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Effectiveness of immune checkpoint inhibitor therapy on bone metastases in non-small-cell lung cancer

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Background: Immune checkpoint inhibitors (ICIs) are standard first-line therapy for patients with advanced metastatic non-small-cell lung cancer (NSCLC). The presence of bone metastases (BoMs) is highly prevalent in patients with metastatic NSCLC and frequently results in intractable pain, pathologic fracture, major surgical interventions, and life-threatening immobility. Patients who have radiological response to ICIs demonstrate meaningful survival improvements, however, there is limited data detailing how BoMs respond to this line of therapy.

Purpose: The primary aim of this study was to compare the therapeutic response of metastatic bone lesions against visceral lesions in patients with NSCLC treated with ICIs. The secondary aim was to evaluate survival in patients treated with ICI with and without BoMs.

Methods: A retrospective, multicenter cohort study was conducted of patients with NSCLC treated with ICI in Alberta, Canada. Patients were identified using the Alberta Cancer Registry and the Alberta Pharmaceutical Information Network from January 2015 to January 2020. The search identified 713 patients with metastatic NSCLC treated with ICIs for potential inclusion. The primary endpoint was the time to progression of bone versus visceral lesions measured with serial imaging studies during ICI treatment. Visceral lesions were categorized by anatomic site as adrenal, brain, liver, lung, lymph node or other intra-abdominal lesions. Response was evaluated retrospectively by analyzing percent changes to the size of visceral lesions according to Response Evaluation Criteria in Solid Tumours version 1.1 and the MD Anderson Criteria was used to assess BoMs. The secondary outcome was to assess the overall survival (OS) amongst patients with and without BoMs.

Results: A total of 573 patients were included in the analysis with a median age of 67.3 years (IQR: 60.6-73.4). ICIs were prescribed as first line therapy in 282 patients (49.6%). All 573 patients had visceral metastases and 243 patients (42.4%) also had BoMs. Median OS for the entire cohort was 8.1 months (95%CI: 6.9-9.1) and median PFS was 3.8 months (95%CI: 3.1-4.4). Median time to BoMs progression was 2.7 months (95%CI: 2.4-3.3), significantly shorter than visceral lesion progression at 3.8 months (95%CI: 3.1-4.4 [p=0.01]). No difference was found between the time to progression of bone, liver and intra-abdominal lesions (p=0.20, p=0.76), however, BoMs demonstrated faster progression than the other sites of disease. Subgroup analysis of patients with high PD-L1 expression (≥50%) demonstrated no significant difference in the time to progression between bone lesions and other extra-thoracic sites of disease. Patients with BoMs had a significantly shorter OS than patients without (6.1 months, 95%CI: 4.9-7.0 versus 10.7 months, 95%CI: 8.3-14.4 [p<0.001]). The presence of BoMs was found to be an independent poor prognostic factor on multivariate analysis in the overall cohort (HR 1.26, 95%CI: 1.05-1.53, p=0.01), however, was not significant in the high PD-L1 expression subgroup (HR: 1.24, 95%CI: 0.92-1.68, p=0.16).

Conclusion: Bone, liver and intra-abdominal lesions demonstrated a significantly shorter time to progression than other visceral lesions, and patients with BoMs had inferior clinical outcomes. PD-L1 status was identified as an important biomarker predicting response, as a subgroup analysis of patients with high PD-L1 expression revealed equivalent responses amongst extra-thoracic sites of disease. As the indications for ICIs continue to increase, understanding how these novel therapies affect BoMs is of critical importance to the multi-disciplinary care of these patients.

Level of Evidence: 3