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Relacorilant + Nab-paclitaxel in Patients With Recurrent, Platinum-resistant Ovarian Cancer: Phase 2 Subgroup Analysis Mirroring the Patient Population of an Upcoming Phase 3 Study

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Summary & Conclusions

- There is a large unmet need for novel, targeted treatments in platinum-resistant ovarian cancer that can extend survival without adding toxicity.
- Selective GR modulation is a promising, new oncologic therapeutic platform.
- This study was the first randomized, controlled, phase 2 trial of the selective GR modulator relacorilant combined with nab-paclitaxel in patients with platinum-resistant/refractory ovarian cancer.
- Benefit was observed with intermittent relacorilant + nab-paclitaxel treatment vs. nab-paclitaxel monotherapy in the entire study population, including improved PFS, DoR, and a trend toward improved OS.
- Greater improvements in PFS, OS, and DoR with intermittent relacorilant + nab-paclitaxel were observed in subgroup analyses, particularly in women without primary platinum-refractory disease who had received ≤3 prior lines of therapy, including prior bevacizumab.
- These phase 2 results informed the patient population, dosing schedule, and comparator agent choices in the ongoing confirmatory phase 3 trial (ROSELLA).

The authors want to thank all those who participated in this study: The study patients and their families, the investigators, and the sponsor team.

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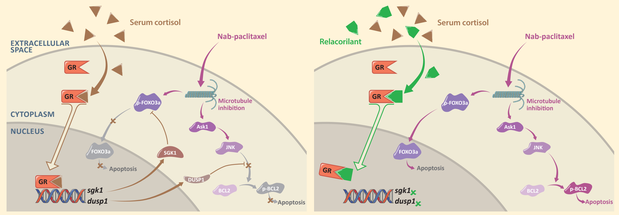
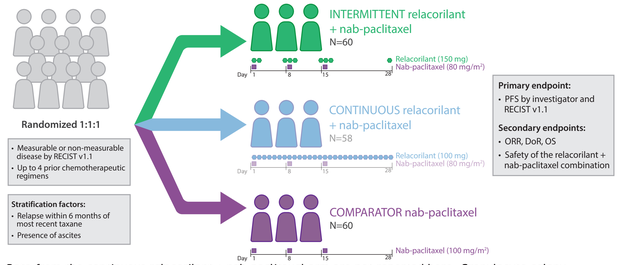
Background

- Platinum resistance occurs in virtually all patients with recurrent ovarian cancer.[1]
- Single-agent chemotherapies are commonly used in this setting, but outcomes are generally poor.[1-3]
  - There is a large unmet need for novel, targeted treatments.
- In preclinical models, cortisol reduces the efficacy of chemotherapies by suppressing the apoptotic pathways used by cytotoxic agents.
  - Cortisol acts by binding to the glucocorticoid receptor (GR), which is abundantly expressed in ovarian tumors.[4]
  - High GR expression is also associated with poor outcomes.[4]
- Preclinical and clinical data indicate that modulation of GR signaling can reverse the anti-apoptotic effects of cortisol, thereby enhancing the efficacy of cytotoxic agents.[5]
- **Relacorilant** is a selective GR modulator (SGRM) that inhibits the anti-apoptotic effects of cortisol.
  - Relacorilant has shown promise in enhancing the efficacy of taxanes (particularly paclitaxel/nab-paclitaxel) in preclinical as well as phase 1 and phase 2 clinical studies in various solid tumors.[5-8]



1 Phase 2 Study of Relacorilant + Nab-paclitaxel in Ovarian Cancer (NCT03776812)



Data from the continuous relacorilant + nab-paclitaxel arm are not reported here. Granulocyte colony stimulating factor (G-CSF) was mandated in the relacorilant arms and administered by investigator decision in the nab-paclitaxel monotherapy arm. PFS, progression-free survival; ORR, objective response rate; DoR, duration of response; OS, overall survival.

- A phase 2, randomized, controlled, open-label, 3-arm study of relacorilant + nab-paclitaxel vs. nab-paclitaxel monotherapy in patients with recurrent, platinum-resistant or platinum-refractory ovarian, primary peritoneal, or fallopian tube cancer

Dosing Schedules

- Nab-paclitaxel: On days 1, 8, 15 of each 28-day schedule; 100 mg/m² as monotherapy, 80 mg/m² when combined with relacorilant[9]
- Intermittent relacorilant + nab-paclitaxel: 150 mg on the day before, the day of, and the day after nab-paclitaxel infusion

Key Findings

- Intermittent administration of relacorilant + nab-paclitaxel resulted in clinically meaningful benefit without increased side effect burden compared to nab-paclitaxel monotherapy.[5,6,*]
  - PFS: HR 0.66 (*P*=0.038; median PFS 5.6 vs. 3.8 months)
  - DoR: HR 0.36 (*P*=0.006; median DoR 5.6 vs. 3.7 months)
  - OS: HR 0.67 (*P*=0.066; median OS 13.9 vs. 12.2 months)

  *Results not adjusted for multiplicity.
- Here, we present results from 3 ad-hoc subgroup analyses that informed the patient population of the ongoing confirmatory phase 3 study of relacorilant + nab-paclitaxel in patients with platinum-resistant ovarian cancer (ROSELLA, NCT05257408).

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2 Patients Without Primary Platinum-refractory Disease Who Had Received 1-3 Prior Lines of Therapy

- Patients with primary platinum-refractory disease and those with >3 prior lines of therapy have particularly poor prognosis and are commonly excluded from clinical trials.
- Patients with primary platinum-refractory disease were randomly overrepresented in the intermittent relacorilant dosing arm vs. nab-paclitaxel monotherapy (n=11 vs. n=1).
- In this subgroup, greater improvements in PFS, DoR, and OS vs. nab-paclitaxel monotherapy were observed.

	Intermittent Relacorilant + Nab-paclitaxel (N=46)	Nab-paclitaxel Monotherapy (N=50)
PFS[1]		
Number of events, (%)	36 (78.3%)	48 (96.0%)
Median PFS (95% CI), months	5.6 (3.7, 7.3)	3.8 (3.5, 5.4)
HR (95% CI)	0.58 (0.37, 0.91)	–
Log-rank test, *P*-value[2]	0.016	–
DoR[1] in patients with objective response		
Number of patients with objective response	18	17
Number of events (%)	13 (72.2%)	16 (94.1%)
Median DoR (95% CI), months	5.6 (3.8, 5.9)	3.6 (1.9, 3.8)
HR (95% CI)	0.26 (0.11, 0.62)	–
Log-rank test, *P*-value[2]	0.001	–
OS[3]		
Number of events, (%)	29 (63.0%)	43 (86.0%)
Median OS (95% CI), months	13.9 (11.1, 18.4)	12.2 (7.7, 15.3)
HR (95% CI)	0.52 (0.31, 0.86)	–
Log-rank test, *P*-value[2]	0.01	–

[1]Data cutoff date for the primary analysis: March 22, 2021; applies to PFS and DoR. [2]Nominal *P*-values are presented. [3]Data cutoff date for the final (OS) analysis: March 7, 2022.

3 Patients Who Had Received Prior Bevacizumab

- Bevacizumab is commonly used and part of the standard of care for recurrent ovarian cancer.
- Patients who had received prior bevacizumab showed greater benefit from adding relacorilant to nab-paclitaxel.
- Prior use of bevacizumab is required for enrollment in the ROSELLA phase 3 trial.

	Intermittent Relacorilant + Nab-paclitaxel (N=31)	Nab-paclitaxel Monotherapy (N=37)
PFS[1]		
Number of events, (%)	24 (77.4%)	36 (97.3%)
Median PFS (95% CI), months	7.2 (3.0, 7.4)	3.7 (3.5, 5.5)
HR (95% CI)	0.44 (0.24, 0.78)	–
Log-rank test, *P*-value[2]	0.005	–
DoR[1] in patients with objective response		
Number of patients with objective response	11	10
Number of events (%)	7 (63.6%)	10 (100.0%)
Median DoR (95% CI), months	5.6 (4.1, NR)	3.4 (1.3, 3.7)
HR (95% CI)	0.25 (0.08, 0.83)	–
Log-rank test, *P*-value[2]	0.006	–
OS[3]		
Number of events, (%)	18 (58.1%)	28 (75.7%)
Median OS (95% CI), months	17.9 (11.9, NR)	12.6 (6.9, 15.9)
HR (95% CI)	0.47 (0.24, 0.94)	–
Log-rank test, *P*-value[2]	0.031	–

[1]Data cutoff date for the primary analysis: March 22, 2021; applies to PFS and DoR. [2]Nominal *P*-values are presented. [3]Data cutoff date for the final (OS) analysis: March 7, 2022. NR, not reached.

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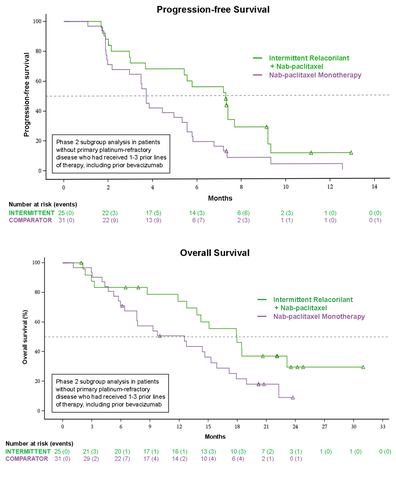
4 Final Phase 3 Population: Patients Without Primary Platinum-refractory Disease Who Had Received 1–3 Prior Lines of Therapy, Including Prior Bevacizumab

- In this subgroup, even greater improvements in PFS, DoR, and OS were observed than in the previous 2 analyses individually.

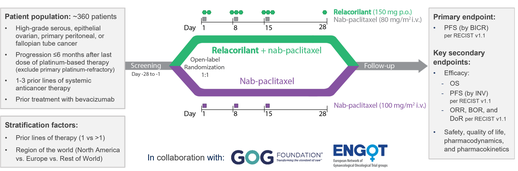
	Intermittent Relacorilant + Nab-paclitaxel (N=25)	Nab-paclitaxel Monotherapy (N=31)
PFS[1]		
Number of events, (%)	20 (80.0%)	30 (96.8%)
Median PFS (95% CI), months	7.3 (3.7, 7.7)	3.7 (2.2, 5.3)
HR (95% CI)	0.40 (0.21, 0.77)	–
Log-rank test, *P*-value[2]	0.005	–
DoR[1] in patients with objective response		
Number of patients with objective response	10	9
Number of events (%)	7 (70.0%)	9 (100.0%)
Median DoR (95% CI), months	5.6 (3.7, NR)	3.1 (1.3, NR)
HR (95% CI)	0.29 (0.09, 0.99)	–
Log-rank test, *P*-value[2]	0.016	–
OS[3]		
Number of events, (%)	15 (60.0%)	25 (80.6%)
Median OS (95% CI), months	17.9 (12.8, NR)	12.6 (6.4, 15.3)
HR (95% CI)	0.38 (0.17, 0.82)	–
Log-rank test, *P*-value[2]	0.011	–

[1]Data cutoff date for the primary analysis: March 22, 2021; applies to PFS and DoR. [2]Nominal *P*-values are presented. [3]Data cutoff date for the final (OS) analysis: March 7, 2022.



5 ROSELLA (GOG-3073, ENGOT-Ov72/MITO) Phase 3 Study Design

- Informed by these analyses, ROSELLA, a phase 3, randomized, controlled, 2-arm, open-label, multicenter study of intermittent relacorilant + nab-paclitaxel vs. nab-paclitaxel, has been initiated and is ongoing.



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

Speaker Disclosures

NC has reported fees for advisory board membership for AstraZeneca, Clovis Oncology, Eisai, GSK, Immunogen, Mersana, MSD/Merck, Nuvation Bio, Onxerna, Pfizer, PharmaMar, Pieris, Roche; fees as an invited speaker for AstraZeneca, Novartis, Clovis Oncology, GSK, MSD/Merck; institutional research grants from AstraZeneca, PharmaMar and Roche. She has also reported non-remunerated activities as member of the ESMO Guidelines Steering Committee and chair of the Scientific Committee of ACTO (Alleanza contro il tumore ovarico).