

LBA40

Randomized dose optimization of ZW191 in heavily pretreated patients with platinum-resistant ovarian cancer (PROC)

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Background

ZWI-ZW191-101 (NCT06555744) is an ongoing, first-in-human study evaluating ZW191, a folate receptor α (FR α)–targeting antibody-drug conjugate. In Part 1 dose escalation, ZW191 was well tolerated and demonstrated antitumor activity across therapeutic doses (6.4-9.6 mg/kg). Here, we report efficacy and safety results from combined Part 1 and Part 2 dose optimization (data cutoff: 17 July 2026; median follow-up 5 months).

Methods

Eligible adults with PROC who had progressed on available systemic therapies were enrolled regardless of histology, FR α expression, or number of prior lines. In Part 2, patients were randomized 1:1 to doses of 6.4 mg/kg and 9.6 mg/kg administered IV every 3 weeks. Primary objectives included safety, tolerability, and antitumor activity.

Results

Eighty patients (Part 1, n=15; Part 2, n=65) received ZW191 at 6.4 mg/kg (n=37) or 9.6 mg/kg (n=43); median age was 61 years (range, 40–79). Median (range) baseline FR α H-score and PS2+ score were 147.5 (0-300) and 45 (0-100), respectively. Median prior lines of therapy were 4 (range, 1-10); patients had received prior platinum and taxane (100%), bevacizumab (84%), PARPi (56%), checkpoint inhibitors (19%), and mirvetuximab (5%). 58% of patients (n=23 per dose) remained on treatment. The most common treatment-emergent adverse events were nausea (6.4 mg/kg, 32%; 9.6 mg/kg, 60%), neutropenia (19%; 42%), and anemia (27%; 26%); Grade $\geq$ 3 events were neutropenia (8%; 23%), anemia (8%; 14%), and pleural effusion (5%; 9%). The objective response rate across all histology except clear cell carcinoma was 58% for both doses (Table). Median duration of response (DOR) was not reached. Updated DOR and progression-free survival with longer follow-up, and efficacy by FR α expression, will be presented. Table: LBA40

ZW191-related efficacy summary in response-evaluable patients

PROC ^a (excluding clear cell carcinoma)	6.4 mg/kg (n=31)	9.6 mg/kg (n=38)	Overall (n=69)
ORR	58%	58%	58%
Confirmed ORR	52%	45%	48%
DCR	100%	92%	96%
All PROC ^a (including clear cell carcinoma)	n=36	n=42	n=78
ORR	53%	52%	53%
Confirmed ORR	47%	41%	44%
DCR	97%	93%	95%

^aPatients had $\geq$ 1 post-baseline scan. DCR, disease control rate; ORR, objective response rate; PROC, platinum-resistant ovarian cancer.

Conclusions

ZW191 showed remarkable antitumor activity in heavily pretreated PROC, with a well-tolerated safety profile. The presented data will guide optimal dosing for further development.

Clinical trial identification

NCT06555744; 15Aug2024.

Editorial acknowledgement

Writing and editorial assistance was provided by Sarah Timmler, PhD, on behalf of Syneos Health, and funded by Zymeworks BC Inc.

Legal entity responsible for the study

Zymeworks BC Inc.

Funding

Zymeworks BC Inc.

Disclosure

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Lee: Financial Interests, Personal, Invited Speaker: AstraZeneca, Takeda, MSD, Roche, AbbVie, GSK; Financial Interests, Personal, Advisory Board: Eisai, GI Innovation, Regeneron, Daiichi Sankyo, Genmab, Sutro, Seagen, AstraZeneca, AbbVie, Corcept, GSK, Lilly, Merck Serono, MSD; Financial Interests, Institutional, Local PI: Alkermes, AstraZeneca, BergenBio, Cellid, Clovis Oncology, Eisai, GI Innovation, ImmunoGen, Janssen, Merck, Mersana, MSD, Novartis, OncoQuest, Roche, Seagen, Synthon, Regeneron, Ascendis Pharma, Advenchen, BMS, Kelun, SUTRO, GSK, AbbVie, Kelun, Lilly, Pfizer, Tori-Bio; Financial Interests, Personal and Institutional, Local PI: BeiGene; Financial Interests, Personal, Steering Committee Member: AstraZeneca, OncoQuest, Seagen, ImmunoGen, MSD; Financial Interests, Institutional, Research Grant: ONO, Takeda, GSK; Financial Interests, Institutional, Other, Sub I: Corcept; Financial Interests, Institutional, Steering Committee Member: AbbVie; Financial Interests, Personal, Local PI: Zymeworks. 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Ended 2025: NEXT Oncology; Financial Interests, Personal, Stocks/Shares, Shareholder: Texas Oncology, IQVIA; Financial Interests, Institutional, Local PI: AbbVie, Acrivon Therapeutics, Alentis Therapeutics, Aprea Therapeutics, Ascentage Pharma Group, Astellas, AstraZeneca, Avenzo Therapeutics, Axion Bio, BJ Biosciences, BioNTech, Biomea Fusion, Boehringer Ingelheim, Bristol-Myers Squibb, CSPC Megalith Biopharma Co, Cartography Biosciences, Compugen, D3 Bio Limited, Day One Biopharma, Dewpoint Therapeutics Inc, Dicerna/Novo Nordisk, Dren Bio Inc, DualityBio Inc, Erasca, Exelixis, Fate Therapeutics, GSK, Gilead Sciences, Haihe Pharma, Iconovir Bio, Ideaya Biosciences, Immuneering, Impact Therapeutics, Incendia, Ipsen, Kura Oncology, MediLink Therapeutics, Mirati Therapeutics, ModeX Therapeutics, Monopteros Therapeutics, NGM Biopharmaceuticals, Navire, Nimbus Saturn, Normunity, OBI Pharmaceuticals, OncoResponse Inc, PMV Pharmaceuticals, Pfizer, ProteinQure, Revolution Medicines, Shanghai Hansoh Biomedical, Step Pharmaceuticals, Sutro, Symphogen, Systimmune, Tachyon Therapeutics, Teon Therapeutics, Tyligand Bioscience, VelaVigo Pharma Co, Vividion Therapeutics, ZielBio, Zymeworks Inc. 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