

# Gastric Carcinoma: Recent Trends in Diagnostic Biomarkers and Molecular Targeted Therapies

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## Abstract

Gastric cancer is generally associated with poor survival rates and accounts for a remarkable proportion of global cancer mortality. The prevalence of gastric carcinoma varies in different regions of world and across the various ethnic groups. On the basis of pathological assessment, gastric cancer can be categorized as intestinal and diffuse carcinomas. The etiology is diverse, including chemical carcinogen exposure and high salt intake *Helicobacter pylori* also plays a vital role in the pathogenesis of certain gastric carcinomas. The development of gastric cancer involves various alterations in mRNAs, genes (*GOLPH3*, *MTA2*) and proteins (Coronins). miRNAs, Hsamir135b, MiR21, miR106b, miR17, miR18a, MiR21, miR106b, miR17, miR18a and MiRNA375, miRNA1955p are the latest diagnostic biomarkers which can facilitate the early diagnosis of gastric carcinomas. Recent development in the treatment strategies for gastric carcinoma include the introduction of monoclonal antibodies, TKI inhibitors, inhibitors of PDGFR  $\beta$ , VEGFR1, VEGFR2, AntiEGFR and antiHER2 agents which can be applied along with conventional therapies.

**Keywords:** Gastric cancer; Carcinoma; *Helicobacter pylori*; Pathogenesis; Proteins; Biomarkers; mRNAs; Monoclonal antibodies

## Introduction

Gastric carcinoma, commonly known as stomach cancer, is one of the leading causes of cancer related deaths worldwide [1]. Over the past few decades, significant advancements have been made in understanding the molecular mechanisms underlying gastric carcinoma development, leading to the identification of novel diagnostic biomarkers and the development of molecular targeted therapies. This article explores the recent trends in diagnostic biomarkers and molecular targeted therapies for gastric carcinoma.

## Diagnostic biomarkers

***Helicobacter pylori* infection markers:** *Helicobacter pylori* is a bacterium known to play a significant role in gastric cancer

development. Recent studies have focused on identifying specific biomarkers associated with *H. pylori* infection, such as CagA, VacA and other virulence factors. Detecting these markers in patients can aid in early diagnosis and prompt intervention.

**Circulating tumor DNA (ctDNA):** Liquid biopsies, which involve the analysis of ctDNA released by tumor cells into the bloodstream, have emerged as a promising non-invasive method for early detection and monitoring of gastric carcinoma. The identification of specific genetic alterations and mutations in ctDNA can provide crucial information for personalized treatment strategies [2].

**MicroRNAs (miRNAs):** miRNAs are small non coding RNA molecules that regulate gene expression. Dysregulation of certain miRNAs has been associated with gastric cancer development. Recent research has unveiled potential miRNA biomarkers that could serve as diagnostic tools and prognostic indicators for gastric carcinoma patients.

## Molecular targeted therapies

**HER2 (Human Epidermal Growth Factor Receptor 2) targeting:** Approximately 20% of gastric carcinoma cases exhibit HER2 overexpression or amplification, making HER2-targeted therapies a vital treatment option. Drugs like trastuzumab have shown improved survival rates and disease control in HER2-positive patients, revolutionizing treatment for this subset of gastric cancer.

**VEGF (Vascular Endothelial Growth Factor) inhibition:** Angiogenesis, the process of forming new blood vessels, is critical for tumor growth and metastasis. Drugs targeting VEGF, such as bevacizumab, have been investigated as potential therapies to inhibit angiogenesis and slow down tumor progression in advanced gastric carcinoma.

**PD-1/PD-L1 immunotherapy:** Immune checkpoint inhibitors, like pembrolizumab and nivolumab, have shown promising results in various cancers, including gastric carcinoma. By blocking the PD-1/PD-L1 interaction, these drugs unleash the patient's immune system to attack cancer cells, leading to durable responses in a subset of patients.

## Description

### Diagnostic biomarkers

**HER2 (Human Epidermal Growth Factor Receptor 2):** HER2 overexpression is found in a subset of gastric carcinomas, similar to breast cancer. Targeted therapies like trastuzumab have shown efficacy in HER2-positive cases, leading to personalized treatment options based on HER2 status [3].

**PD-L1 (Programmed Death-Ligand 1):** Immunotherapy has revolutionized cancer treatment and PD-L1 expression plays a crucial role in determining the response to immune checkpoint inhibitors like pembrolizumab and nivolumab. Testing for PD-L1 expression helps identify patients who may benefit from immunotherapies.

**EBV (Epstein Barr Virus):** Some gastric carcinomas are associated with EBV infection. Detection of EBV related markers can aid in distinguishing this specific subtype and guide therapeutic decisions.

**Micro Satellite Instability (MSI):** MSI-high gastric carcinomas are susceptible to immune checkpoint inhibitors like pembrolizumab. Testing for MSI status is crucial in identifying potential candidates for this treatment approach.

**Circulating tumor DNA ( ctDNA):** Liquid biopsy techniques, such as detecting ctDNA in the blood, have shown promise as non-invasive methods for monitoring treatment response and disease progression.

### Molecular targeted therapies

**HER2-targeted therapy:** As mentioned earlier, trastuzumab, a HER2-targeted monoclonal antibody, has demonstrated efficacy in HER2-positive gastric carcinoma. Other agents like lapatinib and trastuzumab deruxtecan are also being investigated.

**Vascular Endothelial Growth Factor (VEGF) inhibitors:** Agents like ramucirumab, VEGF receptor 2 antagonists, have been approved for advanced gastric carcinoma, showing improved overall survival when combined with chemotherapy.

**MET inhibitors:** *MET* gene amplification and overexpression are present in some gastric carcinomas. *MET* inhibitors like capmatinib and savolitinib are being studied as potential targeted therapies.

**FGFR (Fibroblast Growth Factor Receptor) inhibitors:** Clinical trials are evaluating the efficacy of FGFR inhibitors, such as bemarituzumab and futibatinib, in gastric carcinoma patients with FGFR amplification or mutations.

**Immunotherapies:** Immune checkpoint inhibitors like pembrolizumab and nivolumab have shown promise in subsets of gastric carcinoma patients with high PD-L1 expression or MSI-high status.

**Challenges:** Despite these recent advancements, several challenges persist in the management of gastric carcinoma.

**Heterogeneity:** Gastric carcinoma is a highly heterogeneous disease, making it difficult to develop one size fits all treatments. Personalized medicine approaches are essential to account for individual patient variations.

**Resistance to targeted therapies:** Resistance to molecular targeted therapies can develop over time, limiting their long term effectiveness. Combination therapies and strategies to overcome resistance are under investigation [4].

**Access to biomarker testing:** Not all healthcare settings have easy access to biomarker testing, limiting the availability of targeted therapies to eligible patients.

**Early detection:** The majority of gastric carcinomas are diagnosed at advanced stages, emphasizing the need for improved early detection methods and screening programs.

Recent trends in diagnostic biomarkers and molecular targeted therapies have provided new hope in the management of gastric carcinoma. Personalized treatment approaches based on biomarker status are becoming more common, leading to improved outcomes for some patients. However, challenges related to tumor heterogeneity, resistance and access to testing remain, highlighting the need for ongoing research and collaboration among healthcare professionals and researchers to further advance the field.

## Conclusion

Gastric carcinoma continues to pose a significant global health challenge, but recent advances in diagnostic biomarkers and molecular targeted therapies have provided new hope for patients. Early detection of gastric cancer using specific biomarkers allows for timely intervention, while molecular targeted therapies have shown promising results in improving treatment outcomes and patient survival rates. Continued research and clinical trials are essential to further refine these approaches and develop new strategies to combat this deadly disease effectively. Moreover, multidisciplinary collaborations and precision medicine approaches will be crucial in optimizing individualized treatment plans for gastric carcinoma patients in the future.

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