2022 ASCO® ANNUAL MEETING

OVERALL SURVIVAL DATA FROM A 3-ARM, RANDOMIZED, OPEN-LABEL, PHASE 2 STUDY OF RELACORILANT, A SELECTIVE GLUCOCORTICOID RECEPTOR MODULATOR, COMBINED WITH NAB-PACLITAXEL IN PATIENTS WITH RECURRENT PLATINUM-RESISTANT OVARIAN CANCER

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Platinum-resistant Ovarian Cancer: A Great Unmet Medical Need

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] Luvero et al. 2014

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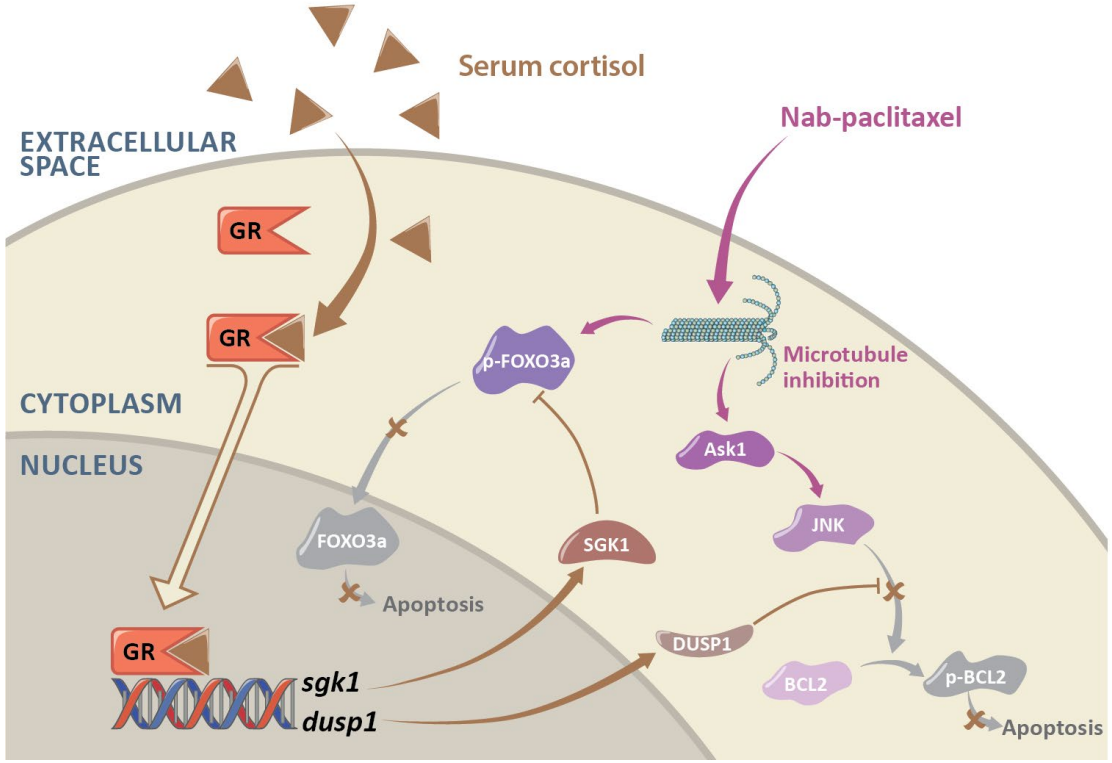
- Cortisol acts by binding to the glucocorticoid receptor (GR)



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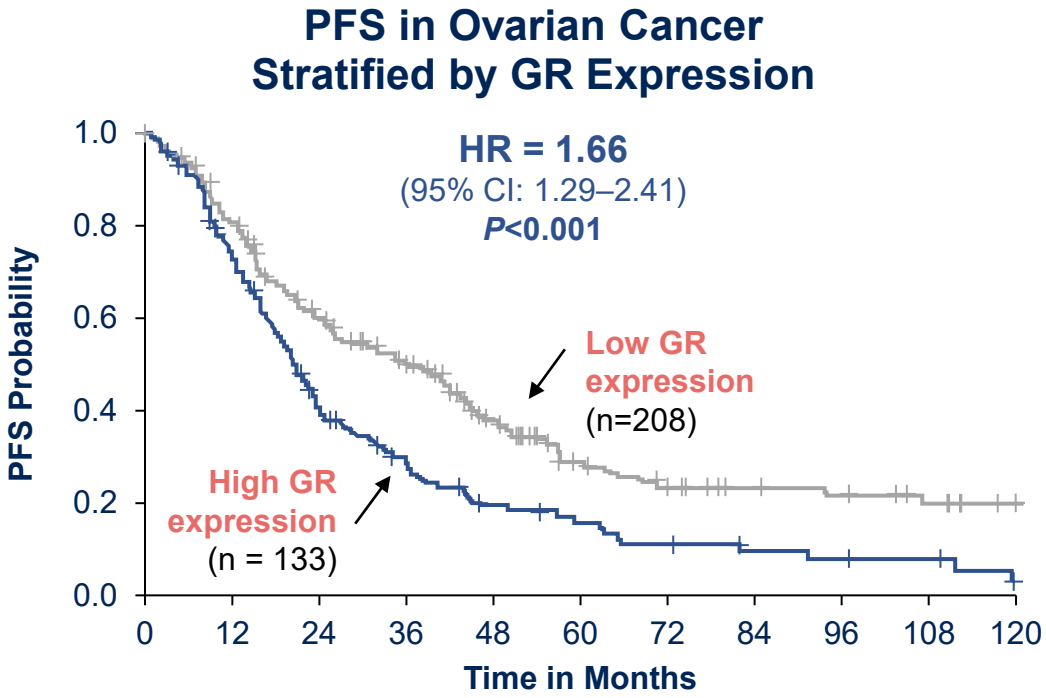
GR is abundantly expressed in ovarian tumors, and high GR expression is associated poor outcomes[2]



Reprinted from Gynecol Oncol. 2017 Jul; 146(1): 153–160. *High glucocorticoid receptor expression predicts short progression-free survival in ovarian cancer.* JT Veneris et al., with permission from Elsevier

[1] Luvero et al. 2014; [2] Veneris et al. 2017; Munster et al. 2022

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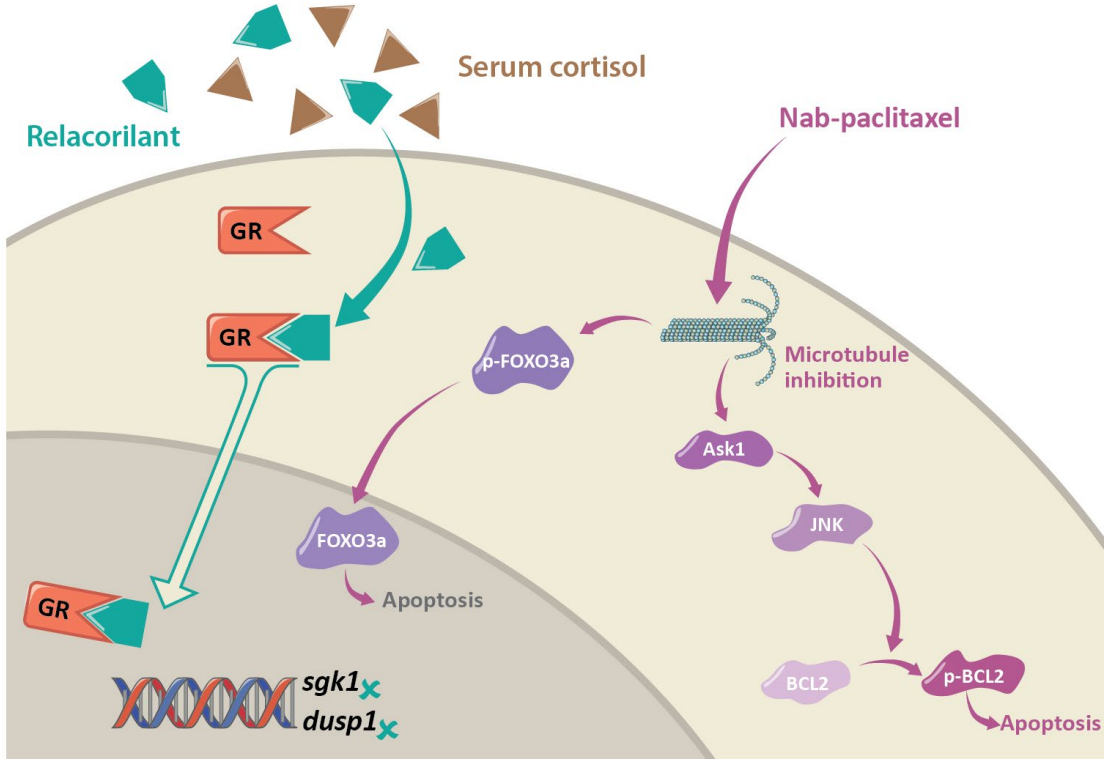
- Cortisol acts by binding to the glucocorticoid receptor (GR)

GR is abundantly expressed in ovarian tumors, and high GR expression is associated poor outcomes[2]

GR modulation with relacorilant inhibits the anti-apoptotic effects of cortisol and enhances the efficacy of cytotoxic agents



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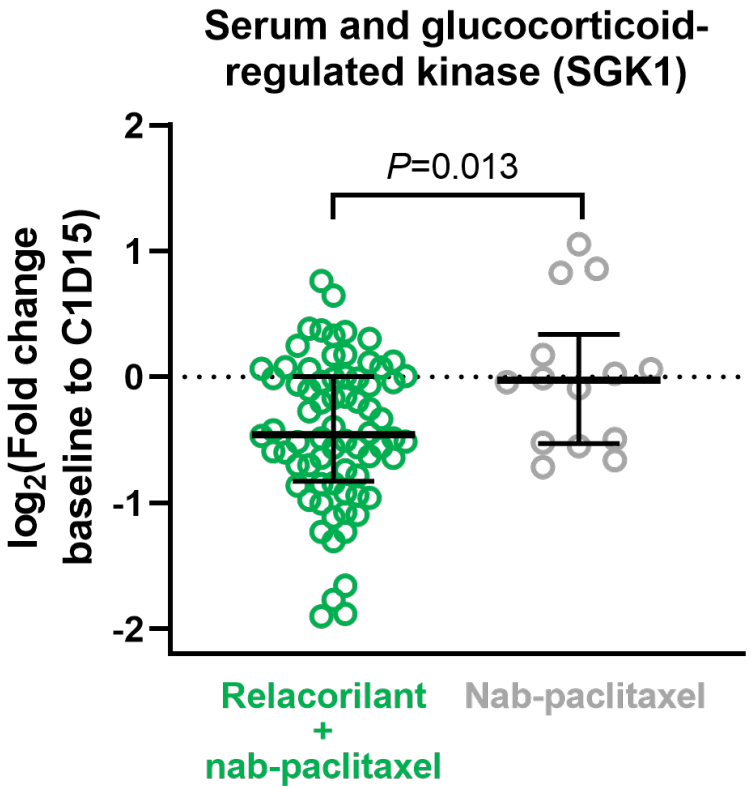
Clinical Studies Support Relacorilant's Hypothesized Mechanism of Action



Relacorilant reduces the expression of anti-apoptotic genes[1]

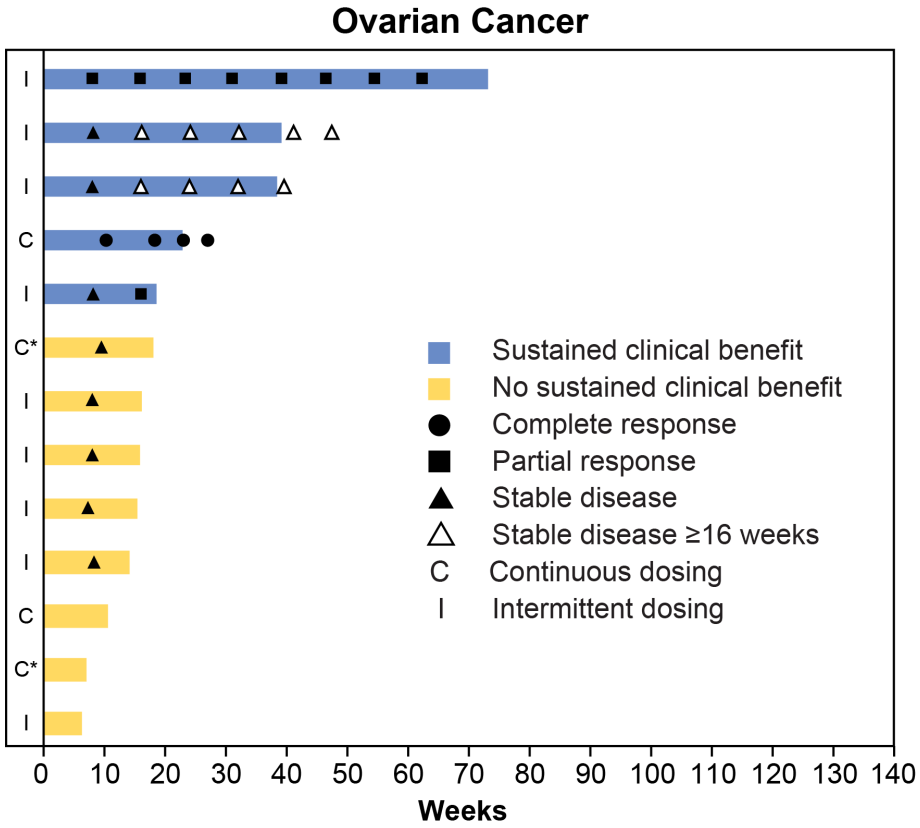
Relacorilant suppressed **significantly more GR target genes**, such as SGK1, than nab-paclitaxel alone (*P*<0.00001)

Assay conducted in whole blood. Error bars are median and interquartile ranges. [1] Analysis of clinical trial NCT03776812.

Clinical Studies Support Relacorilant's Hypothesized Mechanism of Action

Phase 1 study suggests synergy between relacorilant and nab-paclitaxel[1]

Relacorilant + nab-paclitaxel showed **durable disease control** (≥16 weeks) in **38.5% (5/13) of patients with ovarian cancer**



NCT02762981 [1] Munster et al. 2022

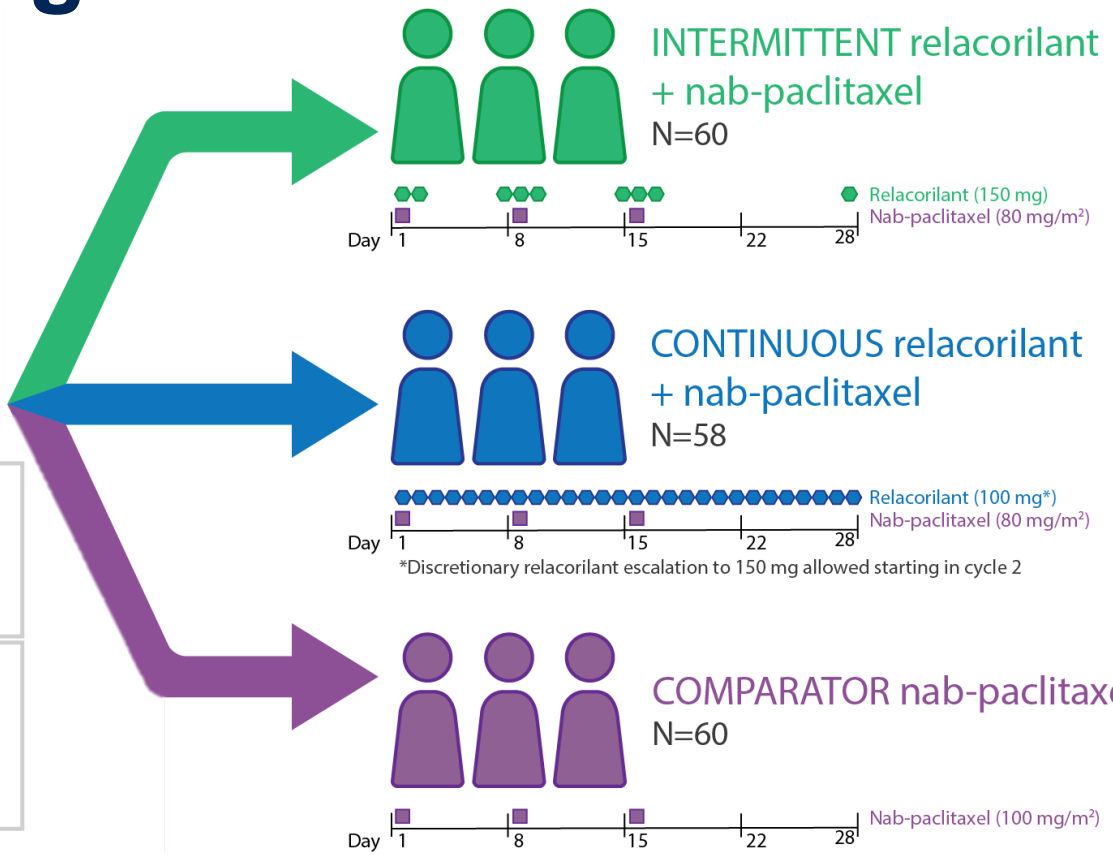
Relacorilant + Nab-paclitaxel Phase 2 Study Design

Randomized 1:1:1

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

Stratification factors:

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



Primary endpoint:

- Progression-free survival (PFS) by investigator and RECIST v1.1

Secondary endpoints:

- Objective response rate (ORR)
- Duration of response (DoR)
- Overall survival (OS)
- Safety of the relacorilant + nap-paclitaxel combination

Statistical assumptions:

- **CONTINUOUS vs COMPARATOR**: 91 PFS events to detect a HR=0.56 (median PFS increase from 3.8 to 6.8 mo)
- **INTERMITTENT vs COMPARATOR**: 92 PFS events to detect a HR=0.7 (median PFS increase from 3.8 to 5.4 mo)

PFS analysis reported at ESMO 2021

Baseline Characteristics

	INTERMITTENT N=60	CONTINUOUS N=58	COMPARATOR N=60	OVERALL N=178
Age, median (range), years	60 (38, 81)	60 (45, 75)	61.5 (41, 81)	61 (38, 81)
Platinum refractory[a], no. (%)	23 (38.3%)	20 (34.5%)	22 (36.7%)	65 (36.5%)
Primary platinum refractory, no. (%)	7 (11.7%)	3 (5.2%)	1 (1.7%)	11 (6.2%)
Number of prior therapies[b], median (range)	2.5 (1, 4)	3 (1, 5)	3 (1, 4)	3 (1, 5)
Prior lines of chemotherapy/myelosuppressive therapy, median (range)	2 (1, 4)	2 (1, 4)[c]	2 (1, 4)	2 (1,4)[c]
Patients with ≥4 prior lines of therapy, no. (%)	7 (11.7%)	15 (25.9%)	9 (15.0%)	31 (17.4%)
Prior taxane therapy, no. (%)	59 (98.3%)	58 (100%)	60 (100%)	177 (99.4%)
Prior bevacizumab therapy, no. (%)	31 (51.7%)	37 (63.8%)	37 (61.7%)	105 (59.0%)
Prior PARP therapy, no. (%)	18 (30.0%)	27 (46.6%)	20 (33.3%)	65 (36.5%)
Molecular profiling (available in a subset of the study population only)				
BRCA1(+), n/N (%)	5/42 (11.9%)	4/42 (9.5%)	7/48 (14.6%)	16/132 (12.1%)
BRCA2(+), n/N (%)	1/36 (2.8%)	3/39 (7.7%)	3/39 (7.7%)	7/114 (6.1%)

[a] Progressing during or within 1 month from last platinum treatment. [b] Chemotherapy or molecularly targeted agents. [c] Data for 1 patient updated after the primary analysis cutoff date.

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

Previously reported at ESMO 2021

Safety of Intermittent Relacorilant + Nab-Paclitaxel Comparable to Nab-Paclitaxel

n, (%)	INTERMITTENT N=60	CONTINUOUS N=57	COMPARATOR N=60
Neutropenia[a]	12 (20.0%)	22 (38.6%)	22 (36.7%)
Grade ≥3	4 (6.7%)	15 (26.3%)	9 (15.0%)
Febrile neutropenia (Grade 3)[b]	0 (0.0%)	0 (0.0%)	1 (1.7%)
Anemia[c]	29 (48.3%)	37 (64.9%)	34 (56.7%)
Grade ≥3	8 (13.3%)	11 (19.3%)	7 (11.7%)
Peripheral neuropathy[d]	22 (36.7%)	31 (54.4%)	21 (35.0%)
Grade ≥3	0 (0.0%)	9 (15.8%)	3 (5.0%)
Fatigue or asthenia	33 (55.0%)	41 (71.9%)	39 (65.0%)
Grade ≥3	7 (11.7%)	5 (8.8%)	1 (1.7%)

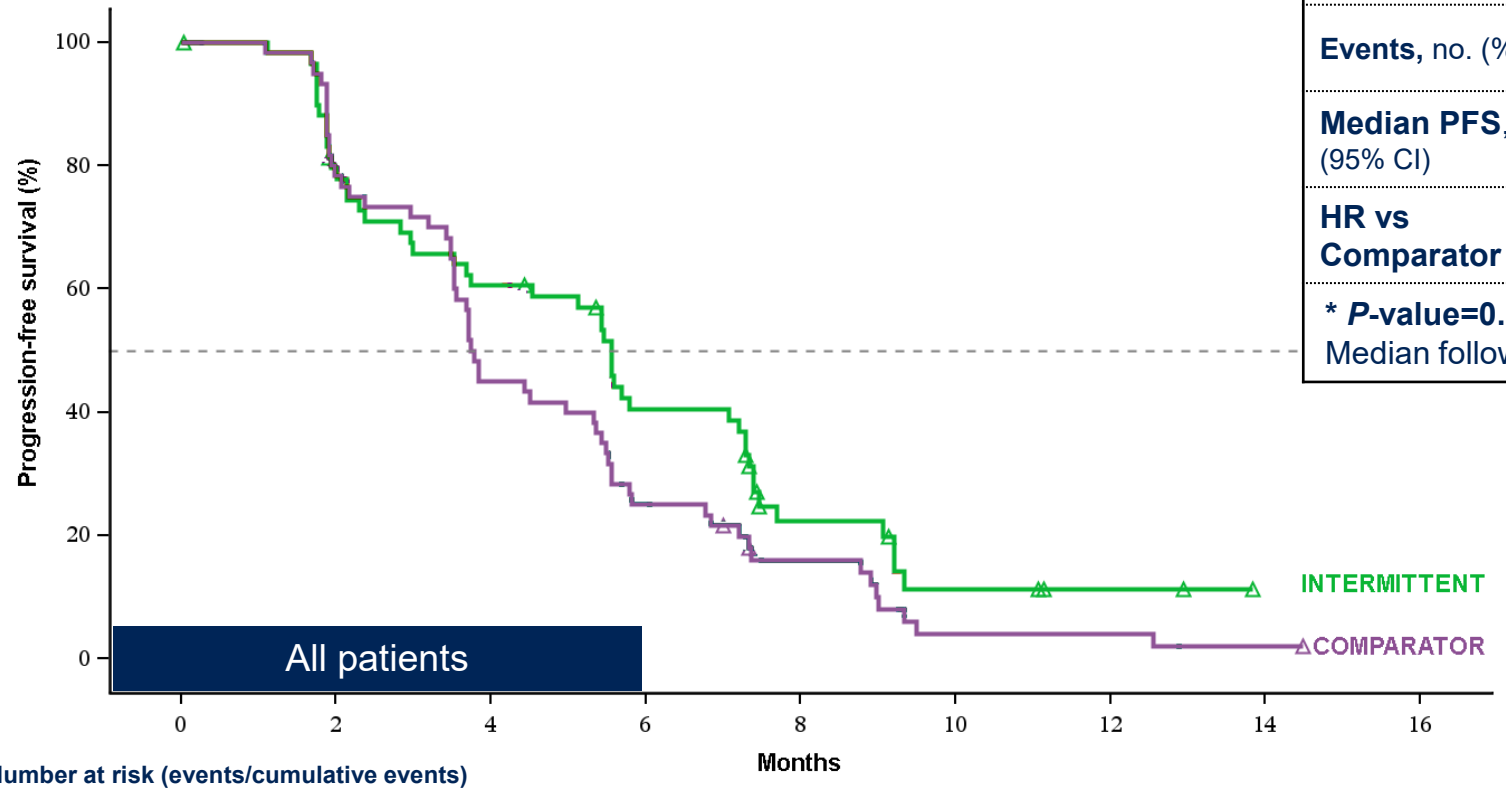
[a] Neutropenia, neutrophil count decreased; [b] Secondary to E.coli urinary sepsis in this patient; [c] Anemia, hemoglobin decreased; [d] Neuropathy peripheral, neurotoxicity, peripheral motor neuropathy, peripheral sensorimotor neuropathy, peripheral sensory neuropathy, hypoesthesia.

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy; G-CSF, granulocyte-colony stimulating factor

- All relacorilant-treated patients received prophylactic G-CSF to reduce the risk of neutropenia
- 46.7% of patients in the comparator arm received G-CSF per the investigator's standard practice

Data cutoff: March 7, 2022

Intermittent Relacorilant + Nab-Paclitaxel Improved PFS



	INTERMITTENT* N=60	COMPARATOR N=60
Events, no. (%)	47 (78.3%)	57 (95.0%)
Median PFS, mo (95% CI)	**5.6** (3.7, 7.2)	3.8 (3.5, 5.4)
HR vs Comparator	**0.66** (0.44, 0.98)	N/A

* ***P*-value=0.038 vs. nab-paclitaxel alone**; no multiplicity adjustment
Median follow-up time: 11.1 months Data cutoff: March 22, 2021

While ORR was similar, **DoR** was **significantly improved in the INTERMITTENT** vs the COMPARATOR arm.

HR 0.36, 95% CI (0.16-0.77), *P*=0.006

Number at risk (events/cumulative events)

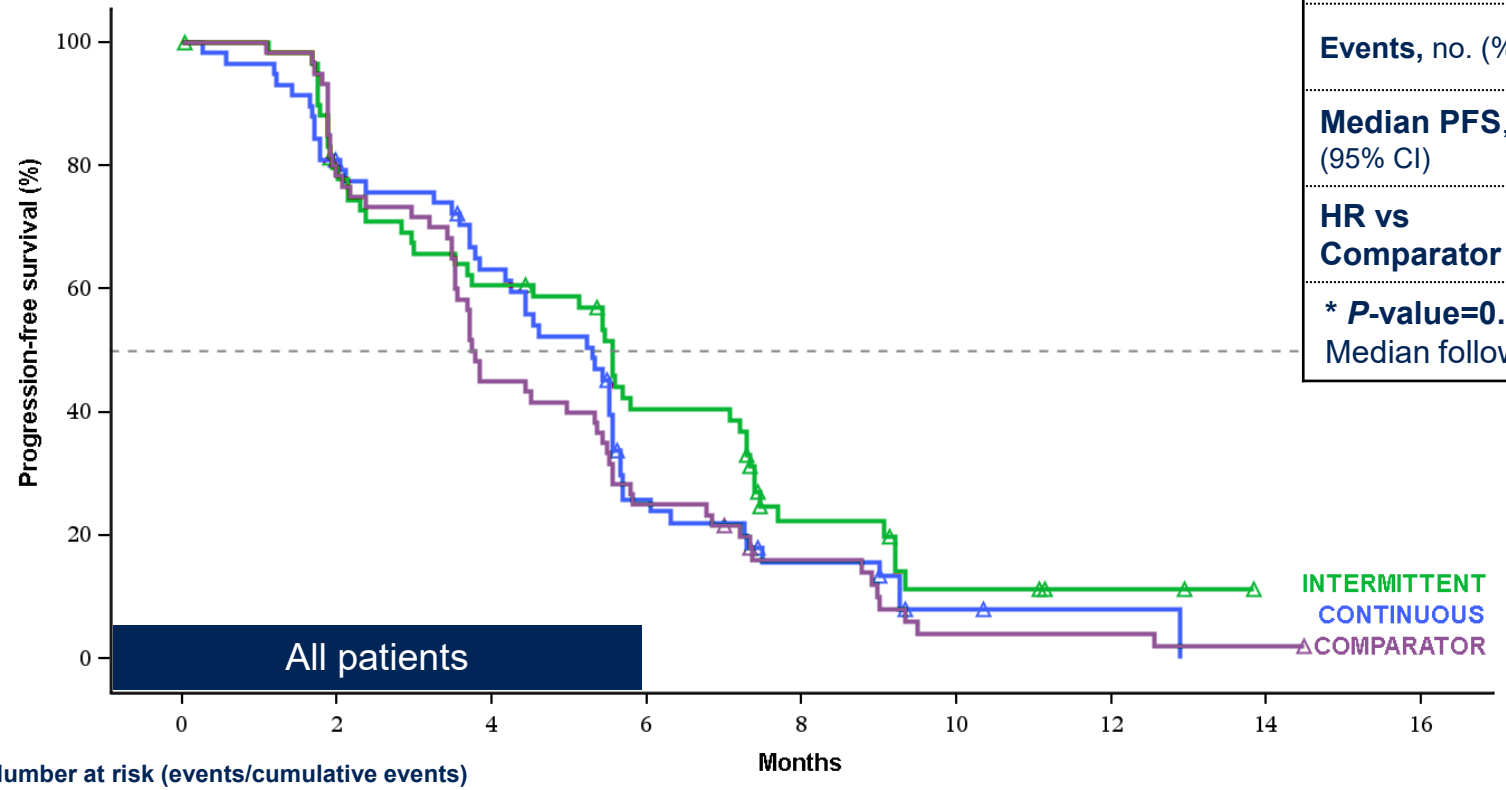
INTERMITTENT	60 (0/0)	46 (12/12)	35 (11/23)	22 (11/34)	9 (9/43)	4 (4/47)	2 (0/47)	0 (0/47)	
COMPARATOR	60 (0/0)	47 (13/13)	27 (20/33)	15 (12/45)	8 (5/50)	2 (6/56)	2 (0/56)	1 (1/57)	0 (0/57)

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

Previously reported at ESMO 2021

PRESENTED BY:
Dr. Nicoletta Colombo

Intermittent Relacorilant + Nab-Paclitaxel Improved PFS



	INTERMITTENT* N=60	CONTINUOUS N=58	COMPARATOR N=60
Events, no. (%)	47 (78.3%)	50 (86.2%)	57 (95.0%)
Median PFS, mo (95% CI)	**5.6** (3.7, 7.2)	5.3 (3.8, 5.6)	3.8 (3.5, 5.4)
HR vs Comparator	**0.66** (0.44, 0.98)	0.83 (0.56, 1.22)	N/A

* ***P*-value=0.038 vs. nab-paclitaxel alone**; no multiplicity adjustment
Median follow-up time: 11.1 months Data cutoff: March 22, 2021

Number at risk (events/cumulative events)

CONTINUOUS	58 (0/0)	46 (11/11)	35 (10/21)	13 (20/41)	7 (5/46)	2 (3/49)	1 (0/49)	0 (1/50)
INTERMITTENT	60 (0/0)	46 (12/12)	35 (11/23)	22 (11/34)	9 (9/43)	4 (4/47)	2 (0/47)	0 (0/47)
COMPARATOR	60 (0/0)	47 (13/13)	27 (20/33)	15 (12/45)	8 (5/50)	2 (6/56)	2 (0/56)	1 (1/57)

0 (0/57)

While ORR was similar, **DoR** was **significantly improved in the INTERMITTENT** vs the COMPARATOR arm.

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Previously reported at ESMO 2021

PRESENTED BY:
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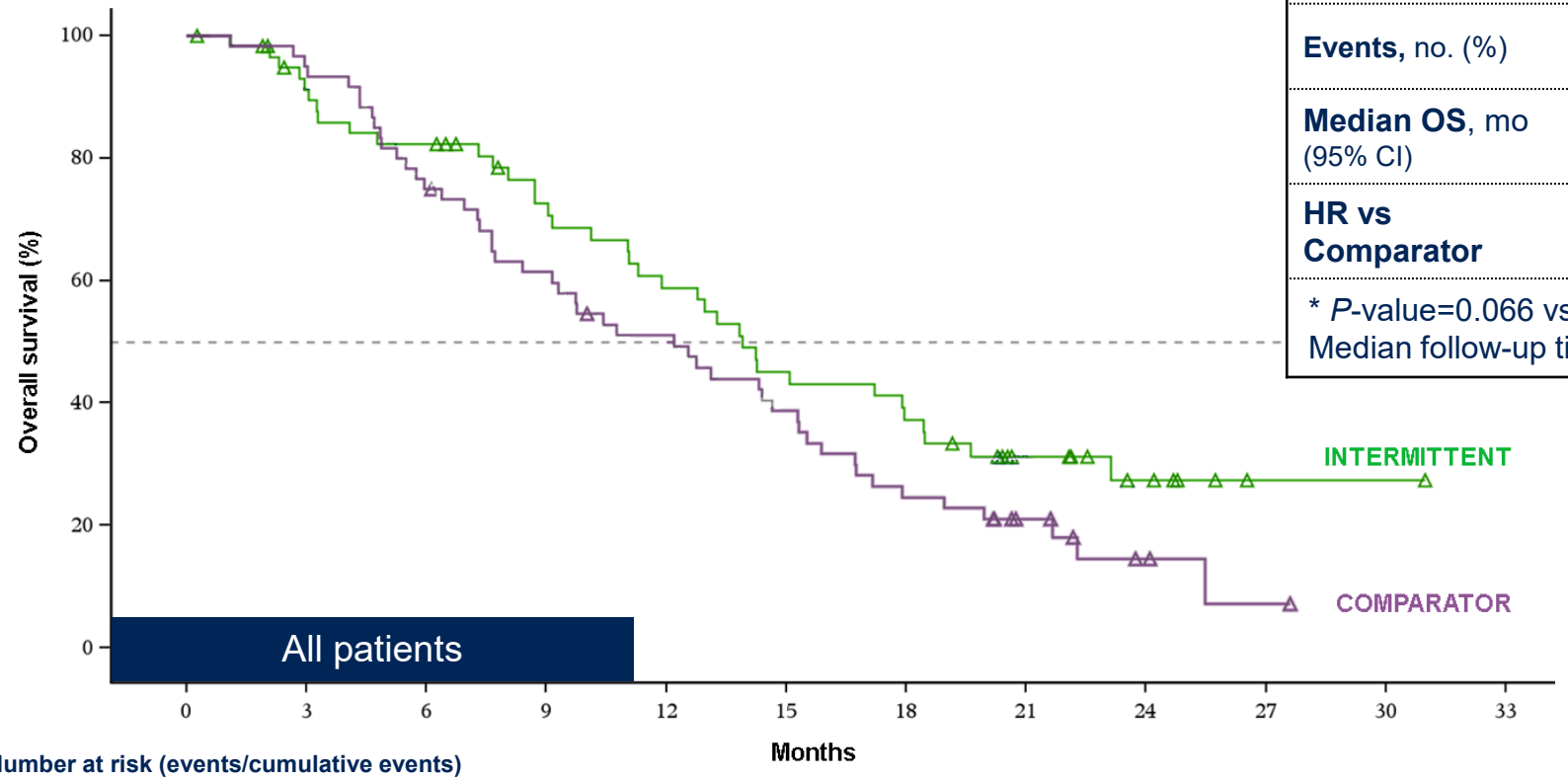
Intermittent Relacorilant + Nab-Paclitaxel Improved OS



	INTERMITTENT* N=60	COMPARATOR N=60
Events, no. (%)	37 (61.7%)	49 (81.7%)
Median OS, mo (95% CI)	13.9 (11.1, 18.4)	12.2 (7.7, 15.3)
HR vs Comparator	0.67 (0.43, 1.03)	N/A

* *P*-value=0.066 vs. nab-paclitaxel alone
Median follow-up time: 22.5 months
Data cutoff: March 7, 2022

Number at risk (events/cumulative events)

INTERMITTENT	60 (0/0)	51 (5/5)	46 (5/10)	37 (5/15)	30 (7/22)	23 (7/29)	19 (4/33)	11 (3/36)	6 (1/37)	1 (0/37)	1 (0/37)	0 (0/37)
COMPARATOR	60 (0/0)	57 (3/3)	45 (12/15)	36 (8/23)	29 (6/29)	22 (7/36)	14 (8/44)	8 (2/46)	3 (2/48)	1 (1/49)	0 (0/49)	

In the **INTERMITTENT arm, 27% of patients were still alive at 24 months** compared to **14% in the COMPARATOR arm**.

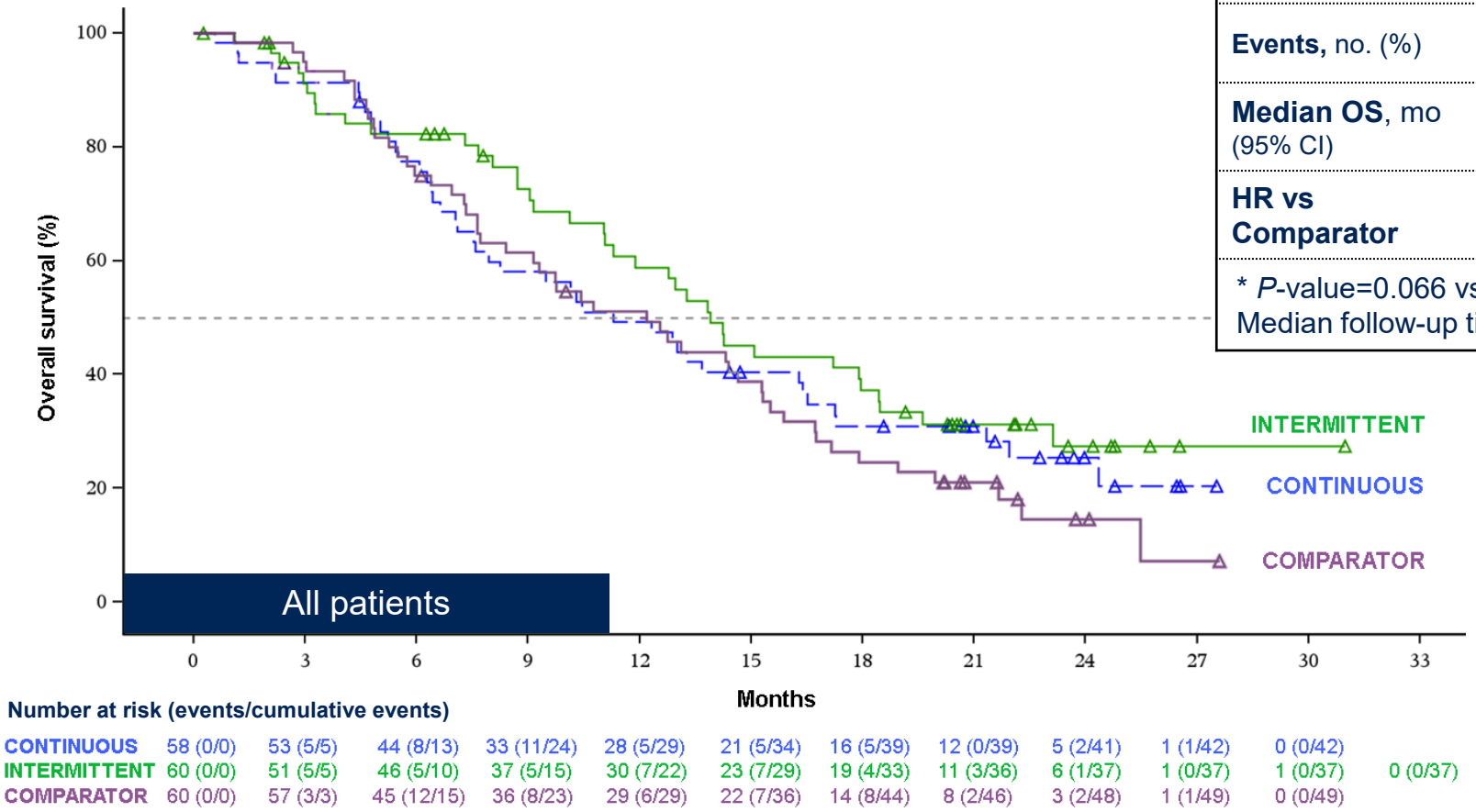
Trend toward **improved OS** consistent at primary and final analyses.

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

Intermittent Relacorilant + Nab-Paclitaxel Improved OS

	INTERMITTENT* N=60	CONTINUOUS N=58	COMPARATOR N=60
Events, no. (%)	37 (61.7%)	42 (72.4%)	49 (81.7%)
Median OS, mo (95% CI)	13.9 (11.1, 18.4)	11.3 (7.5, 16.4)	12.2 (7.7, 15.3)
HR vs Comparator	0.67 (0.43, 1.03)	0.85 (0.56, 1.29)	N/A

* *P*-value=0.066 vs. nab-paclitaxel alone
Median follow-up time: 22.5 months
Data cutoff: March 7, 2022



Number at risk (events/cumulative events)

CONTINUOUS	58 (0/0)	53 (5/5)	44 (8/13)	33 (11/24)	28 (5/29)	21 (5/34)	16 (5/39)	12 (0/39)	5 (2/41)	1 (1/42)	0 (0/42)	
INTERMITTENT	60 (0/0)	51 (5/5)	46 (5/10)	37 (5/15)	30 (7/22)	23 (7/29)	19 (4/33)	11 (3/36)	6 (1/37)	1 (0/37)	1 (0/37)	0 (0/37)
COMPARATOR	60 (0/0)	57 (3/3)	45 (12/15)	36 (8/23)	29 (6/29)	22 (7/36)	14 (8/44)	8 (2/46)	3 (2/48)	1 (1/49)	0 (0/49)	

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Trend toward **improved OS** consistent at primary and final analyses.

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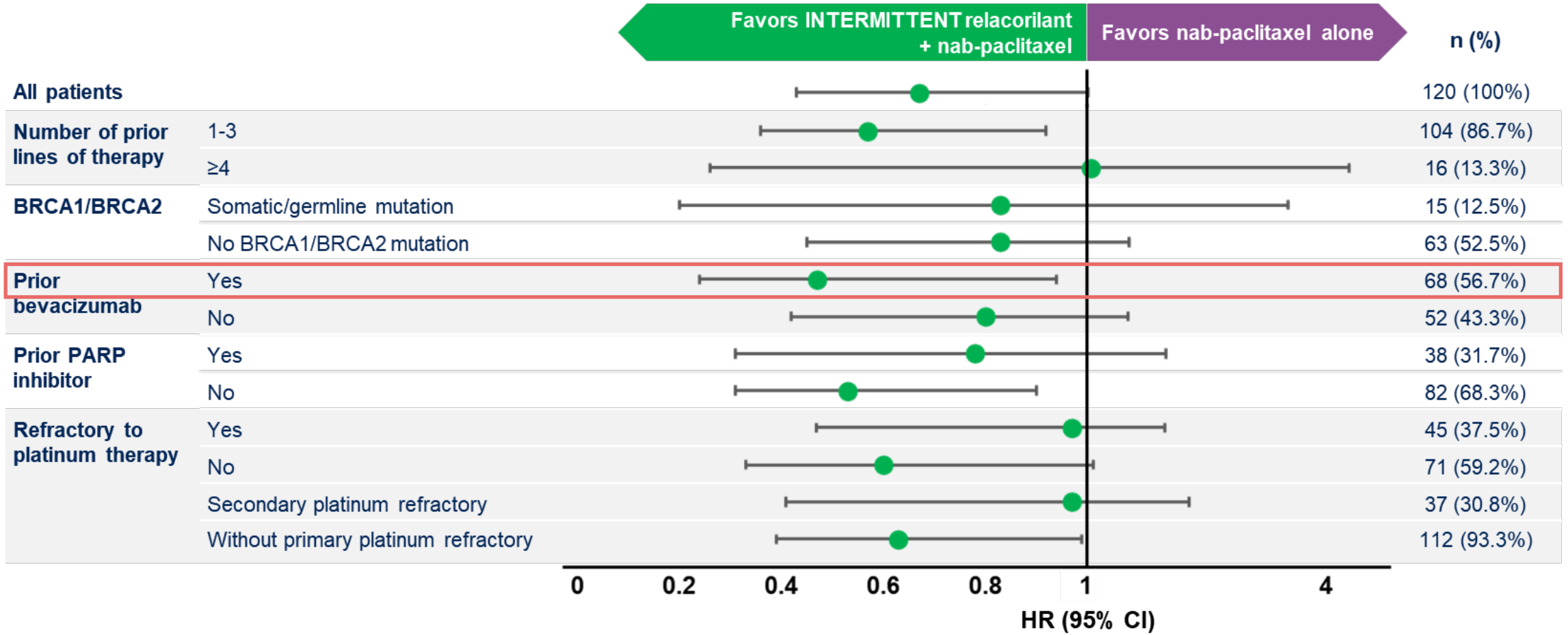
OS in Relevant Subgroups

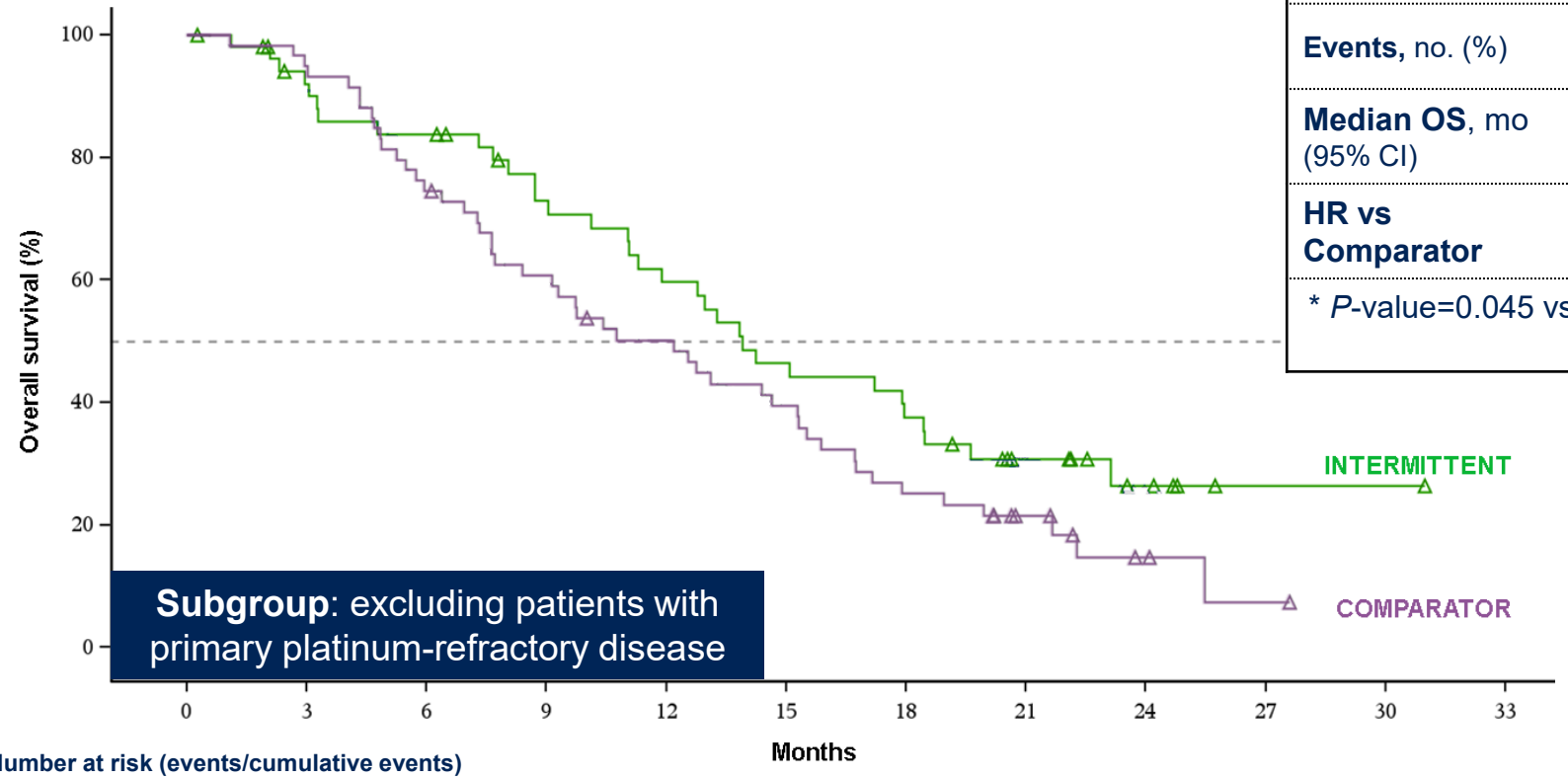


Intermittent Relacorilant + Nab-Paclitaxel Improved OS

	INTERMITTENT* N=53	COMPARATOR N=59
Events, no. (%)	33 (62.3%)	48 (81.4%)
Median OS, mo (95% CI)	13.9 (11.1, 18.4)	12.2 (7.7, 15.3)
HR vs Comparator	0.63 (0.39, 0.99)	N/A

* *P*-value=0.045 vs. nab-paclitaxel alone

Data cutoff: March 7, 2022



Number at risk (events/cumulative events)

INTERMITTENT	53 (0/0)	45 (4/4)	41 (4/8)	33 (5/13)	27 (6/19)	21 (6/25)	17 (4/29)	10 (3/32)	5 (1/33)	1 (0/33)	1 (0/33)	0 (0/33)
COMPARATOR	59 (0/0)	56 (3/3)	44 (12/15)	35 (8/23)	28 (6/29)	22 (6/35)	14 (8/43)	8 (2/45)	3 (2/47)	1 (1/48)	0 (0/48)	

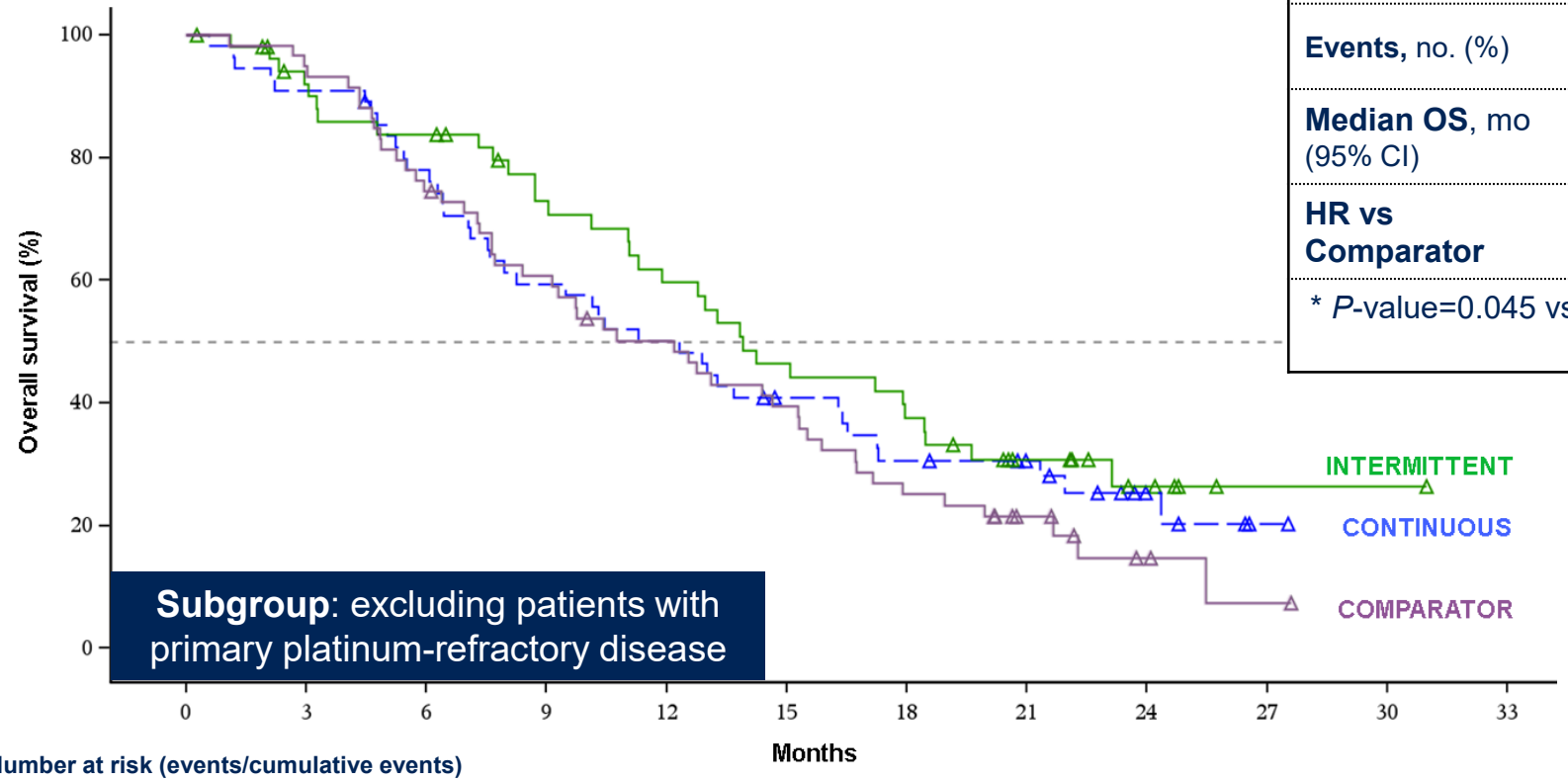
CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

Intermittent Relacorilant + Nab-Paclitaxel Improved OS

	INTERMITTENT* N=53	CONTINUOUS N=55	COMPARATOR N=59
Events, no. (%)	33 (62.3%)	40 (72.7%)	48 (81.4%)
Median OS, mo (95% CI)	13.9 (11.1, 18.4)	12.3 (7.6, 16.4)	12.2 (7.7, 15.3)
HR vs Comparator	0.63 (0.39, 0.99)	0.84 (0.54, 1.29)	N/A

* *P*-value=0.045 vs. nab-paclitaxel alone

Data cutoff: March 7, 2022



Number at risk (events/cumulative events)

CONTINUOUS	55 (0/0)	50 (5/5)	42 (7/12)	32 (10/22)	27 (5/27)	20 (5/32)	15 (5/37)	12 (0/37)	5 (2/39)	1 (1/40)	0 (0/40)
INTERMITTENT	53 (0/0)	45 (4/4)	41 (4/8)	33 (5/13)	27 (6/19)	21 (6/25)	17 (4/29)	10 (3/32)	5 (1/33)	1 (0/33)	1 (0/33)	0 (0/33)
COMPARATOR	59 (0/0)	56 (3/3)	44 (12/15)	35 (8/23)	28 (6/29)	22 (6/35)	14 (8/43)	8 (2/45)	3 (2/47)	1 (1/48)	0 (0/48)	

CONTINUOUS, once-daily relacorilant + nab-paclitaxel; INTERMITTENT, intermittent relacorilant + nab-paclitaxel; COMPARATOR, nab-paclitaxel monotherapy

Conclusions

- Cortisol modulation is a promising novel oncologic therapeutic platform
- This study was the first randomized, controlled, phase 2 trial of relacorilant + nab-paclitaxel in patients with platinum-resistant/refractory ovarian, primary peritoneal, or fallopian tube cancer
- In this heavily pretreated population (up to 4 lines of prior chemotherapy), benefit was observed with intermittent relacorilant + nab-paclitaxel treatment

Primary analysis:

- Improved PFS without additional side-effect burden with intermittent relacorilant + nab-paclitaxel vs. nab-paclitaxel alone
- Despite overrepresentation of primary platinum-refractory patients in the intermittent arm

Final OS analysis:

- Confirmed trend toward improved OS observed at the primary analysis in all patients
- In patients without primary platinum-refractory disease, greater improvement in OS was seen

- A phase 3 trial evaluating intermittent relacorilant + nab-paclitaxel vs. chemotherapy is planned to start in the second quarter of 2022

Thanks to all those who contributed to this study!

The study patients and their families.

The sponsor team:

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