ANNUAL MEETING ON WOMENS' CANCER®

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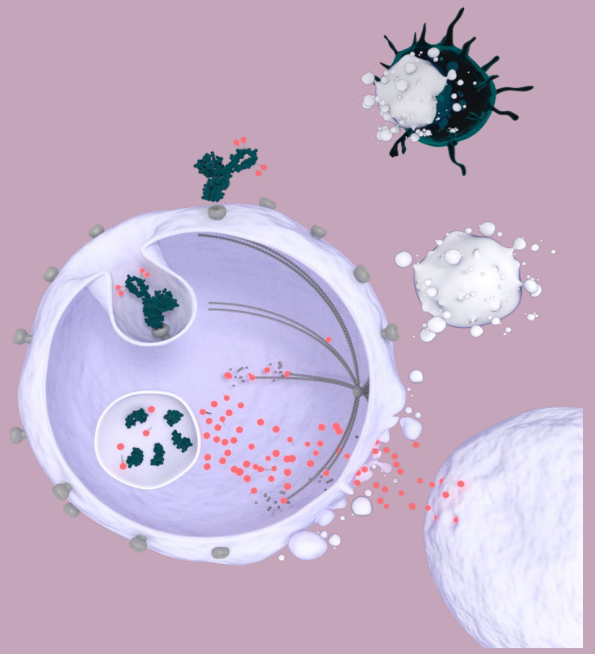
Efficacy and Safety of Mirvetuximab Soravtansine in Patients With Platinum-Resistant Ovarian Cancer With High Folate Receptor Alpha Expression: Results From the SORAYA Study

Ursula A. Matulonis,[1] Domenica Lorusso,[2] Ana Oaknin,[3] Sandro Pignata,[4] Hannelore Denys,[5] Nicoletta Colombo,[6] Toon Van Gorp,[7] Jason A. Konner,[8] Margarita Romeo Marin,[9] Philipp Harter,[10] Conleth G. Murphy,[11] Jiuzhou Wang,[12] Elizabeth Noble,[12] Brooke Esteves,[12] Michael Method,[12] Robert L. Coleman[13]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Fondazione Policlinico Universitario A. Gemelli, IRCCS and Catholic University of Sacred Heart, Rome, Italy; [3]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [4]Istituto Nazionale Tumori di Napoli Fondazione G Pascale IRCCS, Naples, Italy; [5]Ghent University Hospital, Ghent, Belgium; [6]European Institute of Oncology IRCCS, Milan, Italy and University of Milan-Bicocca, Milan, Italy; [7]University Hospital Leuven, Leuven Cancer Institute, Leuven, Belgium; [8]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [9]Institut Català d'Oncologia, Badalona, Spain; [10]Ev. Kliniken Essen-Mitte, Essen, Germany; [11]Bon Secours Hospital and Cancer Trials, Cork, Ireland; [12]ImmunoGen, Inc., Waltham, MA, USA; [13]US Oncology Research, Texas Oncology, The Woodlands, TX, USA



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: Novartis, AstraZeneca, Merck, GSK, Trillium, Blueprint Medicines, and Agenus (all ongoing)
  - Scientific Advisory Boards: ImmunoGen, NextCure, Ovarian Cancer Research Alliance, Rivkin Foundation, and Clearity (all ongoing)
  - Data Safety Monitoring Boards: Symphogen, Alkermes, and Advaxis

Unlabeled/Investigational Uses

- I will be discussing unlabeled/investigational use
  - Mirvetuximab soravtansine is not yet approved for use outside of clinical trials

Background

- Treatment options for platinum-resistant ovarian cancer are limited, consisting primarily of single-agent chemotherapy as many patients will have received prior bevacizumab
  - Single-agent chemotherapy has limited activity (ORR 4%–13%) and considerable toxicity[1–12]
- No biomarker-directed therapy is indicated specifically for patients with platinum-resistant disease
- 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
- Pooled analysis from previous studies with MIRV identified 70 patients with FRα-high platinum-resistant ovarian cancer, 1–3 priors, all with prior bevacizumab: ORR, 31.4%; mDOR, 7.8 months; and mPFS, 4.4 months[11,16–18]

SORAYA is a global, single-arm, phase 3 study evaluating MIRV in adult patients with FRα-high platinum-resistant high-grade serous epithelial ovarian, primary peritoneal, or fallopian tube cancers

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

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SORAYA: 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 enrolled received prior bevacizumab; prior PARP inhibitor was allowed
- Tumor demonstrated FRα-high membrane staining with IHC PS2+ scoring
  - **≥75%** of cells staining positive with **≥2+** staining intensity

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]

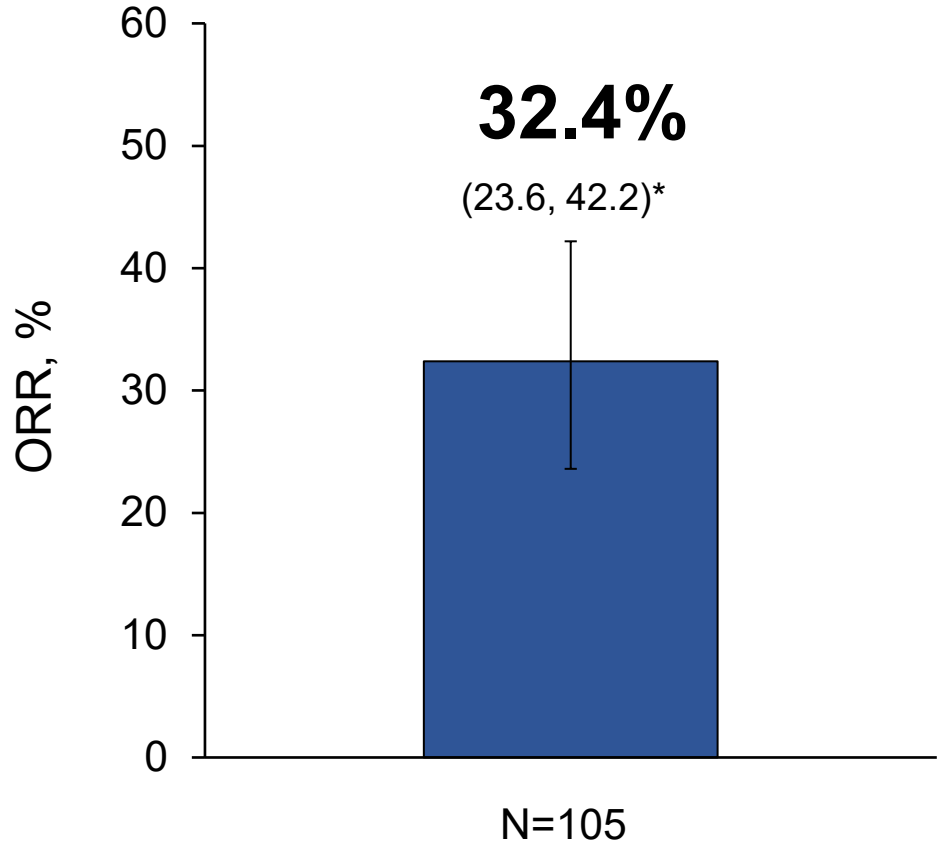
*Defined as disease that did not respond to first-line platinum therapy or progressed within 3 months of the last dose.
FRα, folate receptor alpha; IHC, immunohistochemistry; IV, intravenous; MIRV, mirvetuximab soravtansine; ORR, confirmed objective response rate; PARP, poly ADP-ribose polymerase; PS2+,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

Characteristic		All Patients (N=106)
Age, median (range)		62 (35–85 years)
Primary cancer diagnosis,* n (%)	Epithelial ovarian cancer	85 (80)
	Fallopian tube cancer	8 (8)
	Primary peritoneal cancer	12 (11)
Stage at initial diagnosis,† n (%)	I–II	2 (2)
	III	63 (59)
	IV	40 (38)
BRCA mutation, n (%)	Yes	21 (20)
	No/unknown	85 (80)
No. of prior systemic therapies, n (%)	1	10 (9)
	2	41 (39)
	3	54 (51)
Prior exposure, n (%)	Bevacizumab	106 (100)
	PARP inhibitor	51 (48)
Primary platinum-free interval, n (%)	3–12 months‡	64 (60)
	>12 months	42 (40)
Platinum-free interval, n (%)	0–3 months	39 (37)
	3–6 months	64 (60)

Data cutoff: November 16, 2021.
Patients with ECOG PS of 0, n=60 (57%); 1, n=46 (43%).
*Primary cancer diagnosis includes 1 patient with serous tubal intraepithelial carcinoma. †One patient missing information for stage at initial diagnosis. ‡Includes 1 patient with primary platinum-free interval of 2.8 months.
ECOG PS, Eastern Cooperative Oncology Group performance status; PARP, poly ADP-ribose polymerase.

Investigator-Assessed Objective Response Rate in Overall Efficacy Evaluable Population

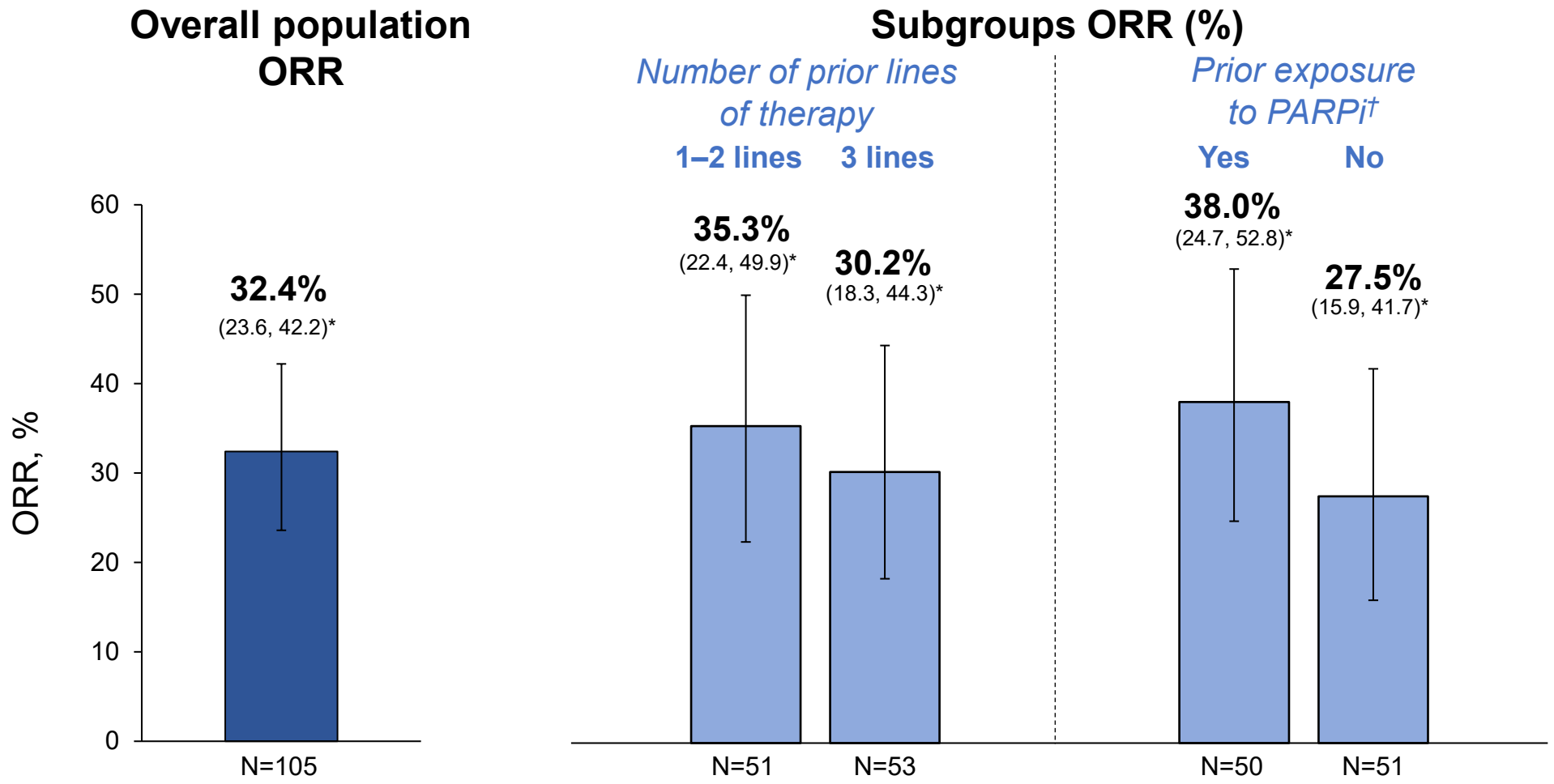


34 responders

- 5 complete responses
- 29 partial responses

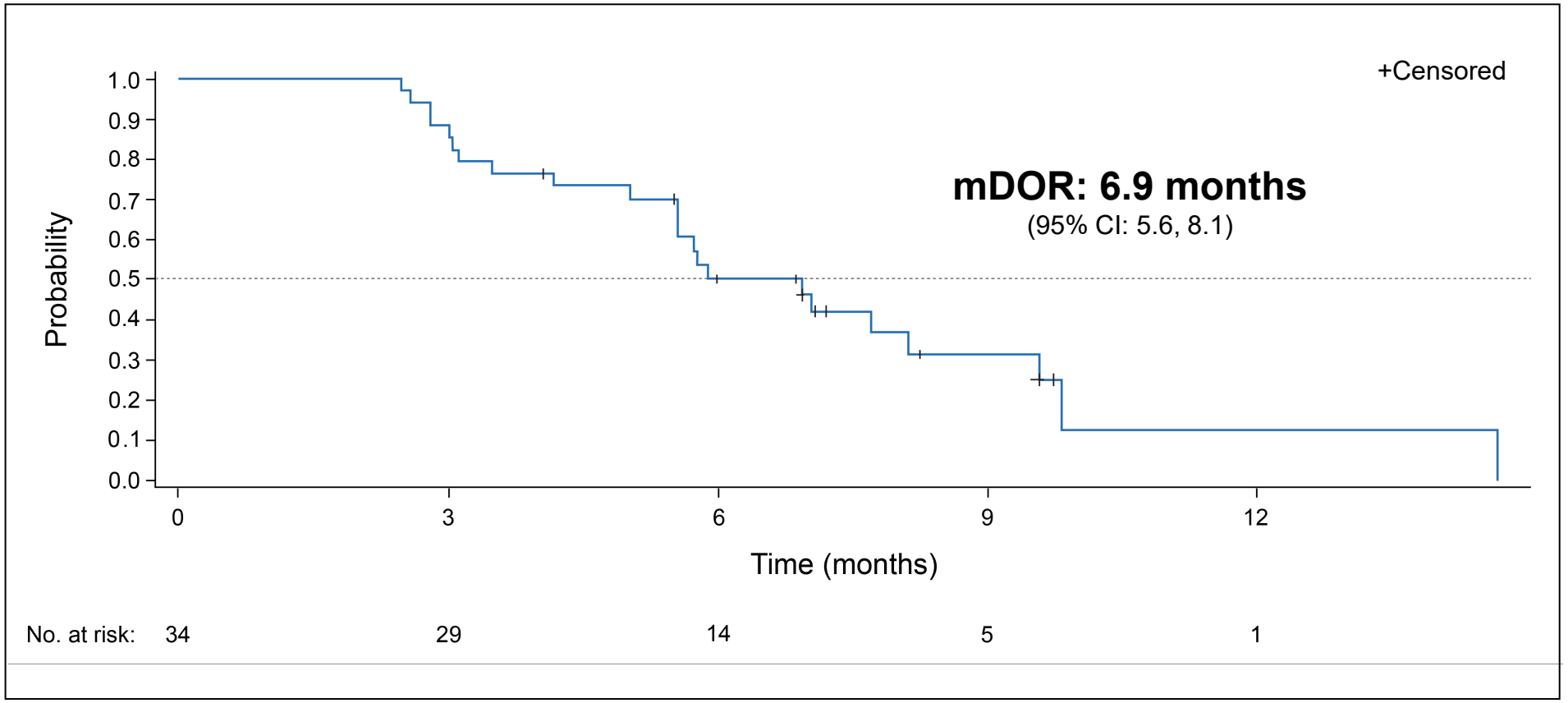
Data cutoff: November 16, 2021.
The denominator for the percentage is the number of patients in the investigator-assessed efficacy evaluable population. Patients without at least 1 postbaseline RECIST assessment were treated as not evaluable.
*95% exact confidence interval is estimated by Clopper-Pearson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

Investigator-Assessed Objective Response Rate by Prior Therapy



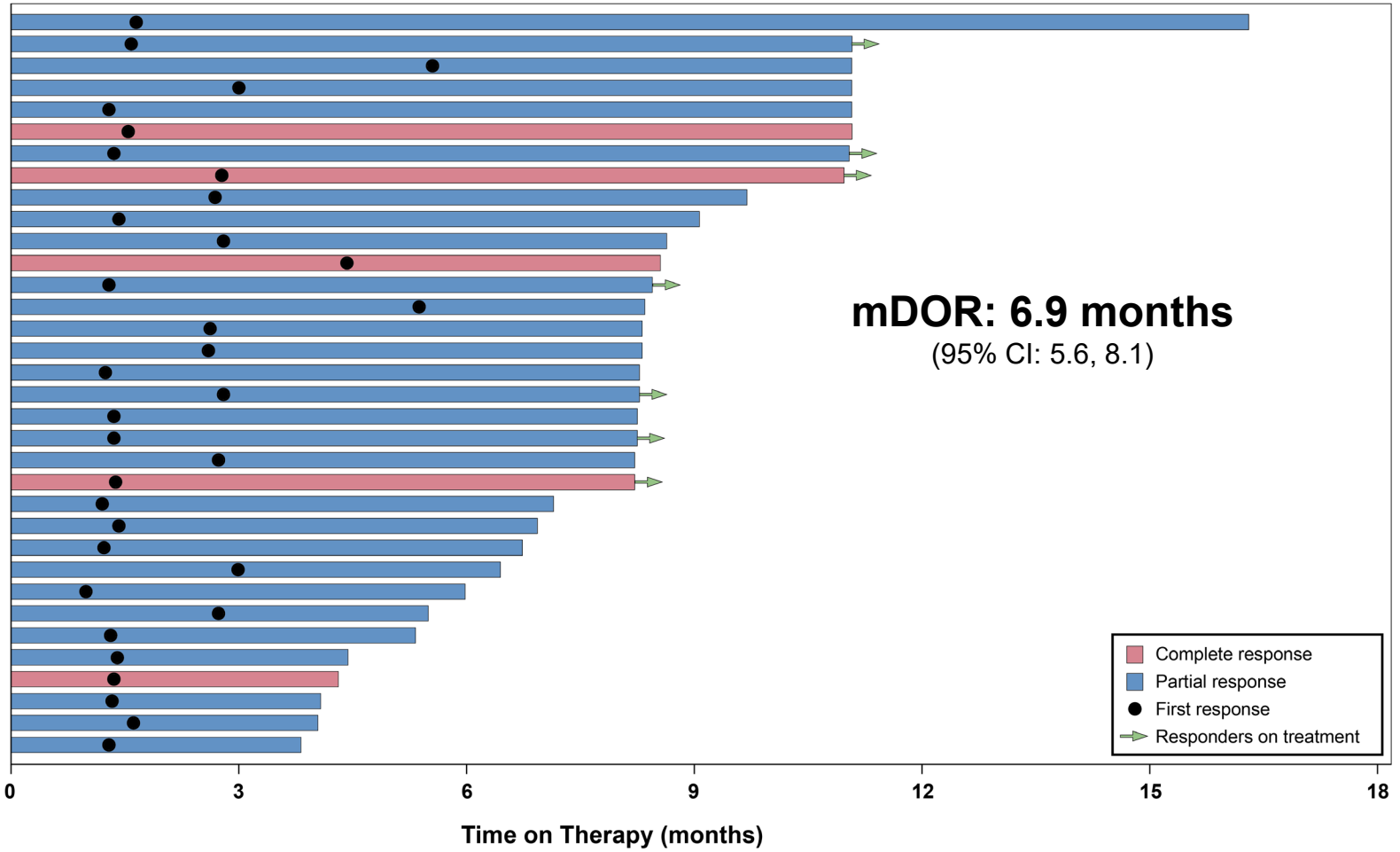
Data cutoff: November 16, 2021.
The denominator for the percentage is the number of patients in the investigator-assessed population in each analysis. Patients without at least 1 postbaseline RECIST assessment were treated as not evaluable.
*95% exact CI is estimated by Clopper-Pearson method (Clopper-Pearson 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.

Investigator-Assessed Duration of Response



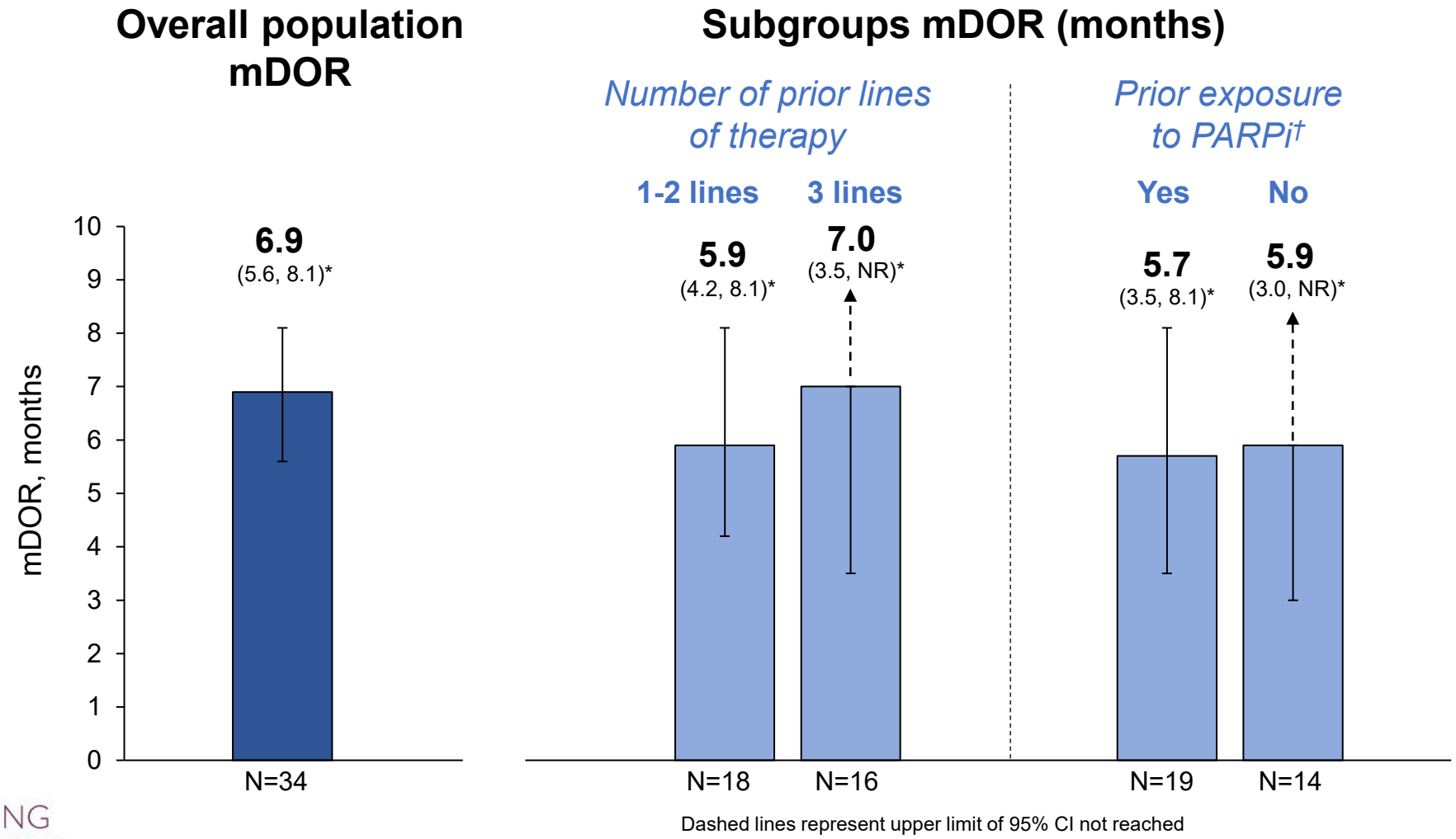
Data cutoff: March 3, 2022.
CI, confidence interval; mDOR, median duration of response.

Investigator-Assessed Duration of Response for Patients With Complete and Partial Responses



Data cutoff: March 3, 2022.
CI, confidence interval; mDOR, median duration of response.

Investigator-Assessed Duration of Response by Prior Therapy



Data cutoff: March 3, 2022.

*95% confidence interval. †Prior PARPi exposure was uncertain for 1 patient in the investigator-assessed population.

CI, confidence interval; mDOR, median duration of response; NR, not reached; PARPi, poly ADP-ribose polymerase inhibitor.

Efficacy Endpoints Assessed by Investigator and BICR

Endpoints	Investigator-Assessed (N=105)	BICR-Assessed (N=95)
ORR, n (%)	**34 (32.4)**	**30 (31.6)**
95% CI	[23.6, 42.2]	[22.4, 41.9]
Best overall response, n (%)		
Complete response	**5 (4.8)**	**5 (5.3)**
Partial response	29 (27.6)	25 (26.3)
Stable disease	48 (45.7)	53 (55.8)
Progressive disease	20 (19.0)	8 (8.4)
Not evaluable	3 (2.9)	4 (4.2)
mDOR, months	**6.9**	**11.7**
95% CI	[5.6, 8.1]	[5.0, NR]
mPFS, months	**4.3**	**5.5**
95% CI	[3.7, 5.1]	[3.8, 6.9]

Data cutoff: November 16, 2021, investigator-assessed DOR: March 3, 2022.
BICR, blinded independent central review; CI, confidence interval; DOR, duration of response; mDOR, median duration of response; MIRV, mirvetuximab soravtansine; mPFS, median progression-free survival; NR, not reached; ORR, confirmed objective response rate; RECIST v1.1, Response Evaluation Criteria in Solid Tumors.

Treatment-Related Adverse Events (≥10%)

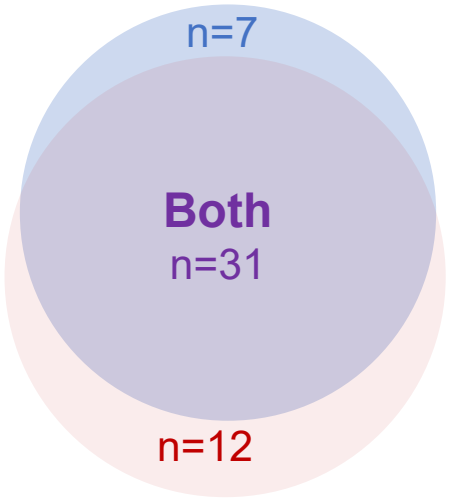
TRAEs, n (%)	All Grades	Grade 3	Grade 4
Patients with any event	91 (86)	29 (27)	1 (1)
Blurred vision	43 (41)	6 (6)	0 (0)
Keratopathy*†	38 (36)	8 (8)	1 (1)
Nausea	31 (29)	0 (0)	0 (0)
Dry eye	24 (23)	2 (2)	0 (0)
Fatigue	24 (23)	1 (1)	0 (0)
Diarrhea	23 (22)	2 (2)	0 (0)
Asthenia	16 (15)	1 (1)	0 (0)
Photophobia	15 (14)	0 (0)	0 (0)
Peripheral neuropathy	13 (12)	0 (0)	0 (0)
Decreased appetite	13 (12)	1 (1)	0 (0)
Vomiting	12 (11)	0 (0)	0 (0)
Neutropenia	11 (10)	1 (1)	0 (0)

- Most AEs were low-grade, reversible ocular and GI events
- Serious grade ≥3 TRAEs were reported in 8% of patients
- TRAEs led to dose delay in 32% and dose reduction in 19%
- 7 patients (7%) 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: November 16, 2021.
*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.
AE, adverse event; GI, gastrointestinal; TRAEs, treatment-related adverse events.

Unique Events Specific to MIRV: Keratopathy and Blurred Vision

Events developed in 50/106 (47%) patients: mostly low grade



- **Proactive supportive care**
  - Lubricating artificial tears
  - Corticosteroid eye drops
- **Predictable**
  - Median time to onset: cycle 2 (~1.5 months)
- **Manageable with dose modifications, if needed**
  - 22% of patients (23/106) had dose delay and/or reduction
- **Reversible**
  - At data cutoff: >80% of patients with grade 2–3 events had resolved to grade 0–1
    - 9 patients still receiving MIRV or being followed up for resolution
- **<1% discontinuation due to ocular events**
  - 1 of 106 patients discontinued due to grade 4 keratopathy,† which resolved within 15 days

Data cutoff: November 16, 2021.
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, mirvetuximab soravtansine.

Conclusions

- MIRV demonstrates clinically meaningful antitumor activity in patients with FRα-high platinum-resistant ovarian cancer
  - **ORR: 32.4%** investigator-assessed, including 5 complete responses
  - **Median DOR: 6.9 months**
  - Consistent antitumor activity regardless of prior number of therapies or prior PARPi
- 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
  - 7 patients (7%) discontinued treatment due to TRAEs
    - Only 1 patient discontinued due to 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

DOR, duration of response; FRα, folate receptor alpha; GI, gastrointestinal; MIRV, mirvetuximab soravtansine; ORR, confirmed objective response rate; PARPi, poly ADP-ribose polymerase inhibitor; 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.

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
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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
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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
Dr. Sudarshan K. Sharma, Ltd. Hinsdale, IL, USA	California Cancer Associates Duarte, CA, USA	Hospital Universitario Vall d'Hebron Barcelona, Spain	Hospital Clínico Universitario Virgen de la Arrixaca Murcia, Spain	Rambam Medical Center Haifa, Israel	University Hospital Waterford Waterford, Munster, Ireland	The Mount Sinai Hospital New York, NY, USA
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