Phase I study of IMM2510, a PD-L1/ VEGF bispecific antibody, in participants with advanced IO-treated SQ-NSCLC

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Background

- Immunotherapy plus Platinum-based chemotherapy (IO + chemo) is the standard first-line treatment for advanced Squamous-cell non-small-cell lung cancer (sq-NSCLC), while therapeutic options for sq-NSCLC patients who failed first-line therapy are limited. Docetaxel has been the standard of care for second-line treatment with a median overall survival (OS) of 6-8 months[1-3]. Novel treatments are urgently needed for this IO-resistant population.
- IMM2510 is a PD-L1/VEGF bispecific fusion protein that incorporates a VEGF-Trap (VEGFR1-D2) into an anti-PD-L1 antibody, retaining an active Fc domain to enhance ADCC/ADCP via Fc-Fcγ receptor interaction and blocking PD-1/PD-L1 signaling with more complete VEGF clearance. This design integrates anti-angiogenesis, T-cell reactivation and innate immune engagement, with the potential to overcome acquired resistance to PD-1 inhibitors.

Methods

- This is an open-label, multicenter phase I study of IMM2510 in patients with advanced solid tumors. A specific cohort was designed to evaluate the efficacy and safety of IMM2510 in patients with advanced SQ-NSCLC who have failed prior PD-1/PD-L1 inhibitor plus platinum-based chemotherapy in the dose expansion stage.
- Key inclusion criteria: pathologically confirmed advanced SQ-NSCLC with documented disease progression following prior PD-1/PD-L1 inhibitor plus platinum-based chemotherapy.
- IMM2510 was administered intravenously once every two weeks
- As of December 31, 2025, a total of 32 patients with IO-pretreated SQ-NSCLC received IMM2510 monotherapy, 7 pts receiving ≤10mg/kg dose at dose escalation and 25 patients at RP2D of 20 mg/kg at dose expansion.
- 22 pts with at least one tumor assessment were included in efficacy analysis.

Baseline Characteristics

Table 1. Baseline Characteristics

	Total (N=32)
Age (years), median (min, max)	61 (46, 78)
male, n (%)	30 (93.8%)
ECOG Score, n(%)	
0	8 (25.0)
1	24 (75.0)
TPS Score, n(%)	
TPS < 1%	10 (31.3)
TPS 1–49%	10 (31.3)
TPS ≥ 50%	4 (12.5)
Disease duration (months), Median(Min, Max)	19.17 (2.76, 153.49)
Prior lines, Median(Min, Max)	2 (1, 5)
Presence of metastasis, n (%)	32 (100)
Sites of metastasis, n (%)	
Lung	11 (34.4)
Bone	11 (34.4)
Liver	4 (12.5)
Brain	2 (6.3)
Other	27 (84.4)
Prior PD-1 therapy, n (%)	28 (87.5)
Prior PD-L1 therapy, n (%)	6 (18.8)
Prior chemotherapy, n (%)	31 (96.9)
Prior Radiotherapy, n (%)	18 (56.3)

Efficacy Results

Twenty-two pts with advanced IO-treated SQ-NSCLC were evaluable for efficacy analysis. With median follow-up time of 8.31 months, ORR was 27.3% (6/22) and DCR was 81.8% (18/22). The median DoR was 11.1 months. The median PFS was 9.40 months, the PFS rate at 6 months was 51.0%. The median overall survival was not reached.

Table 2. Best Overall Response

	Efficacy Evaluable (N=22)
BOR, n (%)	
CR	0
PR	6 (27.3)
SD	12 (54.5)
PD	4 (18.2)
ORR	
n（%)	6 (27.3)
95%CI	10.7, 50.2
DCR	
n（%)	18 (81.8)
95%CI	59.7, 94.8

Figure 1. Percent Changes from Baseline in Target Lesions

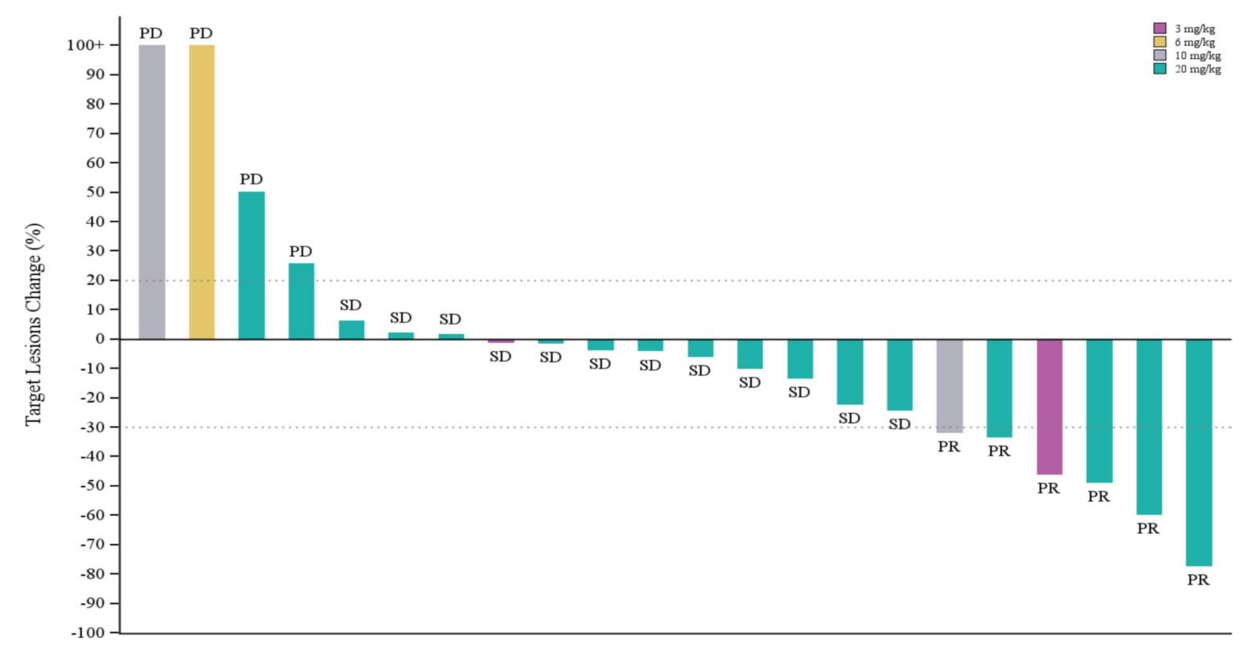


Figure 2. Swimmer Plot

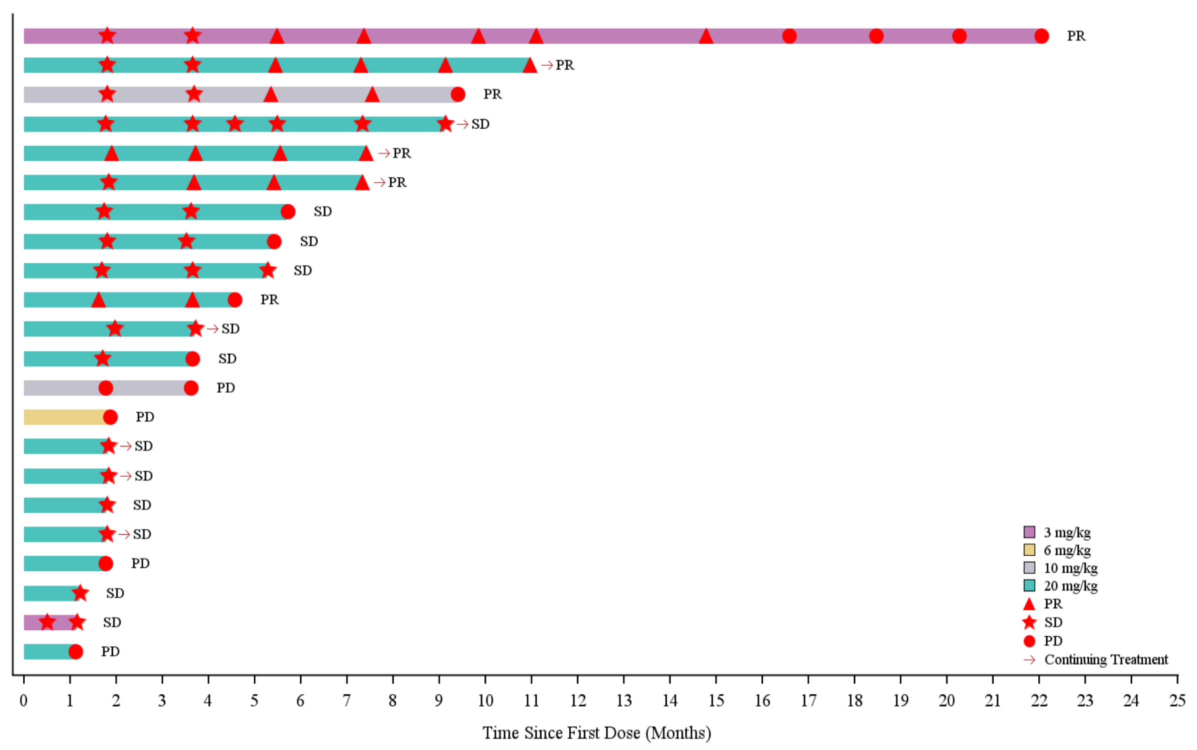


Figure 3. Kaplan-Meier Curve of DoR

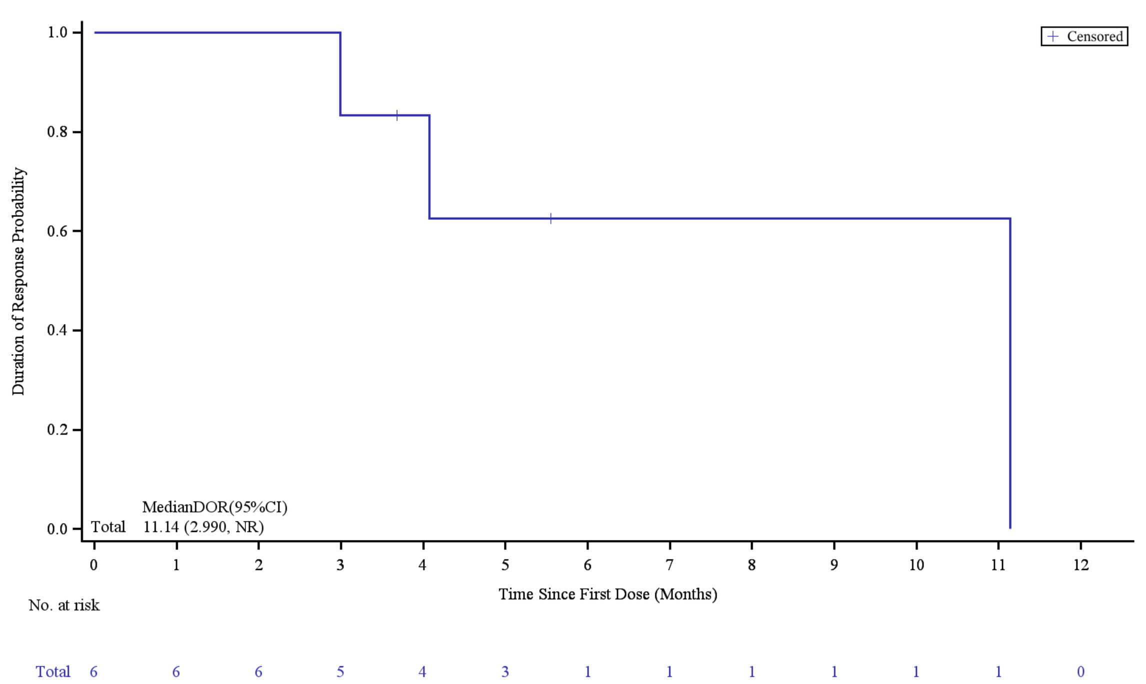


Figure 4. Kaplan-Meier Curve of PFS

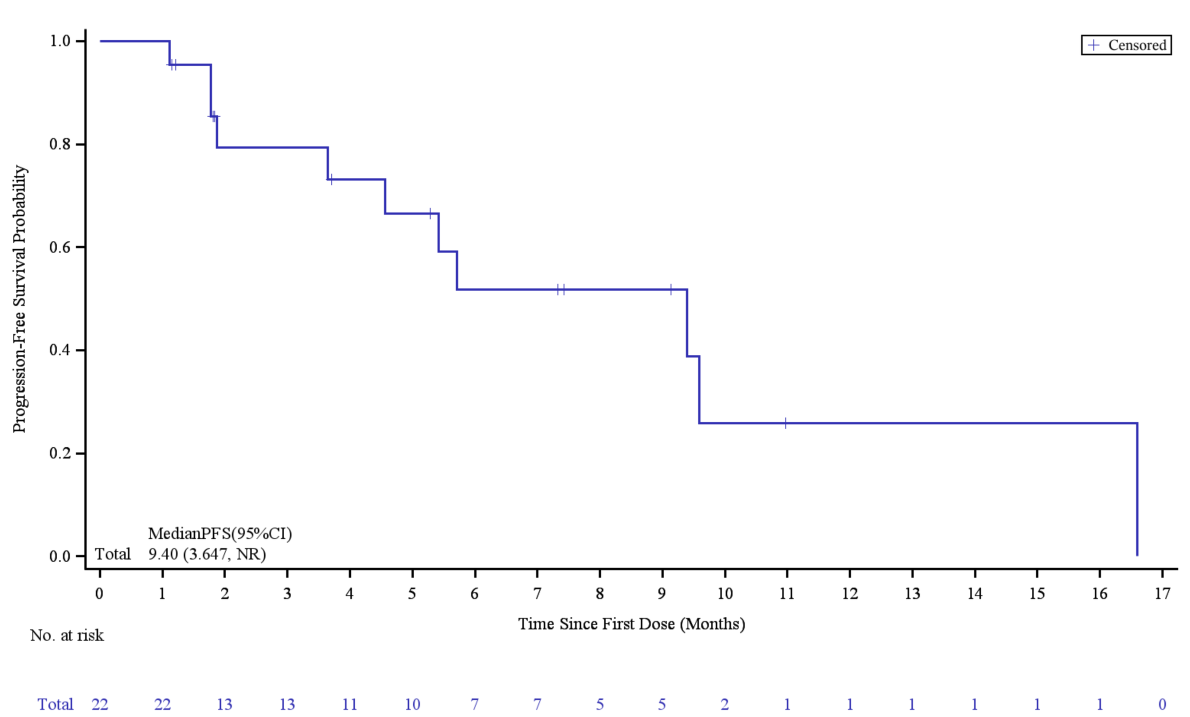
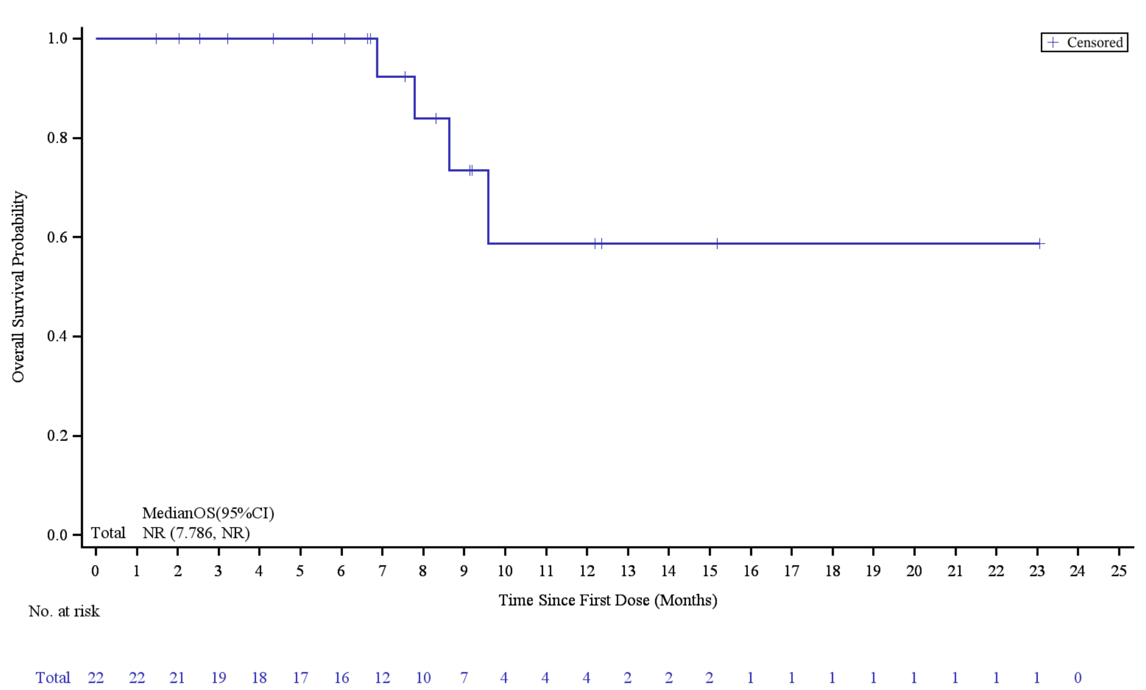


Figure 6. Kaplan-Meier Curve of OS



Safety Results

All 32pts experienced TEAEs. Grade ≥3 TEAEs occurred in 17 (53.1%) pts, 12 (37.5%) considered as treatment related; TRSAEs occurred in 5 (15.6%) pts; 1 (3.1%) TRAEs led to treatment discontinuation. No participant experienced TRAE leading to death.

The most common TRAEs were infusion-related reaction (50.0%), anemia (43.8%), decreased platelet count (34.4%), hypoalbuminemia (34.4%), and decreased lymphocyte count (28.1%), with majority of Grade 1–2.

IRR incidence rate was 40% and no G3 or higher IRR were reported at 20mg/kg dose level with premedication treatment, mainly occurred at the first infusion, and incidence rate significantly reduced at the following infusions.

Table 3. Summary of TRAEs (≥ 20% in total) by PT

PT, n (%)	≤ 10 mg/kg (N=7)		20 mg/kg (N=25)		Total (N=32)	
	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Infusion-related reaction	6 (85.7%)	2 (28.6%)	10 (40.0%)	0	16 (50.0%)	2 (6.3%)
Anemia	5 (71.4%)	0	9 (36.0%)	1 (4.0%)	14 (43.8%)	1 (3.1%)
Platelet count decreased	4 (57.1%)	1 (14.3%)	7 (28.0%)	1 (4.0%)	11 (34.4%)	2 (6.3%)
Hypoalbuminemia	4 (57.1%)	0	7 (28.0%)	0	11 (34.4%)	0
Lymphocyte count decreased	2 (28.6%)	1 (14.3%)	7 (28.0%)	2 (8.0%)	9 (28.1%)	3 (9.4%)
Diarrhea	3 (42.9%)	1 (14.3%)	5 (20.0%)	0	8 (25.0%)	1 (3.1%)
Proteinuria	0	0	8 (32.0%)	1 (4.0%)	8 (25.0%)	1 (3.1%)
White blood cell count decreased	3 (42.9%)	1 (14.3%)	4 (16.0%)	0	7 (21.9%)	1 (3.1%)

Conclusions and main findings

IMM2510, a PD-L1/VEGF bispecific fusion protein, was well tolerated with encouraging and durable efficacy observed in patients with advanced SQ-NSCLC who progressed on anti PD-(L)1 in combination with chemotherapy.

- Encouraging response rate and promising PFS and OS were observed in advanced SQ-NSCLC
- IMM2510 monotherapy was well tolerated and manageable. No TEAE leads to death. Few TRAE led to treatment discontinuation. Main G3 TEAE were lymphocyte decrease and platelet decrease. IRR was well controlled after premedication treatment was given.

Overall, our findings indicated the potential of IMM2510 in immunotherapy-resistant SQ-NSCLC. The data supported a favorable benefit-risk profile of IMM2510.

Reference

1. Lancet. 2017 January 21; 389(10066): 255–265.
2. N Engl J Med. 2015 Jul 9;373(2):123-35.
3. Cancer Commun (Lond). 2022 Dec;42(12):1314-1330.