Poster
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Characterization of Extended Treatment Benefit From Three Phase 1 and 3 Clinical Trials Examining Patients With Folate Receptor Alpha–Positive Recurrent Ovarian Cancer Treated With Single-Agent Mirvetuximab Soravtansine

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BACKGROUND

- Treatment options for platinum-resistant ovarian cancer (PROC) are limited, consisting primarily of single-agent chemotherapy[1,2]
  - Single-agent chemotherapy has limited activity (ORR, 4%-13%) along with considerable toxicity[3-6]
- Folate receptor alpha (FRα; *FOLR1* gene) has limited expression on normal tissues but is elevated in most ovarian cancers, which makes FRα an attractive target for the development of novel therapies[7,8]
- Mirvetuximab soravtansine (MIRV) is an antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and a maytansinoid DM4 payload, a potent tubulin-targeting agent[9]
- Treatment with MIRV demonstrated clinically meaningful antitumor activity and a favorable safety profile in patients with FRα-positive[a] ovarian cancer[10,11]

[a]Antitumor activity with MIRV has been shown with single-agent MIRV in FRα-positive PROC (≥75% tumor cells FRα positive by PS2+)[10] and in combination with other agents in FRα-expressing EOC (≥25% tumor cells FRα-positive by PS2+).[11]

Objective

- Here we report findings from a retrospective pooled analysis of patients who achieved extended treatment benefit (ETB; define as patients with PFS >12 months per investigator assessment) with MIRV monotherapy in the IMGN853-0401 (phase 1),[12] FORWARD I (phase 3),[13] and SORAYA (phase 3)[14] clinical trials

Methods

- Efficacy and safety data were collected from 466 patients in 3 clinical MIRV monotherapy studies (IMGN853-0401, FORWARD I, and SORAYA)
- The ETB analysis of efficacy also included ORR (by RECIST v1.1) and DOR per investigator assessment
- FRα expression levels were evaluated by immunohistochemistry[a]
- 38 of 40 patients (95%) received intravenous MIRV at 6 mg/kg, adjusted ideal body weight,[b] every 3 weeks until disease progression or unacceptable toxicity

[a]In IMGN853-0401 (phase 1) and SORAYA, FRα scoring was by PS2+ with percentage of viable tumor cells with ≥2+ staining intensity.[10,15] In FORWARD I, FRα expression was scored as the percentage of tumor cells with any FRα membrane staining visible at ≥10× microscope objective.[16] [b]Two patients from IMGN853-0401 (phase 1) escalation received 1.8 and 2.0 mg/kg, days 1, 8, and 15 of a 4-week schedule.

Table 1. Clinical Studies in the ETB Analysis

	IMGN853-0401 phase 1 trial[12]	FORWARD I phase 3 trial[13]	SORAYA phase 3 trial[14]
ClinicalTrials.gov identifier	NCT01609556	NCT02631876	NCT04296890
Design/description	First-in-human study with single-agent MIRV[a] Open-label, nonrandomized, dose-escalation and dose-expansion trial	Comparison of single-agent MIRV with investigator's choice of chemotherapy[b] Open-label randomized trial	Single-arm trial with single-agent MIRV[c] Open-label nonrandomized trial
Patients in ETB analysis, n	4	12	24

[a]In patients with relapsed or refractory ovarian cancer or other FRα-expressing solid tumors. [b]In patients with FRα-expressing, platinum-resistant EOC with ≤3 prior systemic anticancer therapies. [c]In patients with bevacizumab-pretreated, FRα-positive, platinum-resistant, advanced, high-grade EOC with 1 to 3 prior systemic anticancer therapies.

Baseline Demographics and Clinical Characteristics

Table 2. Baseline Demographics and Clinical Characteristics in Patients With ETB

Characteristic		Patients with ETB (N=40)
Age, median (range)	Age in years	63 (48-81)
Primary cancer diagnosis, n (%)	Epithelial ovarian cancer Fallopian tube cancer Primary peritoneal cancer	30 (75) 2 (5) 8 (20)
Stage at initial diagnosis, n (%)	IIIA IIIB IIIC III IV	2 (5) 2 (5) 18 (45) 11 (28) 7 (18)
ECOG PS, n (%)	0 1	24 (60) 16 (40)
No. of prior systemic therapies, n (%)	1 2 3	22 (55) 17 (43) 1 (3)
Prior exposure, n (%)	Bevacizumab PARPi	24 (60) 21 (53)
Platinum-free interval, n (%)	0-3 mo 3-6 mo ≥6 mo	9 (23) 22 (55) 9 (23)
FRα expression, n (%)	0%-24% 25%-49% 50%-74% 75%+ Missing	2 (5) 3 (8) 6 (15) 27 (68) 2 (5)

Results: Response Rates

- Patients with ETB had an ORR of 77.5%, with 10 (25.0%) achieving a complete response and 21 (52.5%) achieving a partial response

Figure 1. ORR in Patients With ETB

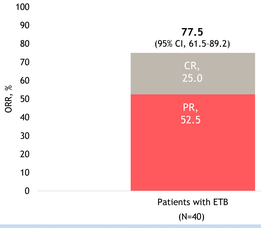


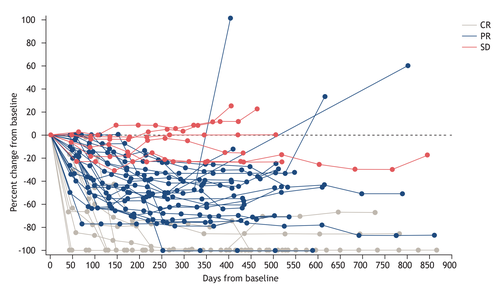
Table 3. Best Overall Response in Patients With ETB

Best overall response, n (%)	Patients with ETB (N=40)
Complete response	10 (25.0)
Partial response	21 (52.5)
Stable disease	8 (20.0)
Progressive disease	0
Not evaluable[a]	1 (2.5)

[a]Patients without at least 1 postbaseline RECIST assessment were treated as not evaluable.

Results: Depth and Duration of Response

Figure 2. Patients With CR, PR, and SD in the ETB Population[a]



[a]Based on the investigator's assessment of the sum of the longest length of target lesions.

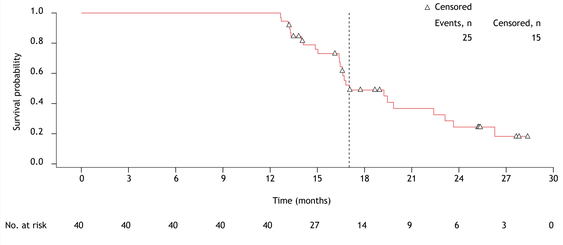
Duration of Response

- Median DOR in patients with ETB was 22.1 months (95% CI, 13.8-60.0)

Results: Progression-Free Survival

- Median PFS in patients with ETB was 17.0 months (95% CI, 16.4-23.1)

Figure 3. Kaplan-Meier Plot for PFS in the ETB Population



Results: Safety

Table 4. Treatment-Related Adverse Events (≥20%, All Grades) (N=40)

TRAEs, n (%)	All grades	Grade 3+
Blurred vision	24 (60)	0
Fatigue	20 (50)	1 (3)
Nausea	20 (50)	0
Keratopathy[a]	16 (40)	1 (3)
Dry eye	14 (35)	0
Peripheral neuropathy[b]	14 (35)	0
Diarrhea	13 (33)	0
Visual acuity reduced	10 (25)	2 (5)
Increased ALT	9 (23)	1 (3)
Increased AST	9 (23)	1 (3)
Asthenia	9 (23)	0
Cataract	8 (20)	6 (15)
Headache	8 (20)	0
Neutropenia	8 (20)	1 (3)
Photophobia	8 (20)	0
Pneumonitis	8 (20)	0
Thrombocytopenia	8 (20)	0

[a]The grouped 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, and punctate keratitis. [b]The grouped term "Peripheral Neuropathy" includes the following preferred terms: neuropathy peripheral, peripheral sensory neuropathy, peripheral motor neuropathy, paresthesia, and hypoesthesia.

- The most common TRAEs included blurred vision (60%), fatigue (50%), and nausea (50%)
- Peripheral neuropathy was present in 35% of patients (no grade 3+ events); pneumonitis occurred in 20% of patients (no grade 3+ events)
- Keratopathy was present in 40% of patients (grade 3 event in 1 patient that resolved within 20 days)
- Grade 3 visual acuity reduction was present in 2 patients, both with grade 3 cataracts. Grade 3 cataracts were present in 6 patients (15%) with a median age of 68 years (range 55-70 years); this was resolved in 5/6 patients and ongoing without surgery in 1 patient
- TRAEs led to:
  - Dose delay in 65%, reduction in 48%, and discontinuation in 15% of patients

CONCLUSIONS

- In a pooled analysis of 466 patients, MIRV monotherapy showed ETB in 40 patients (9%)
  - Most patients with ETB had stage III EOC (83%), 1 prior line of therapy (55%), prior bevacizumab exposure (60%), and prior PARPi exposure (53%)
  - ETB occurred in patients with a wide range of FRα expression but did so predominantly among those with high FRα expression
  - ETB was observed among patients with CR, PR, and SD; ETB was not restricted to patients demonstrating CR
- In patients with ETB, the overall adverse event profile is consistent with the previously reported ISS of 464 patients,[17] with no new safety signals identified
  - Adverse events were primarily low-grade gastrointestinal and ocular events that generally resolved with supportive care or, if needed, dose modifications
- The safety profile of MIRV in these patients suggests minimal cumulative toxicity
- The efficacy and safety outcomes in patients with long-term use supports MIRV's potential to become a new standard of care for FRα-expressing ovarian cancer

Abbreviations: ADC, antibody-drug conjugate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BRCA, BReast CAncer gene; CR, complete response; DM4, N2′-[4-[(3-carboxypropyl)dithio]-4-methyl-1-oxo-2-sulfopentyl]-N2′-deacetylmaytansine; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOC, epithelial ovarian cancer; ETB, extended treatment benefit; *FOLR1*, folate receptor 1; FRα, folate receptor alpha; ISS, integrated safety summary; MIRV, mirvetuximab soravtansine; ORR, objective response rate; PARPi, poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitor; PFS, progression-free survival; PR, partial response; PROC, platinum-resistant ovarian cancer; PS2+, positive staining intensity ≥2; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; SD, stable disease; TRAEs, treatment-related adverse events.

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