FIRST-IN-HUMAN STUDY OF SGN-B7H4V, A B7-H4 DIRECTED VEDOTIN ADC, IN PATIENTS WITH ADVANCED SOLID TUMORS: PRELIMINARY RESULTS OF A PHASE 1 STUDY (SGNB7H4V-001)

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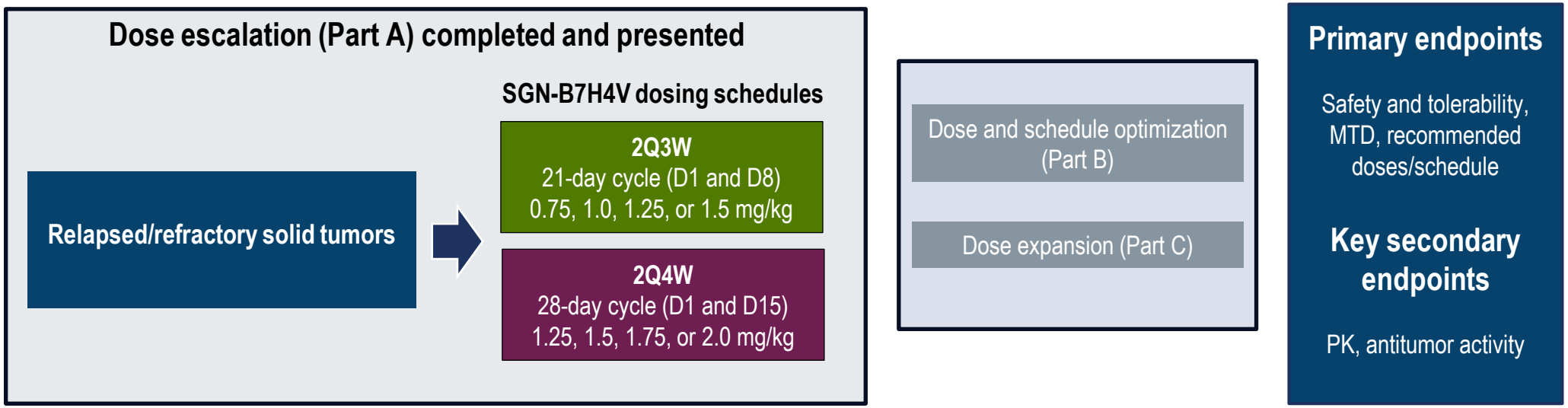
ESMO 2023, Madrid ES, October 20-24; Abstract No. 1546

Background and Study Design

- B7-H4 is an immune checkpoint ligand expressed at low levels in normal tissue and upregulated in solid tumors, including breast, ovarian, and endometrial cancers which show high expression of B7-H4[1-4]
- SGN-B7H4V is an investigational vedotin ADC comprising a B7-H4-directed monoclonal antibody conjugated to MMAE via a protease-cleavable linker[1,5]
- SGN-B7H4V demonstrated antitumor activity in preclinical models[1,6,7]

Study Design

- SGNB7H4V-001 (EudraCT 2021-002107-35; NCT05194072) is a multicenter study evaluating the safety, tolerability, PK, and antitumor activity of SGN-B7H4V in patients with advanced solid tumors[8]



2Q3W, day 1 and day 8 on a 21-day cycle; 2Q4W, day 1 and day 15 on a 28-day cycle; ADC, antibody-drug conjugate; D, day; MMAE, monomethyl auristatin E; MTD, maximum tolerated dose; PK, pharmacokinetics.

1. Gray E, et al. J Immunother Cancer. 2021;9(suppl 2):A895. 2. Liang L, et al. Hum Pathol. 2016;57:1-6. 3. Leong SR, et al. Mol Pharm. 2015;12(6):1717-29. 4. Bregar A, et al. Gynecol Oncol. 2017;145(3):446-52. 5. Klussman K, et al. J Immunother Cancer. 2020;8(suppl 3):A372. 6. Gray E, et al. Cancer Res. 2022;82(suppl 12):1281. 7. Ulrich M, et al. J Immunother Cancer. 2022;10(suppl 2):1234. 8. Patnaik A, et al. J Clin Oncol. 2022;40(suppl 16):TPS3155.

Patient Demographics and Disease Characteristics at Baseline

Part A Dose Escalation	2Q3W 0.75, 1.0, 1.25, 1.5 mg/kg (N = 41)	2Q4W 1.25, 1.5, 1.75, 2.0 mg/kg (N = 45)
Age, median years (range)	63.0 (33 - 86)	62.0 (35 - 78)
Sex, n (%)		
Male	5 (12)	5 (11)
Female	36 (88)	40 (89)
ECOG performance status, n (%)		
0	11 (27)	13 (29)
1	30 (73)	32 (71)
Number of prior systemic LA/m therapies,[a] median (range)	3.0 (1 - 8)	3.0 (1 - 17)
Disease diagnosis, n (%)		
Ovarian cancer[b]	13 (31.7)	8 (17.8)
HR-positive, HER2-negative breast cancer	10 (24.4)	8 (17.8)
Triple negative breast cancer	6 (14.6)	6 (13.3)
Endometrial carcinoma	5 (12.2)	11 (24.4)
Cholangiocarcinoma	3 (7.3)	6 (13.3)
Non-small cell lung cancer	3 (7.3)	3 (6.7)
Gallbladder carcinoma	1 (2.4)	1 (2.2)
Adenoid cystic carcinoma of the head and neck	0 (0)	2 (4.4)

2Q3W, day 1 and day 8 on a 21-day cycle; 2Q4W, day 1 and day 15 on a 28-day cycle; HER2, human epidermal growth receptor 2; HR, hormone receptor; LA/m, locally advanced or metastatic.

[a] Count of unique prior systemic therapies in the LA/m disease setting, excluding maintenance prior therapies

[b] High-grade serous epithelial ovarian cancer, primary peritoneal cancer, or fallopian tube cancer

Data cutoff:10 Jul 2023

Safety Profile

- SGN-B7H4V showed a manageable safety profile across doses evaluated in Part A

Part A Dose Escalation TEAEs, n (%)	2Q3W 0.75, 1.0, 1.25, or 1.5 mg/kg (N = 41)	2Q4W 1.25, 1.5, 1.75, or 2.0 mg/kg (N = 45)
Any grade	**37 (90.2)**	**41 (91.1)**
Treatment-related TEAEs	32 (78.0)	31 (68.9)
Grade ≥3 TEAEs	**19 (46.3)**	**18 (40.0)**
SAEs	**11 (26.8)**	**10 (22.2)**
Treatment-related SAEs	4 (9.8)	1 (2.2)
TEAEs leading to drug discontinuation	**0**	**2 (4.4)[a]**
TEAEs leading to dose reduction	**7 (17.1)**	**6 (13.3)**
Treatment-related deaths	**0**	**0**

[a] TEAEs leading to drug discontinuation were grade 4 diarrhea and unrelated grade 5 respiratory failure.

2Q3W, day 1 and day 8 on a 21-day cycle; 2Q4W, day 1 and day 15 on a 28-day cycle; DLT, dose-limiting toxicity; pt, patient; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Dose-Limiting Toxicities

2Q3W[a]		
Dose Level	**No. Pts Treated**	**No. Pts with DLTs**
0.75 mg/kg	3	0
1.0 mg/kg	6	0
1.25 mg/kg	15	1
1.5 mg/kg	16	3

2Q4W[b]		
Dose Level	**No. Pts Treated**	**No. Pts with DLTs**
1.25 mg/kg	6	1
1.5 mg/kg	20	1
1.75 mg/kg	14	0
2.0 mg/kg	3	1

[a] DLTs occurring in 2Q3W: hyperglycemia (grade 3, 1.25 mg/kg); febrile neutropenia (grade 3, 1.5 mg/kg), neutropenia (grade 3, 1.5 mg/kg); and vomiting (grade 2, 1.5 mg/kg).
[b] DLTs occurring in 2Q4W: acute kidney injury (grade 3), diarrhea (grade 4), and hypotension (grade 4) in a single pt (1.25 mg/kg); peripheral sensory neuropathy (grade 2, 1.5 mg/kg); and transaminitis (grade 3, 2.0 mg/kg).

Treatment-Emergent Adverse Events

Part A Dose Escalation Most common TEAEs, n (%) • >20% Any grade; OR • >2.5% grade ≥3	**2Q3W (N = 41)**		**2Q4W (N = 45)**	
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Fatigue	11 (26.8)	2 (4.9)	15 (33.3)	1 (2.2)
Peripheral sensory neuropathy	10 (24.4)	0 (0)	11 (24.4)	0 (0)
Diarrhea	9 (22.0)	1 (2.4)	5 (11.1)	1 (2.2)
Neutropenia	7 (17.1)	5 (12.2)	1 (2.2)	1 (2.2)
Pleural effusion	4 (9.8)	2 (4.9)	1 (2.2)	1 (2.2)
Anemia	4 (9.8)	1 (2.4)	6 (13.3)	2 (4.4)
Nausea	3 (7.3)	0 (0)	9 (20.0)	0 (0)
Leukopenia	2 (4.9)	2 (4.9)	0 (0)	0 (0)
Pneumonia	1 (2.4)	0 (0)	2 (4.4)	2 (4.4)
Sepsis	1 (2.4)	1 (2.4)	2 (4.4)	2 (4.4)
Hypotension	0 (0)	0 (0)	2 (4.4)	2 (4.4)
Hypoxia	0 (0)	0 (0)	2 (4.4)	2 (4.4)
Pulmonary embolism	0 (0)	0 (0)	2 (4.4)	2 (4.4)

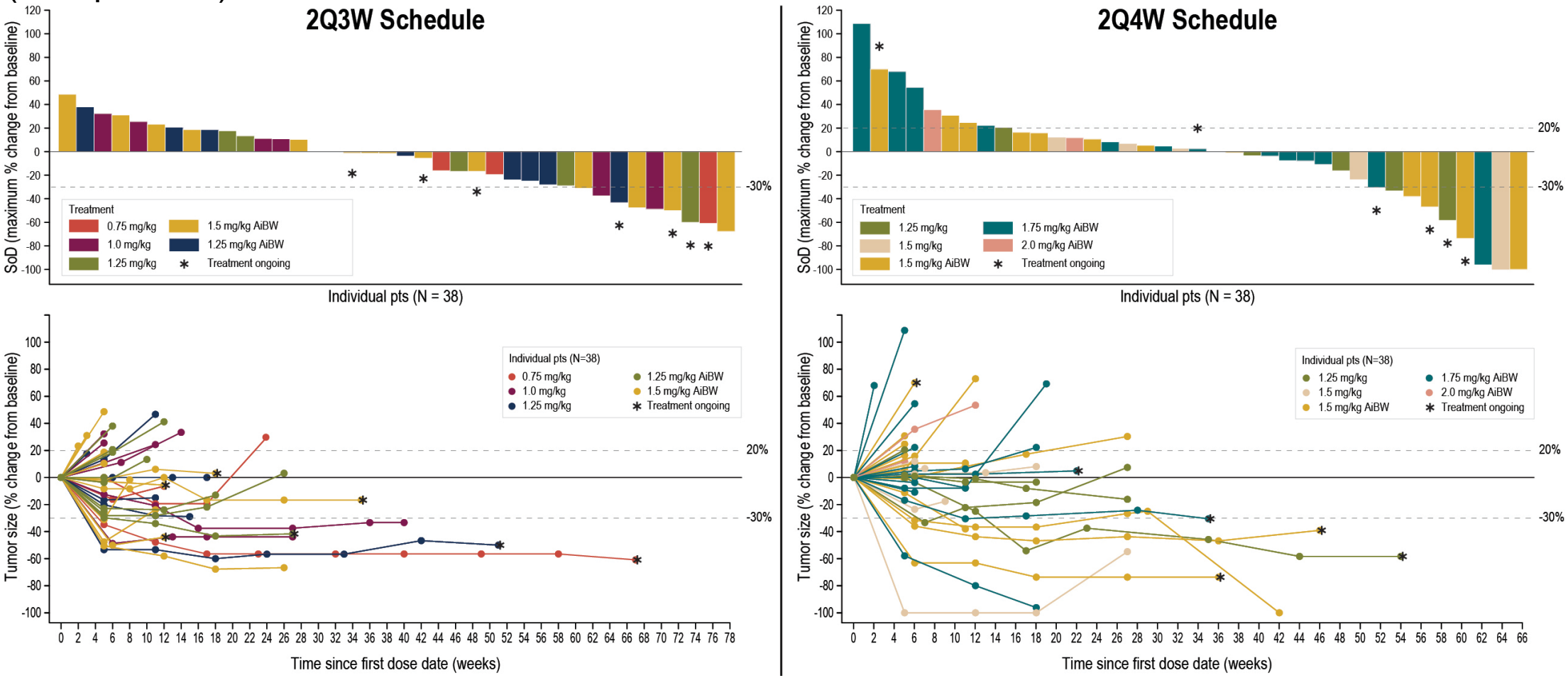
Additional Safety Findings in Part C

- **170 patients treated** in Parts A, B, and C of the ongoing phase 1 study
- After the data cut-off, 2 treatment-related deaths occurred at the 1.5 mg/kg 2Q3W dose in Part C Dose Expansion:
  - Grade 5 hyperglycemia and grade 4 neutropenia in Cycle 1 in a patient with gallbladder carcinoma, type 2 diabetes mellitus, and severe obesity
  - Grade 5 febrile neutropenia in Cycle 1 in a patient with adenoid cystic carcinoma
- Due to the cases of severe neutropenia on the 2Q3W schedule, all patients have been transitioned to 2Q4W dosing

2Q3W, day 1 and day 8 on a 21-day cycle; 2Q4W, day 1 and day 15 on a 28-day cycle; BMI, body mass index; PK, pharmacokinetics; TEAE, treatment-emergent adverse event.

Antitumor Activity in Part A

- Confirmed and durable responses were observed in patients with breast (7/28 patients), ovarian (4/20 patients), endometrial (1 [CR]/16 patients), lung (1/6 patients), and biliary tract cancers (2/11 patients) across dose levels.



2Q3W, day 1 and day 8 on a 21-day cycle; 2Q4W, day 1 and day 15 on a 28-day cycle; AiBW, adjusted ideal body weight.

Authors' Conclusions

SGN-B7H4V is an investigational vedotin ADC directed to the immune checkpoint ligand B7-H4[1]

- In dose escalation, commonly observed AEs include peripheral neuropathy, neutropenia, diarrhea, and nausea, consistent with other vedotin ADCs[2]
- Antitumor activity was observed across doses and tumor types (breast, ovarian, endometrial, lung, and biliary tract cancers)
- Patients continue to receive treatment with SGN-B7H4V on a 2Q4W dosing schedule

2Q4W, day 1 and day 15 on a 28-day cycle; ADC, antibody-drug conjugate; AE, adverse event; pt, patient.

1. Gray E, et al. J Immunother Cancer. 2021;9(suppl 2):A895; 2. ADCETRIS. Prescribing Information [package insert]. Bothell, WA: Seagen Inc.; 2023.

Acknowledgment

- To all patients who participated in the SGNB7H4V-001 trial, their families, and their caregivers
- To investigators and research staff at all SGNB7H4V-001 clinical sites (23 sites in 7 countries)
- This study was sponsored by Seagen Inc., Bothell, WA, USA
- The authors thank Irina Mordukhovich, PhD, of MMS Holdings Inc., who provided medical writing and editorial support with funding from Seagen Inc., in accordance with Good Publication Practice guidelines