Immune checkpoint inhibitors targeting PD-1 have revolutionized cancer treatment, resulting in clinical benefits in a broad range of cancer patients. PD-1 is an inhibitory cell-surface receptor that is upregulated upon T-cell activation. Upon binding to its ligands, the PD-1 pathway can inhibit T-cell proliferation and cytokine production, leading to impaired antitumor immune responses.

Toripalimab, an anti-PD-1 antibody, demonstrates potent T-cell activation and enhanced clinical efficacy irrespective of PD-L1 status. Toripalimab in combination with chemotherapy significantly improved overall survival (OS) in patients with non-small-cell lung cancer (NSCLC) compared to chemotherapy alone. Toripalimab also exhibits a 12-fold higher binding affinity for PD-1 compared to pembrolizumab, which is more potent than nivolumab in enhancing IFN-γ production. This higher affinity allows toripalimab to recruit SHP1 and SHP2 directly, activating the interferon response pathway after 6- and 24-hr treatment.

The interferon response pathway includes expression of unique genes such as IFIT1, IRF5, and IRF9, which are upregulated in response to PD-1 activation. These genes are associated with Th1 and myeloid-derived cytokine secretion, indicating a pro-inflammatory effect. The increased expression of these genes in toripalimab-treated cells compared to pembrolizumab-treated cells suggests that toripalimab may have a more potent immune-stimulating effect.

Overall, toripalimab demonstrates superior efficacy in several cancer indications, including NSCLC, with significant improvements in OS and clinical outcomes. Its unique binding affinity and immune-stimulating properties make it a promising agent in the treatment of PD-1/PD-L1-mediated immune modulation.