



## Advancements in Immunotherapy for Gastric Cancer: Unveiling the Potential of PD-L1 Inhibitors

**Andrea Palacios Navas\***

*Department of General Surgery, Hospital Clinica San Francisco, Ecuador*

**\*Corresponding Author:** Andrea Palacios Navas, Department of General Surgery, Hospital Clinica San Francisco, Ecuador.

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Gastric cancer ranks as the fifth most prevalent cancer globally. While its incidence is declining in the United States, it remains disproportionately high in certain Asian countries, notably Japan, South Korea, and Mongolia [1].

In the domain of oncology, immunotherapy has emerged as a transformative force in cancer treatment, offering renewed hope for patients grappling with various malignancies, including gastric cancer. Programmed death-ligand 1 (PD-L1) inhibitors have garnered substantial attention among immunotherapeutic agents due to their notable efficacy and favorable safety profiles across select cancer types.

Notably, the expression of PD-L1 prior to treatment serves as an immunological biomarker predictive of tumor shrinkage [2].

PD-L1 inhibitors, in particular, have shown promise by blocking the interaction between PD-L1 expressed on tumor cells and PD-1 receptors on immune cells, thereby unleashing an anti-tumor immune response.

The immune checkpoint involves the PD-1 receptor found on activated T cells, which interacts with the PD-L1 ligand expressed on tumor cells, thereby facilitating T cell apoptosis. Antibodies targeting PD-1 and PD-L1, including nivolumab, pembrolizumab, and sintilimab, effectively disrupt this signaling pathway.

Multiple PD-(L)1 inhibitors, including pembrolizumab, nivolumab, and sintilimab, have garnered approval for treating advanced gastric cancer in various regions, including Europe, the USA, and Asia. These inhibitors have been reported to elicit durable responses in patients with advanced gastric cancer [2].

Nivolumab has been approved as a single dose of 2 mg/kg for malignant melanoma and a single dose of 3 mg/kg for non-small cell lung cancer, renal cell carcinoma, non-Hodgkin lymphoma, head and neck cancer, and gastric cancer [3]. It is recommended in combination with platinum-containing chemotherapy and fluoropyrimidine. The dosage regimen typically entails 240 mg IV every 2 weeks or 360 mg IV every 3 weeks alongside a platinum-containing agent (e.g., oxaliplatin) and a fluoropyrimidine (e.g., fluorouracil, capecitabine) [4].

Incorporating anti-PD-1/PD-L1 antibodies into chemotherapy as a primary treatment approach has shown clinical advantages for advanced gastric cancer cases lacking HER2 expression.

In conclusion, the advent of immunotherapy, particularly PD-L1 inhibitors, has ushered in a new era of hope for patients battling gastric cancer. The escalating incidence of gastric cancer, particularly in Asian countries, underscores the urgent need for novel therapeutic strategies. PD-L1 inhibitors have demonstrated remarkable efficacy and safety profiles, offering tangible benefits for patients with advanced gastric cancer. Their ability to disrupt the PD-1/PD-L1 interaction and unleash anti-tumor immune responses represents a significant breakthrough in cancer treatment.

Moreover, the identification of PD-L1 expression as a predictive biomarker for treatment response highlights the potential for personalized medicine approaches in gastric cancer management. Approved PD-(L)1 inhibitors such as pembrolizumab, nivolumab, and sintilimab have expanded treatment options, providing hope for improved outcomes and prolonged survival in patients with advanced disease.

However, challenges persist, including optimizing patient selection, managing immune-related adverse events, and elucidating mechanisms of resistance.

Continued research efforts and collaborative endeavors are essential to address these challenges and further enhance the efficacy of PD-L1 inhibitors in gastric cancer treatment.

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