

EFFICACY AND SAFETY OF EMERGING THERAPIES IN THE TREATMENT OF GASTRIC ADENOCARCINOMA: A SYSTEMATIC REVIEW OF THE LAST 5 YEARS

Emily do Socorro Damasceno Pacheco¹, Paulo Jorge Araújo Pires¹, Erisson de Souza Marques¹, Hammad Sikandar Khan¹, Layane Vitória Santos Ferreira¹, Aluizio Ramos Pereira Neto¹, Kawane Pereira de Souza¹, Sara Martins Pereira¹, Josiel de Araújo Ramos¹, Gilvandro de Jesus Almeida Sanches².

¹ Universidade Federal do Pará (UFPA);

² Universidade da Amazônia (UNIESAMAZ).

Introduction: Gastric cancer remains a leading cause of cancer-related mortality worldwide, particularly in developing countries. Although a gradual decline in incidence has been observed in some nations due to improved sanitation, better control of *Helicobacter pylori* infection, and dietary changes, mortality rates remain high. This is primarily due to late-stage diagnosis and the limited effectiveness of conventional treatments such as surgery alone or empirical chemotherapy. In this context, new, more precise, and personalized therapeutic strategies are being investigated to enhance disease control and patient survival. **Objectives:** To conduct a systematic review of recent advances in gastric cancer treatment, focusing on targeted therapies and immunotherapy. **Methods:** A systematic review was performed by searching PubMed, Scopus, and Web of Science databases for publications from January 2019 to January 2024. MeSH descriptors and specific keywords were combined using Boolean operators. Inclusion criteria encompassed randomized clinical trials, systematic reviews, and meta-analyses on targeted therapies, immunotherapies, or combined strategies in adults with advanced gastric adenocarcinoma. Preclinical studies, case reports, and articles not in English or Portuguese were excluded. The selection process involved three stages: title screening, abstract review, and full-text analysis. Data extracted included study design, interventions, biomarkers, outcomes (overall survival and progression-free survival), and adverse events. Methodological quality was assessed using the Cochrane Risk of Bias Tool and AMSTAR-2, adhering to PRISMA guidelines. **Results:** A total of 36 studies met the inclusion criteria. Significant advancements were noted in immunotherapy, particularly with immune checkpoint inhibitors such as nivolumab and pembrolizumab, which demonstrated efficacy in patients with high *PD-L1* expression (Combined Positive Score ≥ 5) and tumors exhibiting microsatellite instability-high (*MSI-H*), leading to improved overall survival (average hazard ratio: 0.74) and increased objective response rates. Concurrently, targeted therapies continue to be effective, especially in patients with *HER2* overexpression treated with trastuzumab. Ramucirumab, a *VEGFR-2* inhibitor, showed efficacy both as monotherapy and in combination with paclitaxel in second-line

settings, improving progression-free survival (median: 4.4 months vs. 2.9 months in the control arm). Additionally, combining immunotherapy with traditional chemotherapy has shown promise, suggesting a synergistic potential between these approaches.

Conclusion: Findings from this review highlight a paradigm shift in the treatment of advanced gastric cancer, with the progressive incorporation of personalized therapies based on molecular biomarkers. Careful patient selection based on characteristics such as *HER2* and *PD-L1* expression, as well as *MSI-H* status, is crucial to maximize the clinical benefits of these emerging therapies. However, despite encouraging results, further long-term studies with robust methodologies are necessary to validate and consolidate these strategies in clinical oncology practice.

Keywords: Gastric adenocarcinoma; Emerging therapies; Immunotherapy; Targeted therapy; Overall survival.