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

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Background

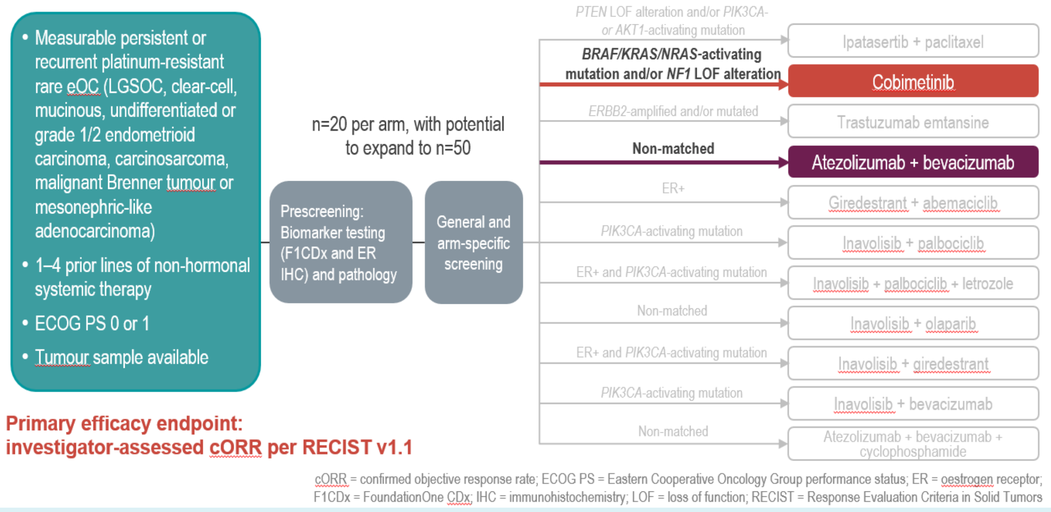
Rare epithelial ovarian cancers (eOC) differs from high-grade serous eOC clinically and molecularly, respond less well to standard therapies for eOC (objective response rate <20% in 2nd line[1–5]) and represents a high unmet need[6] In BOUQUET, treatment is assigned according to tumour-specific molecular 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



cORR = confirmed objective response rate; ECOG PS = Eastern Cooperative Oncology Group performance status; ER = oestrogen receptor; F1CDx = FoundationOne CDx; IHC = immunohistochemistry; LOF = loss of function; RECIST = Response Evaluation Criteria in Solid Tumors

Results

Cobimetinib cohort (n=20)

Median follow-up: 6.9 months

- Oral cobimetinib 60 mg/day, days 1–21 q28d
- 8 LGSOC, 5 MUC, 5 CC, 1 CS, 1 MLA
- 65% ≥3 prior treatment lines
- Median age 57 years (35% ≥65 years old)
- Median treatment duration: 3.6 months (range 0–10 months); ongoing in 9 patients
  - 2 died (1 disease progression, 1 AE)
  - 7 disease progression
  - 1 symptomatic deterioration
  - 1 physician decision

AEs	n (%)
Grade 3/4	7 (35%)
Grade 5	1 (5%)[a]
Treatment-related serious	1 (5%)[b]
Leading to treatment discontinuation	0
Leading to dose reduction	7 (35%)
Leading to treatment interruption	5 (25%)

[a]Cardiac arrest, unrelated to treatment. [b]ECG repolarisation abnormality in a patient with ongoing hypertension, hypercholesterolaemia and arteriosclerosis

Clinical cut-off date: 8 Sep 2022

AE = adverse event; CC = clear-cell; CS = carcinosarcoma; MLA = mesonephric-like adenocarcinoma;

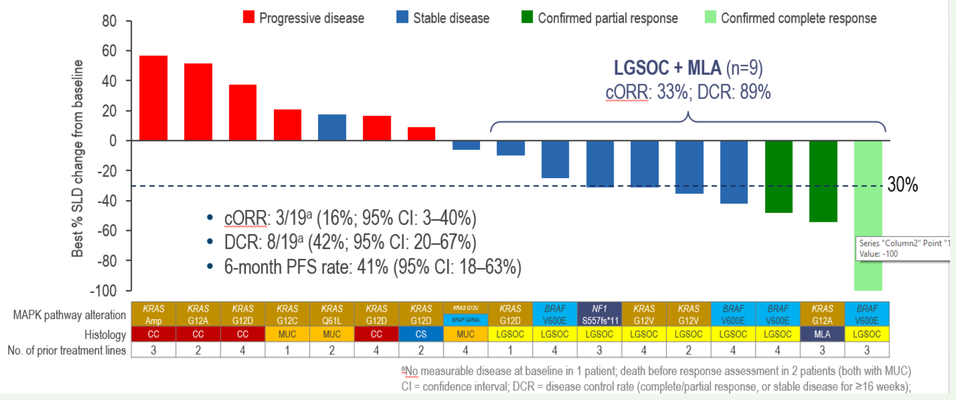
Atezolizumab + bevacizumab cohort (n=21)

- IV atezolizumab 1200 mg day 1 q21d + IV bevacizumab 15 mg/kg day 1 q21d
- 15 LGSOC, 3 CC, 2 MUC, 1 CS
- 48% ≥3 prior treatment lines
- Median age 51 years (24% ≥65 years old)
- Median treatment duration: 6.3/6.9 months atezolizumab/bevacizumab (range 0–10 months); ongoing in 15 patients
  - 1 AE[a]
  - 4 disease progression
  - 1 symptomatic deterioration

AEs	n (%)
Grade 3/4	9 (43)
Grade 5	0
Treatment-related serious	3 (14)[b]
Leading to treatment discontinuation Atezolizumab Bevacizumab	2 (10) 2 (10) 1 (5)
Leading to treatment interruption Atezolizumab Bevacizumab	7 (33) 4 (19) 7 (33)

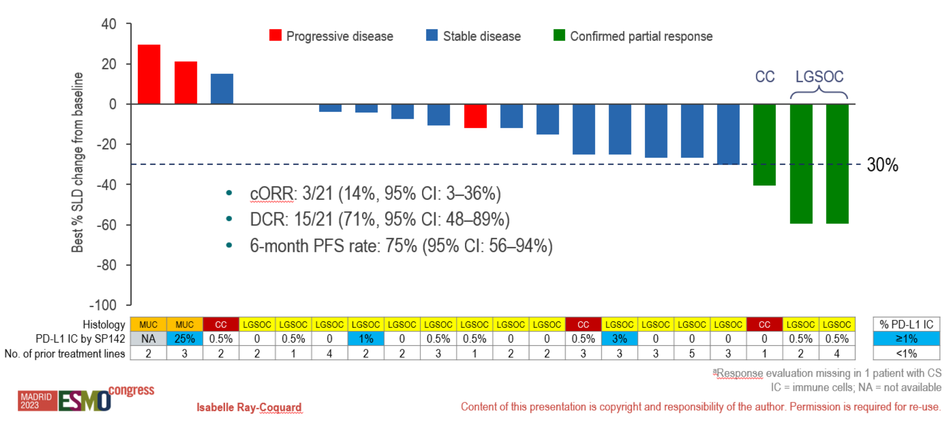
Cobimetinib cohort: best overall response[a]

Promising activity in LGSOC and MLA



[a]No measurable disease at baseline in 1 patient; death before response assessment in 2 patients (both with MUC)
CI = confidence interval; DCR = disease control rate (complete/partial response, or stable disease for ≥16 weeks);

Atezolizumab + bevacizumab cohort: best overall response[a]



[a]Response evaluation missing in 1 patient with CS
IC = immune cells; NA = not available

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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

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