International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

INPLASY202630015

doi: 10.37766/inplasy2026.3.0015

Received: 6 March 2026

Published: 6 March 2026

Predictive Value of PD-L1 Expression and dMMR/pMMR Status for Immune Checkpoint Inhibitor Combined with Chemotherapy in Advanced/Recurrent Endometrial Cancer: A Meta-Analysis

Yang, YH; Lan, LF; Tang, ZY; Yao, XW; Liao, HM.

Corresponding author:
Yihua Yang

workyyh@163.com

Author Affiliation:
Guangxi Reproductive Medical Center, the First Affiliated Hospital of Guangxi Medical University.

ADMINISTRATIVE INFORMATION

Support - This work was supported by the National Natural Science Foundation of China (Nos.82571880 and 82360308), the Guangxi Medical University Training Program for Distinguished Young Scholars provided funding for this work.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202630015

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 6 March 2026 and was last updated on 6 March 2026.

INTRODUCTION

Review question / Objective To systematically evaluate the predictive value of PD-L1 expression and dMMR/pMMR status for the efficacy of immune checkpoint inhibitors (ICIs) combined with chemotherapy in patients with advanced/recurrent endometrial cancer, focusing on progression-free survival (PFS) and overall survival (OS).

Rationale Advanced/recurrent endometrial cancer has limited treatment options and poor prognosis. ICIs combined with chemotherapy have emerged as a promising therapeutic strategy, but their efficacy varies among patients. PD-L1 expression and dMMR/pMMR status are potential biomarkers for ICI response, but their predictive value in combination with chemotherapy remains unclear. This systematic review aims to synthesize evidence from RCTs to clarify the predictive role of these biomarkers, providing a basis for personalized treatment decisions and improving patient outcomes.

Condition being studied Advanced/recurrent endometrial cancer: A malignant tumor originating from the endometrium, with advanced stage (FIGO stage III/IV) or recurrent disease after initial treatment. It is associated with high mortality and limited treatment options, and the prognosis is poor.

METHODS

Participant or population Patients with advanced/recurrent endometrial cancer (FIGO stage III/IV or recurrent disease after initial treatment).

Intervention Immune checkpoint inhibitors (ICIs) combined with chemotherapy.

Comparator Chemotherapy alone.

Study designs to be included Progression-free survival (PFS), overall survival (OS).

Eligibility criteria
Inclusion criteria:
1. Studies published in English.
2.RCTs comparing ICIs + chemotherapy vs. chemotherapy alone in advanced/recurrent endometrial cancer.
3.Studies reporting PD-L1 expression and/or dMMR/pMMR status.
4.Studies providing data on progression-free survival (PFS) and/or overall survival (OS).
Exclusion criteria:
1.Non-RCTs (e.g., observational studies, case reports).
2. Studies focusing on neoadjuvant/adjuvant therapy.
3.Studies without data on PD-L1 expression or dMMR/pMMR status.
4.Studies with overlapping patient populations.

Information sources Electronic databases: PubMed, Embase, Cochrane Library, Web of Science (from inception to October 2025).
Additional sources: Clinical trial registries (e.g., ClinicalTrials.gov), conference proceedings, and reference lists of included studies.

Main outcome(s) 1.Progression-free survival (PFS): Defined as the time from randomization to disease progression or death, measured using hazard ratios (HR).
2. Overall survival (OS): Defined as the time from randomization to death from any cause, measured using hazard ratios (HR).

Additional outcome(s) 1.Objective response rate (ORR): Defined as the proportion of patients achieving a complete or partial response according to RECIST criteria, reported as risk ratios (RR). 2. Treatment-related adverse events (TRAEs): Grade ≥3 adverse events related to treatment, reported as risk ratios (RR).

Data management Two reviewers will independently extract data using a standardized Excel form, including study design, patient demographics, biomarker status, and outcomes. Discrepancies will be resolved by consensus or a third reviewer. All data will be double-checked for accuracy before analysis.1. Two reviewers will independently extract data using a standardized form in Excel, including study characteristics, patient demographics, biomarker status, and outcome data.
2.Discrepancies will be resolved by consensus or consultation with a third reviewer.
3.Data will be double-checked for accuracy before analysis.

Quality assessment / Risk of bias analysis The risk of bias in included RCTs will be assessed using the Cochrane RoB 2 tool, evaluating randomization, allocation concealment, blinding, incomplete outcome data, selective reporting, and other biases. Each study will be rated as “low risk,” “some concerns,” or “high risk” of bias.

Strategy of data synthesis Data synthesis will be performed using Review Manager 5.4. Hazard ratios (HR) with 95% confidence intervals (CI) will be used to pool time-to-event outcomes (PFS, OS), and risk ratios (RR) with 95% CI for dichotomous outcomes (ORR, TRAEs). A random-effects model will be applied if significant heterogeneity ($I^2 > 50\%$) is detected; otherwise, a fixed-effects model will be used. Heterogeneity will be quantified using the I^2 statistic and Cochran’s Q test.

Subgroup analysis Pre-specified subgroup analyses will be conducted to explore the predictive value of biomarkers: – dMMR vs. pMMR status – PD-L1 positive vs. PD-L1 negative expression – Different types of immune checkpoint inhibitors (e.g., anti-PD-1 vs.anti-PD-L1).

Sensitivity analysis Sensitivity analyses will be performed to assess the robustness of the results:
1.Excluding studies with high risk of bias.
2.Excluding small sample size studies ($n < 100$).
3.Using fixed-effects instead of random-effects model.
4.Excluding non-peer-reviewed studies (e.g., conference abstracts).

Language restriction Only studies published in English will beincluded.

Country(ies) involved The study is being carried out in China.

Other relevant information This systematic review will focus on the predictive value of PD-L1 expression and dMMR/pMMR status for the efficacy of immune checkpoint inhibitors combined with chemotherapy in patients with advanced/recurrent endometrial cancer. The findings will be used to inform clinical decision-making and future research directions.

Keywords endometrial cancer; immune checkpoint inhibitor; PD-L1; deficient mismatch

repair (dMMR); proficient mismatch repair (pMMR); meta-analysis.

Dissemination plans The results of this systematic review will be submitted for publication in a peer-reviewed journal and presented at relevant academic conferences. The findings will also be shared with clinical guidelines committees to support evidence-based practice.

Contributions of each author

Author 1 - Yi-hua Yang - Yi-hua Yang coordinated the data collection and conceived the original idea. Li-fang Lan and Hong-mei Liao provided statistical analysis, Li-fang Lan wrote the manuscript, all other Authors facilitated data collection and critically reviewed the manuscript for important intellectual contents. Yi-hua Yang and Li-fang Lan accept direct responsibility for the manuscript.
Email: workyyh@163.com
Author 2 - Li-fang Lan - Li-fang Lan provided statistical analysis and wrote the manuscript.
Email: 354305019@qq.com
Author 3 - Zhuang-yan Tang - Zhuang-yan Tang facilitated data collection and critically reviewed the manuscript for important intellectual contents.
Email: 610915884@qq.com
Author 4 - Xiong-wei Yao - Xiong-wei Yao facilitated data collection and critically reviewed the manuscript for important intellectual contents.
Email: 1034219149@qq.com
Author 5 - Hong-mei Liao - Hong-mei Liao provided statistical analysis.
Email: lhm10047@163.com