

- Primary: PR2D; ORR
- Secondary: TEAE, DCR, DoR, PFS, PK, immunogenicity

## Enrollment

- As of July 31, 2025, 96 patients with OC were enrolled and treated with iza-bren at 2.0 (N=10), 2.3 (N=60), 2.5 (N=26) mg/kg D1D8 Q3W (Table 1).

**Table 1. Patient Characteristics**

| | Total (N=96) | 2.0 mg/kg D1D8Q3W (N=10) | 2.3 mg/kg D1D8Q3W (N=60) | 2.5 mg/kg D1D8Q3W (N=26) |
|---|---|---|---|---|
| Median (range) age, years | 57.0 (29.0, 74.0) | 60.5 (54.0, 74.0) | 58.0 (35.0, 73.0) | 53.0 (29.0, 71.0) |
| Female, n (%) | 96 (100) | 10 (100) | 60 (100) | 26 (100) |
| Median (range) weight, kg | 60.2 (38.1, 93.8) | 62.5 (42.0, 84.0) | 60.0 (38.9, 93.8) | 61.0 (38.1, 79.0) |
| Median (range) BMI, kg/m$^2$ | 23.7 (16.2, 33.6) | 23.8 (16.8, 33.6) | 23.8 (16.2, 32.8) | 23.6 (16.7, 30.9) |
| ECOG performance status, n (%) | | | | |
| 0 | 20 (20.8) | 1 (10.0) | 13 (21.7) | 6 (23.1) |
| 1 | 76 (79.2) | 9 (90.0) | 47 (78.3) | 20 (76.9) |
| Median (range) baseline SOD, mm | 38.5 (13.0, 181.2) | 61.0 (24.2, 147.1) | 36.4 (14.6, 180.6) | 39.9 (13.0, 181.2) |
| Platinum-resistant*, n (%) | 83 (86.5) | 10 (100) | 49 (81.7) | 24 (92.3) |
| Prior PARP inhibitor therapy, n (%) | 46 (47.9) | 4 (40.0) | 31 (51.7) | 11 (42.3) |
| Prior Bevacizumab, n (%) | 79 (82.3) | 9 (90.0) | 48 (80.0) | 22 (84.6) |

*: disease progression within 6 months after last platinum-based chemotherapy (PBC).

## Safety

- Most common Grade 3 and above AEs were hematologic toxicities, which were effectively managed with standard supportive care.
- Treatment-related adverse events (TRAEs) occurred in all patients, and grade≥3 TRAEs occurred in 87.5% of patients (Table 2). In total, 2 (2.1%) patients discontinued iza-bren treatment due to TRAEs.
- Dose reductions due to anemia, neutropenia, and thrombocytopenia occurred in 3.1%, 8.3%, and 20.8% of patients, respectively; no patients discontinued treatment due to any of these events.
- The median time to resolution of Grade ≥3 anemia, neutropenia, and thrombocytopenia was 238, 7, and 13 days, respectively. Most patients experienced 1, 2, and 2 episodes of anemia, neutropenia, and thrombocytopenia, respectively.
- Neutropenic fever was 5.2%.
- Grade 3 or higher infection related AEs was 3.1%.

**Table 2. Treatment-related adverse events (>25% in all patients)**

| Preferred terms, n (%) | Total (N=96) | | 2.0 mg/kg D1D8Q3W (N=10) | | 2.3 mg/kg D1D8Q3W (N=60) | | 2.5 mg/kg D1D8Q3W (N=26) | |
|---|---|---|---|---|---|---|---|---|
| | All grade | Grade≥3 | All grade | Grade≥3 | All grade | Grade≥3 | All grade | Grade≥3 |
| Any TRAEs | 96 (100) | 84 (87.5) | 10 (100) | 9 (90.0) | 60 (100) | 52 (86.7) | 26 (100) | 23 (88.5) |
| Anemia | 92 (95.8) | 34 (35.4) | 8 (80.0) | 1 (10.0) | 59 (98.3) | 23 (38.3) | 25 (96.2) | 10 (38.5) |
| Leukopenia | 82 (85.4) | 36 (37.5) | 5 (50.0) | 2 (20.0) | 54 (90.0) | 20 (33.3) | 23 (88.5) | 14 (53.8) |
| Thrombocytopenia | 79 (82.3) | 45 (46.9) | 7 (70.0) | 2 (20.0) | 52 (86.7) | 32 (53.3) | 20 (76.9) | 11 (42.3) |
| Neutropenia | 76 (79.2) | 43 (44.8) | 6 (60.0) | 3 (30.0) | 48 (80.0) | 23 (38.3) | 22 (84.6) | 17 (65.4) |
| Nausea | 59 (61.5) | 5 (5.2) | 5 (50.0) | 0 | 38 (63.3) | 5 (8.3) | 16 (61.5) | 0 |
| Asthenia | 55 (57.3) | 12 (12.5) | 4 (40.0) | 0 | 37 (61.7) | 9 (15.0) | 14 (53.8) | 3 (11.5) |
| Decreased appetite | 48 (50.0) | 3 (3.1) | 3 (30.0) | 0 | 35 (58.3) | 3 (5.0) | 10 (38.5) | 0 |
| Vomiting | 45 (46.9) | 4 (4.2) | 5 (50.0) | 0 | 31 (51.7) | 4 (6.7) | 9 (34.6) | 0 |
| Stomatitis | 36 (37.5) | 6 (6.3) | 5 (50.0) | 1 (10.0) | 24 (40.0) | 2 (3.3) | 7 (26.9) | 3 (11.5) |
| Hypokalemia | 30 (31.3) | 9 (9.4) | 2 (20.0) | 1 (10.0) | 18 (30.0) | 5 (8.3) | 10 (38.5) | 3 (11.5) |
| Constipation | 28 (29.2) | 0 | 3 (30.0) | 0 | 16 (26.7) | 0 | 9 (34.6) | 0 |
| AST increased | 27 (28.1) | 0 | 3 (30.0) | 0 | 13 (21.7) | 0 | 11 (42.3) | 0 |
| Lymphocyte count decreased | 25 (26.0) | 10 (10.4) | 2 (20.0) | 1 (10.0) | 16 (26.7) | 7 (11.7) | 7 (26.9) | 2 (7.7) |
| Diarrhea | 25 (26.0) | 2 (2.1) | 2 (20.0) | 1 (10.0) | 19 (31.7) | 1 (1.7) | 4 (15.4) | 0 |

## Efficacy

- All pts who received at least one dose of iza-bren are included in the analysis (Table 3, Figures 1 and 2).
- All patients have progressed on at least one line of PBC with 86.5% of the patients had platinum-resistant OC. In total population (N=96), confirmed ORR (cORR) was 46.9% and 2 responders (2.1%) were pending confirmation. Median DoR was 8.5 months. Median PFS was 7.0 months. Median duration of follow-up for OS was 12.5 months, and median OS had not been reached.
- In the 2.3 mg/kg D1D8 Q3W group, cORR was 55.0%. Median DoR was 8.5 months. Median PFS was 8.3 months.
  - A total of 49 patients (81.7%) had platinum-resistant OC, including 26 patients who progressed on or within 3 months of PBC (platinum-refractory). The cORR in the platinum-resistant subgroup was 49.0%, median DoR was 8.2 months, median PFS was 7.0 months. In the remaining 11 patients with platinum-sensitive OC, cORR was 81.8%, median DoR has not been reached, median PFS was 14.0 months.0

**Table 3. Summary of Efficacy Results**

| | Total | | | 2.0 mg/kg D1D8Q3W | 2.3 mg/kg D1D8Q3W | | | 2.5 mg/kg D1D8Q3W |
|---|---|---|---|---|---|---|---|---|
| | Total (N=96) | Platinum-resistant (N=83) | Platinum-sensitive (N=13) | (N=10) | Total (N=60) | Platinum-resistant (N=49) | Platinum-sensitive (N=11) | (N=26) |
| Median (range) prior line of therapy | 2 (1, 10) | 3 (1, 10) | 2 (1, 3) | 3 (2, 10) | 2 (1, 5) | 2 (1, 5) | 2 (1, 3) | 3 (1, 7) |
| BOR, n (%) | | | | | | | | |
| PR | 51 (53.1) | 41 (49.4) | 10 (76.9) | 2 (20.0) | 34 (56.7) | 25 (51.0) | 9 (81.8) | 15 (57.7) |
| Confirmed | 45 (46.9) | 35 (42.2) | 10 (76.9) | 0 | 33 (55.0) | 24 (49.0) | 9 (81.8) | 12 (46.2) |
| Ongoing | 2 (2.1) | 2 (2.4) | 0 | 1 (10.0) | 0 | 0 | 0 | 1 (3.8) |
| SD | 33 (34.4) | 31 (37.4) | 2 (15.4) | 6 (60.0) | 19 (31.7) | 18 (36.7) | 1 (9.1) | 8 (30.8) |
| PD | 4 (4.2) | 4 (4.8) | 0 | 1 (10.0) | 2 (3.3) | 2 (4.1) | 0 | 1 (3.8) |
| NE | 8 (8.3) | 7 (8.4) | 1 (7.7) | 1 (10.0) | 5 (8.3) | 4 (8.2) | 1 (9.1) | 2 (7.7) |
| ORR, % (95% CI) | 53.1 (42.7, 63.4) | 49.4 (38.2, 60.6) | 76.9 (46.2, 95.0) | 20.0 (2.5, 55.6) | 56.7 (43.2, 69.4) | 51.0 (36.3, 65.6) | 81.8 (48.2, 97.7) | 57.7 (36.9, 76.6) |
| cORR, % (95% CI) | 46.9 (36.6, 57.3) | 42.2 (31.4, 53.5) | 76.9 (46.2, 95.0) | 0 (0, 30.8) | **55.0 (41.6, 67.9)** | **49.0 (34.4, 63.7)** | **81.8 (48.2, 97.7)** | 46.2 (26.6, 66.6) |
| DCR, % (95% CI) | 87.5 (79.2, 93.4) | 86.7 (77.5, 93.2) | 92.3 (64.0, 99.8) | 80.0 (44.4, 97.5) | 88.3 (77.4, 95.2) | 87.8 (75.2, 95.4) | 90.9 (58.7, 99.8) | 88.5 (69.8, 97.6) |
| CBR, % (95% CI) | 66.7 (56.3, 76.0) | 62.7 (51.3, 73.0) | 92.3 (64.0, 99.8) | 20.0 (2.5, 55.6) | 71.7 (58.6, 82.5) | 67.3 (52.5, 80.1) | 90.9 (58.7, 99.8) | 73.1 (52.2, 88.4) |
| Median time to response, months | 1.5 | 1.5 | 1.5 | / | 1.5 | 1.6 | 1.4 | 1.5 |
| Median DoR, mo, (95% CI) | 8.5 (5.6, 9.9) | 8.2 (5.2, 9.9) | 8.5 (4.0, NR) | / | **8.5 (5.3, 10.0)** | **8.2 (5.2, 8.7)** | **NR (4.0, NR)** | 6.8 (2.5, 10.4) |
| Median PFS, mo, (95% CI) | 7.0 (5.7, 9.8) | 6.8 (5.6, 9.7) | 14.0 (7.1, NR) | 5.5 (1.2, 5.7) | **8.3 (6.1, 11.2)** | **7.0 (5.7, 9.9)** | **14.0 (5.3, NR)** | 8.3 (3.7, 11.9) |
| Median FU for OS, mo, (95% CI) | 12.5 (11.3, 13.1) | 12.9 (11.3, 13.6) | 12.3 (8.3, 12.9) | 16.3 (1.4, NR) | 11.3 (11.0, 12.3) | 11.3 (11.0, 12.5) | 12.0 (8.2, 12.6) | 14.9 (13.6, 15.3) |
| Median OS, mo, (95% CI) | NR (14.6, NR) | 15.5 (13.8, NR) | NR (NR, NR) | 10.0 (6.5, 15.5) | NR (14.6, NR) | NR (14.6, NR) | NR (NR, NR) | NR (9.1, NR) |

TTR was evaluated for responders (confirmed CR or PR) only. CBR is defined as the percentage of patients who have achieved CR, PR or SD ≥ 6 months.

**Figure 1. Waterfall plot (All patients)**

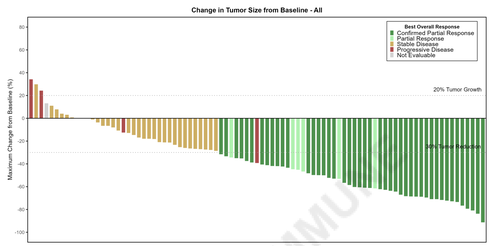
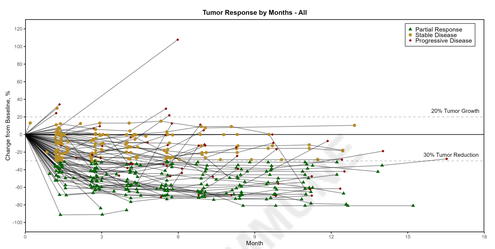



**Figure 2. Spider plot (All patients)**




- 81.3% of patients (78/96) with tumor shrinkage and the median (range) shrinkage (%) was -42.9 (-91.3, -0.1).

## Conclusions

- In patients with heavily pre-treated OC, iza-bren demonstrated promising efficacy with a manageable safety profile in patients with both platinum-resistant (including platinum-refractory) and platinum-sensitive OC. Phase III clinical study (NCT06994195) in platinum-resistant recurrent epithelial OC patients is ongoing in China.

## Acknowledgments

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