al., 2025). Consequently, traditional surgery-plus-chemotherapy paradigms, while indispensable, are insufficient to secure durable disease control for most patients with stage III-IV disease.

2.2 Targeted therapy and unresolved problems of recurrence and resistance

Over the past decade, targeted therapies have been incorporated into frontline and recurrent treatment, partially reshaping the therapeutic landscape of advanced ovarian cancer. Anti-angiogenic agents, particularly bevacizumab, are now used in selected high-risk patients both concurrently with chemotherapy and as maintenance, improving progression-free survival, especially in those with suboptimal debulking or extensive disease. In parallel, PARP inhibitors such as olaparib, niraparib, and rucaparib have fundamentally changed maintenance strategies by exploiting homologous recombination deficiency, with landmark trials (SOLO1, PRIMA, VELIA, PAOLA-1, ATHENA) demonstrating substantial delays in recurrence, particularly among BRCA-mutated and HRD-positive tumors. These agents are increasingly deployed in both first-line and recurrent settings, and combinations of PARP inhibitors with anti-angiogenic drugs have shown synergistic activity and secured regulatory approvals in defined biomarker-selected populations (Papageorgiou et al., 2025).

Nevertheless, even with modern targeted agents, long-term disease eradication remains rare, and recurrence, often within two to three years, continues to drive mortality in advanced ovarian cancer. Platinum-based chemotherapy achieves initial response rates of up to 80%, but most advanced-stage patients eventually relapse due to acquired or intrinsic drug resistance, transforming the disease into a pattern of repeated remissions and recurrences. Molecular studies highlight that resistance mechanisms are multifactorial, involving enhanced DNA damage repair, altered drug transport, evasion of apoptosis, cancer stem cell populations, and remodeling of the tumor microenvironment (Nunes et al., 2024). These complex resistance networks limit the durability of benefit from both cytotoxic agents and targeted therapies, including PARP inhibitors and bevacizumab, and underscore the need for novel modalities capable of overcoming or bypassing established resistance pathways.

2.3 Toward individualized and precision treatment strategies

The persistent challenge of relapse and resistance has accelerated a shift from “one-size-fits-all” protocols toward more individualized treatment strategies grounded in molecular profiling and risk stratification. Contemporary guidelines increasingly recommend universal germline BRCA testing and expanded somatic profiling to identify homologous recombination deficiency, actionable mutations, and other genomic features that can guide selection of PARP inhibitors, anti-angiogenic agents, or enrollment in biomarker-driven clinical trials (Wang et al., 2025). Treatment decisions in the recurrent setting now explicitly incorporate platinum-free interval, residual toxicity, prior exposure to targeted agents, and patient preferences, allowing differentiation between platinum-sensitive and platinum-resistant pathways, with tailored combinations of chemotherapy, targeted therapy, and, in select cases, surgery or radiotherapy (Papageorgiou et al., 2025).

Beyond genomics, emerging approaches aim to integrate multi-omics data, tumor microenvironment characteristics, and artificial-intelligence-based analyses to refine subtype classification and predict drug response at the individual level (Nunes et al., 2024). Single-cell and spatial profiling have begun to delineate resistant cellular phenotypes that persist after first-line therapy and seed lethal recurrences, opening avenues for rational combination strategies targeting both tumor cells and stromal or immune components (Zhang et al., 2024; Whipman et al., 2025). This precision-medicine trend also extends to the development of novel targeted agents, such as antibody-drug conjugates, PI3K/AKT/mTOR inhibitors, and dual-targeted nanomedicines, that seek to improve selectivity, mitigate systemic toxicity, and overcome resistance (Wang et al., 2025). Within this evolving, increasingly personalized framework, immunotherapy is being actively explored as an integral component of comprehensive treatment, with the goal of achieving more durable control and potentially transforming advanced ovarian cancer into a truly manageable chronic or even curable condition.

3 Basis and Mechanisms of Immunotherapy

3.1 Tumor immune microenvironment in advanced ovarian cancer

The tumor immune microenvironment (TIME) of ovarian cancer is highly complex and profoundly shapes responses to immunotherapy. It comprises malignant cells, stromal components such as cancer-associated fibroblasts, endothelial cells, and a dense infiltrate of innate and adaptive immune cells embedded within an