INPLASY PROTOCOL

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Immune Checkpoint Inhibitors in Pretreated Metastatic Endometrial Cancer

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Review question / Objective: **Efficacy and safety of immune checkpoint inhibitors alone or in combination with tyrosine kinase inhibitors in patients with pretreated advanced, persistent, or recurrent metastatic endometrial cancer.**
Condition being studied: **Advanced, persistent, or recurrent metastatic endometrial cancer.**
Study designs to be included: **Non-randomized studies of monotherapy in populations selected for relevant biomarkers such as MMR, microsatellite stability, and PD-L1 expression status and randomized trials of ICI combinations in unselected patients.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 January 2023 and was last updated on 13 January 2023 (registration number INPLASY202310038).

INTRODUCTION

Review question / Objective: **Efficacy and safety of immune checkpoint inhibitors alone or in combination with tyrosine kinase inhibitors in patients with pretreated advanced, persistent, or recurrent metastatic endometrial cancer.**

Rationale: **Endometrial cancer is a common malignancy and recurrences can be fatal. Although platinum-pretreated endometrial tumors are commonly treated with anthracyclines and taxanes, there is no current standard of care. Both immune checkpoint inhibitors (ICIs) and tyrosine kinase inhibitors (TKIs) have been extensively assessed in this setting,**

including tumors selected for DNA mismatch repair (MMR)/microsatellite instability (MSI) and programmed death-ligand 1 (PD-L1) expression status.

Condition being studied: Advanced, persistent, or recurrent metastatic endometrial cancer.

METHODS

Search strategy: A search of published and presented literature was conducted to identify potentially practice-changing studies with outcomes assessing ICIs in pretreated metastatic endometrial cancer. Potentially practice-changing investigations included non-randomized studies of monotherapy in populations selected for relevant biomarkers such as MMR, microsatellite stability, and PD-L1 expression status and randomized trials of ICI combinations in unselected patients. PubMed (all time to February 2, 2022), the proceedings from the 2020 and 2021 American Society of Clinical Oncology (ASCO), the European Society for Medical Oncology (ESMO) annual meetings and the 2020, 2021 and 2022 Society of Gynecologic Oncology (SGO) annual meeting were searched using the key search terms ("immune checkpoint inhibitors") AND "endometrial cancer" AND "advanced" AND "phase I-III" OR respective aliases. A supplemental bibliographic search of review articles and pooled/meta-analyses was also conducted. In addition, directed searches were performed after the database search cut-off date to ensure that the most up-to-date reports of eligible studies were considered.

Participant or population: Patients with petreated advanced, persistent, or recurrent metastatic endometrial cancer.

Intervention: Immune checkpoint inhibitors alone or in combination with tyrosine kinase inhibitors.

Comparator: Any.

Study designs to be included: Non-randomized studies of monotherapy in populations selected for relevant biomarkers such as MMR, microsatellite stability, and PD-L1 expression status and randomized trials of ICI combinations in unselected patients.

Eligibility criteria: None.

Information sources: PubMed/MEDLINE; Conference abstract databases (ASCO, ESMO, SGO).

Main outcome(s): Efficacy measures: overall survival, progression-free survival, duration of response and overall response rate.

Additional outcome(s): Safety, adverse event profile.

Quality assessment / Risk of bias analysis: Descriptive.

Strategy of data synthesis: Tabulation of efficacy and safety outcomes. Plotting of select adverse event data.

Subgroup analysis: Available subgroup analyses by MMR, MSI or PD-(L)1 status were assessed.

Sensitivity analysis: None.

Language restriction: English.

Country(ies) involved: Canada.

Keywords: endometrial cancer, advanced, metastatic, pretreated, immune checkpoint inhibitors, biomarker selection.

Contributions of each author:
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Author 2 - Neesha C. Dhani.
Author 3 - Prafull Ghatage.
Author 4 - Deanna McLeod.
Author 5 - Vanessa Samouëlian.
Author 6 - Stephen A. Welch.
Author 7 - Alon D. Altman.

Conflicts of interest: Ion Altman reports grants AstraZeneca, Pfizer, Clovis, CCMB foundation, Canadian Clinical Trials Group, Merck, and GSK, outside the submitted

work. He has also received advisory role for AstraZeneca, Merck and GSK and speaker fees from AstraZeneca and Merck.
Neesha C. Dhani has nothing to disclose.
Prafull Ghatage has served in a consultancy or advisory role for Eisai, AstraZeneca and GSK and has received research funding from AstraZeneca.
Deanna McLeod has nothing to disclose.
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