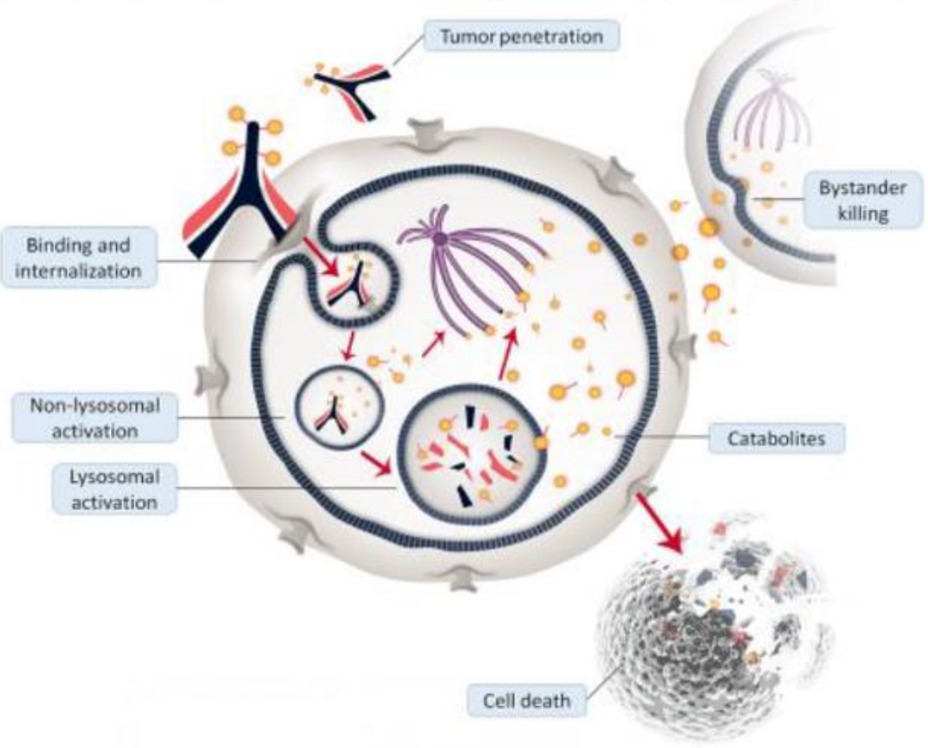
2021 ASCO ANNUAL MEETING

Mirvetuximab Soravtansine, a folate receptor alpha-targeting antibody drug conjugate, in combination with bevacizumab in patients with platinum-agnostic ovarian cancer: final analysis



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Background

- The incorporation of PARPi into the treatment paradigm has resulted in an increasing population of women with recurrent ovarian cancer for whom a non-platinum based regimen would be appropriate
- Mirvetuximab soravtansine (MIRV) is a folate receptor-α (FRα) targeting ADC that delivers the potent tubulin-targeting maytansinoid DM4 directly to the tumor
- MIRV has encouraging activity in platinum-resistant ovarian cancer (PROC):
  - Monotherapy in high FRα patients: 24% to 47% confirmed objective response rate (ORR)[1,2]
  - With bevacizumab (BEV) in medium and high FRα patients: 39% to 56% confirmed ORR[3]
- The AURELIA trial[4] showed that in patients with platinum-resistant ovarian cancer, the addition of BEV to chemotherapy:
  - Significantly improved progression-free survival (PFS) in comparison to chemotherapy alone (median PFS: 6.7 months vs. 3.4 months); and
  - Demonstrated a higher ORR over chemotherapy alone (27% vs. 12%)
- In this trial, MIRV was combined with BEV as a novel, targeted, non-platinum based regimen designed to address the unmet need in a broader population of recurrent ovarian cancer patients

[1]Moore ASCO 2017; [2]Moore ESMO 2019; [3]O'Malley *Gyn Onc* 2020; [4]Pujade-Lauraine *J Clin Oncol* 2014

Objectives and Patient Population

Primary objective:

- Assess preliminary response-based anti-tumor activity of MIRV in combination with BEV in recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer

Patient population:

- Recurrent ovarian cancer with up to three prior regimens (prior BEV allowed)
- Patients for whom a non-platinum-based doublet with BEV would be appropriate
    - Platinum-sensitive ovarian cancer (PSOC): responded to the last platinum therapy and did not progress within 6 months; or
    - PROC: recurrence within 6 months after last platinum dose
- Tumor demonstrated medium or high FRα membrane staining with IHC PS2+ scoring* (% of cells staining positive and intensity of staining)
    - Medium expressors ≥ 50% - <75%, ≥ 2+ intensity
    - High expressors ≥ 75%, ≥ 2+ intensity

Treatment schedule:

- MIRV (6 mg/kg, adjusted ideal body weight) + BEV (15 mg/kg) administered intravenously on Day 1 of a 3-week cycle (Q3W)

*IHC PS2+ scoring: immunohistochemistry percent staining 2+ or 3+

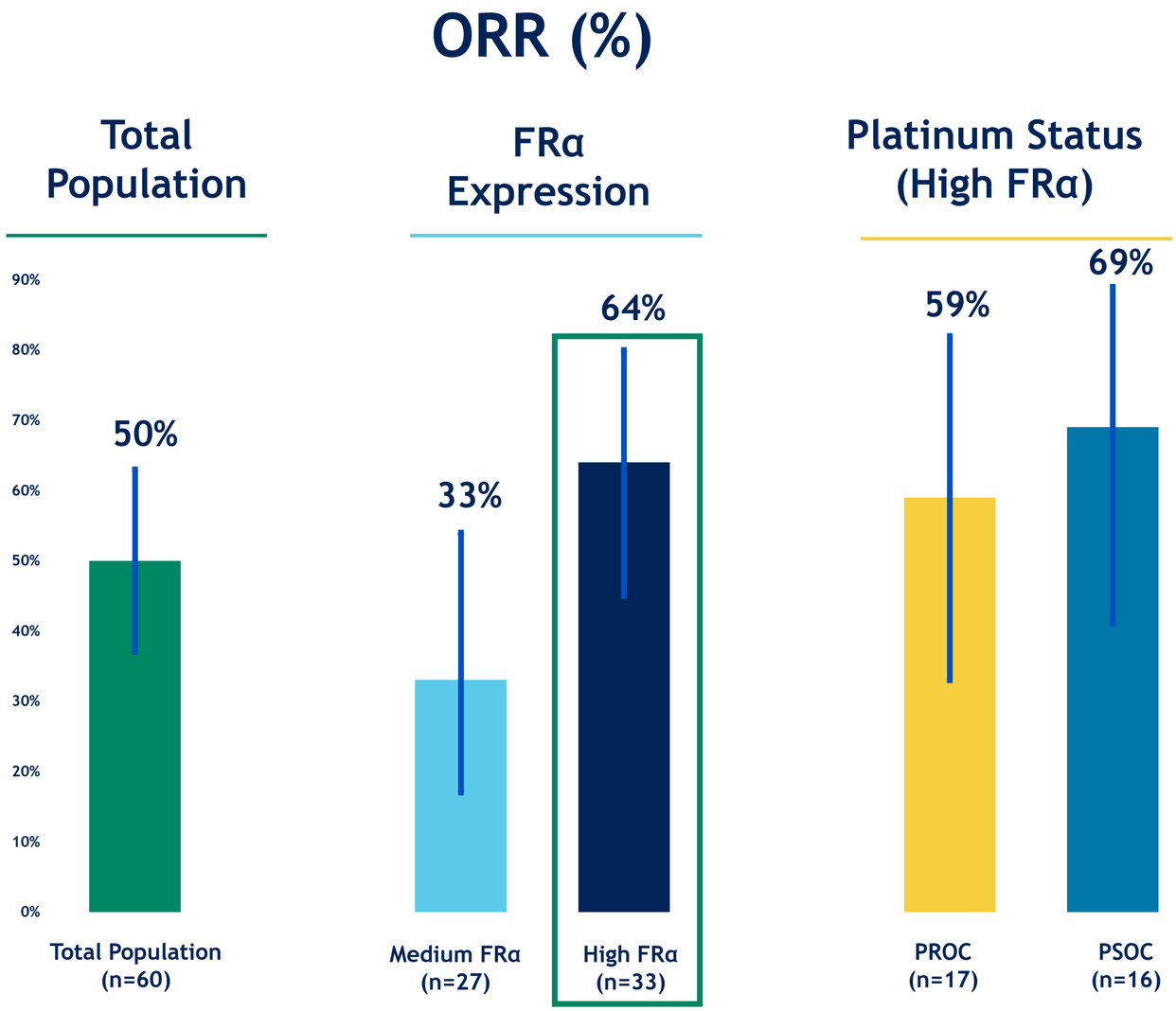
Patient Demographics

Characteristic		All Patients (N = 60)
Age median (range)		60 (44-83 years)
Primary cancer diagnosis n (%) (Recurrent, High Grade)	Epithelial ovarian cancer	41 (68)
	Fallopian tube cancer	15 (25)
	Primary peritoneal	4 (7)
ECOG PS, n (%)	0	44 (73)
	1	16 (27)
No. of prior systemic therapies, n (%)	1	20 (33)
	2	21 (35)
	≥3*	19 (32)
	Median (range)	2 (1-4)
FRα expression n (%)	High (≥75% PS2+) **	33 (55)
	Medium (≥50% PS2+) **	27 (45)
Prior exposure, n (%)	Platinum compounds	60 (100)
	Taxanes	60 (100)
	Bevacizumab	24 (40)
	PARP inhibitor	21 (35)
Platinum free interval	≤ 6 months	32 (53)
	> 6 - ≤ 12 months	20 (33)
	> 12 months	8 (13)

*1 patient had 4 priors

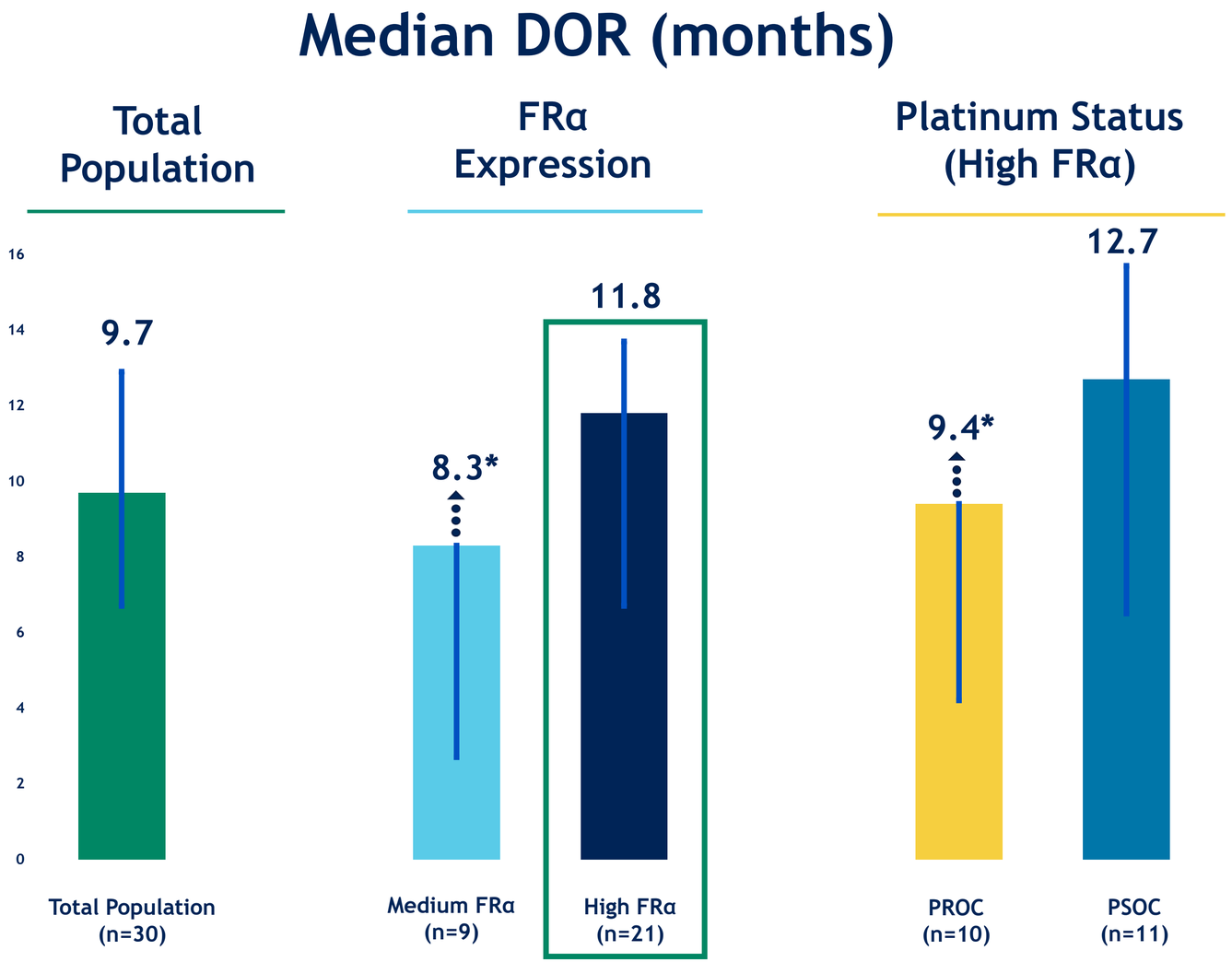
PS2+ Scoring: ≥50 or ≥75% of tumor cells with FRα membrane staining with ≥ 2+ intensity

Confirmed ORR by FRα Expression and Platinum Status



- **50% ORR** (30/60) for overall cohort
- **64% ORR** (21/33) in high FRα tumors
  - **59% ORR** (10/17) in PROC subset
  - **69% ORR** (11/16) in PSOC subset

Median Duration of Response (mDOR) by FRα Expression and Platinum Status

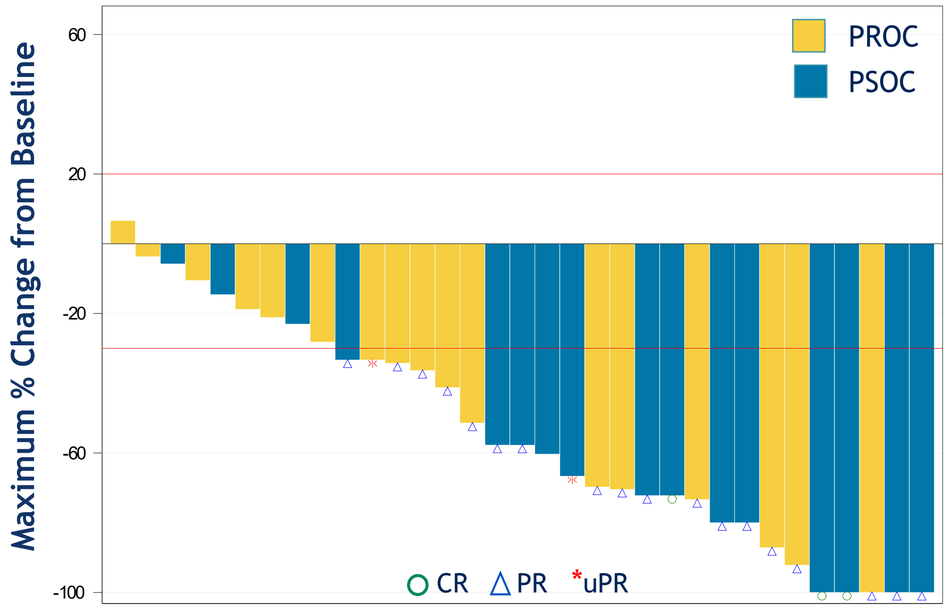


- **9.7 mo mDOR** for overall cohort
- **11.8 mo mDOR** in high FRα tumors
  - **9.4 mo mDOR** in PROC subset
  - **12.7 mo mDOR** in PSOC subset

*Upper limit of 95% confidence interval not reached

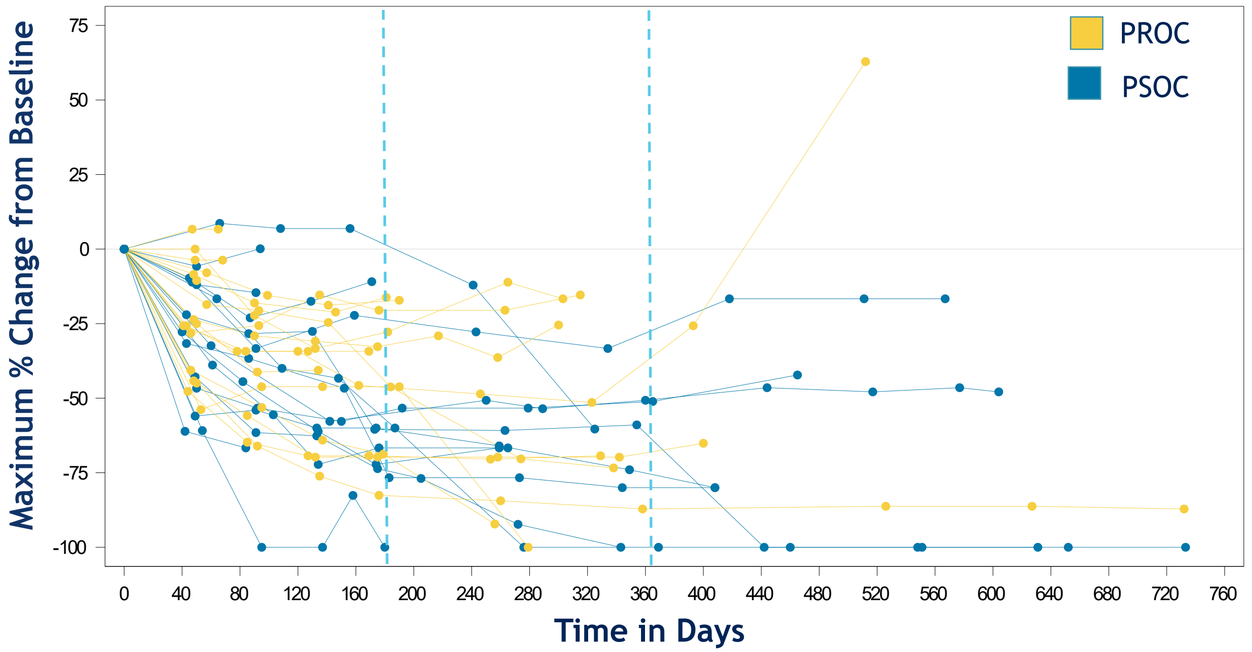
High FRα Tumors Showed a Deep Response and Durable Benefit

Maximum % Change from Baseline



- **97% (32/33)** of patients demonstrated tumor burden reduction

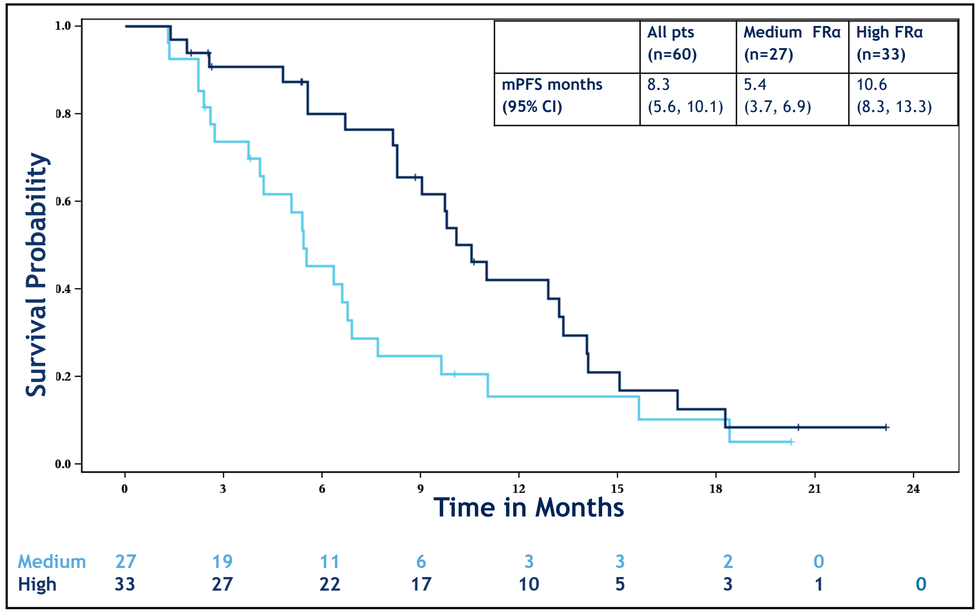
Percent Change and Duration from Baseline



- Rapid tumor shrinkage, with early responses
- Durable benefit in both PSOC and PROC

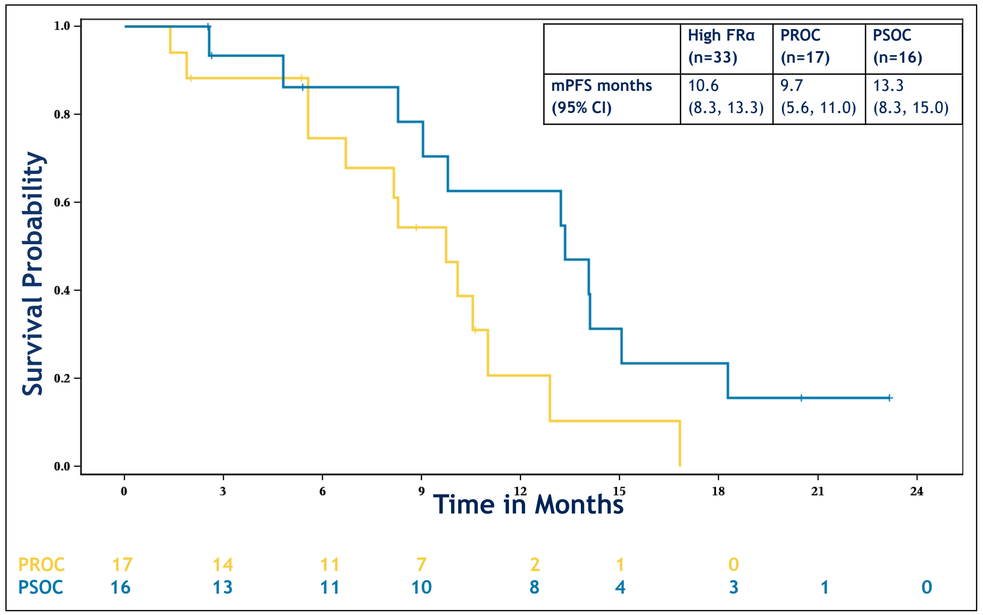
Longer PFS in High FRα Tumors Regardless of Platinum Status

Medium and High FRα Tumors



- mPFS 10.6 months in high FRα tumors
- mPFS 5.4 months in medium FRα tumors
- High FRα 6-month and 12-month PFS rate of 80% and 42%, respectively

High FRα Tumors (PROC and PSOC)



- mPFS 9.7 months in high FRα PROC tumors
- mPFS 13.3 months in high FRα PSOC tumors

mPFS = median progression free survival

Treatment-Related Emergent Adverse Events >20%

N=60	All Grades	Grade 3/4
Adverse Event	N (%)	N (%)
Diarrhea^	37 (62)	1 (2)
Blurred vision	36 (60)	0 (0)
Fatigue^	36 (60)	2 (3)
Nausea	34 (57)	0 (0)
Keratopathy†	26 (43)	0 (0)
Peripheral neuropathy*	24 (40)	1 (2)
Dry eye	20 (33)	3 (5)
Decreased appetite	20 (33)	0 (0)
Hypertension^	19 (32)	10 (17)
Headache	17 (28)	0 (0)
AST increased	17 (28)	2 (3)
Vomiting	17 (28)	0 (0)
Abdominal pain	16 (27)	0 (0)
Visual acuity reduced	14 (23)	0 (0)
Thrombocytopenia	14 (23)	2 (3)
Neutropenia	13 (22)	8 (13)
ALT increased	13 (22)	3 (5)
Dysphonia^	13 (22)	0 (0)
Asthenia	13 (22)	0 (0)
Weight decrease^	13 (22)	1 (2)

AST, aspartate aminotransferase; ALT, alanine aminotransferase;
*Includes neuropathy peripheral, peripheral sensory neuropathy, paresthesia, and hypoesthesia
† Includes keratopathy, keratitis, corneal deposits, and corneal epithelial microcysts

- **Most AEs were low grade**
  - GI and Ocular were most frequent
  - Ocular AE class effect of ADC manageable with eye drops
- **Grade 3+ events were infrequent**
  - 17% hypertension
  - 13% neutropenia
- **Eighteen patients (30%) discontinued BEV and/or MIRV** due to treatment-related AEs
  - Discontinuations occurred after a median of 13 cycles of treatment
  - Discontinuations by agent
    - MIRV: 23%
    - BEV: 18%

AE rates are similar for MIRV/BEV compared with MIRV alone (n=243 from FORWARD I), when adjusted for exposure
^Exceptions (p <0.05, not adjusted for multiplicity testing) include Diarrhea, Fatigue, Hypertension, Dysphonia, and Weight Decrease

Conclusions

- MIRV was combined with BEV in a broad population of recurrent ovarian cancer patients in need of more effective non-platinum based treatments

- With a 64% ORR, 11.8 month mDOR, and 10.6 month mPFS, the combination of MIRV with BEV has promising activity in high FRα recurrent ovarian cancer with up to 3 priors, irrespective of platinum status, and is compelling in light of available therapies reported in less heavily pre-treated populations[4,5,6]
    - In high FRα PSOC patients, which represents a growing patient population, the combination of MIRV with BEV achieved a 69% ORR, 12.7 month mDOR and a 13.3 month mPFS
    - In high FRα PROC patients the combination of MIRV with BEV achieved a 59% ORR, 9.4 month mDOR and a 9.7 month mPFS

- Adverse events were manageable and consistent with the side effect profiles of each agent

- The strength of these mature data in a broader population of recurrent ovarian cancer, warrants further development of this novel, targeted combination and supports MIRV as the combination partner of choice for BEV

[4]Pujade-Lauraine *J Clin Oncol* 2014; [5]Aghajanian *J Clin Oncol* 2012; [6]Coleman *Lancet Oncol* 2017

We are indebted to the women and their families who chose to participate on the mirvetuximab plus bevacizumab clinical trial.

Thank you to all the clinical investigators.