pseudoprogression rates vary modestly by tumor type, definition, and response criteria, and are somewhat more common with PD-1/PD-L1 monotherapy than with other ICI regimens (Park et al., 2020). Conversely, hyperprogression and dissociated responses have also been described, complicating decisions about treatment beyond progression. In practice, most guidelines still recommend RECIST-based assessment, reserving treatment continuation after apparent progression for carefully selected, clinically stable patients, ideally supported by confirmatory imaging consistent with immune-related criteria.

5.3 Biomarkers for efficacy evaluation: PD-L1, TMB, BRCA and HRD

Biomarker-driven patient selection is central to improving the risk-benefit profile of immunotherapy in advanced ovarian cancer, with PD-L1 expression, tumor mutational burden (TMB), and homologous recombination-related markers (including BRCA1/2) among the most widely studied. Across cancer types, large genomic datasets indicate that PD-L1 expression and TMB are largely independent biomarkers with limited correlation at the tumor level, and each exerts non-overlapping effects on ICI response rates. In ovarian cancer, PD-L1 positivity on tumor or immune cells is relatively common and has been associated with an inflamed microenvironment, but clinical trials such as KEYNOTE-100 and others have shown only modest enrichment of pembrolizumab responses at higher PD-L1 combined positive scores, with overall ORR remaining low (Matulonis et al., 2019). Global analyses of ICI trials therefore support PD-L1 as an imperfect, context-dependent biomarker whose predictive value in ovarian cancer is weaker than in highly ICI-sensitive tumors like non-small cell lung cancer.

TMB and BRCA/HRD status provide additional, but also imperfect, layers of prognostic and predictive information. Mechanistically, BRCA1/2-mutated high-grade serous ovarian cancers exhibit higher neoantigen loads, increased $CD8^+$ T-cell infiltration, and elevated PD-1/PD-L1 expression in tumor-associated immune cells, and these features correlate with improved survival and a more immunogenic phenotype. However, biomarker analyses from the phase III IMagyn050 trial demonstrated that most newly diagnosed ovarian cancers have low TMB regardless of BRCA or HRD status, that TMB ≥10 mut/Mb is rare, and that neither BRCA1/2 mutations nor HRD predicted enhanced benefit from adding atezolizumab to bevacizumab-chemotherapy. Collectively, current evidence suggests that PD-L1, TMB, and BRCA/HRD primarily function as prognostic or weakly predictive markers in ovarian cancer; meaningful efficacy evaluation and individualized immunotherapy strategies will likely require composite algorithms integrating multiple biomarkers with tumor-infiltrating lymphocytes, gene-expression signatures, and clinical features (Figure 3) (Morand et al., 2021; Pizarro et al., 2023).

6 Clinical Progress and Efficacy Analysis

6.1 Major recent clinical trial outcomes

Over the past decade, multiple phase I–III trials have evaluated PD-1/PD-L1 and CTLA-4 inhibitors in advanced ovarian cancer, either as monotherapy or in combination with chemotherapy, anti-angiogenic agents, or PARP inhibitors. A comprehensive review of 20 clinical studies (16 phase I/II and 4 phase III) confirmed that single-agent ICIs achieved low response rates and did not improve survival, with several trials halted early due to toxicity or lack of efficacy. In contrast, combination regimens, particularly those integrating ICIs with platinum-based chemotherapy, bevacizumab, or PARP inhibitors, generally produced higher objective response rates and longer progression-free survival (PFS), albeit at the cost of increased treatment-related adverse events.

Large randomized phase III programs have further clarified the magnitude of benefit from immune-based strategies. A recent meta-analysis of eight phase II–III randomized trials including 6205 patients found that adding PD-1/PD-L1 inhibitors to chemotherapy or placebo did not significantly improve PFS in either first-line or recurrent settings (overall HR 1.02), and subgroup analyses by PD-L1 status also failed to show a clinically meaningful advantage (Vida et al., 2025). Consistently, a systematic review of seven phase III trials in newly diagnosed and recurrent epithelial ovarian cancer concluded that PD-L1 inhibitor monotherapy lacked efficacy in the frontline setting, while CPI-based combinations delivered, at best, modest PFS gains without clear overall survival (OS) benefit to date (Bogani et al., 2025). These results underscore that, although immunotherapy is firmly established in many solid tumors, its clinical impact in ovarian cancer remains constrained and highly regimen-dependent.