Several new treatment options for gastric cancer have been introduced but the prognosis of patients diagnosed with gastric cancer is still poor. Disease prognosis could be improved for high-risk individuals by implementing earlier screenings. Because many patients are asymptomatic during the early stages of gastric cancer, the diagnosis is often delayed and patients present with unresectable locally advanced or metastatic disease. Cytotoxic treatment has been shown to prolong survival in general, but not all patients are responders. The application of targeted therapies and multimodal treatment has improved prognosis for those with advanced disease. However, these new therapeutic strategies do not uniformly benefit all patients. Predicting whether patients will respond to specific therapies would be of particular value and would allow for stratifying patients for personalized treatment strategies. Metabolic imaging by positron emission tomography was the first technique with the potential to predict the response of esophago-gastric cancer to neoadjuvant therapy. Exploring and validating tissue-based biomarkers are ongoing processes. In this review, we discuss the status of several targeted therapies for gastric cancer, as well as proteomic and metabolic methods for investigating biomarkers for therapy response prediction in gastric cancer.