of ORR, PFS, and OS in ovarian cancer immunotherapy trials but emphasize the need to interpret early endpoints cautiously and in conjunction with immune-specific response metrics and biomarker data (Shahnam et al., 2023).

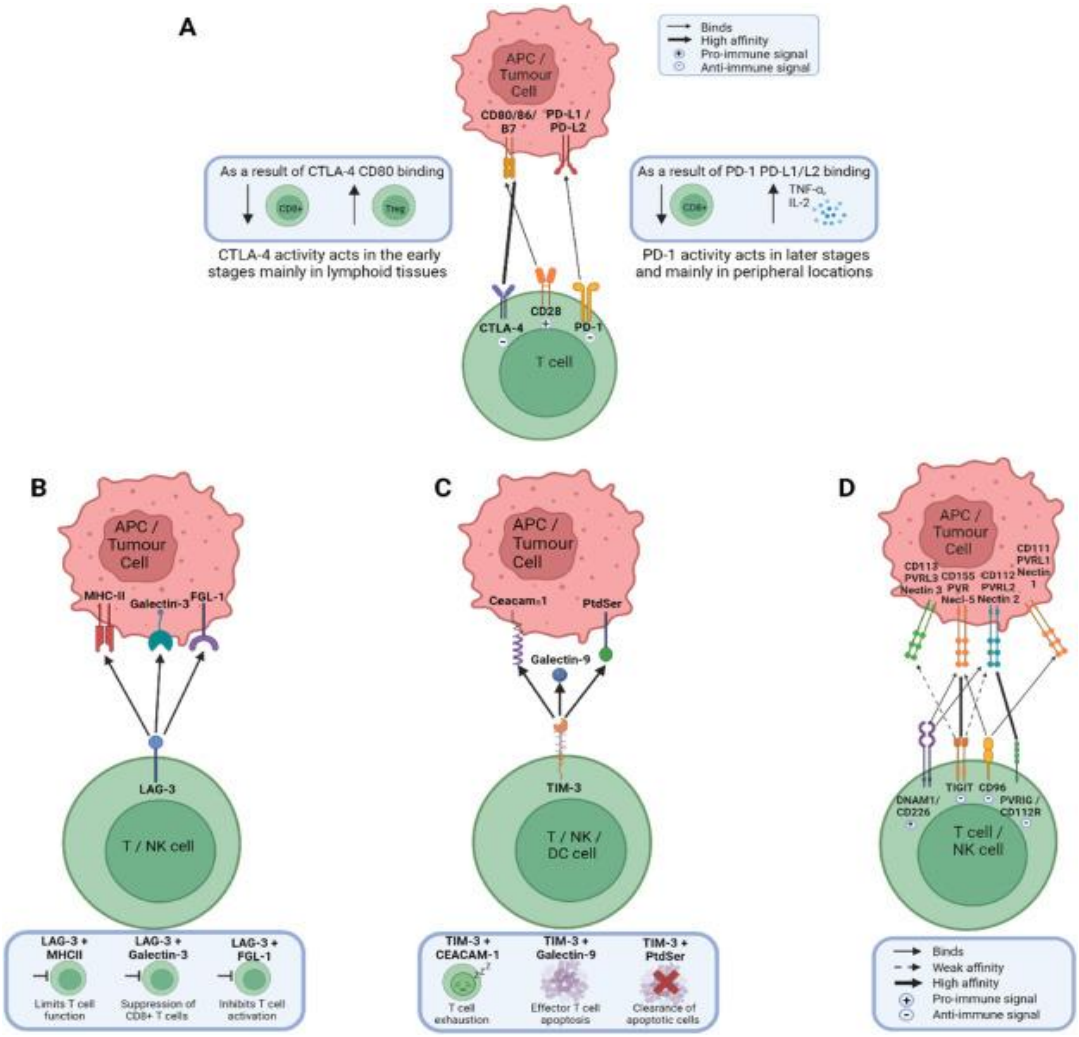

Figure 2 Immune checkpoint receptors and binding ligands, and their immunologic effect (Adopted from Connor et al., 2024)
Image caption: A) The B7-CD28 family: The binding interactions of three of the receptors in this family; CTLA-4, CD28 and PD-1 to the ligands CD80, CD86, PD-L1 and PD-L2. B) LAG3 receptor binding ligands and their immunologic effect. C) TIM-3 receptor binding ligands and their immunological effect. D) TIGIT family receptors: The binding interactions and affinity between receptors and their corresponding ligands (Adopted from Connor et al., 2024)

5.2 Immune-related response criteria and pseudoprogression

Because immune checkpoint blockade can induce unconventional patterns of response, conventional RECIST 1.1 criteria may misclassify some patients who ultimately benefit from treatment. Immune-related criteria such as irRC, irRECIST, and iRECIST were developed to address phenomena like transient tumor enlargement, new lesions followed by regression, and delayed responses. In a large pooled analysis of patients treated with the PD-L1 inhibitor avelumab, approximately 8% of patients categorized as having progressive disease (PD) by RECIST 1.1 actually achieved immune-related disease control by irRECIST, and this discordant subgroup displayed a distinct, more favorable survival curve. Nonetheless, immune-related PFS did not outperform conventional PFS as a surrogate for OS at the population level, indicating that immune-adapted criteria add clinical nuance but do not fundamentally replace standard endpoints (Manitz et al., 2022).

Pseudoprogression, initial radiologic progression followed by tumor regression without treatment change, is an established but relatively infrequent phenomenon in patients receiving ICIs, with pooled estimates around 6% across solid tumors and reported rates rarely exceeding 10%. Systematic reviews and meta-analyses show that