Abstract TPS5622

GLORIOSA: A randomized, open-label, phase 3 study of mirvetuximab soravtansine with bevacizumab vs. bevacizumab as maintenance in platinum-sensitive ovarian, fallopian tube or primary peritoneal cancer

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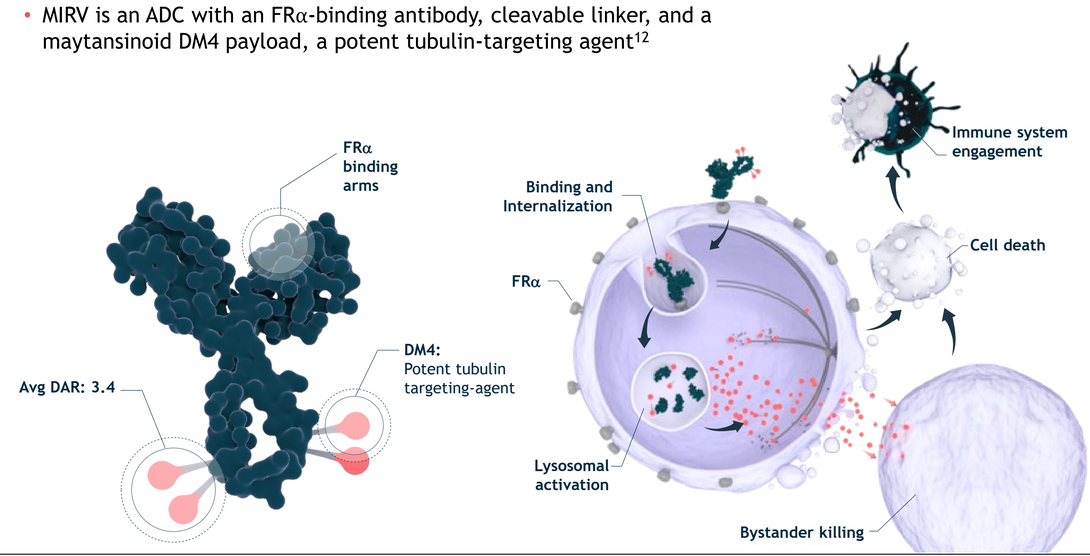
BACKGROUND

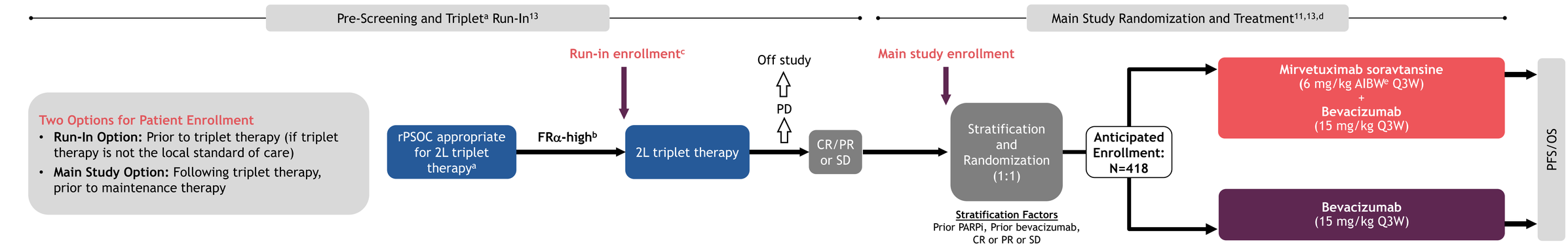
- Epithelial ovarian cancer, primary peritoneal cancer, and fallopian tube cancer (together referred to as EOC) are a leading cause of death from gynecologic cancers worldwide[1]
- Mirvetuximab soravtansine (MIRV), an antibody-drug conjugate (ADC), received accelerated FDA approval in November 2022 for the treatment of adult patients with folate receptor alpha (FRα)-positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received 1 to 3 prior systemic treatment regimens[2]
- FRα, also known as folate receptor 1 (FOLR1), has limited expression on normal tissues but is elevated in most ovarian cancers, which makes it an attractive target for the development of novel therapies[3-5]
- MIRV treatment has demonstrated clinically meaningful antitumor activity in patients with platinum-resistant ovarian cancer (PROC) regardless of the number of prior lines of therapy or PARPi use[6,7]
  - SORAYA (phase 2, single-arm trial): Investigator-assessed objective response rate (ORR) was 32.4% (95% CI, 23.6%-42.2%), including 5 complete responses (CRs), and median duration of response (DOR) was 6.9 months[7]
  - MIRASOL (phase 3 randomized, confirmatory trial): The primary endpoint of progression-free survival (PFS) was met with MIRV vs investigator's choice of chemotherapy (median, 5.62 vs 3.98 mo; HR 0.65; *P*<0.0001). MIRV also demonstrated a statistically significant improvement in overall survival ([OS] median, 16.46 vs 12.75 mo; HR 0.67; *P*=0.0046).[8] These results are reported in the ASCO 2023 late-breaking abstract #LBA5507[9]
- In the FORWARD II trial among patients with recurrent platinum-sensitive ovarian cancer (rPSOC), combination therapy with MIRV + bevacizumab conferred an ORR of 48% (95% CI, 30%-67%), including 3 CRs and a median DOR of 12.7 months[10]
- The GLORIOSA trial will evaluate maintenance therapy with MIRV + bevacizumab vs. bevacizumab in patients with FRα-high rPSOC who demonstrated CR, partial response (PR), or stable disease (SD) following 2L triplet therapy[11]

MIRV Mechanism of Action

- MIRV is an ADC with an FRα-binding antibody, cleavable linker, and a maytansinoid DM4 payload, a potent tubulin-targeting agent[12]



GLORIOSA Trial Design



[a]Triplet treatment consists of platinum+chemotherapy+bevacizumab for planned 6 cycles (minimum 4 and maximum 8 cycles), including at least 3 cycles of bevacizumab. [b]Pre-screening consent must be obtained for tissue testing for FRα expression by Ventana FOLR1 Assay. [c]FRα-high patients who desire to be treated and followed while on their run-in triplet therapy must sign a run-in consent as part of the main consent form if they meet eligibility criteria as assessed by the investigator. [d]Maintenance treatment must begin ≤12 weeks from last dose of triplet therapy and within 30 days of randomization. Treatment continues until PD, unacceptable toxicity, withdrawal of consent, death, or sponsor study termination. [e]AIBW, also known as AdjBW, is calculated as IBW (kg) + 0.4 (actual weight − IBW). IBW for females is calculated as 0.9*height (cm) − 92.

Eligibility Criteria, Objectives, and Endpoints

Inclusion Criteria[11,a]

- Patients ≥18 years old
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Confirmed high-grade serous epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer
- FRα detected by IHC with PS2+ intensity among ≥75% of viable tumor cells
- Prior PARPi required if positive for *BRCA* mutation
- 1 prior platinum treatment
- Relapsed after 1L platinum-based chemotherapy
- Platinum-sensitive disease (PFI >6 months)
- Appropriate for, currently be on, or have completed 2L platinum-based triplet therapy
- Received 4-8 cycles of 2L platinum-based triplet therapy, which included ≥3 cycles of bevacizumab in combination with platinum-based chemotherapy[b,c]
- CR, PR, or SD after prior treatment with platinum-based doublet + bevacizumab
- Randomized no later than 8 weeks from the last dose of platinum-based triplet therapy in second line
- Stabilized or recovered (Grade 1 or baseline) from all prior therapy-related toxicities (except alopecia) and not had any major surgeries for at least 4 weeks prior to the first dose of maintenance therapy
- Adequate hematologic, liver, and kidney functions

[a]List of inclusion criteria is not comprehensive of all criteria. [b]If the number of cycles received is <6 due to toxicity, this must be documented, and toxicity assessed as unlikely related to bevacizumab. [c]In the case of interval secondary cytoreductive surgery, patients are permitted to receive only 2 cycles of bevacizumab in combination with the last 3 cycles of 2L platinum-based triplet therapy. In the case of primary cytoreductive surgery before 2L platinum-based triplet therapy, patients must have no less than 3 cycles of bevacizumab in combination with platinum-based chemotherapy after their surgery and before randomization.

Exclusion Criteria[11,a]

- Endometrioid, clear cell, mucinous, or sarcomatous histology, mixed tumors containing any of the above histologies, or low-grade/borderline ovarian tumor
- >1 line of prior chemotherapy[b]
- PD while on or following platinum-based triplet therapy
- Active or chronic corneal disorders, history of corneal transplantation, or active ocular conditions requiring ongoing treatment/monitoring
- >Grade 1 peripheral neuropathy per CTCAE
- History of bowel obstruction related to underlying disease within 6 months before the start of maintenance study treatment
- Prior treatment with MIRV or other FRα-targeting agents

[a]List of exclusion criteria is not comprehensive of all criteria. [b]Neoadjuvant ± adjuvant therapies are considered 1 line of therapy. Maintenance therapy will be considered part of the preceding line of therapy.

Primary Objective[13]

To compare PFS, as assessed by the investigator per the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) criteria, after platinum-based chemotherapy (doublet) plus bevacizumab and randomized to maintenance MIRV plus bevacizumab versus bevacizumab alone

Primary Efficacy Endpoint[11]

Investigator-assessed PFS, defined as the time from date of randomization until investigator-assessed progressive disease or death

Key Secondary Endpoint[11]

OS, defined as the time from randomization to death

Other Secondary Endpoints[11,13]

- Evaluation of AEs according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0
- PFS2, defined as the time from date of randomization until second disease progression or death
- ORR, which includes best response for CR or PR
- DOR, defined as patients who achieved best overall response of CR or PR upon completion of triplet therapy
- DFS, defined as patients who have no measurable disease per RECIST v1.1 at randomization
  - BICR sensitivity analyses of efficacy endpoints (ORR, DOR, DFS) will also be performed
- CA-125 response, determined using the Gynecologic Cancer Intergroup Criteria
- Patient-reported outcome health-related quality of life of disease-related symptoms using the NCCN-FACT Ovarian Symptom Index (NFOSI-18) DRS-P (disease-related symptom subscale—physical) questionnaire

Statistical Assumptions[13]

- Anticipated enrollment: N=418, providing 90% power to detect a hazard ratio of 0.7

GLORIOSA Trial Status

Overall Status and Enrollment[11,13]

- This is a global study that is currently open and enrolling

Trial Tracking Information[11,14,15]

- ClinicalTrials.gov ID: NCT05445778
- ENGOT.ESGO.org ID: ENGOT-ov76
- GOG.org ID: GOG-3078

Additional Information

- This trial will be performed according to the principles of the Joint ENGOT and GOG Foundation requirements for trials with industry partners. A model C design will be utilized.
- For more information, please contact medicalinformation@immunogen.com

GLORIOSA

ENGOT European Network of Gynaecological Oncological Trial groups

GOG FOUNDATION®

Abbreviations: 2L, second-line; AEs, adverse events; ADC, antibody-drug conjugate; AdjBW, adjusted body weight; AIBW, adjusted ideal body weight; Avg, average; BICR, blinded independent central review; *BRCA*, breast cancer gene; CA-125, cancer antigen 125; CR, complete response; CTCAE, Common Terminology Criteria for Adverse Events; DAR, drug to antibody ratio; DFS, disease-free survival; DOR, duration of response; DRS-P, disease-related symptom subscale—physical; ECOG, Eastern Cooperative Oncology Group; ENGOT, The European Network of Gynaecological Oncological Trial groups; EOC, epithelial ovarian cancer; FOLR1, folate receptor 1; FRα, folate receptor alpha; GOG, Gynecologic Oncology Group; IBW, ideal body weight; MIRV, mirvetuximab soravtansine; NFOSI-18, NCCN-FACT Ovarian Symptom Index 18; ORR, objective response rate; PARPi, poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitor; PD, progressive disease; PFI, platinum-free interval; PFS, progression-free survival; PFS2, progression-free survival 2; PR, partial response; PS2+, positive staining 2+; Q3W, three times per week; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; rPSOC, recurrent platinum-sensitive ovarian cancer; SD, stable disease.

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