Neoadjuvant Immunotherapy in Bladder Cancer: Ushering in a New Era of Treatment – A Systematic Review of Current Evidence

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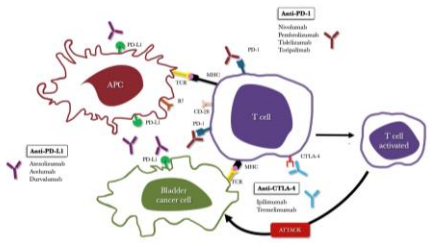
INTRODUCTION

Bladder cancer is a global challenge, being the sixth most common cancer in the USA. Muscle-invasive bladder cancer (MIBC) is diagnosed in 30% of cases and has a high risk of progression. Radical cystectomy with cisplatin-based neoadjuvant chemotherapy improves survival. However, approximately 50% of patients experience disease recurrence within three years. Recent studies have evaluated immune checkpoint inhibitors (ICIs) as an alternative. The NIAGARA trial (phase 3) showed survival benefits with neoadjuvant ICI therapy. These findings suggest a new potential treatment standard for MIBC. This systematic review

Figura 1. Mechanism of action of checkpoint inhibitors targeting the PD-1/PDL-L1 and CTLA-4 pathways.



MATERIALS AND METHODS

This systematic review, conducted in October 2024 and registered on the PROSPERO platform, adhered to PRISMA guidelines. Only prospective studies on neoadjuvant immunotherapy for BC were included. Extracted variables encompassed study design,clinical-pathological characteristics, perioperative, pathological complete response (pCR) rates, overall survival (OS), event-free survival, and immune- and treatment-related adverse events (irAEs and TRAEs).

RESULTS

From 726 records, 35 studies met the inclusion criteria. The highest pCR rate observed was 54%, utilizing durvalumab. Perioperative chemoimmunotherapy with durvalumab plus cisplatin/gemcitabine showed greater overall survival over chemotherapy alone in the NIAGARA trial. The NEMIO trial achieved the highest 12-month OS of 97% using Durvalumab with Tremelimumab and dose-dense MVAC, followed by the AURA trial (95%) and the LCCC1520 trial (91%). At 24 months, the NEBULA trial reported 100% OS with three doses of Atezolizumab, while PrECOG PrE0807 reached 89% OS with Nivolumab and Lirilumab. The highest rates of grade 3 and 4 irAEs were reported with Nivolumab combined with Ipilimumab (54%) and Durvalumab combined with Tremelimumab (64%). The most common grade 3/4 irAEs were hepatitis (2%–27%), kidney injury (2%–100%), and skin rash (1.1%–41%). Grade 3/4 TRAEs were comparable between ICI and chemotherapy groups.

CONCLUSIONS

Neoadjuvant immunotherapy for BC has shown promising efficacy and a manageable adverse event profile. However, financial toxicity, the absence of predictive biomarkers, and the risk of significant irAEs remain challenges. Future research should focus on optimizing treatment protocols and biomarker identification to enhance safety and response.