Tumour-infiltrating lymphocyte density is associated with favourable outcome in patients with advanced non-small cell lung cancer treated with immunotherapy

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Abstract

Background: The established role of morphological evaluation of tumour-infiltrating lymphocytes (TILs) with immune checkpoint inhibitors (ICIs) in non-small cell lung cancer (NSCLC) is unknown. We aimed to determine TIL association with the outcome for ICIs and for chemotherapy in advanced NSCLC.

Methods: This is a multicenter retrospective study of a nivolumab cohort of 221 patients treated between November 2012 and February 2017 and a chemotherapy cohort of 189 patients treated between June 2009 and October 2016. Patients with available tissue for stromal TIL evaluation were analysed. The presence of a high TIL count (high-TIL) was defined as ≥10% density. The primary end-point was overall survival (OS).

Results: Among the nivolumab cohort, 64% were male, with median age of 63 years, 82.3% were smokers, 77% had performance status ≤1 and 63% had adenocarcinoma histology. High-TIL was observed in 22% patients and associated with OS (hazard ratio [HR] 0.48; 95% confidence interval [95% CI]: 0.28-0.81) and progression-free survival [PFS] (HR = 0.40; 95% CI: 0.25-0.64). Median PFS was 13.0 months (95% CI: 5.0-not reached) with high-TIL versus 2.2 months (95% CI: 1.7-3.0) with the presence of a low TIL count (low-TIL). Median OS for high-TIL was not reached (95% CI: 12.2-not reached) versus 8.4 months (95% CI: 5.0-11.6) in the low-TIL group. High-TIL was associated with the overall response rate (ORR) and disease control rate (DCR) (both, $P < .0001$). Among the chemotherapy cohort, 69% were male, 89% were smokers, 86% had performance status ≤1 and 90% had adenocarcinoma histology. High-TIL was seen in 37%. Median PFS and OS were 5.7 months (95% CI: 4.9-6.7) and 11.7 months (95% CI: 9.3-13.0), respectively, with no association with TILs.

Conclusions: High-TIL was associated with favourable outcomes in a real-world immunotherapy cohort of patients with NSCLC, but not with chemotherapy, suggesting that TILs may be useful in selecting patients for immunotherapy.

Keywords: Biomarkers; Immune checkpoint inhibitor; Immunotherapy; Lung cancer; NSCLC; Nivolumab; Non–small cell lung cancer; Prognostic; TIL; Tumor-infiltrating lymphocytes.