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Final Overall Survival Data From a Randomized, Open-Label, Phase 2 Study of Relacorilant, a Selective Glucocorticoid Receptor Modulator, in Combination With Nab-Paclitaxel in Patients With Recurrent Platinum-Resistant Ovarian Cancer

PRESENTER:
Prof.ssa Nicoletta Colombo, MD
Contact: nicoletta.colombo@ieo.it

Nicoletta Colombo,[1,2] Toon Van Gorp,[3] Ursula A. Matulonis,[4] Ana Oaknin,[5] Rachel N. Grisham,[6] Diane Provencher,[7] Gini F. Fleming,[8] Alexander B. Olawaiye,[9] Hristina I. Pashova,[10] Iulia Cristina Tudor,[10] Lyndah Dreiling,[10] Domenica Lorusso[11]

Summary & Conclusions

- There is a high unmet need for novel therapies for patients with advanced, platinum-resistant ovarian cancer
- The selective glucocorticoid receptor modulator (SGRM) relacorilant has shown potential in restoring chemosensitivity and enhancing chemotherapy efficacy
- With an additional ~16 months of follow-up, the findings from the primary OS analysis of this randomized, open-label, phase 2 study were confirmed
  - After a median follow-up of 38 months, intermittent relacorilant + nab-paclitaxel had improved OS compared to nab-paclitaxel monotherapy (HR: 0.69 [95% CI: 0.46—1.02])
- In the overall population, the chance of survival at 24 months was doubled for patients receiving relacorilant + nab-paclitaxel vs nab-paclitaxel monotherapy, and the frequency and nature of AEs were similar across study arms
  - This trend continued at 36 months
- In the subgroup of patients with 1—3 prior therapies, including prior bevacizumab, without primary platinum-refractory disease, median OS was prolonged by 5 months in the intermittent relacorilant + nab-paclitaxel arm (17.9 months) vs nab-paclitaxel monotherapy (12.6 months)
- These promising results have paved the way for the currently enrolling phase 3 ROSELLA trial

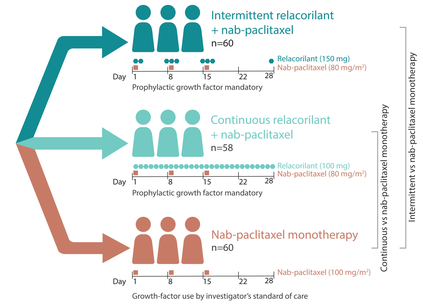
AE, adverse event; CI, confidence interval; HR, hazard ratio; OS, overall survival.

Background

- Effective treatment options remain limited for patients with advanced, platinum-resistant ovarian cancer[1]
  - Most patients relapse and eventually die of treatment-resistant disease
  - There is a high unmet need for novel therapies
- Glucocorticoid receptor (GR) modulation is a promising new mechanism of action for oncology therapies
  - Many chemotherapy agents, such as nab-paclitaxel, elicit anti-tumor effects by activating signaling pathways that induce tumor cell apoptosis
  - Even physiologic cortisol levels can reduce chemotherapy efficacy and promote tumor cell survival by suppressing apoptosis[2]
  - In preclinical and early-phase clinical trials, the selective GR modulator (SGRM) relacorilant has shown potential in restoring chemosensitivity and enhancing chemotherapy efficacy by competing with cortisol for binding at the GR[2-4]
    - When cortisol activates the GR, target genes are upregulated and suppress apoptotic pathways used by cytotoxic agents[2]
    - Modulation of GR signaling can reverse the anti-apoptotic effects of cortisol, which may enhance chemotherapy efficacy

1 Randomized, Open-label Phase 2 Study of Relacorilant + Nab-paclitaxel in Ovarian Cancer

- 178 women with recurrent, platinum-resistant/refractory, high-grade serous or endometrioid epithelial ovarian, primary peritoneal, or fallopian tube cancer or ovarian carcinosarcoma were enrolled in this study (NCT03776812)



Key Inclusion Criteria

- Measurable or non-measurable disease by RECIST v1.1
- ≤4 prior chemotherapeutic regimens

Stratification Factors

- Relapse within 6 months of most recent taxane
- Presence of ascites

Primary Endpoint

- PFS by investigator and RECIST v1.1

Secondary Endpoints

- ORR
- DOR
- OS
- Safety of the relacorilant + nab-paclitaxel combination

Primary Study Results[5]

- Intermittently dosed relacorilant + nab-paclitaxel improved PFS, DOR, and OS compared with nab-paclitaxel monotherapy
  - mPFS: 5.6 months vs 3.8 months (HR: 0.66 [95% CI: 0.44—0.98])[a,b]
  - mDOR: 5.6 months vs 3.7 months (HR: 0.36 [95% CI: 0.16—0.77])[a,b]
  - mOS: 13.9 months vs 12.2 months (HR: 0.67 [95% CI: 0.43—1.03])[b,c]
- Continuous relacorilant + nab-paclitaxel showed numerically improved mPFS but did not result in significant improvement over nab-paclitaxel monotherapy
- AEs were similar across study arms, with the most common grade ≥3 AEs being neutropenia, anemia, peripheral neuropathy, and fatigue/asthenia

Here, we report the end-of-study OS analysis for the intermittent relacorilant + nab-paclitaxel vs nab-paclitaxel monotherapy arms, after the study was closed and the study database was locked on August 25, 2023

- This is the treatment regimen being evaluated in the phase 3 ROSELLA trial (NCT05257408)

AE, adverse event; CI, confidence interval; HR, hazard ratio; mDOR, median duration of response; mOS, median overall survival; mPFS, median progression-free survival; ORR, objective response rate. [a]Median follow-up of 11.1 months; [b]No multiplicity adjustement; [c]Median follow-up of 22.5 months.

2 Baseline Characteristics

	Intermittent relacorilant (150 mg) + nab-paclitaxel (80 mg/m²) n=60	Nab-paclitaxel monotherapy (100 mg/m²) n=60
Age, median (range), years	60 (38, 81)	61.5 (41, 81)
Platinum refractory[a], n (%)	23 (38.3)	22 (36.7)
Primary platinum refractory[b], n (%)	7 (11.7)	1 (1.7)
Number of prior systemic anticancer therapies[c,d], median (range)	2.5 (1, 4)	3 (1, 4)
Number of prior chemo-therapies, median (range)	2 (1, 4)	2 (1, 4)
≥4 prior lines of therapy[d], n (%)	7 (11.7)	9 (15.0)
Bevacizumab, n (%)	31 (51.7)	37 (61.7)
PARP inhibitor, n (%)	18 (30.0)	20 (33.3)
Molecular profiling[b]		
BRCA1(+), n/N (%)	5/42 (11.9)	7/48 (14.6)
BRCA2(+), n/N (%)	1/36 (2.8)	3/39 (7.7)

[a]Progressing during or within 1 month from last platinum treatment; [b]Retrospectively collected and available in a subset of the study population only; [c]Across all three study arms, 177/178 (99.4%) patients had received prior taxane (1 unknown); [d]Chemotherapy, myelosuppressive therapy, or molecularly targeted agents.
BRCA; breast cancer gene; PARP, poly (ADP-ribose) polymerase.

3 Safety

- The safety profile in the end-of-study analysis remained consistent with the primary analysis[5], with the frequency and nature of AEs similar across study arms

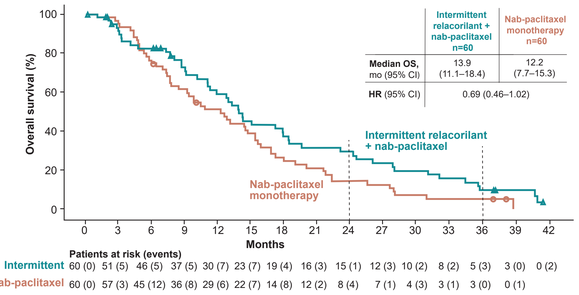
n, (%)	Intermittent relacorilant (150 mg) + nab-paclitaxel (80 mg/m²) n=60	Nab-paclitaxel monotherapy (100 mg/m²) n=60
Neutropenia[a]	12 (20.0)	23 (38.3)
Grade ≥3	4 (6.7)	9 (15.0)
Febrile neutropenia (Grade 3)[b]	0	1 (1.7)
Anemia	29 (48.3)	34 (56.7)
Grade ≥3	8 (13.3)	7 (11.7)
Peripheral neuropathy[c]	22 (36.7)	21 (35.0)
Grade ≥3	0	3 (5.0)
Fatigue or asthenia	33 (55.0)	39 (65.0)
Grade ≥3	7 (11.7)	1 (1.7)

[a]Neutropenia, neutrophil count decreased; [b]Secondary to *E. coli* urinary sepsis in this patient; [c]Neuropathy peripheral, neurotoxicity, peripheral motor neuropathy, peripheral sensorimotor neuropathy, peripheral sensory neuropathy, hypoesthesia.
n, number of patients.

4 Overal Survival for Intermittent Relacorilant + Nab-Paclitaxel vs Nab-Paclitaxel Monotherapy at the End-of-Study Analysis

Full Study Population

- Kaplan-Meier estimates of OS in the intermittent relacorilant + nab-paclitaxel and nab-paclitaxel monotherapy arms:
  - At 24 months: 29.4% (95% CI: 17.7—42.1) and 14.1% (6.6—24.3)
  - At 36 months: 9.8% (3.6—19.7) and 5.3% (1.4—13.2)



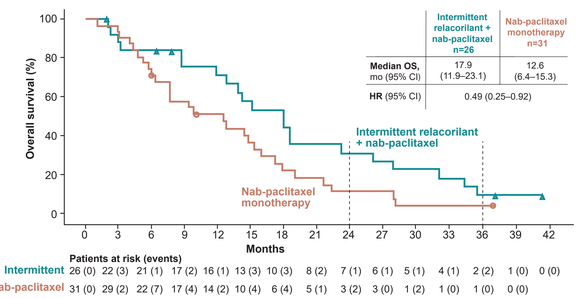
Patients at risk (events)

Intermittent	60 (0)	51 (5)	46 (5)	37 (5)	30 (7)	23 (7)	19 (4)	16 (3)	15 (1)	12 (3)	10 (2)	8 (2)	5 (3)	3 (0)	0 (2)
Nab-paclitaxel	60 (0)	57 (3)	45 (12)	36 (8)	29 (6)	22 (7)	14 (8)	12 (2)	8 (4)	7 (1)	4 (3)	3 (1)	3 (0)	0 (1)	

*Kaplan-Meier methods were used to estimate OS and probability of survival at milestones (24 and 36 months). Median follow-up was 38.1 months.
CI, confidence interval; HR, hazard ratio; mo, months; mOS, median overall survival.

Patients with 1—3 Prior Therapies, Including Prior Bevacizumab, Excluding Primary Platinum-Refractory Disease

- In this subgroup, mOS was prolonged by 5 months in the intermittent relacorilant + nab-paclitaxel arm vs nab-paclitaxel monotherapy
- This population is similar to that being enrolled in the phase 3 ROSELLA study



Patients at risk (events)

Intermittent	26 (0)	22 (3)	21 (1)	17 (2)	16 (1)	13 (3)	10 (3)	8 (2)	7 (1)	6 (1)	5 (1)	4 (1)	2 (2)	1 (0)	0 (0)
Nab-paclitaxel	31 (0)	29 (2)	22 (7)	17 (4)	14 (2)	10 (4)	6 (4)	5 (1)	3 (2)	3 (0)	1 (2)	1 (0)	1 (0)	0 (0)	

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Author Affiliations

[1]Gynecologic Oncology Program, European Institute of Oncology, IRCCS, Milan, Italy.
[2]Department of Medicine and Surgery, University Milan-Bicocca, Milan, Italy.
[3]Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium.
[4]Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA.
[5]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain.
[6]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical Center, New York, NY, USA.
[7]CHUM, Université de Montréal, Montréal, QC, Canada.
[8]The University of Chicago, Chicago, IL, USA.
[9]Department of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA.
[10]Corcept Therapeutics, Inc., Menlo Park, CA, USA.
[11]Fondazione Policlinico Universitario Gemelli IRCCS and Catholic University of Sacred Heart, Rome, Italy.

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