

LBA1
INterpath-001: Phase 3 study of the mRNA-based individualized neoantigen therapy (INT) intismeran autogene (intismeran) plus pembrolizumab (pembro) vs pembro alone for adjuvant treatment of resected stage IIB-IV melanoma (MEL)

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Background

Many patients (pts) with resected high-risk MEL experience recurrence despite adjuvant therapy. Enhancing immune activation may improve efficacy. Intismeran is an mRNA-based INT designed to expand pre-existing and generate de novo neoantigen-specific antitumor T-cell responses by targeting pt-specific tumor-derived antigens. INterpath-001 (NCT05933577) is a double-blind phase 3 study of intismeran + pembro as adjuvant therapy for resected stage IIB–IV MEL.

Methods

Eligible adults with surgically resected stage IIB/IIC (pathologic or clinical) or III/IV cutaneous MEL and a tumor sample suitable for next-generation sequencing were randomized 2:1 to pembro 400 mg (9 cycles, IV Q6W) + intismeran 1 mg or placebo (9 doses, IM Q3W). Pembro started at randomization, intismeran or placebo upon availability. Primary endpoint: RFS. Secondary endpoints: DMFS, OS, and safety.

Results

1137 pts were randomized: 757 to intismeran + pembro, 380 to placebo + pembro; 726 (95.9%) received ≥1 dose of intismeran and 365 (96.1%) received ≥1 dose of placebo as planned. Median follow-up as of 30Jun2026 was 24.6 mo. Intismeran + pembro significantly improved RFS and DMFS compared with placebo + pembro (Table). Benefit was similar in stage IIB–IIIB and IIIC–IV MEL and other subgroups. For intismeran + pembro vs placebo + pembro, AEs were grade ≥3 in 23.6% vs 20.3%; 6.5% vs 5.3% discontinued both drugs simultaneously due to an AE. Most common AEs were pyrexia (52.2% vs 8.2%), injection site pain (51.0% vs 9.5%), and fatigue (38.5% vs 29.7%).Table: LBA1

	Intismeran + pembro (N = 757)	Placebo + pembro (N = 380)
Recurrence-free survival (RFS)		
24-mo rate, % (95% CI)	82.2 (79.3–84.8)	70.0 (65.0–74.5)
HR (95% CI)	0.58 (0.45–0.75)	—
Two-sided P	<0.001	—

	Intismeran + pembro (N = 757)	Placebo + pembro (N = 380)
Distant metastasis-free survival (DMFS)		
24-mo rate, % (95% CI)	88.5 (86.0–90.6)	80.2 (75.6–84.0)
HR (95% CI)	0.62 (0.45–0.85)	—
Two-sided P	0.002	—

Conclusions

Intismeran + pembro significantly improved RFS and DMFS compared with placebo + pembro and was generally well tolerated when given as adjuvant therapy for stage IIB–IV MEL. These findings set a new benchmark for adjuvant MEL and are a pivotal advance in personalized medicine and cancer treatment.

Clinical trial identification

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