and increase neoantigen load and type I interferon signaling, providing a rationale for PARP-ICI combinations that have demonstrated encouraging activity, especially in BRCA-mutated or homologous-recombination-deficient disease (Chen et al., 2025). Radiotherapy is also being explored as an immunogenic adjuvant capable of inducing in situ vaccination and abscopal effects, with nanoparticle-based radiosensitizers and toll-like receptor agonists under investigation to further amplify systemic immune responses when combined with ICIs.

4.3 Multimodal and individualized immunotherapy strategies

The convergence of clinical and translational data has driven a shift toward multimodal and personalized immunotherapy strategies that integrate ICIs with other immune-based and conventional modalities. Multi-immunotherapy concepts combine checkpoint blockade with adoptive cell therapies, cancer vaccines, or oncolytic viruses to simultaneously expand tumor-specific T-cell clones, enhance their effector function, and dismantle immunosuppressive networks within the tumor microenvironment. Early-phase studies of PD-1/CTLA-4 dual blockade have shown higher response rates and more durable remissions than monotherapy in some recurrent and platinum-resistant cohorts, at the expense of increased immune-related toxicity, prompting careful exploration of optimal dosing and patient selection (Li et al., 2025). Parallel efforts are evaluating ICIs alongside CAR-T or TCR-engineered T cells, dendritic-cell vaccines, and antibody-drug conjugates in order to provide complementary mechanisms of tumor recognition and killing while exploiting immunologic memory for long-term control (Chen et al., 2025).

A central theme in contemporary strategy design is individualized treatment based on immunophenotype and molecular biomarkers. Stratification by $CD8^+$ T-cell infiltration, PD-L1 expression, homologous-recombination status, tumor mutational burden, and gene-expression signatures allows classification of ovarian cancers into “inflamed”, “immune-excluded” and “immune-desert” phenotypes, each requiring distinct combination approaches (Ghisoni et al., 2024). For example, inflamed tumors may be suitable for ICI-based doublets or multi-immunotherapy, whereas immune-desert lesions might first need priming with vaccines, epigenetic modulators, or radiotherapy to recruit effector cells before checkpoint blockade is effective (Figure 2) (Connor et al., 2024). Emerging technologies such as single-cell sequencing, spatial transcriptomics, organoids, and nanomedicine-enabled drug delivery further support the design of tailored regimens, optimize dosing and sequencing, and help predict benefit versus toxicity on an individual basis. Within this framework, ICIs are no longer viewed as standalone agents but as flexible components of comprehensive, patient-specific treatment architectures that combine surgery, chemotherapy, targeted therapy, and diverse immunotherapies to maximize durable benefit in advanced ovarian cancer.

5 Efficacy Evaluation of Immunotherapy

5.1 Traditional endpoints

Objective response rate (ORR), progression-free survival (PFS), and overall survival (OS) remain the core endpoints for evaluating the efficacy of immunotherapy in advanced ovarian cancer, largely inherited from chemotherapy and targeted-therapy trial design. In recurrent ovarian cancer, ORR has historically shown a strong correlation with PFS and a moderate association with OS, supporting its use as a surrogate endpoint in later-line settings. However, large cross-tumor meta-analyses of contemporary immunotherapy trials indicate that, for checkpoint inhibitors and their combinations, trial-level correlations between ORR, PFS, and OS are generally weak, suggesting that conventional radiologic shrinkage does not fully capture long-term benefit from immune-based treatments (Shahnam et al., 2023). This discrepancy is particularly relevant in immuno-oncology, where durable disease stabilization and delayed responses may translate into survival gains despite modest ORR.

The limitations of ORR and PFS are further highlighted by pooled analyses of randomized immunotherapy trials submitted to the FDA. Across multiple agents and tumor types, associations between treatment effects on ORR or PFS and OS were low (R^2 values around 0.13), and attempts to modify PFS definitions by altering progression thresholds did not materially improve surrogacy for OS. Broader meta-analyses of phase III studies confirm that ORR and PFS are poor trial-level surrogates for OS across diverse malignancies and treatment classes, although correlations can be somewhat stronger in specific disease-treatment subsets. These findings support continued use