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Perioperative Outcomes and Tumor-Lymph Node Immune Microenvironment in Neoadjuvant NSCLC: A Real-World Study

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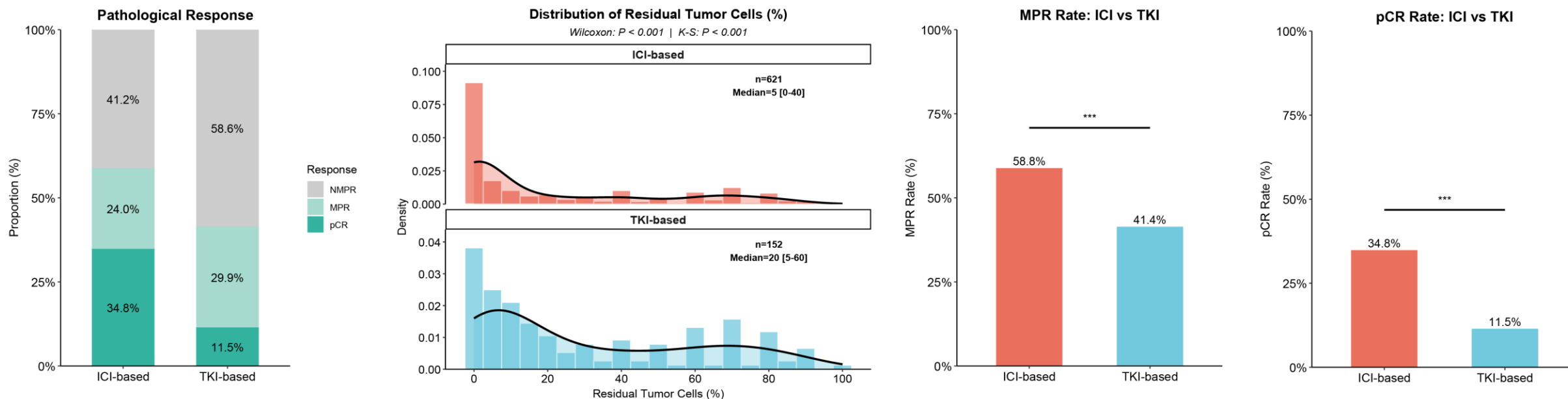
INTRODUCTION

- Neoadjuvant therapy is a key strategy for resectable non-small cell lung cancer (NSCLC).
- Differences between immunotherapy and targeted therapy in pathological response, nodal control, and immune microenvironment remodeling remain insufficiently characterized.
- As central sites of adaptive immunity, lymph nodes play a critical role in treatment response and prognosis, yet most studies have focused primarily on primary tumors.

METHODS

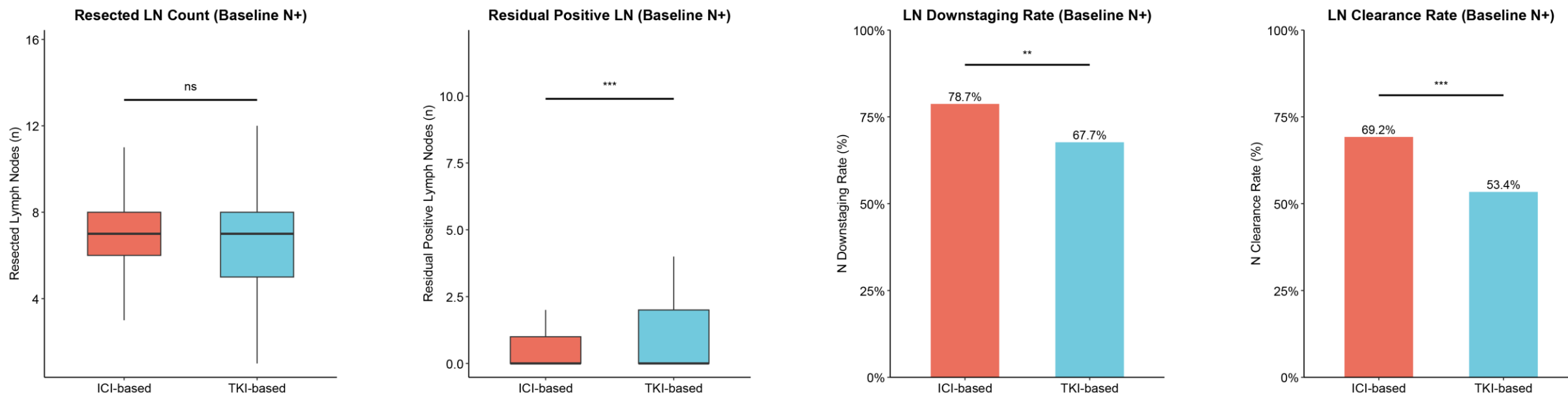
- This two-part study retrospectively included 786 patients with resectable NSCLC who underwent surgery after neoadjuvant immunotherapy or targeted therapy. Pathological response and lymph node outcomes were compared between the two treatment groups.
- In addition, matched tumor and lymph node samples from 23 patients across the immunotherapy, targeted therapy, and treatment-naïve groups were analyzed using single-cell RNA sequencing and T-cell receptor sequencing to characterize immune remodeling.

RESULTS



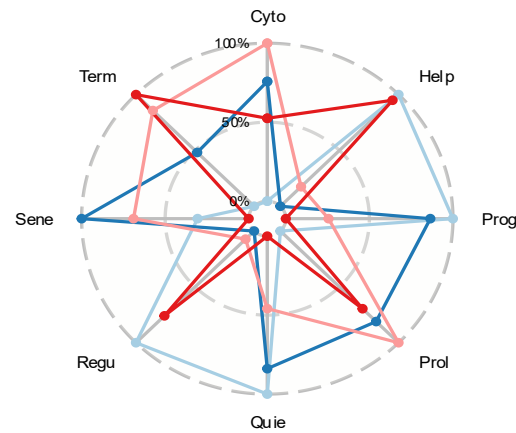
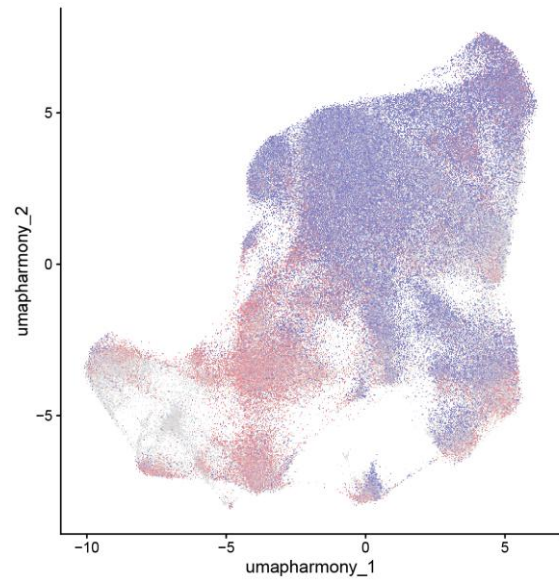
- Patients receiving immunotherapy achieved significantly higher rates of MPR (58.8% vs. 41.4%, $P < 0.001$) and pCR (34.8% vs. 11.5%, $P < 0.001$) than those receiving targeted therapy.

RESULTS

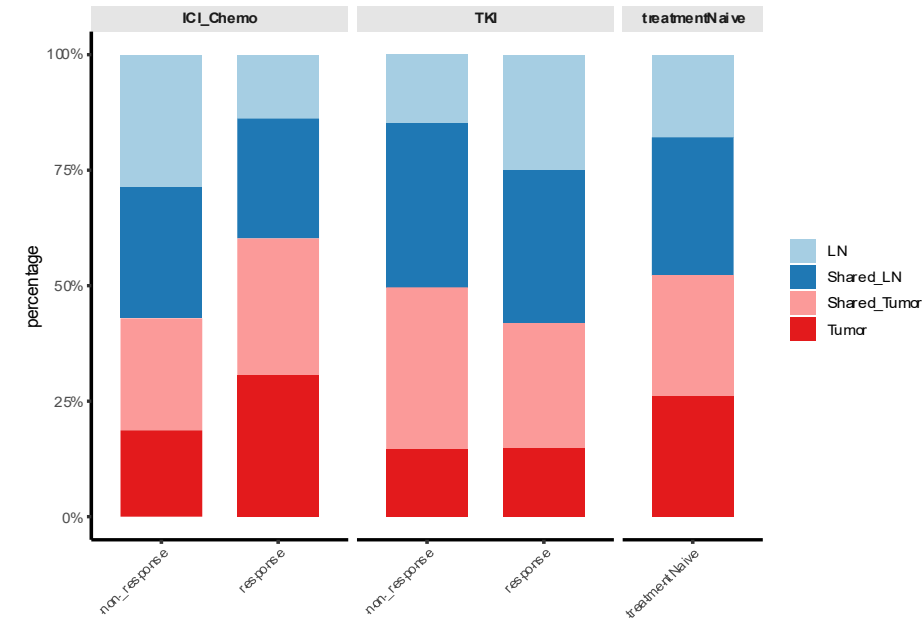


- Among patients with baseline node-positive disease, immunotherapy resulted in improved nodal downstaging (78.7% vs. 67.7%, $P < 0.01$) and clearance (69.2% vs. 53.4%, $P < 0.001$).

RESULTS

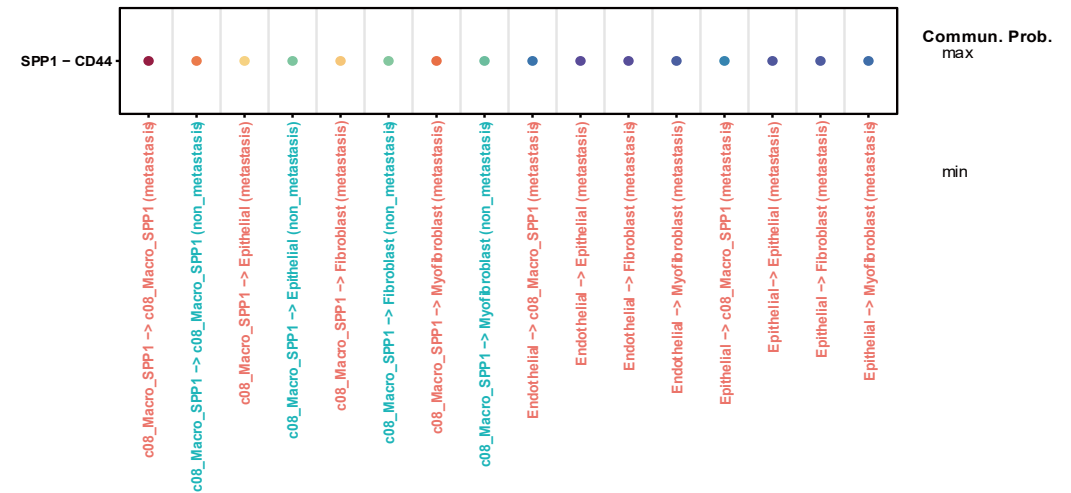
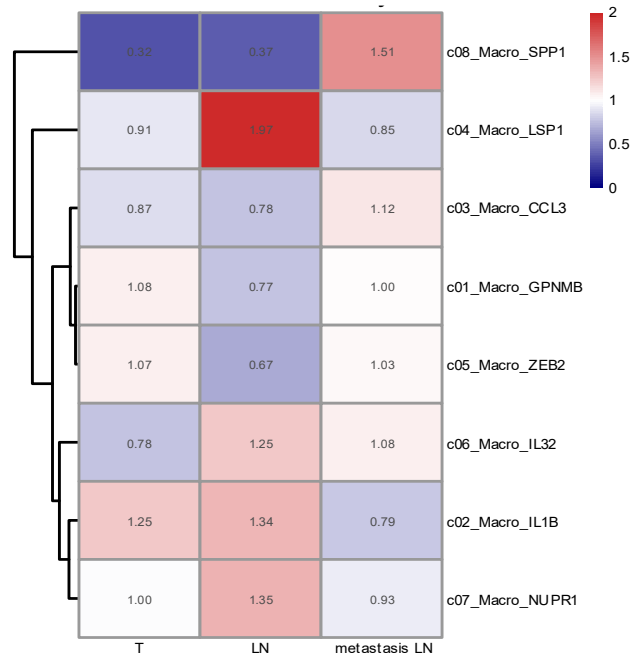


— LN
— Shared_LN
— Shared_Tumor
— Tumor



- T-cell clones showed progressive functional transitions from lymph nodes to tumors. Tumor-biased enrichment was observed only in immunotherapy responders.

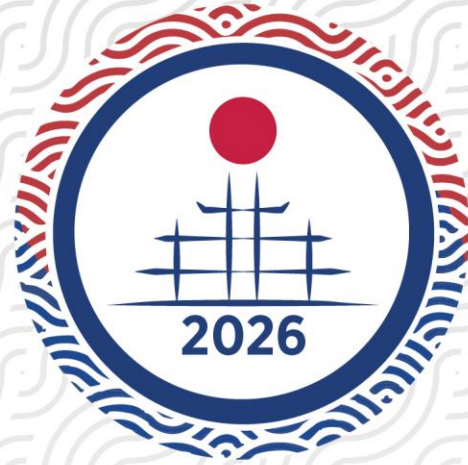
RESULTS



- In targeted therapy, SPP1⁺ macrophages formed stromal networks that supported an immunosuppressive microenvironment.

CONCLUSION

- Immunotherapy achieved superior pathological response and nodal clearance, potentially driven by enhanced mobilization of antitumor T cells from lymph nodes to tumors.
- In contrast, targeted therapy induced an SPP1⁺ macrophage-associated immunosuppressive niche in residual lymph nodes.
- These findings highlight lymph nodes as an important immune reservoir and provide a biological basis for optimizing individualized lymph node management strategies.



Thank You.