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Characterization of tumor and peripheral biomarkers in patients (pts) with resectable melanoma (MEL) treated with adjuvant nivolumab + relatlimab (NIVO + RELA) or NIVO alone in RELATIVITY-098

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Background

RELA-098 (NCT05002569) evaluated adj NIVO + RELA fixed dose combination (FDC) vs NIVO in pts with resected stage III–IV MEL. NIVO + RELA did not significantly improve recurrence-free survival (RFS) vs NIVO alone. In advanced (adv) MEL, LAG-3+ CD8 T cells were primarily located in tumor tissue; on-treatment expansion of LAG-3+ CD8 T cells in blood was lower in adj vs adv MEL (Long, ASCO 2025). Here we characterized BM for pharmacodynamic (PD) effects of adj NIVO + RELA and NIVO alone and association of BM with RFS.

Methods

Pts received NIVO 480 mg + RELA 160 mg FDC or NIVO 480 mg. Baseline (BL) and post-treatment blood samples were analyzed for PD changes in immune cell populations by flow cytometry and cytokines by immunoassays. Tissue samples collected at BL resection and recurrence were analyzed by immunohistochemistry for tumor cell PD-L1, LAG-3, and CD8.

Results

Blood inflammatory cytokines (eg IFNγ, CXCL9, and CXCL10) were significantly increased in both arms, but to a greater degree by NIVO + RELA vs NIVO. Immunosuppressive cytokines (eg IL-10, CRP, and CCL8) were also elevated by NIVO + RELA. Blood LAG-3+ T cells were more significantly increased by adj NIVO + RELA vs NIVO. Higher PD-L1, LAG-3, and CD8 expression in BL resected tumors enriched for RFS benefit in both arms. 72% of resected tumors were LAG-3-positive but only 28% were PD-L1-positive despite most tumors being CD8 infiltrated (>95%). Pts with lower CD8 infiltration (lowest tertile) in resected tumors demonstrated a trend for RFS benefit of NIVO + RELA vs NIVO. BM expression in resected tumors compared with that in recurrent tumors is underway.

Conclusions

In resected stage III-IV MEL (RELA-098), NIVO + RELA induced similar PD changes as those reported for adv MEL (RELA-047) though smaller magnitude, and inflammation-related TME BM in resected tumors similarly enriched for efficacy to adj IO therapy. Despite the similarities, BM analyses, as previously reported, support that LAG-3+ tumor infiltrating lymphocytes at therapy initiation are likely needed for NIVO + RELA vs NIVO benefit. The significance of NIVO + RELA benefit in pts whose resected tumors have lower CD8 infiltration is being investigated.

Clinical trial identification

NCT05002569.

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Legal entity responsible for the study

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