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INPLASY

Prognostic Significance of Circulating Tumor DNA in Urothelial Carcinoma Patients Undergoing Immune Checkpoint Inhibitor Therapy: A Systematic Review and Meta-Analysis

INPLASY202520058

doi: 10.37766/inplasy2025.2.0058

Received: 10 February 2025

Published: 10 February 2025

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202520058

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 February 2025 and was last updated on 10 February 2025.

INTRODUCTION

Review question / Objective This meta-analysis reveals a significant association between detectable ctDNA and its dynamic changes with OS and PFS/DFS in UC patients undergoing ICI therapy. Consequently, ctDNA serves as a valuable tool for diagnostic assessment and patient stratification before treatment, as well as for evaluating therapeutic response and tracking disease progression.

Rationale Circulating tumor DNA (ctDNA) has emerged as a novel biomarker with the advantages of being non-invasive and enabling dynamic monitoring, providing significant clinical insights into the prognosis and management of malignancies. However, its prognostic role in patients with urothelial carcinoma (UC) receiving immune checkpoint inhibitors (ICI) remains controversial. This study aims to systematically review and perform a meta-analysis to evaluate the prognostic significance of ctDNA levels in this specific patient population.

Condition being studied We conducted a comprehensive search of the PubMed, Cochrane Library, CNKI, and EMBASE databases to include studies published up to November 14, 2024, assessing the prognostic value of ctDNA in UC patients treated with ICI. Fixed-effects or random-effects models were used to evaluate the association between ctDNA levels and overall survival (OS), progression-free survival (PFS)/ disease-free survival (DFS). Funnel plots, Begg's test, and Egger's test were employed to assess publication bias.

METHODS

Search strategy To investigate the predictive value of ctDNA in UC patients treated with ICI, we used the following keywords: "Urothelial Carcinoma," "Bladder Neoplasms," "Transitional

Cell Carcinoma," "Urinary Tract Neoplasms," "Urothelial cancer," "Bladder cancer," "Transitional cell carcinoma of the bladder," "Urothelial carcinoma prognosis," as well as "ctDNA," "circulating tumor DNA," "PD-L1 inhibitors," "immune checkpoint inhibitors," "programmed cell death ligand-1 inhibitors," and "immunotherapy." In addition to using free-text terms and Medical Subject Headings (MeSH) for searching titles and abstracts.

Participant or population Urothelial carcinoma (UC) patients receiving immune checkpoint inhibitor (ICI) therapy.

Intervention ctDNA levels.

Comparator The ctDNA test was negative.

Study designs to be included OS and PFS/DF.

Eligibility criteria (1) Studies focusing solely on cfDNA data without providing outcome data;(2) Case reports, conference abstracts, animal studies, or review articles;(3) Studies lacking sufficient data to estimate HR and 95% CI;(4) Duplicate publications of data.

Information sources PubMed, Cochrane Library, CNKI, and EMBASEdatabases.

Main outcome(s) OS and PFS/DFS.

Quality assessment / Risk of bias analysis Funnel plots, Egger's linear regression, and Begg's regression.

Strategy of data synthesis Two independent researchers extracted relevant data from eligible studies, and any discrepancies were resolved through discussion or consultation with a third researcher. The extracted data included the first author's name, publication year, study location, study design, sample size, mean or median patient age, cancer stage, treatment methods, detection techniques, timing of sample collection, target genes, median follow-up period (in months), and survival analysis (including hazard ratios and 95% confidence intervals for OS and PFS/DFS). Study quality was assessed using the Newcastle-Ottawa Scale (NOS), which evaluates three key domains: selection (0–4 points), comparability (0–2 points), and outcome assessment (0–3 points). Each researcher independently scored the eight questions across these domains, with a total score range of 0 to 9. Studies scoring more than 6 points were classified as high quality[25].

Subgroup analysis Country ,Sample size,Median, age, Gender (M/F), ICI, Detection, methods.

Sensitivity analysis Sensitivity analysis demonstrated that no individual study significantly impacted the effect size of the association between ctDNA and OS or PFS/DFS in UC patients before and after ICI therapy. The removal of any single study did not lead to substantial changes, reinforcing the reliability of the study's findings.

Country(ies) involved China.

Keywords urothelial carcinoma；circulating tumor DNA；immune checkpoint inhibitors；overall survival；progression-free survival.

Contributions of each author

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