Factors Associated With Decision-Making in the Second-Line Treatment of Patients With Advanced/Metastatic Gastric and GE Junction Cancers

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Learning Objectives

- Evaluate which patient populations may benefit from anti-angiogenic therapy as a second-line treatment for advanced or metastatic gastric and gastroesophageal junction (GEJ) cancers

- Select appropriate second- and subsequent-line therapy for the management of gastric/GEJ cancers

- Assess clinical trials findings in patients who could benefit from anti-angiogenic treatment for advanced or metastatic GEJ cancers

- Apply clinical practice guidelines for second-line treatment in patients with advanced and metastatic gastrointestinal cancers to maximize patient outcomes through proper sequencing of therapy

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Gastric Cancer (GC)

United States

- Estimated 26,500 people will be diagnosed with GC and 11,130 will die from stomach cancer in 2023
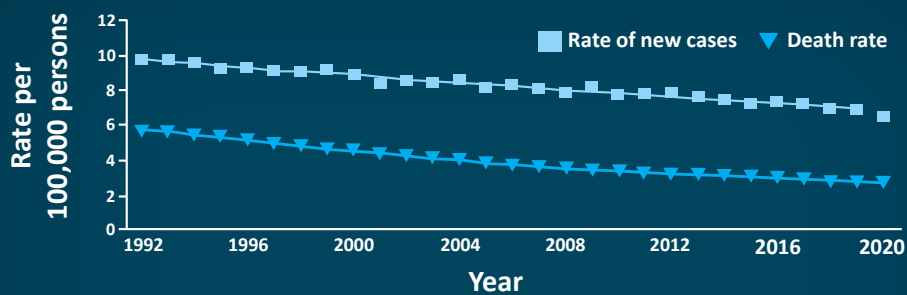
Worldwide (2020 data)

- GC is the **6th most common malignancy,** with **1.09 million new cases worldwide**

- **GC is 4th most common cause of cancer mortality,** with nearly 769,000 deaths

American Cancer Society (ACS). About stomach cancer (www.cancer.org/content/dam/CRC/PDF/Public/8838.00.pdf). World Health Organization (WHO). Cancer. 2022. (www.who.int/news-room/fact-sheets/detail/cancer). World Cancer Research Fund International. Stomach cancer statistics. (www.wcrf.org/cancer-trends/stomach-cancer-statistics/). URLs accessed 6/21/23.

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Trends in Stomach Cancer Statistics

Incidence and mortality rates (1992–2020)

- 5-year relative rate survival varies by staging
  - **localized = 74.7%, regional = 34.6%, distant = 6.6%,** and unknown = 31.1%
- Median age at diagnosis is 68 years
- New case incidence per 100,000 persons (of all races) is greater in males (9.0) compared with females (5.2)

National Cancer Institute (NCI). Stomach cancer stat facts (https://seer.cancer.gov/statfacts/html/stomach.html. Accessed 6/21/23.

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Evidence-Based Management of Advanced G/GEJ Cancer
1st-Line NCCN Recommendations

- HER2– disease
  - Fluoropyrimidine* + oxaliplatin + nivolumab (PD-L1 CPS ≥5)
  - Fluoropyrimidine* + oxaliplatin
  - Fluoropyrimidine* + cisplatin

- HER2+ disease (15–20% of advanced G/GEJ cancers)
  - Fluoropyrimidine* + oxaliplatin + trastuzumab†
  - Fluoropyrimidine* + oxaliplatin + trastuzumab† + pembrolizumab (other preferred)
  - Fluoropyrimidine* + cisplatin + trastuzumab† (category 1)
  - Fluoropyrimidine* + cisplatin + trastuzumab† + pembrolizumab

*fluoropyrimidines are fluorouracil or capecitabine; †NCCN guidelines support an FDA-approved biosimilar as an appropriate substitute for trastuzumab.

CPS = combined positive score; G = gastric; GEJ = gastroesophageal junction; HER2 = human epidermal growth factor 2; NCCN = National Comprehensive Cancer Network; PD-L1 = programmed (cell) death 1 ligand.

NCCN. Clinical practice guidelines for gastric cancer. Version 1.2023 (www.nccn.org/professionals/physician_gls/pdf/gastric.pdf). Accessed 6/21/23. Van Cutsem E, et al. *Gastric Cancer.* 2015;18:476-484.

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Advanced Gastric and Gastroesophageal Junction Cancers: Second-Line Treatment Considerations

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2L Treatment Option Benefits in Gastric and GEJ Cancers
Benefits of Second-Line Therapy

- Understanding first-line therapy benefits and limitations
  - Up to 25–30% have progression in early response evaluation visits
  - Median PFS is 4–7 months
  - Newer, more effective 1st-line regimens may extend survival and preserve performance status, potentially resulting in more candidates for 2nd-line therapy

- RCTs show second-line therapy may improve OS and QoL when compared with basic supportive care

2L = second line; OS = overall survival; PFS = progression-free survival; QoL = quality of life; RCT = randomized controlled trial.

Cotes Sanchis A, et al. *PLoS One*. 2020;15:e0235848.

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2L Treatment Considerations After Progression on
1L Therapy in Gastric and GEJ Cancers

- Prior treatment response and first-line TTF may predict second-line TTF and second-line overall survival

- Treatment choices are often based on molecular characteristics (eg, HER2), along with other factors like
  - Toxicity profile of regimens
  - Patient comorbidities
  - Patient performance status
  - Patient goals

1L = first line; TTF = time to treatment failure.

van Velzen MJM, et al. *Eur J Cancer*. 2021;156:60-69. American Cancer Society. Treating Stomach Cancer. (https://www.cancer.org/cancer/types/stomach-cancer/treating/by-stage.html) Accessed 7.13.23

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We look forward to seeing you at our ECHO presentation to discuss 2nd line therapies in the treatment of Gastric and GEJ cancers!

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