

PHASE III TRIAL OF LETROZOLE VERSUS PACLITAXEL AND CARBOPLATIN FOLLOWED BY LETROZOLE AS INITIAL TREATMENT FOR PATIENTS WITH ADVANCED-STAGE LOW-GRADE SEROUS OVARIAN CARCINOMA

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Abstract Body: Objectives: To assess the efficacy and toxicity of Letrozole alone (L) versus paclitaxel and carboplatin followed by L (PC/L) as initial treatment for patients with stage II-IV, p53 wildtype, low-grade serous carcinoma of the ovary, fallopian tube, or peritoneum. **Methods:** NRG-GY019 is a phase III, noninferiority (NI) trial. After primary cytoreductive surgery (CRS), eligible subjects were randomized 1:1 to PC/L (paclitaxel and carboplatin IV, for up to six 21-day cycles) followed by L (PO once daily) or L alone (PO once daily). The randomization was stratified by 1) Country and 2) Residual disease following CRS (no gross—NGR--vs any residual disease). Progression-free survival (PFS) was the primary endpoint. The targeted 450 patient accrual supported 80% power (1-sided $\alpha=0.1$) to assess the NI of L (NI margin=1.18) compared to PC/L. Two interim analyses were planned. **Results:** Of 450 patients accrued, 3 were deemed ineligible, and 26 withdrew consent. The median patient age was 52, 92% had stage III/IV disease, and 64% had no gross residual (NGR) disease after CRS. In cycles 1-6, 100 PC/L and 38 L patients experienced at least one grade 3/4 event. Two grade 5 events on the Letrozole arm were considered unrelated to treatment. The odds of observing at least one grade 3/4 event was 4.26 (95%CI: 2.74, 6.62) higher in the PC/L patients than the L patients. The protocol-specified 2nd interim analysis assessed the futility or efficacy of L vs PC/L against a prespecified futility margin of $HR \geq 1.213$ (lower values favor L). The interim analysis included 63 (L) and 50 (PC/L) PFS events, with median follow-up time of 27.3 months. The HR estimate for L vs PC/L was 1.3 [95% CI: 0.9, 1.89], and the DSMB closed the study for futility of L. However, in the 64% (286/450) patients who underwent CRS to NGR, 29/142 (20.4%) of L patients experienced a progression event compared to 27/144 (18.8%) of PC/L patients, with an estimated HR at 1.15 [95% CI: 0.68-1.94]. The median PFS has not been reached in either treatment arm. At 18 months from randomization, 84% PC/L and 74% L patients were alive and progression free. At the Jan 5, 2026 data cut off, 77.9% of PC/L and 71.9% of L patients remained alive and progression-free, with overall survival of 95% and 92%, respectively. **Conclusion:** In the intent-to-treat population, the trial met the pre-specified criteria for early termination for futility and did not demonstrate noninferiority of L

compared with PC/L. Ongoing follow up and translational research are in progress. These results are practice defining for PC/L as the current standard of care.

PRELIMINARY SAFETY AND EFFICACY OF IXOTATUG VEDOTIN (TORL-1-23), A CLAUDIN 6-TARGETED ADC, IN COMBINATION WITH BEVACIZUMAB IN RECURRENT OVARIAN CANCER

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Abstract Body: Background: Claudin-6 (CLDN6) is a cell surface protein and member of the claudin family of tight junction molecules expressed at high levels in multiple human cancers including high-grade serous ovarian cancer, with little or no expression in normal adult tissues. CLDN6 overexpression is associated with worse progression-free survival and overall survival in ovarian cancer. Ixotatug vedotin (Ixo-V) is a first-in-class IgG1-vc-MMAE antibody drug conjugate that specifically targets CLDN6 positive (CLDN6+) disease. Ixo-V monotherapy has demonstrated promising antitumor activity with a manageable safety profile in heavily pretreated CLDN6+ ovarian cancer, supporting combination strategies. As part of an ongoing Phase 1 study, the combination of Ixo-V plus bevacizumab (BEV) is being evaluated in CLDN6+ recurrent ovarian cancer. **Method:** Patients (pts) with recurrent ovarian cancer, including platinum-resistant (PROC) and platinum-sensitive (PSOC) disease, received Ixo-V (2.4 or 3.0 mg/kg) and BEV (15 mg/kg) intravenously on Day 1 of a 21-day cycle. Responses were assessed by investigator per RECIST 1.1; adverse events (AEs) were graded using CTCAE v5.0. **Results:** A total of 29 pts were treated, with 21 pts remaining on treatment. Median age was 63 years. Median number of prior lines was 2 (range 1-5), 20 pts had received prior BEV, 13 prior PARP inhibitors, 1 prior mirvetuximab; 20 pts were PROC and 9 PSOC. Of 28 CLDN6+ evaluable pts, 11 had initial responses. Disease control rate was 96%. Median duration of response has not been reached. Most common non-laboratory AEs (all grades) included alopecia (48%), nausea (45%), arthralgia (41%), constipation (31%), and fatigue (31%). Most common grade 3/4 AEs included hypertension (10%), neutropenia (7%), and ileus (7%). Discontinuation rate due to AE was 10%; 3% were treatment-related. **Conclusions:** Preliminary results with Ixo-V plus BEV show favorable tolerability, characterized by a manageable safety profile, and demonstrate encouraging activity in pts with CLDN6+ recurrent ovarian cancer. These results suggest that Ixo-V and

BEV may expand combination therapy options for CLDN6+ disease in the PROC and PSOC settings. Clinical trial information: NCT05103683.

MIRVETUXIMAB SORAVTANSINE PLUS CARBOPLATIN IN FOLATE RECEPTOR ALPHA-EXPRESSING RECURRENT PLATINUM-SENSITIVE OVARIAN CANCER

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Abstract Body: Objectives: The IMGN853-0420 trial (NCT05456685) was a phase 2, single-arm, multicenter study that investigated the efficacy and safety of the folate receptor alpha (FRa)-directed antibody-drug conjugate mirvetuximab soravtansine (MIRV) plus carboplatin in platinum-sensitive ovarian cancer (PSOC). **Methods:** Patients (pts) with

measurable, recurrent FRA-expressing PSOC ($\geq 25\%$ tumor cells with $\geq 2+$ membrane intensity by immunohistochemistry [VENTANA FOLR1 (FOLR1-2.1) RxDx Assay, Roche Diagnostics]) and 1 prior line of platinum-based chemotherapy (PBC) received 6–8 cycles of combination Q3W MIRV (6 mg/kg adjusted ideal body weight) plus carboplatin (AUC 5) followed by single-agent MIRV as continuation therapy. Primary and key secondary endpoints were objective response rate (ORR) by the end of 6 combination cycles in the FRA $\geq 50\%$ subgroup and overall population (ie, FRA $\geq 25\%$), respectively. Additional secondary endpoints included duration of response (DOR), progression-free survival (PFS), overall survival (OS), and treatment-emergent adverse events (AEs). **Results:** Among 125 pts in the overall population, 102 had FRA $\geq 50\%$; 49% had prior poly (ADP-ribose) polymerase inhibitor (PARPi) exposure. Confirmed ORR by the end of 6 combination cycles was 62.7% (95% CI, 52.6–72.1) in the FRA $\geq 50\%$ group, including 9 complete and 55 partial responses. In the overall population, confirmed ORR by the end of 6 combination cycles was 62.4% (95% CI, 53.3–70.9). Among the 81% (101/125) of pts who continued on MIRV monotherapy, 7 additional responses were observed (ORR, 68.0%). Median number of MIRV cycles was 12 (range, 1–33). Across both phases in the overall population, median DOR was 11.2 mo (95% CI, 8.6–13.9); median PFS was 11.0 mo (95% CI, 9.8–13.1). Notable activity was present in subgroups including in pts who progressed on or after PARPi (**Table**). OS data are immature. The most common treatment-emergent AEs were grade (gr) 1 or 2 blurred vision (81%) and corneal AEs (74%), resolving to gr ≤ 1 in $>90\%$ of pts. Gr ≥ 3 AEs occurred in 65% of pts, largely driven by hematologic AEs (26%), 81% of which occurred during combination treatment. 54% of pts had a dose reduction of MIRV and/or carboplatin and 20% discontinued treatment, mainly driven by hematologic (7%), respiratory (7%), and ocular (2%) AEs. The rate of adjudicated pneumonitis was 15% (gr ≥ 3 , 4%), including 2 deaths in pts with preexisting cardiopulmonary disorders. **Conclusions:** MIRV plus carboplatin in recurrent FRA $\geq 25\%$ PSOC can be safely administered with dose modifications and AE management, achieved favorable ORR and PFS, showed comparable efficacy to pre-PARPi era benchmarks, and established for the first time the safety and efficacy of continuing MIRV after carboplatin. Notably, efficacy was maintained across subgroups, including in those with prior PARPi exposure, a population where PBC rechallenge may have diminished clinical activity. These findings support further evaluation of MIRV plus carboplatin as a meaningful treatment option in recurrent PSOC. Funded by

AbbVie.

Table

Data cutoff: June 20, 2025*	FR α $\geq$ 50%	Overall population (ie, FR α $\geq$ 25%)				
	Total patients (n=102)	Total patients (N=125) ^a	PARPi naïve (n=62)	PARPi treated (n=61)	PD on PARPi (n=37)	PD after PARPi (n=24)
ORR, n (%) [95% CI] [†]	69 (67.6) [57.7–76.6]	85 (68.0) [59.1–76.1]	45 (72.6) [59.8–83.1]	39 (63.9) [50.6–75.8]	22 (59.5) [42.1–75.2]	17 (70.8) [48.9–87.4]
Median PFS, mo [95% CI] [‡]	11.0 [9.8–13.7]	11.0 [9.8–13.1]	12.4 [9.8–18.0]	10.4 [7.5–12.5]	7.7 [6.3–10.8]	12.7 [7.8–16.3]

*Results from the overall study (combination + continuation phases).

[†]Investigator-assessed ORR per RECIST v1.1 in the overall study.

‡Time from 1st dose to radiological PD or any-cause death in the overall study.

[§]2 patients were censored from PFS analysis due to missing tumor scans.

FR α , folate receptor alpha; ORR, objective response rate; PARPi, poly (ADP-ribose) polymerase inhibitor; PD, progressive disease; PFS, progression-free survival.

A RANDOMIZED PHASE II TRIAL OF MIRVETUXIMAB SORAVTANSINE IN FOLATE RECEPTOR ALPHA (FRA)-HIGH RECURRENT OVARIAN CANCER ELIGIBLE FOR PLATINUM-BASED CHEMOTHERAPY (MIROVA/AGO-OVAR 2.34)

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Abstract Body: Background: Mirvetuximab soravtansine (MIRV) has demonstrated single agent activity in patients with platinum-resistant ovarian cancer with FRA high expression. However, its activity and safety in combination with carboplatin has not been defined in platinum eligible patients so far. **Methods:** Randomized phase II trial comparing 6 cycles of carboplatin AUC5+MIRV 6 mg/kg AIBW every 3 weeks followed by MIRV versus 6 cycles of carboplatin combined with either paclitaxel, gemcitabine or pegylated liposomal doxorubicin followed by maintenance PARP inhibitor (PARPi) if applicable. All histologic subtypes were eligible with a platinum-free interval >3 months and FRA high expression ($\geq 75\%$ with PS2+ scoring) confirmed by central laboratory. Prior PARPi therapy in BRCAmut patients was mandatory. Strata were BRCA-Status, TFIp and number of prior lines of chemotherapy. The primary endpoint was PFS. **Results:** In total, 145 patients were randomized. Of them, 112/145 (77.2%) patients had received prior bevacizumab and

97/145 (66.9%) had prior PARPi, 15.2% were BRCAmut. In the standard arm, 39.15% received PARPi as maintenance. Median PFS in the standard arm was 9.79 months versus 9.53 months in the experimental arm ($p=0.996$; HR=1.00; 95% CI: 0.68;

1.46). **Conclusion:** MIROVA/AGO-OVAR 2.34 is the first randomized trial evaluating the activity and safety of the combination of carboplatin with an antibody-drug conjugate in the setting of platinum-eligible relapsed ovarian cancer. The primary endpoint regarding improvement of PFS was not met. Further analysis will be presented.

MAINTENANCE DOSTARLIMAB AFTER CHEMORADIATION (CRT) FOR PATIENTS WITH HIGH-RISK LOCALLY ADVANCED CERVICAL CANCER: GEICO 78-C/ATOMICC RANDOMIZED PHASE 2 TRIAL

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Abstract Body: Background When ATOMICC was designed (2018), CRT was standard for LACC and the impact of adding immunotherapy was unknown. **Methods** This ongoing open-label randomized phase 2 trial is investigating maintenance dostarlimab in patients with high-risk locally advanced cervical cancer (LACC; FIGO 2009 definition) with complete/partial response after standard concurrent CRT. Patients were randomized 1:2 to observation or dostarlimab (500 mg q3w for 4 cycles → 1000 mg q6w for up to 2 years in

total), stratified by histology, response to CRT, and combined FIGO 2009 stage/nodal status. The primary endpoint is progression-free survival (PFS) per RECIST v1.1, with final analysis prespecified after 74 PFS events. The protocol was amended to add an interim analysis after ≥ 32 PFS events, reported here. Overall survival (OS) is a secondary endpoint. **Results** In 134 patients randomized Aug 2019–Jun 2023, FIGO 2009 stage at diagnosis was IB–IIB/III/IVA in 61%/34%/5%, 69% had pelvic and 28% paraaortic positive lymph nodes, and 69% were in complete response. Patients received current standard CRT and 79% underwent 3D HR-CTV brachytherapy. Median cisplatin duration was 4.3 (IQR 4.1–5.1) weeks. By the data cutoff (17 Sep 2025; median follow-up 40.6 months), all patients had discontinued dostarlimab (56% after 2 years of treatment, 18% disease progression, 15% toxicity related). Median dostarlimab duration was 24.7 (IQR 8.4–25.1) months. At the interim analysis with 34/74 (46%) of the PFS events required for final analysis, PFS numerically but non-significantly favored dostarlimab (stratified hazard ratio 0.64, 95% CI 0.31–1.31; 3-year PFS rate 67% [observation] vs 77% [dostarlimab]) (Table). The most common grade ≥ 3 adverse events with dostarlimab were diarrhea (5%) and asthenia (3%); 1 patient died from duodenal perforation unrelated to treatment. **Conclusions** In patients with high-risk LACC, PFS at the interim analysis exceeded expectations in both arms. PFS numerically favored dostarlimab, although not reaching statistical significance.

	PFS	
	Observation (n=46)	Dostarlimab (n=28)
Events, n (%)	14 (30)	20 (23)
Stratified HR (95% CI)	0.64 (0.31–1.31); 1-sided p=0.11	
Rates, % (95% CI)		
1-year	80 (68–92)	82 (74–90)
2-year	75 (62–88)	79 (70–87)
3-year	67 (52–83)	77 (68–86)
4-year	62 (45–79)	74 (63–84)

AVUTOMETINIB AND DEFACTINIB IN RECURRENT LOW-GRADE SEROUS OVARIAN CANCER (LGSOC): A PHASE II STUDY IN JAPANESE PATIENTS (RAMP201J)

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Abstract Body: Introduction: Avutometinib (oral RAF/MEK dual inhibitor) + defactinib (oral selective FAK inhibitor), is approved for treatment of recurrent *KRAS*-mutated low-grade serous ovarian cancer (LGSOC) based on results from RAMP 201 conducted in the US, Europe, and Canada (NCT04625270). We evaluated the efficacy, safety, and pharmacokinetics of avutometinib + defactinib in Japanese patients with advanced/recurrent LGSOC. **Methods:** RAMP 201J is an ongoing, single-arm, phase II study in Japanese patients with advanced/recurrent LGSOC who progressed on platinum-based chemotherapy. Patients received avutometinib 3.2 mg orally twice weekly + defactinib 200 mg orally twice daily for 3 weeks followed by 1 week off (4-week cycle). The primary endpoint was objective response rate (ORR) assessed by blinded independent central review. This ad hoc interim efficacy analysis evaluated investigator-assessed (INV) response. **Results:** As of May 2026, 16 patients were enrolled (median follow-up: 12.4 months); 11/16 patients remain on treatment. Median age was 47 years, 44% of patients had *KRAS* mutations, and 44% had ≥ 4 prior lines of therapy. INV ORR was 44% (*KRAS* mutant, 71%; *KRAS* wild-type, 22%). INV disease control rate was 94% (*KRAS* mutant, 100%; *KRAS* wild-type, 89%). Pharmacokinetic profile (maximum concentration and steady-state exposure) was similar between patients in RAMP 201 and RAMP 201J. The most common treatment-related adverse events (AEs; **Table**) were managed with conservative treatment or dose interruptions/reductions. No treatment discontinuations due to AEs were reported. **Conclusion:** Avutometinib + defactinib demonstrated promising efficacy, similar pharmacokinetics, and manageable safety profile in Japanese patients with advanced/recurrent LGSOC, consistent with results from RAMP

201.

Table. Treatment-related AEs

Treatment-related AEs, ^a n (%)	All patients (N=16)	
Preferred term	All grades	Grade 3 ^b
Any treatment-related AE	16 (100)	9 (56)
Treatment-related AEs (≥25% of patients)		
Nonlaboratory AEs		
Peripheral edema	9 (56)	0
Stomatitis	9 (56)	0
Diarrhea	8 (50)	0
Nausea	8 (50)	0
Rash	8 (50)	3 (19)
Malaise	7 (44)	2 (13)
Paronychia	6 (38)	0
Vision blurred	5 (31)	0
Rash maculopapular	5 (31)	1 (6)
Acne	4 (25)	0
Dermatitis acneiform	4 (25)	1 (6)
Dry eye	4 (25)	0
Laboratory-related AEs		
Increased CPK	15 (94)	3 (19)
Increased ALT	5 (31)	2 (13)
Increased blood bilirubin	5 (31)	0

^aMost common AEs (preferred term) considered by the investigator to be related to study drug (either avotemetinib or defactinib). ^bOther grade 3 events included back pain, neck pain, anemia, hypoalbuminemia, and pyogenic granuloma (1 patient each).

AE, adverse event; ALT, alanine aminotransferase; CPK, creatine phosphokinase.

MOCERTATUG REZETECAN (GSK5733584), A B7-H4-TARGETED ANTIBODY-DRUG CONJUGATE (ADC), IN PLATINUM-RESISTANT OVARIAN CANCER (PROC) AND ENDOMETRIAL CANCER (EC): FIRST RESULTS FROM THE GLOBAL BEHOLD-1 STUDY

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Abstract Body: Objective: Mocertatug rezetecan (Mo-Rez, GSK5733584) is a novel ADC comprised of a humanised IgG1 monoclonal anti-B7-H4 antibody conjugated to rezetecan (topoisomerase 1 inhibitor-payload complex) via a protease cleavable linker (Drug-Antibody ratio: 6) that has shown promising antitumour activity in Chinese patients (pts) with PROC.¹ We report first data from the global BEHOLD-1 (NCT06431594) trial of Mo-Rez monotherapy in pts with PROC or recurrent EC unselected for B7-H4 tumour expression. **Methods:** BEHOLD-1 is a 2-part, open-label, Phase 1 study. Phase 1a dose escalation (rolling 6 design to determine maximum tolerated dose [MTD]) planned to assess up to 4 Mo-Rez dose levels given intravenously every 3 weeks (Q3W) until progression/toxicity in pts with advanced solid tumours. In Phase 1b dose expansion, pts

with PROC or EC (1–3 prior lines of therapy) were randomised to 3 or 2 Mo-Rez dose levels, respectively. Primary endpoints: incidence of dose-limiting toxicity (DLT-evaluable; Phase 1a); confirmed objective response rate (ORR) by investigator per RECIST 1.1 (Phase 1b). **Results:** A total of 224 pts were enrolled (Phase 1a: n=44 [21 OC], data cut-off [DCO] 1 Jul 2025; Phase 1b: n=180 [n=131 PROC, n=49 EC]; DCO 12 Nov 2025). In Phase 1a, of 16 DLT-evaluable pts, 1 experienced 2 DLTs (febrile neutropenia and thrombocytopenia) at 5.8 mg/kg Q3W. MTD was not reached; maximum applicable dose was 5.8 mg/kg Q3W. In Phase 1b, 130 pts with PROC and 48 pts with EC received ≥ 1 dose at DCO. Median follow-up was 6.1 and 4.0 months in PROC and EC, respectively. At highest dose levels, 5.8 mg/kg Q3W for PROC and 4.8 mg/kg Q3W for EC, confirmed ORR was 62% and 67%, respectively (**Table**). Median duration of response was not reached. In Phase 1b, the most common treatment-related adverse event (TRAE) was nausea (68%, PROC; 67%, EC). Gr ≥ 3 TRAEs occurred in 42% and 35% of pts with PROC and EC, respectively, and were mostly haematological (most common: neutrophil count decrease [15% in both PROC and EC]; neutropenia [12% and 6%]; and anaemia [8% and 15%]); frequency of these events was dose-dependent as were dose delay/reductions, indicating a dose-dependent impact on tolerability. Treatment discontinuation due to TRAEs was low (2% in PROC, 4% in EC). **Conclusions:** Mo-Rez showed encouraging antitumour activity in pts with PROC and EC and had a manageable safety profile. Mo-Rez is being evaluated in global Phase 3 trials in PROC (NCT07286266) and recurrent EC (NCT07286331). **Funding:** GSK (222730). Writing support provided by Avalere Health, funded by GSK. **Reference:** 1. Yuan G, et al. *Ann Oncol.* 2025;36(Suppl 2):S717–18.

Table. ORR by investigator per RECIST 1.1

	Phase 1b				
	PROC			EC	
Dose (mg/kg, Q3W)	2.8 (n=35)	4.8 (n=34)	5.8 (n=34)	2.8 (n=11)	4.8 (n=12)
Confirmed ORR, n (%), [95% CI]	11 (31) [16.9, 49.3]	18 (53) [35.1, 70.2]	21 (62) [43.6, 77.8]	1 (9) [0.2, 41.3]	8 (67) [34.9, 90.1]

ORR reported in all randomised pts who had the opportunity for ≥ 18 weeks of follow up. CI, confidence interval. © **Society of Gynecologic Oncology (2026). Reproduced with permission.**