First results from the ENGOT-GYN2/GOG 305/BOUQUET phase 2 biomarker-directed platform study: cobimetinib or atezolizumab + bevacizumab for persistent/recurrent rare epithelial ovarian cancer


Background
Rare epithelial ovarian cancers (eOC) differs from high-grade serous eOC clinically and molecularly, respond less well to standard therapies for eOC (objective response rate <20% in 2nd line\textsuperscript{1–5}) and represents a high unmet need\textsuperscript{6} In BOUQUET, treatment is assigned according to tumour-specific molecular alterations. Non-matched arms are designated for tumours without corresponding biomarkers.

Primary Aim
Confirmed overall response rate, defined as the proportion of patients with a confirmed radiologic CR or PR.

Methods

**ENGOT-GYN2/GOG-3051/BOUQUET (NCT04931342) design**

- Possibly provided a radiologic or pathologic confirmatory response (R/RPCD, CR/PR)
- Non-matched arm for patients without corresponding biomarkers
- Tumour sample available
- Primary efficacy endpoint: investigator-assessed cORR per RECIST v1.1

**Results**

**Cobimetinib cohort (n=20)**

- Median follow-up: 6.9 months
- Oral cobimetinib 40 mg, days 1-21 q2w
- 8 LGSOCC: 5 MESO: 5 OC: 1 CSE: 1 MLA
- 65% ≥2 prior treatment lines
- Median age 57 years (28-65 years old)
- Median treatment duration: 3.6 months (range 0.1-11 months), ongoing in 5 patients
- 2 (15.5% disease progression, 1 AE)
- 7 disease progression
- 1 symptomatic deterioration
- 1 physician decision

**Atezolizumab + bevacizumab cohort (n=21)**

- IV atezolizumab 1200 mg day 1 q2w +
- IV bevacizumab 15 mg/kg day 1 q2w +
- 15 LGSOCC: 3 OC: 2 MLA: 1 CSE
- 48% ≥3 prior treatment lines
- Median age 51 years (24-65 years old)
- Median treatment duration: 6.9 (0-10 months) atezolizumab/bevacizumab (range 0-15 months), ongoing in 15 patients
- 4 AE
- 4 disease progression
- 1 symptomatic deterioration

**Conclusions**

- Cobimetinib monotherapy showed a promising 33% cORR and 89% DCR at 6 months in heavily pretreated low-grade serous ovarian cancer/mesonephric-like adenocarcinoma despite a modest cORR (16%) in the overall population
- Tolerability consistent with prior experience; no new safety signals identified
- The cobimetinib arm will be expanded (excluding mucinous and clear cell carcinoma and carcinosarcoma) to a total of 50 evaluable patients with target histologies
- Modest cORR (14%) with atezolizumab + bevacizumab but 75% 6-month PFS rate warrants exploration of the combination with metronomic cyclophosphamide to promote tumour cell death and potentiate the anti-tumour immune response
- Large global collaboration between industry and academia (14 countries, 62 sites) enables efficient evaluation of biomarker-directed therapies in patients with poor-prognosis rare tumours
- Enrolment in BOUQUET is ongoing and additional arms are opening for accrual