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IGCS20_1398
Poster

Safety and Activity of the Anti-Mesothelin Antibody–Drug Conjugate Anetumab Ravtansine in Combination with Pegylated-Liposomal Doxorubicin in Platinum-Resistant Ovarian, Fallopian Tube or Primary Peritoneal Cancer

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Introduction: Treatment options for platinum-resistant ovarian cancer (PROC) remain a high medical need. Mesothelin is highly expressed in PROC. Anetumab ravtansine (ARv) is an antibody–drug conjugate that selectively targets mesothelin, consisting of a fully human anti-mesothelin monoclonal antibody conjugated to the cytotoxic maytansinoid tubulin inhibitor DM4.

Methods: This phase Ib, open-label, dose-escalation (modified 3+3 design, n=9) and expansion study (n=56) evaluated the safety/tolerability and clinical activity of ARv and pegylated liposomal doxorubicin (PLD, 30 mg/m² Q3W) in PROC. Mesothelin expression was assessed by central immunohistochemistry. Adverse events, tumor response (RECIST v1.1), and progression-free survival (PFS) were determined. Biomarker samples were assessed by ELISA, next-generation sequencing, and expression profiling.

Results: ARv/PLD combination was safe and tolerated. No DLT was observed. MTD of ARv was 6.5 mg/kg Q3W. The most common ARv-related adverse events were nausea (38.5%), decreased appetite (30.8%), corneal disorder (29.2%), fatigue (29.2%), diarrhea (24.6%), and AST increase (21.5%).

In all measurable or evaluable patients (n=65), objective response rate (ORR) was 28% (95% CI 16.0–38.5%), including one complete and 17 partial responses with a median PFS of 5.1 months. In an exploratory subset of patients (n=19) who received ≤3 prior lines of therapy with high mesothelin expression, the ORR was 42% with a median duration of response of 36 weeks. Median PFS was 8.5 months.

Conclusions/Implications: These results established the RP2D, schedule, and mesothelin-positive target population of the ARv/PLD combination for the phase III study in PROC. Molecular profiling and correlation with observed clinical activity will be presented.