Check for updates

Primary Analysis of EPIK-O/ENGOT-ov61: Alpelisib Plus Olaparib Versus Chemotherapy in Platinum-Resistant or Platinum-Refractory High-Grade Serous Ovarian Cancer Without *BRCA* Mutation

Panagiotis A. Konstantinopoulos, MD, PhD[1]; Jae Weon Kim, MD, PhD[2]; Gilles Freyer, MD, PhD[3,4]; Jung Yun Lee, MD, PhD[5]; Lydia Gaba, MD[6]; Rachel N. Grisham, MD[7]; Nicoletta Colombo, MD, PhD[8,9,10]; Xiaohua Wu, MD, PhD[11]; Jalid Sehouli, MD[12,13]; Felipe Cruz, MD, PhD[14]; David Cibula, MD, PhD[15]; Bradley J. Monk, MD[16]; Gitte-Bettina Nyvang, MD[17,18]; Michael Friedlander, MBChB, PhD[19]; Domenica Lorusso, MD, PhD[20,21,22]; Els Van Nieuwenhuysen, MD, PhD[23,24]; Rozita Malik, MBBS[25]; Rosalind Glasspool, MD, PhD[26,27]; Christian Marth, MD, PhD[28]; Alexandra Leary, MD, PhD[4,29]; Alfonso Cortés-Salgado, MD[30]; Claudio Zamagni, MD[31]; Frederik Marmé, MD, PhD[32]; Jozef Sufliarsky, MD, PhD[33]; Patsy Hinson[34]; Monica Zuradelli, MD[35]; Craig Wang, PhD[35]; Fei Su, PhD[36]; Ines Paule, PhD[35]; Michelle Miller, MD, MPH[35]; Ursula A. Matulonis, MD[1]; and Antonio González-Martín, MD, PhD[37,38]

DOI https://doi.org/10.1200/JCO-25-00225

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

ABSTRACT

PURPOSE Patients with platinum-resistant/platinum-refractory high-grade serous ovarian cancer (HGSOC) without a *BRCA* mutation have poor prognosis and limited treatment options. We report efficacy and biomarker data from EPIK-O, which investigated alpelisib + olaparib versus single-agent chemotherapy in these patients.

PATIENTS AND METHODS EPIK-O was an open-label, phase III trial that randomly assigned patients with platinum-resistant/platinum-refractory HGSOC with no germline or known somatic *BRCA* mutation 1:1 to alpelisib 200 mg once daily + olaparib 200 mg twice daily or treatment of physician's choice (TPC; paclitaxel 80 mg/m² once weekly or pegylated liposomal doxorubicin 40-50 mg/m² once every 28 days). Patients had 1-3 previous systemic therapies. Previous bevacizumab was required (unless contraindicated); previous poly(adenosine diphosphate-ribose) polymerase inhibitors were allowed. Primary end point was progression-free survival (PFS) per RECIST 1.1 (blinded independent review committee [BIRC]). Secondary efficacy end points included overall response rate (ORR; per BIRC), duration of response (per BIRC), and overall survival (OS; key secondary end point).

RESULTS A total of 358 patients (alpelisib + olaparib [n = 180], TPC [n = 178]) were included. The median follow-up time was 9.3 months. At data cutoff (April 21, 2023), 33 (18.3%) and 30 (16.9%) patients remained on treatment with alpelisib + olaparib and TPC, respectively. The median PFS (BIRC) was 3.6 versus 3.9 months (hazard ratio [HR], 1.14 [95% CI, 0.88 to 1.48]; one-sided $P = .84$) for alpelisib + olaparib versus TPC. The ORR was 15.6% (95% CI, 10.6% to 21.7%) versus 13.5% (95% CI, 8.8% to 19.4%). The median OS was 10.0 versus 10.6 months (HR, 1.22; 95% CI, 0.87 to 1.71). The safety profile of alpelisib + olaparib was consistent with that observed for the individual agents.

CONCLUSION The primary objective, PFS improvement, was not met in EPIK-O. No new or unexpected adverse events were observed. Biomarker analyses provided new insights for responders to alpelisib + olaparib.

ACCOMPANYING CONTENT

Data Sharing Statement

Data Supplement

Protocol

Accepted June 6, 2025
Published July 23, 2025

J Clin Oncol 43:2908-2917
© 2025 by American Society of Clinical Oncology

View Online Article

Creative Commons Attribution Non-Commercial No Derivatives 4.0 License

INTRODUCTION

Platinum-resistant high-grade serous ovarian cancer (HGSOC) has poor prognosis, with a median overall survival (OS) of 12-15 months.[1] Treatment options are very limited for these patients; platinum-free chemotherapy is considered standard of care, but response rates remain low and mostly temporary, with progression-free survival (PFS) and overall response rate (ORR) decreasing with increasing lines of therapy.[2,3] In patients with platinum-resistant disease, poly(adenosine diphosphate-ribose) polymerase inhibitors (PARPis) have shown activity only in *BRCA*-mutated tumors;

CONTEXT

Key Objective

Is the combination of alpelisib + olaparib more effective than single-agent chemotherapy (treatment of physician's choice [TPC]: paclitaxel or pegylated liposomal doxorubicin) for patients with platinum-resistant/platinum-refractory high-grade serous ovarian cancer without BRCA mutation?

Knowledge Generated

There was no significant difference in progression-free survival (PFS) with alpelisib + olaparib versus TPC. The safety profile of the combination of alpelisib + olaparib was consistent with what was observed previously with the individual agents. Biomarker analyses provided new insights for responders to alpelisib + olaparib.

Relevance *(G.F. Fleming)*

This phase III trial, one product of many attempts to "sensitize" ovarian cancers to poly(adenosine diphosphate-ribose) polymerase inhibitors, showed no evidence that alpelisib plus olaparib was superior to TPC, and re-demonstrated the dismal PFS (3.6 *v* 3.9 months) overall for women with platinum-resistant ovarian cancer.*

*Relevance section written by *JCO* Associate Editor Gini F. Fleming, MD.

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

PARPis have shown minimal benefit in patients with *BRCA* wild-type (wt) platinum-resistant tumors—ORRs of <5% have been reported.[4-7] The low response rate in this group highlights the urgent need for novel strategies to expand PARPi use in patients with platinum-resistant *BRCA*-wt tumors.

Alpelisib is an orally bioavailable, α-specific phosphatidylinositol-3-kinase (PI3K) inhibitor that inhibits both mutated and wt PI3K isoforms.[8] Alpelisib selectively inhibits p110α with 50-fold greater potency than other PI3K isoforms (β, δ, ɣ).[8-10] PI3K inhibitors have shown effectiveness in advanced solid tumors when used in combination therapies.[11] The synergism between PARPis and PI3K inhibitors has been demonstrated in breast and ovarian cancer preclinical studies; PI3K inhibition, through downregulation of *BRCA1* and *BRCA2*, inactivation of homologous recombination repair (HRR), increased DNA damage, and increased poly (ADP-ribose) levels, led to sensitization to PARPis.[12-14] Based on these preclinical and early clinical data in recurrent ovarian and breast cancers, it was hypothesized that alpelisib may sensitize platinum-resistant *BRCA*-wt HGSOC to PARPis.[10-14]

Here, we present the results from the phase III EPIK-O/ENGOT-ov61 trial (ClinicalTrials.gov identifier: NCT04729387), which studied alpelisib + olaparib versus physician's choice single-agent chemotherapy in patients with platinum-resistant or platinum-refractory HGSOC with *BRCA*-wt.

PATIENTS AND METHODS

Study Design

EPIK-O was a phase III, multicenter, open-label, randomized study. Women 18 years and older were randomly assigned 1:1 to alpelisib (200 mg orally once daily [28-day cycle]) + olaparib (200 mg orally twice daily [28-day cycle]) or investigator's choice of cytotoxic chemotherapy (treatment of physician's choice [TPC]). Alpelisib and olaparib doses were chosen based on the maximum tolerated dose from the phase 1b study.[14] Chemotherapy options were paclitaxel (80 mg/m^2 intravenously once weekly [28-day cycle]) or pegylated liposomal doxorubicin (PLD; 40-50 mg/m^2 intravenously once every 28 days). Switching between chemotherapy agents after the first dose of chemotherapy and crossover between arms were not permitted. Random assignment was stratified by relapse from last platinum dose (<3/3-6 months), previous PARPi use (yes/no), and previous bevacizumab use (yes/no). Patients received study treatment until disease progression (per RECIST version 1.1 as assessed by the blinded independent review committee [BIRC]), unacceptable toxicity, or discontinuation because of any other reason.

Patients

Patients were eligible if they had histologically confirmed HGSOC or high-grade endometrioid ovarian, fallopian tube, or primary peritoneal cancer; germline *BRCA*-wt and no known somatic *BRCA* mutation (testing not required); and measurable platinum-resistant or platinum-refractory disease. In the absence of measurable disease, the disease had to be evaluable by Gynecologic Cancer InterGroup criteria for CA-125. Platinum-resistant disease was defined as disease progression 1-6 months after completion of platinum-based therapy; platinum-refractory disease was defined as disease progression during treatment or within 4 weeks of the last dose. Patients who never responded to platinum and whose disease progressed during initial platinum-based chemotherapy were ineligible. Patients were required to have one to three previous systemic therapies. Previous bevacizumab was

required unless contraindicated. Previous PARPi exposure was allowed. Patients were included regardless of *PIK3CA* mutation status.

Outcome Measures

The primary end point was PFS (time from random assignment to first documented progression or death because of any cause), assessed by BIRC per RECIST 1.1. PFS was censored at the date of last adequate tumor assessment if a patient did not have an event at the time of analysis.

OS (time from random assignment to death because of any cause) was a key secondary end point. Patients who did not have an OS event were censored at the latest date they were known to be alive. Other secondary end points included ORR (per BIRC), duration of response (DOR; per BIRC), clinical benefit rate (CBR; confirmed complete response, partial response, or stable disease ≥24 weeks; per BIRC), and safety.

Biomarker Responder Analyses

In a prespecified exploratory analysis, next-generation sequencing (NGS) was used to identify biomarkers associated with response to alpelisib + olaparib (Supplementary Methods, online only).

Safety

Adverse events (AEs) were coded using the Medical Dictionary for Regulatory Activities v26.0 and were assessed and graded with the Common Terminology Criteria for Adverse Events v4.03.

Statistical Methods

All randomly assigned patients were included for primary and secondary efficacy analyses. Safety was assessed in all randomly assigned patients who received ≥1 dose of study treatment.

The study was powered at 93.5% to detect a hazard ratio (HR) of 0.6 (at a one-sided 2.5% level of significance) for PFS at final analysis using ≈224 events. The study design included an interim futility analysis for efficacy (PFS). PFS and OS were evaluated by the Kaplan-Meier method and stratified Cox models. A stratified log-rank test with an overall one-sided 2.5% level of significance was used for hypothesis testing of PFS. A hierarchical testing procedure was used for OS analysis and was planned to be performed only if the primary end point (PFS) was statistically significant. Exploratory analysis by chemotherapy choice was performed to evaluate efficacy results in paclitaxel and PLD groups separately. Additional details are provided in the Supplementary Methods and described elsewhere.[10]

All studies were conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki. The trial protocol and all amendments were approved by the respective institutional review boards. All patients provided written informed consent.

RESULTS

Study Population and Disposition

A total of 358 patients were randomly assigned to alpelisib + olaparib (n = 180) or TPC (n = 178). All patients in the alpelisib + olaparib arm received treatment. In the TPC arm, 14 patients (7.9%) did not receive treatment, 70 (39.3%) received paclitaxel, and 94 (52.8%) received PLD (Fig 1). At data cutoff (April 21, 2023), 33 (18.3%) patients in the alpelisib + olaparib arm and 30 (16.9%) patients in the TPC arm were still receiving treatment. Baseline characteristics were balanced between the two arms (Table 1). Most patients in both arms had predominantly serous adenocarcinoma histology/cytology (92.2% and 97.2%). Overall, 35.2% of patients had received previous PARPi, and 79.6% previous bevacizumab.

The overall median follow-up time (random assignment to data cutoff) was 9.3 months (range, 2.8-20.3 months). The median duration of exposure for alpelisib + olaparib was 3.2 months (range, 0.1-18.5 months); the median relative dose intensity was >90% for both arms (Data Supplement, Table S1, online only). The discontinuation rate was 81.7% for the alpelisib + olaparib arm and 75.3% for the TPC arm. Discontinuations were primarily due to disease progression (alpelisib + olaparib, 70 [38.9%]; TPC, 85 [47.8%]), followed by AEs (24 [13.3%] and eight [4.5%]), patient decision (21 [11.7%] and 10 [5.6%]), and physician decision (17 [9.4%] and 16 [9.0%]).

Efficacy

The trial met its PFS futility criteria, but considering that the futility rule was nonbinding and enrollment had been completed, the data monitoring committee did not recommend stopping the study. The protocol-specified final PFS analysis was conducted based on 244 events observed at the data cutoff date: 134 (74.4%) in the alpelisib + olaparib arm and 110 (61.8%) in the TPC arm.

The median PFS per BIRC was 3.6 months (95% CI, 3.4 to 4.3 months) in the alpelisib + olaparib arm and 3.9 months (95% CI, 3.7 to 5.4 months) in the TPC arm (HR, 1.14; 95% CI, 0.88 to 1.48; one-sided $P = .84$; Fig 2A). The prespecified boundary for demonstrating statistical significance for the primary end point (PFS) was not crossed. Consistent with the primary analysis, supportive analysis for PFS based on local investigator assessment demonstrated a median PFS of 3.7 months in both arms (HR, 1.02 [95% CI, 0.79 to 1.30]; descriptive one-sided $P = .54$; Fig 2B). PFS in prespecified subgroups was consistent with that observed in the intent-to-treat population (Fig 3). Exploratory analysis of PFS (BIRC) by chemotherapy choice using weighted analysis to

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

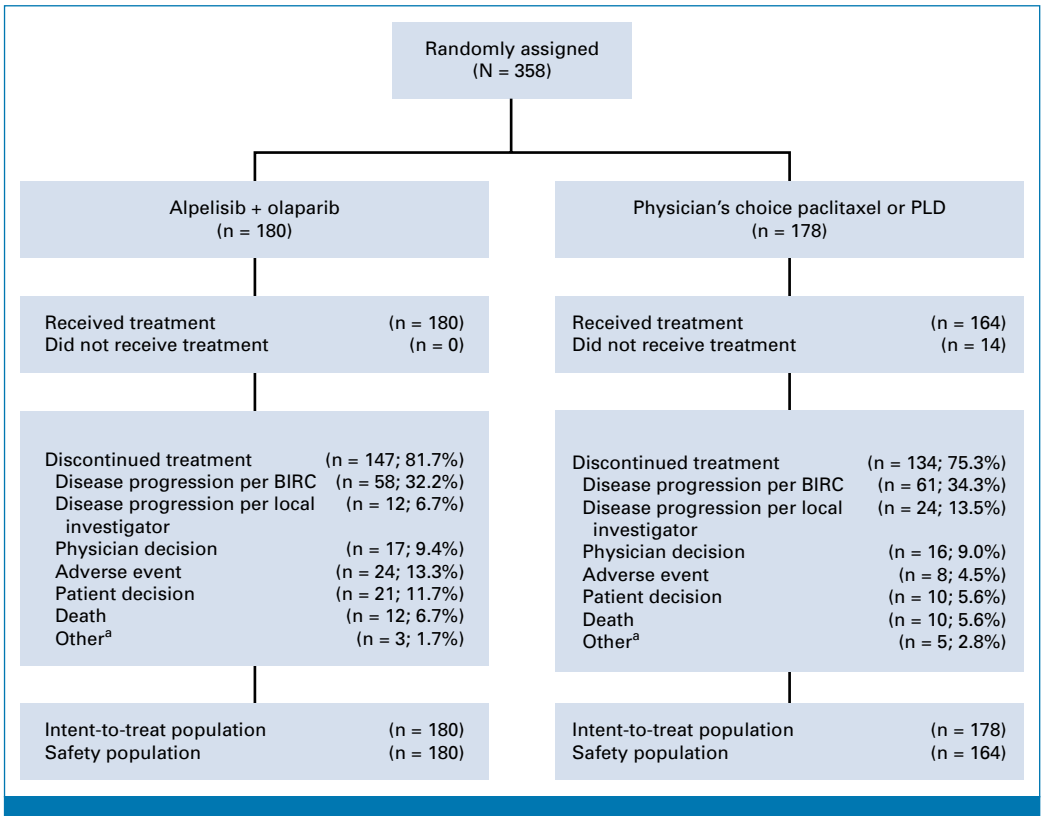

FIG 1. CONSORT diagram. [a]Includes progressive disease reported shortly after the end of treatment disposition. BIRC, blinded independent review committee; PLD, pegylated liposomal doxorubicin.

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

match the alpelisib + olaparib arm to paclitaxel and PLD groups using baseline covariates revealed that HR was worse for alpelisib + olaparib versus paclitaxel (HR, 1.41; 95% CI, 0.99 to 2.00). For PLD, the HR was 0.86 (95% CI, 0.63 to 1.19; Data Supplement, Fig S1).

The ORR was 15.6% (95% CI, 10.6% to 21.7%) in the alpelisib + olaparib arm versus 13.5% (95% CI, 8.8% to 19.4%) in the TPC arm (Table 2). Within the TPC arm, the ORR was 28.6% with paclitaxel and 4.3% with PLD. These chemotherapy subgroup data should be interpreted with caution given the nonrandomized assignment to paclitaxel versus PLD. The CBR was 21.1% versus 19.1% for alpelisib + olaparib versus TPC, respectively. The median DOR was 7.4 months (95% CI, 5.0 to 12.9 months) for alpelisib + olaparib versus 5.6 months for TPC (95% CI, 3.8 months to not evaluable).

OS was not formally tested since the primary end point of PFS was not statistically significant; therefore, OS results are presented descriptively. There were 75 (41.7%) OS events in the alpelisib + olaparib arm versus 63 (35.4%) in the TPC arm. The median OS was 10.0 versus 10.6 months (HR, 1.22; 95% CI, 0.87 to 1.71) for alpelisib + olaparib versus TPC (Data Supplement, Fig S2).

Safety

The safety population comprised 180 patients in the alpelisib + olaparib arm and 164 patients in the TPC arm. The safety profile of alpelisib + olaparib was consistent with that of the individual agents. At least one AE (any grade) occurred in 178 patients (98.9%) in the alpelisib + olaparib arm versus 160 patients (97.6%) in the TPC arm. Serious AEs were reported in 92 patients (51.1%) versus 50 patients (30.5%), respectively. The most common AEs (occurring in >40% in either arm) of any grade in the alpelisib + olaparib arm included nausea (61.7%), hyperglycemia (52.2%), vomiting (41.7%), and diarrhea (41.1%) (Table 3). The most common grade ≥3 AEs in the alpelisib + olaparib arm were hyperglycemia (18.9%), followed by vomiting (10.0%), nausea (9.4%), and anemia (7.2%).

The most common alpelisib AEs of special interest included gastrointestinal toxicity (nausea, vomiting, diarrhea) in 75.6% of patients, hyperglycemia in 55.6%, and rash in 20.6% (Data Supplement, Table S2). No patients in either arm developed myelodysplastic syndromes or acute myeloid leukemia.

Alpelisib, olaparib, and TPC (paclitaxel or PLD) dose reductions occurred in 36.7%, 45.6%, and 20.1% of patients,

TABLE 1. Demographics and Baseline Characteristics

Characteristic	Alpelisib + Olaparib, n = 180	TPC, n = 178
Age, years		
Median (range)	61 (32-81)	61 (37-84)
<65, No. (%)	113 (62.8)	112 (62.9)
≥65, No. (%)	67 (37.2)	66 (37.1)
ECOG performance status, No. (%)		
0	115 (63.9)	109 (61.2)
1	64 (35.6)	68 (38.2)
Presence of ascites, No. (%)		
Yes	39 (21.7)	30 (16.9)
No	141 (78.3)	148 (83.1)
No. of previous regimens, No. (%)		
1	39 (21.7)	43 (24.2)
2	84 (46.7)	79 (44.4)
3	54 (30.0)	54 (30.3)
4	3 (1.7)	2 (1.1)
Predominant histology/cytology, No. (%)		
Serous adenocarcinoma	166 (92.2)	173 (97.2)
Endometrioid	7 (3.9)	2 (1.1)
Clear cell adenocarcinoma	1 (0.6)	0
Other	5 (2.8)	3 (1.7)
Current extent of disease (metastatic sites), No. (%)		
Intra-abdominal	153 (85.0)	155 (87.1)
Lymph nodes	92 (51.1)	83 (46.6)
Other	123 (68.3)	121 (68.0)
Extra-abdominal	109 (60.6)	106 (59.6)
Liver	33 (18.3)	42 (23.6)
Lymph nodes	55 (30.6)	53 (29.8)
Other	25 (13.9)	17 (9.6)
Pleural effusion	34 (18.9)	22 (12.4)
Spleen	9 (5.0)	5 (2.8)
No. of metastatic sites, No. (%)		
1	73 (40.6)	79 (44.4)
2	70 (38.9)	49 (27.5)
3	19 (10.6)	35 (19.7)
4	10 (5.6)	6 (3.4)
≥5	8 (4.4)	7 (3.9)
Patients with measurable/nonmeasurable disease at baseline, No. (%)		
Measurable disease	163 (90.6)	154 (86.5)
Nonmeasurable disease	12 (6.7)	14 (7.9)
Stratification factors based on eCRF data		
Time to relapse from last platinum dose, No. (%)		
<3 months	73 (40.6)	77 (43.3)
≥3 to ≤6 months	85 (47.2)	75 (42.1)
>6 months	7 (3.9)[a]	7 (3.9)[a]
Unknown[b]	15 (8.3)	19 (10.7)
Previous PARPi use, No. (%)		
Yes	60 (33.3)	66 (37.1)
No	120 (66.7)	112 (62.9)
Previous bevacizumab use, No. (%)		
Yes	145 (80.6)	140 (78.7)
No	35 (19.4)	38 (21.3)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; eCRF, electronic case report form; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; TPC, treatment of physician's choice.
[a]Protocol violation.
[b]This category includes patients whose last platinum dose dates or the associated progression dates are partially missing or completely missing.

respectively; dose interruptions occurred in 66.7%, 52.8%, and 20.1%. Among patients treated with paclitaxel (n = 70), 34.3% and 40.0% had a dose reduction and dose interruption; among patients treated with PLD (n = 94), the rates were 9.6% and 5.3%. AEs leading to dose adjustment or interruption occurred in 139 patients (77.2%) in the alpelisib + olaparib arm versus 66 patients (40.2%) in the TPC arm. The most common AEs of any grade that led to dose adjustment or interruption were hyperglycemia (20.6%), nausea (16.7%), vomiting (13.3%), and diarrhea (10.0%) in the alpelisib + olaparib arm and neutropenia (9.1%), anemia (5.5%), neutrophil count decreased (4.9%), peripheral neuropathy (3.7%), asthenia (3.7%), and COVID-19 disease (3.7%) in the TPC arm. A total of 14.4% of patients in the alpelisib + olaparib arm and 7.3% of patients in the TPC arm discontinued because of an AE (Data Supplement, Table S3; these percentages are from safety analysis and may differ slightly from the patient disposition analysis of the primary reason for discontinuation). The most common AEs of any grade that led to discontinuation of any trial treatment in the alpelisib + olaparib arm were vomiting (5.0%), blood creatinine increased (1.7%), and nausea (1.7%). One patient had acute kidney injury leading to study drug discontinuation in the alpelisib + olaparib arm. Two patients treated with paclitaxel discontinued because of peripheral neuropathy.

There were 26 (14.4%) on-treatment deaths (defined as up to 30 days after the last dose) in the alpelisib + olaparib arm and seven (4.3%) in the TPC arm; the most common cause in both the alpelisib + olaparib (19 [10.6%]) and TPC (four [2.4%]) arms was progressive disease. Treatment-related fatal serious AE (pneumonia) occurred in one patient in the alpelisib + olaparib arm. Further analysis did not reveal any individual factors or specific safety patterns leading to the imbalance of on-treatment deaths.

Biomarker Responder Analyses

Among 358 patients who were randomly assigned, 202 had NGS data for analysis (alpelisib + olaparib, 106; TPC, 96;

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

additional details are provided in the Supplementary Methods). The majority (>95%) were from archived samples, with few from new biopsies. Prespecified biomarkers of interest were homologous recombination deficiency (HRD) status, PI3K, and HRR pathway genes. For the biomarker analyses, responders were defined as being progression-free at cycle 7, day 1 visit (24 weeks) and being alive for at least 9 months. Among patients in the biomarker population, 26 in the alpelisib + olaparib arm and 18 in the TPC arm were responders. Six patients in the alpelisib + olaparib arm (four responders) and four patients in the TPC arm (three responders) had a somatic *BRCA1/2* mutation (Data Supplement, Table S4). A PI3K pathway alteration was observed in 35% (71 of 202), and HRD positivity in 36% (72 of 202). HRD status was not associated with response (Data Supplement, Table S5). PI3K pathway alterations were associated with HRD-negative status (P = .017, Pearson's chi-squared test); among 71 patients with PI3K pathway alteration, 73% were HRD-negative (52 total: alpelisib + olaparib, 27; TPC, 25) versus 25% HRD-positive (total 18: alpelisib + olaparib, 10; TPC, 8; Data Supplement, Figs S3 and S4). In patients with PI3K-altered/HRD-negative tumors, 33% (9 of 27) with alpelisib + olaparib and 16% (4 of 25) with TPC were responders (P = .15; Data Supplement, Fig S4D). The HR (alpelisib + olaparib *v* TPC) for PFS for patients with PI3K-altered/HRD-negative tumors was 0.84 (95% CI, 0.41 to 1.7; P = .63); the HR for OS was 0.79 (95% CI, 0.32 to 1.96; P = .61).

When evaluating alterations of individual genes in PI3K, HRR, and DNA damage/repair pathways, there was no association with response to alpelisib + olaparib with the exception of *AKT2* amplification (P = .04; Data Supplement, Table S5). As with the other PI3K pathway gene alterations, *AKT2* amplification was associated with HRD-negative status (P = .008; 94% HRD-negative among 16 patients with *AKT2* amplification; Data Supplement, Fig S4C). *AKT2* amplification was associated with better response to alpelisib + olaparib; however, patient numbers were low (Data Supplement, Table S5 and Fig S5).

DISCUSSION

In this analysis of the EPIK-O/ENGOT-ov61 trial, the primary end point was not met; the combination of alpelisib and olaparib did not have a PFS benefit compared with single-agent chemotherapy of physician's choice in patients with platinum-resistant/platinum-refractory HGSOC with no *BRCA* mutation. Similar ORR and DOR were observed between the two arms. Descriptive OS analysis found a similar median OS between the two arms (≈10.0 months). In addition, the safety profile with alpelisib + olaparib was similar to that reported for the individual agents.[4,14]

The rationale for this study was based on the premise that alpelisib may sensitize ovarian cancer cells to PARPis.[12-14] Activity of alpelisib + olaparib among patients with *BRCA*-wt platinum-resistant/platinum-refractory disease from a phase Ib study (ORR, 31%) provided support for conducting this larger phase III study.[14] By contrast, an ORR of 15.6% was observed in EPIK-O. Differences in the phase Ib and EPIK-O study populations might have contributed to this discordance of results. The percentage of patients with relapse >6 months after last platinum-based therapy was 7.1% in the phase Ib trial versus 3.9% in EPIK-O. The percentage of patients with relapse <2 months from last

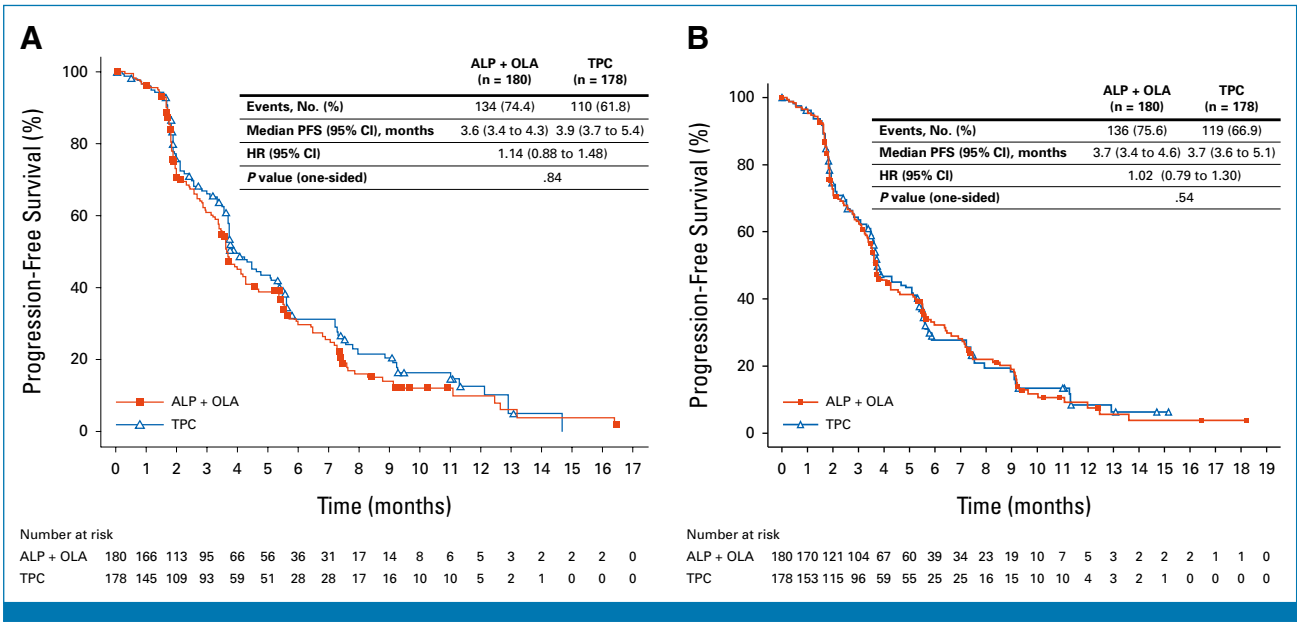

FIG 2. PFS (A) per BIRC assessment and (B) per local investigator assessment. ALP, alpelisib; BIRC, blinded independent review committee; HR, hazard ratio; OLA, olaparib; PFS, progression-free survival; TPC, treatment of physician's choice of paclitaxel or pegylated liposomal doxorubicin.

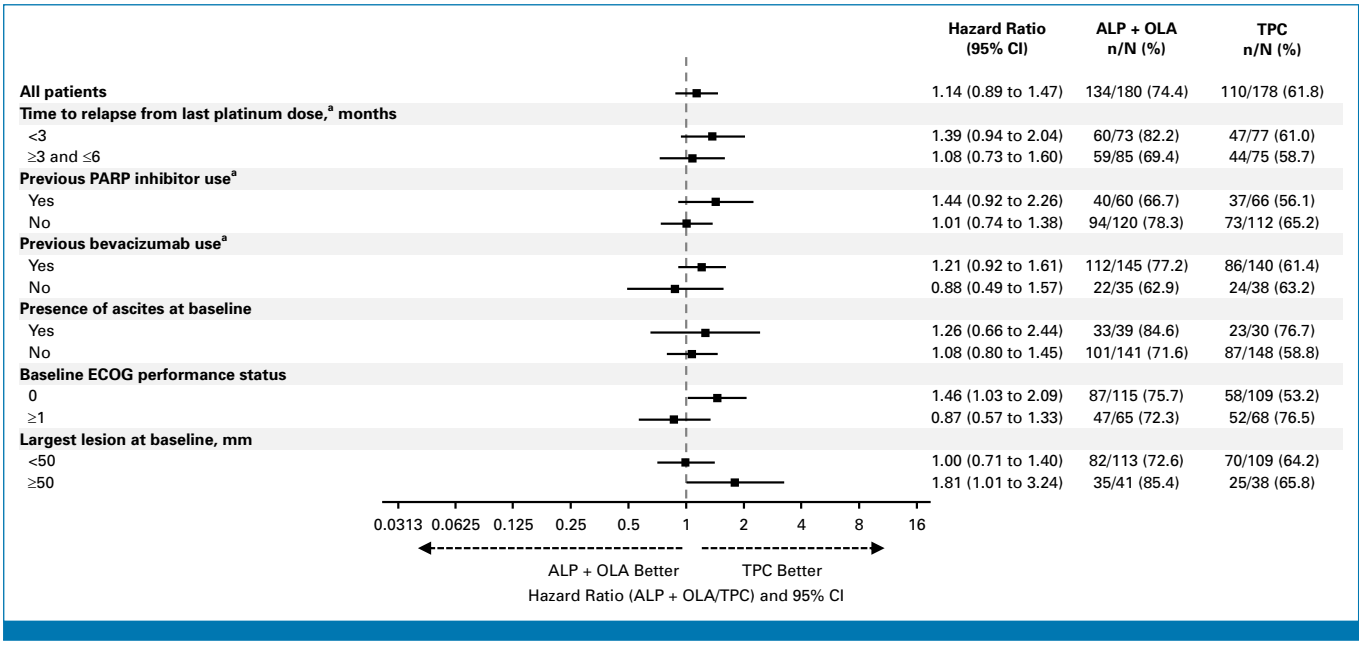

FIG 3. Forest plot of PFS per BIRC assessment by subgroup. [a]Stratification factors. ALP, alpelisib; BIRC, blinded independent review committee; ECOG, Eastern Cooperative Oncology Group; OLA, olaparib; PARP, poly(adenosine diphosphate-ribose) polymerase; PFS, progression-free survival; TPC, treatment of physician's choice of paclitaxel or pegylated liposomal doxorubicin.

platinum therapy was 10.7% in the phase Ib trial. In EPIK-O, the percentage of patients with relapse <3 months was 42%. None of the patients in the phase Ib trial had received previous PARPi therapy versus 35% in EPIK-O. In addition, while EPIK-O required that patients have previous treatment with bevacizumab (unless medically contraindicated), there was no such stipulation in the phase 1b trial. It should also be noted that the doses of alpelisib and olaparib used in EPIK-O were chosen based on the phase Ib study and were lower than their standard doses (alpelisib, 300 mg once daily [as indicated for breast cancer]; olaparib, 300 mg twice daily).[15,16]

EPIK-O evaluated a clinically and biologically aggressive population with *BRCA*-wt platinum-resistant disease, with previous bevacizumab exposure in 80%, previous PARPi therapy in 35%, and progression within 3 months from last platinum therapy in 42%. More recent studies in analogous populations with platinum-resistant disease have demonstrated poor ORR to multiple types of therapies (eg, 3% with niraparib in QUADRA, 4% with liposomal doxorubicin in JAVELIN 200, 7.3% with niraparib + dostarlimab in MOONSTONE), much lower than historical controls (ORR, ≈15%) based on pre-AURELIA single-agent chemotherapy trials.[5,17,18] However, the 28.6% ORR to once weekly

TABLE 2. Best Overall Response per BIRC Assessment

Response, No. (%)	Alpelisib + Olaparib, n = 180	TPC, n = 178
CR	2 (1.1)	3 (1.7)
PR	26 (14.4)	21 (11.8)
SD	69 (38.3)	61 (34.3)
PD	37 (20.6)	41 (23.0)
Non-CR/Non-PD	6 (3.3)	8 (4.5)
Not evaluable	40 (22.2)	44 (24.7)
ORR[a]	28 (15.6)	24 (13.5)
Clinical benefit rate[b]	38 (21.1)	34 (19.1)
Median duration of response	7.4 months (95% CI, 5.0 to 12.9)	5.6 months (95% CI, 3.8 to NE)

Abbreviations: BIRC, blinded independent review committee; CR, complete response; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; TPC, treatment of physician's choice of paclitaxel or pegylated liposomal doxorubicin.

[a]ORR = CR + PR.

[b]Clinical benefit rate = CR + PR + SD ≥24 weeks.

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

TABLE 3. Adverse Events (>20% in either arm)

	Alpelisib + Olaparib, n = 180		TPC, n = 164	
Adverse Event	All Grades, No. (%)	Grade ≥3, No. (%)	All Grades, No. (%)	Grade ≥3, No. (%)
Nausea	111 (61.7)	17 (9.4)	52 (31.7)	2 (1.2)
Hyperglycemia	94 (52.2)	34 (18.9)	6 (3.7)	0
Vomiting	75 (41.7)	18 (10.0)	34 (20.7)	2 (1.2)
Diarrhea	74 (41.1)	5 (2.8)	30 (18.3)	3 (1.8)
Anemia	62 (34.4)	13 (7.2)	60 (36.6)	8 (4.9)
Decreased appetite	60 (33.3)	6 (3.3)	26 (15.9)	0
Fatigue	52 (28.9)	6 (3.3)	31 (18.9)	1 (0.6)
Abdominal pain	45 (25.0)	7 (3.9)	29 (17.7)	4 (2.4)
Constipation	40 (22.2)	3 (1.7)	28 (17.1)	1 (0.6)
Asthenia	34 (18.9)	5 (2.8)	36 (22.0)	1 (0.6)

Abbreviation: TPC, treatment of physician's choice of paclitaxel or pegylated liposomal doxorubicin.

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

paclitaxel observed in EPIK-O was very similar to that observed in GOG-3018 (29.6%).[19] Furthermore, in the AURELIA trial, investigators selected chemotherapy (PLD, paclitaxel, or topotecan) before patients were randomly assigned to bevacizumab + chemotherapy or chemotherapy alone; subanalysis of patients treated with paclitaxel in the chemotherapy-alone arm demonstrated an ORR of 30.2%.[20] These data suggest that weekly paclitaxel clearly stands out as a treatment option for platinum-resistant disease with a consistent ORR of ≈30% across different trials regardless of the previous number of lines of therapy and previous bevacizumab and/or PARPi exposure.

Exploratory biomarker analyses indicated a significant association between PI3K pathway alterations and HRD-negative status in HGSOC. HRD-negative disease is a large, heterogeneous subset of HGSOCs that derives minimal benefit from currently approved maintenance therapies (PARPi or bevacizumab), for which there is a critical unmet need for novel treatments.[21–23] Our study suggests that PI3K-altered/HRD-negative tumors may represent a unique subset of HGSOCs that may respond to alpelisib + olaparib; this was more evident with *AKT2* amplification for which a significant association with response to alpelisib + olaparib was observed. Of note, all but one (94%) of the *AKT2*-amplified tumors were HRD-negative. These hypothesis-generating observations should be interpreted with caution and require further confirmation. In addition, based on the safety profile (although it should be noted that the combination had higher interruptions and discontinuations than the chemotherapy arm), alpelisib + olaparib may be explored in HRD-negative tumors with other histologic subtypes (including low-grade ovarian cancer).

In conclusion, this protocol-specified final PFS analysis of EPIK-O/ENGOT-ov61 did not meet its primary efficacy end point of PFS improvement with alpelisib + olaparib versus TPC in patients with platinum-resistant/platinum-refractory HGSOC with no *BRCA* mutation. Additional treatment strategies are being explored in platinum-resistant HGSOC, and additional research into novel targeted therapies is warranted to address the unmet needs in this patient population.[24–27]

AFFILIATIONS

[1]Dana-Farber Cancer Institute, Boston, MA
[2]Seoul National University, Seoul, South Korea
[3]HCL Cancer Institute, Lyon, France
[4]GINECO, Paris, France
[5]Yonsei Cancer Center and Severance Hospital, Yonsei University, Seoul, South Korea
[6]Medical Oncology Department, Hospital Clinic, and Translational Genomics and Targeted Therapies in Solid Tumors, IDIBAPS, Barcelona, Spain
[7]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY
[8]European Institute of Oncology IRCSS, Milan, Italy
[9]Department of Medicine and Surgery, University of Milan-Bicocca, Milan, Italy
[10]MaNGO, Milan, Italy
[11]Fudan University Shanghai Cancer Center, Shanghai, China
[12]Charité Universitätsmedizin Berlin, Berlin, Germany
[13]NOGGO, Berlin, Germany
[14]Instituto Brasileiro de Controle do Câncer, São Paulo, Brazil
[15]Department of Gynecology, Obstetrics and Neonatology, General University Hospital in Prague, First Faculty of Medicine, Charles University, Prague, Czech Republic
[16]Florida Cancer Specialists and Research Institute, West Palm Beach, FL
[17]Odense University Hospital, Odense, Denmark
[18]NSGO-CTU, Copenhagen, Denmark
[19]Department of Medical Oncology, Prince of Wales Hospital and Prince of Wales Clinical School, University of New South Wales, Sydney, NSW, Australia
[20]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy
[21]Gynaecological Oncology Medical Unit, Humanitas San Pio X Hospital, Milan, Italy

[22]Department of Women and Child Health, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy
[23]UZ Leuven, Leuven, Belgium
[24]BGOG, Leuven, Belgium
[25]University of Malaya, Kuala Lumpur, Malaysia
[26]Beatson West of Scotland Cancer Centre and University of Glasgow, Glasgow, United Kingdom
[27]GTG-UK/SGCTG, London, United Kingdom
[28]Medizinische Universität Innsbruck, Innsbruck, Austria
[29]Gustave Roussy, Villejuif, France
[30]Medical Oncology Department, Hospital Universitario Ramón y Cajal (IRYCIS), Madrid, Spain
[31]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
[32]Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany
[33]Comenius University Bratislava, National Cancer Institute, Bratislava, Slovakia
[34]Ovarian Cancer Research Alliance (OCRA), New York, NY
[35]Novartis Pharma AG, Basel, Switzerland
[36]Novartis Pharmaceuticals Corporation, East Hanover, NJ
[37]Medical Oncology Department, and Programme in Solid Tumours-CIMA, Cancer Center Clínica Universidad de Navarra, Madrid, Spain
[38]GEICO, Madrid, Spain

CORRESPONDING AUTHOR

Panagiotis A. Konstantinopoulos, MD, PhD; e-mail: panagiotis_konstantinopoulos@dfci.harvard.edu.

SUPPORT

Supported by Novartis Pharmaceuticals Corporation.

CLINICAL TRIAL INFORMATION

NCT04729387 (EPIK-O)

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at DOI https://doi.org/10.1200/JCO-25-00225.

DATA SHARING STATMENT

A data sharing statement provided by the authors is available with this article at DOI https://doi.org/10.1200/JCO-25-00225.

AUTHOR CONTRIBUTIONS

Conception and design: Panagiotis A. Konstantinopoulos, Jung Yun Lee, Bradley J. Monk, Monica Zuradelli, Michelle Miller, Ursula A. Matulonis
Administrative support: Jalid Sehouli, Bradley J. Monk
Provision of study materials or patients: Jae Weon Kim, Xiaohua Wu, Jalid Sehouli, Michael Friedlander, Els Van Nieuwenhuysen, Rosalind Glasspool, Christian Marth, Alexandra Leary, Claudio Zamagni, Frederik Marmé, Ursula A. Matulonis
Collection and assembly of data: Panagiotis A. Konstantinopoulos, Jae Weon Kim, Jung Yun Lee, Rachel N. Grisham, Nicoletta Colombo, Xiaohua Wu, Felipe Cruz, David Cibula, Bradley J. Monk, Gitte-Bettina Nyvang, Michael Friedlander, Domenica Lorusso, Rozita Malik, Rosalind Glasspool, Christian Marth, Alfonso Cortés-Salgado, Claudio Zamagni, Frederik Marmé, Jozef Sufliarsky, Monica Zuradelli, Craig Wang, Michelle Miller, Antonio González-Martín
Data analysis and interpretation: Panagiotis A. Konstantinopoulos, Jae Weon Kim, Gilles Freyer, Jung Yun Lee, Lydia Gaba, Nicoletta Colombo, Jalid Sehouli, Felipe Cruz, David Cibula, Michael Friedlander, Domenica Lorusso, Els Van Nieuwenhuysen, Christian Marth, Alexandra Leary, Patsy Hinson, Monica Zuradelli, Craig Wang, Fei Su, Ines Paule, Michelle Miller, Ursula A. Matulonis, Antonio González-Martín
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

ACKNOWLEDGMENT

We thank the patients who participated in this trial and their families and caregivers from sites across 26 countries. We also thank the data monitoring committee members, study steering committee members, and staff who assisted with the trial at each site. We thank Novartis for providing alpelisib and AstraZeneca for providing olaparib. We also thank William Ho, PhD, and Safiyya Mohamed Ali, MSc, of Nucleus Global for medical editorial assistance with the manuscript.

REFERENCES

1. Pujade-Lauraine E, Banerjee S, Pignata S: Management of platinum-resistant, relapsed epithelial ovarian cancer and new drug perspectives. J Clin Oncol 37:2437-2448, 2019
2. Griffiths RW, Zee YK, Evans S, et al: Outcomes after multiple lines of chemotherapy for platinum-resistant epithelial cancers of the ovary, peritoneum, and fallopian tube. Int J Gynecol Cancer 21: 58-65, 2011
3. Hanker LC, Loibl S, Burchardi N, et al: The impact of second to sixth line therapy on survival of relapsed ovarian cancer after primary taxane/platinum-based therapy. Ann Oncol 23:2605-2612, 2012
4. Gelmon KA, Tischkowitz M, Mackay H, et al: Olaparib in patients with recurrent high-grade serous or poorly differentiated ovarian carcinoma or triple-negative breast cancer: A phase 2, multicentre, open-label, non-randomised study. Lancet Oncol 12:852-861, 2011
5. Moore KN, Secord AA, Geller MA, et al: Niraparib monotherapy for late-line treatment of ovarian cancer (QUADRA): A multicentre, open-label, single-arm, phase 2 trial. Lancet Oncol 20:636-648, 2019
6. Matulonis UA, Penson RT, Domchek SM, et al: Olaparib monotherapy in patients with advanced relapsed ovarian cancer and a germline BRCA1/2 mutation: A multistudy analysis of response rates and safety. Ann Oncol 27:1013-1019, 2016
7. Oza AM, Tinker AV, Oaknin A, et al: Antitumor activity and safety of the PARP inhibitor rucaparib in patients with high-grade ovarian carcinoma and a germline or somatic BRCA1 or BRCA2 mutation: Integrated analysis of data from Study 10 and ARIEL2. Gynecol Oncol 147:267-275, 2017
8. Fritsch C, Huang A, Chatenay-Rivauday C, et al: Characterization of the novel and specific PI3Kα inhibitor NVP-BYL719 and development of the patient stratification strategy for clinical trials. Mol Cancer Ther 13:1117-1129, 2014
9. André F, Ciruelos E, Rubovszky G, et al: Alpelisib for *PIK3CA*-mutated, hormone receptor-positive advanced breast cancer. N Engl J Med 380:1929-1940, 2019
10. Konstantinopoulos PA, Gonzalez-Martin A, Cruz FM, et al: EPIK-O/ENGOT-OV61: Alpelisib plus olaparib vs cytotoxic chemotherapy in high-grade serous ovarian cancer (phase III study). Future Oncol 18:3481-3492, 2022
11. Matulonis UA, Wulf GM, Barry WT, et al: Phase I dose escalation study of the PI3kinase pathway inhibitor BKM120 and the oral poly (ADP ribose) polymerase (PARP) inhibitor olaparib for the treatment of high-grade serous ovarian and breast cancer. Ann Oncol 28:512-518, 2017
12. Ibrahim YH, García-García C, Serra V, et al: PI3K inhibition impairs BRCA1/2 expression and sensitizes BRCA-proficient triple-negative breast cancer to PARP inhibition. Cancer Discov 2:1036-1047, 2012
13. Juvekar A, Burga LN, Hu H, et al: Combining a PI3K inhibitor with a PARP inhibitor provides an effective therapy for BRCA1-related breast cancer. Cancer Discov 2:1048-1063, 2012
14. Konstantinopoulos PA, Barry WT, Birrer M, et al: Olaparib and α-specific PI3K inhibitor alpelisib for patients with epithelial ovarian cancer: A dose-escalation and dose-expansion phase 1b trial. Lancet Oncol 20:570-580, 2019

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

15. Novartis Pharmaceuticals Corporation: PIQRAY® (alpelisib) [prescribing information]. 2024
16. AstraZeneca Pharmaceuticals: LYNPARZA (olaparib) [prescribing information]. 2023
17. Pujade-Lauraine E, Fujiwara K, Ledermann JA, et al: Avelumab alone or in combination with chemotherapy versus chemotherapy alone in platinum-resistant or platinum-refractory ovarian cancer (JAVELIN Ovarian 200): An open-label, three-arm, randomised, phase 3 study. Lancet Oncol 22:1034-1046, 2021
18. Randall LM, O'Malley DM, Monk BJ, et al: Niraparib and dostarlimab for the treatment of recurrent platinum-resistant ovarian cancer: Results of a phase II study (MOONSTONE/GOG-3032). Gynecol Oncol 178:161-169, 2023
19. Arend RC, Monk BJ, Shapira-Frommer R, et al: Ofranergene obadenovec (Ofra-Vec, VB-111) with weekly paclitaxel for platinum-resistant ovarian cancer: Randomized controlled phase III trial (OVAL study/GOG 3018). J Clin Oncol 42:170-179, 2024
20. Poveda AM, Selle F, Hilpert F, et al: Bevacizumab combined with weekly paclitaxel, pegylated liposomal doxorubicin, or topotecan in platinum-resistant recurrent ovarian cancer: Analysis by chemotherapy cohort of the randomized phase III AURELIA trial. J Clin Oncol 33:3836-3838, 2015
21. Ray-Coquard I, Pautier P, Pignata S, et al: Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. N Engl J Med 381:2416-2428, 2019
22. Tewari KS, Burger RA, Enserro D, et al: Final overall survival of a randomized trial of bevacizumab for primary treatment of ovarian cancer. J Clin Oncol 37:2317-2328, 2019
23. González-Martín A, Pothuri B, Vergote I, et al: Niraparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med 381:2391-2402, 2019
24. Meric-Bernstam F, Makker V, Oaknin A, et al: Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: Primary results from the DESTINY-PanTumor02 phase II trial. J Clin Oncol 42:47-58, 2024
25. Moore KP, Philipovskiy A, Harano K, et al: Raludotatug deruxtecan (R-DXd) monotherapy in patients with previously treated ovarian cancer: Subgroup analysis of a first-in-human phase 1 study. Gynecol Oncol 190:S6-S7, 2024
26. Matulonis UA, Lorusso D, Oaknin A, et al: Efficacy and safety of mirvetuximab soravtansine in patients with platinum-resistant ovarian cancer with high folate receptor alpha expression: Results from the SORAYA study. J Clin Oncol 41:2436-2445, 2023
27. Moore KN, Angelergues A, Konecny GE, et al: Mirvetuximab soravtansine in FRα-positive, platinum-resistant ovarian cancer. N Engl J Med 389:2162-2174, 2023

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Primary Analysis of EPIK-O/ENGOT-ov61: Alpelisib Plus Olaparib Versus Chemotherapy in Platinum-Resistant or Platinum-Refractory High-Grade Serous Ovarian Cancer Without *BRCA* Mutation

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Panagiotis A. Konstantinopoulos
Consulting or Advisory Role: Merck, Vertex, AstraZeneca, Pfizer/EMD Serono, Tesaro, Bayer, Alkermes, Repare Therapeutics, Kadmon, Mersana, Novartis, AADi, ARTIOS, Immunogen, Scorpion Therapeutics, Gilead Sciences, Nimbus Therapeutics, Mural Oncology
Research Funding: Pfizer (Inst), Lilly (Inst), Tesaro (Inst), Merck Serono (Inst), AstraZeneca (Inst), Merck (Inst), Bayer (Inst), Bristol Myers Squibb/Sanofi (Inst), Novartis (Inst)

Gilles Freyer
Honoraria: AstraZeneca, Pfizer, BMS, Amgen, Novartis, GlaxoSmithKline, Biogaran Pharmaceuticals, Veracyte, Seagen, Gilead Sciences, Menarini Group
Consulting or Advisory Role: Lilly, BeiGene
Research Funding: AstraZeneca (Inst), MYLN (Inst), BMS (Inst)

Jung Yun Lee
Honoraria: AstraZeneca, MSD, Regeneron, Merck Serono, Genmab, Seagen
Consulting or Advisory Role: AstraZeneca (Inst), MSD, Roche (Inst), Takeda (Inst), Regeneron (Inst), Merck Serono (Inst), Genmab (Inst), Seagen (Inst), AbbVie (Inst), Advenchen Laboratories (Inst), Ascendis Pharma (Inst), Alkermes (Inst), BeiGene (Inst), BerGenBio (Inst), BMS (Inst), CanariaBio (Inst), Corcept Therapeutics (Inst), Cellid (Inst), CKD Pharm (Inst), Clovis Oncology (Inst), Daiichi Sankyo/AstraZeneca (Inst), Eisai (Inst), Genemedicine (Inst), GI Innovation (Inst), GlaxoSmithKline (Inst), Immunogen (Inst), Janssen Oncology (Inst), Kelun (Inst), Merck Serono (Inst), Novartis (Inst), Onconic Therapeutics (Inst), Ono Pharmaceutical (Inst), Sutro Biopharma (Inst), Synthon (Inst), TORL Biotherapeutics (Inst), Zymeworks (Inst)
Speakers' Bureau: AstraZeneca, Eisai, MSD, Roche, Takeda
Research Funding: Clovis Oncology (Inst), Immunogen (Inst), Janssen Oncology (Inst), Merck (Inst), MSD (Inst), Synthon (Inst), MSD (Inst), Eisai (Inst), Mersana (Inst), Ascendis Pharma (Inst), AstraZeneca (Inst), Novartis (Inst), OncoQuest Pharmaceuticals (Inst), Roche (Inst), Seagen (Inst), Takeda (Inst)

Lydia Gaba
Consulting or Advisory Role: GlaxoSmithKline, MSD Oncology, AstraZeneca Spain, AbbVie, Daiichi Sankyo Europe GmbH
Travel, Accommodations, Expenses: GlaxoSmithKline/Tesaro, MSD/AstraZeneca

Rachel N. Grisham
Employment: Memorial Sloan Kettering Cancer Center
Consulting or Advisory Role: GlaxoSmithKline, AstraZeneca, Signatera, Corcept Therapeutics, IntelliSphere, SpringWorks Therapeutics, Verastem
Research Funding: Context Therapeutics (Inst), Verastem (Inst), SpringWorks Therapeutics (Inst), Bayer (Inst), Novartis (Inst)
Travel, Accommodations, Expenses: EMD Serono
Other Relationship: Prime Oncology, MCM Education, OncLive, Aptitude Health, Cardinal Health
Uncompensated Relationships: Verastem

Nicoletta Colombo
Employment: Sarepta Therapeutics (I)
Honoraria: Roche/Genentech, AstraZeneca, GlaxoSmithKline, MSD Oncology, Clovis Oncology, Immunogen, Mersana, Eisai, Nuvation Bio, OncXerna, Pieris Pharmaceuticals, Novocure, BioNTech, Incyte, Gilead Sciences
Consulting or Advisory Role: Roche/Genentech, AstraZeneca, Clovis Oncology, MSD Oncology, GlaxoSmithKline, Immunogen, Mersana, Eisai, Nuvation Bio, OncXerna, Pieris Pharmaceuticals, Novocure
Speakers' Bureau: AstraZeneca, Clovis Oncology, GlaxoSmithKline, MSD Oncology, Eisai
Research Funding: AstraZeneca (Inst), Roche (Inst), GlaxoSmithKline (Inst)
Travel, Accommodations, Expenses: GlaxoSmithKline, AstraZeneca, Corcept Therapeutics

Jalid Sehouli
Honoraria: AstraZeneca, Eisai, Johnson & Johnson, PharmaMar, Pfizer, MSD Oncology, GlaxoSmithKline, Bayer, Clovis Oncology, Roche, Vifor Pharma, Hexal, Novartis, Esteve Pharmaceuticals, Incyte, Phytolife Nutrition, Jenapharm, Kyowa Kirin International, Oncoinvent, Daiichi, Medtronic Covidien, Amgen, AbbVie, Corcept Therapeutics, Gilead Sciences, Myriad Pharmaceuticals
Consulting or Advisory Role: AstraZeneca, Clovis Oncology, PharmaMar, Merck, Pfizer, MSD Oncology, Lilly, Novocure, Johnson & Johnson, Roche, Ingress Health, Sobi, GlaxoSmithKline, Alkermes, Eisai, Oncoinvent, Intuitive Surgical, Seagen, Bayer/Vital, Mundipharma, Sanofi Aventis GmbH, Immunogen, Tubulis GmbH, Daiichi Sankyo, Bristol Myers Squibb, Karyopharm Therapeutics, Corcept Therapeutics
Research Funding: AstraZeneca (Inst), Clovis Oncology (Inst), Merck (Inst), Bayer (Inst), PharmaMar (Inst), Pfizer (Inst), MSD Oncology (Inst), Roche (Inst), GlaxoSmithKline (Inst), Lilly (Inst), IQVIA (Inst), Mural (Inst), MSD (Inst)
Travel, Accommodations, Expenses: AstraZeneca, Clovis Oncology, PharmaMar, Roche Pharma AG, MSD Oncology, Olympus

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

© 2025 by American Society of Clinical Oncology

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

Felipe Cruz
Consulting or Advisory Role: Pfizer, Bayer, Astellas Pharma, Janssen, MSD
Travel, Accommodations, Expenses: Janssen Oncology, Novartis

David Cibula
Consulting or Advisory Role: Roche, GlaxoSmithKline, MSD, AstraZeneca, Karyopharm Therapeutics, AbbVie

Gitte-Bettina Nyvang
Travel, Accommodations, Expenses: GlaxoSmithKline

Michael Friedlander
Honoraria: AstraZeneca, MSD, Novartis, GlaxoSmithKline
Consulting or Advisory Role: AstraZeneca, MSD, AbbVie, Lilly, Takeda, Novartis, GlaxoSmithKline, Eisai, Incyclix Bio, Gilead Sciences
Speakers' Bureau: AstraZeneca, GlaxoSmithKline, MSD Oncology
Research Funding: BeiGene (Inst), AstraZeneca (Inst), Novartis (Inst)

Domenica Lorusso
Consulting or Advisory Role: PharmaMar, AstraZeneca, Clovis Oncology, GlaxoSmithKline, MSD, Genmab, Seagen, Immunogen, Oncoinvest, Corcept Therapeutics, Sutro Biopharma, Novartis, Novocure, Daiichi Sankyo/Lilly
Speakers' Bureau: AstraZeneca, Clovis Oncology, GlaxoSmithKline, MSD, ImmunoGen, Seagen
Research Funding: PharmaMar (Inst), Clovis Oncology (Inst), GlaxoSmithKline (Inst), MSD (Inst), AstraZeneca (Inst), Clovis Oncology (Inst), GlaxoSmithKline (Inst), MSD (Inst), Genmab (Inst), Seagen (Inst), Immunogen (Inst), Incyte (Inst), Novartis (Inst), Roche (Inst), Pharma& (Inst), Corcept Therapeutics (Inst), Alkermes (Inst)
Travel, Accommodations, Expenses: AstraZeneca, Clovis Oncology, GlaxoSmithKline, Menarini
Uncompensated Relationships: Gynecological Cancer InterGroup, MITO, ENGOT

Els Van Nieuwenhuysen
Consulting or Advisory Role: Regeneron (Inst), Oncoinvent, AstraZeneca (Inst), Merck Serono (Inst)
Speakers' Bureau: GlaxoSmithKline (Inst), AstraZeneca (Inst), MSD
Research Funding: AstraZeneca (Inst), Lilly (Inst), Merck (Inst), Seagen (Inst), Roche (Inst), Novartis (Inst), Regeneron (Inst), Oncoinvent (Inst)
Travel, Accommodations, Expenses: Regeneron (Inst), GlaxoSmithKline (Inst)

Rozita Malik
Research Funding: Novartis (Inst), Roche (Malaysia) Sdn Bhd (Inst), Janssen Research & Development (Inst), Merck Sharp & Dohme (Malaysia) Sdn Bhd (Inst), AstraZeneca (Inst)

Rosalind Glasspool
Honoraria: GlaxoSmithKline
Consulting or Advisory Role: GlaxoSmithKline, Pharma&
Research Funding: GlaxoSmithKline (Inst), Immunogen (Inst), Allarity Therapeutics (Inst), AstraZeneca (Inst), Verastem (Inst), Novartis (Inst)
Travel, Accommodations, Expenses: AbbVie, GlaxoSmithKline, MSD Oncology

Christian Marth
Honoraria: AstraZeneca, GlaxoSmithKline, MSD, Eisai
Consulting or Advisory Role: MSD, GlaxoSmithKline, AbbVie, Eisai, BioNTech, Seagen, Genmab, BeiGene

Alexandra Leary
Honoraria: Medscape, Gerson Lehrman Group, PeerVoice
Consulting or Advisory Role: Clovis Oncology (Inst), AstraZeneca (Inst), Tesaro (Inst), MSD (Inst), GlaxoSmithKline (Inst), Merck Serono (Inst), Zentalis (Inst), PEGASCY, Blueprint Medicines (Inst), Apmonia Therapeutics (Inst), Seagen (Inst), Immunogen (Inst), AbbVie (Inst), Pharma& (Inst)
Research Funding: Inivata (Inst), Sanofi (Inst), AstraZeneca (Inst), MSD Oncology (Inst), OSE Immunotherapeutics (Inst), Adaptimmune (Inst), Owkin (Inst)
Travel, Accommodations, Expenses: AstraZeneca, Tesaro, Oseimmuno

Alfonso Cortés-Salgado
Consulting or Advisory Role: GlaxoSmithKline, AstraZeneca, Daiichi Sankyo/AstraZeneca, Eisai, Pharma&
Speakers' Bureau: GlaxoSmithKline, AstraZeneca Spain, MSD, Eisai, Pfizer, Novartis
Travel, Accommodations, Expenses: Pfizer, GlaxoSmithKline, MSD

Claudio Zamagni
Consulting or Advisory Role: Roche, Eisai, Novartis, AstraZeneca, Pfizer, Lilly, Daiichi Sankyo, Exact Sciences, MSD Oncology, Seagen, Gilead Sciences, Menarini, GlaxoSmithKline
Research Funding: Roche/Genentech (Inst), Roche (Inst), AstraZeneca (Inst), Novartis (Inst), AbbVie (Inst), Pfizer (Inst), Synthon (Inst), Seagen (Inst), Daiichi Sankyo (Inst), Gilead Sciences (Inst), Greenwich LifeSciences (Inst), Lilly (Inst), MSD Oncology (Inst), Merck (Inst), Immunogen (Inst), Karyopharm Therapeutics (Inst)
Travel, Accommodations, Expenses: Roche, Novartis, Pfizer, AstraZeneca, Daiichi Sankyo, Gilead Sciences, MSD Oncology

Frederik Marmé
Honoraria: Roche/Genentech, Novartis, Pfizer, AstraZeneca, Clovis Oncology, Eisai, Genomic Health, MSD Oncology, Immunomedics (Inst), Seagen, Myriad Genetics, Pierre Fabre, GlaxoSmithKline, Agendia, Lilly, Gilead Sciences, Daiichi Sankyo, Menarini Group, Boehringer Ingelheim, Novocure, Pharma&, BioNTech, Gilead Sciences, Immunogen
Consulting or Advisory Role: AstraZeneca (Inst), Pfizer, Roche (Inst), Genomic Health, CureVac, Amgen, Vaccibody (Inst), Immunomedics (Inst), Eisai, GlaxoSmithKline, Gilead Sciences, Seagen, Clovis Oncology, BioNTech, Boehringer Ingelheim, Incyte (Inst), Gilead Sciences (Inst), Gilead Sciences
Research Funding: Roche/Genentech (Inst), Novartis (Inst), AstraZeneca (Inst), Tesaro (Inst), Clovis Oncology (Inst), MSD Oncology (Inst), Vaccibody (Inst), Gilead Sciences (Inst), GlaxoSmithKline (Inst)
Travel, Accommodations, Expenses: Roche, Pfizer, AstraZeneca, Gilead Sciences, Menarini Group

Jozef Sufliarsky
Honoraria: Novartis, Roche, AstraZeneca
Consulting or Advisory Role: Novartis, Lilly, Pfizer
Travel, Accommodations, Expenses: Immedica Pharma CEE, MSD, Novartis

Monica Zuradelli
Employment: Novartis
Stock and Other Ownership Interests: Novartis

Craig Wang
Employment: Novartis
Stock and Other Ownership Interests: Novartis

Fei Su
Employment: Novartis
Stock and Other Ownership Interests: Novartis

Ines Paule
Employment: Novartis
Stock and Other Ownership Interests: Novartis

Michelle Miller
Employment: Novartis
Stock and Other Ownership Interests: Novartis
Travel, Accommodations, Expenses: Novartis

Ursula A. Matulonis
Honoraria: Alkermes, Symphogen, MacroGenics
Consulting or Advisory Role: Merck, NextCure, Blueprint Medicines, Agenus, Boehringer Ingelheim, CureLab Oncology, Allarity Therapeutics, Immunogen, Eisai, ProfoundBio, GlaxoSmithKline, Tango Therapeutics, Lilly
Speakers' Bureau: Med Learning Group
Research Funding: Merck, Novartis, Tesaro, Syndax, Immunogen, Mersana, Leap Therapeutics, Fujifilm, SQZ Biotech
Travel, Accommodations, Expenses: AstraZeneca, Immunogen

Antonio González-Martín
Consulting or Advisory Role: Roche, Tesaro/GSK, Clovis Oncology, AstraZeneca, MSD, Genmab, Immunogen, Oncoinvent, Pfizer/EMD Serono, Amgen, Mersana, SOTIO, Sutro Biopharma, MacroGenics, Novartis, Alkermes, Hedera Dx, Novocure, Seagen, Takeda, Kartos Therapeutics, Tubulis GmbH, Pharma&, AbbVie, Regeneron, BioNTech SE, Eisai, Daiichi Sankyo, Incyte, TORL Biotherapeutics
Speakers' Bureau: Roche, AstraZeneca, Tesaro/GSK, PharmaMar, Clovis Oncology, MSD Oncology, Pharma&
Research Funding: Roche (Inst), Tesaro/GSK (Inst)
Travel, Accommodations, Expenses: Roche, AstraZeneca, PharmaMar, Tesaro/GSK, MSD Oncology

No other potential conflicts of interest were reported.

Downloaded from ascopubs.org by Yonsei University on November 2, 2025 from 116.089.178.139
Copyright © 2025 American Society of Clinical Oncology. All rights reserved.

© 2025 by American Society of Clinical Oncology