

Topic: AS06. Tumor Types / AS06c. Ovarian Cancer

BIOMARKERS OF RESPONSE TO RIBOCICLIB PLUS LETROZOLE IN RECURRENT LOW-GRADE SEROUS OVARIAN CARCINOMA: A GOG-3026 CORRELATIVE STUDY

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Introduction: Ribociclib plus letrozole demonstrated meaningful activity in recurrent low-grade serous ovarian carcinoma (LGSOC) in the phase II GOG-3026 trial. However, predictive biomarkers for CDK4/6 inhibitor response remain undefined. We conducted an exploratory translational analysis to identify molecular and immune biomarkers associated with outcomes.

Methods: Archival FFPE tumors from 24 GOG-3026 patients were analyzed. Immunohistochemistry assessed ER, PR, p16, phosphorylated RB (pRB), and Ki-67. Whole-exome sequencing (n=14) and RNA sequencing (n=12) evaluated genomic alterations and immune transcriptional profiles. Associations between biomarkers and objective response rate (ORR), clinical benefit rate (CBR), progression-free survival (PFS) and overall survival were evaluated using 2-sided tests at a 5% significance level, without multiple testing adjustment.

Preliminary Data or Expected Results: Among 24 patients, ORR was 37.5% and CBR was 87.5%. Lower Ki-67 expression was significantly associated with CBR ($r = -0.437$, $p=0.0326$) (Table 1). Lower p16 expression showed a trend toward longer PFS (HR 0.36, 95% CI 0.109–1.045; $p=0.0633$) (Figure 1). ER, PR, pRB expression and MAPK pathway alterations were not associated with response or survival. The most common mutations involved *BRAF*, *KRAS*, *NRAS* and *FANCD2*. RNA sequencing identified three immune phenotypes: immune-hot, intermediate, and immune-cold. No partial responders had an immune-hot phenotype, while four of five partial responders clustered in the intermediate group.

Significance and Impact: Lower Ki-67 expression may predict clinical benefit from ribociclib plus letrozole, while higher p16 expression may be associated with shorter PFS. Distinct immune phenotypes may also influence response, supporting prospective validation of proliferation-, cell-cycle-, and immune-based biomarkers for patient selection in recurrent LGSOC.

Biomarker	No clinical benefit (n=3) Median (IQR)	Clinical benefit (n=21) Median (IQR)	<i>P-value</i>	Correlation coefficient
p16	6.0 (0-8)	4.0 (3-5)	0.388	-0.195
PR	6.0 (0-8)	0 (0-5)	0.138	-0.282
ER	7.0 (5-8)	6.0 (4-7)	0.341	-0.225
pRB	4.0 (3-5)	4.0 (3-5)	0.914	0.046
Ki-67	6.9 (6-10.1)	4.5 (2.9-5.9)	0.0326	-0.4371

Table 1. Association of Biomarker Expression with Clinical Benefit

Values are presented as median (IQR). Associations were evaluated using Spearman rank correlation.

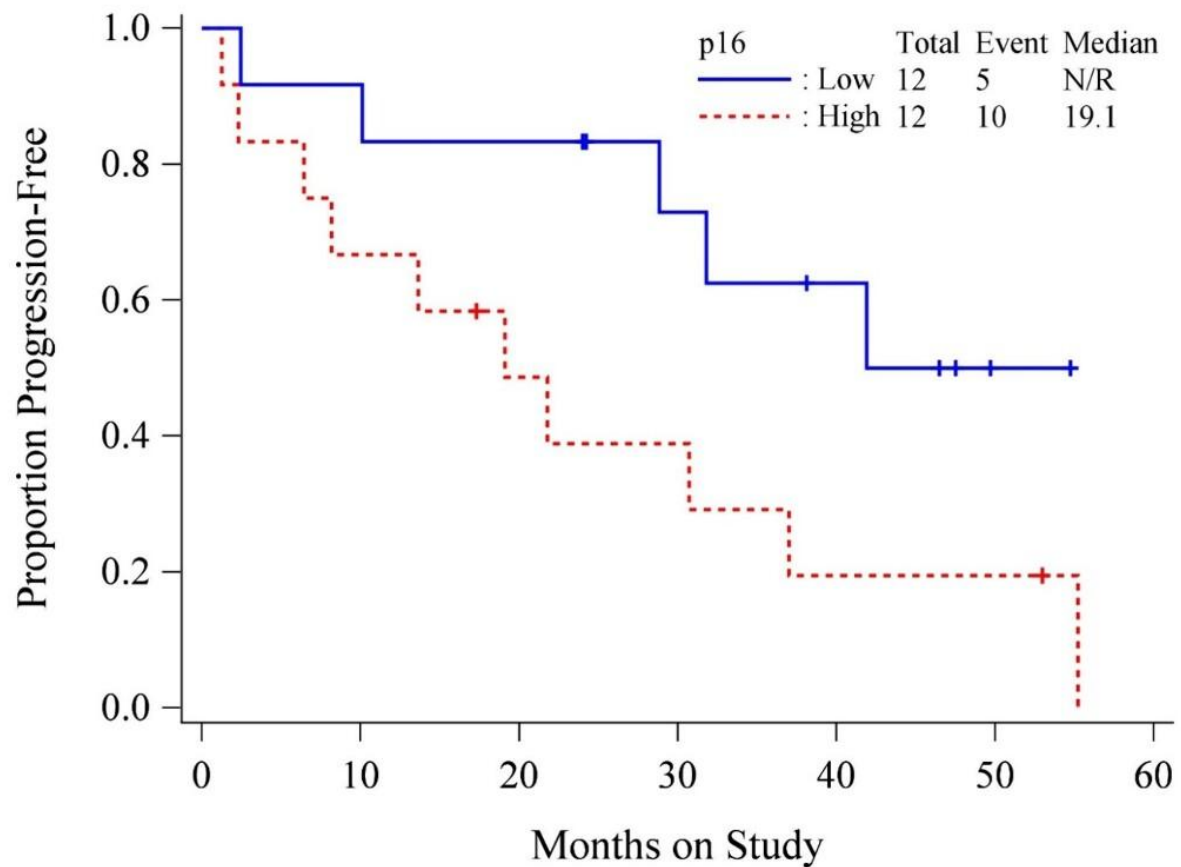


Figure 1. Kaplan–Meier curves for progression-free survival (PFS) stratified by p16 expression, dichotomized at the median. Patients with lower p16 expression showed a trend toward longer PFS (Cox proportional hazard regression: HR 0.36, 95% CI 0.109–1.045; Monte Carlo permutation log-rank test: $p=0.0633$). NR: not reached.

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UBAMATAMAB (MUCIN-16×CLUSTER OF DIFFERENTIATION 3 BISPECIFIC ANTIBODY) ACTIVITY IN LOW-GRADE SEROUS OVARIAN CANCER

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Introduction: Recurrent low-grade serous ovarian cancer (LGSOC) treatment options are limited. Ubamatamab bridges MUC16-positive tumor cells and CD3-expressing T cells, promoting MHC-independent cytotoxicity.

Phase 1/2 subset data (NCT03564340) evaluating ubamatamab ± cemiplimab in recurrent LGSOC previously treated with platinum-containing therapy are presented.

Methods: Among participants enrolled before June 2025, BOR, ORR, DOR, and PFS (RECIST 1.1) were evaluated. Safety and cytokine release syndrome (CRS) were graded (CTCAE and Lee criteria, respectively). MUC16 tumor cell expression was evaluated via immunohistochemistry (Ventana, clone SP426).

Preliminary Data or Expected Results: Overall, 19 participants were included (DCO June 1, 2026): 14 received ubamatamab (3–20 mg QW, 250 mg Q3W, or 800 mg QW/Q3W IV) and 5 received ubamatamab (3–20 mg QW or 250 mg Q3W IV) plus cemiplimab (350 mg Q3W IV). Median prior regimens was 4. Median (IQR) follow-up and treatment duration were 9.8 months (7.9–15.5) and 33.0 weeks (17.4–58.0), respectively. Median (IQR) baseline MUC16 tumor cell expression was 100.0% (94.0–100.0). For ubamatamab 800 mg (n=11), ORR was 72.7% (95% CI 39.0–94.0), median DOR was 9.0 months (95% CI 6.9–NE), and PFS was 11.1 months (95% CI 3.0–NE; **Table/Figure**). TRAEs occurred in all participants; 8 reported Grade ≥3 (42.1%;

neutropenia, anemia, increased ALT/AST, abdominal pain, ileus). CRS occurred in 17 participants (89.5%; all Grade 1/2). No TEAEs resulted in death.

Significance and Impact: In recurrent LGSOC, ubamatamab showed marked antitumor activity, durable responses, and an acceptable safety profile. A prospective, 100-participant LGSOC cohort study evaluating ubamatamab 800 mg Q3W is ongoing.

Table. Study exposure, follow-up, and efficacy by ubamatamab dose level

Measure	3–20 mg QW (n=5)*	250 mg Q3W (n=3) [†]	800 mg		800 mg QW/Q3W (n=11)
			QW (n=8)	Q3W (n=3)	
Study exposure and follow-up					
Median follow-up duration (IQR), months	7.9 (6.8–9.5)	9.0 (5.1–19.1)	14.1 (10.4–15.7)	9.9 (7.9–19.0)	13.3 (8.5–15.9)
Median treatment duration (IQR), weeks	17.4 (11.3–18.3)	19.0 (11.9–81.0)	54.7 (36.5–63.0)	43.0 (33.0–82.4)	– [‡]
Response (per RECIST 1.1) [§]					
BOR, n (%)					
CR	0	0	0	0	0
PR	0	1 (33.3)	6 (75.0)	2 (66.7)	8 (72.7)
SD	3 (60.0)	2 (66.7)	1 (12.5)	1 (33.3)	2 (18.2)
PD	2 (40.0)	0	0	0	0
NE	0	0	1 (12.5)	0	1 (9.1)
ORR, n (%)	0	1 (33.3)	6 (75.0)	2 (66.7)	8 (72.7)
95% CI	0.0–52.2	0.8–90.6	34.9–96.8	9.4–99.2	39.0–94.0
Median KM-estimated DOR (95% CI), months [§]	–	12.5 (NE–NE) [n=1]	9.0 (6.9–NE) [n=6]	10.5 (7.2–NE) [n=2]	9.0 (6.9–NE) [n=8]
Median KM-estimated PFS (95% CI), months [§]	3.8 (2.2–NE)	4.2 (2.8–NE)	11.8 (2.2–NE)	8.4 (3.0–NE)	11.1 (3.0–NE)
DCO: June 1, 2026.					
*Four participants received ubamatamab plus cemiplimab 350 mg IV Q3W; [†] One participant received ubamatamab plus cemiplimab 350 mg IV Q3W; [‡] Treatment duration was not reported for the 800 mg QW/Q3W combined group due to differing dosing frequency; [§] By					

investigator assessment.

BOR, best overall response; CI, confidence interval; CR, complete response; DCO, data cut-off;

DOR, duration of response; IQR, interquartile range; IV, intravenous; KM, Kaplan–Meier; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response;

QW, once weekly; Q3W, once every 3 weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease.

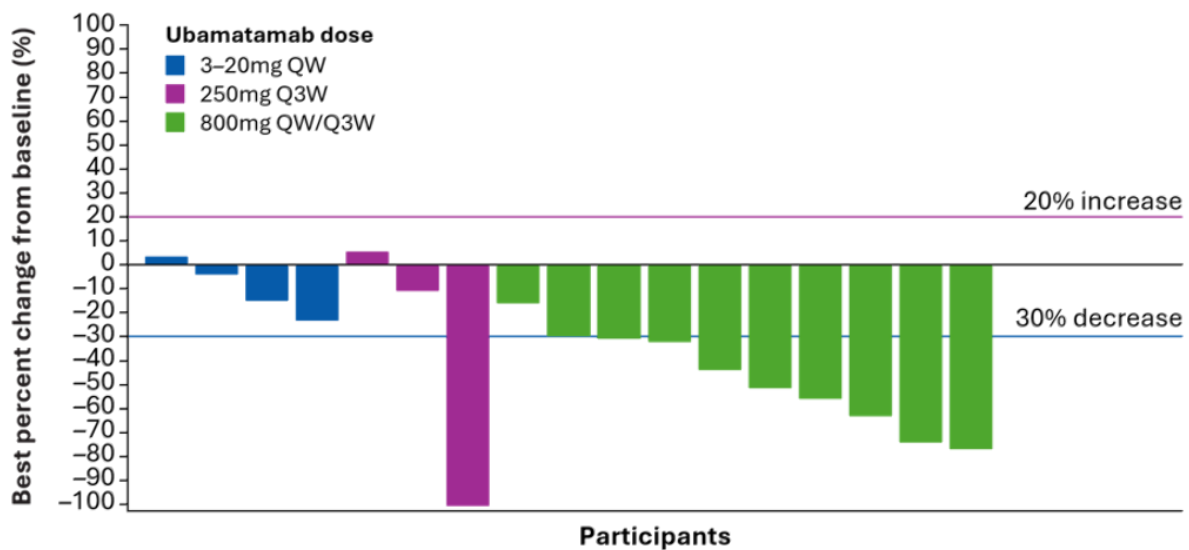


Figure. BOR per RECIST 1.1 by investigator assessment

DCO: June 1, 2026. Increase in sum of target lesion diameters greater than 100% is reported as 100%.

BOR, best overall response; QW, once weekly; Q3W, once every 3 weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

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DOSE OPTIMIZATION, EFFICACY, AND SAFETY OF CUSP06, A CADHERIN-6-DIRECTED ANTIBODY-DRUG CONJUGATE, IN PLATINUM-RESISTANT OVARIAN CANCER

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Introduction: Platinum-resistant ovarian cancer (PROC) is associated with poor prognosis and limited durable treatment options. CUSP06 is a CDH6-directed ADC delivering a topoisomerase I inhibitor payload (exatecan). In Ph1a of CUSP06-1001, CUSP06 demonstrated preliminary antitumor activity with a manageable safety profile.

Methods: CUSP06-1001 is an ongoing Ph1a/1b, open-label, multicenter dose escalation, dose expansion study in patients with PROC and other CDH6-positive tumors. In Ph1b dose optimization, PROC patients (1-4 prior lines) were randomized 1:1 across 2 cohort pairs: 3.6 mg/kg and 4.4 mg/kg + G-CSF; and 4.0 mg/kg and 4.0 mg/kg + G-CSF (~20 patients/cohort). Endpoints include ORR, DOR, PFS, and safety and PK parameters.

Preliminary Data or Expected Results: As of 15 June 2026, 181 patients have been treated, including 82 PROC Ph1b patients. Enrollment to all Ph1b PROC cohorts is complete. The 4.0 mg/kg and 4.0 mg/kg + G-CSF cohorts remain immature with limited follow-up. Safety remains consistent with Ph1a with no new safety signals observed;

prophylactic G-CSF reduced high-grade neutropenia. Although efficacy data are still maturing, encouraging clinical activity has been observed in all cohorts, with ORRs of 50.0% (10/20) and 40.0% (8/20) in the 3.6 mg/kg and 4.4 mg/kg + G-CSF cohorts, respectively. The ORR in the post-mirvetuximab population is 45.0% (9/20). Among responders, four Ph1b patients achieved CR, one after 7 months in PR. Nine patients remain on treatment $\geq$ 12 months; one ongoing response is approaching 2 years.

Significance and Impact: CUSP06 demonstrates durable antitumor activity and a manageable safety profile in heavily pre-treated PROC, supporting continued development in CDH6 and FR α unselected patients.

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PEMBROLIZUMAB VS PLACEBO PLUS PACLITAXEL WITH OR WITHOUT BEVACIZUMAB FOR PLATINUM-RESISTANT RECURRENT OVARIAN CANCER: RESULTS BY HISTOLOGIC SUBTYPE FROM THE PHASE 3 ENGOT-OV65/KEYNOTE-B96 STUDY

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Introduction: Certain histologic subtypes of ovarian cancer (eg, clear cell carcinoma [CCC]) are associated with poor prognosis and survival outcomes. In the phase 3 ENGOT-ov65/KEYNOTE-B96 study (NCT05116189), pembrolizumab (vs placebo) plus weekly paclitaxel ± bevacizumab significantly improved PFS and OS in participants with platinum-resistant recurrent ovarian cancer (PROC), both in the overall study population and in participants with PD-L1 combined positive score (CPS) ≥1. We evaluated the benefit across different PROC histologic subtypes.

Methods: Eligible participants had histologically confirmed, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma of multiple histologic subtypes, including high-grade serous or predominantly serous, CCC, low-grade serous, any-grade endometrioid, and carcinosarcoma. Participants were randomized 1:1 to pembrolizumab 400 mg IV or placebo Q6W, each combined with weekly paclitaxel (80 mg/m² on days 1, 8, and 15 of each 3-week cycle) ± bevacizumab (10 mg/kg Q2W) until PD or unacceptable toxicity. Primary endpoint was investigator-assessed PFS per RECIST v1.1 in participants with PD-L1 CPS ≥1 and in all participants. OS was the key secondary endpoint in both populations. Efficacy outcomes by histologic subtypes were predefined exploratory endpoints.

Preliminary Data or Expected Results: Efficacy outcomes at the final analysis are shown by histologic subtype in the **table**.

Significance and Impact: Pembrolizumab (vs placebo) plus weekly paclitaxel ± bevacizumab demonstrated consistent PFS and OS benefit across histologic subtypes in both the PD-L1 CPS ≥1 population and all participants. Results were consistent with those for the overall study population.

Table. Efficacy by Histologic Subtype^a

	PD-L1 CPS ≥1		All Participants	
Endpoint	Pembrolizumab	Placebo	Pembrolizumab	Placebo
PFS (Primary)				
Overall				
Events, n/N (%)	198/234 (84.6)	206/232 (88.8)	276/322 (85.7)	286/321 (89.1)
HR (95% CI)	0.76 (0.62–0.92)		0.73 (0.62–0.87)	
High-grade serous				
Events, n/N (%)	173/206 (84.0)	184/208 (88.5)	238/278 (85.6)	245/275 (89.1)
HR (95% CI)	0.79 (0.64–0.98)		0.77 (0.64–0.92)	
CCC				
Events, n/N (%)	13/14 (92.9)	13/13 (100)	22/24 (91.7)	24/26 (92.3)
HR (95% CI)	0.53 (0.23–1.24)		0.59 (0.31–1.09)	
Other ^b				

Events, n/N (%)	12/14 (85.7)	9/11 (81.8)	16/20 (80.0)	17/20 (85.0)
HR (95% CI)	0.64 (0.27–1.54)		0.67 (0.34–1.33)	
OS (Key Secondary)				
Overall				
Events, n/N (%)	174/234 (74.4)	192/232 (82.8)	247/322 (76.7)	266/321 (82.9)
HR (95% CI)	0.76 (0.62–0.93)		0.82 (0.69–0.97)	
High-grade serous				
Events, n/N (%)	155/206 (75.2)	171/208 (82.2)	215/278 (77.3)	228/275 (82.9)
HR (95% CI)	0.79 (0.64–0.99)		0.83 (0.69–1.00)	
CCC				
Events, n/N (%)	9/14 (64.3)	11/13 (84.6)	18/24 (75.0)	21/26 (80.8)
HR (95% CI)	0.52 (0.21–1.26)		0.78 (0.41–1.47)	
Other ^b				
Events, n/N (%)	10/14 (71.4)	10/11 (90.9)	14/20 (70.0)	17/20 (85.0)
HR (95% CI)	0.47 (0.19–1.18)		0.62 (0.30–1.28)	

^aSubgroup analyses were based on an unstratified Cox regression model with the Efron method of tie handling and treatment as a covariate.

^bOther histology categories included low-grade serous, any-grade endometrioid, and carcinosarcoma.

Data cutoff: September 5, 2025

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RINATABART SESUTECAN (RINA-S®) FOR PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER: FIRST EFFICACY AND SAFETY RESULTS FROM THE PHASE 2 COHORT OF THE RAINFOL™-01 STUDY

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Introduction: Rinatabart sesutecan (Rina-S) is an investigational FRα-directed ADC with a topoisomerase I inhibitor payload and a hydrophilic protease-cleavable linker. Dose optimization identified 120 mg/m² as the RP2D for Rina-S in platinum-resistant ovarian cancer (PROC). Here, we report single-arm phase 2 results from RAINFOL-01™ (NCT05579366) evaluating Rina-S 120 mg/m² Q3W monotherapy in patients with PROC.

Methods: Patients had metastatic or unresectable PROC and received 1-3 prior lines of therapy (pLOT) or up to 4 pLOT if mirvetuximab (MIRV) was the most recent pLOT for patients with FRα ≥75% expression. Enrollment was not restricted by FRα expression level. Primary endpoint was ORR. Secondary endpoints included DOR, PFS, OS, and safety.

Preliminary Data or Expected Results: Overall, 109 patients were treated (median follow-up, 13.6 months). Over half (53%) of patients received 3 or 4 pLOT. All patients had received prior bevacizumab and taxane; 33% had received prior MIRV. The investigator-assessed confirmed ORR was 45.9% (95% CI, 36.3-55.7), including 5 CRs; DCR was 94.5% (95% CI, 88.4-98.0). Median DOR was 12.1 months (95% CI, 6.5-15.4) with 42% of responses ongoing at data cutoff, including all CRs. Median PFS was 9.5 months (95% CI, 7.6-11.3). Grade ≥ 3 treatment-emergent adverse events (TEAEs) were primarily neutropenia (33.9%), anemia (30.3%), or thrombocytopenia (23.9%). No fatal TEAEs occurred. TEAEs led to Rina-S discontinuation in 7 (6.4%) patients.

Significance and Impact: Rina-S 120 mg/m² Q3W led to substantial and durable antitumor activity, translating into meaningful PFS, with a tolerable safety profile in a broad population of patients with PROC who have an unmet need for effective new treatment options.

SURVIVAL AFTER RELAPSE IN PATIENTS WITH ENDOMETRIAL CANCER IN THE INTERNATIONAL RANDOMISED PORTEC-4A TRIAL

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Introduction: PORTEC-4a demonstrated non-inferiority and cost-effectiveness of molecular-profile-guided adjuvant-treatment in early-stage high-intermediate-risk endometrial cancer (HIR-EC). In the molecular-profile arm, 46% had favourable profile and received observation, 14% unfavourable profile and received pelvic-radiotherapy (EBRT); 40% intermediate profile and received vaginal-brachytherapy (VBT), as did all patients in the standard arm. This analysis evaluates outcomes after relapse.

Methods: HIR-EC patients were randomised (2:1) to molecular-profile or standard arm. In patients with recurrent disease, descriptive analyses evaluated patterns of relapse,

subsequent treatment, tumour control and survival after relapse. Time-to-event outcomes were analysed using Kaplan-Meier methods.

Preliminary Data or Expected Results: After a median follow-up of 5 years, 69 recurrences were diagnosed among 564 patients (figure 1A). Recurrences were observed in 10/168 (6.0%) and 5/109 (4.6%) patients with favourable profile in molecular-profile and standard arms; and in 12/51 (23.5%) versus 10/23 (43.5%) in patients with unfavourable profile, treated with EBRT or VBT respectively (figure 1B-C). Three-year overall survival after recurrence was 42% overall; 46% in molecular-profile arm versus 30% in standard arm (HR 0.67 (95%CI 0.35-1.30)). Most recurrences after observation for favourable profile were successfully salvaged (figure 2A). In case of complete remission, 3-year survival after recurrence was 93%.

Significance and Impact: Most of the 6% recurrences during observation in patients with favourable profile were successfully salvaged, corresponding with an excellent survival after recurrence in this subgroup. In contrast, patients with unfavourable profile appeared to benefit from EBRT, with fewer recurrences compared to patients receiving VBT. These findings further support molecular-profile-guided adjuvant treatment as a strategy to reduce over- and undertreatment in women with HIR-EC.

Topic: AS06. Tumor Types / AS06a. Cervical Cancer

LOW-DOSE NIVOLUMAB WITH NEOADJUVANT CHEMOTHERAPY FOLLOWED BY CONCURRENT CHEMORADIATION IN STAGE IIIC–IVA CERVICAL CANCER: A PHASE II STUDY

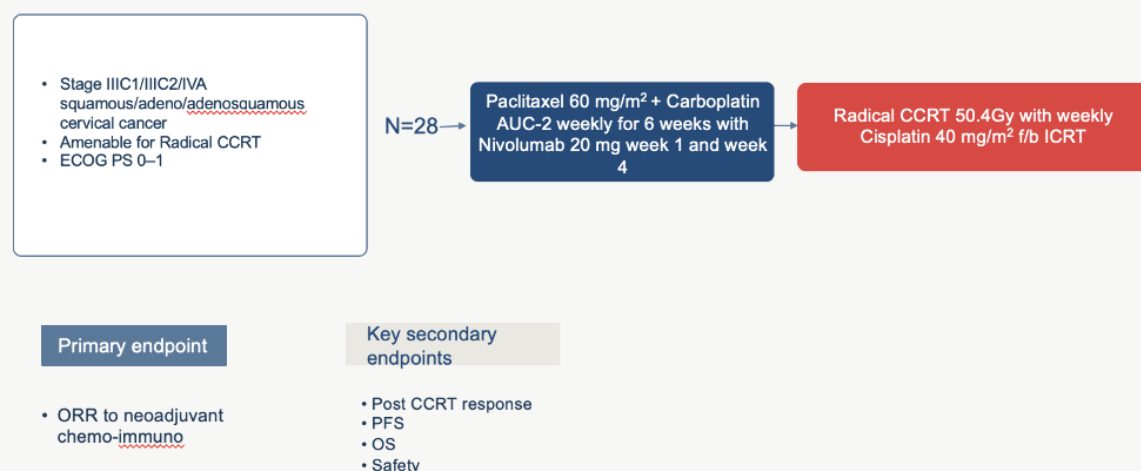
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Introduction: Locally advanced cervical cancer, particularly stage IIIC–IVA disease, continues to have suboptimal outcomes with current standards of care. We initiated a prospective phase II study to evaluate the feasibility and antitumor activity of low-dose nivolumab combined with neoadjuvant chemotherapy followed by definitive CCRT.

Methods: This single-arm phase II study used Simon's two-stage design. Eligible patients with stage IIIC–IVA disease received weekly paclitaxel 60 mg/m² and carboplatin AUC 2 for 6 weeks with low-dose nivolumab (20 mg flat, 2 doses three weeks apart), followed by definitive CCRT. The primary endpoint was response to neoadjuvant chemo-immunotherapy; secondary endpoints included post-CCRT response, PFS, OS and safety.

LOW-DOSE NIVOLUMAB WITH NEOADJUVANT CHEMOTHERAPY FOLLOWED BY CONCURRENT CHEMORADIATION IN STAGE IIIC–IVA CERVICAL CANCER: A PHASE II STUDY



Preliminary Data or Expected Results: Twenty-eight patients were evaluable for response. ORR after neoadjuvant chemo-immunotherapy was 96.4% (CR 25.0%, PR 71.4%), with no new safety signals. Among patients who completed CCRT, 88.0% received at least 4 doses of cisplatin. Three patients were not evaluable post-CCRT: one defaulted, one progressed before CCRT and transitioned to palliative treatment, and one had not completed CCRT at data cutoff. Among 25 patients evaluable post-CCRT, ORR was 92.0% (CR 80.0%, PR 12.0%). At a median follow-up of 14.0 months, median PFS and OS were not reached; estimated 12-month PFS and OS were 85.3% (95% CI, 65.4–94.2) and 91.6% (95% CI, 69.9–97.9), respectively.

Significance and Impact: Neoadjuvant low-dose nivolumab with chemotherapy demonstrated excellent response rates, high post-CCRT complete response rates, and preserved definitive CCRT deliverability, supporting early chemo-immunotherapy intensification as a promising strategy for stage IIIC–IVA cervical cancer.

Topic: AS06. Tumor Types / AS06c. Ovarian Cancer

**COMPARATIVE EFFECTIVENESS OF CARBOPLATIN PLUS MIRVETUXIMAB
SORAVTANSINE VERSUS REAL-WORLD PLATINUM-BASED CHEMOTHERAPY IN
PATIENTS WITH FIRST RECURRENCE PLATINUM-SENSITIVE OVARIAN CANCER**

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Introduction: Carboplatin combined with mirvetuximab soravtansine (MIRV) demonstrated clinically meaningful activity and manageable safety in the single-arm phase 2 IMGN853-0420 trial in patients with folate receptor alpha (FRA)-positive platinum-sensitive ovarian cancer (PSOC) with one prior line of platinum-based chemotherapy. Efficacy was compared between trial-treated patients and real-world patients in routine US oncology practice.

Methods: Data from IMGN853-0420 were compared with real-world evidence using de-identified electronic health record data from the US-based Flatiron Database. Key prognostic and clinical characteristics were aligned to minimize confounding factors. The real-world platinum-based chemotherapy (rwPBC) cohort received standard platinum doublets ($\pm$ maintenance) and was not selected for FRA. Primary endpoint was trial-based investigator-assessed progression-free survival (PFS) vs real-world PFS (rwPFS). Additional endpoints included blinded independent central review (BICR)-assessed PFS vs rwPFS and safety.

Preliminary Data or Expected Results: Patient characteristics of the trial cohort (N=124) and trial-eligible rwPBC cohort (N=223) were balanced using inverse probability of treatment weighting (IPTW). After IPTW, effective sample sizes were 90.3 (72.8%) and 202.3 (90.7%), respectively. Median investigator-assessed PFS was 10.7 months with carboplatin plus MIRV, and median rwPFS was 7.9 months with rwPBC (Table and Figure; adjusted HR=0.67 [95% CI: 0.49-0.91]; $P=0.0109$). Median BICR-assessed PFS was 12.7 months (Table; adjusted HR=0.51 [95% CI: 0.35-0.75]; $P=0.0006$). Descriptive safety analyses will be presented.

Significance and Impact: In patients with FRA-positive first recurrence PSOC, treatment with carboplatin plus MIRV was associated with improved median PFS relative to non-FRA-selected real-world platinum-based doublets ($\pm$ maintenance), after IPTW balancing of key prognostic factors. These findings provide real-world comparative evidence for treatment efficacy in this population.

Table: IPTW-Weighted^a PFS Estimates in Trial Cohort vs Real-World Cohort^b

Investigator-assessed		
Endpoint Estimate	Trial cohort (n=120)	Real-world cohort (n=222)
Events, n (%)	74.8 (62.3)	159.4 (71.7)
Censor, n (%)	45.4 (37.7)	63.0 (28.3)
Median PFS (95% CI), months	10.7 (9.49, 13.70)	7.9 (6.67, 8.74)
Endpoint	Estimate	
Log-rank <i>P</i> value	0.0073	
Hazard ratio (95% CI); Cox PH adjusted for BRCA status <i>P</i> value	0.67 (0.49, 0.91); <i>P</i> =0.0109	
E-value ^c (point estimate / CI limit closest to null)	1.97 / 1.34	
ECOG 0-1 Subgroup		
Endpoint Estimate	Trial cohort (n=122)	Real-world cohort (n=137)
Events, n (%)	76.5 (62.7)	92.9 (68.0)
Censor, n (%)	45.4 (37.3)	43.8 (32.0)
Median PFS (95% CI), months	10.8 (9.66, 13.70)	7.9 (6.24, 9.49)
Endpoint	Estimate	
Log-rank <i>P</i> value	0.0101	
Hazard ratio (95% CI); Cox PH <i>P</i> value	0.66 (0.48, 0.91); <i>P</i> =0.0118	
E-value ^c (point estimate / CI limit closest to null)	2.00 / 1.34	

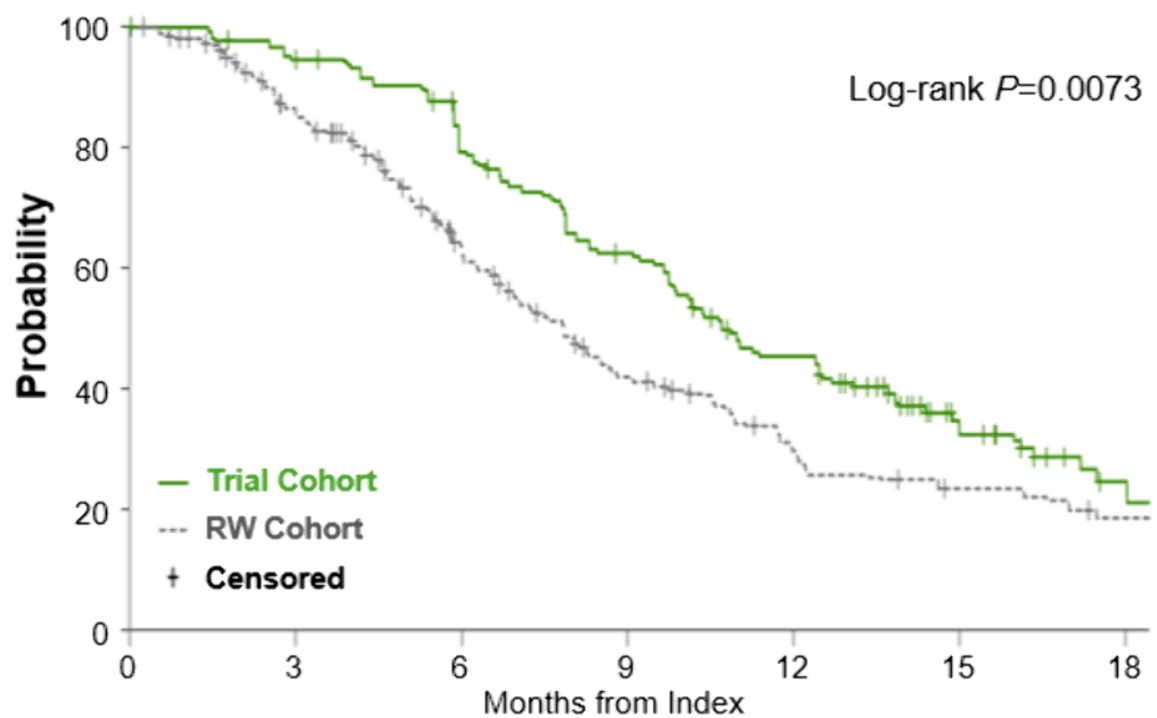
BICR-assessed		
Endpoint Estimate	Trial cohort (n=106)	Real-world cohort (n=222)
Events, n (%)	46.9 (44.2)	159.5 (71.8)
Censor, n (%)	59.1 (55.8)	62.7 (28.2)
Median PFS (95% CI), months	12.7 (10.15, 19.02)	7.9 (6.67, 8.74)
Endpoint	Estimate	
Log-rank <i>P</i> value	0.0001	
Hazard ratio (95% CI); Cox PH adjusted for BRCA status <i>P</i> value	0.51 (0.35, 0.75); <i>P</i> =0.0006	
E-value ^c (point estimate / CI limit closest to null)	2.56 / 1.74	

PFS was defined as the time from the index date to the earliest occurrence of investigator-assessed disease progression or death from any cause. Patients without progression or death were censored at the last eligible follow-up date according to the cohort-specific censoring rules.

Abbreviations: 2L, second line; BICR, blinded independent central review; BRCA, breast cancer gene; CI, confidence interval; Cox PH, Cox proportional hazards; ECOG, Eastern Cooperative Oncology Group; IPTW, inverse probability of treatment weighting; PARPi, poly (ADP-ribose) polymerase inhibitor; PBC, platinum-based chemotherapy; PFS, progression-free survival.

^aInverse probability of treatment weighting was applied to balance baseline demographics and clinical characteristics including age, time from diagnosis to 2L, prior surgery, platinum-free interval, prior bevacizumab and PARPi exposure, and BRCA status. ^bThe real-world cohort included adult women with histologically confirmed serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who relapsed after one prior line of PBC, had a platinum-free interval greater than 6 months, and initiated 2L platinum-based doublet therapy ± maintenance. ^cE-values quantify the minimum strength of association, on the risk-ratio scale, that an unmeasured confounder would need to have with both the treatment and the outcome — conditional on the measured covariates — to fully explain away the observed treatment–outcome association.

Figure: IPTW-Weighted Kaplan-Meier Curve for PFS: Investigator-Assessed PFS (Trial) vs Real-World PFS



Number at Risk

Trial Cohort

120 109 89 69 47 17 7

RW Cohort

222 176 114 70 45 35 26

Abbreviations: IPTW, inverse probability of treatment weighting; PFS, progression-free survival; RW, real-world.

Topic: AS01. Basic & Translational Science / AS01b. Translational Findings

MOLECULAR PROFILING AND TUMOR BIOMARKER ANALYSIS OF RAMP 201, A STUDY DEMONSTRATING EFFICACY OF AVUTOMETINIB IN COMBINATION WITH DEFACTINIB IN RECURRENT LOW-GRADE SEROUS OVARIAN CANCER

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Introduction: Low-grade serous ovarian cancer (LGSOC) harbors KRAS mutations in ~30% of patients. The ENGOT-OV60/GOG-3052/RAMP-201 study led to accelerated approval of avutometinib (RAF/MEK clamp) and defactinib (FAK inhibitor) for KRAS-mutated recurrent LGSOC. In the GOG-281 study, for KRAS wild-type patients who were also wild-type for NRAS/BRAF, limited clinical benefit was observed with either the MEK inhibitor trametinib (8% [4/48] ORR; 7 months mPFS) or chemo/endocrine therapy (7% [3/42] ORR; 6 months mPFS). We performed molecular profiling of baseline tumors from RAMP 201 to determine activity of avutometinib with defactinib in subgroups within the KRAS wild-type population.

Methods: Genomic alterations and gene-expression profiles were characterized in tumor samples using Tempus xT/xR assays.

Preliminary Data or Expected Results: Among patients with KRAS-mutated LGSOC, antitumor activity was observed across multiple KRAS mutation variants. Among patients with KRAS wild-type LGSOC, the majority (81%) were also wild-type for NRAS/BRAF. In this KRAS/NRAS/BRAF wild-type population, clinically meaningful efficacy was observed with avutometinib plus defactinib (18% [7/39] ORR; 13 months mPFS). Among patients with KRAS wild-type LGSOC harboring NRAS or BRAF mutations, avutometinib plus defactinib achieved a confirmed ORR of 22% (2/9). Molecular profiling showed that in KRAS/NRAS/BRAF wild-type patients, lower expression of genes related to fibroblast activation and extracellular matrix remodeling correlated with longer PFS.

Significance and Impact: These data demonstrate that the combination of avutometinib with defactinib provides clinically meaningful efficacy for patients with recurrent LGSOC that do not harbor mutations in KRAS, NRAS or BRAF, a population with historically poorer prognosis and lower response rates to single agent MEK inhibitors.