

EFFICACY OF COMBINATION OF ANTI-PD-1/L1 AGENTS WITH CHEMOTHERAPY IN ADVANCED OR RECURRENT ENDOMETRIAL CANCER WITH DEFICIENT MISMATCH REPAIR: AN INDIRECT TREATMENT COMPARISON

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BACKGROUND AND IMPORTANCE

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Several drugs targeting PD-1 or PD-L1, in combination with platinum-based chemotherapy (ChT), are under evaluation for the treatment of recurrent or advanced endometrial cancer (EC) with deficient mismatch repair (dMMR). However, there are currently no head-to-head trials comparing these regimens, which limits the ability to establish their therapeutic positioning.

AIM AND OBJECTIVES

To evaluate whether pembrolizumab, dostarlimab, durvalumab, durvalumab plus olaparib, and atezolizumab –each in combination with chemotherapy– can be considered equivalent therapeutic alternatives (ETAs) for patients with advanced or recurrent dMMR EC, through an adjusted indirect treatment comparison (ITC).

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 identified

Treatment	Progression Free Survival H.R (95% CI)	Overall Survival H.R (95% CI)
Dostarlimab + ChT	Reference	Reference
Pembrolizumab + ChT	0,8 (0,381 – 1,678)	0,526 (0,172 – 1,608)
Atezolizumab + ChT	0,778 (0,379 – 1,597)	0,73 (0,255 – 2,1)
Durvalumab + ChT	0,667 (0,284 – 1,565)	0,882 (0,255 – 3,054)
Durvalumab+ ChT + Olaparib	0,683 (0,293 – 1,593)	1,071 (0,297 – 3,865)

CONCLUSION AND RELEVANCE

- No statistically or clinically significant differences among the therapies.
- Pembrolizumab showed clinically relevant difference compared to the reference treatment, but no statistically significant improvement in OS in the clinical trial.
- Durvalumab plus olaparib (only therapy that add two drugs to ChT) was consequently associated with higher toxicity, without providing significant statistical or clinical benefits over the other therapies.