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First-Line or Maintenance Immune Checkpoint Inhibitors in Older Patients with Advanced Urothelial Carcinoma: A Systematic Review and Meta-Analysis

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Background & Objective

Evidence on immune-based treatment in older patients with advanced urothelial carcinoma is limited, as age-specific outcomes are usually exploratory. We assessed the efficacy of first-line and maintenance immune-based strategies in patients aged ≥65 years.

Methods

PubMed/MEDLINE, Embase, Cochrane and major oncology congresses were searched from Jan 2015 to May 2026 for randomized trials reporting age-specific hazard ratios (HRs) for overall survival (OS) or progression-free survival (PFS). The primary analysis pooled first-line combination regimens versus platinum-based chemotherapy using random-effects models. For maintenance treatment, an anchored Bucher indirect comparison used avelumab as the shared treatment node, evaluating PFS as the primary endpoint.

Results

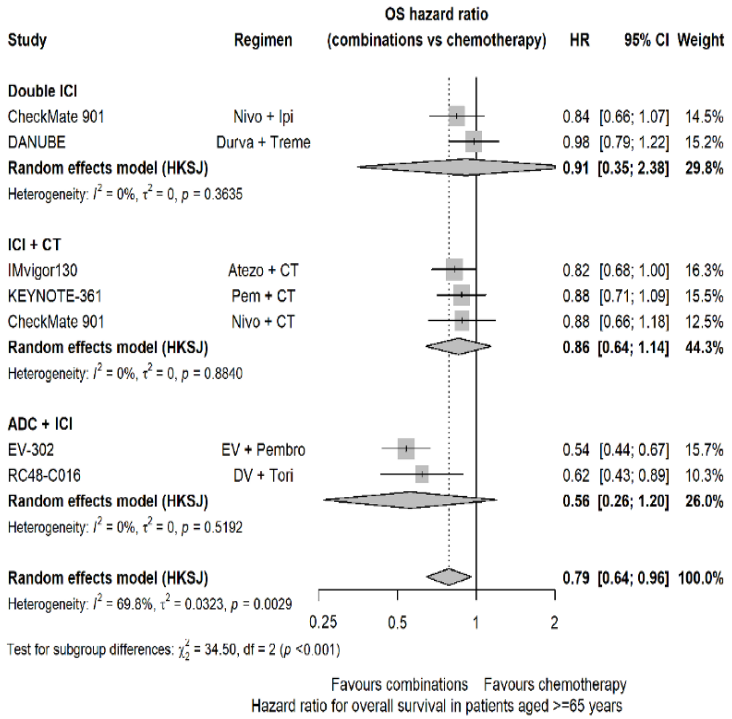
Six first-line randomized trials were identified, representing 2,678 patients aged ≥65 years across experimental and control groups (exploratory age-subgroup analyses).

Combination first-line regimens improved OS versus chemotherapy: HR 0.79 (95% CI 0.64–0.96), with substantial heterogeneity (I^2=69.8%; p=0.0029).

- ADC + immunotherapy: HR 0.56 (95% CI 0.26–1.20)
- ICI + chemotherapy: HR 0.86 (95% CI 0.64–1.14)
- Dual ICI combinations: HR 0.91 (95% CI 0.35–2.38)

ICI monotherapy showed no OS benefit (pembrolizumab HR 1.15, 95% CI 0.84–1.59; atezolizumab HR 0.98, 95% CI 0.79–1.21).

In maintenance, avelumab improved PFS vs. best supportive care (HR 0.46, 95% CI 0.37–0.57). Indirect comparison: avelumab + sacituzumab govitecan vs. best supportive care, HR 0.31 (95% CI 0.18–0.54; p<0.0001).



Pooled OS hazard ratio for first-line treatment combinations vs. chemotherapy in patients aged ≥65 years, by regimen category.

Conclusions In clinically fit older patients, combination-based first-line and maintenance treatment were associated with improved OS and PFS, while ICI monotherapy showed no survival benefit — arguing against routine de-escalation on the basis of age alone. Further age-specific efficacy, safety, and geriatric assessment data are needed to guide treatment selection.