Mirvetuximab soravtansine (MIRV), a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in combination with bevacizumab (BEV) in patients (pts) with platinum-agnostic ovarian cancer

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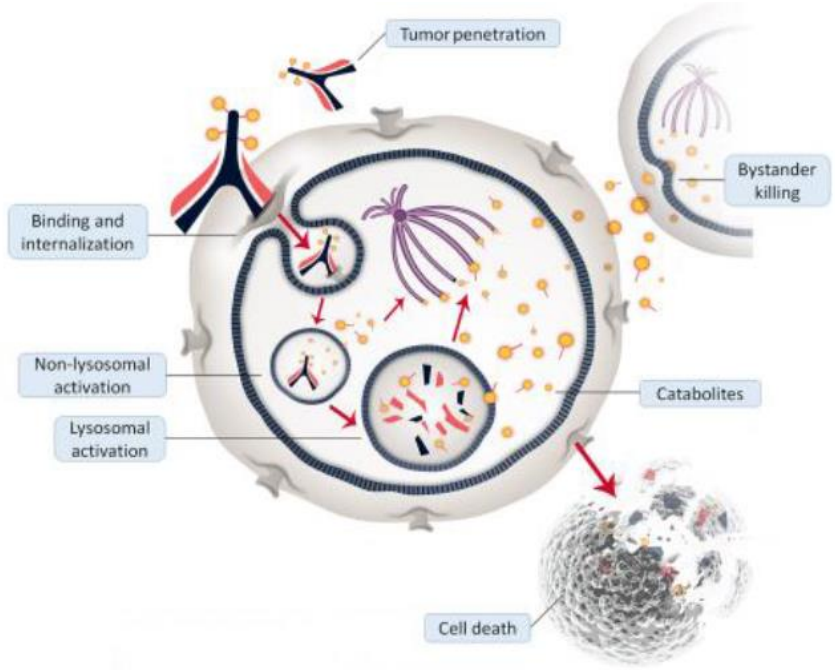
Background

- Unmet need remains in recurrent high-grade epithelial ovarian cancer
- 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
  - Monotherapy in high FRα patients : 24% to 47% confirmed ORR [1,2]
  - With bevacizumab in medium and high FRα patients 39% to 56% confirmed ORR [3]
- In this trial, MIRV was combined with bevacizumab for a broader segment of recurrent ovarian cancer patients, regardless of platinum status



[1]Moore, ASCO 2017; [2]Moore, ESMO 2019; [3]O'Malley ASCO 2019

Objectives and Patient Population

Primary objective:

- Evaluate the safety and tolerability of MIRV in combination with bevacizumab in recurrent epithelial ovarian cancer (EOC), primary peritoneal cancer, or fallopian tube cancer

Patient population – recurrent ovarian cancer:

- Patients for whom a non-platinum-based doublet with bevacizumab would be appropriate
- Includes both platinum-sensitive and platinum-resistant disease
- Tumor demonstrated medium or high FRα membrane staining with IHC -PS2+ scoring (intensity and %)
  - Medium expressors ≥ 50% <75%, ≥ 2+
  - High expressors ≥ 75%, ≥ 2+

Treatment schedule:

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

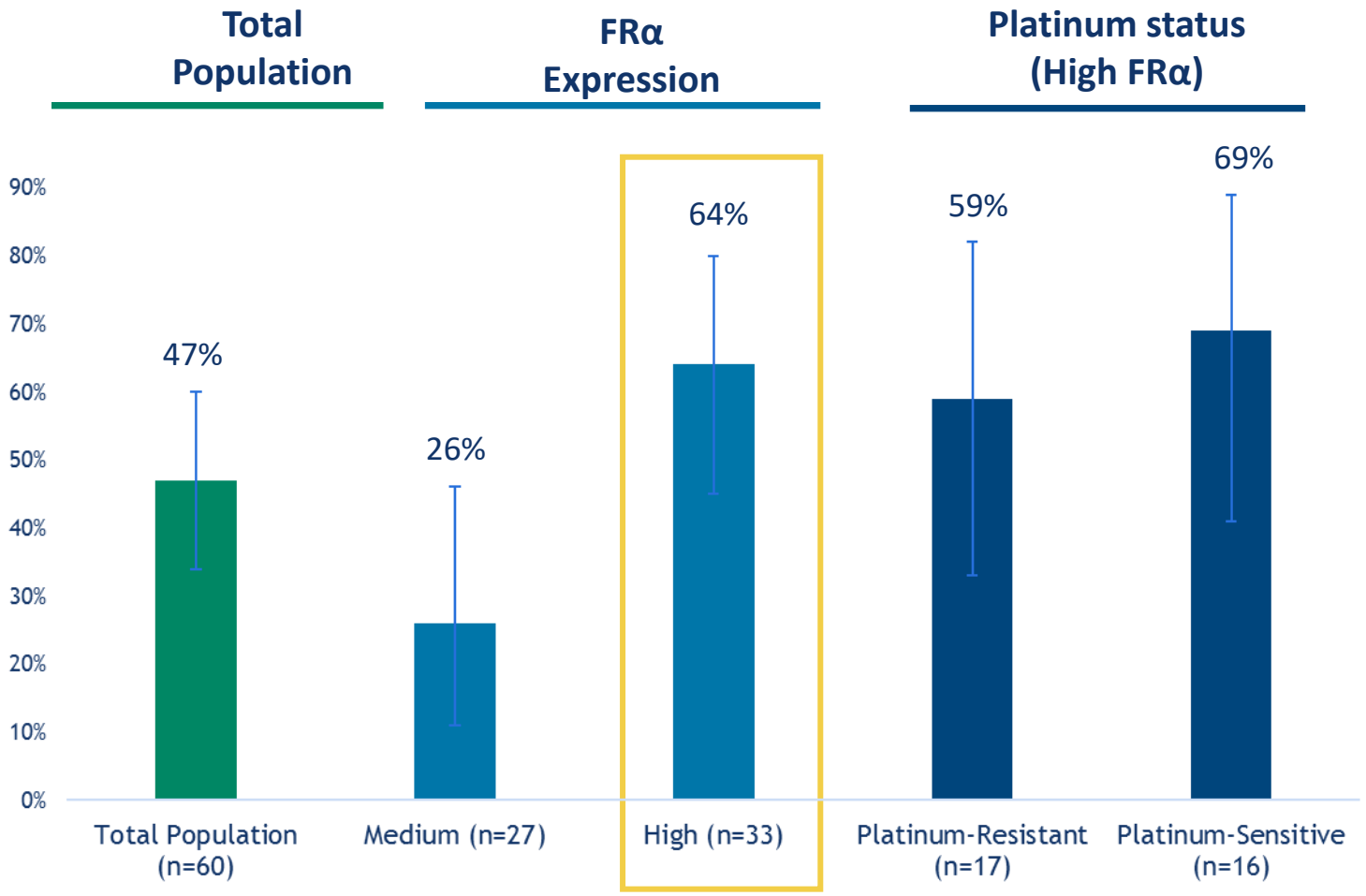
Patient Demographics

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	45 (75)
	1	15 (25)
No. of prior systemic therapies, n (%)	1	20 (33)
	2	22 (37)
	≥3*	18 (30)
	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	59 (98)
	Bevacizumab	24 (40)
	PARP inhibitor	19 (32)
Platinum free interval	≤ 6 months	32 (53)
	> 6 - ≤ 12 months	20 (33)
	> 12 months	8 (13)

*1 patient had 4 priors

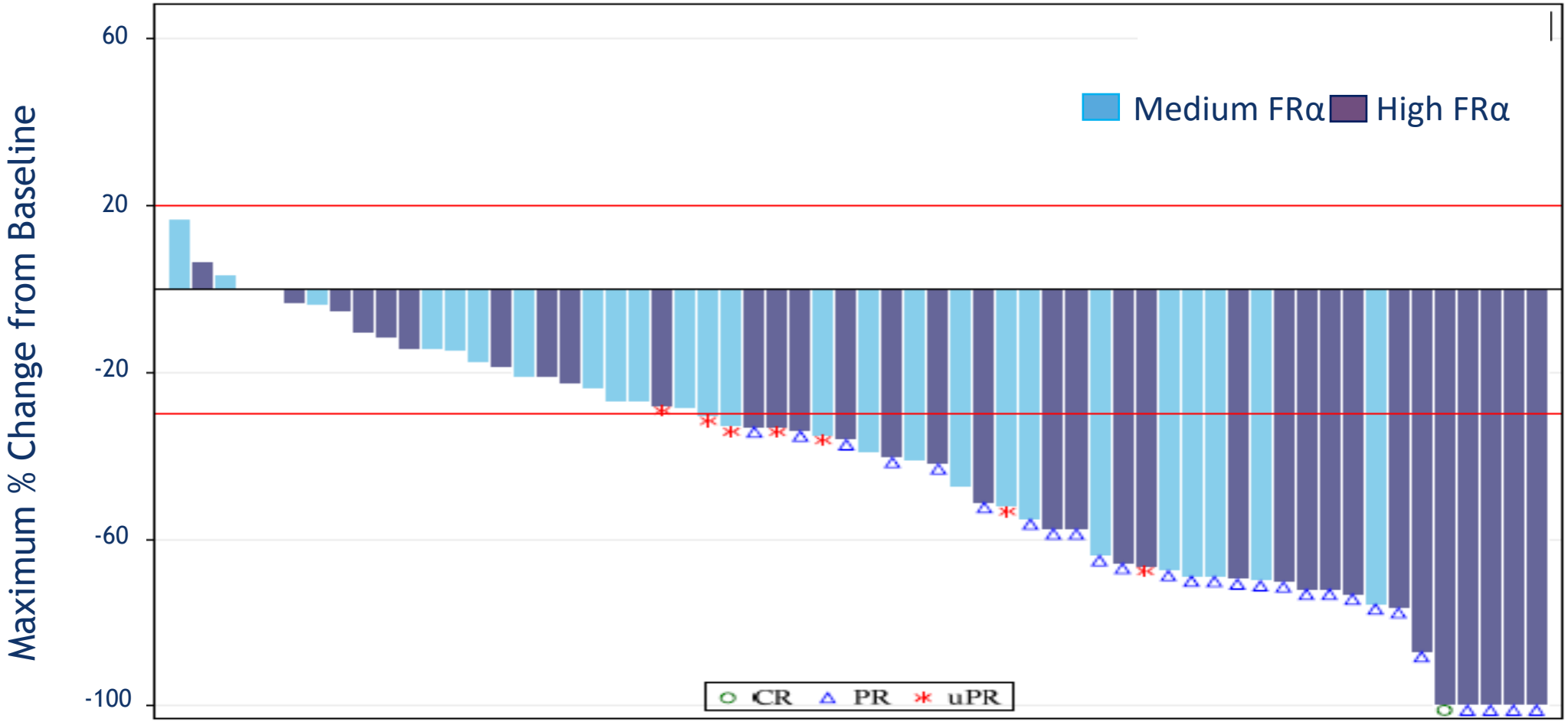
PS2+ Scoring: ≥50 or ≥75% of tumor cells with FRα membrane staining with ≥ 2+ intensity

ORR by FRα Expression and Platinum Status



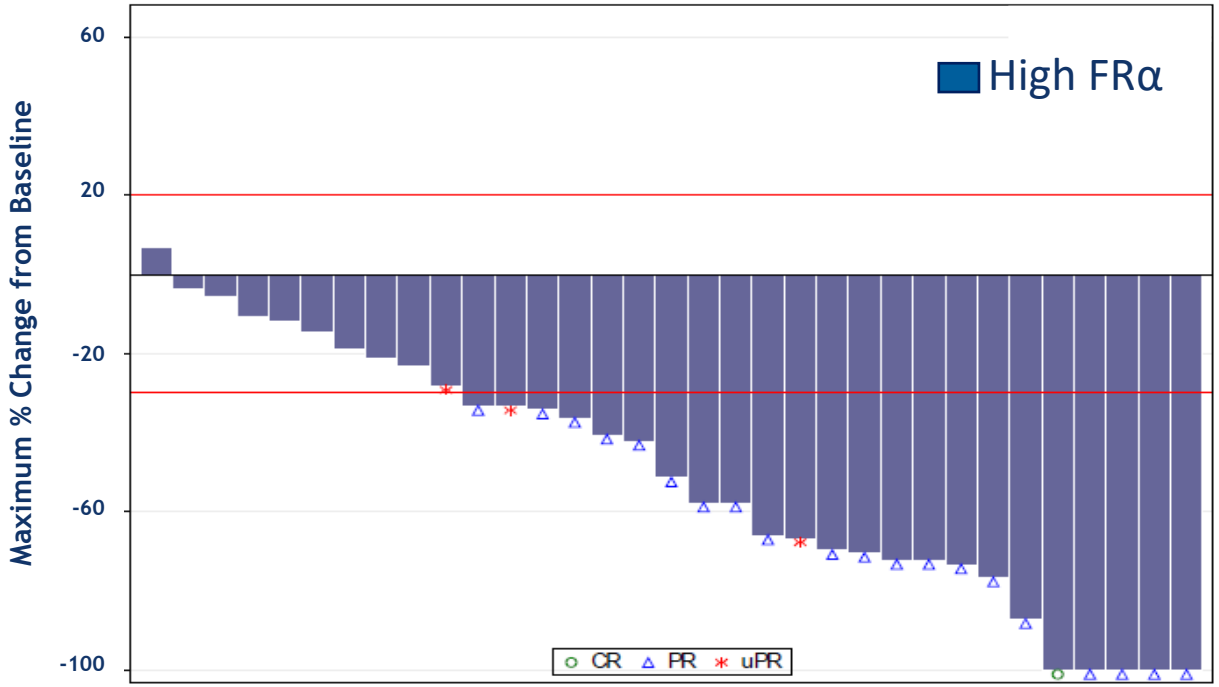
- 47% ORR (28/60) for overall cohort
- 64% ORR (21/33) in high FRα pts
  - 59% ORR (10/17) in platinum-resistant subset
  - 69% ORR (11/16) in platinum-sensitive subset

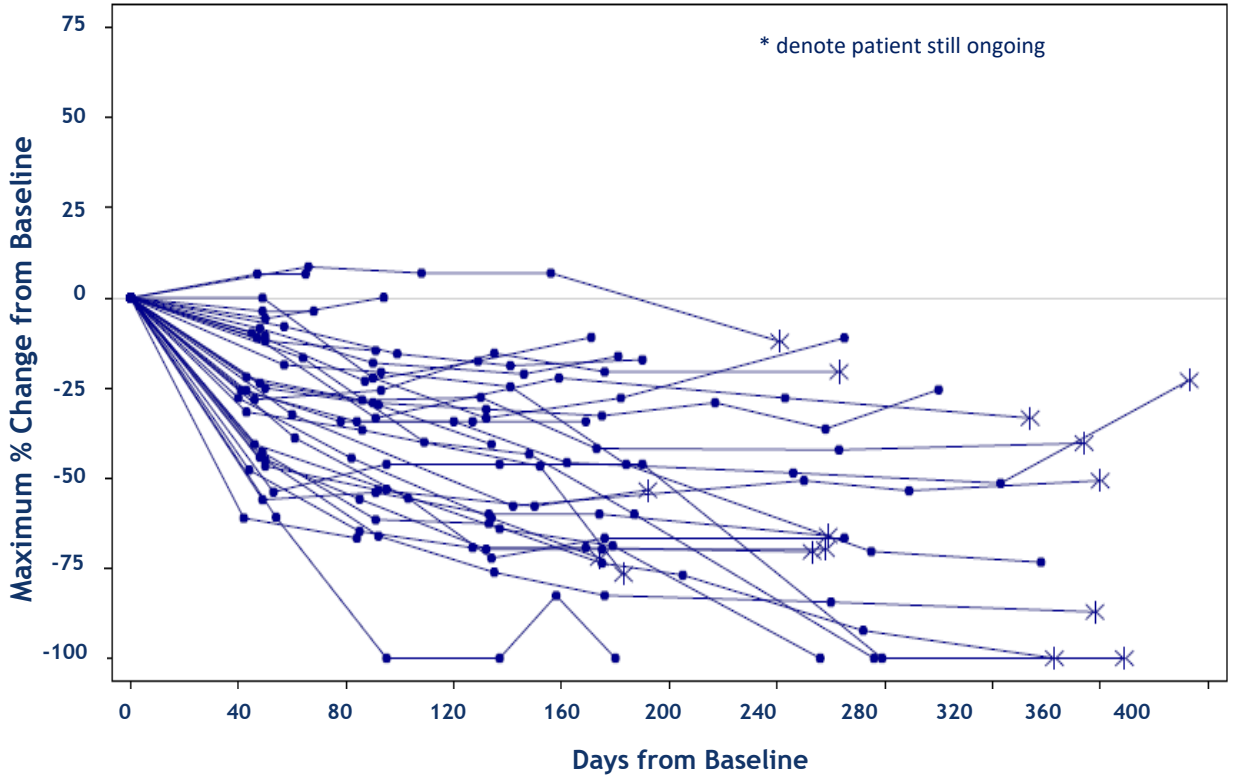
Maximum Tumor Change (%) in Target Lesions from Baseline



- 92% (55/60) of patients demonstrated tumor burden reduction
- Deeper and more durable tumor burden reduction in high FRα pts

Depth and Duration of Tumor Reduction in High FRα Patients





- Most responses begin by the first tumor assessment at 6 weeks
- 5pts showed 100% ↓Target lesions, CR in 1
- 46% of high FRα still on treatment, many on for 9 months and some still on at over a year
- With a median duration of follow-up of 8.5 months, duration of response (DOR) and progression-free survival (PFS) are immature

Treatment-Related Emergent Adverse Events >20% N=60

	All Grades		Grade 3/4	
Adverse Event	N	%	No.	%
Diarrhea	41	68	1	2
Blurred vision	38	63	1	2
Fatigue	35	58	3	5
Nausea	33	55	0	0
Peripheral neuropathy*	26	43	1	2
Keratopathy†	26	43	0	0
Dry eye	21	35	3	5
Headache	21	35	0	0
Decreased appetite	19	32	0	0
Hypertension	17	28	7	12
AST increased	17	28	2	3
Vomiting	16	27	0	0
Abdominal pain	16	27	0	0
Neutropenia	14	23	6	10
ALT increased	13	22	3	5
Dysphonia	13	22	0	0
Visual acuity reduced	13	22	0	0
Thrombocytopenia	13	22	2	3

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
  - Ocular AE class effect of ADC but manageable with local drops
- Grade 3+ events were infrequent
  - 12% hypertension
  - 10% myelosuppression
  - Pneumonitis
    - Grade 3: None
    - Grade 1: 3pts
    - Grade 2: 1pt
- Thirteen patients (22%) discontinued bevacizumab and/or MIRV due to treatment-related AEs

Conclusions

- Mirvetuximab soravtansine combines well with bevacizumab
  - The adverse events observed were manageable and consistent with the side effect profiles of each agent
- With a confirmed 64% ORR, the combination of MIRV with bevacizumab has promising activity in high FRα recurrent ovarian cancer, regardless of platinum status, and is encouraging with respect to available therapies reported in similar populations
- The clinical activity is consistent with previously reported MIRV plus bevacizumab data demonstrating greater depth and duration of response in high FRα tumors
- With almost half of high FRα patients still on treatment and a median duration of follow-up of 8.5 months, the DOR and PFS data are immature
- The combination of MIRV and bevacizumab may benefit an increasing population of recurrent ovarian cancer for whom a non-platinum based regimen would be appropriate