SGN-B6A, An Integrin Beta-6 Targeted Antibody-Drug Conjugate, in Patients With Advanced Solid Tumors: Updated Results From a Phase 1 Study (SGNB6A-001)

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Objectives

- To present updated safety and efficacy results, including durability, with an additional 7 months of follow-up, from an ongoing phase 1 first-in-human study of SGN-B6A, an integrin beta-6 directed ADC, in patients with advanced solid tumors
- Updated results as of March 30, 2023, include:
  - Safety in all patients treated in dose escalation and expansion (N=220)
  - Efficacy in dose escalation in NSCLC (N=33) and EC (N=12), and combined dose escalation and expansion in HNSCC (N=56)

Conclusions

SGN-B6A continues to demonstrate a tolerable and manageable safety profile

SGN-B6A demonstrates encouraging antitumor activity and durable responses in a heavily pretreated patient population with NSCLC, EC, and HNSCC

Multiple expansion cohorts are ongoing to determine the recommended dose and schedule and further evaluate safety and efficacy

The combination cohort of SGN-B6A and pembrolizumab has been initiated

Abbreviations

2Q3W: days 1 and 8, 21-day cycle; 2Q4W: days 1 and 15, 28-day cycle; AiBW: adjusted ideal body weight; ADC: antibody-drug conjugate; BOR: best overall response; CI: confidence interval; cORR: confirmed objective response rate; CPS: combined positive score; CR: complete response; cSCC: cutaneous squamous cell carcinoma; EAC: esophageal adenocarcinoma; EC: esophageal cancer; ECOG PS: eastern cooperative oncology group performance status; ESCC: esophageal squamous cell carcinoma; GEJ: gastroesophageal junction; GPP3: good publication practice; HNSCC: head and neck squamous cell carcinoma; ICMJE: International Committee of Medical Journal Editors; MMAE: monomethyl auristatin E; NA: no assessment; NE: not evaluable; NSCLC: non-small cell lung carcinoma; PD: progressive disease; PD-(L)1: programmed cell death (ligand) 1; PR: partial response; Q1W: days 1, 8, and 15, 21-day cycle; Q3W: day 1, 21-day cycle; RECIST: response evaluation criteria in solid tumors; SD: stable disease; SOC: standard of care; SoD: sum of diameters; TEAEs: treatment-emergent adverse events; TBW: total body weight; TPS: tumor positive score

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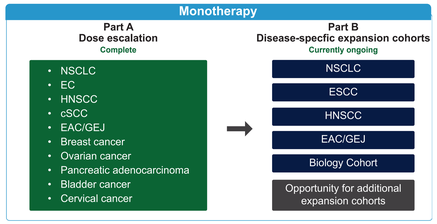
Background

- The receptor integrin beta-6 plays a role in tumor pathogenesis and invasiveness, and overexpression is correlated with poor outcomes[1,2]
- NSCLC, HNSCC, and EC are among tumors with high integrin beta-6 expression[1,2]
- SGN-B6A is an investigational ADC designed to deliver MMAE to integrin beta-6-expressing cells via selective binding to the target, to elicit MMAE-directed cytotoxicity, bystander effect, and immunogenic cell death[3]
- SGN-B6A has shown encouraging preliminary safety and efficacy results in dose escalation[4]

Methods

Study Design



Key Eligibility Criteria

- Histologically or cytologically confirmed metastatic or unresectable solid tumor
- No prior MMAE-containing agent or agent targeting integrin beta-6

Part A

- Relapsed or refractory disease or intolerance to SOC therapies, and no appropriate SOC option, per investigator

Part B

- Must have received prior platinum-based therapy and PD-(L)1 inhibitor, if applicable and available per local SOC

Demographics and Characteristics at Baseline

Dose Escalation and Expansion, All Tumor Types

	Total[a,b] N=220
Age, median years (range)	62 (30-84)
Male sex, n (%)	126 (57.3)
ECOG PS of 1, n (%)	155 (70.5)
Disease diagnosis, n (%)	
NSCLC	96 (43.6)
HNSCC	62 (28.2)
EC	36 (16.4)
Breast cancer	15 (6.8)
cSCC	3 (1.4)
Other[c]	8 (3.6)

[a]Total includes all patients who received any amount of SGN-B6A
[b]SGN-B6A TBW Dosing: 0.8/1.0/1.2 mg/kg (Q1W), 1.2/1.25 mg/kg (2Q3W), 1.5/1.8 mg/kg (Q3W), 1.5/1.8/2.0 mg/kg (2Q4W); SGN-B6A AiBW Dosing: 1.8 mg/kg (2Q4W)
[c]Ovarian cancer (n=3), exocrine pancreatic cancer (n=2), cervical cancer (n=2), bladder cancer (n=1)
Data cutoff: March 30, 2023

Results

Overall TEAEs and Treatment-Related TEAEs

	Total[a,b] N=220
All TEAEs, n (%)	196 (89.1)
Treatment-related TEAEs	145 (65.9)
≥ Grade 3 TEAE, n (%)	98 (44.5)
Treatment-related ≥ grade 3 TEAE	43 (19.5)
Serious TEAEs, n (%)	70 (31.8)
Treatment-related serious TEAEs	16 (7.3)
TEAEs leading to treatment discontinuation	12 (5.5)
Discontinuation due to treatment-related TEAEs	7 (3.2)
TEAEs leading to death, n (%)	4 (1.8)
Treatment-related TEAEs leading to death	0

[a]Total includes all patients who received any amount of SGN-B6A
[b]SGN-B6A TBW Dosing: 0.8/1.0/1.2 mg/kg (Q1W), 1.2/1.25 mg/kg (2Q3W), 1.5/1.8 mg/kg (Q3W), 1.5/1.8/2.0 mg/kg (2Q4W); SGN-B6A AiBW Dosing: 1.8 mg/kg (2Q4W)
Data cutoff: March 30, 2023

Any grade TEAEs occurring in ≥10% or grade ≥3 occurring in ≥3% of patients

	Total N=220	
	All grades	Grade ≥3
Fatigue	78 (35.5)	13 (5.9)
Diarrhea	62 (28.2)	4 (1.8)
Nausea	59 (26.8)	0
Peripheral sensory neuropathy	53 (24.1)	4 (1.8)
Decreased appetite	46 (20.9)	4 (1.8)
Alopecia	45 (20.5)	0
Dyspnea	44 (20.0)	15 (6.8)
Anemia	40 (18.2)	9 (4.1)
Weight decreased	32 (14.5)	0
Constipation	31 (14.1)	0
Cough	29 (13.2)	0
Hypokalemia	28 (12.7)	6 (2.7)
Vomiting	26 (11.8)	2 (0.9)
Abdominal pain	25 (11.4)	2 (0.9)
Neutropenia	24 (10.9)	17 (7.7)
Hypophosphatemia	23 (10.5)	1 (0.5)
Aspartate aminotransferase increased	23 (10.5)	1 (0.5)
Pneumonia	12 (5.5)	8 (3.6)

Safety Summary

- The most common TEAEs are fatigue (35.5%), diarrhea (28.2%), nausea (26.8%), peripheral sensory neuropathy (24.1%), and decreased appetite (20.9%)
- The most common grade ≥3 TEAEs are neutropenia (7.7%), dyspnea (6.8%), fatigue (5.9%), anemia (4.1%), and pneumonia (3.6%)
- TEAEs leading to treatment discontinuation occurred in 5.5% of patients (3.2% treatment-related)
- No treatment-related deaths were reported

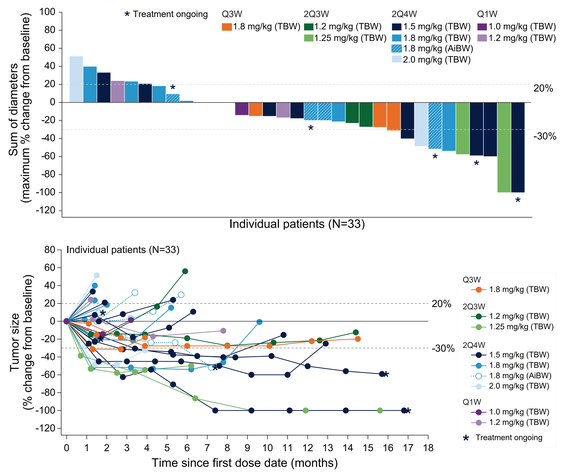
Antitumor Activity in NSCLC Dose Escalation

All (100%) patients received prior systemic therapy, with 78.8% (26 of 33 patients) receiving at least 2 lines of systemic therapy in the locally advanced or metastatic setting

	NSCLC dose escalation TBW N=27	NSCLC dose escalation TBW + AiBW N=33
cORR (CR or PR), n(%)	9 (33.3)	9 (27.3)
95% CI	(16.5, 54.0)	(13.3, 45.5)
BOR, n (%)		
CR	3 (11.1)	3 (9.1)
PR	6 (22.2)	6 (18.2)
SD[a]	8 (29.6)	12 (36.4)
PR pending confirmation	0	1 (3.0)
PD	9 (33.3)	11 (33.3)
NE	1 (3.7)	1 (3.0)
Median duration of response, months (range)	8.3 (2.5, 15.0+)	8.3 (2.5, 15.0+)

The efficacy-evaluable analysis set includes all treated subjects who had both a baseline and at least 1 evaluable post baseline disease assessment per RECIST v1.1 (assessed by investigator) or discontinued the study treatment.
[a]Including 1 patient whose initial response (CR or PR) is pending confirmation
Data cutoff: March 30, 2023

Best Percentage Change in Target Lesions SoD From Baseline per RECIST v1.1



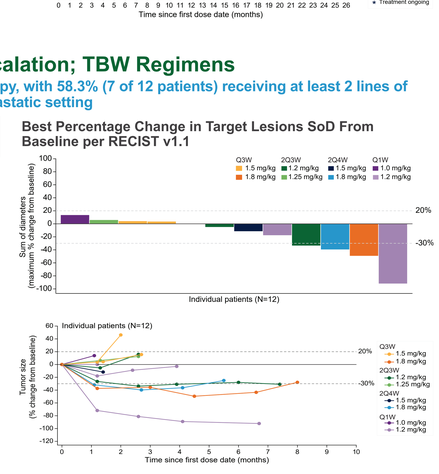
Antitumor Activity in HNSCC Dose Escalation and Dose Expansion

All (100%) patients received prior systemic therapy, with 85.7% (48 of 56 patients) receiving at least 2 lines of systemic therapy in the locally advanced or metastatic setting

	HNSCC dose escalation and expansion N=56
cORR (CR or PR), n(%)	13 (23.2)
95% CI	(13.0, 36.4)
BOR, n (%)	
PR	13 (23.2)
SD[a]	21 (37.5)
PR pending confirmation	4 (7.1)
PD	15 (26.8)
NE	2 (3.6)
NA	5 (8.9)
Median duration of response, months (range)	5.5 (1.4+, 23.3)

The efficacy-evaluable analysis set includes all treated subjects who had both a baseline and at least 1 evaluable post baseline disease assessment per RECIST v1.1 (assessed by investigator), or discontinued the study treatment
[a]Including 4 patients whose initial response (CR or PR) is pending confirmation
Data cutoff: March 30, 2023

Best Percentage Change in Target Lesions SoD From Baseline per RECIST v1.1



Antitumor Activity in EC Dose Escalation; TBW Regimens

All (100%) patients received prior systemic therapy, with 58.3% (7 of 12 patients) receiving at least 2 lines of systemic therapy in the locally advanced or metastatic setting

	EC dose escalation N=12
cORR (CR or PR), n(%)	4 (33.3)
95% CI	(9.9, 65.1)
BOR, n (%)	
PR	4 (33.3)
SD	4 (33.3)
PD	4 (33.3)
Median duration of response, months (range)	5.6 (3.5, 9.8)

The efficacy-evaluable analysis set includes all treated subjects who had both a baseline and at least 1 evaluable post baseline disease assessment per RECIST v1.1 (assessed by investigator), or discontinued the study treatment
Data cutoff: March 30, 2023

Best Percentage Change in Target Lesions SoD From Baseline per RECIST v1.1