ANNUAL MEETING ON WOMEN'S CANCER

TAMPA, FL • 2023

PATIENTS • PURPOSE • PROGRESS

Mirvetuximab Soravtansine (MIRV) in Patients with Platinum-Resistant Ovarian Cancer with High Folate Receptor Alpha (FRα) Expression: Evaluation of Sequence of Therapy on Anti-Tumor Activity in the SORAYA Study

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SORAYA

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Financial Disclosures

- I have the following financial relationships with ACCME-defined ineligible companies to report over the past 24 months:
  - Consulting: AstraZeneca, GSK, ImmunoGen, Novocure, OncXerna, Onconova, Epsilogen, Pfizer, Merck, Alkermes, Gradalis, Agenus, Mersana, Karyopharm, Deciphera, Roche Genentech, Genelux
  - Grants: Clovis Oncology, AbbVie, AstraZeneca, ImmunoGen, Seagen, Merck
  - Independent Data Monitoring Committees: Eisai, VBL Therapeutics
  - Board Membership: GOG Foundation

Unlabeled/Investigational Use

I will not be discussing unlabeled/investigational uses

Background

- Traditional treatment options for platinum-resistant ovarian cancer are limited, consisting primarily of single-agent chemotherapy or combinations with bevacizumab
  - Single-agent chemotherapy has limited activity (ORR 4%–13%) and considerable toxicity[1–12]
- Greater than 90% of ovarian cancer overexpresses folate receptor α (FRα); FRα is associated with poor clinical outcomes[13–15]
- Mirvetuximab soravtansine (MIRV) is a first-in-class antibody-drug conjugate comprising an FRα-binding antibody, cleavable linker, and maytansinoid DM4, a potent tubulin-targeting agent
- SORAYA was a global, single-arm study evaluating MIRV in adult patients with FRα-high platinum-resistant high-grade serous epithelial ovarian, primary peritoneal, or fallopian tube cancers[16]
- MIRV received FDA approval November 2022 for the treatment of adult patients with FRα positive, platinum-resistant ovarian cancer who have received one to three prior systemic treatment regimens
- With the addition of new agents for the treatment of ovarian cancer, sequence of therapies may be important to optimize patient outcomes

FRα, folate receptor alpha; mDOR, median duration of response; ORR, confirmed objective response rate; mPFS, median progression-free survival.

1. ten Bokkel Huinink W, et al. *J Clin Oncol*. 1997;15(6):2183-2193. 2. Gore M, et al. *Eur J Cancer*. 2002;38(1):57-63. 3. Mutch DG, et al. *J Clin Oncol*. 2007;25(19):2811-2818. 4. Vergote I, et al. *Eur J Cancer*. 2009;45(13):2324-2332. 5. Vergote I, et al. *Int J Gynecol Cancer*. 2010;20(5):772-780. 6. Sehouli J, et al. *J Clin Oncol*. 2011;29(2):242-248. 7. Colombo N, et al. *J Clin Oncol*. 2012;30(31):3841-3847. 8. Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308. 9. Gaillard S, et al. *Gynecol Oncol*. 2021;163(2):237-245. 10. Hamanishi J, et al. *J Clin Oncol*. 2021;39(33):3671-3681. 11. Moore KN, et al. *Ann Oncol*. 2021;32(6):757-765. 12. Pujade-Lauraine E, et al. *Lancet Oncol*. 2021;22(7):1034-1046. 13. Crane LM, et al. *Cell Oncol (Dordr)*. 2012;35(1):9-18. 14. Kalli KR, et al. *Gynecol Oncol*. 2008;108(3):619-626. 15. Chen YL, et al. *Mol Oncol*. 2012;6(3):360-369. 16. Matulonis UA, et al. *JCO*. 2023; published online January 30, 2023.

Study Design and Patient Population

Objective: Evaluate efficacy and safety of MIRV in patients with FRα-high platinum-resistant ovarian cancer

Primary endpoint: Confirmed ORR by investigator

- ORR by blinded independent central review for sensitivity analysis

Key secondary endpoint: Duration of response

Patient population

- Platinum-resistant ovarian cancer (recurrence within 6 months after last platinum dose) treated with 1 to 3 prior regimens
  - Primary platinum-refractory disease* was excluded
- High-grade serous histology
- All patients enrolled received prior bevacizumab; prior PARP inhibitor was allowed
- Tumor demonstrated FRα-high membrane staining by the Ventana FOLR1 assay with at least 75% of viable tumor cells exhibiting at least 2+ staining intensity with IHC

Treatment schedule

- Patients received MIRV 6 mg/kg adjusted ideal body weight, IV once every 3 weeks

Sample size calculation: 105 patients

- 110 patients planned to result in approximately 105 efficacy-evaluable patients
- 90% power to detect a difference in ORR of 24% vs 12% using a 1-sided binomial test and a 1-sided α level of 0.025
- 12% was chosen as the ORR to rule out based on the ORR for single-agent chemotherapy reported in prior trials of platinum-resistant ovarian cancer, which ranges from 4% to 13%[1-4]

FRα, folate receptor alpha; IHC, immunohistochemistry; IV, intravenous; MIRV, mirvetuximab soravtansine; ORR, confirmed objective response rate; PARP, poly ADP-ribose polymerase; PS2+, sum of staining of 2+ and 3+ intensity.
*Defined as disease that did not respond to first-line platinum therapy or progressed within 3 months of the last dose.

1. Pujade-Lauraine E, et al. *J Clin Oncol*. 2014;32(13):1302-1308. 2. Gaillard S, et al. *Gynecol Oncol*. 2021;163(2):237-245. 3. Moore KN, et al. *Ann Oncol*. 2021;32(6):757-765. 4. Pujade-Lauraine E, et al. *Lancet Oncol*. 2021;22(7):1034-1046.

Baseline Demographics and Clinical Characteristics

Characteristics		All Patients (N=106)
Age, median (range)	Age in years	62 (35–85)
Primary cancer diagnosis, n (%)[a]	Epithelial ovarian cancer Fallopian tube cancer Primary peritoneal cancer	85 (80) 8 (8) 12 (11)
Stage at initial diagnosis, n (%)[b]	I–II III **IV**	2 (2) 63 (59) **40 (38)**
BRCA mutation, n (%)	Yes No	21 (20) 85 (80)
No. of prior systemic therapies (%)	1 2 **3[c]**	10 (9) 41 (39) **55 (52)**
Prior exposure, n (%)	**Bevacizumab** **PARPi** Taxanes	**106 (100)** **51 (48)** 105 (99)
MIRV as first treatment for PROC, n (%)	Yes No	67 (63) 39 (37)
Prior bevacizumab treatment setting, n (%)[d]	PSOC PROC	95 (90) 17 (16)
Platinum-free interval, n (%)[e]	**0–3 mo** 3– >6 mo	**39 (37)** 64 (60)

Analysis Population

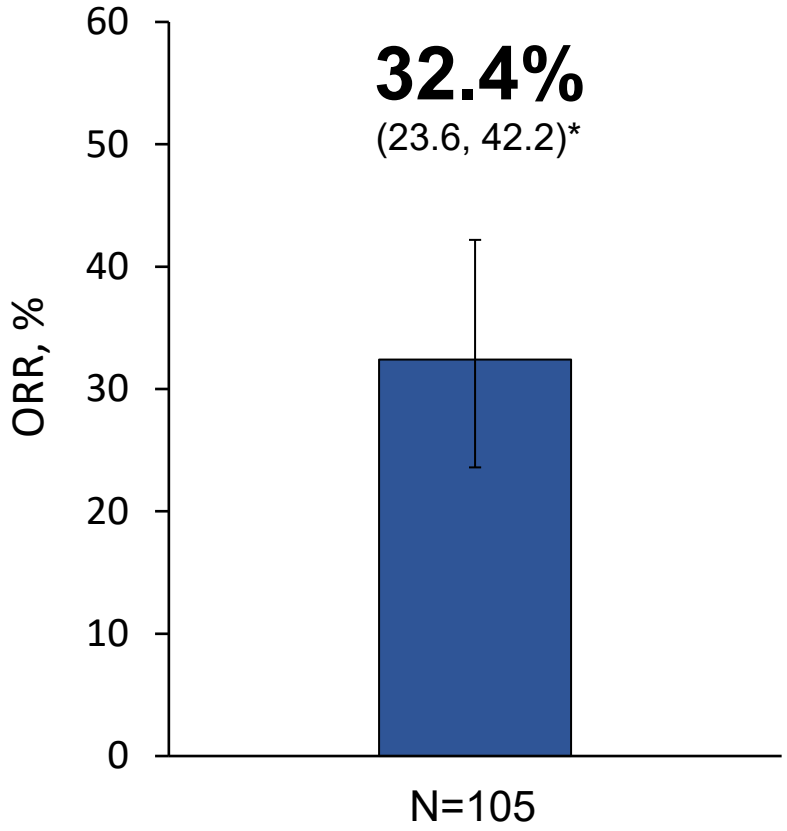
- **Efficacy-evaluable population:** 105 patients who had measurable disease at baseline by investigator assessment per RECIST v1.1
- **Safety population:** 106 patients who received ≥1 dose of MIRV

Data cutoff: April 29, 2022.

BRCA, BReast CAncer gene; ECOG PS, Eastern Cooperative Oncology Group Performance Status; MIRV, mirvetuximab soravtansine; PROC, platinum resistant ovarian cancer; PARPi, poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitor; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1.

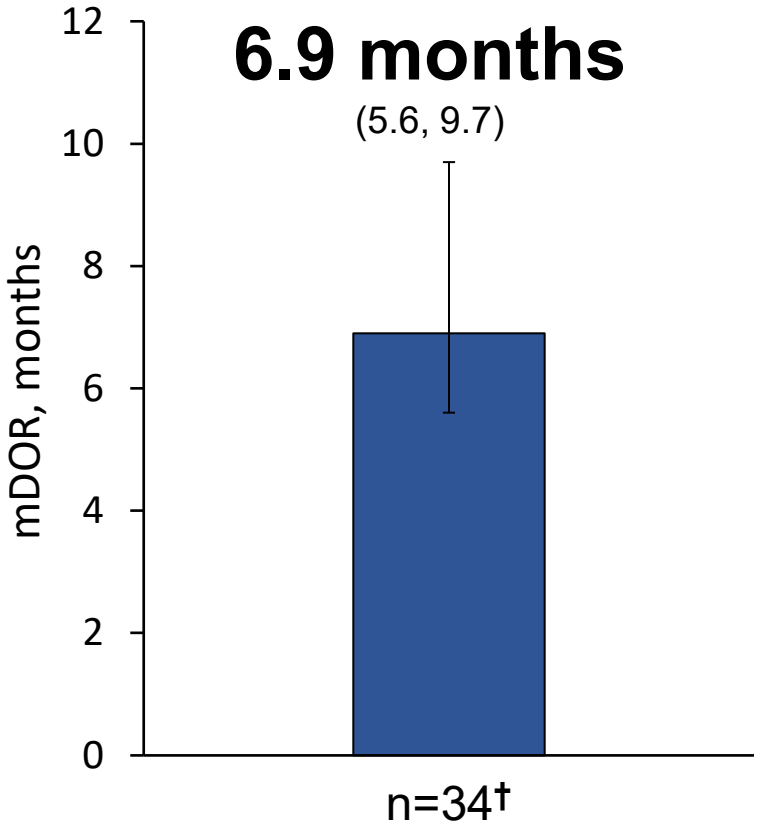
[a]Primary cancer diagnosis includes 1 patient with serous tubal intraepithelial carcinoma. [b]One patient missing information for stage at initial diagnosis; none of the patients were at stage II when initially diagnosed. [c]Includes 1 patient with >3 prior lines. [d]6 patients received bevacizumab in both the PSOC and PROC settings. [e]3 patients were enrolled with platinum-free interval of >6 months.

Investigator-Assessed Objective Response Rate and Median Duration of Response in Overall Efficacy Evaluable Population



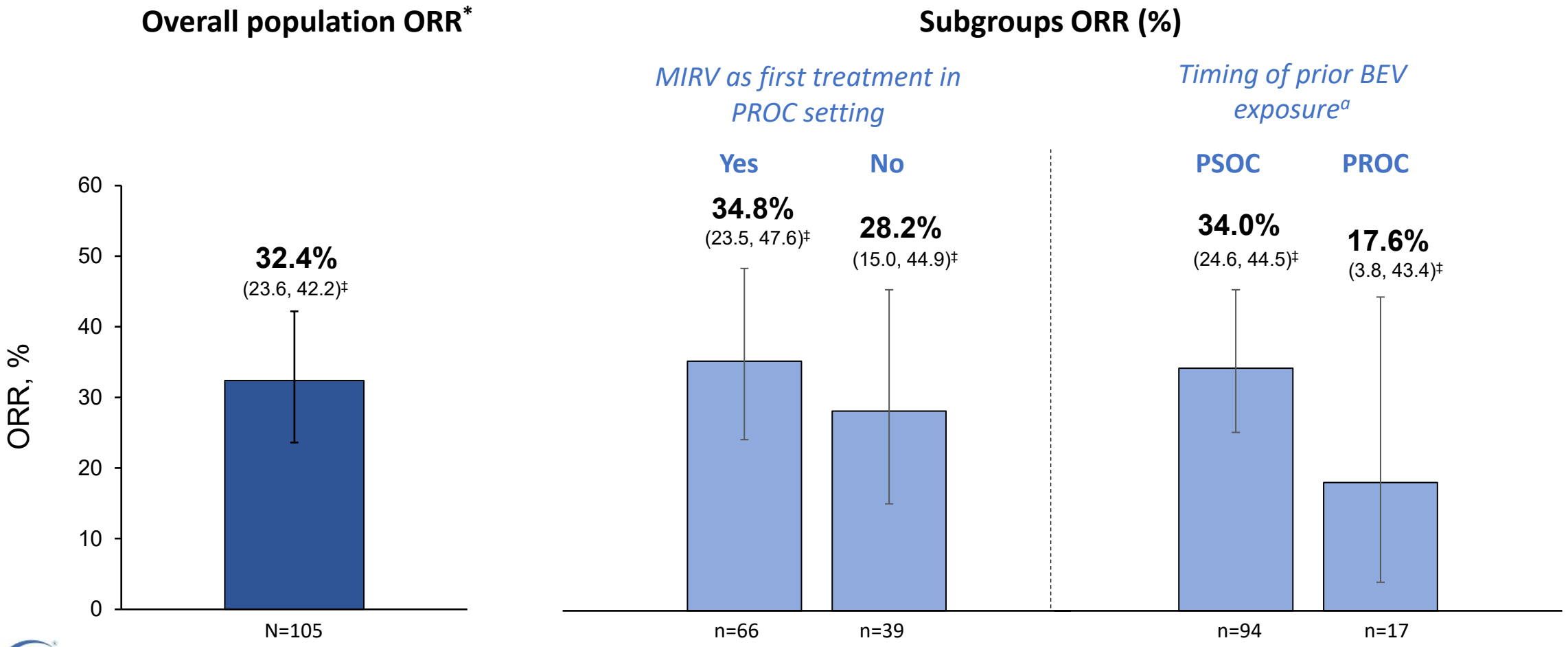
ORR: 34 responders

- 5 complete responses
- 29 partial responses



Data cutoff: April 29, 2022.
CR, complete response; DOR, duration of response; mDOR, median duration of response; ORR, confirmed objective response rate; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors.
The denominator for the percentage is the number of patients in the investigator-assessed efficacy evaluable population. Patients without at least 1 postbaseline RECIST assessment were treated as not evaluable.
*95% exact confidence interval is estimated by Clopper-Pearson method (Clopper-Pearson exact CI); †mDOR for overall patients was calculated amongst 34 responders

Investigator-Assessed Objective Response Rate by Prior Therapy



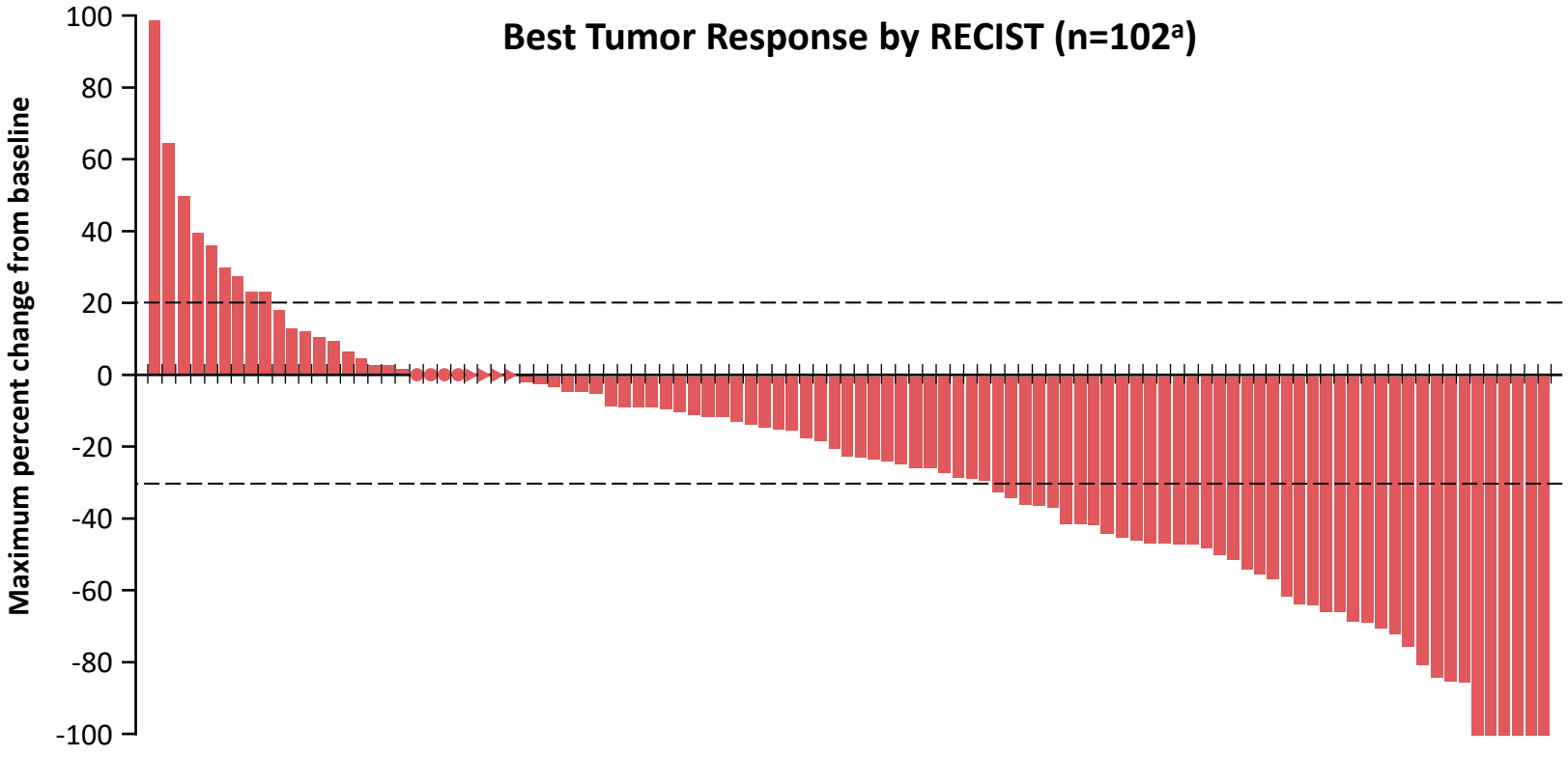
*Data cutoff: April 29, 2022.

CI, confidence interval; ORR, confirmed objective response rate; PROC platinum resistant ovarian cancer; PSOC, platinum sensitive ovarian cancer; RECIST, Response Evaluation Criteria in Solid Tumors. 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.

[a]6 patients received bevacizumab in both the PSOC and PROC settings. ‡95% exact CI is estimated by Clopper-Pearson method (Clopper-Pearson exact CI).

Best Tumor Response

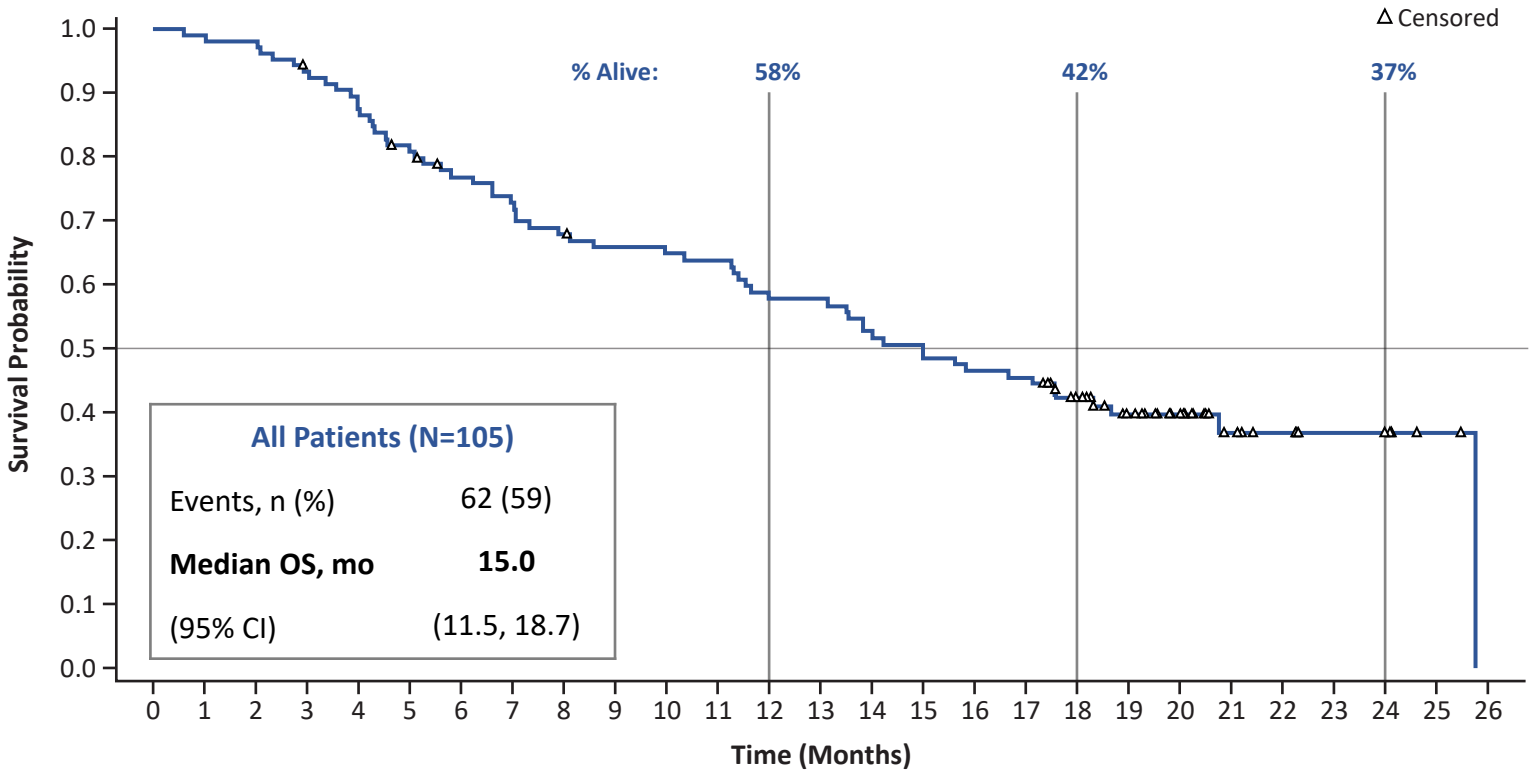
- 71% of patients experienced tumor reduction
- 51% of patients had disease control (defined as CR, PR, or SD for ≥12 weeks)



Data cutoff: April 29, 2022
CR, complete response; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.
[a]Three patients had no postbaseline tumor assessment.

Overall Survival

Final Overall Survival* in INV Efficacy Evaluable Population



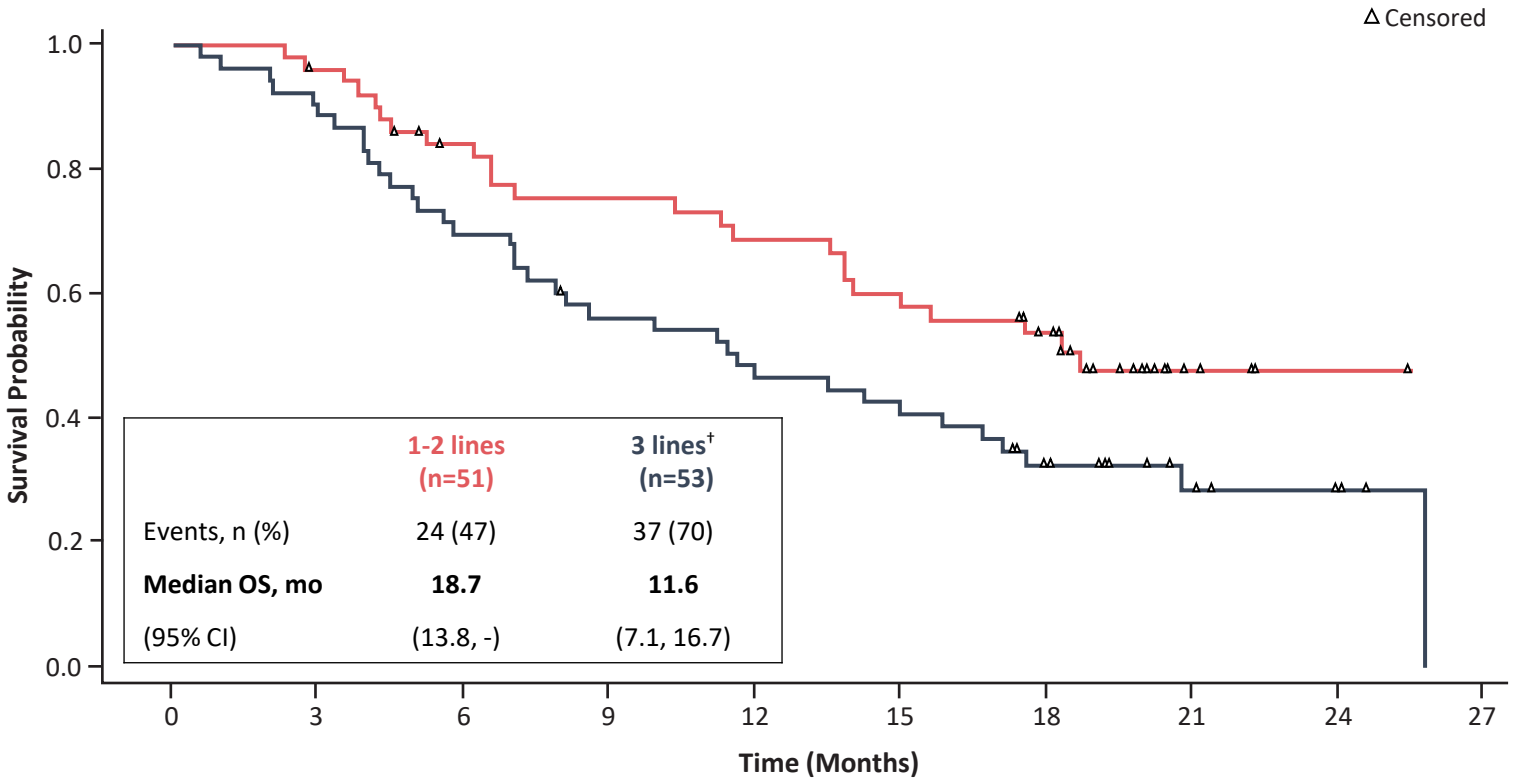
Number of Patients at Risk

MIRV	105	104	103	97	91	83	77	73	68	65	64	63	57	57	52	48	46	45	36	27	21	12	9	6	5	2	0

Data cutoff: December 22, 2022.
INV, investigator; MIRV, mirvetuximab soravtansine; OS, overall survival
*Overall survival defined as the time from the date of first dose until the date of death from any cause.

Overall Survival in 1-2 vs 3 Prior Therapies

Final Overall Survival* by Number of Prior Lines of Therapy



Number of Patients at Risk										
1–2 lines	51	48	39	35	32	27	22	5	1	0
3 lines	53	48	37	29	24	21	14	7	4	0

Data cutoff: December 22, 2022.
OS, overall survival.
*Overall survival defined as the time from the date of first dose until the date of death from any cause. †1 patient had >3 prior lines and was not included in this analysis.

TRAEs Reported in ≥10% of Patients (N=106)[1-2]

TRAEs, n (%)	All Grades	Grade 3	Grade 4
Patients with any event	91 (86)	30 (28)	1 (1)
Blurred vision	43 (41)	6 (6)	0 (0)
Keratopathy*†	31 (29)	8 (8)	1 (1)
Nausea	31 (29)	0 (0)	0 (0)
Dry eye	26 (25)	2 (2)	0 (0)
Fatigue	25 (24)	1 (1)	0 (0)
Diarrhea	23 (22)	2 (2)	0 (0)
Asthenia	16 (15)	1 (1)	0 (0)
Photophobia	14 (13)	0 (0)	0 (0)
Peripheral neuropathy	14 (13)	0 (0)	0 (0)
Decreased appetite	14 (13)	1 (1)	0 (0)
Neutropenia	14 (13)	2 (2)	0 (0)
Vomiting	12 (11)	0 (0)	0 (0)

- Most AEs were low-grade, reversible ocular and GI events
- Serious grade ≥3 TRAEs were reported in 9% of patients
- TRAEs led to dose delay in 33% and dose reduction in 20%
- 10 patients (9%) discontinued treatment due to TRAEs
- 1 death was recorded as possibly related to study drug
  - Respiratory failure
  - Autopsy: No evidence of drug reaction; lung metastases

Data cutoff: April 29, 2022.
AE, adverse event; GI, gastrointestinal; TRAEs, treatment-related adverse events.
*The grouped preferred term "Keratopathy" includes the following preferred terms: "corneal cyst," "corneal disorder," "corneal epithelial microcysts," "keratitis," "keratopathy," "limbal stem cell deficiency," "corneal opacity," "corneal erosion," "corneal pigmentation," "corneal deposits," "keratitis interstitial," "punctate keratitis," and "corneal epithelial defect." †One patient experiencing a grade 4 event recorded as keratopathy was based upon the visual acuity evaluation of one eye (20/200). This patient had confirmed grade 2 corneal changes, and both the visual acuity and these corneal changes resolved completely (grade 0) in 15 days by ophthalmic exam.

MIRV Ocular AE Profile: Keratopathy and Blurred Vision

- **52% of patients experienced any-grade blurred vision or keratopathy***
- **Predictable**
  - Median time to onset: cycle 2 (~1.4 months)
- **Manageable with dose modifications, if needed**
  - 11% of patients had dose reduction
- **Reversible**
  - At time of data cutoff, 96% of patients with grade 2 or greater ocular events had resolved to grade 1 or 0
- **<1% discontinuation due to ocular events**
  - 1 of 106 patients discontinued due to an ocular treatment-emergent adverse event†
  - No corneal ulcers or corneal perforations were identified, and no patients had permanent ocular sequelae

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Data cutoff: April 29, 2022.
AE; Adverse events; MIRV, mirvetuximab soravtansine.
*The grouped preferred term "Keratopathy" includes the following preferred terms: "corneal cyst," "corneal disorder," "corneal epithelial microcysts," "keratitis," "keratopathy," "limbal stem cell deficiency," "corneal opacity," "corneal erosion," "corneal pigmentation," "corneal deposits," "keratitis interstitial," "punctate keratitis," and "corneal epithelial defect." †One patient experiencing a grade 4 event recorded as keratopathy was based upon the visual acuity evaluation of one eye (20/200). This patient had confirmed grade 2 corneal changes, and both the visual acuity and these corneal changes resolved completely (grade 0) in 15 days by ophthalmic exam.

Conclusions

- MIRV demonstrates clinically meaningful antitumor activity in patients with FRα-high platinum-resistant ovarian cancer
  - **ORR: 32.4%** and **Median DOR: 6.9 months**
  - **Median OS of 15 months; 37% patients alive at 24 months**
  - MIRV as first treatment for PROC demonstrated an ORR of 34.8%; in patients with prior treatment(s) for PROC, MIRV demonstrated an ORR of 28.2%
  - In patients with prior bevacizumab in the platinum-sensitive setting, MIRV has an ORR of 34.0%; in patients with prior bevacizumab in the platinum-resistant setting, MIRV has an ORR of 17.6%
- The safety and tolerability profile of MIRV in SORAYA is consistent with that observed in previous studies
  - Low-grade, reversible ocular and GI events, manageable with supportive care
  - No appreciable myelosuppression and limited low-grade neuropathy
  - 10 patients (9%) discontinued treatment due to TRAEs
    - Only 1 patient discontinued due to an ocular event
- **These results position MIRV to become a practice-changing, biomarker-driven standard of care treatment option for patients with FRα-positive platinum-resistant ovarian cancer**

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MIRV, mirvetuximab soravtansine; FRα, folate receptor alpha; ORR, confirmed objective response rate; DOR, duration of response; OS, overall survival; PROC, platinum resistant ovarian cancer; GI, gastrointestinal; TRAEs, treatment-related adverse events

This presentation is dedicated to the patients and their families who participated in the SORAYA clinical trial.

Thank you to all of the clinical investigators and research teams.

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Participating Sites

Massachusetts General Hospital Boston, MA, USA	Medical Center at Mount Sinai New York, NY, USA	Stanford Health Care Stanford, CA, USA	Hospital Universitari Germans Trias i Pujol Barcelona, Spain	SP ZOZ Ministerstwa Spraw Wewnętrznych z Warmińsko – Mazurskim Centrum Onkologii Olsztyn, Poland	Policlinico S. Orsola-Malpighi Bologna, Italy	St James's Hospital Dublin, Leinster, Ireland
Tennessee Oncology Nashville, TN, USA	USOR, Investigational Product Center Irving, TX, USA	Universitair Ziekenhuis Leuven Leuven, Belgium	Institut Català d'Oncologia Badalona Barcelona, Spain	Instytut Centrum Zdrowia Matki Polki Łódź, Poland	Istituto Nazionale Tumori - G. Pascale Napoli, Italy	Všeobecná fakultní nemocnice v Praze Prague, Czech Republic
University of Kansas Hospital Westwood, KS, USA	St. Tammany Parish Hospital Pharmacy Covington, LA, USA	Universitair Ziekenhuis Ghent Ghent, Belgium	Hospital Teresa Herrera A Coruña, Spain	Specjalistyczna Przychodnia Lekarska Medicus Chorzow, Silesia Province, Poland	Istituto Oncologico Candiolo - I.R.C.C.S Candiolo (Torino), Italy	Universitätsklinikum Mannheim, Baden-Württemberg, Germany
Dana-Farber Cancer Institute Boston, MA, USA	Research Medical Center Kansas City, MO, USA	Cliniques Universitaires Saint Luc Bruxelles, Belgium	IOR-Hospital Quiron Dexeus Barcelona, Spain	Sheba Medical Center Ramat Gan, Israel	ASST degli Spedali Civili di Brescia Brescia, Italy	Kliniken Essen Mitte Apotheke Essen, Germany
Sarasota Memorial Health Cancer Center Sarasota, FL, USA	Holy Name Medical Center Teaneck, NJ, USA	Centre Hopsitalier de l'Ardenne Luxembourg, Belgium	Hospital Clínico San Carlos Madrid, Spain	Meir Medical Center Kfar Saba, Israel	Ospedale Cannizzaro di Catania Catania, Italy	River City Pharmacy (ICON Cancer Care) Auchenflower, QLD, Australia
Center of Hope Reno, NV, USA	Florida Cancer Specialists West Palm Beach, FL, USA	CHU UCL Namur / St. Elisabeth Namur, Belgium	Hospital Universitario Reina Sofia, Córdoba, Spain	Hadassah Ein Kerem Medical Center Jerusalem, Israel	Bon Secours Hospital Cork, Munster, Ireland	St John of God Subiaco Hospital Subiaco, WA, Australia
Memorial Sloan-Kettering Cancer Center New York, NY, USA	UW Health - University Hospital Madison, WI, USA	MD Anderson Cancer Center Madrid, Spain	Hospital Clínico de Valencia Valencia, Spain	Ziv Medical Center Safed, Israel	Mater Misericordiae University Hospital Dublin, Leinster, Ireland	PSEHOG - Slade Pharmacy Subiaco, WA, Australia
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ICO Hospitalet Barcelona, Spain	Complex Oncology Center Burgas, Bulgaria	Fondazione Policlinico Universitario Agostino Gemelli Rome, Italy	Beaumont Hospital Dublin, Ireland			

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