Strategies in Platinum Resistant Ovarian Cancer

	Trial	Phase	Regimen	Tumor testing/ Prevalence
Taxanes	**GOG-3018 (OVAL)**	3	VB-111/placebo D1 (56 day cycle) + weekly paclitaxel vs. weekly Paclitaxel	no
	GOG-3029 (INNOVATE-3)	3	TTFields >18 hr/day + weekly paclitaxel vs. weekly Paclitaxel	no
	GOG-3044 (PROFECTA)	3	Afuresertib PO QD + Paclitaxel D1,8,15 Q3W vs. weekly Paclitaxel	yes
	GOG-3059 (AXLerate-OC)	3	AVB-S6-500 (D1&15) +Weekly paclitaxel (D 1, 8, 15 on a 28d cycle) vs. weekly Paclitaxel	no
	GOG-3073 (ROSELLA)	3	Relacorilant + nab-paclitaxel vs. nab-paclitaxel	no
Antibody Drug Conjugates	**GOG-3045 (MIRASOL)**	3	Mirvetuximab vs Investigator Choice chemotherapy	yes
	GOG-3048 (UPLIFT)	1b	XMT-1536 (Upifitimab) every 4 weeks	no
Immunotherapy	**NRG-GY009**	2/3	PLD/Atezolizumab (D1&15) vs. PLD/Bevacizumab(D1&15)/Atezo (D1&15) vs. PLD/Bevacizumab (D1&15)	no
	GOG-3063 (ARTISTRY 7)	3	Nemvaleukin + Pembrolizumab vs. Pembrolizumab vs. Nemvaleukin vs. Investigator Choice chemotherapy	no
Targeting DDR/ PARPi resistance	**NRG-GY005**	2/3	Olaparib vs. Olaparib/Cediranib vs. Cediranib vs. Investigator Choice chemotherapy	no
	NRG-GY023	2	Durvalumab/Olaparib/Cediranib vs. Olaparib/Cediranib vs. Durvalumab/Cediranib vs. Investigator Choice chemotherapy	no
	NRG-GY029 (approved)	2	Olaparib + copanlisib vs. Investigator Choice chemotherapy (PARPi resistant)	no
	GOG-3072	1b	ZN-c3 in combination with chemotherapy in patients with PROC	no

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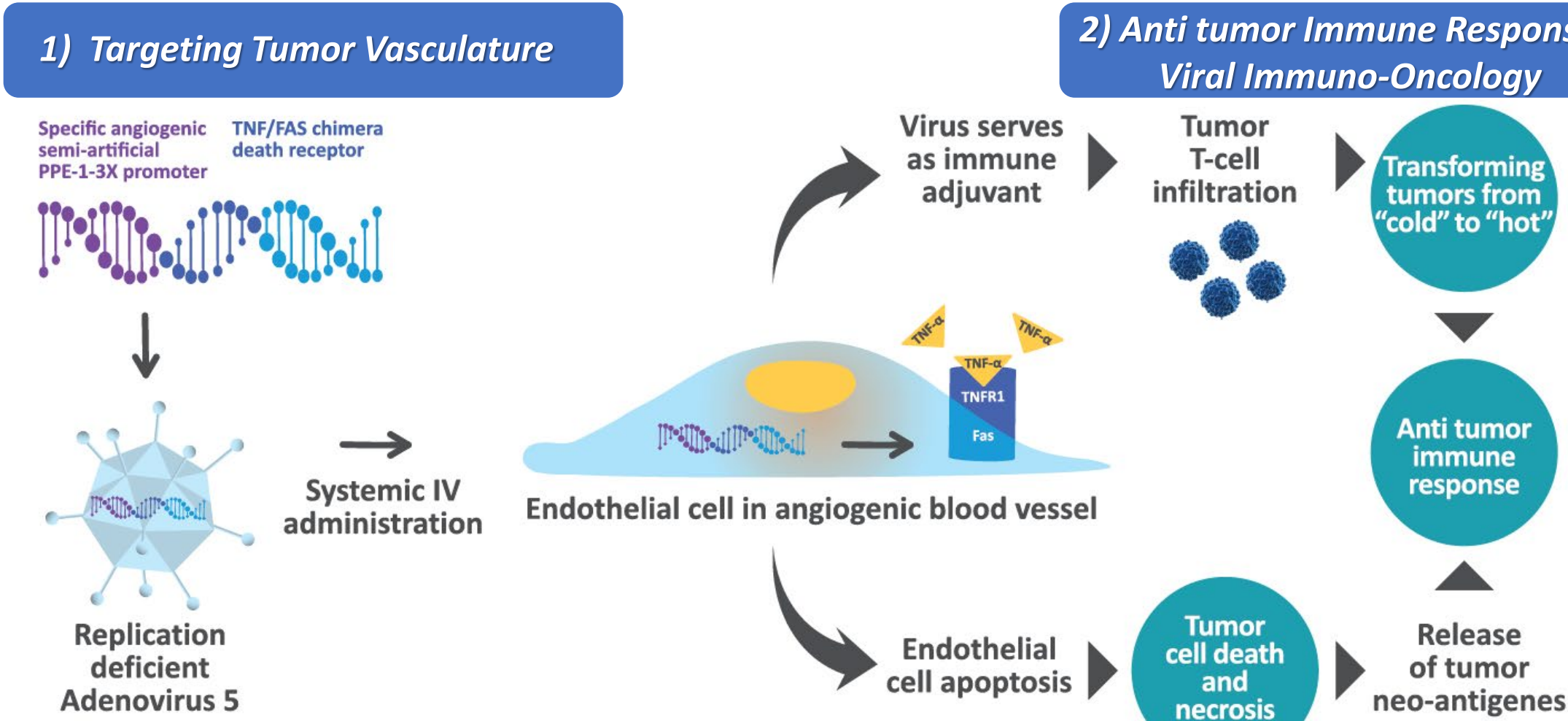
VB-111: Novel, Dual Mechanism for Targeting Solid Tumors



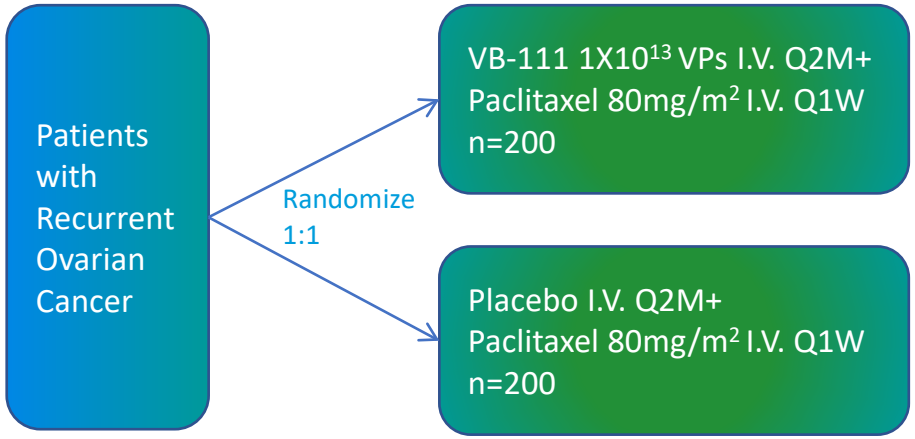
https://www.vblrx.com/cancer-programs/cancer-platform-technology/

Arend RC et alGynecol Oncol. 2020 Jun;157(3):578-584.

OVAL

GOG 3018: OVAL Design and Population

- Randomized, Controlled, Double-Blind Phase 3 Registration Trial in Platinum-Resistant Ovarian Cancer
- Approx. 110 sites (65 US, 5 Israel, 30 EU, 10 Japan), 400 subjects
- Population: Recurrent platinum resistant / refractory epithelial ovarian cancer; ≤ 5 prior lines ; Prior anti-angiogenic therapy is allowed ; ECOG 0-1 ; Measurable disease per RECIST



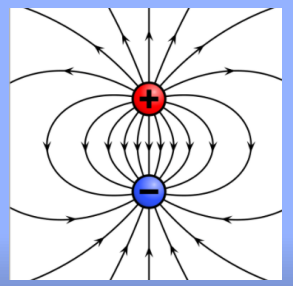
NCT03398655

TTFields Disrupt Localization and Orientation of Polar Molecules and Organelles

Forces Are Exerted on Cell Components During Cell Division

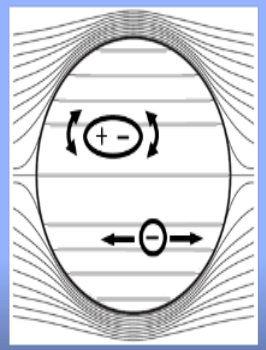
The 3 main types of cytoskeletal filaments in eukaryotic cells are microfilaments, microtubules, and intermediate filaments

physical dipole of electric charges

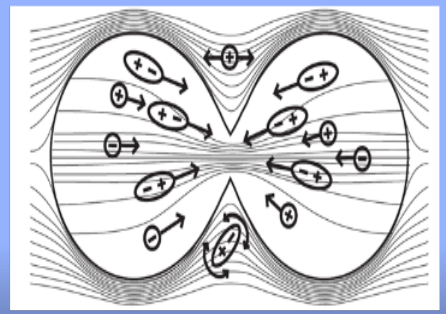


The electric dipole moment is the measure of the electrical polarity of a system of charges

Uniform electric field leads to **dipole alignment**



Nonuniform electric field leads to **dielectrophoresis**



Adapted from Gutin PH et al. 2012

Tubulin and Septin are two examples of polar molecules with very high dipole moments. In the presence of TTFields, the electric field exerted on the cancer cell "disrupts or perturbs" the function of Tubulin and Septin during mitosis

1. Kirson ED et al. *Cancer Res*. 2004;64(9):3288-3295. 2. Kirson ED et al. *Proc Natl Acad Sci U S A*. 2007;104(24):10152-10157.
3. Gera N et al. *PLoS One*. 2015;26;10(5):e0125269. 4. Giladi M et al. *Sci Rep*. 2015;5:18046.

ENGOT-ov50/ GOG-3029/ INNOVATE-3 (EF-28)
Study Design

Enrollment target (n=540)

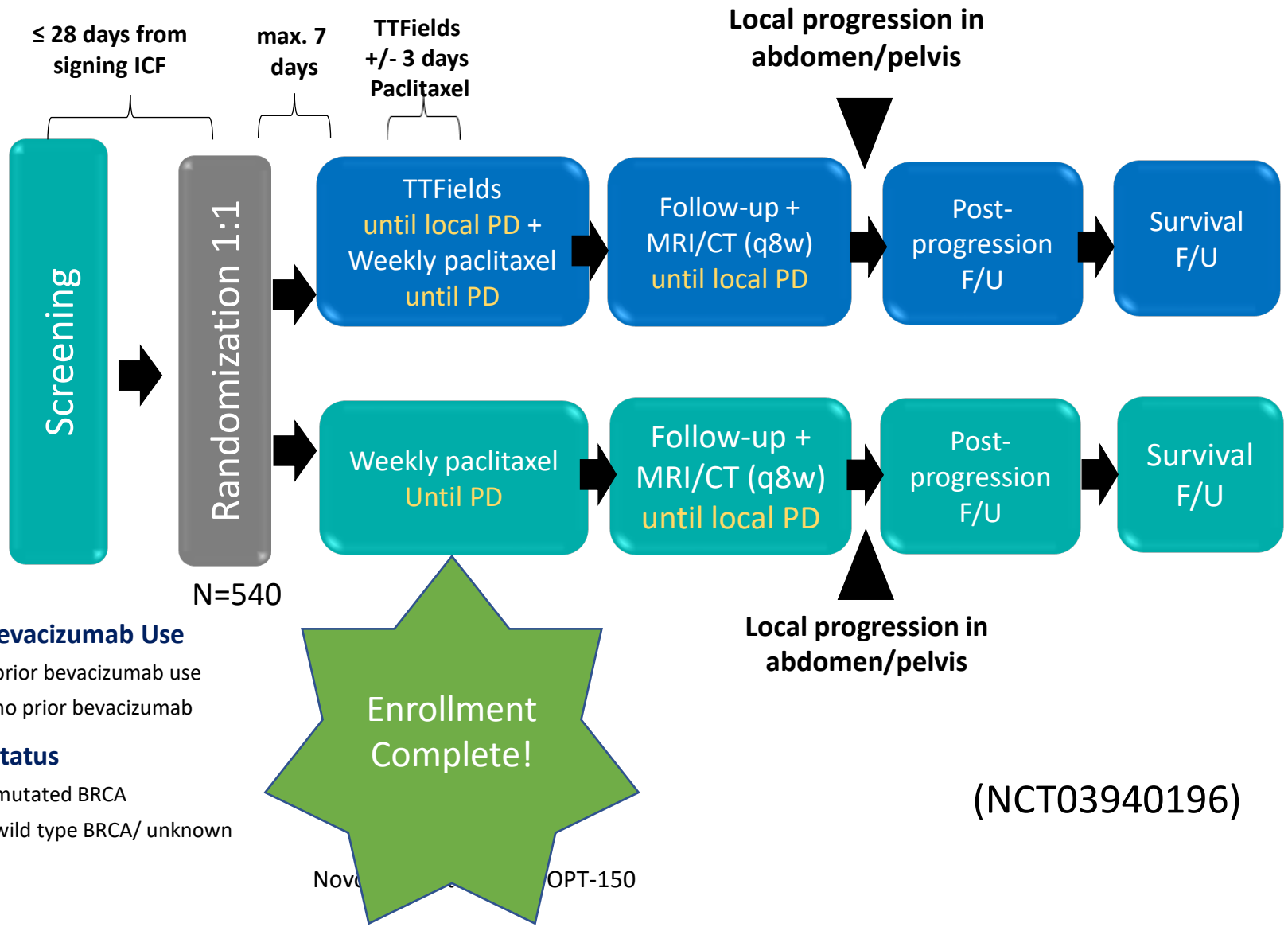
- ENGOT (60%)
- GOG (40%)
- HR estimate (<0.75)

Number of sites (n=110)

- ENGOT enrollment began March 2019
- GOG enrollment began February 2020

Stratification

- **Prior therapy**
  - no prior systemic therapy following PROC
  - one prior line
  - two prior lines
- **Prior Bevacizumab Use**
  - prior bevacizumab use
  - no prior bevacizumab
- **BRCA Status**
  - mutated BRCA
  - wild type BRCA/ unknown



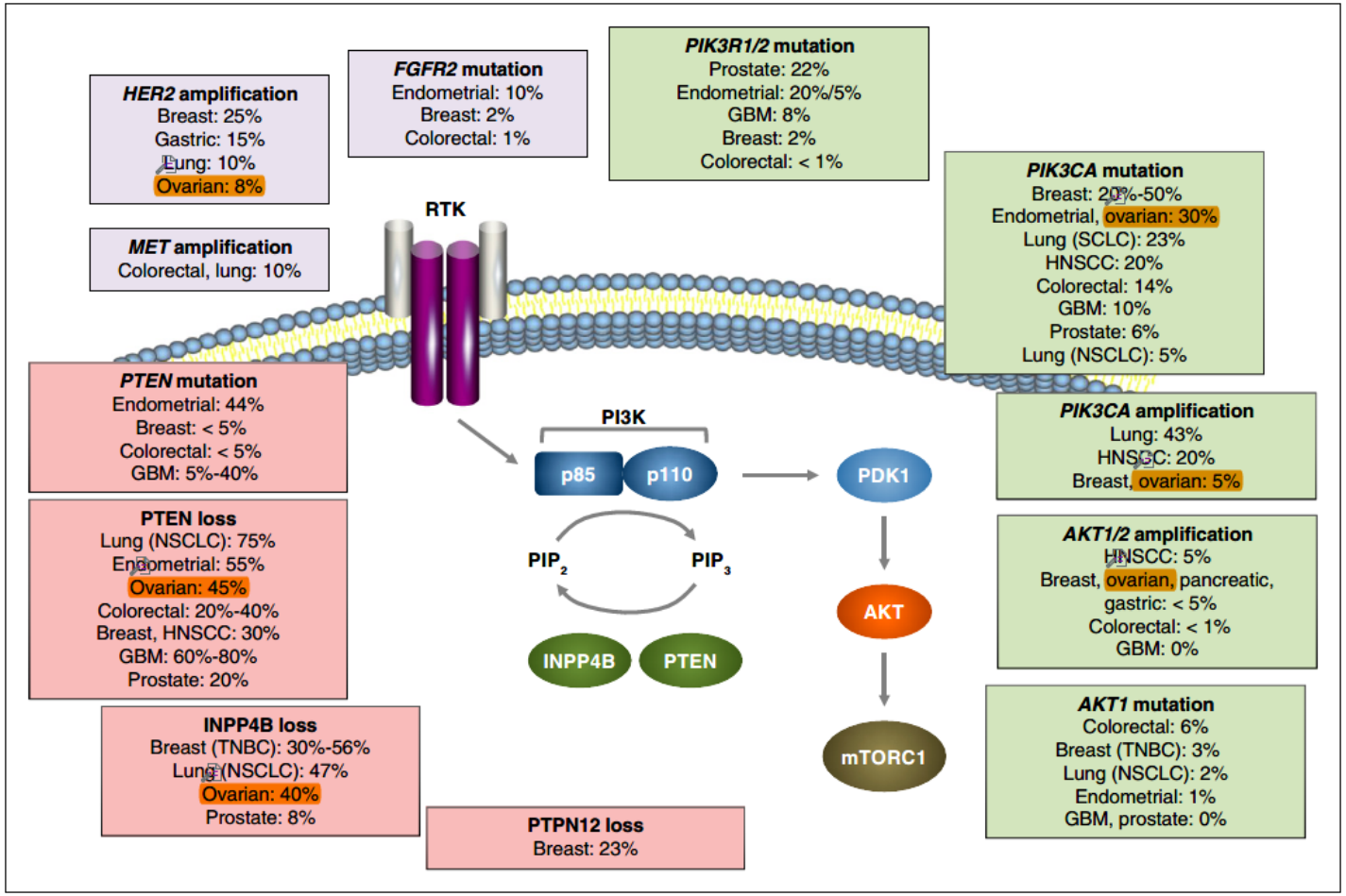
(NCT03940196)

PI3K/AKT Pathway Alterations Leading To Ovarian Tumor Growth, Survival And Resistance

PI3K/AKT pathway activation in up to 30% of ovarian cancers

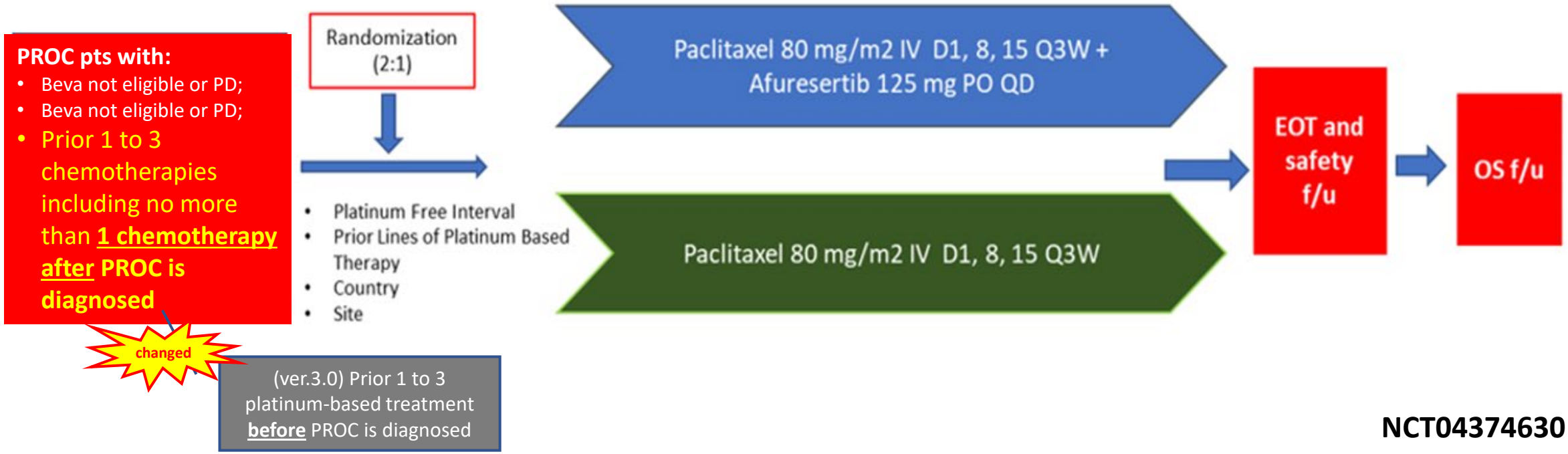
- PIK3CA or AKT mutation/amplification
- PTEN loss
- Overexpression and copy number alterations in PI3K/AKT/mTOR pathways are common in high grade serous EOC (~46%)
- PI3K/AKT/mTOR pathway is also a driver of treatment resistance
  - Preclinical evidence that platinum resistance is AKT mediated → AKT phosphorylation and activation
  - Activation inhibits platinum/paclitaxel-mediated apoptosis

LoRusso, 2016



GOG 3044: LAE002INT2001 Study Design

PROFECTA-II



NCT04374630

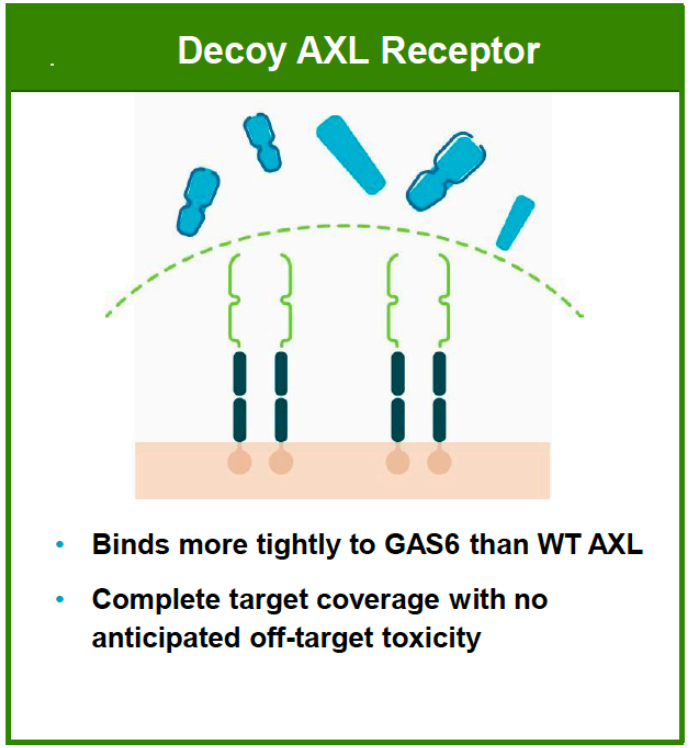
D = Day; EOT = End of treatment; f/u = Follow-up; OS = Overall survival; PARPi = Poly ADP ribose polymerase inhibitor; PD: Progressive disease; PO = Per os (oral); PROC = Platinum-resistant ovarian cancer; Q3W = Once every 3 weeks; QD = Once daily.
EOT visit and safety follow-up: within 30 days (± 7 days) of last dose.
OS follow-up: every 12 weeks (± 7 days) continuing after EOT.
The afuresertib plus paclitaxel combination therapy arm starts from the first day (Day 1) after randomization. The PK study will be performed in both the afuresertib plus paclitaxel arm and paclitaxel alone arm.

LAEKNA 来凯医药 Laekna Therapeutics

GOG-3059/AVB500-OC-004

A Phase 3, Randomized, Double-Blind, Adaptive, Placebo/Paclitaxel-Controlled Study of AVB-S6-500 in Combination with Paclitaxel in Patients with Platinum-Resistant Recurrent Ovarian Cancer

- Phase III, double blind randomized trial comparing AVB-500 + Paclitaxel vs. Placebo + weekly paclitaxel sponsored by Aravive
- AVB-500 is high-affinity AXL decoy receptor that binds to GAS6, the sole ligand of AXL
- AXL is highly expressed in metastatic and advanced stage tumors in ovarian cancer
- Phase IB data demonstrated little to no added side effects of AVB-500 to paclitaxel
- Serum based biomarker will be used to correlate response to targeted agent
- GOG and study sponsor are looking for approximately 70 US sites.
- First site activated and patient randomized to be targeted for February 2021.



NCT04729608

PI: Katherine Fuh, MD, PhD

2022 ASCO® ANNUAL MEETING

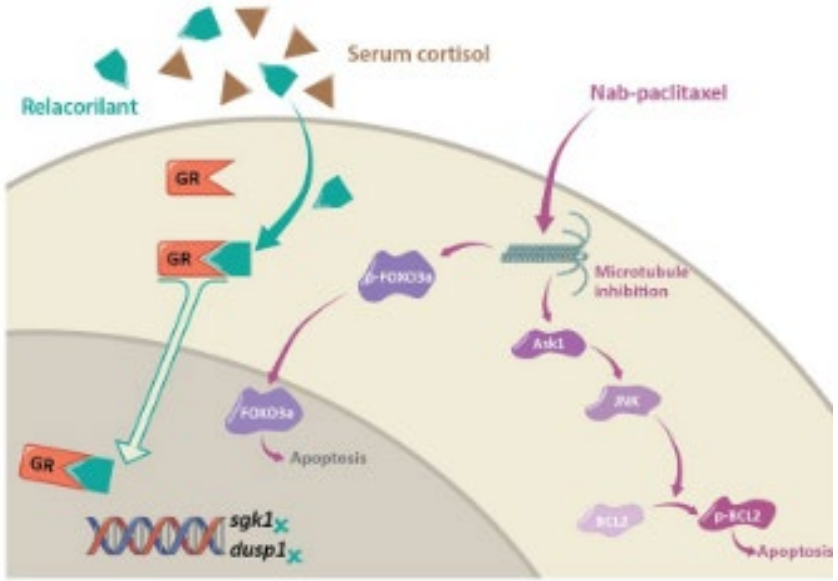
OVERALL SURVIVAL DATA FROM A 3-ARM, RANDOMIZED, OPEN-LABEL, PHASE 2 STUDY OF RELACORILANT, A SELECTIVE GLUCOCORTICOID RECEPTOR MODULATOR, COMBINED WITH NAB-PACLITAXEL IN PATIENTS WITH RECURRENT PLATINUM-RESISTANT OVARIAN CANCER

Nicoletta Colombo, Toon Van Gorp, Ursula A. Matulonis, Ana Oaknin, Rachel N. Grisham, Gini F. Fleming, Alexander B. Olawaiye, Hristina I. Pashova, Dorothy D. Nguyen, Domenica Lorusso

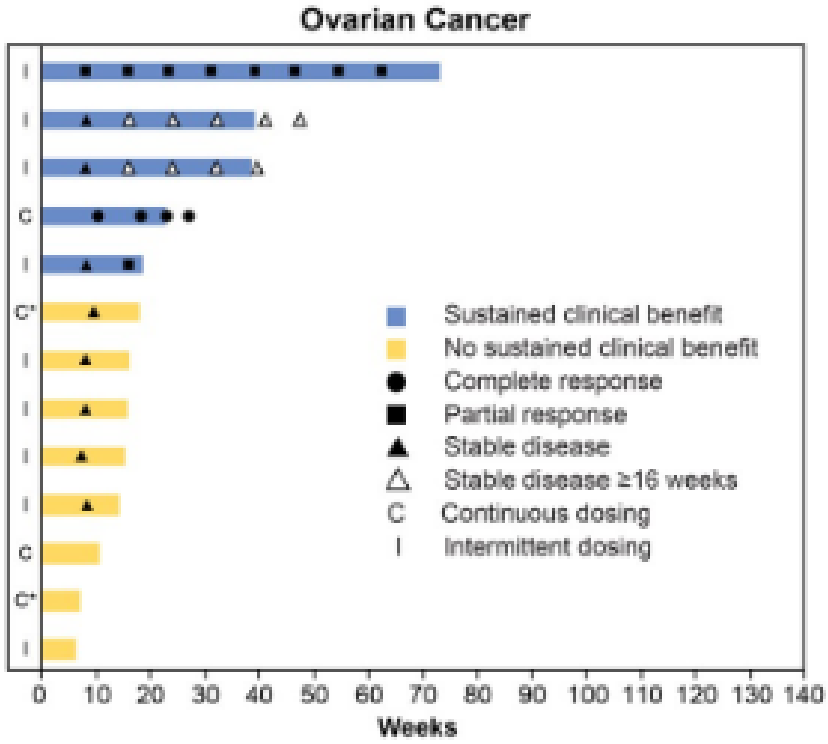
Glucocorticoid Receptor Modulation as a Target in Ovarian Cancer

Cortisol contributes to chemotherapy resistance by suppressing apoptotic pathways that cytotoxic agents such as nab-paclitaxel utilize

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



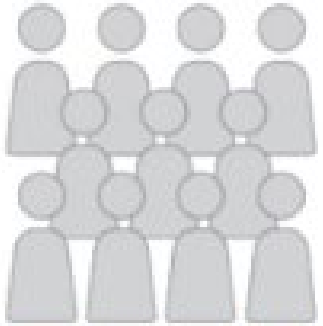
Phase 1 study of relacorilant and nab-paclitaxel suggested synergy:
~ 38.5% (5/13) pts with clinical benefit at 16 weeks



Colombo et al. ASCO 2022 Abstract LBA 5503

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

CONTINUOUS vs COMPARATOR

INTERMITTENT vs COMPARATOR

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

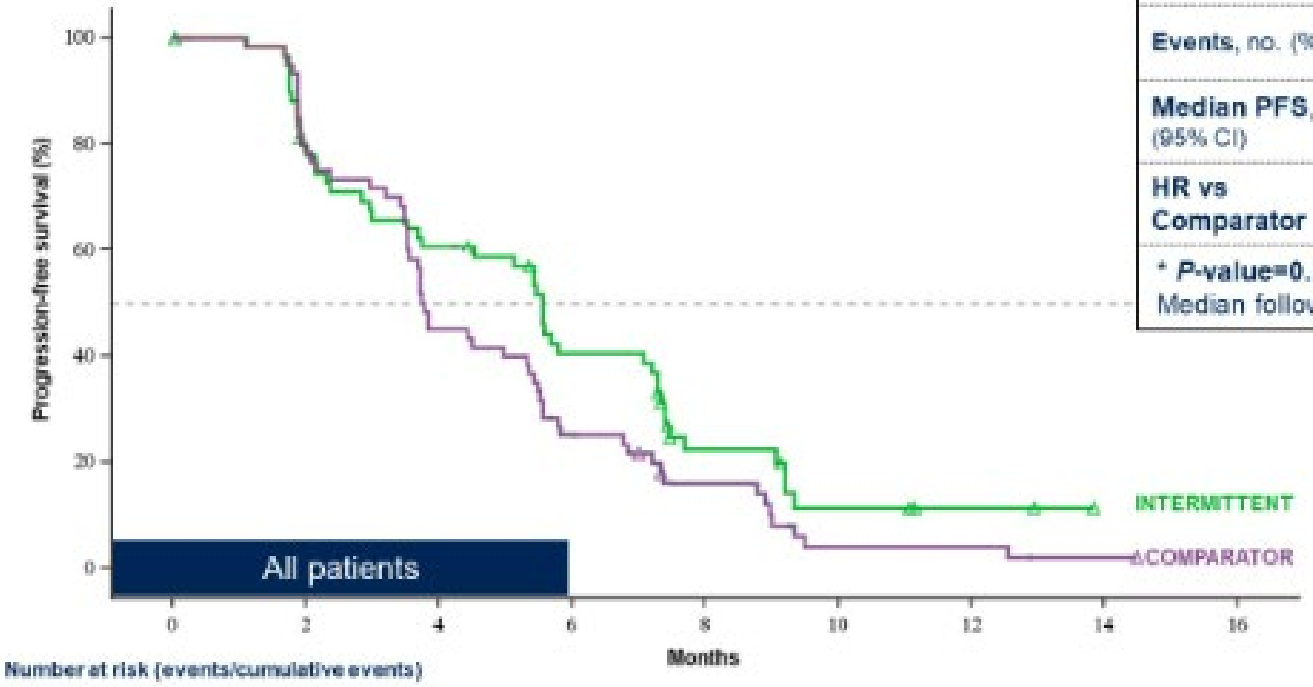
Statistical assumptions:

- **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

Colombo et al. ASCO 2022 Abstract LBA 5503

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, 0.99)	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

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

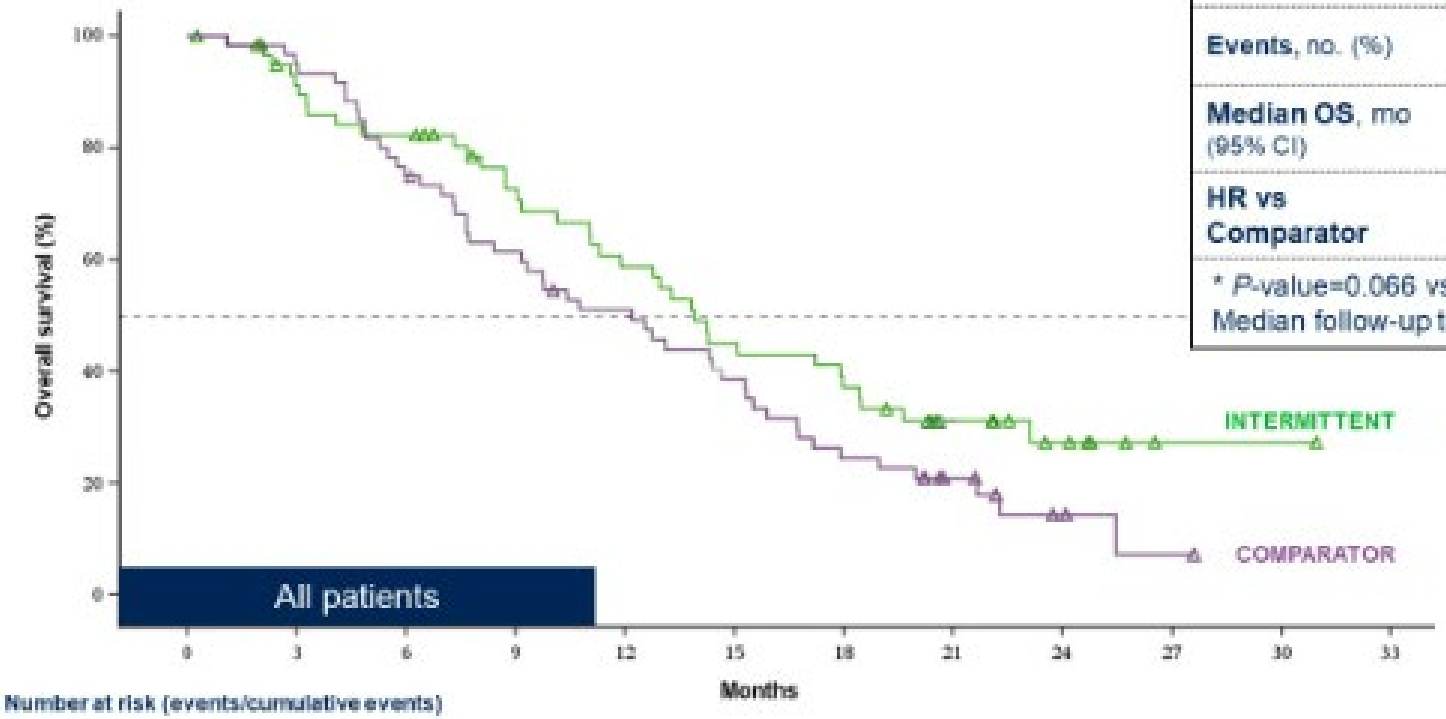
Previously reported at ESMO 2021

Colombo et al. ASCO 2022 Abstract LBA 5503

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



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

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

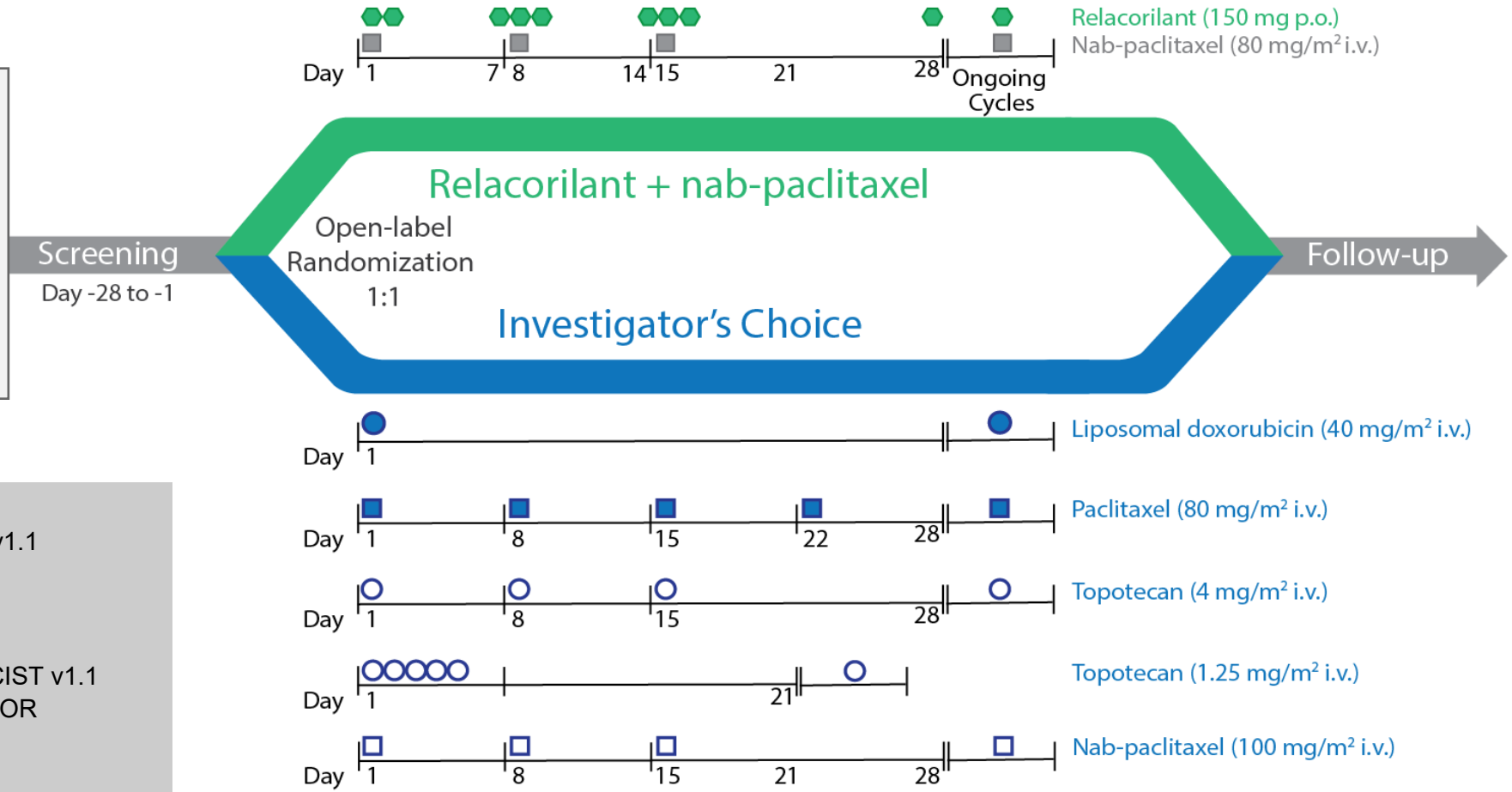
Trend toward **improved OS** consistent at primary and final analyses.

Colombo et al. ASCO 2022 Abstract LBA 5503

GOG 3073 ROSELLA
Phase 3 Study Design: Open-label, Randomized, 2-Arm Study

Patient population, n=360

- HG serous, Gr3 Endometrioid epithelial ovarian, primary peritoneal, or fallopian tube cancer
- Progression ≤6 mos after last dose of plat-based therapy (exclude primary-platinum refractory)



Primary Endpoint:
- Progression free survival (BICR) per RECIST v1.1

Secondary:
- Efficacy
  - Overall Survival
  - Progression-Free Survival (by INV) per RECIST v1.1
  - Overall Response Rate per RECIST v1.1, BOR
  - Duration of Response per RECIST v1.1
  - Clinical Benefit Rate per RECIST v1.1
  - Combined response according to RECIST v1.1 + GCIG criteria
- Safety, QOL, Ca-125, PD, PK

NCT05257408

2022 ASCO ANNUAL MEETING

Randomized phase III trial on Trabectedin (ET-743) single agent vs clinician's choice chemotherapy in recurrent ovarian, primary peritoneal or fallopian tube cancers in BRCA mutated or BRCAness phenotype patients: the MITO 23 study

Giovanni Scambia[1], Francesco Raspagliesi[2], Giorgio Valabrega[3], Nicoletta Colombo[4], Carmen Pisano[5], Chiara Cassani[6], Germana Tognon[7], Stefano Tamberi[8], Giorgia Mangili[9], Serafina Mammoliti[10], Ugo De Giorgi[11], Filippo Greco[12], Anna Maria Mosconi[13], Enrico Breda[14], Grazia Artioli[15], Claudia Andreetta[16], Claudia Casanova[17], Rita Ceccherini[18], Antonio Frassoldati[19], Domenica Lorusso[1]

[1] Fondazione Policlinico Universitario A. Gemelli IRCCS Università Cattolica, Rome, Italy; [2]Fondazione IRCCS Istituto Nazionale Tumori Milan, Milan, Italy; [3]Ospedale Umberto I, Turin, Italy; [4]European Institute of Oncology IRCCS and Università degli Studi di Milano Bicocca, Milan, Italy; [5]National Cancer Institute, IRCCS, "Fondazione G. Pascale", and MITO, Naples, Italy; [6]Fondazione IRCCS Policlinico San Matteo-University of Pavia, Pavia, Italy; [7]Azienda Ospedaliera "Spedali Civili" Di Brescia, Brescia, Italy; [8]Ospedale degli Infermi – AUSL, Ravenna, Italy; [9]IRCCS San Raffaele Hospital, Milan, Italy; [10]IRCCS Az. San Martino, Genova, Italy; [11]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori", Meldola, Italy; [12]Mater Salutis Hospital, Legnago, Italy; [13]Azenda Ospedaliera Perugia, Perugia, Italy; [14]MITO and Fatebenefratelli Hospital, Rome, Italy; [15]Ulss 2 Marca Trevigiana, Treviso, Italy; [16]Royal Marsden Hospital, London, United Kingdom; [17]Azienda USL della Romagna, Ravenna, Italy; [18]Cancer Center, Trieste, Italy; [19]S Anna University Hospital, Ferrara, Italy.

Study Design

Eligibility criteria

- Recurrent epithealial ovarian, primary peritoneal or fallopian tube cancers
- gBRCAm or
- BRCAness phenotype (patients who had received and responded to ≥2 previous platinum-based chemotherapy lines)

Stratification criteria

- Platinum sensitivity (≤ 6 months vs > 6 months)
- Measurable disease (yes/no)
- N. of previous chemotherapy lines (<3 vs ≥3)
- BRCA mutational status (gBRCA vs BRCAness phenotype)

R (1:1)

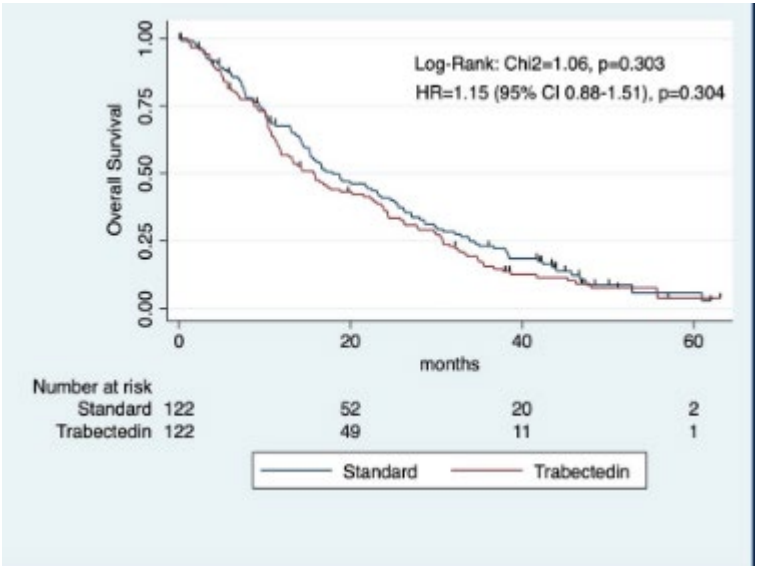
EXPERIMENTAL ARM

- **Trabectedin 1.3 mg/sqm Iv day 1 Q3W**

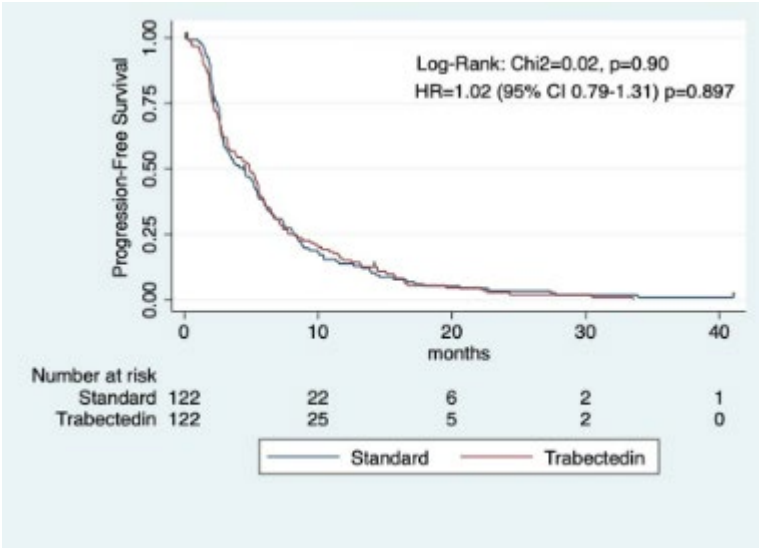
CONTROL ARM

- **Investigator's choice** (any of the following) :
  - **Paclitaxel 80 mg/sqm days 1-8-15 Q4W**
    OR
  - **Pegylated liposomal doxorubicin 40 mg/sqm day 1 Q4W**
    OR
  - **Topotecan 4 mg/sqm days 1-8-15 Q4W**
    OR
  - **Gemcitabine 1000 mg/sqm days 1-8-15 Q4W**
    OR
  - **Carboplatin AUC 5-6 day 1 Q3W or Q4W**

Lorusso et al. ASCO 2022 LBA 5504



Median OS 15.8 vs. 17.9 in Trabec vs IC
HR 1.15 (95% CI 0.88-1.51)



Median PFS 4.9 vs 4.4 in Trabec vs IC
HR 1.02 (95% CI 0.79-1.31)

Strategies in Platinum Resistant Ovarian Cancer

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	NRG-GY029 (approved)	2	Olaparib + copanlisib vs. Investigator Choice chemotherapy (PARPi resistant)	no
	GOG-3072	1b	ZN-c3 in combination with chemotherapy in patients with PROC	no

SORAYA

SINGLE-ARM PIVOTAL TRIAL FOR MIRVETUXIMAB IN FRα-HIGH PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER

TARGET TIMELINES

- FULLY ENROLLED
- TOP-LINE DATA Q4 2021
- BLA Q1 2022

*BLA submission expected in Q1 2022

BLA: Biologics License Application; BICR: blinded independent central review; DOR: duration of response; BRCA: BReast CAncer gene

https://www.clinicaltrials.gov/ct2/show/NCT04296890

PRIMARY ENDPOINT

ORR by Investigator

BICR for Sensitivity Analysis

SECONDARY ENDPOINT

DOR by Investigator

ENROLLMENT AND KEY ELIGIBILITY

~110 patients

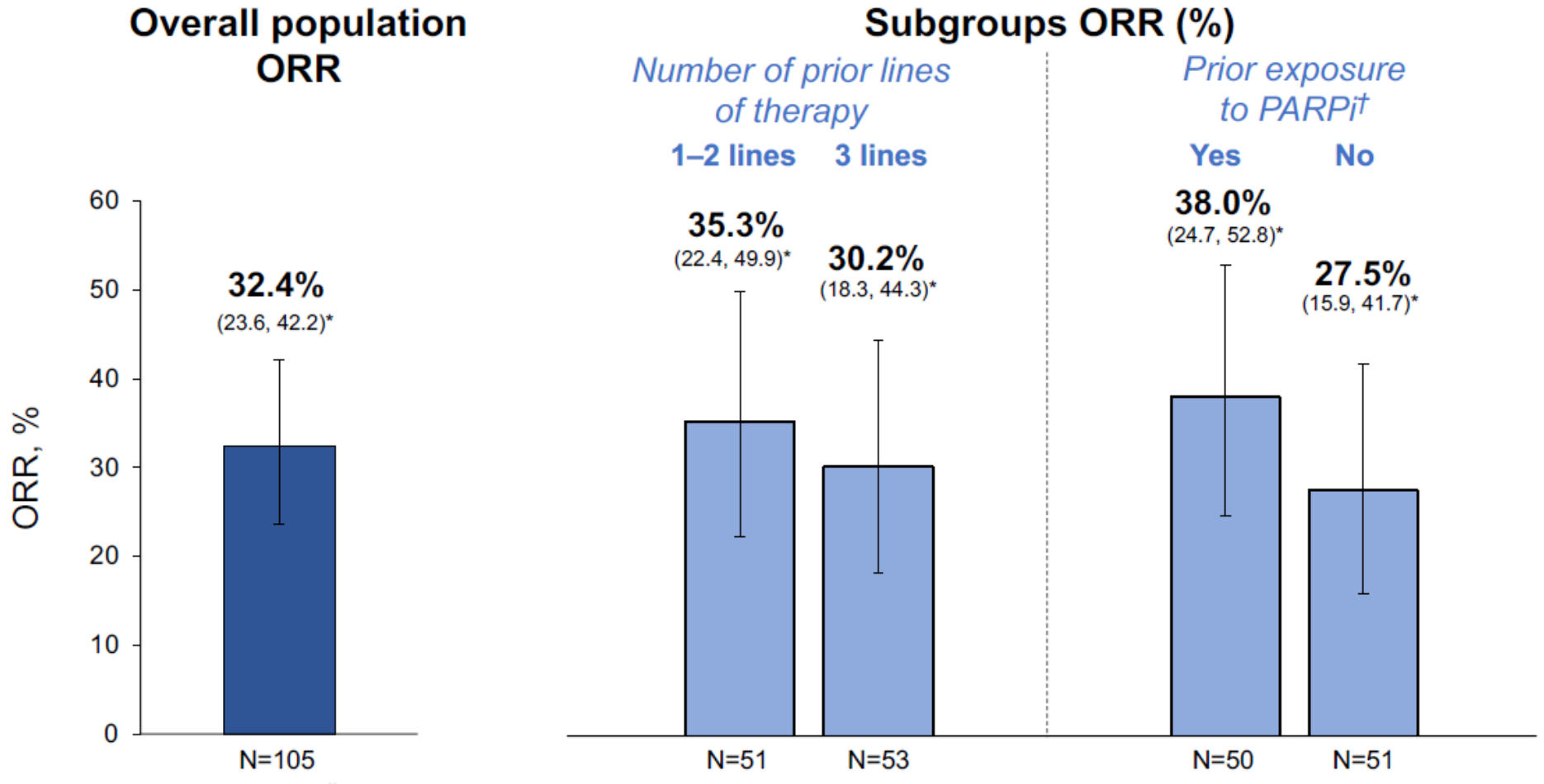
Platinum-resistant disease (primary PFI >3 mos)

1-3 lines of prior systemic lines of therapy

~~Prior bevacizumab required~~

11 COUNTRIES / 85 SITES

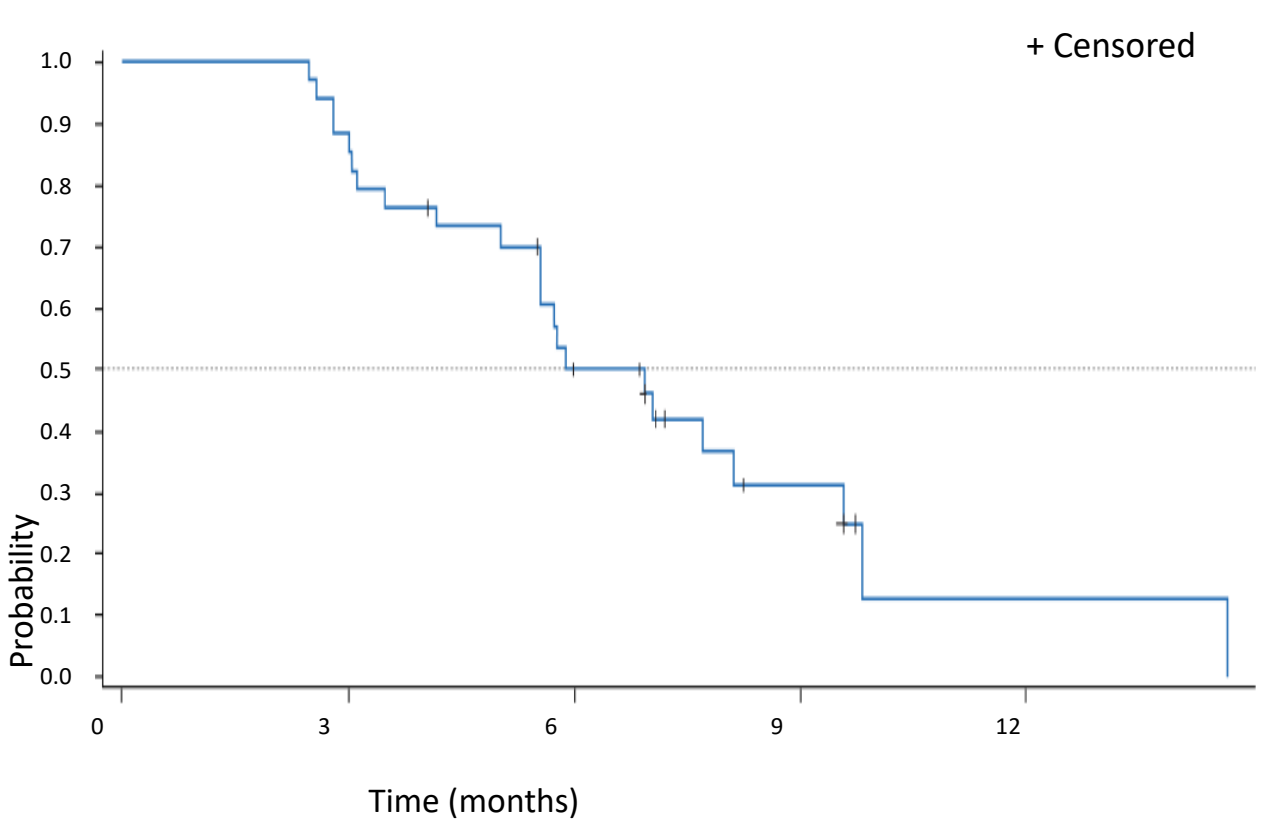
Investigator-Assessed Objective Response Rate by Prior Therapy

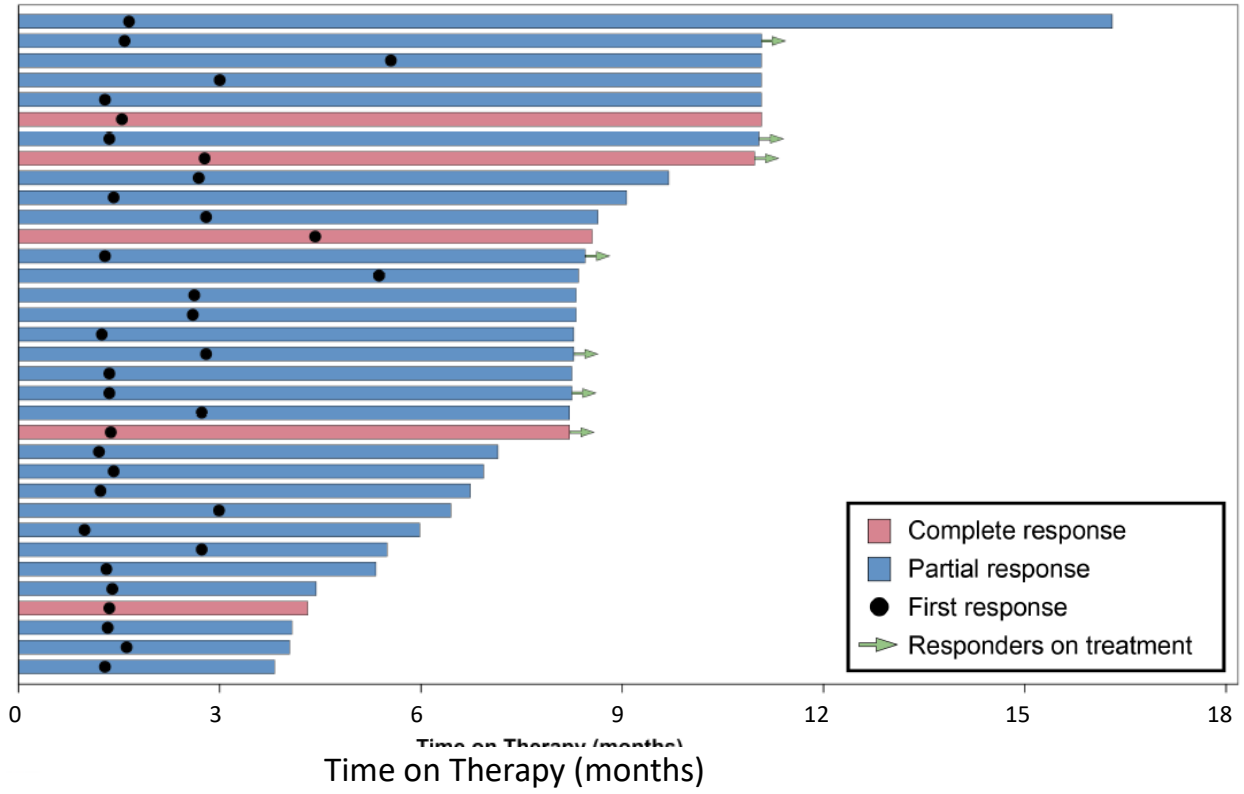


Data cutoff: November 16, 2021.
The denominator for the percentage is the number of patients in the investigator-assessed population in each analysis. Patients without at least 1 postbaseline RECIST assessment were treated as not evaluable.
*95% exact CI is estimated by Clopper-Pearson method (Clopper-Pearson exact CI). †Prior PARPi exposure was uncertain for 4 patients in the investigator-assessed population.
CI, confidence interval; ORR, confirmed objective response rate; PARPi, poly ADP-ribose polymerase inhibitor; RECIST, Response Evaluation Criteria in Solid Tumors.

SORAYA Duration of Response

mDOR: 6.9 months (95% CI: 5.6, 8.1)

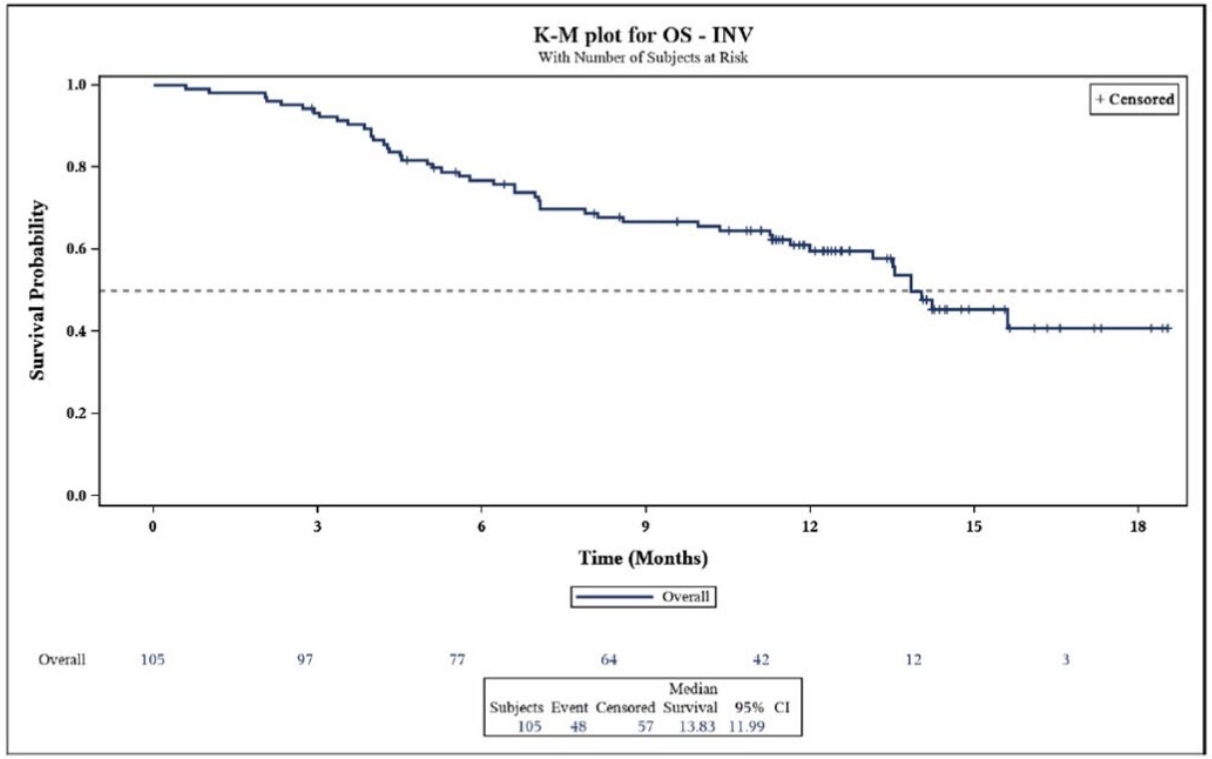




SORAYA ASCO Update 2022

Investigator-Assessed Outcomes	N=105
Disease control rate (DCR)[a], n (%) 95% CI[b]	54 (51.4) [41.5-61.3]
Tumor reduction[c], n (%)	75 (71.4)
CA-125 Response	**N=86**
CA-125 response, % 95% CI	46.5% [35.7-57.6]

[a]Proportion of patients who achieved a CR, PR, or stable disease maintained for ≥12 weeks.
[b]Clopper-Pearson exact CI. [c]Occurred if the sum of the diameters of target lesions was reduced from the baseline value during the study.



Matulonis et al. ASCO 2022 Abs 5512

Integrated Safety Summary of Single Agent Mirvetuximab Soravtansine in FRα + Recurrent Ovarian Cancer

Most Common (≥10%) TRAEs

	Integrated Safety Population (N=464)		SORAYA Safety Population* (N=106)	
Adverse event	All Grades, n (%)	Grade ≥3, n (%)	All Grades, n (%)	Grade ≥3, n (%)
Patients with any TRAE	**431 (93)**	**121 (26)**	**91 (86)**	**32 (30)**
Most common TRAEs (all-grade, ≥10% of patients)				
Vision blurred	195 (42)	12 (3)	43 (41)	6 (6)
Nausea	187 (40)	7 (2)	31 (29)	0
Diarrhea	151 (33)	10 (2)	23 (22)	2 (2)
Fatigue	143 (31)	9 (2)	25 (24)	1 (<1)
Keratopathy	121 (26)	12 (3)	31 (29)	9 (9)
Dry eye	104 (22)	5 (1)	26 (25)	2 (2)
AST increased	73 (16)	6 (1)	7 (7)	2 (2)
Decreased appetite	72 (16)	4 (<1)	14 (13)	1 (<1)
Vomiting	71 (15)	7 (2)	12 (11)	0
Headache	64 (14)	1 (<1)	8 (8)	0
Neuropathy peripheral	64 (14)	4 (<1)	14 (13)	0
Asthenia	63 (14)	3 (<1)	16 (15)	1 (<1)
ALT increased	57 (12)	5 (1)	6 (6)	1 (<1)
Visual acuity reduced	56 (12)	4 (<1)	3 (3)	0
Photophobia	49 (11)	2 (<1)	14 (13)	0
Eye pain	48 (10)	3 (<1)	8 (8)	0
Abdominal pain	45 (10)	4 (<1)	7 (7)	2 (2)

n=464	Vision Blurred n (%)	Keratopathy n (%)
All Grades	206 (44.4)	166 (35.8)
Grade 1	100 (21.6)	75 (16.2)
Grade 2	92 (19.8)	76 (16.4)
Grade 3	14 (3.0)	14 (3.0)
Grade 4	None	1

Ocular AEs in the Integrated Safety Population

- An ophthalmic exam was performed at baseline for all patients. All patients with any ocular symptoms were referred to an eye care specialist for evaluation and were monitored with ocular exams every other cycle (every 6 weeks) thereafter
- 231 of 464 patients (50%) had any reported ocular event (all grades; blurred vision or keratopathy[a])
  - 208 patients (45%) experienced ocular events that were grade ≤2 in severity; 22 patients (5%) experienced a grade 3 event
  - One patient had a grade 4 event, which was recorded as keratopathy, based upon the visual acuity evaluation of one eye (20/200). This patient had nonconfluent corneal deposits treated as dry eye syndrome. Visual acuity and corneal changes both resolved completely (grade 0) in 15 days
- Onset of ocular events typically occurred during cycle two of treatment (median time to onset approximately 1.5 months)
  - Median time to onset of vision blurred was 41.5 days (range, 1-394), and median time to onset of keratopathy was 50.0 days (range, 23-394)

[a]Keratopathies included corneal cyst, corneal deposits, corneal disorder, corneal epithelial microcysts, corneal epithelium defect, corneal erosion, corneal opacity, corneal pigmentation, keratitis, keratitis interstitial, keratopathy, limbal stem cell deficiency, and punctate keratitis.

Moore et al. ASCO 2022 Abs 5512

MIRASOL

GOG-3045 / ENGOT-Ov55 PHASE 3 RANDOMIZED TRIAL FOR MIRVETUXIMAB IN FRα-HIGH PATIENTS WITH PLATINUM-RESISTANT OVARIAN CANCER

TARGET TIMELINES

- ENROLLING GLOBALLY
- TOP-LINE DATA Q3 2022
- sBLA 2023

2:1 RANDOMIZATION

Mirvetuximab

STRATIFICATION FACTORS
IC Chemotherapy (Paclitaxel, PLD, Topotecan)
Prior Therapies (1 vs 2 vs 3)

Investigator's Choice Chemotherapy
Paclitaxel, PLD, or Topotecan

PRIMARY ENDPOINT
PFS by Investigator
BICR for Sensitivity Analysis

SECONDARY ENDPOINTS
ORR by Investigator, OS, and PRO

ENROLLMENT AND KEY ELIGIBILITY
22 countries /159 sites
430 patients/330 events for PFS by Investigator
Platinum-resistant disease (primary PFI >3 mos)
Prior bevacizumab allowed*
Prior PARPi allowed
Patients with BRCA mutations allowed

*Eligibility criterion different than SORAYA; potential sBLA approval in 2023
sBLA: Supplemental Biologics License Application; IC: investigator's choice; PLD: pegylated liposomal doxorubicin; OS: overall survival; PRO: patient-reported outcomes

GLORIOSA

RANDOMIZED PHASE 3 TRIAL FOR MIRVETUXIMAB + BEVACIZUMAB MAINTENANCE IN FRα-HIGH PSOC PATIENTS

TARGET TIMELINES

- Targeting first site in Q2 2022
- Global trial
- POTENTIAL APPROVAL 2026

PRIMARY ENDPOINT

PFS

SECONDARY ENDPOINT

OS by BICR

ENROLLMENT AND KEY ELIGIBILITY

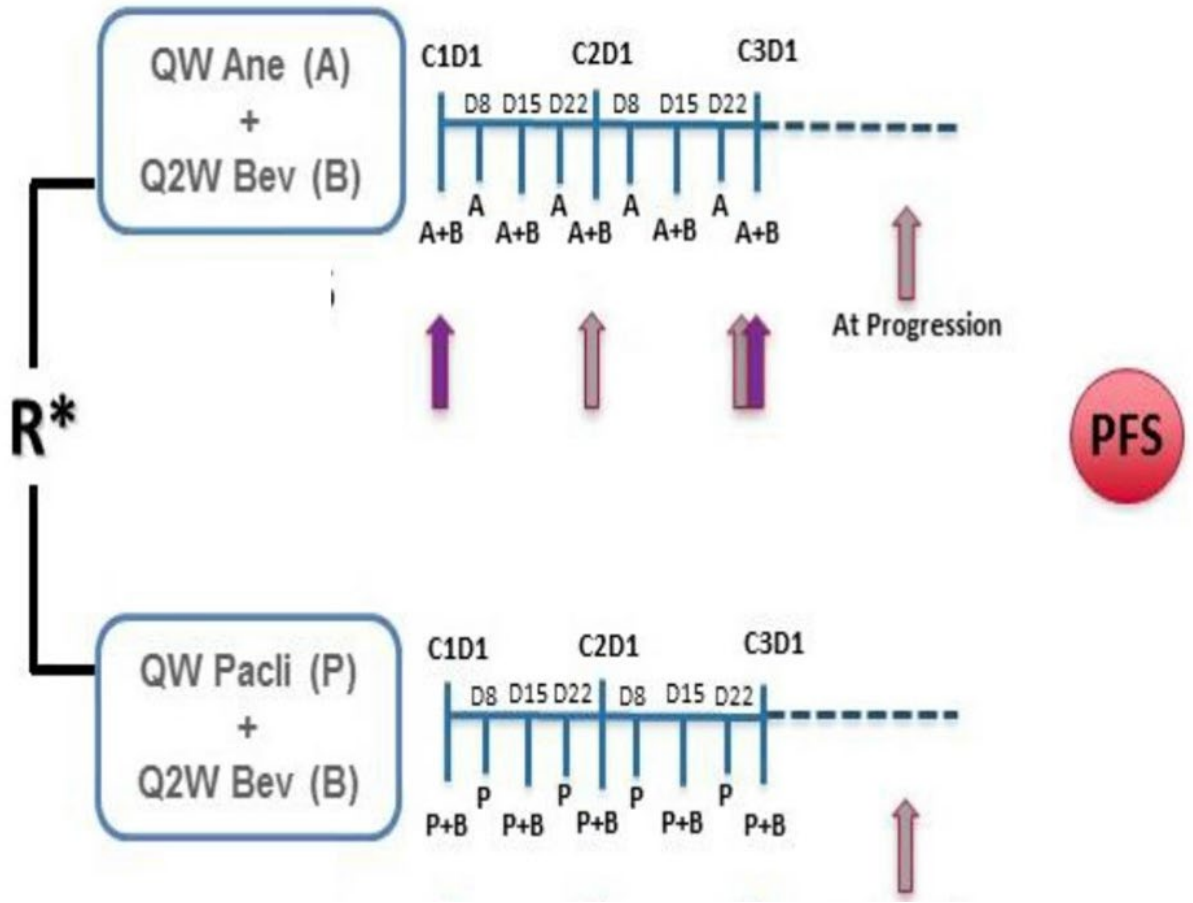
438 patients
Platinum-sensitive ovarian cancer
1 prior systemic treatment
Prior PARPi required if BRCA+
CR, PR, or SD after treatment with platinum-based doublet + bevacizumab required

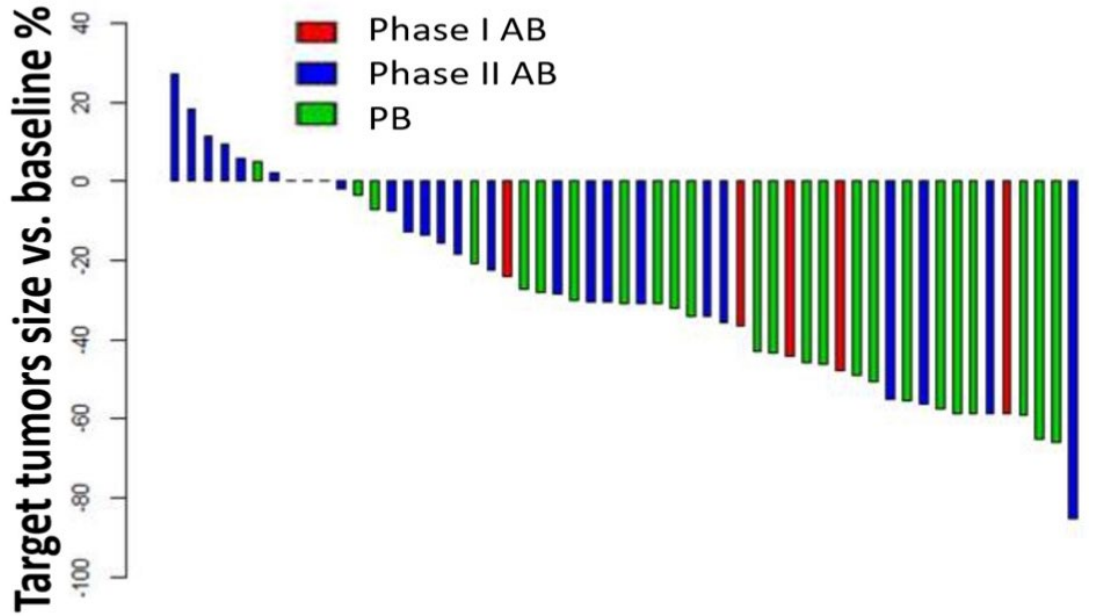
PRIOR MIRV EXPERIENCE

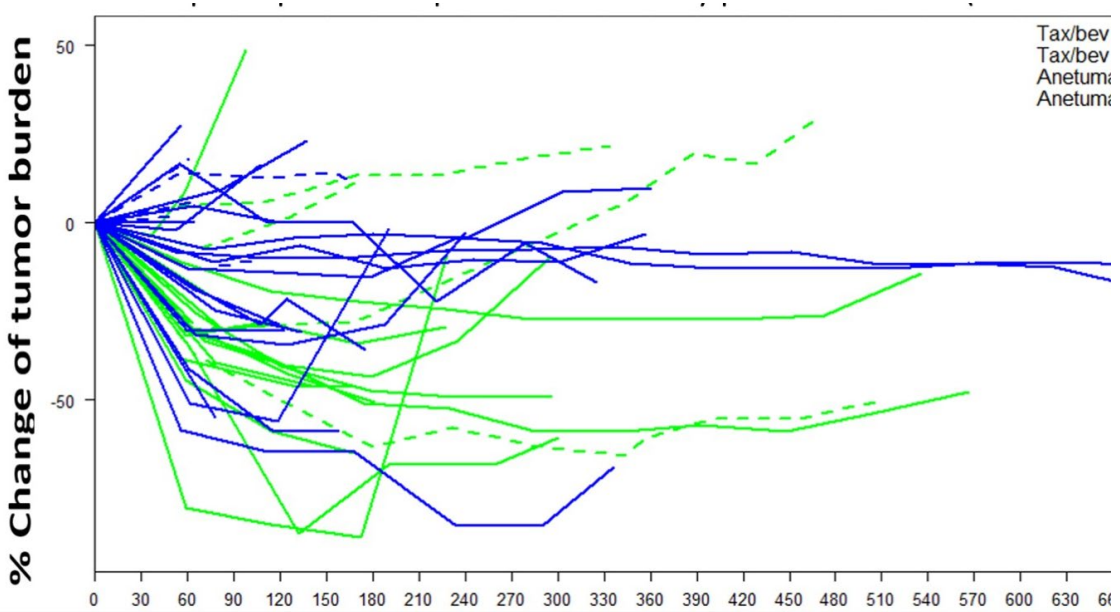
Strong MIRV/BEV treatment efficacy and tolerability in > 120 patients
FRα high rPSOC, MIRV/BEV has an ORR of 69% and mPFS of 13.3 months

PFS (progression-free survival); BICR (blinded independent central review); OS (overall survival); CR (complete response); PR (partial response); SD (stable disease); BRCA (BReast CAncer gene); MIRV (mirvetuximab soravtansine); DOR: duration of response; ORR: overall response rate

Randomized Phase 2 Study of Bevacizumab and Weekly Anetumab ravtansine vs. Bevacizumab + Weekly Paclitaxel







Median PFS 5.3 vs. 9.6 months for anetumab vs. weekly PAC + bev

ORR is 21% vs. 59% for anetumab vs. weekly PAC + bev

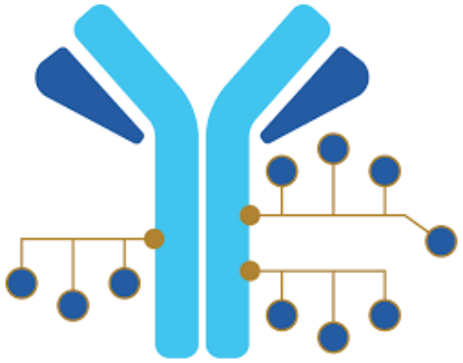
Lheureux et al. ASCO 2022 abstract 5514

Efficacy Comparison of Mirvetuximab + Bevacizumab Combo

	AURELIA	FORWARD II	Anetumab/Bev
Regimen	Chemo/Bev	**Mirv/Bev**	**Anetumab/Bev**
Median age	61	**60**	**63**
Patient population	Platinum resist 1-2 priors **60% - 1 prior** **40% - 2 prior**	**Median of 2 priors** **33%-1 prior** **37% -2 prior** **30% 3 or more**	**Median of 3 priors (1-8)**
Prior bevacizumab	7%	**64%**	**43%**
ORR	27%	**59%**	**22%**
mPFS	6.7 (95% 5.7, 7.9)	**immature**	**5.3 months (comparison PAC/Bev = 9.6 mos)**

Aghajanian C et al. JCO. 2012;30: 2039-2045,

Upifitamab Rilsodotin (UpRi) – First-in-Class ADC Targeting NaPi2b



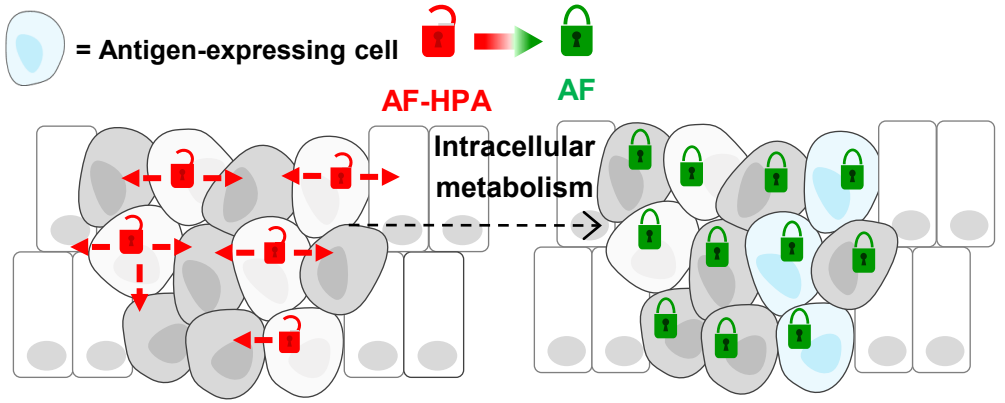
UpRi

Antibody: Humanized monoclonal anti-NaPi2b[1]

Linker: Polymer scaffold; cleavable ester linker[2]

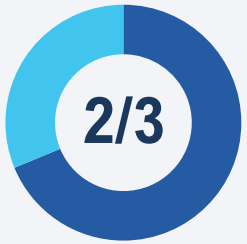
Payload: AF-HPA (DolaLock-controlled bystander effect)[1]

Drug-to-Antibody Ratio: ~10

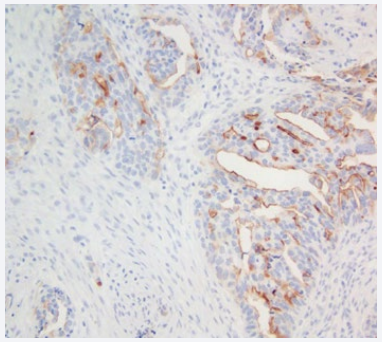


Upon ADC internalization into tumor cells and efficient release of payload, AF-HPA payload is metabolized to AF that remains highly potent but loses the ability to cross the cell membrane, locking it in the tumor, controlling the bystander effect, and consequently limiting impact on adjacent healthy cells[2,3]

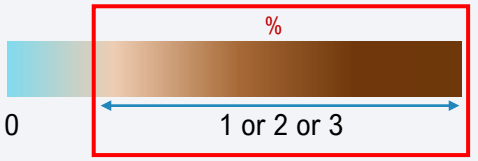
NaPi2b Is a Sodium-Dependent Phosphate Transporter Broadly Expressed in Ovarian Cancer With Limited Expression in Healthy Tissues[4]



- NaPi2b expressed by tumor cells in two-thirds of patients with high-grade serous ovarian cancer[2]
- NaPi2b is a lineage antigen (not an oncogene)[1]



NaPi2b IHC assay in development *– an optimal diagnostic assay would be robust, predictive, reproducible, easily able to distinguish a wide range of expression using* ***TPS scoring method***[2]

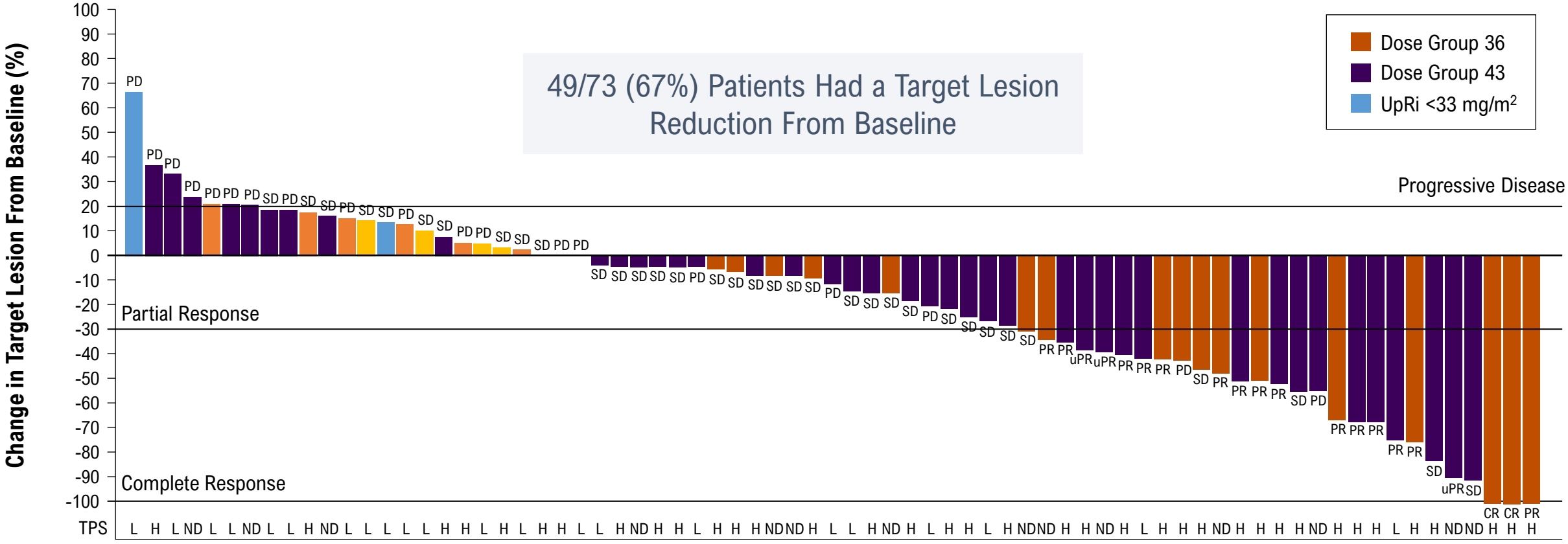


ADC, antibody drug conjugate; AF, auristatin F; AF-HPA, auristatin F-hydroxypropylamide; IHC, immunohistochemistry; NaPi2b, sodium-dependent phosphate transport protein 2B; TPS, tumor proportion score; UpRi, upifitamab rilsodotin.

1. Bodyak ND et al. *Mol Cancer Ther.* 2021;20(5):885–895. 2. Mersana. Data on File. 2022. 3. Tolcher AW et al. ASCO Annual Meeting 2019; Abstract 3010. 4. Lin K et al. *Clin Cancer Res*. 2015;21(22):5139–5150.

Best Response by UpRi Dose Group

Similar Tumor Reduction in Both Dose Groups: Two-thirds of Patients Had Reductions in Target Tumor Lesions by RECIST 1.1



Data cut: June 10, 2021. Analysis with 73 evaluable patients. Two patients excluded as post-baseline tumor measurement shows “Not Measurable”, yet “PD” was assigned by investigator in response dataset. There were 22 unevaluable patients: 4 in Dose Group 36, 2 patient withdrawals (1 enrolled in hospice), 2 patient deaths; 18 in Dose Group 43, 5 patient withdrawals, 1 clinical progression, 3 due to adverse events, 8 deaths, 1 had not reached first scan.

CR, complete response; H, high; L, low; ND, not yet determined; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; TPS, tumor proportion score; uPR, unconfirmed partial response; UpRi, upifitamab rilsodotin.

ENGOT-ov67 / GOG-3048

UpRi Single-Arm Registrational Trial in Platinum-Resistant Ovarian Cancer

Patient Population: HGSOC[a] progressing after standard treatments; measurable disease per RECIST v1.1; ECOG PS 0 or 1; enrolling regardless of NaPi2b expression

Global
US, Europe, Australia, Canada

Key Inclusion Criteria

- Platinum-resistant ovarian cancer (PROC)
- 1–4 prior lines of therapy
- Grade ≤2 peripheral neuropathy
- Archival or fresh tissue required for biomarker evaluation

Key Exclusion Criteria

- 1–2 prior lines bevacizumab-naive
- Primary platinum-refractory disease

UpRi 36 mg/m^2 up to max 80 mg; IV Q4W

Primary Endpoint

- Confirmed ORR in NaPi2b-high (N = ~100)

Secondary Endpoint

- Confirmed ORR in overall population (N = up to ~180 including 100 NaPi2b-high)

Other Secondary Endpoints

- DoR
- Safety

Prospectively-defined retrospective analysis to validate NaPi2b biomarker cutoff

NCT03319628: Trial Currently Enrolling Patients

[a] HGSOC including fallopian tube and primary peritoneal cancer.
DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; HGSOC, high-grade serous ovarian cancer; IV, intravenous; NaPi2b, sodium-dependent phosphate transport protein 2B; ORR, overall response rate, PROC, platinum-resistant ovarian cancer; PS, performance score; Q4W, every 4 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; UpRi, upifitamab rilsodotin.

NCT03319628; Trial currently enrolling patients (FPD April 2021)

2022 ASCO ANNUAL MEETING

Abstract No. 5513

Safety and Efficacy of MORAb-202 in Patients With Platinum-Resistant Ovarian Cancer: Results From the Expansion Part of a Phase 1 Trial

Shin Nishio[1], Mayu Yunokawa[2], Koji Matsumoto[3], Kazuhiro Takehara[4], Kosei Hasegawa[5], Yasuyuki Hirashima[6], Hidenori Kato[7], Hiroki Ikezawa[8], Maiko Nomoto[8], Seiichi Hayato[8], Yohei Otake[8], Takuma Miura[8], Kan Yonemori[9]

[1]Department of Obstetrics and Gynecology, Kurume University School of Medicine, Fukuoka, Japan; [2]Department of Gynecologic Oncology, Cancer Institute Hospital, Tokyo, Japan; [3]Division of Medical Oncology, Hyogo Cancer Center, Hyogo, Japan; [4]Department of Gynecologic Oncology, National Hospital Organization Shikoku Cancer Center, Ehime, Japan; [5]Department of Gynecologic Oncology, Saitama Medical University International Medical Center, Saitama, Japan; [6]Department of Gynecology, Shizuoka Cancer Center, Shizuoka, Japan; [7]Department of Gynecologic Oncology, Hokkaido Cancer Center, Sapporo, Japan; [8]Eisai Co. Ltd., Tokyo, Japan; 9Department of Breast and Medical Oncology, National Cancer Center Hospital, Tokyo, Japan

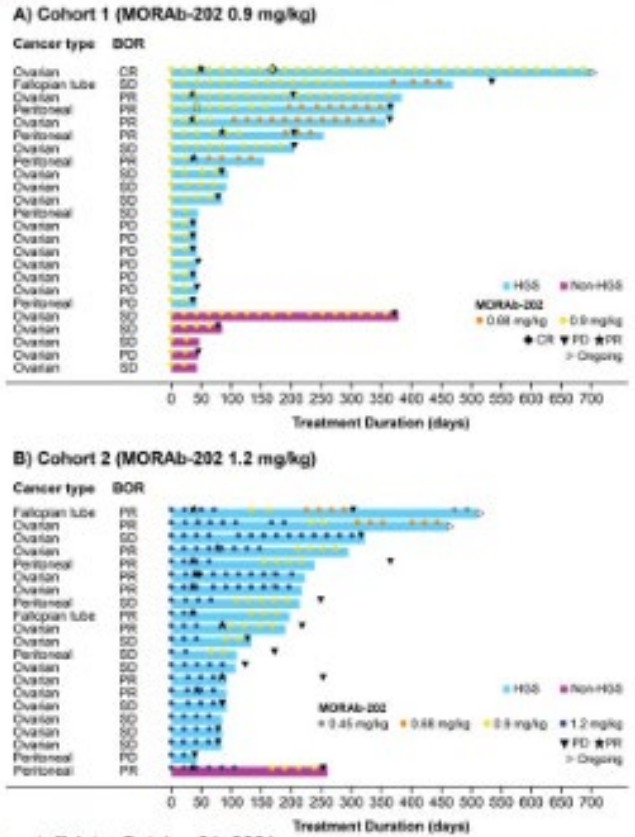
MORAb-202 is farletuzumab ecteribulin

Targets FR and conjugated to eribulin (microtubule toxin)

ORR is 25.0% in cohort 1 and 52.4% in cohort 2

Efficacy

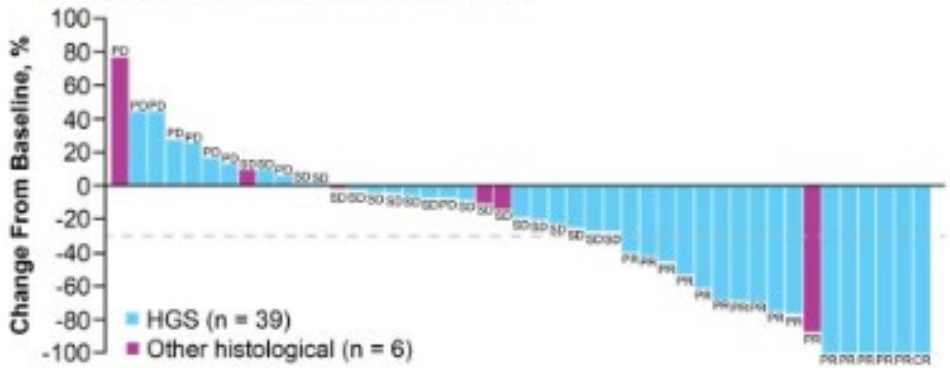
Figure 2. Duration of Treatment and Best Overall Response



Data cutoff date: October 31, 2021.

- Duration of treatment and best overall responses are shown in **Figure 2**.
- Most patients demonstrated reductions in the sums of tumor diameters (**Figure 3**).
- Median PFS in Cohort 1 was 6.7 months (95% CI 1.5–12.0) and in Cohort 2 was 8.2 months (95% CI 4.2–10.4).
- Median OS in Cohort 1 was 10.5 months (95% CI 6.4–15.1) and in Cohort 2 was not estimable (95% CI 12.5–NE).

Figure 3. Best Overall Response and Maximum Shrinkage in Tumor Volume From Baseline



Data cutoff date: October 31, 2021.

Nishio et al. ASCO 2022 abstract 5513

MORAb-202 is farletuzumab ecteribulin

Targets FR and conjugated to eribulin (microtubule toxin)

Parameter, n (%)		Cohort 1 (n = 24) MORAb-202 0.9 mg/kg	Cohort 2 (n = 21) MORAb-202 1.2 mg/kg
Any ILD/Pneumonitis event		9 (37.5)	14 (66.7)
Severity:	Grade 1	8 (33.3)	6 (28.6)
	Grade 2	1 (4.2)	7 (33.3)
	Grade 3	0	1 (4.8)
	Grade 4	0	0
	Grade 5	0	0
Serious respiratory event[a]		2 (8.3)	3 (14.3)
ILD/Pneumonitis event leading to MORAb-202:			
Discontinuation		1 (4.2)	5 (23.8)
Dose reduction		5 (20.8)	9 (42.9)
Dose interruption		1 (4.2)	4 (19.0)

Data cutoff date: October 31, 2021.
[a]Includes pneumonitis, ILD, dyspnea.

Nishio et al. ASCO 2022 abstract 5513

Strategies in Platinum Resistant Ovarian Cancer

	Trial	Phase	Regimen	Tumor testing/ Prevalence
Taxanes	**GOG-3018 (OVAL)**	3	VB-111/placebo D1 (56 day cycle) + weekly paclitaxel vs. weekly Paclitaxel	no
	GOG-3029 (INNOVATE-3)	3	TTFields >18 hr/day + weekly paclitaxel vs. weekly Paclitaxel	no
	GOG-3044 (PROFECTA)	3	Afuresertib PO QD + Paclitaxel D1,8,15 Q3W vs. weekly Paclitaxel	yes
	GOG-3059 (AXLerate-OC)	3	AVB-S6-500 (D1&15) +Weekly paclitaxel (D 1, 8, 15 on a 28d cycle) vs. weekly Paclitaxel	no
	GOG-3073 (ROSELLA)	3	Relacorilant + nab-paclitaxel vs. nab-paclitaxel	no
Antibody Drug Conjugates	**GOG-3045 (MIRASOL)**	3	Mirvetuximab vs Investigator Choice chemotherapy	yes
	GOG-3048 (UPLIFT)	1b	XMT-1536 (Upifitimab) every 4 weeks	no
Immunotherapy	**NRG-GY009**	2/3	PLD/Atezolizumab (D1&15) vs. PLD/Bevacizumab(D1&15)/Atezo (D1&15) vs. PLD/Bevacizumab (D1&15)	no
	GOG-3063 (ARTISTRY 7)	3	Nemvaleukin + Pembrolizumab vs. Pembrolizumab vs. Nemvaleukin vs. Investigator Choice chemotherapy	no
Targeting DDR/ PARPi resistance	**NRG-GY005**	2/3	Olaparib vs. Olaparib/Cediranib vs. Cediranib vs. Investigator Choice chemotherapy	no
	NRG-GY023	2	Durvalumab/Olaparib/Cediranib vs. Olaparib/Cediranib vs. Durvalumab/Cediranib vs. Investigator Choice chemotherapy	no
	NRG-GY029 (approved)	2	Olaparib + copanlisib vs. Investigator Choice chemotherapy (PARPi resistant)	no
	GOG-3072	1b	ZN-c3 in combination with chemotherapy in patients with PROC	no

Efficacy and safety of Lucitanib + Nivolumab in Patients with Advanced Gynecologic Malignancies

Endometrial Cancer[b]
- Recurrent disease
- ≥1 prior platinum-based chemotherapy regimen
- Up to 10 patients who have progressed on treatment with 1 prior PD-(L)1 inhibitor administered as monotherapy

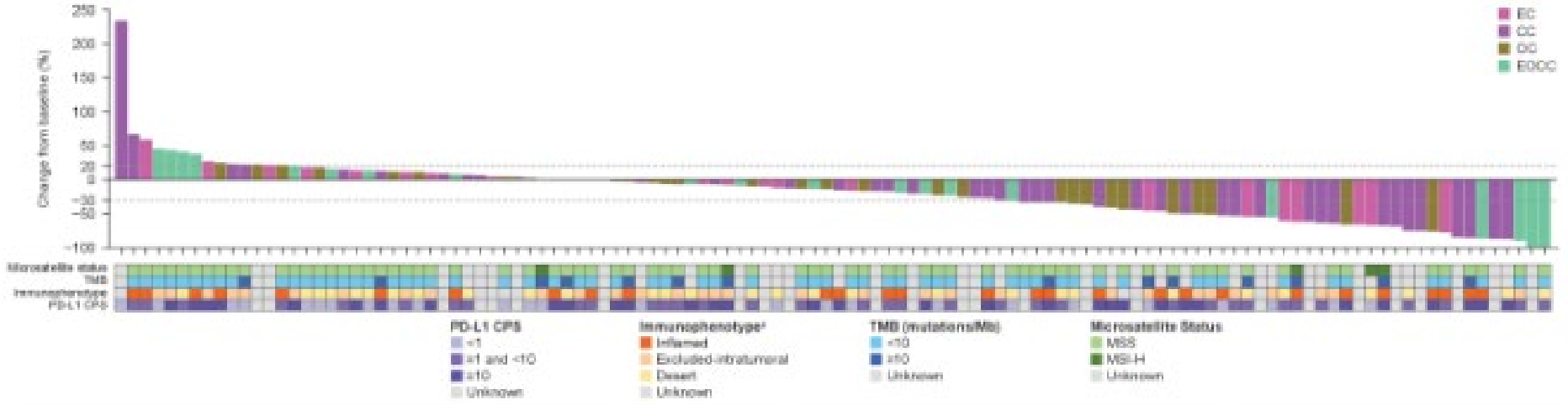
Cervical Cancer
- Persistent or recurrent disease
- ≥1 prior regimen of platinum-based chemotherapy, with or without bevacizumab

Ovarian Cancer[b]
- Recurrent high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer
- ≥2 prior chemotherapy regimens (including ≥1 platinum doublet) OR disease progression ≤6 months after completing 1L platinum-based chemotherapy ie, primary platinum resistance (up to 10 patients)

Endometrial or Ovarian Cancer With Clear-Cell Histology
- Recurrent, metastatic clear-cell carcinoma of ovarian, fallopian tube, primary peritoneal, or endometrial origin
- ≥1 prior platinum- and taxane-based chemotherapy regimen

	EC (n=22)	CC (n=46)	OC (n=33)	EOCC (n=23)
Confirmed ORR, n (%)	**5 (22.7%)**	**12 (26.1%)**	**4 (12.1%)**	**6 (26.1%)**
[95% CI]	[7.8–45.4]	[14.3–41.1]	[3.4–28.2]	[10.2–48.4]
CR	0	2 (4.3)	0	1 (4.3)
PR	5 (22.7)	10 (21.7)	4 (12.1)	5 (21.7)
SD	8 (36.4)	19 (41.3)	18 (54.5)	7 (30.4)
PD	9 (40.9)	12 (26.1)	7 (21.2)	9 (39.1)
NE	0	3 (6.5)	4 (12.1)	1 (4.3)
DCR, n (%)	**11 (50.0%)**	**22 (47.8%)**	**11 (33.3%)**	**11 (47.8%)**
[95% CI]	[28.2–71.8]	[32.9–63.1]	[18.0–51.8]	[26.8–69.4]

CC, cervical cancer; CR, complete response; DCR, disease control rate (CR/PR/SD ≥16 weeks); EC, endometrial cancer; EOCC, endometrial/ovarian clear-cell cancer; NE, not evaluable; OC, ovarian cancer; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.



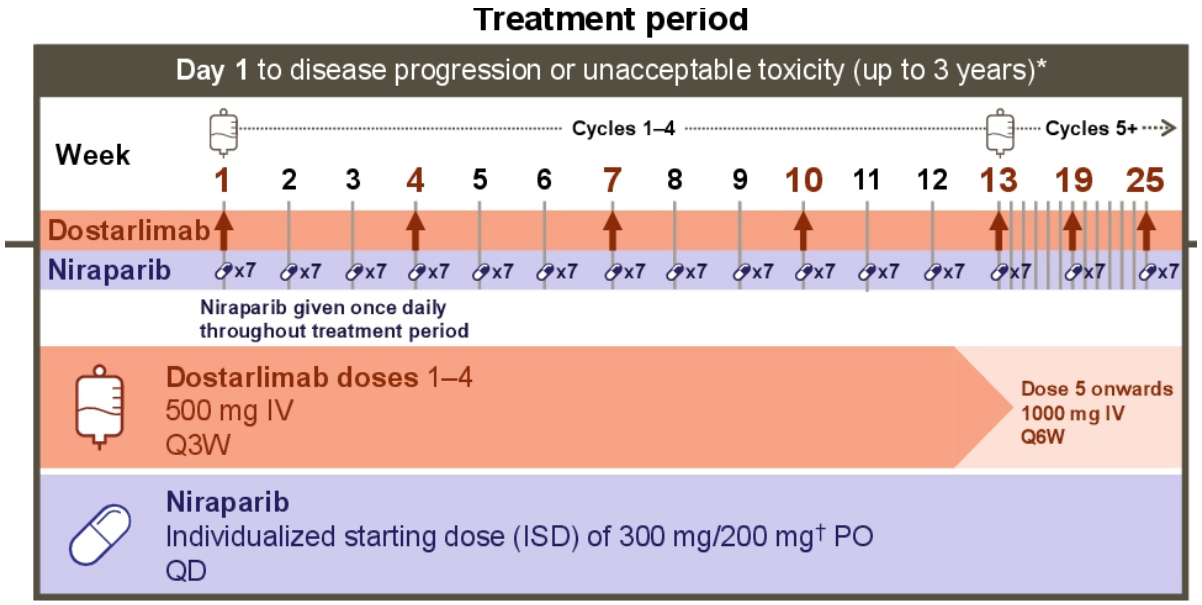
Patel et al. ASCO 2022 Abstract 5517

Pembrolizumab + Anlotinib in Refractory or Platinum Resistant HGSOC

Best Response	anlotinib+pembrolizumab N=15	pembrolizumab N=18
Partial Response (PR)	5 (33.3%)	0
Stable Disease (SD)	10 (66.7%)	16 (88.9%)
Progression Disease (PD)	0	2 (11.1%)
ORR (CR+PR),95% CI	33.3% (95% CI, 0.118-0.616)	0
DCR (CR+PR+SD),95% CI	100% (95% CI, 0.782-1.0)	88.9% (95% CI, 0.653-0.986)

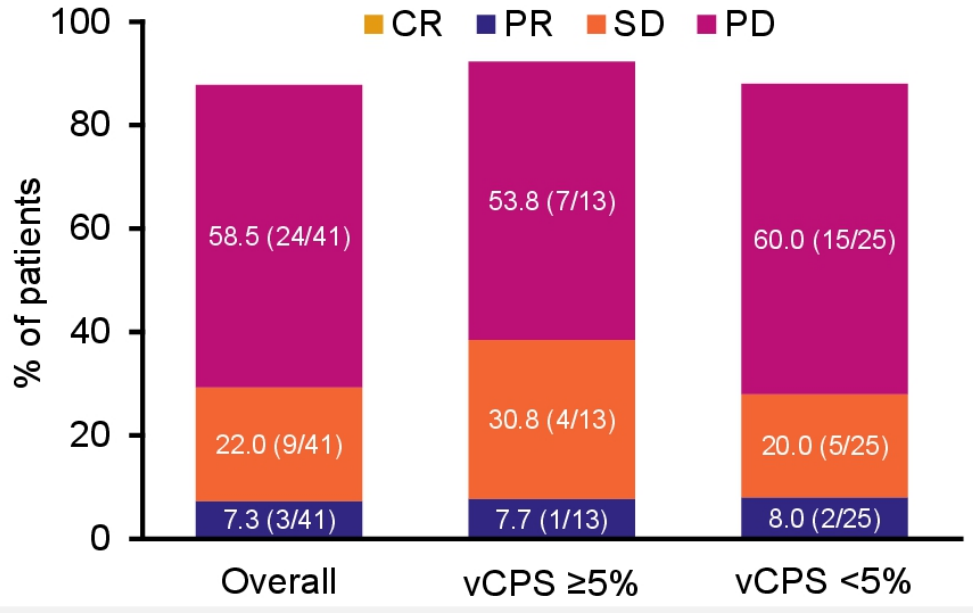
Jiang et al. ASCO 2022 Abstract 5543

Niraparib and Dostarlimab in PROC: MOONSTONE/GOG 3032



Efficacy, n (%) [95% CI]*	Overall N=41	PD-L1 status	
		vCPS ≥5% n=13	vCPS <5% n=25
ORR (CR + PR)	3 (7.3) [1.5–19.9]	1 (7.7) [0.2–36.0]	2 (8.0) [1.0–26.0]
DCR (CR + PR + SD)	12 (29.3) [16.1–45.5]	5 (38.5) [13.9–68.4]	7 (28.0) [12.1–49.4]
Median PFS, months (95% CI)	2.1 (2.0–2.2)	2.2 (1.6–not evaluable)	2.1 (1.8–2.2)

CI, confidence interval; CR, complete response; DCR, disease control rate; ORR, overall response rate; PFS, progression-free survival; PR, partial response; SD, stable disease.



Randall eta l. ASCO 2022 Abstract 5573

Nemvaleukin Alfa ("Nemvaleukin"): Unique Cytokine Designed to Harness Validated IL-2 Pathway Biology

Design derives from natural biology, utilizing native IL-2 and IL-2Rα sequences to confer differentiated properties

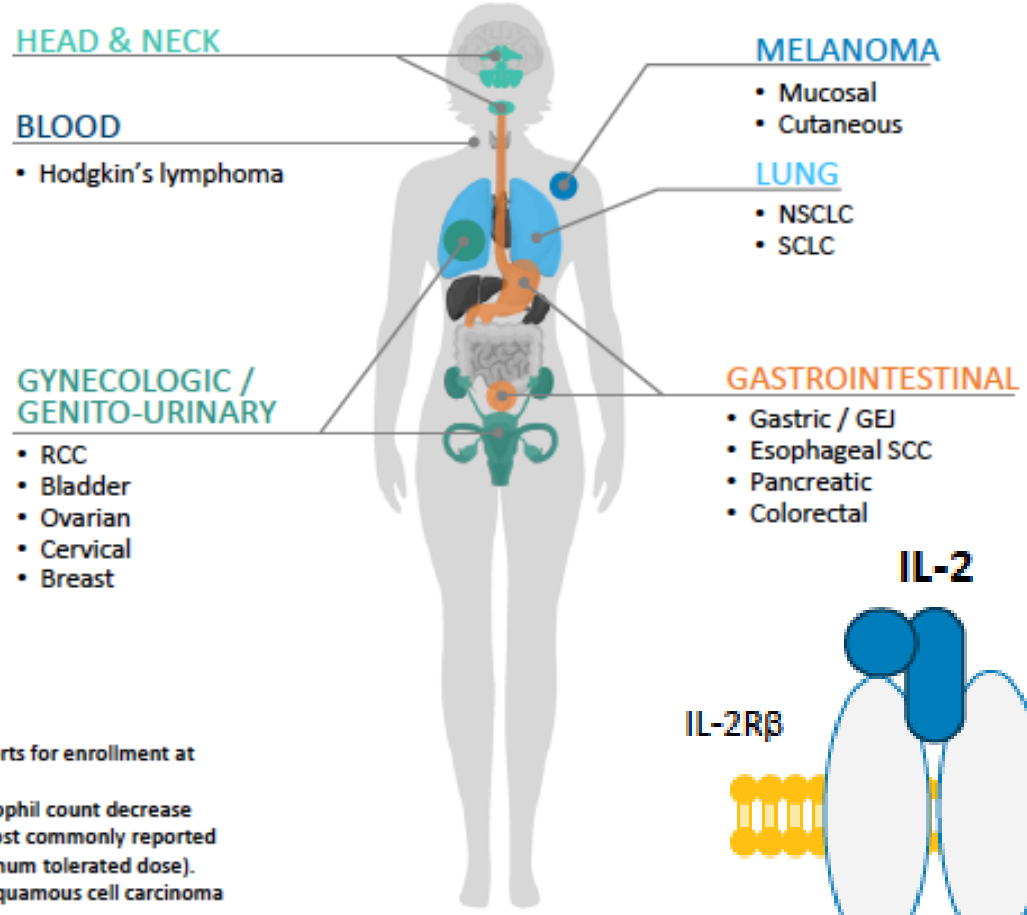
- **Inherently active, stable fusion protein**: Does not require metabolic or proteolytic conversion; does not degrade to native IL-2

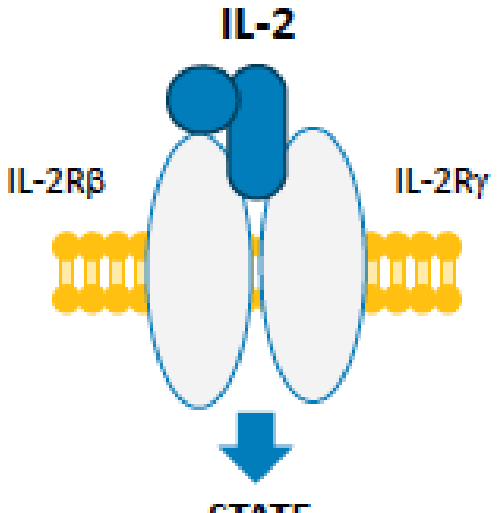
Demonstrated **durable and deepening responses** in high unmet need populations with **monotherapy** and in **combination with pembrolizumab** in a range of tumors

- Treatment-related adverse events (AEs) across the program have been consistent with expectations based on nemvaleukin's mechanism of action and were mostly transient and manageable**

Differentiated and rapidly advancing clinical development program in high unmet need, difficult-to-treat populations, including patients with checkpoint inhibitor (CPI)-unapproved tumor types and in post-CPI settings

Monotherapy and Combination Responses*



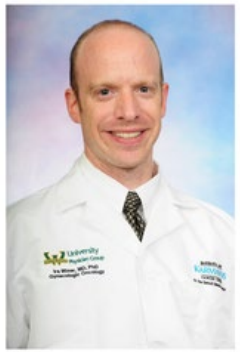


*Includes one response from ARTISTRY-2 study evaluating subcutaneous nemvaleukin, which has recently opened expansion cohorts for enrollment at the recommended phase 2 dose.

**ARTISTRY-1: Pyrexia, chills and nausea were the most commonly reported AEs. Transient and asymptomatic neutropenia/neutrophil count decrease were the most commonly reported events of grade ≥3; ARTISTRY-2: Pyrexia, fatigue, chills and injection site reactions were the most commonly reported AEs. Three dose-limiting toxicities were reported, all in the highest doses evaluated in each dosing regimen (declared as the maximum tolerated dose).

NSCLC: Non-Small Cell Lung Cancer; SCLC: Small Cell Lung Cancer; RCC: Renal cell carcinoma; GEJ: Esophagogastric junction; SCC: Squamous cell carcinoma

ARTISTRY-1 Study Design and PROC Cohort



Ira S. Winer

Cinical Outcomes of Ovarian Cancer Patients Treated With the Novel Engineered Cytokine Nemvaleukin Alfa in Combination With the PD-L1 Inhibitor Pembrolizumab: Recent Data From ARTISTRY-1

Sat, March 19, 200
SGO

Monotherapy cohort
Nemvaleukin dose escalation
Dose cohorts: 0.1-10 µg/kg IV

Combination therapy cohort (N=162)[a]
Nemvaleukin + pembrolizumab

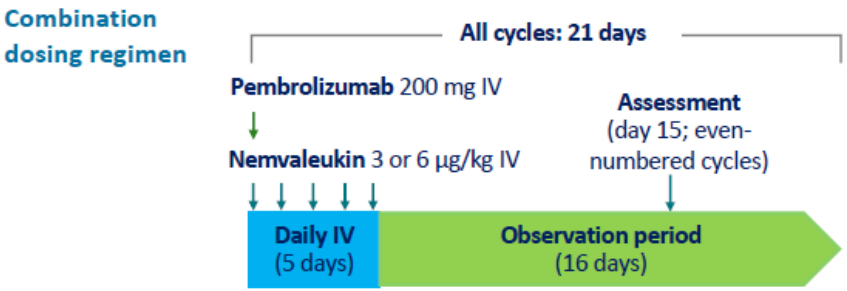
- **Objectives:** Characterize safety profile and antitumor activity by ORR[b]
- **Cohorts:** Mixed tumor types based on PD-(L)1 indication and prior treatment received nemvaleukin 3 µg/kg IV; additional tumor-specific cohorts received nemvaleukin 6 µg/kg IV

PD-(L)1 unapproved cohort (n=42)

- 9 different tumor types, primarily CRC, PROC, and sarcoma

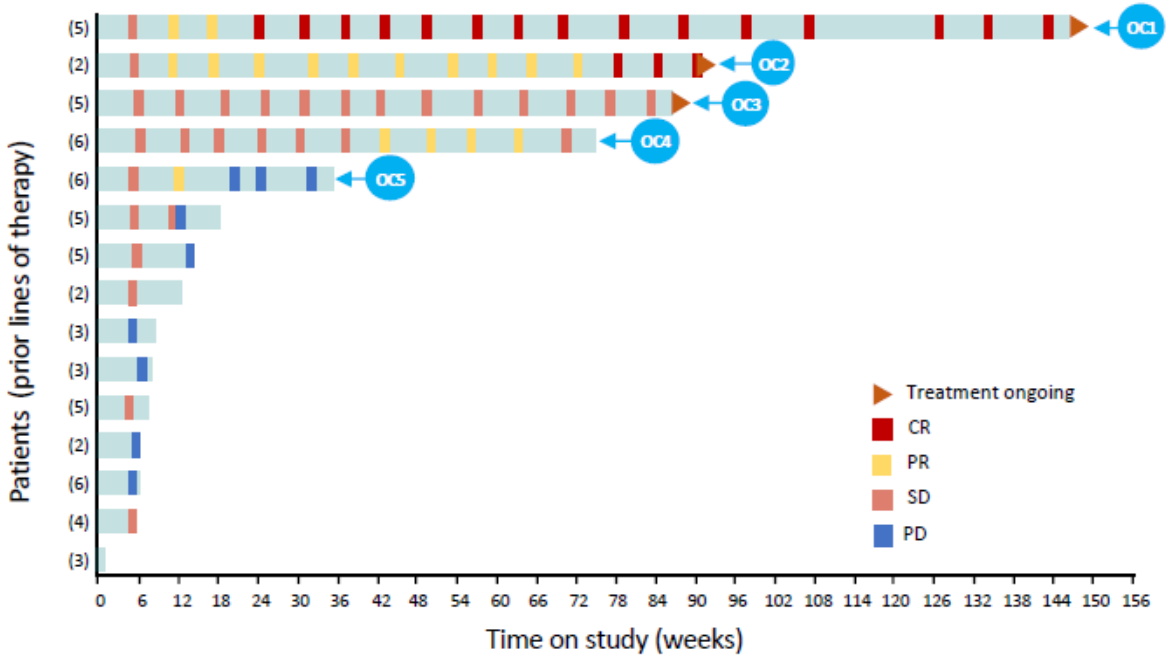
PROC population (n=16[c])

- Advanced solid tumors, refractory to or intolerant of established therapies known to provide clinical benefit
- Prior therapy with platinum-based regimens
- ECOG PS 0 or 1 with life expectancy ≥3 months
- Adequate hematologic reserve, hepatic function, and renal function



[a]3 patients received nemvaleukin 1 µg/kg. [b]Assessed by investigator (RECIST v1.1). [c]1 patient had platinum-refractory disease and 1 patient received nemvaleukin 1 µg/kg.
CRC, colorectal cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; ORR, objective response rate; PD-(L)1, programmed death (ligand) 1; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria In Solid Tumors.

4 Objective Responses: 2 CRs, 2 PRs



Summary of patient experience

Patient	Age (years)	Number of prior regimens/ Prior therapies	Best overall response[a]	Maximum change in target lesions (%)	Time on therapy (weeks)
OC1	48	5: CBP/PAC/BEV, CDDP/GEM, CBP/ PLD, PCA, CBP/DOC	CR	↓ 70	146 ▶
OC2	83	2: CBP/PAC/DOC, CBP/DOC/NIR/TAM	CR	↓ 100	90 ▶
OC3	83	5: CBP/PAC, CBP, CBP/PAC/CAP, CBP/PLD/PEG, CBP/PLD	SD	↓ 28	86 ▶
OC4	75	6: CBP/PAC, NIR, PLD/BEV, CBP/GEM, TOP, NIR	PR	↓ 41	75
OC5	60	6: CBP/PAC, CBP/PLD, CBP/BEV, PAC/BEV, BEV, PLD	uPR	↓ 45	36

▶ Treatment ongoing.

- 5 patients with PROC had clinically meaningful benefit, 4 of whom were on treatment >1 year
  - 4 objective responses: 2 CRs, 2 PRs (1 unconfirmed); 1 SD for >1.5 years
  - 3 of these patients remain on treatment
- ORR was 28.6% and DCR was 71.4% in 14 evaluable patients[b] who received nemvaleukin 3 µg/kg IV + pembrolizumab

Data cutoff October 29, 2021. [a]Assessed by investigator. [b]Patients who received nemvaleukin 3 µg/kg IV + pembrolizumab and had ≥1 post-baseline scan.
BEV, bevacizumab; CAP, capecitabine; CBP, carboplatin; CDDP, cisplatin; DCR, disease control rate (CR+PR+SD); DOC, docetaxel; GEM, gemcitabine; NIR, niraparib; PAC, paclitaxel; PCA, paclitaxel albumin; PEG, pegfilgrastim; PLD, pegylated liposomal doxorubicin hydrochloride; TAM, tamoxifen; TOP, topotecan; uPR, unconfirmed PR.

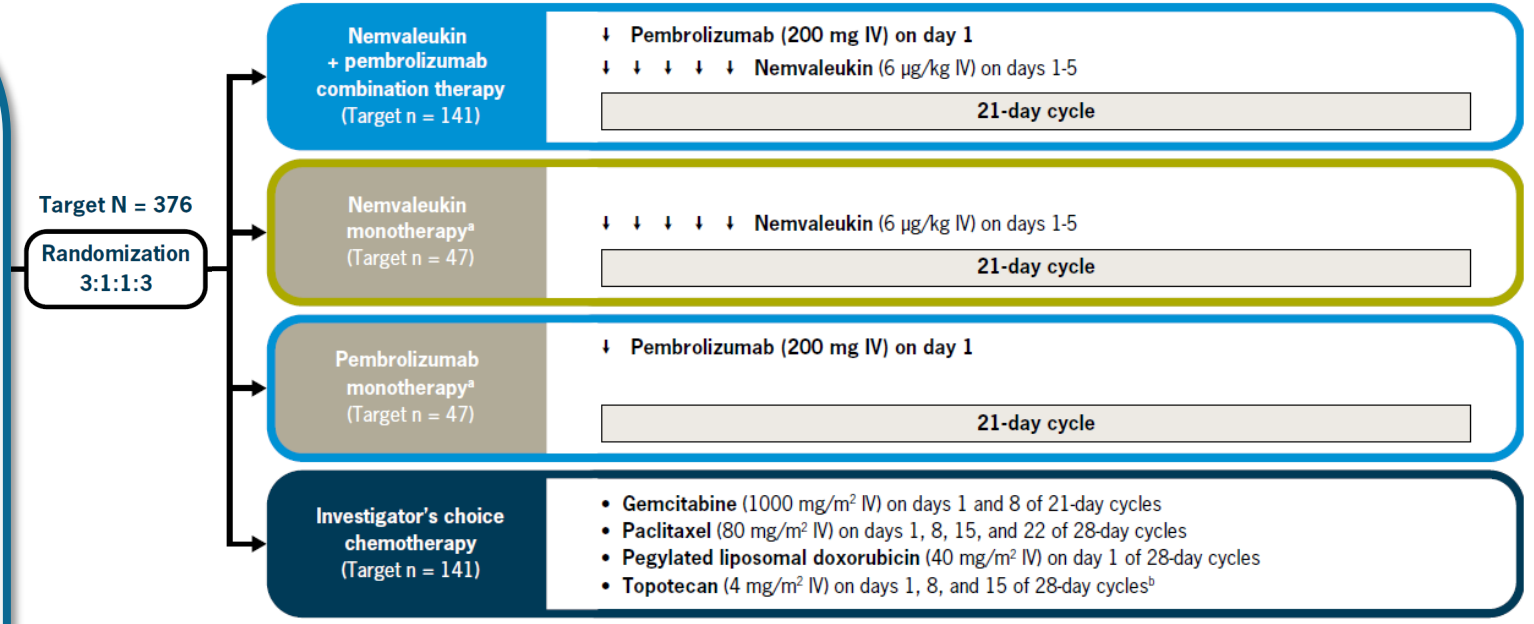
ARTISTRY-7: Phase 3 Nemvaleukin Alfa in Combination With Pembrolizumab Versus Chemotherapy in Patients With Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer: (ARTISTRY-7, NCT05092360, GOG-3063, ENGOT-ov68)

Key Inclusion Criteria

- Females aged ≥18 years with platinum-resistant epithelial OC (high-grade serous, endometrioid, clear cell), fallopian tube cancer, or primary peritoneal cancer
- Must have received:
  - ≥1 prior line of systemic anticancer therapy in the platinum-sensitive setting
  - ≤5 prior lines in the platinum-resistant setting
  - Prior bevacizumab
  - Prior PARP inhibitor for patients with BRCA mutation
- Evidence of radiographic progression on or after most recent therapy
- ECOG performance status of 0 or 1
- Estimated life expectancy of ≥3 months
- Adequate hematologic reserve and hepatic and renal function

Key Exclusion Criteria

- Primary platinum-refractory disease (progression during first-line platinum-based therapy)
- Primary platinum resistance (progression <3 months after completion of first-line platinum-based therapy)
- Prior programmed death (ligand) 1 (PD-[L]1) therapy
- Prior IL-2, IL-15, and IL-12 therapy
- Epithelial OC with mucinous or carcinosarcoma subtype, nonepithelial tumors
- Fluid drainage (eg, paracentesis, thoracentesis, pericardiocentesis) of ≥500 mL within 6 weeks of study drug initiation



[a]Futility analyses planned to stop the monotherapy arms earlier. [b]1.25 mg/m2 on days 1-5 of 21-day cycles is also an option.

Treatment Groups

- Patients will be stratified according to PD-L1 status, histologic subtype, and chemotherapy.
- Patients will continue treatment in the absence of disease progression or intolerable toxicity (maximum 35 cycles for pembrolizumab; nemvaleukin can be continued).
- Patients will be followed for survival beyond treatment discontinuation.

Primary Endpoint

• Investigator-assessed progression-free survival (RECIST v1.1) in patients treated with nemvaleukin plus pembrolizumab vs chemotherapy

Secondary/Exploratory Endpoints

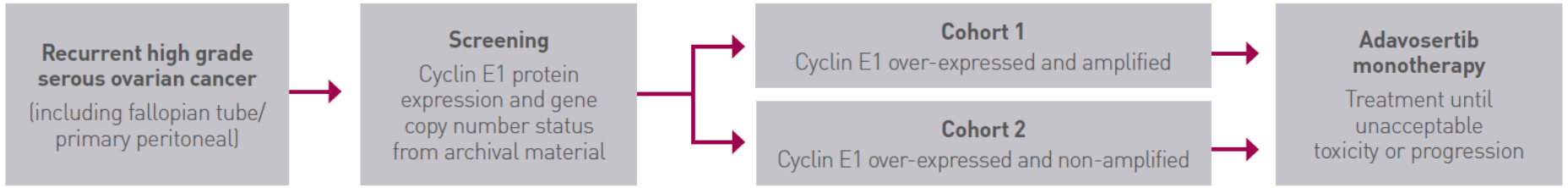
• Characterization of antitumor activity (objective response rate, overall survival, disease control rate, duration of response, and time to response) of nemvaleukin and pembrolizumab in combination and as monotherapy

• Safety, health-related quality of life, pharmacokinetic/pharmacodynamic effects

Strategies in Platinum Resistant Ovarian Cancer

	Trial	Phase	Regimen	Tumor testing/ Prevalence
Taxanes	**GOG-3018 (OVAL)**	3	VB-111/placebo D1 (56 day cycle) + weekly paclitaxel vs. weekly Paclitaxel	no
	GOG-3029 (INNOVATE-3)	3	TTFields >18 hr/day + weekly paclitaxel vs. weekly Paclitaxel	no
	GOG-3044 (PROFECTA)	3	Afuresertib PO QD + Paclitaxel D1,8,15 Q3W vs. weekly Paclitaxel	yes
	GOG-3059 (AXLerate-OC)	3	AVB-S6-500 (D1&15) +Weekly paclitaxel (D 1, 8, 15 on a 28d cycle) vs. weekly Paclitaxel	no
	GOG-3073 (ROSELLA)	3	Relacorilant + nab-paclitaxel vs. nab-paclitaxel	no
Antibody Drug Conjugates	**GOG-3045 (MIRASOL)**	3	Mirvetuximab vs Investigator Choice chemotherapy	yes
	GOG-3048 (UPLIFT)	1b	XMT-1536 (Upifitimab) every 4 weeks	no
Immunotherapy	**NRG-GY009**	2/3	PLD/Atezolizumab (D1&15) vs. PLD/Bevacizumab(D1&15)/Atezo (D1&15) vs. PLD/Bevacizumab (D1&15)	no
	GOG-3063 (ARTISTRY 7)	3	Nemvaleukin + Pembrolizumab vs. Pembrolizumab vs. Nemvaleukin vs. Investigator Choice chemotherapy	no
Targeting DDR/ PARPi resistance	**NRG-GY005**	2/3	Olaparib vs. Olaparib/Cediranib vs. Cediranib vs. Investigator Choice chemotherapy	no
	NRG-GY023	2	Durvalumab/Olaparib/Cediranib vs. Olaparib/Cediranib vs. Durvalumab/Cediranib vs. Investigator Choice chemotherapy	no
	NRG-GY029 (approved)	2	Olaparib + copanlisib vs. Investigator Choice chemotherapy (PARPi resistant)	no
	GOG-3072	1b	ZN-c3 in combination with chemotherapy in patients with PROC	no

IGNITE: Phase 2 trial of adavosertib in recurrent HGSOC with CCNE1 amplification



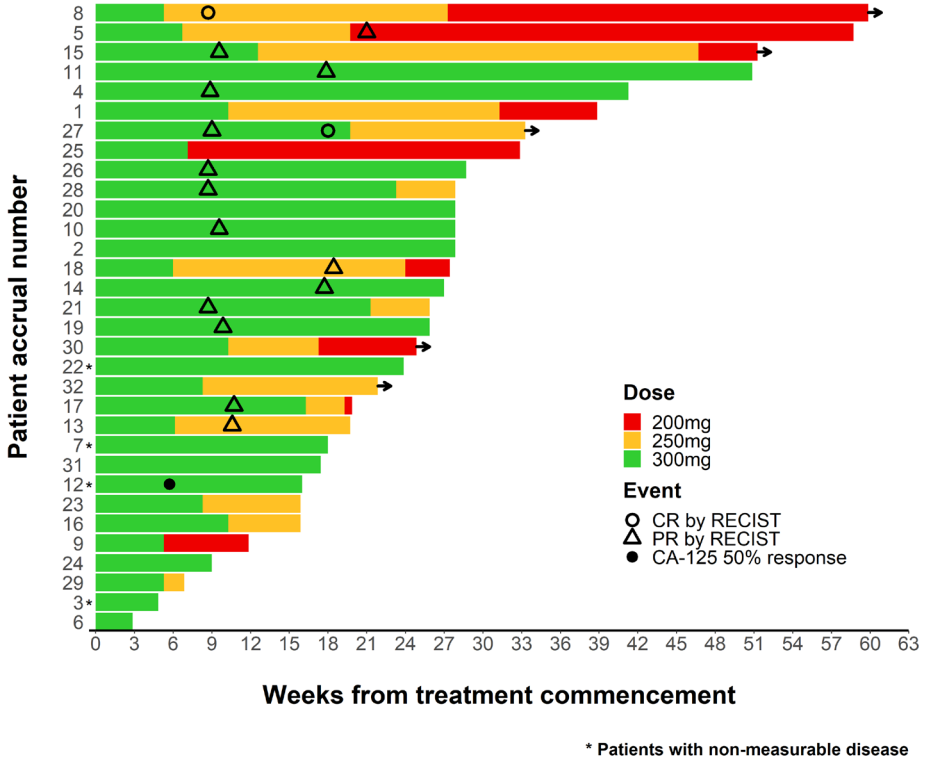
- Screening of archival FFPE material
- Assess Cyclin E1 expression (IHC) followed by copy number (FISH)

Treatment	Dose	Dose frequency	Route of administration	Treatment period
Adavosertib	300mg	Daily	Oral	Days 1-5 and 8-12 of each 21-day cycle

Table 2. Clinical activity

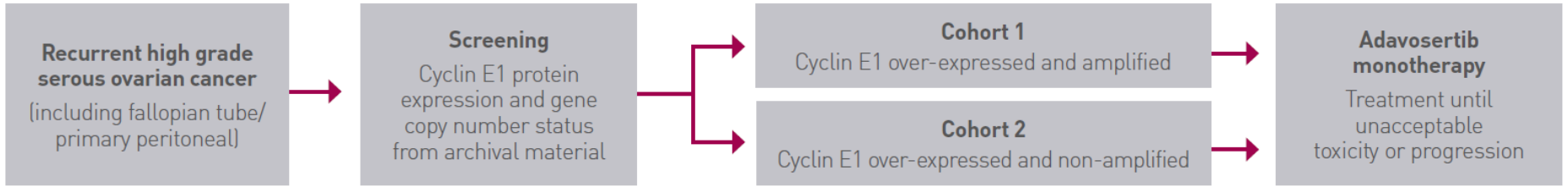
Response	Response evaluable patients (n=32)	CA125 evaluable only patients (n=4)	RECIST measurable patients (n=28)
Complete Response (CR)	2 (6%)	-	2 (7%)
Partial Response (PR)	14 (44%)	-	14 (50%)
CA125 50% Response	1 (3%)	1 (25%)	-
Stable Disease (SD)	8 (25%)	-	8 (29%)
No CA-125 response and no PD	3 (9%)	3 (75%)	-
Progressive disease (PD)	4 (12%)	0 (0%)	4 (14%)
OR (CR/PR/CA-125 50% response)	17 (53% [35, 71])	1 (25% [0, 81%])	16 (57% [37, 76])
Clinical Benefit (No PD>18 weeks)[a]	19 (61% [42, 78])	1 (25% [0, 81%])	18 (67% [46, 83])

a - One patient withdrew consent at week 15 when ceased treatment due to toxicity. This patient was considered not evaluable for clinical benefit and the CB rate was calculated excluding this patient.



Au-Yeung et al. ASCO 2022 Abs 5515

IGNITE: Phase 2 trial of adavosertib in recurrent HGSOC with CCNE1 amplification



- Screening of archival FFPE material
- Assess Cyclin E1 expression (IHC) followed by copy number (FISH)

Treatment	Dose	Dose frequency	Route of administration	Treatment period
Adavosertib	300mg	Daily	Oral	Days 1-5 and 8-12 of each 21-day cycle

- The most common treatment related adverse events experienced were nausea, fatigue and diarrhea (Table 3)
- Dose reductions were required in 17 (53%) patients (Fig 2) and dose delays occurred in 26 (81%) patients
- Four (15%) patients discontinued adavosertib due to toxicity
- Since data cut-off, there have been additional significant hematologic adverse events resulting in recruitment halt pending protocol amendment

Table 3. Treatment related adverse events of any grade occurring in >10% of patients (CTCAE v5.0)

Adverse Event	Any grade, n (%)	Grade 3-4, n (%)
Nausea	26 (81)	1 (3)
Fatigue	20 (62)	4 (12)
Diarrhea	19 (59)	3 (9)
Vomiting	15 (47)	1 (3)
Neutrophil count reduced*	13 (41)	3 (9)
Dysgeusia	9 (28)	0
Constipation	7 (22)	0
Peripheral sensory neuropathy	5 (16)	0
Dizziness	5 (16)	0
Platelet count reduced	4 (12)	3 (9)
Anemia	4 (12)	0
Insomnia	4 (12)	0
Tremor	4 (12)	0
*One patient (3%) experienced a Grade 3 febrile neutropenia event		

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Which of the following novel agents/ trials are clinically most promising in PROC?

- Afuresertib/GOG-3044 Profecta-II

1. AVB-500/ GOG-3059 AXLerate-OC
2. Mirvetuximab/ GOG-3045 MIRASOL
3. Nemvaleukin-alpha/ GOG-3063 ARTISTRY-7
4. VB-111 - Ofranergene Obadenove/ GOG 3018 OVAL
5. Relacorilant/ GOG-3073 ROSELLA
6. Tumor Treating Fields/ GOG 3029
7. XMT-1536/ GOG 3048 UPLIFT
8. ZN-c3/ GOG-3067 MAMMOTH