Emerging opportunities in platinum-resistant recurrent ovarian cancer

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UC San Diego

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New & Emerging Data…

Mirvetuximab + Bevacizumab

Patient population (N=126):
Patients with FRα-positive epithelial ovarian, primary peritoneal, or fallopian tube cancer

- FRa expression (PS2+ scoring), scored as the percent of viable tumor cells staining with ≥2+ intensity
  - FRa Low: ≥25% to 49%
  - FRa Medium: 50% to 74%
  - FRa High: ≥75%
- Platinum status was stratified by platinum-free interval as PFI > 6 months or PFI ≤ 6 months
- BEV treatment defined as BEV-naïve or BEV-treated (BEV in any line of therapy)

- 46% had **≥3 prior lines of therapy**
- 52% had received prior BEV
- 75% had a most recent PFI of ≤6 months
- **40% had low or medium** FRa **expression** **(25%–74% of tumor cells with ≥2+ intensity** FRa **staining)**

Escalation

MIRV 5 mg/kg + BEV 15 mg/kg (N=3)

MIRV 6 mg/kg + BEV 15 mg/kg (N=11)

Expansion

BEV-naïve (N=21)
BEV-pretreated (N=34)

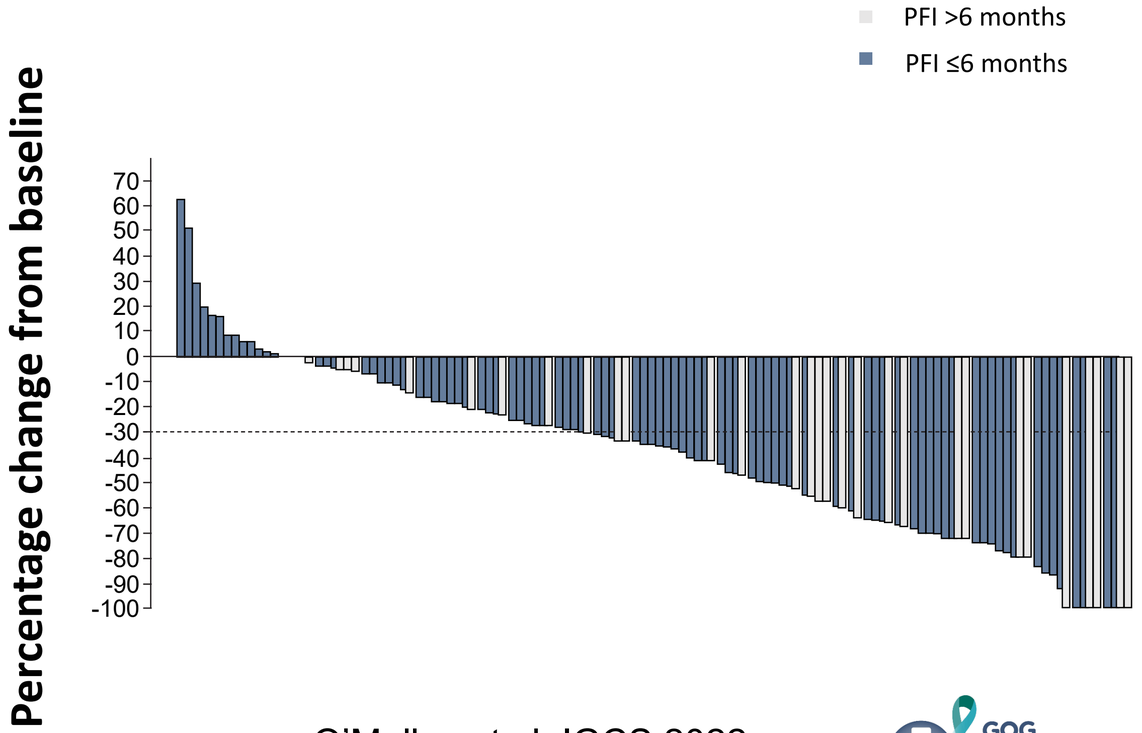
Platinum-agnostic (N=60)

Treatment schedule

MIRV 6 mg/kg, adjusted ideal body weight + BEV 15 mg/kg intravenously on day 1 of a 3-week cycle[1]

Endpoints:

Primary: Confirmed ORR by RECIST v1.1
Secondary: DOR, PFS, Safety



O'Malley et al. IGCS 2022

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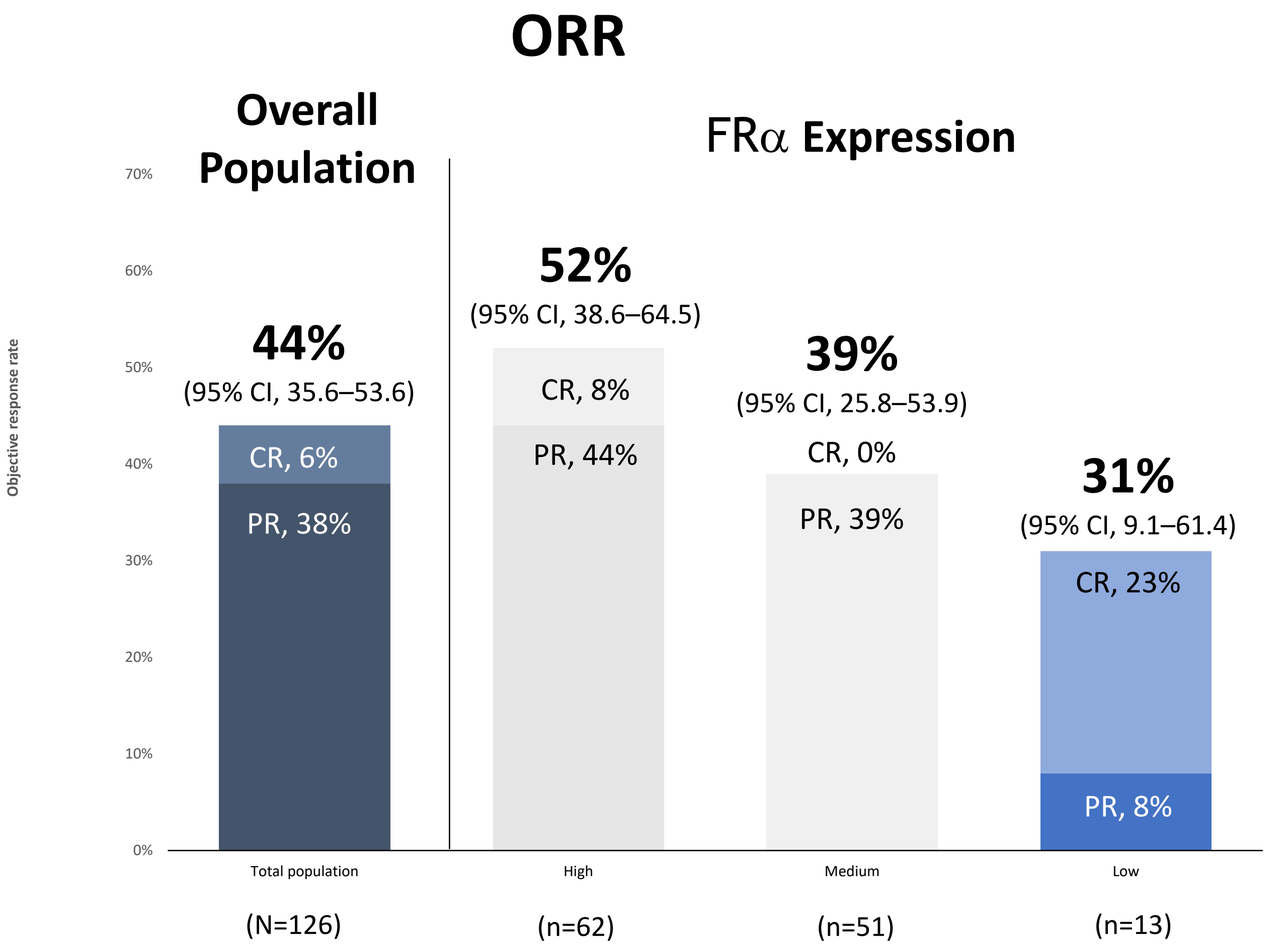
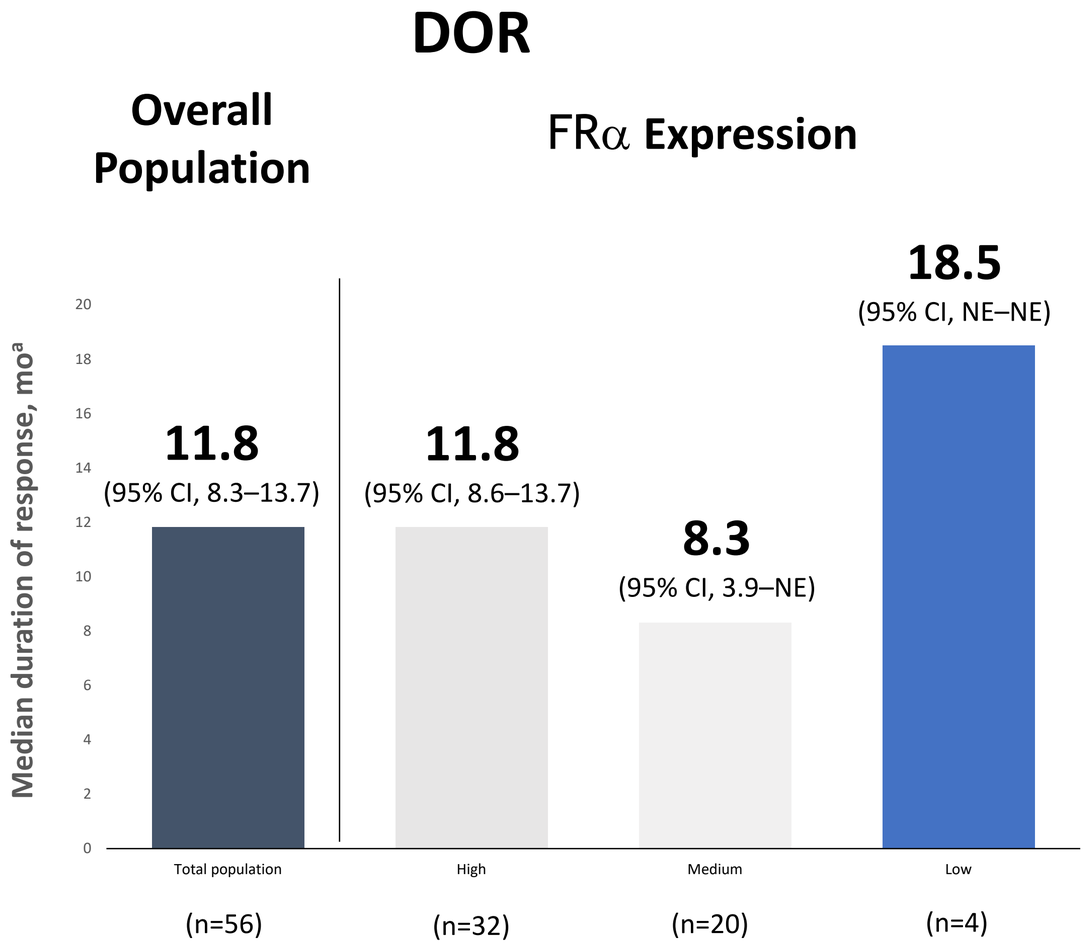
Mirvetuximab + Bevacizumab (ORR and DOR)





- Most TRAEs were low grade. GI, ocular, and fatigue were the most common
- 48% of patients experienced grade ≥3 events; the most common was hypertension (16%)

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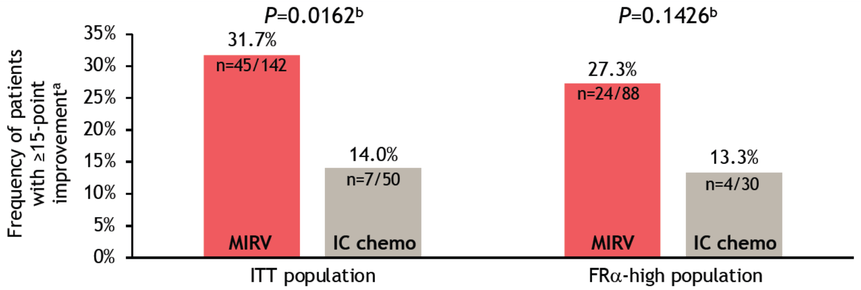
- Due to treatment-emergent AEs, 30% discontinued MIRV and 37% discontinued BEV
  - 4 patients (3%) discontinued MIRV due to blurred vision
- Patients received a median of 8 cycles of MIRV+ BEV (range 1–35 cycles)
- One patient had a death that was deemed related to a study treatment (intestinal perforation possibly related to BEV)

Forward-1 PRO: Phase 3, open-label, randomized (2:1) trial (N=366), in patients with FR-alpha + PROC

- Patients completed PRO assessments during screening, on day 1 of cycle 1, every 9 weeks thereafter until disease progression, and at the end of treatment visit

PRO assessment	Description
EORTC QLQ-C30 (C30)	A 30-item questionnaire designed to assess the QoL in patients with cancer by measuring functional domains, symptoms, and global QoL/health status
EORTC QLQ-OV28 (OV28)	A 28-item ovarian cancer supplemental module developed to augment the C30 with 3 multi-item functional scales and 5 multi-item symptom scales
FOSI	An 8-item measure of symptom response to treatment for ovarian cancer

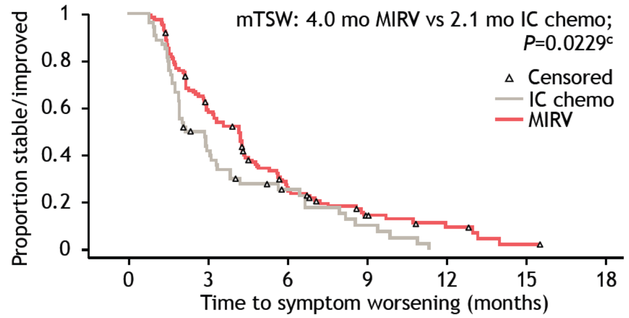
Figure 1. Improvement in the OV28 Abdominal/GI Symptom Subscale by Treatment Group at Week 8/9



[a]Improvement was defined as ≥15-point increase from baseline. Any change <15 points was categorized as unimproved.
[b]*P* value from chi-square test or Fisher exact test if necessary.

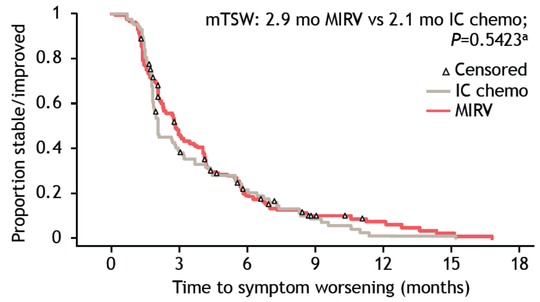
- Positive PRO findings, further support MIRV as a potential novel treatment strategy in the PROC space

Figure 2b. FRα-High Population: TSW on the OV28 Abdominal/GI Symptom Subscale



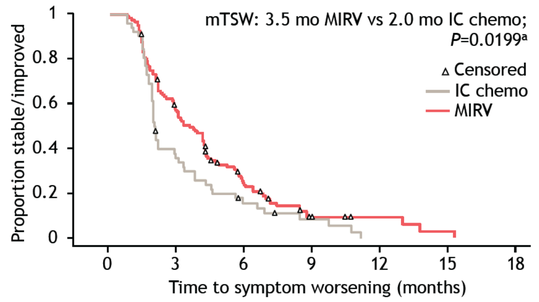
- Categorical change analyses of FOSI scores demonstrated that by cycle 7:
  - 88.9% of ITT population patients on IC chemo had declined vs 70.3% with MIRV
  - 88.1% of FRα-high population patients on IC chemo had declined vs 65.0% with MIRV

Figure 4a. ITT Population: TSW on the FOSI



[a]*P* value based on stratified log-rank test using randomization stratification factors.

Figure 4b. FRα-High Population: TSW on the FOSI



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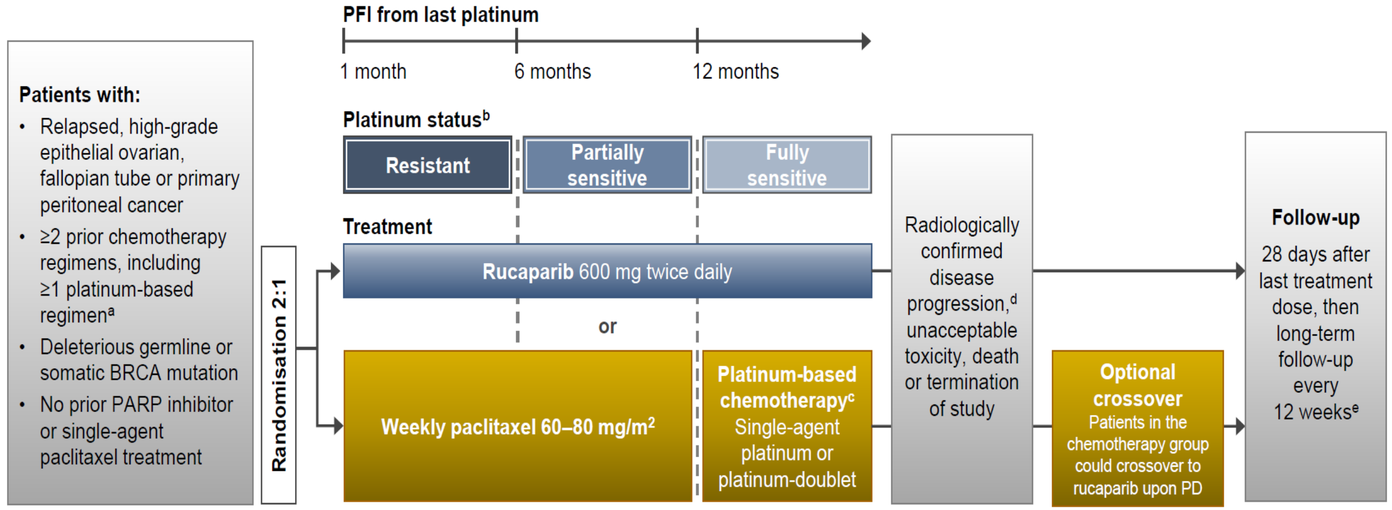
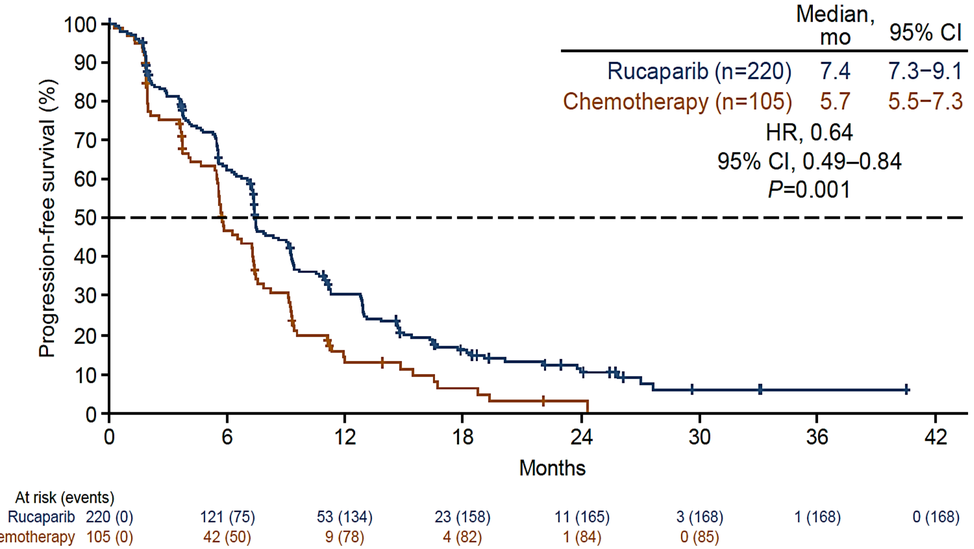
ARIEL-4

Trial eligibility and design



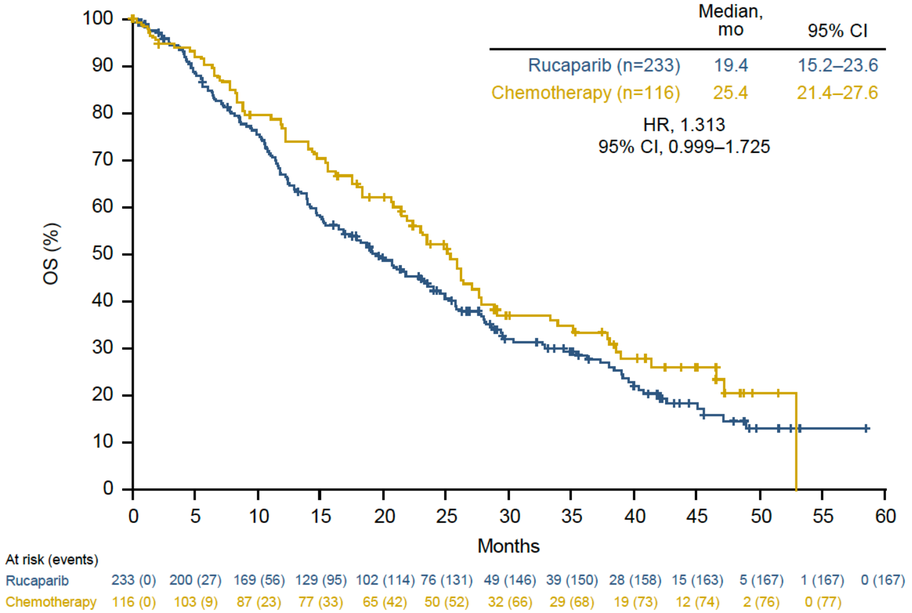
- Efficacy endpoints
  - Prespecified secondary endpoint: OS in the ITT population
  - Exploratory endpoints: OS in platinum-status subgroups; PFS2 in the ITT population and in platinum-status subgroups

Investigator-assessed PFS: Efficacy population

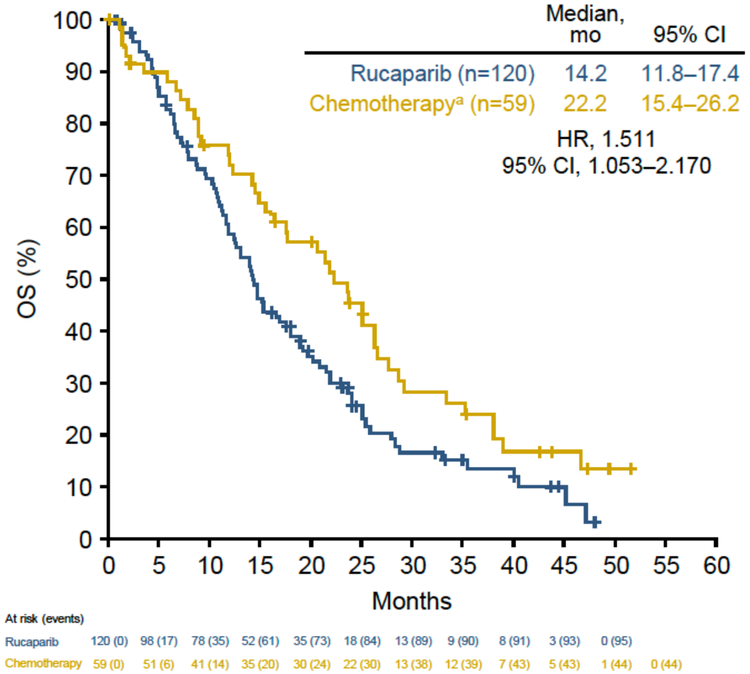


ARIEL-4: OS data

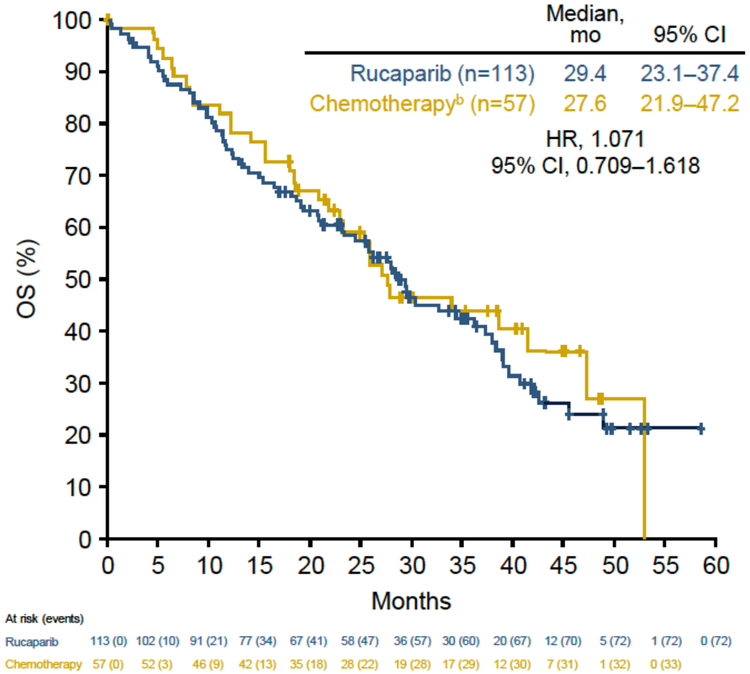
OS: ITT Population



Platinum Resistant



Platinum Sensitive



- **45%** of fully platinum sensitive patients receiving Rucaparib **DID NOT report receiving a subsequent anti-cancer txt**
- **38%** of partially platinum sensitive…
- **43%** of platinum resistant…

- **If you exclude cross over from chemotxt to Rucaparib, the Rucaparib arm had a median OS of 19.4 mo compared to 9.1 mo for chemotherapy (HR 0.432; 95% CI 0.276-0.659). 90% received rucaparib after randomization or crossover**

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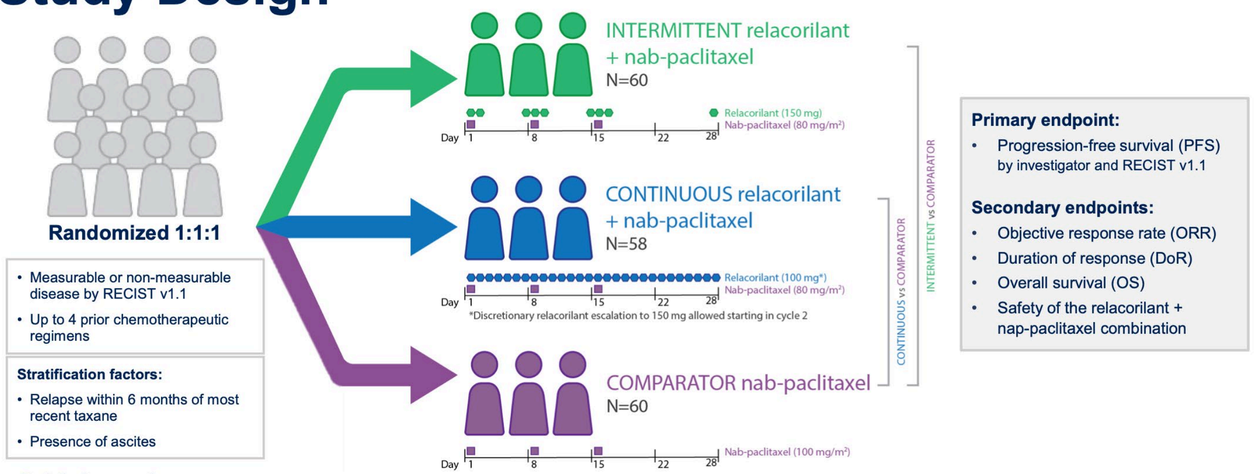
Corcept Phase 2

Relacorilant + Nab-paclitaxel Phase 2 Study Design



- 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

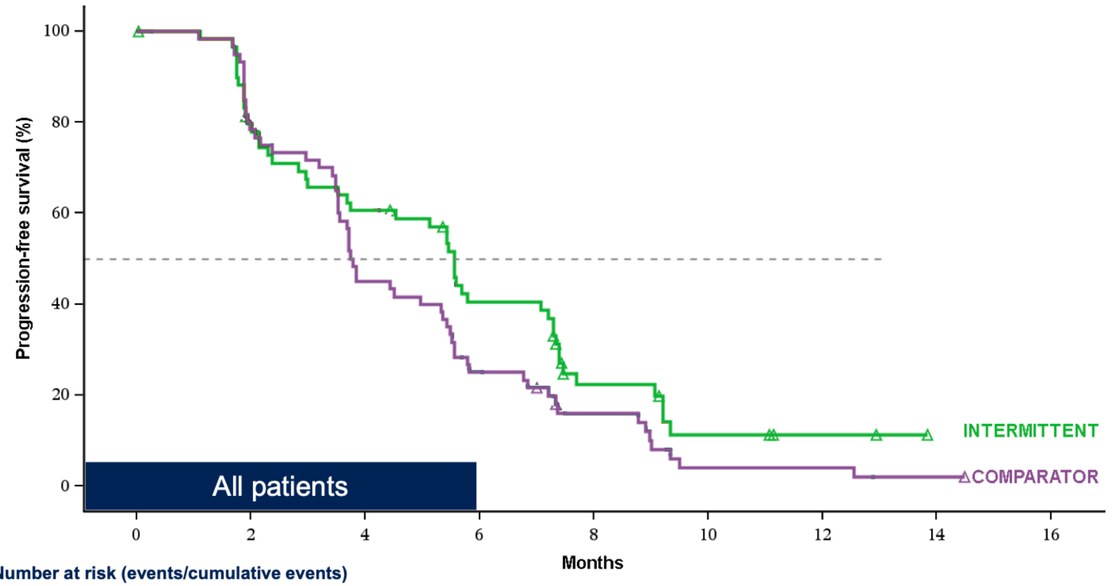
Secondary endpoints:
- Objective response rate (ORR)
- Duration of response (DoR)
- Overall survival (OS)
- Safety of the relacorilant + nap-paclitaxel combination

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

	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)

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)

Biologic Rational

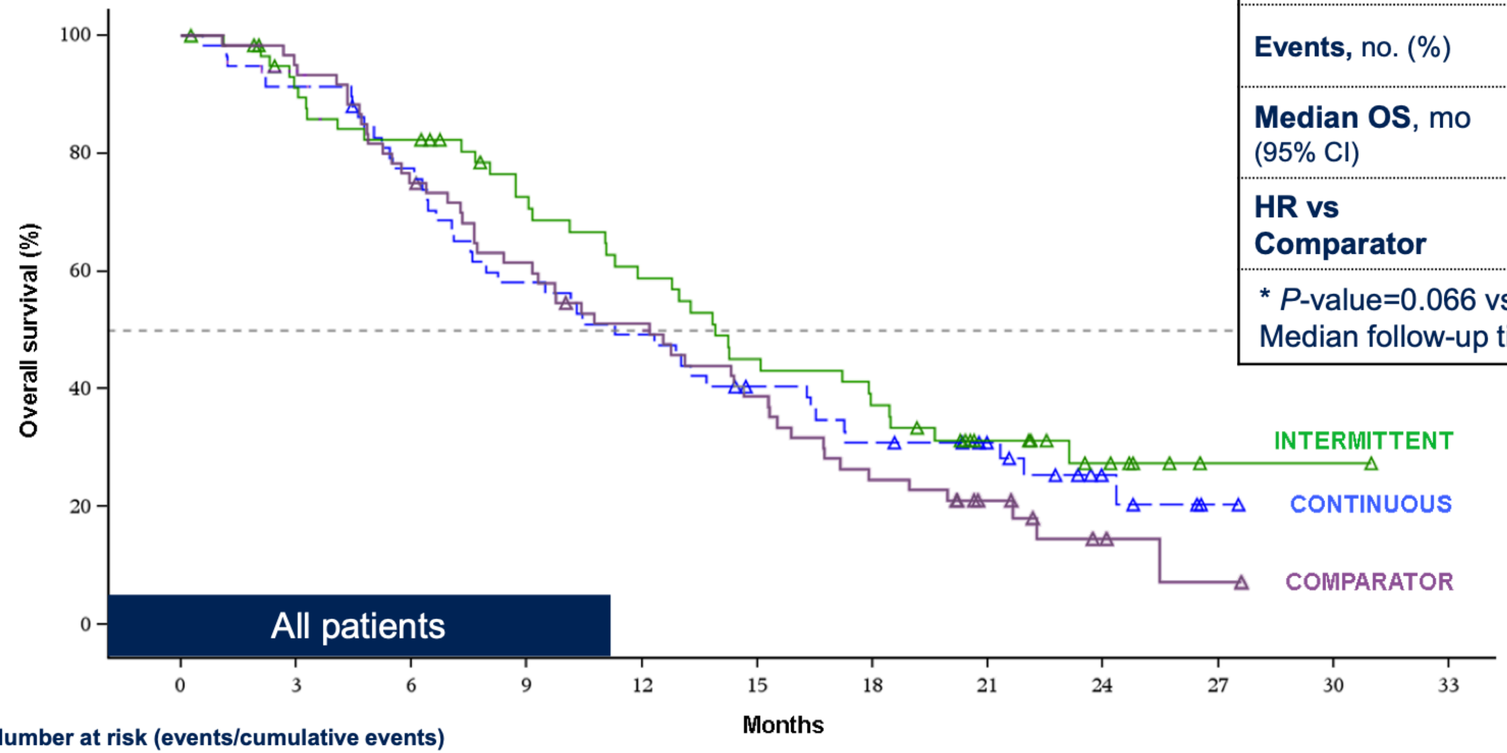
- Cortisol contributes to Chemotherapy resistance by suppressing apoptotic pathways
- GR is abundantly expressed in ovarian malignancies, and high expression is associated with poor outcomes
- GR modulation with relacorilant inhibits antiaopototic affects and enhances activity of cytotoxic chemoTx

Corcept Phase 2

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)	

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

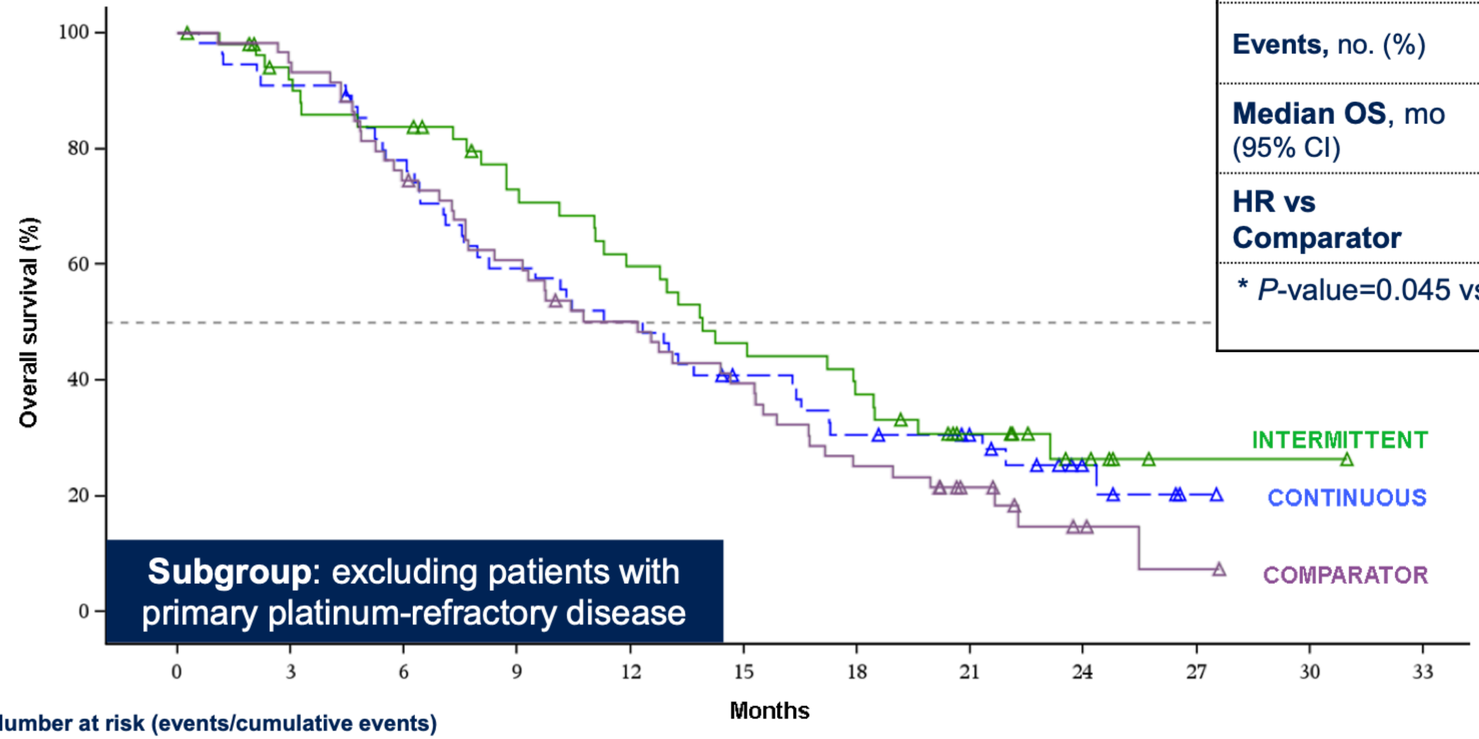
Corcept Phase 2

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

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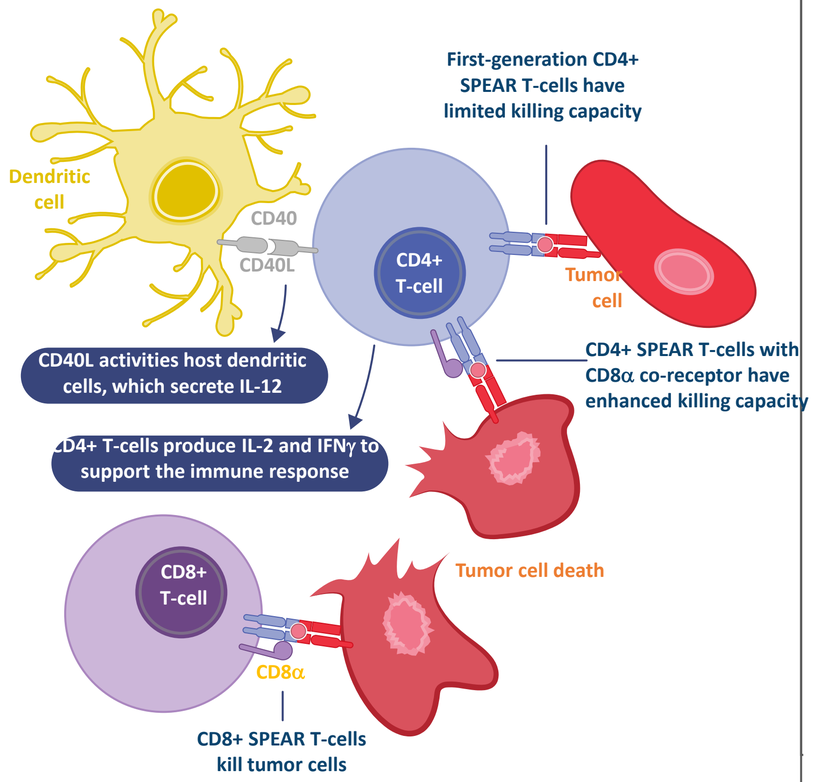
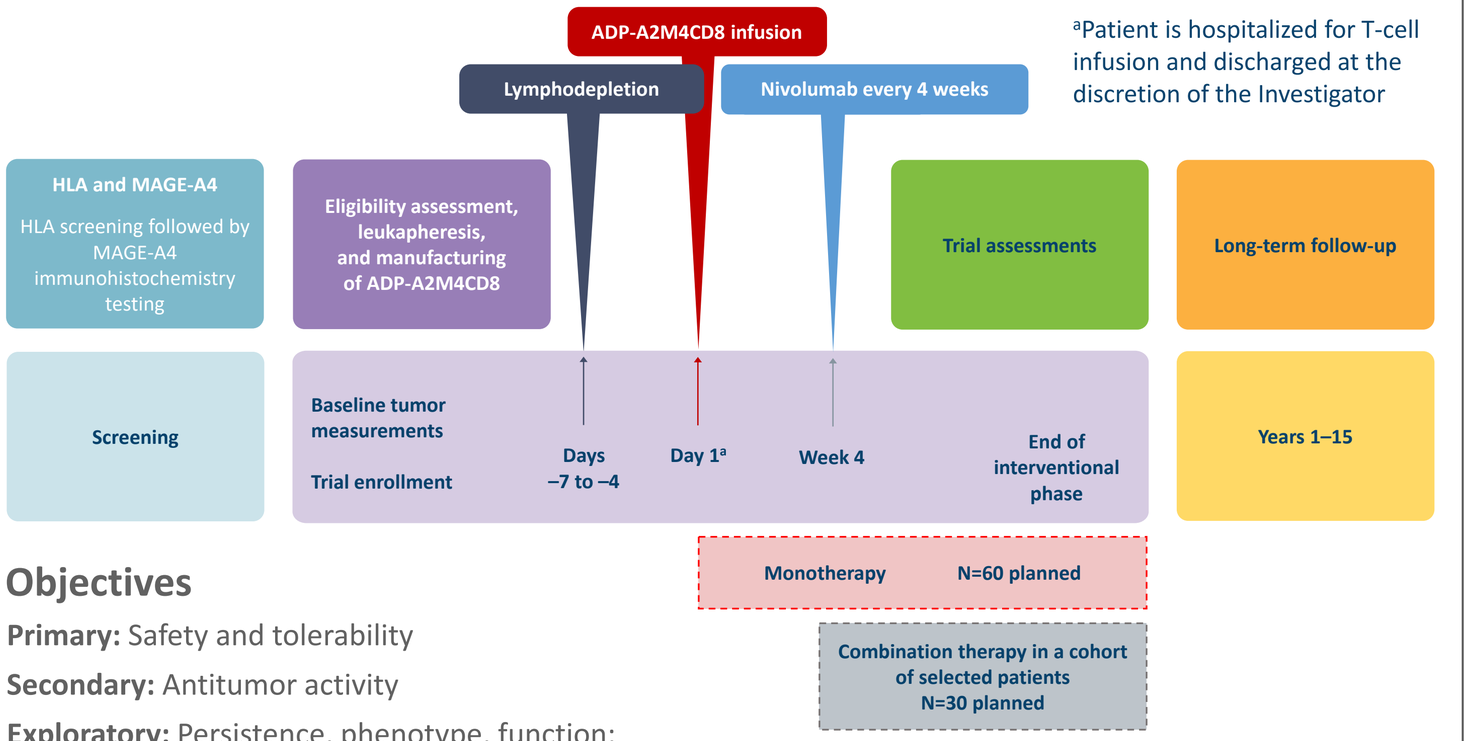
Surpass (Adaptimmune): Preliminary Clinical Outcomes of ADP-A2M4CD8, a Next-Generation Autologous T-Cell Receptor T-Cell Therapy, in Patients With Advanced Epithelial Ovarian Cancer

Designed to increase potency by expressing a CD8α co-receptor



SURPASS trial design



Objectives

Primary: Safety and tolerability

Secondary: Antitumor activity

Exploratory: Persistence, phenotype, function; tumor and serum factors that may influence response or resistance

NCT04044859

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Surpass (Adaptimmune): Preliminary Clinical Outcomes of ADP-A2M4CD8, a Next-Generation Autologous T-Cell Receptor T-Cell Therapy, in Patients With Advanced Epithelial Ovarian Cancer

Eligibility in ovarian cancer based on HLA and MAGE-A4 inclusion criteria (NCT02636855)

- HLA eligible: 49%
- MAGE-A4 positive: 24%

Baseline patient and disease characteristics

	N=14
Median age, years (range)	59 (40, 75)
H-score,[a] median (range)	237.5 (95, 300)
Transduced T-cells × 10^9, median (range)	3.17 (1.14, 9.95)
ECOG performance status, n (%)	
0	6 (42.9)
1	8 (57.1)
No. of prior lines of therapy, median (range)	4 (2, 8)

Overall response rate

- 36% (5 of 14 patients)*

Disease control rate

- 79% (11 of 14 patients)

*1 patient was not evaluable (died prior to their first scan)

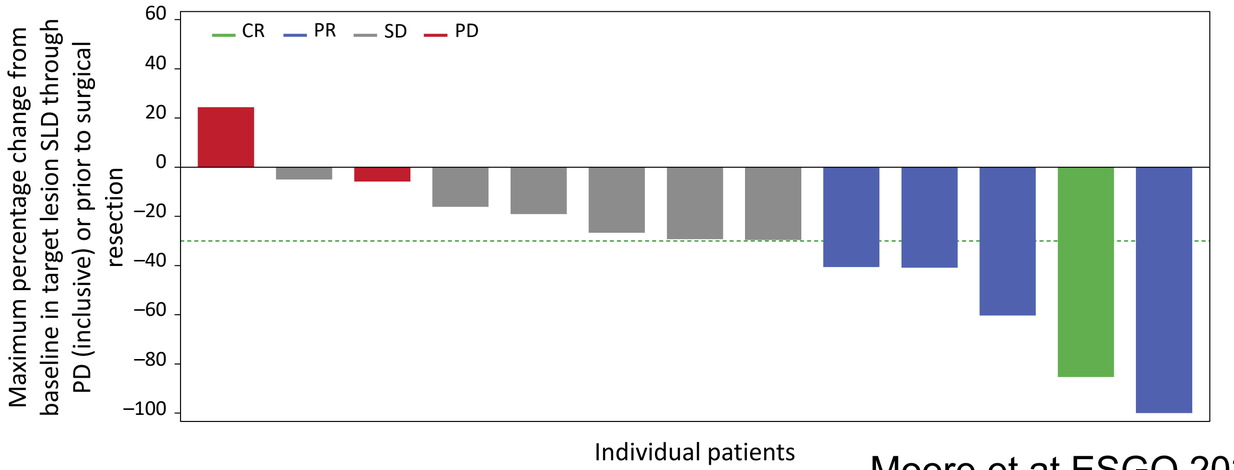
Duration of response (range)

- 9+ to 30 weeks

Serious adverse events and those related to T-cell infusion in ≥5% of patients

Preferred term	N=44, n (%)	
	SAE	Related SAE
Any SAE	27 (61.4)	21 (47.7)
CRS	14 (31.8)	14 (31.8)
Hypoxia	3 (6.8)	3 (6.8)
ICANS	3 (6.8)	3 (6.8)
Pyrexia	3 (6.8)	2 (4.5)

There were 2 related Grade 5 (fatal) SAEs: CRS and Pancytopernia



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Discussion

GOG-P Trials in the PROC Space…

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PROC Space: Mirasol (GOG-3045)

GOG-3045

MIRASOL

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

TARGET TIMELINES

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

1:1 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

PI: Kathleen Moore, MD
ClinicalTrials.gov Identifier: NCT04209855

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*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

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PROC Space: UPLIFT (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 (FPD April 2021) – Study has completed accrual

[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.

ENGOT European Network of Gynaecological Oncological Trial groups
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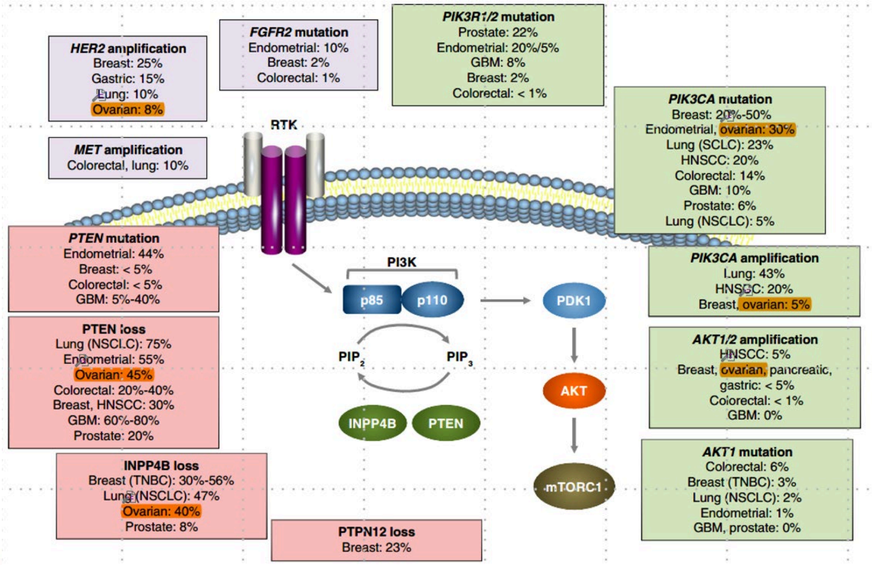
PROC Space: PROFECTA-II (GOG-3044) Open Label Randomized Phase II trial of Afuresertib plus Palcitaxel versus Paclitaxel

- Afuresertib MOA: Pan AKT inhibitor
  - Inhibits Akt 1/2/3
- Hypothesized to restore chemosensitivity
- PROC is a rational therapeutic population
- Can be combined with a chemoTx backbone (Phase 1B data)



N=141; Primary Endpoint PFS

PROC pts with:
- **Bev ineligible or PD;**
- **PARPi ineligible or PD;**
- **Failed prior 1 to 3 chemotherapies including no more than one chemo after PROC is diagnosed.**

Randomization (2:1)

- Platinum Free Interval
- Prior Lines of Platinum Based Therapy
- Country
- Site

Paclitaxel 80 mg/m2 IV D1, 8, 15 Q3W + Afuresertib 125 mg PO QD

Paclitaxel 80 mg/m2 IV D1, 8, 15 Q3W

EOT and safety f/u

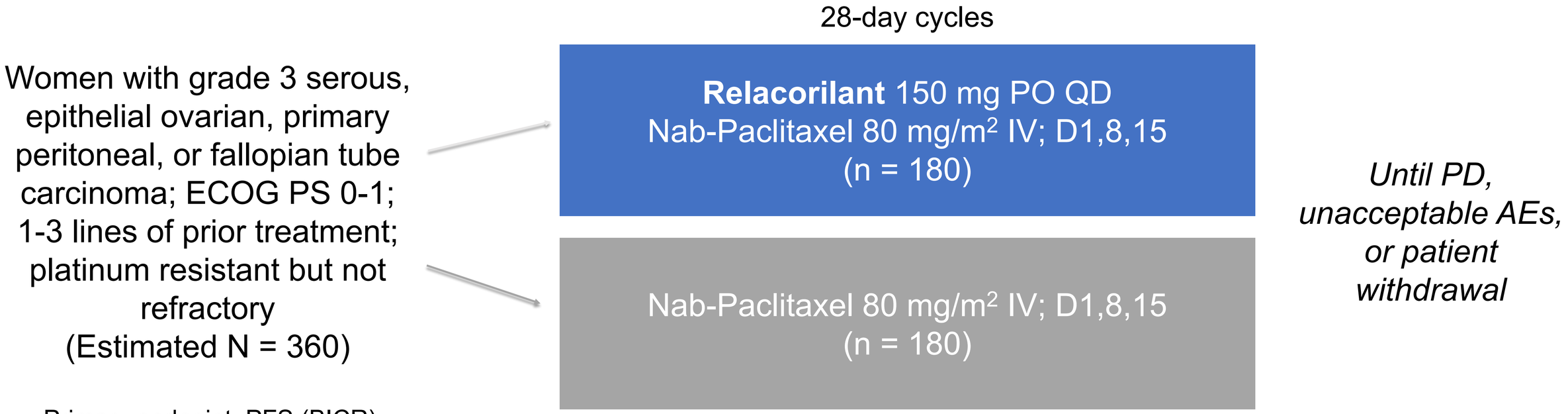
OS f/u

Accrual is currently on hold.

PI: Tom Herzog, MD; NCT04374630

PROC Space: Phase III ROSELLA (GOG3073): Relacorilant + Nab-Paclitaxel vs. Nab-Paclitaxel

- Open-label, randomized study of relacorilant, a selective glucocorticoid receptor modulator



- Primary endpoint: PFS (BICR)
- Secondary endpoints: OS, PFS (investigator), ORR, DoR, CBR, CA-125

ClinicalTrials.gov. NCT05257408. Colombo. ASCO 2022. Abstr LBA5503.