INDIRECT COMPARISON OF PEMBROLIZUMAB PLUS ENFORTUMAB VEDOTIN AND NIVOLUMAB PLUS GEMCITABINE-CISPLATIN INUROTHELIAL CARCINOMA

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Background and importance

The European Medicines Agency recently approved new treatments such as enfortumab vedotin plus pembrolizumab (EV-Pembrolizumab) and nivolumab in combination with gemcitabine-cisplatin (Nivolumab-CT) for urothelial carcinoma (UC).
Indirect comparisons between these regimens might support the therapeutic positioning of the schemes in this clinical context.

Aim and objectives

To evaluate whether EV-Pembrolizumab and Nivolumab-CT are equivalent therapeutic alternatives (ETA) in untreated carcinoma patients with UC through an indirect comparison.

Material and methods

- A bibliographic search was conducted in PubMed® database until September-2025.
- Inclusion criteria: phase III, randomised clinical trials (RCTs), untreated patients with unresectable locally advanced or metastatic UC.
- Exclusion criteria: RCTs without a comparator common to alternatives considered.
- Overall survival (OS) was selected as the main variable.
- ESMO-Magnitude of Clinical Benefit Scale was used to define the maximum acceptable difference as a clinical non-inferiority standard Delta (Δ).
- ETA guidelines were applied.

Results

Δ = 0.70 – 1.43

Bucher method

EV-302 trial: EV-Pembrolizumab vs chemotherapy (HR 0.47; 95% Confidence Interval 0.38-0.58; p <0.001)
CheckMate 901 trial assessed Nivolumab-CT vs chemotherapy (HR 0.78; 95% CI 0.63-0.96; p=0.02).
Common comparator: chemotherapy (gemcitabine plus cisplatin)
Limitations identified in the RCTs: follow-up (17.2 months in EV-302 trial and 33.6 months in CheckMate 901 trial), patients over 65 years of age (67.47% and 49.70%, respectively) and metastatic stage (95.20% and 85.90%, of patients).

Indirect comparison
HR 0.60
(95% CI, 0.45-0.81; p=0.0009)

ATE guide: degree of equivalence F (probably relevant difference), since statistically significant and clinically relevant differences were found (most of the 95% CI is outside the equivalence interval).

Conclusion and relevance

- Our indirect comparison provide comparative efficacy data between among therapeutic alternatives for untreated patients with unresectable locally advanced or metastatic UC.
- EV-Pembrolizumab and Nivolumab-CT showed clinically relevant differences and could not be considered ETA.

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