

# Management of Metastatic Gastric Cancer

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## KEYWORDS

- Gastric cancer • Metastases • Chemotherapy • Radiotherapy • Surgery • Doublet • Triplet • Sequence

## KEY POINTS

- In metastatic gastric cancer, chemotherapy is part of the palliative care concept. A platinum compound (cisplatin or oxaliplatin) plus a fluoropyrimidine (fluorouracil [5-FU], capecitabine, or S-1) is the global standard.
- HER2 is the only predictive marker, and HER2 testing of the primary tumor and/or metastases is warranted before initiation of first-line treatment.
- Selected patients can benefit from triplet combinations, but increased side effects must be considered. Comorbidity, concomitant diseases, and prior therapies should be taken into account for selecting the appropriate therapeutic approach.
- Recent data support the routine use of second-line chemotherapy, either as mono chemotherapy or as a combination of ramucirumab and paclitaxel.

## INTRODUCTION

According to the EUROCARE-5 study, 4 of 5 patients with gastric cancer in Europe die within the first 5 years after diagnosis.<sup>1</sup> With 42,280 new cases and 26,420 deaths, gastric and esophageal cancers rank among the most deadly malignant diseases in the United States in 2016.<sup>2</sup> The high mortality rate indicates that a majority of patients diagnosed with gastric and esophageal cancer are primarily diagnosed in stage IV or eventually recur with metastases. The management of metastatic disease is an important health problem. From a patient perspective, prolongation of life, symptom control,

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and quality of life matter. From a society perspective, cost-related and resource-related issues also are important.

Data from the Netherlands indicate that the use of palliative chemotherapy increased, from 5% in 1990 to 36% in 2011, with a strong increase in particular after 2006 ( $P < .0001$ ).<sup>3</sup> Disappointingly, median overall survival for all noncardia gastric cancers remained constant between 15 weeks (95% CI, 11.9–17.7) and 17 weeks (95% CI, 15.0–20.0) ( $P = .10$ ). Systemic chemotherapy was revealed, however, as an independent positive prognostic factor in this disease and patients who received chemotherapy had a longer survival.

The options for patients with metastatic disease are increasing. In the past 5 years several new drugs were made available based on positive study results, including targeted drugs like trastuzumab for human epidermal growth factor receptor 2 (HER2)-positive gastric cancer and ramucirumab for cancers that progressed on first-line treatment. As a consequence, median survival has improved from approximately 6 months to 7 months in early studies to approximately 11 months to 12 months in modern studies. This can be seen as the beginning of a new era for treatment of patients with metastatic gastric cancer. Classic chemotherapy is still an important backbone of treatment but — with an increasing knowledge about gastric cancer biology — more biologically targeted options are to come in the near future.

## TREATMENT GOALS

According to the World Health Organization, “palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.”<sup>4</sup> (Box 1). In metastatic gastric cancer, chemotherapy can be part of the palliative care concept. Physicians who apply chemotherapy should follow these goals.

### Box 1

#### Definition of palliative care according to the World Health Organization

- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process
- Intends neither to hasten or postpone death
- Integrates the psychological and spiritual aspects of patient care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help the family cope during patients' illness and in their own bereavement
- Uses a team approach to address the needs of patients and their families, including bereavement counseling, if indicated
- Enhances quality of life and may also positively influence the course of illness
- Is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications

From World Health Organization (WHO). WHO definition of palliative care. Available at: <http://www.who.int/cancer/palliative/definition/en/>. Accessed July 29, 2016; with permission.

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