596 AMBER, PART 2B: A PHASE 1 STUDY OF COBOLIMAB PLUS DOSTARLIMAB IN PATIENTS WITH ADVANCED/METASTATIC NON-SMALL CELL LUNG CANCER (NSCLC) PREVIOUSLY TREATED WITH ANTI-PD(L)-1 THERAPY

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Background T-cell immunoglobulin- and mucin-domain-containing-3 (TIM-3) expression on tumor-infiltrating lymphocytes and myeloid-derived cells is associated with immune exhaustion and poor prognosis in patients with NSCLC.[1 2] Cobolimab, an anti-TIM-3 monoclonal antibody, in combination with dostarlimab (a PD-1 inhibitor), has been shown to enhance T-cell activity in preclinical assessments.[3]

Objectives To assess the safety and efficacy of cobolimab plus dostarlimab in patients with advanced/metastatic NSCLC.

Methods AMBER (NCT02817633) is a dose escalation and expansion, multicenter, open-label, Phase 1 study assessing cobolimab monotherapy and combinations in patients with advanced solid tumors. AMBER part 2B tested cobolimab and dostarlimab combination in patients with advanced/metastatic NSCLC previously treated with anti-PD(L)-1 therapy. Eligible patients received cobolimab (100, 300, or 900 mg IV) plus dostarlimab (500 mg IV) Q3W. The primary endpoint included objective response rate (ORR) per RECIST v1.1; secondary endpoints included disease control rate (DCR), immune-related (ir)-ORR and irDCR per irRECIST, overall survival (OS), and safety; exploratory endpoints included biomarker assessments (post hoc).

Results Eighty-four patients were treated (mean age 65.9 years [range: 35–86]). The most common histologies were adenocarcinoma (69.0%) and squamous cell (26.2%), and 58.3% of patients had ≥3 prior treatment lines. At data cut-off (February 2023), across all doses, ORR was 8.3%, irORR was 9.5%, DCR was 21.4%, and irDCR was 25.0% (table 1). The highest ORR (9.8%) was observed in the cobolimab 300 mg cohort, which was ultimately selected as the recommended Phase 2 dose. Patients with irRECIST defined partial response or stable disease (n=12) had higher baseline TIM-3 immunohistochemistry (research use only assay) levels versus patients with progressive disease (n=22; p=0.013); a similar trend was observed for ORR. Patients with lower than median baseline systemic interleukin (IL)-6 and IL-8 correlated with a higher OS versus patients with higher than median baseline systemic IL-6 and IL-8 (table 2).

Treatment-emergent adverse events (TEAEs) ≥1 occurred in 98.8% of patients, most commonly: fatigue (42.9%), dyspnea (31.0%), and decreased appetite (27.4%); 54.8% of patients had Grade ≥3 TEAEs. In total, 52.4%, 13.1%, and 7.1% of patients had treatment-related adverse events (TRAEs), Grade ≥3 TRAEs, and serious TRAEs respectively; no TRAEs deaths were observed.

Conclusions Cobolimab plus dostarlimab showed early evidence of efficacy and acceptable safety in patients with advanced/metastatic NSCLC. Cobolimab plus dostarlimab and docetaxel versus standard of care is being evaluated in COSTAR, an ongoing Phase 2/3 study (NCT04655976) for patients with advanced NSCLC.

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Trial Registration NCT02817633

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Ethics Approval The study was approved by respective IRB/IEC/Competent authorities prior to approval (GSK study 213348).

Abstract 596 Table 1 Efficacy outcomes in patients who received 100,300, and 900 mg doses of cobolimab in combination with dostarlimb (500 mg)

n (%)	Cobolimab 100 mg + dostarlimab (500 mg) cohort (n=14)	Cobolimab 300 mg + dostarlimab (500 mg) cohort (n=41)	Cobolimab 900 mg + dostarlimab (500 mg) cohort (n=29)	Total N=84*
ORR†	1 (7.1)	4 (9.8)	2 (6.9)	7 (8.3)
irORR‡	1 (7.1)	5 (12.2)	2 (6.9)	8 (9.5)
DCR†	3 (21.4)	9 (22.0)	6 (20.7)	18 (21.4)
irDCR‡	3 (21.4)	11 (26.8)	7 (24.1)	21 (25.0)

*14 patients had no post-baseline tumor assessments; †6 patients were not evaluable; ‡7 patients were not evaluable.

DCR, disease control rate; ir, immune-related; ORR, objective response rate.

Abstract 596 Table 2 OS associated with baseline systemic IL-6 and IL-8

	Patients with <median baseline systemic IL-6 (n=31)	Patients with >median baseline systemic IL-6 (n=31)	Patients with <median baseline systemic IL-8 (n=32)	Patients with >median baseline systemic IL-8 (n=32)
OS, months	14.95	5.95	14.95	6.47
HR	0.31		0.49	
p	0.0001		0.01	

HR, hazard ratio; IL, interleukin; OS, overall survival.

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