

INDIRECT TREATMENT COMPARISON OF ANTI-PD-1/L1 PLUS CHEMOTHERAPY IN ADVANCED OR RECURRENT ENDOMETRIAL CANCER WITH PROFICIENT MISMATCH REPAIR

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BACKGROUND AND IMPORTANCE

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In the setting of recurrent or advanced endometrial cancer (EC) with proficient mismatch repair (pMMR), several immune checkpoint inhibitors targeting PD-1 or PD-L1 are being investigated in combination with platinum-based chemotherapy (ChT). The absence of direct comparative studies limits informed decision-making regarding their relative clinical benefit.

AIM AND OBJECTIVES

To explore the comparative efficacy of immunotherapy-based combinations with chemotherapy – specifically those including pembrolizumab, dostarlimab, durvalumab, durvalumab plus olaparib, and atezolizumab–, in the treatment of pMMR EC, through an adjusted indirect treatment comparison (ITC), with the goal of assessing their potential equivalence as equivalent therapeutic alternatives (ETAs).

MATERIALS AND METHODS:

Systematic bibliographic search
PubMed for Clinical trials:
Indirect Comparison

Bucher method

Dostarlimab + ChT selected for showing the best numerical HR value among those that add a single drug to chemotherapy

Inclusion criteria:

-phase II/III
-randomised

-similar populations, comparator, follow-up period and EC definition.

Efficacy endpoint: Overall survival (OS) and Progression Free Survival (PFS) (Both expressed as Hazard Ratio (H.R))
 Δ : 0.65-1.54

(In accordance with the ETA guideline and the ESMO-MCBS (form 2b))

RESULTS/KEY FINDINGS

Five randomized CTs were finally selected, one per treatment

The rest were not included in the ITC because they did not meet the inclusion criteria

Treatment	Progression Free Survival HR (95% CI)	Overall Survival HR (95% CI)
Dostarlimab + ChT	Reference	Reference
Pembrolizumab + ChT	1,027 (0,741 – 1,423)	0,912 (0,578 – 1,441)
Atezolizumab + ChT	0,826 (0,587 – 1,162)	0,73 (0,463 – 1,151)
Durvalumab + ChT	0,987 (0,698 – 1,397)	0,802 (0,49 – 1,313)
Durvalumab+ ChT + Olaparib	1,101 (0,7 – 1,733)	1,058 (0,636 – 1,761)

CONCLUSION AND RELEVANCE

- No clinically or statistically meaningful differences were observed between the evaluated PD-1/PD-L1 inhibitor combinations in patients with pMMR advanced or recurrent endometrial cancer.
- Durvalumab + ChT + olaparib showed a higher toxicity burden without demonstrating superiority over the other treatment options which only add one drug to chemotherapy, suggesting limited added clinical value.