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Mocertatug rezetecan (Mo-Rez) in patients with platinum-resistant ovarian cancer (PROC): Updated results with longer follow-up from the global BEHOLD-1 study

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Background

B7-H4 is a transmembrane protein widely expressed in gynaecological tumours but with low expression in normal tissue; it carries immunoregulatory and tumour promoting functions making it a promising therapeutic target. Mo-Rez is an investigational ADC composed of a humanised anti-B7-H4 IgG1 mAb conjugated to a TOP1 inhibitor. Results from BEHOLD-1 showed encouraging antitumour activity in patients (pts) with PROC and advanced/recurrent endometrial cancer leading to selection of Mo-Rez 5.8 mg/kg Q3W as the recommended dose for expansion. Updated data for the PROC cohort at longer follow-up are presented.

Methods

BEHOLD-1 is a 2-part, open-label, phase 1 study (NCT06431594). In phase 1b (dose selection) pts with PROC were randomised to 3 Mo-Rez dose levels (2.8, 4.8, or 5.8 mg/kg Q3W). Primary endpoint is confirmed ORR by investigator per RECIST 1.1.

Results

In total, 136 pts with PROC were randomised in the dose selection phase (data cut-off, 30 June 2026); pts had received a median (range) of 2 (1, 5) prior lines of therapy. At median follow-up of 13.4 months, confirmed ORR was 62% (95% CI: 46.5, 76.2) at the 5.8 mg/kg dose level, which showed longer DoR of 12.2 months and PFS of 11.1 months versus other doses (Table). Among 135 pts who received at least one dose of Mo-Rez, Grade ≥3 treatment-related adverse events (TRAEs) occurred in 64 pts (47%) across all doses and in 32 pts (71%) who received Mo-Rez 5.8 mg/kg. Treatment discontinuation due to TRAEs was low (3% in overall dose selection; 2% for pts receiving 5.8 mg/kg). Efficacy by prespecified B7-H4 expression cut-offs will be presented.Table: LBA41

|                               | Mo-Rez dose, mg/kg Q3W |                      |                      |
|-------------------------------|------------------------|----------------------|----------------------|
|                               | 2.8 (N=45)             | 4.8 (N=46)           | 5.8 (N=45)           |
| Median follow-up, mos         | 13.4                   | 13.4                 | 13.4                 |
| Confirmed ORR, % (n) [95% CI] | 36 (16) [21.9, 51.2]   | 57 (26) [41.1, 71.1] | 62 (28) [46.5, 76.2] |
| Median DoR, mos [95% CI]      | 7.8 [4.4, NE]          | 6.9 [5.7, 9.7]       | 12.2 [7.0, 12.7]     |
| Median PFS, mos [95% CI]      | 5.6 [4.0, 5.8]         | 8.3 [7.4, 10.9]      | 11.1 [8.3, 13.9]     |

N, number of randomised pts; CI, confidence interval; DoR, duration of response; ORR, objective response rate; PFS, progression free survival; Q3W, every three weeks.

Conclusions

In pts with PROC, Mo-Rez 5.8 mg/kg showed encouraging long-term activity, with median DoR of 12 months and median PFS of 11 months, and with an acceptable safety profile. Enrolment in the 5.8 mg/kg expansion cohorts is ongoing.

**Clinical trial identification**

NCT06431594.

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**Legal entity responsible for the study**

GSK.

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