

LBA68
Phase 3 study of sigvotatug vedotin (SV) vs docetaxel (DTX) in previously treated nonsquamous non-small cell lung cancer (NSCLC)

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Background

SV, a novel integrin beta-6 (IB6)-directed ADC, showed promising antitumor activity in patients (pts) with heavily pretreated advanced NSCLC in the phase 1 SGNB6A-001 study. Phase 3 SigVie-002 (NCT06012435) results are reported.

Methods

Pts with nonsquamous NSCLC were randomized to SV (1.8 mg/kg by AiBW IV Q2W) or DTX (75 mg/m² IV Q3W). Eligible pts received prior platinum-based chemotherapy; prior PD-(L)-1 inhibitor was required by pts with no known actionable genomic alterations (AGAs); and ≥1 targeted therapy was required for known AGAs. Endpoints: primary, overall survival (OS); secondary, progression-free survival (PFS) and safety.

Results

As of May 18, 2026, 703 pts were assigned to SV (n=354) or DTX (n=349) with balanced baseline characteristics. Overall, ≥1 AGA, 30%; *EGFR* mutation, 19%. Median OS: 11.9 mo with SV and 11.5 mo with DTX (HR=0.929; one-sided *P*=0.226). Median PFS by BICR: 4.7 mo with SV and 4.2 mo with DTX (HR=0.844). Post-hoc analysis in second line (2L) subgroup (68% of overall; 90% non-AGAs) showed median OS of 13.6 mo with SV and 11.1 mo with DTX (HR=0.831), along with PFS benefit (HR=0.795). In contrast, in third line or later (3L+) subgroup (32% of overall; 72% AGAs), no similar benefit trends were observed. There was no clear relationship between IB6 expression level and efficacy. Any-grade and grade≥3 treatment-related adverse events (TRAEs) occurred in 91% and 33% with SV and 87% and 36% with DTX, respectively. TRAEs led to treatment discontinuation in 11% with SV and 9% with DTX. Table: LBA68

	SV	DTX	Hazard ratio (95% CI)
Overall population, n	354	349	
Median OS (95% CI), mo	11.9 (10.1-14.0)	11.5 (10.2-13.3)	0.929 (0.767-1.126) one-sided p=0.226
Median PFS (95% CI), mo	4.7 (4.2-6.0)	4.2 (4.0-6.0)	0.844 (0.699-1.019)
2L patients, n	236	241	
Median OS (95% CI), mo	13.6 (10.7-16.4)	11.1 (9.6-13.3)	0.831 (0.658-1.049)
Median PFS (95% CI), mo	5.9 (4.3-6.3)	4.2 (4.0-6.0)	0.795 (0.634-0.996)
3L+ patients, n	117	105	
Median OS (95% CI), mo	10.0 (8.2, 12.0)	11.9 (8.9, 16.8)	1.187 (0.850, 1.657)

SV	DTX	Hazard ratio (95% CI)
Median PFS (95% CI), mo 4.2 (3.9, 5.0)	4.2 (3.3, 6.0)	1.024 (0.739, 1.419)

Conclusions

SV did not significantly improve OS over DTX in overall population. Notably, favorable OS and PFS trends were observed with SV in 2L subgroup, which consisted primarily of non-AGA pts. Taken together with phase 1 data showing manageable safety and promising preliminary efficacy in combination with pembrolizumab, these results support further development of SV in combination with pembrolizumab or PF-0864404 (PD1/VEGF bispecific) in earlier settings.

Clinical trial identification

NCT06012435.

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Legal entity responsible for the study

Pfizer.

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Disclosure

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