Gastric Cancer (GC) remains one of the deadliest diagnosable cancers, and commonly has poor prognoses with traditional chemotherapy, radiation, and surgical resection. Micro-Satellite Instability (MSI) subtype GC and Epstein Barr Virus (EBV) positive GC contribute to increased tumor mutational burdens, accelerating pathogenesis, and treatment resistance, but these subtypes also present prime targets for immune modulation due to their high prevalence of tumor neoantigens. One ligand-receptor interaction of interest is the programmed cell death protein (PD-1) receptor and its ligand PD-L1. This interaction prevents full T cell activation and contributes to immune escape in solid tumors. Current PD-1 and PD-L1 inhibitors are monoclonal antibodies which bind to either PD-1 or PD-L1 to prevent tolerant tumor micro-environment (TME) and cytotoxic lymphocyte (CTL) interactions. Inhibiting PD-1 and PDL-1 can thereby increase tumor infiltrating lymphocyte (TIL) immunoreactivity to tumors, and these inhibitors can be given in combination with established CTLA-4 inhibitor ipilimumab. These inhibitors are undergoing current clinical trials to determine their role in gastric cancer treatment, and a few will herein be evaluated according to recent pooled meta-analysis data: nivolumab, pembrolizumab, avelumab, avelozulubam, and durvalumab. According to pooled 2020 clinical trial data, nivolumab showed modest increases in overall survival compared to placebo and in conjunction with ipilimumab, but response rates remained below 27%. Pembrolizumab was more effective among different study designs, but still only obtained modest results when compared to paclitaxel therapy, yet pembrolizumab showed promise in PD-L1 overexpressing patients. Avelumab did not significantly increase overall survival or response rates in metastatic GC patients when compared against paclitaxel and irinotecan chemotherapies. Atezolizumab and durvalumab clinical trial results are pending but trials are active.

Further investigation into these PD-1 and PD-L1 inhibitors remains to been seen in clinical settings alongside tissue histology and IHC analysis of PD-L1 expression. As demonstrated, PD-1/PD-L1 complete clinical data is emerging at a rapid pace, and many studies will emerge which may further elucidate upon the findings presented within this work. Careful consideration for subtypes and TME expression profiles may yield more significant results in pembrolizumab and nivolumab clinical trials, as the discussed factors can greatly affect gastric tumor sensitivity to the PD-1 blockade immunotherapeutic strategy. This avenue of treatment yields great promise for patients and physicians due to increased survivability and tolerability for patients, and contributions to this field will continue to expand knowledge and treatment paradigms for gastric cancer in the coming years.