Abstract 8522

Sigvotatug vedotin (SV), an investigational integrin beta-6 (IB6)–directed antibody-drug conjugate (ADC), plus pembrolizumab: updated results from phase 1 study (SGNB6A-001)

Jesus Corral Jaime,[1] Kartik Sehgal,[2] Javier-David Benitez-Fuentes,[3] Muh-Hwa Yang,[4] Joseph Z. Ye,[5] Edwin C. Kingsley,[6] Elisa Fontana,[7] Michael Mark,[8] Solange Peters,[9] Francesca Toffalorio,[10] Tianhua Wang,[11] Sona Ghorashi,[12] Anthony Lee,[11] Steven Powell[13]

[1]Hospital Universitario de Jerez de la Frontera, Cádiz, Spain; [2]Dana-Farber Cancer Institute, Boston, MA; [3]Hospital General Universitario de Elche, Elche, Spain; [4]National Yang Ming Chiao Tung University, Taipei, Taiwan; [5]Vista Oncology, AON, Olympia, WA; [6]Comprehensive Cancer Centers of Nevada, Las Vegas, NV; [7]Sarah Cannon Research Institute, London, UK; [8]Kantonsspital Graubünden, Chur, Switzerland, and Faculty of Biomedical Sciences, Università della Svizzera Italiana, Lugano, Switzerland; [9]Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [10]Pfizer, Milan, Italy; [11]Pfizer, South San Francisco, CA; [12]Pfizer, New York, NY; [13]Sanford Cancer Center, Sioux Falls, SD

Conclusions

- As a first-line treatment, SV plus pembrolizumab had a manageable safety profile that was generally consistent with that of each individual component[1,2]
  - Immune-related AEs were as expected based on pembrolizumab monotherapy[2]
- The combination of SV plus pembrolizumab continued to show encouraging antitumor activity in treatment-naive aNSCLC across programmed death ligand 1 (PD-L1) scores and histology
  - PD-L1 TPS ≥50%: ORR was 86%
  - PD-L1 TPS ≥1%: ORR was 47%
  - PD-L1 TPS <1%: ORR was 56%
- Responses were durable (median duration, 8.1 months), including responses lasting ≥12 months
- These results support the ongoing phase 3 SigVie-003 study (NCT06758401)[3] as well as further investigation in the enrolling phase 1 cohorts and future studies
  - SigVie-003 is evaluating SV plus pembrolizumab vs pembrolizumab monotherapy for treatment-naive aNSCLC with PD-L1 tumor proportion score (TPS) ≥50%[3]

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Correspondence: Jesus Corral Jaime, jesuscorraljaime@hotmail.com

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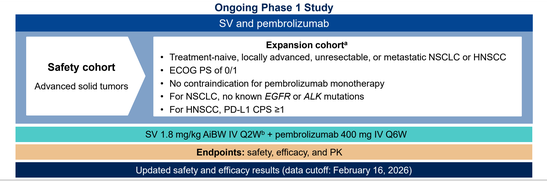
Background

- IB6 is overexpressed in many solid tumors, including non-small cell lung cancer (NSCLC) and head and neck squamous cell carcinoma (HNSCC)[1,4-9]
- SV, an IB6-directed, vedotin-based ADC, showed encouraging antitumor activity and manageable safety as monotherapy in advanced NSCLC (aNSCLC) in the ongoing phase 1 SGNB6A-001 study (NCT04389632) [1]
- Based on the rationale that SV demonstrated the ability to induce immunogenic cell death and also enhanced antitumor activity in combination with immunotherapy in preclinical studies,[10,11] the SGNB6A-001 study is also evaluating SV plus pembrolizumab[12]
- Initial results with SV plus pembrolizumab (N=51) showed encouraging antitumor activity and manageable safety in aNSCLC and HNSCC[12]
- Here, we present pooled safety data for HNSCC and aNSCLC and clinical activity in treatment-naive NSCLC from an expanded cohort with longer follow-up

Methods

- SGNB6A-001 is an open-label, multicenter, dose-escalation and dose-expansion study evaluating the safety, recommended dose, pharmacokinetics (PK), and antitumor activity of SV as a monotherapy or in a combination
- SV plus pembrolizumab is being evaluated in safety and expansion cohorts in treatment-naive, locally advanced, unresectable, or metastatic NSCLC across PD-L1 scores and HNSCC combined positive score (CPS) ≥1 (**Figure 1**)
- This analysis describes patients who received SV at the recommended dose of 1.8 mg/kg AiBW IV Q2W and pembrolizumab 400 mg IV Q6W in either the safety or expansion portion of this study
- The primary endpoint is safety, and key secondary endpoints include antitumor activity

Figure 1. SGNB6A-001 Study Design



AiBW, adjusted ideal body weight; ALK, anaplastic lymphoma kinase; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; Q2W, days 1, 15, 29 of a 42-day cycle; Q6W, day 1 of a 42-day cycle.
[a]Additional cohorts are currently enrolling and are not included in this analysis. [b]While other SV doses were used, this analysis includes only patients who received the SV 1.8 mg/kg AiBW Q2W dose.

Results

- As of February 16, 2026, 89 patients across cohorts received ≥1 dose of SV + pembrolizumab (55 aNSCLC, 33 HNSCC, 1 esophageal cancer; **Table 1**) and 34 were still on treatment

Table 1. Baseline Characteristics

NSCLC and patient characteristics	n=55[a]
Median age (range), years	67.0 (34.0-86.0)
Male, n (%)	37 (67)
ECOG PS of 1, n (%)	35 (64)
Disease stage, n (%)	
Locally advanced/recurrent	3 (5)
Metastatic	52 (95)
PD-L1 status, n (%)	
TPS ≥50%	8 (15)
TPS ≥1%-49%	26 (47)
TPS <1%	21 (38)
Treatment naive in locally advanced/recurrent or metastatic setting, n (%)	54 (98)
Histology, n (%)	
Nonsquamous	39 (71)
Squamous	16 (29)
HNSCC and patient characteristics	**n=33[a]**
Median age (range), years	63.0 (34.0-78.0)
Male, n (%)	23 (70)
ECOG PS of 1, n (%)	15 (45)
Disease stage, n (%)	
Locally advanced/recurrent	18 (55)
Metastatic	15 (45)
PD-L1 status, n (%)	
CPS 1-19	17 (52)
CPS ≥20	16 (48)
Treatment naive in locally advanced/recurrent or metastatic setting, n (%)	32 (97)

CPS, combined positive score.
[a]One patient with esophageal cancer received study treatment. Data for that patient are not shown here.

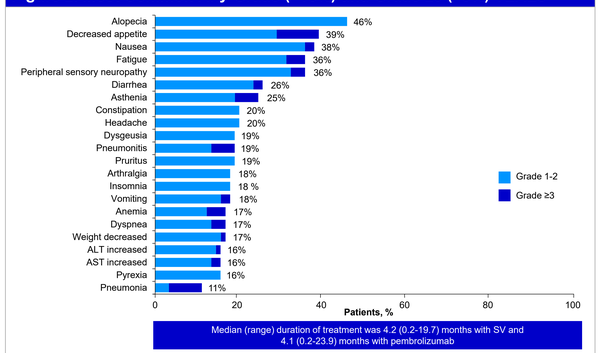
- Overall, all cause any-grade treatment-emergent adverse events (TEAEs) occurred in 98% of patients, with predominantly low-grade events; grade ≥3 TEAEs occurred in 64% of patients (**Table 2**)
  - Six patients (7%) had fatal TEAEs, with 2 treatment-related events (Stevens-Johnson syndrome [SJS] and cardiac arrest)
- The most common TEAEs (>30%) were alopecia, decreased appetite, nausea, fatigue, and peripheral sensory neuropathy (**Figure 2**)

Table 2. Safety Overview

	All patients (N=89)	
n (%)	All cause	Treatment related
Any-grade TEAE	87 (98)	83 (93)
Grade ≥3 TEAE	57 (64)	40 (45)
SAE	50 (56)	28 (31)
TEAE leading to death	6 (7)	2 (2)[a]
TEAEs leading to discontinuation of any drug	30 (34)	23 (26)[b]
TEAEs leading to discontinuation of SV	26 (29)	19 (21)
TEAEs leading to discontinuation of pembrolizumab	27 (30)	20 (22)

SAE, serious adverse event.
[a]Cardiac arrest (n=1) and SJS (n=1). [b]The most common reasons for discontinuation were pneumonitis (n=6 [7%]), interstitial lung disease (n=3 [3%]), and peripheral sensory neuropathy (n=3 [3%]).

Figure 2. Most Common Any-Grade (>15%) and Grade ≥3 (>5%) TEAEs



ALT, alanine aminotransferase; AST, aspartate aminotransferase.

- AEs of interest by composite term were determined using pooled search terms (**Table 3**)
  - The composite terms of peripheral neuropathy and interstitial lung disease (ILD) were reported by 45% and 24% of patients, respectively
- Any-grade and grade ≥3 immune-related AEs occurred in 73% and 25% of patients, respectively (**Table 4**)

Table 3. AEs of Interest by Composite Term[a]

	All patients (N=89)	
Adverse drug reaction, n (%)	Any grade	Grade ≥3
Peripheral neuropathy	40 (45)	4 (4)
ILD/pneumonitis	21 (24)	6 (7)
Hepatotoxicity	19 (21)	3 (3)
Hyperglycemia	7 (8)	3 (3)
Other events of interest, n (%)	**Any grade**	**Grade ≥3**
Neutropenia	15 (17)	11 (12)
Anemia	15 (17)	4 (4)
Infusion-related reaction	4 (4)	1 (1)
Injection site reaction	2 (2)	0

PT, preferred term; SMQ, standardized MedDRA query.
[a]Composite terms: peripheral neuropathy [peripheral neuropathy SMQ (broad)]; ILD/pneumonitis [ILD SMQ (narrow) + PT of organizing pneumonia]; hepatoxicity [cholestasis and jaundice of hepatic origin SMQ (narrow); liver-related investigations, signs, and symptoms SMQ (narrow); hepatic failure, fibrosis, and cirrhosis and other liver damage–related conditions SMQ (narrow); hepatitis, noninfectious SMQ (narrow)]; hyperglycemia [hyperglycemia/new-onset diabetes mellitus SMQ (narrow) + PTs of blood glucose abnormal, blood glucose fluctuation, metabolic syndrome]; neutropenia [hematopoietic leukopenia SMQ (narrow)]; anemia [hematopoietic erythropenia SMQ (broad)]; infusion-related reaction [PT of infusion-related reaction]; and injection site reaction [extravasation events (injections, infusions, and implants) SMQ (broad)].

Table 4. Immune-Related AEs

	All patients (N=89)	
TEAE, n (%)	Any grade (≥10%)	Grade ≥3 (≥2%)
Any event	65 (73)	22 (25)
Fatigue	17 (19)	3 (3)
Pneumonitis	15 (17)	5 (6)
Asthenia	13 (15)	2 (2)
Arthralgia	12 (13)	0
Decreased appetite	12 (13)	4 (4)
Hypothyroidism	11 (12)	0
Pruritus	11 (12)	0
ALT increased	9 (10)	0
AST increased	9 (10)	0
Diarrhea	9 (10)	2 (2)
Colitis	7 (8)	4 (4)
SJS[a]	2 (2)	2 (2)

[a]Confounded by exposure to pembrolizumab and antibiotics associated with SJS.

- In the aNSCLC expansion cohort, median follow-up for the 53 patients was 11.2 months (95% CI, 4.2-15.2)
- Objective response rate (ORR) with SV + pembrolizumab was 50% in efficacy-evaluable patients (n=46) (**Table 5; Figure 3**)
  - 86% with TPS ≥50% (n=7)
  - 47% with TPS ≥1% (n=30)
  - 56% with TPS <1% (n=16)
- ORR was similar across nonsquamous (n=33 [52%]) and squamous (n=13 [46%]) histologies
- Durable responses were seen across subgroups, including responses lasting ≥12 months

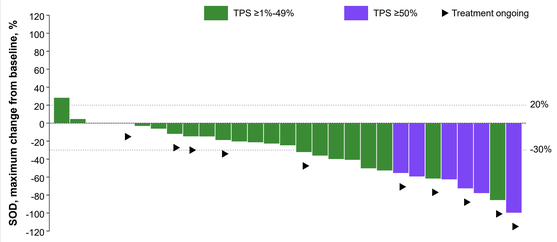
Table 5. Antitumor Activity in Treatment-Naive aNSCLC Across Subgroups

	Treatment-naive aNSCLC (expansion cohort)			
	All efficacy evaluable[a] (n=46)	PD-L1 TPS ≥50% (n=7)	PD-L1 TPS ≥1% (n=30)	PD-L1 TPS <1% (n=16)
ORR (95% CI), %	50 (35-65)	86 (42-100)	47 (28-66)	56 (30-80)
cORR (95% CI), %	46 (31-61)	86 (42-100)	43 (26-63)	50 (25-75)
BOR, n (%)				
CR	1 (2)	1 (14)	1 (3)	0
PR	22 (48)	5 (71)	13 (43)	9 (56)
SD	16 (35)	0	11 (37)	5 (31)
PD	4 (9)	0	3 (10)	1 (6)
NE	1 (2)	0	1 (3)	0
No assessment	2 (4)	1 (14)	1 (3)	1 (6)
Median DOR (95% CI),[b] months	8.1 (4-NR)	NR (4.3-NR)	NR (4.2-NR)	5.7 (2.9-NR)

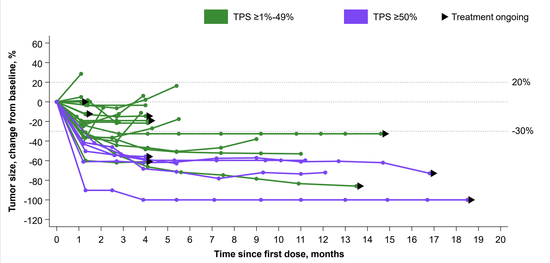
BOR, best overall response; cORR, confirmed objective response rate; CR, complete response; DOR, duration of response; NE, not evaluable; NR, not reached; PD, progressive disease; PR, partial response; SD, stable disease.
[a]Efficacy-evaluable patients had both a baseline and ≥1 evaluable postbaseline disease assessment per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (assessed by investigator) or discontinued the study treatment. [b]Calculated from among those with confirmed response.

Figure 3. Antitumor Activity in Treatment-Naive aNSCLC[a]

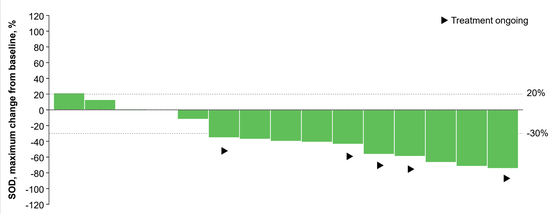
A. Maximum percent change from baseline[b] in patients with PD-L1 TPS ≥1%



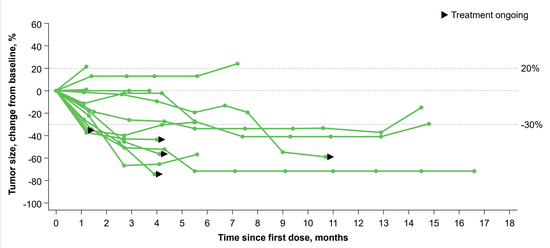
B. Percent change over time in patients with PD-L1 TPS ≥1%



C. Maximum percent change from baseline[b] in patients with PD-L1 TPS <1%



D. Percent change over time in patients with PD-L1 TPS <1%



[a]Efficacy-evaluable patients had both a baseline and ≥1 evaluable postbaseline disease assessment per RECIST 1.1 (assessed by investigator) or discontinued the study treatment. [b]Change from baseline in sums of diameters of target lesions.