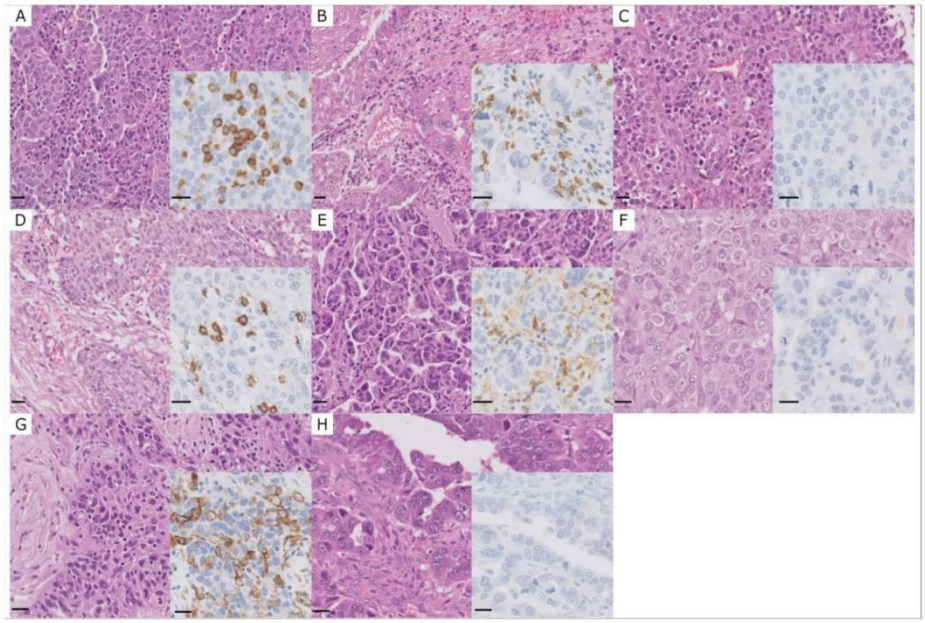

Figure 3 Histopathological and immunohistochemical analysis of the immune microenvironment and immune marker expression in advanced ovarian cancer tissue (Adopted from Pizarro et al., 2023)

Image caption: (A) Case with high iTILs CD8+, Inset: CD8 immunohistochemistry; (B) Case with high sTILs CD8+; Inset: CD8 immunohistochemistry; (C) Case with no CD8+lymphocytes; Inset: CD8 immunohistochemistry; (D) Case with high iTILs CD4+; Inset: CD4 immunohistochemistry; (E) Case with high sTILs CD4+; Inset: CD4 immunohistochemistry; (F) Case with no CD4+lymphocytes; Inset: CD4 immunohistochemistry; (G) PD-L1-positive case; Inset: PD-L1 immunohistochemistry; (H) PD-L1-negative case; Inset: PD-L1 immunohistochemistry; Scale bar 20 μm (Adopted from Pizarro et al., 2023)

6.2 Comparative efficacy of different treatment strategies

Comparative analyses across monotherapy, dual checkpoint blockade, and multi-drug combinations reveal important differences in clinical efficacy. Pooled clinical experience indicates that single-agent PD-1/PD-L1 or CTLA-4 blockade in unselected advanced ovarian cancer yields modest objective response rates and no survival improvement over historical chemotherapy benchmarks, positioning monotherapy primarily as an investigational option for highly selected biomarker-defined subgroups (Ghisoni et al., 2024). In contrast, dual PD-1/CTLA-4 blockade (such as nivolumab plus ipilimumab or durvalumab plus tremelimumab) has shown higher response rates and more durable responses, particularly in recurrent and platinum-resistant disease, although at the expense of greater immune-related toxicity and with notable heterogeneity across histologic subtypes (Li et al., 2025).

Combination regimens that layer ICIs onto established standards, chemotherapy, bevacizumab, and PARP inhibitors, have emerged as the most clinically mature strategies and allow direct comparison with non-immunotherapy controls. The FIRST/ENGOT-OV44 phase III trial demonstrated that adding dostarlimab to first-line platinum-based chemotherapy followed by dostarlimab-niraparib maintenance resulted in a statistically significant but clinically modest PFS extension (20.6 vs. 19.2 months; HR 0.85) without OS improvement, and with toxicity profiles consistent with the component agents (Hardy-Bessard et al., 2025). Similarly, a systematic review of CPI incorporation into epithelial ovarian cancer showed that triplet maintenance with bevacizumab, olaparib, and durvalumab prolonged PFS compared with bevacizumab alone in BRCA-wild-type patients, whereas CPI addition to standard therapy in platinum-sensitive and platinum-resistant settings generally failed to improve outcomes (Bogani et al., 2025). Collectively, these data suggest a gradient of efficacy from least with monotherapy, intermediate with dual checkpoint blockade, and modest but most clinically relevant benefit with carefully selected multi-agent combinations.

6.3 Survival benefits and current evidence

From a survival standpoint, the aggregate evidence indicates that immunotherapy has not yet replicated in ovarian cancer the transformative OS gains seen in melanoma or lung cancer. The meta-analysis of randomized