PHASE 2 RESULTS OF RELACORILANT + NAB-PACLITAXEL IN PATIENTS WITH RECURRENT, PLATINUM-RESISTANT OVARIAN CANCER WITH AND WITHOUT PRIOR BEVACIZUMAB

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Conclusions

- An unmet need persists for treatments in platinum-resistant ovarian cancer that can extend a woman's survival without adding toxicity.
- Selective GR modulation is a promising, new oncologic therapy.
- This was the first randomized, controlled trial to evaluate relacorilant in combination with nab-paclitaxel in women with platinum-resistant/ refractory ovarian cancer.
- Improved PFS and a trend toward improved OS were observed with intermittent relacorilant + nab-paclitaxel versus nab-paclitaxel monotherapy.
- In this pre-planned subgroup analysis, patients with prior BEV exposure treated with intermittent relacorilant + nab-paclitaxel experienced greater improvements in PFS, OS, and DOR versus those treated with nab-paclitaxel monotherapy.

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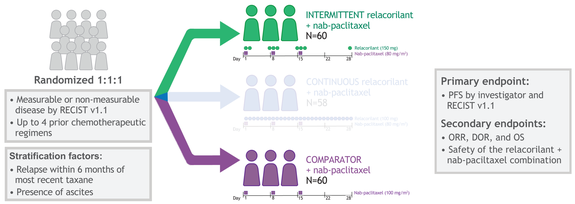
Background

- Current treatment for ovarian cancer generally begins with a platinum-based chemotherapy regimen with or without bevacizumab (BEV); however, most patients ultimately progress and succumb to the disease due to the emergence of chemotherapy resistance.[1,2]
  - Single-agent chemotherapies are commonly used in platinum-resistant disease, but generally have limited efficacy and poor outcomes.[3]
- Binding of cortisol to the glucocorticoid receptor (GR) can reduce the efficacy of chemotherapies by activating anti-apoptotic pathways, such as those activated by SGK1 and DUSP1.[4,5]
- Relacorilant is an investigational, reversible, selective GR modulator (SGRM) that competes with cortisol at the GR.[6,7]
  - Preclinical and clinical data indicate that modulation of GR signaling can reverse the anti-apoptotic effects of cortisol, thereby restoring or enhancing chemotherapy efficacy.[6,7]
- In a recent phase 2 study in patients with recurrent, platinum-resistant ovarian cancer, intermittently dosed relacorilant + nab-paclitaxel resulted in clinically meaningful benefit compared to nab-paclitaxel monotherapy, including[8,9,*]:
  - Improved progression-free survival (PFS; hazard ratio [HR] 0.66; *P*=0.038; median PFS 5.6 months [95% confidence interval (CI) 3.7, 7.2] versus 3.8 months [95% CI 3.5, 5.4]),
  - Improved duration of response (DOR; HR 0.36; *P*=0.006), and
  - A trend toward improved overall survival (OS; HR 0.67; *P*=0.066; median OS 13.9 months [95% CI 11.1, 18.4] versus 12.2 months [95% CI 7.7, 15.3]).
- Here, we present a pre-planned subgroup analysis of this phase 2 study based on prior treatment with or without BEV.

*Results not adjusted for multiplicity

1 Study Design

- This was a phase 2, randomized, controlled, open-label, 3-arm study (ClinicalTrials.gov Identifier: NCT03776812) in patients with recurrent, platinum-resistant/refractory ovarian, primary peritoneal, or fallopian tube cancer or ovarian carcinosarcoma.
  - Patients were randomized as follows:
    - Intermittent relacorilant + nab-paclitaxel, with relacorilant administered on the day before, the day of, and the day after nab-paclitaxel (intermittent arm),
    - Continuous relacorilant administered daily + nab-paclitaxel (continuous arm; results from this arm will not be reported here),
    - Nab-paclitaxel monotherapy (comparator arm).
- In a pre-planned subgroup analysis, efficacy outcomes were compared between the intermittent and comparator arms based on whether or not patients had received prior BEV.
  - Among the 120 patients randomized to the intermittent or comparator arms, 68 had received prior BEV (31 and 37, respectively) and 52 had not (29 and 23, respectively).



Granulocyte colony-stimulating factor (G-CSF) was mandated in the relacorilant arms and administered by investigator decision in the nab-paclitaxel monotherapy arm.

ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors.

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2 Baseline Characteristics in All Study Patients, by Prior BEV Use

- Baseline characteristics in patients with or without prior BEV were generally balanced, with the exception that a higher proportion (~70%) of patients who had received prior BEV were in Europe.

	Prior BEV (N=105)	No prior BEV (N=73)
Age, median (range), years	62 (38, 81)	60 (43, 81)
≥65, n (%)	43 (41.0)	19 (26.0)
Race, n (%)*		
White	96 (91.4)	63 (86.3)
Other	5 (4.8)	5 (6.8)
Baseline weight, mean (SD), kg	65.5 (13.1)	70.7 (19.4)
Geographic region, n (%)		
North America	32 (30.5)	35 (47.9)
Europe	73 (69.5)	38 (52.1)
Stage at initial diagnosis, n (%)†		
Stage <IIIA	5 (4.8)	4 (5.5)
Stage ≥IIIA	98 (93.3)	69 (94.5)
Platinum refractory, n (%)‡	38 (36.2)	27 (37.0)
Molecular profiling, n/N (%)		
BRCA1 (+)	11/85 (12.9)	5/47 (10.6)
BRCA2 (+)	4/75 (5.3)	3/39 (7.7)

*Race data were missing or not reported for 4 (3.8%) patients who had received prior BEV and 5 (6.8%) of patients without prior BEV.
†Cancer stage at initial diagnosis data were missing for 2 (1.9%) patients who had received prior BEV.
‡Progressing during or within 1 month from last platinum treatment.
SD, standard deviation.

3 Prior Anticancer Therapy in All Study Patients, by Prior BEV Use

- The previous platinum-free interval for most patients was <6 months (prior BEV 99.0%; no prior BEV 100.0%).

	Prior BEV (N=105)	No prior BEV (N=73)
Number of prior therapies, median (range)	3 (1, 5)	2 (1, 5)
Time from initial diagnosis to first study treatment, median (SD), months	32.0 (18.4)	29.2 (22.1)
Previous treatment-free interval,* n (%)		
≤6 months	102 (97.1)	71 (97.3)
>6-12 months	2 (1.9)	2 (2.7)
>12 months	1 (1.0)	0
Treatment-free interval from most recent taxane, n (%)		
Relapse ≤6 months	48 (45.7)	39 (53.4)
Relapse >6 months	57 (54.3)	34 (46.6)
Prior primary debulking surgery, n (%)	46 (43.8)	27 (37.0)
Outcome of primary debulking surgery, n (%)		
No visible disease (R0)	31 (29.5)	15 (20.5)
≤1 cm residual disease	5 (4.8)	7 (9.6)
>1 cm residual disease	8 (7.6)	2 (2.7)
Prior PARPi, n (%)	43 (41.0)	22 (30.1)

*From the most recent treatment to this study treatment.
PARPi, poly (ADP-ribose) polymerase inhibitor.

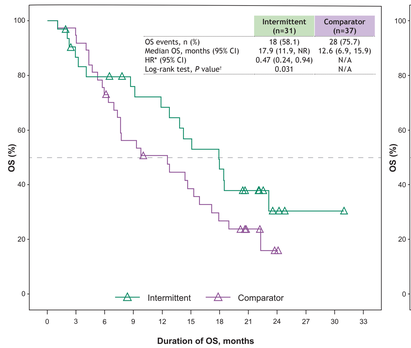
4 Efficacy Outcomes Based on Prior BEV Use

- In this pre-planned subgroup analysis, patients in the intermittent arm who had received prior BEV experienced longer PFS and OS versus those with no prior exposure to BEV.
- ORR was similar across both BEV subgroups, but DOR improved in the intermittent arm versus nab-paclitaxel monotherapy among patients who had received prior BEV.

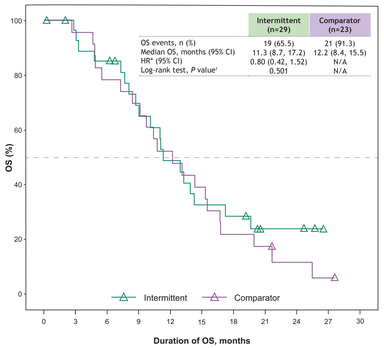
	Prior BEV		No prior BEV	
	Intermittent relacorilant + nab-paclitaxel (n=31)	Nab-paclitaxel monotherapy (n=37)	Intermittent relacorilant + nab-paclitaxel (n=29)	Nab-paclitaxel monotherapy (n=23)
PFS				
Median PFS, months (95% CI)	7.2 (3.0, 7.4)	3.7 (3.5, 5.5)	5.4 (2.8, 5.7)	3.8 (3.4, 5.5)
HR* (95% CI)	0.44 (0.24, 0.78)	N/A	0.91 (0.48, 1.72)	N/A
Log-rank test, *P* value†	0.005	N/A	0.767	N/A
ORR				
ORR in patients with measurable disease at baseline, n/N (%)	11/27 (40.7)	10/30 (33.3)	9/29 (31.0)	9/23 (39.1)
DOR				
Median DOR, months (95% CI)	5.6 (4.1, NR)	3.4 (1.3, 3.7)	3.8 (3.6, NR)	3.8 (2.9, 5.1)
HR* (95% CI)	0.25 (0.08, 0.83)	N/A	0.47 (0.13, 1.68)	N/A
Log-rank test, *P* value†	0.006	N/A	0.234	N/A

*Comparing intermittent relacorilant + nab-paclitaxel versus nab-paclitaxel monotherapy.
†Nominal *P* values are presented.
Data from the study arm treated with continuous, daily relacorilant + nab-paclitaxel are not reported here. The data cutoff date for the primary analysis (PFS, ORR, and DOR) was March 22, 2021; median follow-up was 11.1 months. The data cutoff date for the final analysis (OS) was March 7, 2022; median follow-up was 22.5 months.
N/A, not applicable; NR, not reported.

A. OS in patients with prior BEV



B. OS in patients without prior BEV



Limitations

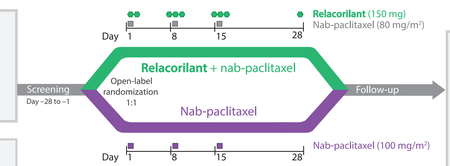
- While this analysis showed consistent improvements in PFS, OS, and DOR in women with prior BEV treatment and intermittently dosed relacorilant + nab-paclitaxel versus nab-paclitaxel monotherapy, interpretation of these findings is limited by the small number of patients in this pre-planned subgroup analysis.
- Patient characteristics beyond those discussed here, or recognized as impactful factors, may also contribute to these findings.

5 Ongoing Phase 3 Study: ROSELLA

- Results from this phase 2 subgroup analysis informed the patient population for the confirmatory phase 3 trial of intermittent relacorilant + nab-paclitaxel versus nab-paclitaxel monotherapy (ROSELLA [GOG-3073, ENGOT-Ov72/MITO]; NCT05257408), with an enrollment inclusion criterion for prior treatment with BEV.

Patient population: ~360 patients
- High-grade serious, epithelial ovarian, primary peritoneal, or fallopian tube cancer
- Progression ≤6 months after last dose of platinum-based therapy (exclude primary platinum-refractory)
- 1-3 prior lines of systemic anticancer therapy
- Must have received prior BEV

Stratification factors
- Prior lines of therapy (1 vs >1)
- Region of the world (North America versus Europe versus the rest of the world)



Primary endpoint:
- PFS (by BICR) per RECIST v1.1

Key secondary endpoints:
- Efficacy:
  - OS
  - PFS (by investigator) per RECIST v1.1
  - ORR, BOR, and DOR per RECIST v1.1
- Safety, quality of life, pharmacodynamics, and pharmacokinetics

In collaboration with: GOG FOUNDATION ENGOT

BICR, blinded independent central review; BOR, best overall response.