Highlights in Gynecologic Cancer

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Pembrolizumab Plus Chemotherapy Provides Overall Survival Benefit in Advanced Endometrial Cancer

Adding pembrolizumab (Keytruda, Merck) to chemotherapy with carboplatin/paclitaxel (CP) provides an overall survival (OS) benefit to patients with advanced or recurrent endometrial cancer (EC), according to long-term results from the phase 3 NRG-GY018 trial.

The trial previously demonstrated significant improvements in progression-free survival (PFS) with the addition of pembrolizumab to CP in both mismatch repair–deficient (dMMR) and mismatch repair–proficient (pMMR) EC populations, findings that led to US Food and Drug Administration (FDA) and European Medicines Agency approval of the regimen in 2024. OS data were immature.

In the updated OS analysis, the median follow-up was 49 months in the dMMR cohort (n=222) and 44 months in the pMMR cohort (n=588). In the dMMR cohort, pembrolizumab plus CP reduced the risk of death by 44% vs placebo plus CP (hazard ratio [HR], 0.56; 95% CI, 0.34-0.92). The 48-month OS rate was 78.6% with pembrolizumab vs 60.4% with placebo; median OS was not reached in either arm. In the pMMR cohort, median OS was 44.4 months with pembrolizumab vs 35.1 months with placebo (HR, 0.86; 95% CI, 0.69-1.08); this result was directionally favorable but did not reach statistical significance.

Notably, the OS benefit persisted despite substantially greater post-study immune checkpoint inhibitor (ICI) use in the control arm. A total of 93.2% of the dMMR and 81.1% of the pMMR placebo patients who received subsequent therapy received an ICI. The median time on post-progression ICI therapy was 5.5 months (95% CI, 4.1-5.7) in the pembrolizumab arm and 6 months (95% CI, 4.8-8.1) in the placebo arm.

Presenter Ramez N. Eskander, MD, of the Moores Cancer Center at UC San Diego Health, in La Jolla, California, concluded that these data add "great confidence" to the current US and international approvals of pembrolizumab plus CP, followed by pembrolizumab maintenance, in patients with advanced or recurrent EC, irrespective of MMR status.

Eskander RN, Sill M, Beffa L, et al. Updated overall survival analysis and examination of subsequent therapy in endometrial cancer patients treated with pembrolizumab plus carboplatin/paclitaxel as compared to CP plus placebo in the NRG-GY018 trial [ASCO abstract 5502]. *J Clin Oncol*. 2026;44(16)(suppl).

Relacorilant Plus Nab-paclitaxel Improves Overall Survival in Platinum-Resistant Ovarian Cancer Regardless of Prior Taxane History

Relacorilant (Lifyorli, Corcept Therapeutics), a first-in-class selective glucocorticoid receptor antagonist, added to nab-paclitaxel (Abraxane, Bristol Myers Squibb) significantly improved OS vs nab-paclitaxel alone in patients with platinum-resistant ovarian cancer (PROC); a consistent benefit was observed across subgroups defined by prior taxane use, according to final OS results from the phase 3 ROSELLA trial.

The open-label trial randomized 381 patients with PROC 1:1 to receive relacorilant (150 mg orally the day before, of, and after nab-paclitaxel) plus nab-paclitaxel (80 mg/m^2 intravenously [IV] on days 1, 8, and 15 of each 28-day cycle) or nab-paclitaxel monotherapy (100 mg/m^2 IV on the same schedule). All patients had previously received bevacizumab and 1 to 3 lines of therapy. The trial met both its primary endpoints: PFS and OS.

At a median follow-up of 24.8 months, relacorilant plus nab-paclitaxel reduced the risk of death by 35% vs monotherapy (HR, 0.65; 95% CI, 0.51-0.83; *P*=.0004). Median OS was 16.0 months with the combination vs 11.9 months with nab-paclitaxel alone, an increase of 4.1 months. Prior taxane use was nearly universal (99.5%), and the OS benefit was consistent irrespective of whether the taxane-free interval was short (≤6 months: HR, 0.60; median difference, 5.7 months) or long (>6 months: HR, 0.66; median difference, 3.6 months) and regardless of whether a taxane had been used in the most recent regimen (HR, 0.67) or had not been used (HR, 0.63).

The safety profile was favorable and consistent with that in the primary analysis; no new signals were identified, and no relacorilant-related fatal adverse events or cases of adrenal insufficiency occurred. The most common adverse reactions, defined by an incidence of at least 20%, were decreased hemoglobin, decreased neutrophils, fatigue, nausea, diarrhea, decreased platelets, rash, and

decreased appetite.

Presenter Lucy Gilbert, MD, of McGill University Health Centre, in Montreal, Canada, concluded that this study supports the use of relacorilant plus nab-paclitaxel as a new treatment option for patients with advanced EC, without the need for biomarker selection.

Relacorilant plus weekly nab-paclitaxel received FDA approval on March 25, 2026, for the treatment of patients with PROC who previously received 1 to 3 systemic treatment regimens, at least one of which included bevacizumab.

Gilbert L, You B, Olawaiye A, et al. Overall survival subgroup analyses for prior taxane use in the phase 3 ROSELLA trial of relacorilant plus nab-paclitaxel versus nab-paclitaxel monotherapy in patients with platinum-resistant ovarian cancer [ASCO abstract 5503]. *J Clin Oncol*. 2026;44(16)(suppl).

Shifting More Chemotherapy Cycles to Neoadjuvant Setting Does Not Improve DFS in Advanced Ovarian Cancer

Delaying cytoreductive surgery until after 6 cycles of neoadjuvant chemotherapy (NAC) did not improve disease-free survival (DFS) vs the standard approach of interval cytoreductive surgery after 3 cycles in patients with advanced high-grade epithelial ovarian cancer, according to results from the phase 2 CHRONO trial.

The randomized multicenter trial enrolled 209 patients with stage IIIB to IVA high-grade epithelial ovarian cancer who were not candidates for complete primary surgery but whose cancer became amenable to complete resection after 3 cycles of platinum-based NAC. Patients were randomized 1:1 to a control arm of interval cytoreductive surgery followed by 5 additional cycles of chemotherapy or to an experimental arm of 3 further cycles of NAC followed by delayed cytoreductive surgery and 2 additional cycles of chemotherapy. Maintenance therapy was administered per standard of care in both arms.

After a median follow-up of 40.4 months, median DFS was 20.2 months (95% CI, 18.2-23.6) in the control arm vs 23.4 months (95% CI, 19.0-30.4) in the experimental arm, a difference that was not statistically significant (HR, 0.88; 95% CI, 0.63-1.24; *P*=.48). The complete resection rate was numerically higher in the delayed surgery arm (90% vs 83.2%), but the rate of major postoperative complications within 30 days was also higher (11% vs 5%), although this difference likewise did not reach significance (*P*=.11). No deaths occurred within 30 days after surgery in either arm. Quality-of-life analyses revealed no significant differences between the arms, although trends toward improved social functioning and sexuality and decreased insomnia were noted with delayed surgery.

"Further studies are needed to explore which patients may benefit from surgery following 6 cycles of neoadjuvant chemotherapy based on tumor biology and chemosensitivity," concluded presenter Jean-Marc Classe, MD, of the Institut de Cancérologie de l'Ouest, in Saint-Herblain, France.

Ferron G, Dupre P-F, Georgeac C, et al. CHRONO: a randomized phase II trial of the chronology of surgery after neoadjuvant chemotherapy for ovarian cancer [ASCO abstract 5505]. *J Clin Oncol*. 2026;44(16)(suppl).

TUB-040 Demonstrates High Response Rates and Durable Benefit in Platinum-Resistant Ovarian Cancer

TUB-040, a novel antibody-drug conjugate (ADC) targeting NaPi2b, achieved high response rates and durable disease control with a manageable safety profile in heavily pretreated patients with PROC, according to phase 1 dose-escalation results from the NAPISTAR 1-01 trial.

NaPi2b is a rapidly internalizing sodium phosphate transporter expressed in more than 95% of high-grade serous ovarian cancers (HGSOCs). TUB-040 is an ADC with a drug-to-antibody ratio of 8 comprising a humanized, Fc-silenced immunoglobulin G1 monoclonal antibody conjugated to exatecan via a cleavable, cysteine-selective P5 linker, engineered to minimize off-target toxicity while providing strong bystander activity.

As of April 5, 2026, 67 patients with PROC had received TUB-040 for a median of 10 cycles. The patients were heavily pretreated with a median of 4 prior lines of therapy and prior exposure to bevacizumab (84%), poly(ADP-ribose) polymerase (PARP) inhibitors (76%), and mirvetuximab soravtansine (Elahere, AbbVie; 13%). Among the 46 patients treated at dose levels of 1.67 to 3.3 mg/kg, the unconfirmed and confirmed objective response rates (ORRs) were 67% (95% CI, 50.2%-80.5%) and 61% (95% CI, 45.4%-74.9%), respectively, with 2 complete responses. The disease control rate was 96% (95% CI, 85.2%-99.5%), and 79% of the responders maintained a response beyond 6 months, with median duration of response (DOR) not yet reached. In the overall population, median PFS was 11.0 months (95% CI, 7.5 to not available). Responses were consistent across subgroups regardless of prior treatment history or level of NaPi2b expression.

The safety profile was favorable, with predominantly low-grade hematologic events and no clinically relevant pneumonitis, neuropathy, ocular toxicity, or treatment discontinuations due to adverse events. Dose optimization is currently ongoing.

"These encouraging results in platinum-resistant ovarian cancer support the rapid development of TUB-40 in a non–biomarker-restricted ovarian cancer population," concluded presenter Toon Van Gorp, MD, of the

Leuven Cancer Institute, in Leuven, Belgium.

Several other topoisomerase inhibitors are in testing for ovarian cancer irrespective of a biomarker, including rinatabart sesustecan and raludotatug deruxtecan.

Van Gorp T, Sehouli J, Richardson DL, et al. NAPISTAR 1-01: results of phase 1 dose escalation of monotherapy with TUB-040, a novel NaPi2b-targeting exatecan ADC, in patients with platinum-resistant ovarian cancer [ASCO abstract 5513]. *J Clin Oncol*. 2026;44(16)(suppl).

Telisotuzumab Adizutecan Shows Antitumor Activity Across Histologies in Platinum-Resistant Ovarian Cancer

In phase 1 results from a basket study, telisotuzumab adizutecan (Temab-A), an ADC that targets c-Met protein, demonstrated meaningful antitumor activity and a manageable safety profile in patients with PROC, including those with clear cell carcinoma, which is a histology with limited treatment options.

The open-label study enrolled 41 patients with recurrent PROC, who received Temab-A at 2.4 mg/kg IV every 3 weeks. The patients were heavily pretreated, with a median of 3 prior lines of therapy; 73% had previously received bevacizumab, and 59% had received a PARP inhibitor. Tumor histologies included HGSOC (n=26) and clear cell carcinoma (n=8).

At a median follow-up of 9.5 months, the confirmed ORR (cORR) was 44% overall (95% CI, 28%-60%), comprising 18 partial responses and no complete responses. The cORR was 46% (95% CI, 27%-67%) in the HGSOC subgroup and 50% (95% CI, 16%-84%) in the clear cell subgroup. The confirmed clinical benefit rate (CBR) was 85% overall and 100% in the patients with clear cell carcinoma. Median DOR was 5.7 months (95% CI, 2.8 to not estimable), and median PFS was 5.4 months (95% CI, 4.1-6.8). Exploratory biomarker analyses suggested a higher level of activity in tumors with greater c-Met protein expression.

The most common treatment-related adverse events (TRAEs) of any grade were anemia (59%), nausea (59%), and fatigue (39%). Grade 3 or higher TRAEs occurred in 59% of patients and were predominantly hematologic; no TRAEs led to death, and the adjudicated rate of interstitial lung disease/pneumonitis was 5% (both grade 1).

"These results support further development of Temab-A for patients with ovarian cancer," concluded presenter Gini F. Fleming, MD, of UChicago Medicine, in Chicago, Illinois.

Fleming GF, Kurnit K, Pelster M, et al. Phase 1 basket study of telisotuzumab adizutecan (Temab-A, ABBV-400), a c-Met protein–targeting antibody-drug conjugate: results from patients with platinum-resistant ovarian/primary peritoneal/fallopian tube cancer [ASCO abstract 5514]. *J Clin Oncol*. 2026;44(16)(suppl).

Abemaciclib Plus Hormonal Therapy Shows Durable Benefit in Low-Grade Serous Ovarian Cancer and ER-Positive Endometrial Cancer

Abemaciclib (Verzenio, Lilly) combined with hormonal therapy demonstrated promising and durable clinical activity in patients with low-grade serous ovarian cancer (LGSOC) and estrogen receptor–positive (ER+) EC, with activity in LGSOC independent of *KRAS* mutational status, according to final results from a single-center phase 2 study.

The trial enrolled 43 evaluable patients: 21 with ER+ EC, 14 with LGSOC, and 8 with HGSOC selected for CDK4/6 molecular activation features. Patients were heavily pretreated, with a median of 3 prior lines of therapy. Abemaciclib was administered at 150 mg twice daily with physician's choice of hormonal therapy.

In the patients with LGSOC, the 24-week PFS rate was 71% (95% CI, 48%-95%), and median PFS was 17.5 months (95% CI, 3.5 to not reached). The CBR was 79%. Notably, benefit was observed regardless of *KRAS* mutational status, with median PFS of 11.9 months in *KRAS*-mutant patients vs 17.5 months in *KRAS* wild-type patients (P=.89). Impressively, 28% of patients with LGSOC remained on treatment for more than 3 years, with the longest treatment still ongoing at 4.6 years.

In the patients with ER+ EC, the 24-week PFS rate was 56% (95% CI, 35%-78%), and median PFS was 9.0 months (95% CI, 2.4-11.2). Exploratory biomarker analyses identified the no specific molecular profile (NSMP) subgroup as deriving the greatest benefit, with a median PFS of 10.4 months vs 1.9 months in the non-NSMP group (P=.02). In contrast, little activity was observed in the HGSOC cohort, with a 24-week PFS rate of 12.5% and a median PFS of 1.6 months. No new safety signals were identified across subgroups.

"Abemaciclib demonstrated promising clinical activity in patients with LGSOC regardless of *KRAS* mutational status and in ER+ EC, with the greatest activity observed in the NSMP group," concluded presenter Jordyn Silverstein, MD, of the University of California, Los Angeles.

Silverstein J, Tseng C-H, Grande I, et al. Updated efficacy, safety, and exploratory biomarker analyses of a phase II trial of abemaciclib plus hormonal therapy in recurrent ovarian and endometrial cancer [ASCO abstract 5516]. *J Clin Oncol*. 2026;44(16)(suppl).