A Phase 1/2 Study of Surzebiclimab in Combination with Tislelizumab With or Without LBL-007 in Advanced Solid Tumors

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Background

Despite the substantial clinical benefit of anti-programmed cell death protein-1 (PD-1) and anti-programmed death ligand-1 (PD-L1) monoclonal antibodies for patients, an unmet need remains to address resistance to these treatments. This phase 1/2 trial investigated the efficacy and safety of surzebiclimab (anti-T-cell immunoglobulin and mucin-domain containing-3 [TIM-3]), tislelizumab (anti-PD-1) and LBL-007 (anti-lymphocyte activation gene-3 [LAG-3]) combinations in patients with advanced solid tumors.

Methods

In this phase 1/2 trial, patients with solid tumors received surzebiclimab plus tislelizumab in the phase 1 dose escalation and tislelizumab plus LBL-007 with or without surzebiclimab in the phase 2 safety lead-in, and patients with head and neck squamous cell cancer (HNSCC) or non-small cell lung cancer (NSCLC) received surzebiclimab plus tislelizumab with LBL-007 (Cohort 4 [HNSCC] and Cohort 5 [NSCLC]) or without LBL-007 (Cohort 1 [HNSCC] and Cohort 2 [NSCLC]) (NCT03744468). Primary endpoints included treatment-emergent adverse events (TEAEs) and the maximum tolerated dose (MTD) for phase 1 and the phase 2 safety lead-in, and objective response rate (ORR) per RECIST v1.1 for the phase 2 dose expansion.

Results

A total of 147 patients were enrolled (phase 1: n=33; phase 2 safety lead-in: n=31; phase 2 dose expansion: n=83). One DLT was reported in phase 1. MTD was not reached for surzebiclimab in phase 1 or for LBL-007 in the phase 2 safety lead-in. Grade ≥3 treatment-related TEAEs occurred in 9.1% (3/33), 16.1% (5/31), and 10.8% (9/83) of patients in phase 1, phase 2 safety lead-in, and phase 2 dose expansion, respectively. Antitumor activity was observed in the phase 2 dose expansion cohorts, with confirmed ORRs (95% confidence interval [CI]) of 4.8% (0.1-23.8), 9.1% (1.1-29.2), 0 (0-16.8), and 10.5% (1.3-33.1%) in Cohorts 1, 2, 4, and 5, respectively. Biomarker analysis showed that patients who responded or had stable disease tended to have higher baseline expression of PD-L1, TIM-3, or LAG-3.

	Cohort 1: HNSCC Surzebiclimab + tislelizumab (N = 21)	Cohort 2: NSCLC Surzebiclimab + tislelizumab (N = 22)	Cohort 4: HNSCC Surzebiclimab + tislelizumab + LBL-007 (N = 20)	Cohort 5: NSCLC Surzebiclimab + tislelizumab + LBL-007 (N = 20)
Patients with any TEAE, n (%)	20 (95.2)	21 (95.5)	20 (100.0)	20 (100.0)
Grade ≥3	11 (52.4)	11 (50.0)	9 (45.0)	9 (45.0)
Serious	9 (42.9)	8 (36.4)	6 (30.0)	9 (45.0)
Leading to death	3 (14.3)	1 (4.5)	0 (0.0)	4 (20.0)
Leading to treatment discontinuation	1 (4.8)	4 (18.2)	2 (10.0)	4 (20.0)
Patients with any treatment-related TEAE, n (%)	16 (76.2)	10 (45.5)	11 (55.0)	16 (80.0)
Grade ≥3	4 (19.0)	4 (18.2)	0 (0.0)	1 (5.0)
Serious	2 (9.5)	0 (0.0)	0 (0.0)	1 (5.0)
Leading to death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patients with IRRs, n (%)	0 (0.0)	1 (4.5)	0 (0.0)	0 (0.0)

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ORR, n (%)	1 (4.8)	2 (9.1)	0 (0.0)	2 (10.5)
95% CI, %[a]	0.1-23.8	1.1-29.2	0.0-16.8	1.3-33.1
Best overall response, n (%)				
CR	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.3)
PR	1 (4.8)	2 (9.1)	0 (0.0)	1 (5.3)
SD	8 (38.1)	8 (36.4)	9 (45.0)	12 (63.2)
PD	11 (52.4)	11 (50.0)	9 (45.0)	4 (21.1)
NE	1 (4.8)	1 (4.5)	2 (10.0)	1 (5.3)
DCR, n (%)	9 (42.9)	10 (45.5)	9 (45.0)	14 (73.7)
95% CI, %[a]	21.8-66.0	24.4-67.8	23.1-68.5	48.8-90.9
Median DoR (95% CI), months[b]	4.0 (NE-NE)	6.9 (5.6-NE)	NE (NE-NE)	NE (2.8-NE)

Conclusion

Surzebiclimab plus tislelizumab with or without LBL-007 was generally well tolerated in patients with previously treated advanced solid tumors. The observed antitumor activity was modest in patients with anti-PD-1/PD-L1-treated HNSCC and NSCLC. Further research to optimize combination strategies and identify predictive biomarkers is needed.

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