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GYNAECOLOGICAL CANCERS

721O Relacorilant, a selective glucocorticoid receptor modulator, in combination with nab-paclitaxel improves progression-free survival in patients with recurrent platinum-resistant ovarian cancer: A 3-arm, randomized, open-label, phase II study

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Background: Pre-clinical and clinical data indicate that glucocorticoid receptor (GR) antagonism may enhance/restore chemotherapy sensitivity. This is the first randomized, controlled study to explore the efficacy and safety of relacorilant (RELA), a selective GR modulator, in combination w/ nab-paclitaxel (nab-pac) compared to nab-pac alone.

Methods: Women w/ recurrent platinum-resistant/refractory high grade serous or endometroid epithelial ovarian, primary peritoneal, or fallopian tube cancer or ovarian carcinosarcoma w/ measurable or non-measurable disease and up to 4 chemotherapeutic regimens were 1:1:1 randomized to: -CONTINUOUS 100mg RELA daily (w/discretionary escalation to 150mg) + 80mg/m^2 nab-pac on days 1, 8, and 15 of a q28-day schedule; or -INTERMITTENT 150mg RELA the day before, of, and after 80mg/m^2 nab-pac on days 1, 8, and 15, of a q28-day schedule; or -COMPARATOR,100mg/m^2 nab-pac on days 1, 8, and 15, of a q28-day schedule. A lower nab-pac dose was used with RELA because RELA inhibits the metabolism of nab-pac. The primary endpoint was progression-free survival (PFS) determined by the investigator per RECIST 1.1.

Results: 178 women were randomized. At median follow-up of 11.07 mos, the INTERMITTENT regimen significantly improved median PFS compared to nab-pac alone (HR, 0.66, 95%CI 0.44-0.98, log-rank test p=0.038). While ORR was similar, Duration of Response (DoR) was significantly improved (HR 0.36, 95% 0.16-0.77, p=0.006) in the INTERMITTENT regimen vs. nab-pac alone. Overall survival will be assessed at maturity. Most common grade ≥3 adverse events were neutropenia, anemia, and peripheral sensory neuropathy.

Conclusions: INTERMITTENT RELA + nab-pac improved PFS and had a favorable safety profile in recurrent platinum-resistant and/or platinum-refractory ovarian cancer patients.

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Legal entity responsible for the study: Corcept Therapeutics.

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722O Randomised phase II trial of olaparib compared to weekly paclitaxel or olaparib plus cediranib in patients with platinum-resistant ovarian cancer (OCTOVA)

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Background: The main aims of the OCTOVA trial were to compare the efficacy and toxicity of olaparib (O) with weekly paclitaxel (wP) and also the oral combination of olaparib plus cediranib (O+C) in recurrent ovarian cancer (OC).

Table: 721O

	CONTINUOUS RELA + Nab-Pac N=58	INTERMITTENT RELA + Nab-Pac N=60	COMPARATOR Nab-Pac N=60
PFS Median, mos (95% CI)	5.29 (3.84, 5.55)	5.55* (3.68, 7.20)	3.76 (3.52, 5.36)
ORR % (95% CI)	n=19 35.2 (22.68, 49.38)	n=20 35.7 (23.36, 49.64)	n=19 35.8 (23.14, 50.20)
DoR Median, mos (95% CI)	3.79 (2.33, 5.55)	5.55** (3.75, 5.88)	3.65 (2.89, 5.09)
*P<0.05 vs. Nab-Pac alone **P<0.01 vs. Nab-Pac alone			
Grade 3+ TEAEs by Preferred term n,%	n=57	n=60	n=60
Neutropenia	14 (24.6%)	4 (6.7%)	8 (13.3%)
Anemia	11 (19.3%)	8 (13.3%)	7 (11.7%)
Peripheral Sensory Neuropathy	9 (15.8%)	0 (0%)	3 (5.0%)
TEAEs=Treatment-Emergent Adverse Events			

Methods: Participants with high grade ovarian, fallopian tube, primary peritoneal cancer who relapsed within 12 months of previous platinum-based therapy were randomised, with stratification for germline *BRCA1/2* mutation status, prior PARP inhibitor (PARPi) or anti-angiogenic therapy, to receive O (300mg daily) or either wP (80mg/m^2 d1,8,15, q28) or O+C (300mg/20mg daily respectively). Treatment continued until disease progression or unacceptable toxicity. Primary endpoint was Progression Free Survival (PFS). Secondary endpoints were safety and tolerability of the combination of O+C, overall survival, objective response rate, and quality of life. A sample size of 138 (46 per arm) was sufficient to observe HR 0.64 in favour of O+C compared to O alone and 1.44 for wP compared to O (20% one-sided type I error, 80% power, 15% dropout, one-sided p-value <0.2).

Results: OCTOVA recruited 139 participants, median 65 years (IQR:38-84), from 15 UK centres over 34 months. 31 (22%) had had prior PARPi therapy, 47 (34%) prior anti-angiogenic therapy. 41 (29%) had known germline *BRCA1/2* mutations. 125 (90%) had relapsed <6 months after prior platinum. Median 2 prior lines of chemotherapy (range 1-7). There was no difference in PFS between wP and O (HR=0.97, 60%CI: 0.79, 1.19; p=0.55). PFS was increased for O+C compared to O (HR=0.70; 60%CI: 0.57, 0.86; p=0.08). There were 239, 176, and 137 treatment related adverse events (all grades) in the O+C, wP and O arms respectively.

Conclusions: The OCTOVA trial demonstrated that the combination of O+C showed greater efficacy than O alone, but we did not find evidence that wP was inferior to O in women with multiply relapsed OC.

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723MO Tisotumab vedotin (TV) + carboplatin (Carbo) in first-line (1L) or + pembrolizumab (Pembro) in previously treated (2L/3L) recurrent or metastatic cervical cancer (r/mCC): Interim results of ENGOT-Cx8/GOG-3024/innovaTV 205 study

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Background: TV demonstrated durable activity (objective response rate [ORR]=24%; median duration of response [mDOR]=8.3 mo) with manageable safety in previously treated r/mCC (Lancet Oncol. 2021; 22:609-619). Here we report results for the 1L TV + carbo and 2L/3L TV + pembro cohorts of the 2-part, multi-cohort phase Ib/II trial ENGOT-cx8/GOG-3024/innovaTV 205 clinical trial in r/mCC.

Methods: In the 1L TV + carbo cohort, pts with no prior systemic therapy (excluding chemoradiation) for r/mCC received TV 2.0 mg/kg + carbo AUC 5 IV every 3 weeks (Q3W). In the 2L/3L TV + pembro cohort, pts with r/mCC, with disease progression on/after 1–2 prior systemic therapies, received TV 2.0 mg/kg + pembro 200 mg IV Q3W. The primary endpoint was ORR per RECIST v1.1.

Results: There were 33 pts treated with 1L TV + carbo (median 5 cycles). Confirmed ORR was 55% (Table). All treated pts had adverse events (AEs) with 76% reporting grade (gr) $\geq$3 AEs regardless of causality. Prespecified AEs of interest (gr 1-2/ gr $\geq$3) included ocular (55%/3%), peripheral neuropathy (27%/12%) and bleeding events (48%/6%). There were 35 pts treated with 2L/3L TV + pembro (median 6 cycles), with most having received 1 prior systemic treatment for r/mCC (57%) and prior bevacizumab (57%). Confirmed ORR was 35% (Table). All treated pts had AEs with 74% reporting gr $\geq$3 AEs regardless of causality. AEs of interest included (gr 1-2/ gr $\geq$3) ocular (51%/3%), peripheral neuropathy (37%/3%) and bleeding events (54%/9%). There were no treatment-related deaths in either cohort.

Conclusions: Both 1L TV + carbo and 2L/3L TV + pembro had encouraging antitumor activity with acceptable safety profiles in pts with r/mCC.

Clinical trial identification: NCT03786081.

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Table: 723MO Summary of efficacy

Parameters	1L TV + Carbo (N = 33) Median FU: 4.8 months	2L/3L TV + Pembro (N = 34)[a] Median FU: 10.2 months
Objective response rate, n (%) [95% CI]	18 (55) [36–72]	12 (35) [20–54]
Complete response, n (%)	2 (6)	2 (6)
Partial response, n (%)	16 (48)	10 (29)
Median duration of response, months (range)	5.6 (2.7-NE)	NE
Median time to response, months (range)	1.4 (1.1–4.4)	1.4 (1.3–5.8)
Median PFS, months (range)	6.9 (3.9–NE)	5.6 (2.7–9.6)

NE, not estimable. [a]1 pt was excluded from the full analysis set as they didn't have any target or non-target lesions at baseline. Response ongoing in 13/18 pts with 1L TV + carbo and 8/12 pts with 2L/3L TV + pembro.