## 746MO Randomized phase II trial of durvalumab in combination with olaparib and cediranib (DOC) compared to olaparib and cediranib (OC) or durvalumab and cediranib (DC) or standard of care chemotherapy (SOC) in platinum-resistant ovarian cancer with prior bevacizumab (NRG-GY023)

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**Background:** In platinum-resistant ovarian cancer, non-platinum chemotherapy is the standard of care after progression on combination bevacizumab and chemotherapy. We assessed the activity of DOC, DC or OC compared to SOC in bevacizumab pre-exposed population.

**Methods:** NRG-GY023 is an open-label, randomized, phase II trial conducted in the United States with a targeted sample size of 164 patients (pts). Eligibility included high-grade serous/endometrioid, or clear cell platinum-resistant ovarian cancer with 2-5 prior systemic therapies. Prior use of bevacizumab is required. Treatments were randomly assigned 1:2:2:2 to SOC (weekly paclitaxel, topotecan or liposomal doxorubicin), DOC, DC or OC. The primary end point was progression-free survival (PFS). Secondary end points included overall survival and overall response rate. Interim futility analysis was planned when 28 PFS events (60% information) were available in any pair of one experimental arm with the SOC; arms with a hazard ratio (HR) estimate (ref: SOC) $>$ 0.87 would be discontinued.

**Results:** By the data cutoff (10/31/2022), 120 pts were enrolled with a median age 65 yo [IQR: 58-69] and 10% were with germline or somatic BRCA mutation. All received prior bevacizumab in either the upfront or recurrent setting. Other prior therapies included PARP inhibitor (49%) and immunotherapy (11%). 103 pts were treated (15 SOC, 30 DOC, 28 DC, and 30 OC, respectively). At the data cutoff, median follow-up time was 4.3 months (IQR: 2.0-7.9). Median PFS was 4.2 (95% CI, 1.9-5.0), 2.6 (95% CI, 2-4.2), 2.3 (95% CI, 2-4.6), and 2.3 (95% CI, 2.1-3.9) months with SOC, DOC, DC and OC, respectively. The HR estimates (ref: SOC) were 1.01 (95% CI, 0.44-2.31), 1.21 (95% CI, 0.52-2.84), and 1.34 (95%CI, 0.58-3.08) for DOC, DC and OC, respectively. Hematologic adverse events were more common with SOC. Safety signals were consistent with past experience.

**Conclusions:** None of the experimental arms improved PFS compared with SOC. SOC was active in this heavily pretreated population.

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## 747MO First results from the ENGOT-GYN2/GOG-3051/BOUQUET phase II biomarker-directed platform study: Cobimetinib (cobi) or atezolizumab (atezo) + bevacizumab (bev) for persistent/recurrent rare epithelial ovarian cancer (eOC)

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**Background:** BOUQUET (NCT04931342) is an ongoing platform study evaluating multiple treatments in biomarker-selected patients (pts) with rare eOC that tends to respond less well to standard therapies. We report interim results from the cobi (MEK1 inhibitor) and atezo (anti-PD-L1) + bev (anti-VEGF) arms.

**Methods:** Eligible pts had measurable persistent/recurrent platinum-resistant (not primary-refractory) non-high-grade serous/non-high-grade endometrioid eOC by central pathological assessment and had received 1–4 prior lines of non-hormonal systemic therapy. Tumour samples were tested centrally using the FoundationOne CDx NGS assay. Pts with *BRAF*/*KRAS*/*NRAS* or *NF1* alterations were treated with oral cobi 60 mg/d, d1–21 q28d. Pts ineligible for any open biomarker-selected arm received IV atezo 1200 mg + bev 15 mg/kg both on d1 q21d. The primary efficacy endpoint is investigator-assessed confirmed objective response rate (cORR) per RECIST v1.1.

**Results:** As of the clinical cut-off date, 20 pts have received cobi (8 low-grade serous ovarian cancer [LGSOC], 5 mucinous carcinoma [MUC], 5 clear-cell carcinoma [CCC], 1 carcinosarcoma [CS], 1 mesonephric-like adenocarcinoma [MLA]) and 21 atezo + bev (15 LGSOC, 3 CCC, 2 MUC, 1 CS). Pts were heavily pretreated ($\geq$3 prior lines: 65% of cobi pts, 48% of atezo + bev pts). cORRs were 16% with cobi and 14% with atezo + bev (Table). For cobi-treated LGSOC + MLA, cORR was 33% (3/9) and disease control rate (complete/partial response [CR/PR] or stable disease $\geq$16 wks) was 89% (8/9). At data cut-off, treatment was ongoing in 9 pts in the cobi arm and 15 in the atezo + bev arm; all CR/PR in both arms were ongoing.

**Table: 747MO**

| Parameter | Cobi (n = 20)[a] | Atezo + bev (n = 21) |
|---|---|---|
| Clinical cut-off date | 8 Sep 2022 | 13 Oct 2022 |
| Median follow-up, mo (range) | 6.9 (0–10) | 7.4 (2–10) |
| cORR, n/N (%) [95% CI] | 3/19 (16) [3–40] | 3/21 (14) [3–36] |
| CR, n (%) | 1 (5) | 0 |
| PR, n (%) | 2 (11) | 3 (14) |
| Disease control rate, n (%) [95% CI] | 8 (42) [20–67] | 15 (71) [48–89] |
| 6-month progression-free survival rate, % (95% CI) | 41 (18–63) | 75 (56–94) |
| Median treatment duration, mo (range) | 3.6 (0–10) | Atezo/bev: 6.3/6.9 (1–10) |
| Adverse events, n (%) | | |
| Grade 3/4 | 7 (35) | 9 (43) |
| Grade 5 | 1 (5)[b] | 0 |
| Leading to any treatment discontinuation | 0 | 2 (10) |

[a]n=19 for efficacy (no measurable disease at baseline in 1 pt).
[b]Cardiac arrest, not considered treatment related.