Noninterventional cohort study of biomarker testing and treatment patterns in patients with advanced gastric or gastroesophageal junction cancer

462P

Samuel J. Klempner[1], Rupali M. Fuldeore[2], Adrienne Brackey[3], Chithra Sangli[3], Sneha Nishtala[3], David Nimke[2], Stephanie Braun[2], Rutika Mehta[4]

[1]Department of Medicine, Division of Hematology-Oncology, Massachusetts General Cancer Center, Boston, MA, USA; [2]Astellas Pharma Global Development, Inc., Northbrook, IL, USA; [3]Tempus AI, Inc., Chicago, IL, USA; [4]Department of Gastrointestinal Oncology, Moffitt Cancer Center, Tampa, FL, USA

BACKGROUND

- Combining biomarker-directed therapies with chemotherapy has been shown to improve survival in patients with advanced gastric or gastroesophageal junction cancer (G/GEJC)[1-5]
- Thus, timely testing for actionable biomarkers is needed to match patients with appropriate treatments
- The National Comprehensive Cancer Network guidelines recommend matched therapies for patients with advanced G/GEJC who have positive biomarker test results for human epidermal growth factor receptor 2 (HER2), programmed cell death ligand 1 (PD-L1), and microsatellite instability (MSI)[5]
- Although treatment guidelines include these recommendations, data on real-world biomarker testing rates and treatment patterns with matched, or possibly unmatched therapies, are limited

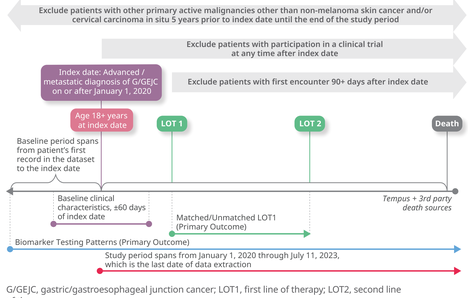
OBJECTIVE

- This study aimed to describe actionable biomarker testing and treatment patterns with matched therapies in patients with locally advanced or metastatic G/GEJC

METHODS

- The study was conducted using de-identified, patient-level, real-world electronic health record data from the Tempus database (**Figure 1**), which consists of longitudinal, multimodal data on patients treated by cancer care providers in the US, including those at a mix of academic and community-based cancer centers
- Biomarker testing patterns were identified in patients with advanced G/GEJC from any time before the advanced G/GEJC diagnosis until 90 days after initiating the first line of therapy (LOT1) or until 180 days after advanced diagnosis in patients not initiating LOT1
- Biomarker testing consisted of evaluating the following actionable biomarkers and their matched or unmatched therapies:
  - HER2
  - PD-L1
  - MSI/mismatch repair (MMR)

Figure 1. Study Design Using De-identified Health Record Data From the Tempus Database in the United States

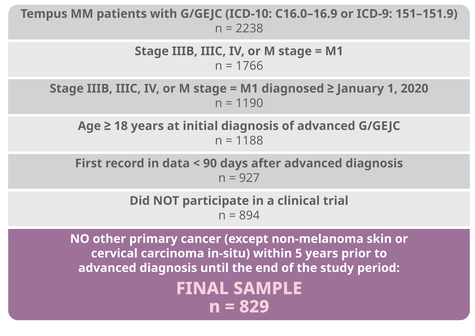


G/GEJC, gastric/gastroesophageal junction cancer; LOT1, first line of therapy; LOT2, second line of therapy.

RESULTS

- The study included 829 patients with advanced G/GEJC (**Figure 2**); baseline characteristics for the population are shown in **Table 1**

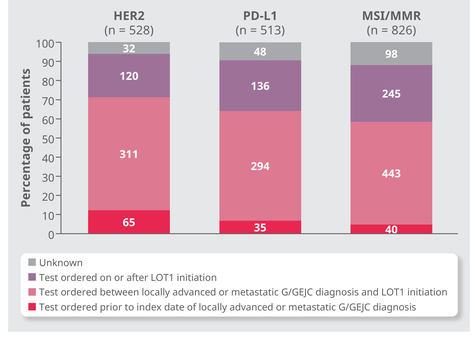
Figure 2. Selection Criteria and Cohort Attrition for the Inclusion of Patients With Advanced G/GEJC From the Tempus Database



G/GEJC, gastric/gastroesophageal junction cancer; ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision; MM, multimodal.

- Documented testing for all 3 biomarkers (HER2, PD-L1, and MSI/MMR) occurred in 363/829 (43.8%) patients with advanced G/GEJC in the Tempus database
- Many patients were tested for actionable biomarkers either prior to advanced G/GEJC diagnosis or between advanced G/GEJC diagnosis and initiating their first line of therapy (LOT1); however, some patients were tested on or after initiating LOT1 (120/528 [22.7%] for HER2, 136/513 [26.5%] for PD-L1, and 245/826 [29.7%] for MSI/MMR), meaning that there may have been a missed opportunity to use matched therapy in these patients (**Figure 3**)

Figure 3. Biomarker Testing by Time of Advanced G/GEJC Diagnosis and Initiation of LOT1



G/GEJC, gastric/gastroesophageal junction cancer; HER2, human epidermal growth factor receptor 2; LOT1, first line of therapy; MSI/MMR, microsatellite instability/mismatch repair; PD-L1, programmed cell death ligand 1.

Table 1. Baseline Demographics and Clinical Characteristics of Patients With Advanced G/GEJC in the Tempus Database

		Patients with advanced G/GEJC n = 829
Age at index date,[a] years	Median	62
	Minimum, maximum	21, 87
Female, n (%)		283 (34.1)
Race, n (%)	Asian	38 (4.6)
	Black or African American	57 (6.9)
	White or Caucasian	367 (44.3)
	Other or unknown	87 (10.5)
	Not documented	280 (33.8)
Provider setting,[b] n (%)	Academic	311 (37.5)
	Community	518 (62.5)
Primary tumor site at initial diagnosis, n (%)	GEJ	299 (36.1)
	Stomach	530 (63.9)
Primary histology at initial diagnosis, n (%)	Adenocarcinoma[c]	610 (73.6)
	Signet ring cell carcinoma	44 (5.3)
	Carcinoma, diffuse type	40 (4.8)
	Carcinoma, no subtype	36 (4.3)
	Carcinoma, metastatic	11 (1.3)
	Malignant neoplasm, primary	9 (1.1)
	Other[d]	73 (8.8)
	Not documented/unknown	6 (0.7)
Number of metastatic sites at index date,[a] n (%)	1	366 (44.1)
	2	89 (10.7)
	3+	39 (4.7)
	Not documented/unknown	335 (40.4)
Metastatic site(s) at index date,[a] n (%)	Brain metastases	6 (0.7)
	Bone metastases	28 (3.4)
	Liver metastases	189 (22.8)
	Lung metastases	38 (4.6)
	Other metastases	310 (37.4)
	Not documented/unknown	335 (40.4)
Time of biomarker testing in relation to LOT1 initiation, months	*On or before LOT1 initiation*	
	n	175
	Median	–0.39
	Minimum, maximum	–20.05, 0.01
	After LOT1 initiation	
	n	544
	Median	2.34
	Minimum, maximum	0.04, 37.12
	Not documented/unknown	
	n	110
Time of biomarker testing in relation to index date,[a] months	*On or before index date[e]*	
	n	31
	Median	–3.26
	Minimum, maximum	–19.00, –0.03
	After index date[e]	
	n	798
	Median	2.14
	Minimum, maximum	0.16, 37.94
Follow-up time from index date,[a] months	Median	6.60
	Minimum, maximum	0.19, 40.69

[a]Index date: date of diagnosis for locally advanced or metastatic G/GEJC. [b]Patients may have received care at multiple sites and were prioritized using the following hierarchy: 1. Academic 2. Community. [c]Included adenocarcinoma, adenocarcinoma (metastatic), adenocarcinoma (intestinal type), mucinous adenocarcinoma, and intramucosal adenocarcinoma. [d]Included gastrointestinal stromal tumor, uncertain malignant potential (n = 25); neuroendocrine tumor (n = 13); tumor cells, malignant (n = 10); tubular adenocarcinoma (n = 5); adenosquamous carcinoma (n = 3); adenocarcinoma with mixed subtypes; adenocarcinoma with squamous metaplasia; large cell neuroendocrine carcinoma; poorly differentiated carcinoma (each n = 2); adenocarcinoma with neuroendocrine differentiation; goblet cell carcinoid; linitis plastica; metastatic signet ring cell carcinoma; neuroendocrine carcinoma, grade 1; neuroendocrine carcinoma, grade 3; neuroendocrine carcinoma, metastatic; neuroendocrine tumor grade 2; spindle cell carcinoma (each n = 1).
G/GEJC, gastric/gastroesophageal junction cancer; GEJ, gastroesophageal junction; LOT1, first line of therapy.

- Test results for HER2, PD-L1, and MSI/MMR are shown in **Table 2**

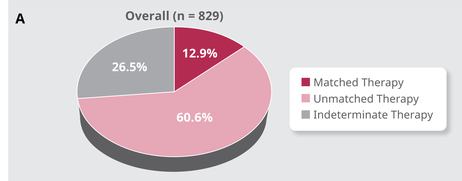
Table 2. Biomarker Testing Results for Patients With Advanced G/GEJC in the Tempus Database

	Patients with advanced G/GEJC n = 829
Tested for HER2, n (%)	**528 (63.7)**
Positive	82 (15.5)
Negative	416 (78.8)
Unknown	30 (5.7)
Tested for PD-L1,[a] n (%)	**513 (61.9)**
CPS = 0	32 (6.2)
CPS ≤ 1[b]	174 (33.9)
1 < CPS < 5	75 (14.6)
5 ≤ CPS < 10	54 (10.5)
CPS ≥ 10	90 (17.5)
Positive	21 (4.1)
Negative	31 (6.0)
Unknown	36 (7.0)
Tested for MSI/MMR, n (%)	**826 (99.6)**
High	29 (3.5)
Stable	693 (83.9)
Unknown	104 (12.6)

[a]CPS data were reported by the cutoff values if available; otherwise, categorical result (ie, positive and negative) were reported.
[b]If the laboratory/pathology reported the number of positive cells as '≤ 1' for a sample, a CPS could not be calculated exactly, but it could be concluded that CPS was also '≤ 1' (n = 94).
CPS, combined positive score; G/GEJC, gastric/gastroesophageal junction cancer; HER2, human epidermal growth factor receptor 2; MSI/MMR, microsatellite instability/mismatch repair; PD-L1, programmed cell death ligand 1.

- Use of matched therapy based on actionable biomarkers occurred in 107/826 (12.9%) patients with advanced G/GEJC (**Figure 4**)
  - Details on how matched therapy was evaluated can be found in the supplementary material, via the quick response (QR) code

Figure 4. Biomarker Testing Results by Matched Therapy Status in Patients With Advanced G/GEJC: Overall (A) and PD-L1 Tested by HER2 Tested Status (B)



B

	HER2 Positive		HER2 Negative	
	Matched (n = 52)	Unmatched (n = 23)	Matched (n = 39)	Unmatched (n = 287)
PD-L1 tested, n (%)				
CPS < 5	17 (32.7)	8 (34.8)	4 (10.3)	121 (42.2)
5 ≤ CPS < 10	2 (3.8)	1 (4.3)	10 (25.6)	16 (5.6)
CPS ≥ 10	8 (15.4)	6 (26.1)	22 (56.4)	25 (8.7)
Positive	0 (0)	1 (4.3)	0 (0)	5 (1.7)
Negative	1 (1.9)	1 (4.3)	0 (0)	18 (6.3)
Unknown	5 (9.6)	0 (0)	1 (2.6)	11 (3.8)
Not tested	19 (36.5)	6 (26.1)	2 (5.1)	91 (31.7)

CPS, combined positive score; G/GEJC, gastric/gastroesophageal junction cancer; HER2, human epidermal growth factor receptor 2; PD-L1, programmed cell death ligand 1.

STRENGTHS/LIMITATIONS

- This was a multicenter study that included a diverse patient population from a mix of academic and community-based cancer centers
- Results of this study were based on data from the Tempus database and may not be generalizable to other populations or datasets
- Data were collected from medical records designed to support billing and continuity of patient care; thus, data completeness could have been affected. For instance, HER2 test results may be missing from the data if they were not recorded by the health care provider

CONCLUSIONS

- Contrary to current treatment guidelines, not all patients with advanced G/GEJC had documentation of testing for actionable biomarkers, and of those who did, not all were treated with appropriate matched therapies
- In addition, many patients with advanced G/GEJC started therapy prior to obtaining biomarker testing results, which represents an important missed opportunity for guideline-directed treatment
- Increased biomarker testing and use of matched therapies would likely improve survival in these patients
- Further research is needed to understand nonadherence to treatment guidelines

References

1. Drugs.com. Accessed June 7, 2024. Available at https://www.drugs.com/newdrugs/fda-approves-herceptin-her2-positivemetastatic-stomach-cancer-2375.html
2. Merck. Accessed June 7, 2024. Available at https://www.merck.com/news/fda-approves-mercks-keytruda-pembrolizumab-plus-platinum-and-fluoropyrimidine-based-chemotherapy-for-treatment-of-certain-patients-with-locally-advanced-or-metastatic-esophageal-or-g/
3. Bristol Myers Squibb. Accessed June 7, 2024. Available at https://news.bms.com/news/details/2021/U.S.-Food-and-Drug-Administration-Approves-Opdivo-nivolumab-in-Combination-with-Chemotherapy-for-Patients-with-Advanced-or-Metastatic-Gastric-Cancer-Gastroesophageal-Junction-Cancer-and-Esophageal-Adenocarcinoma/default.aspx
4. US Food & Drug Administration. Accessed June 7, 2024. Available at https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nivolumab-combination-chemotherapy-metastatic-gastric-cancer-and-esophageal
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Gastric Cancer. v2.2022. Accessed February 7, 2023. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf

Funding

This study was sponsored by Astellas Pharma Inc.

Medical writing support, conducted in accordance with Good Publication Practice (GPP 2022) and the International Committee of Medical Journal Editors (ICMJE) guidelines, was provided by Steven F. Merkel, PhD, of Oxford PharmaGenesis Inc., Newtown, PA, USA, and funded by Astellas Pharma Inc.

Conflicts of Interest

SJK reports receiving consulting fees from Astellas Pharma and Novartis; receiving honoraria from Merck Sharp & Dohme; serving a consulting or advisory role for Amgen, Astellas Pharma, Novartis, Pfizer, Sanofi-Aventis, Merck Sharp & Dohme, Bristol Myers Squibb, IMAB, Mersana Therapeutics, Natera, AstraZeneca, Daiichi Sankyo, Laboratoires Servier, Coherus BioSciences; serving as a committee member for National Comprehensive Cancer Network; and had received stocks from Turning Point Therapeutics (by June 2022) and Nuvalent (by November 2022).

RMF, **DN**, and **SB** are full-time employees of Astellas Pharma Global Development, Inc.

AB, **CS**, and **SN** are full-time employees of Tempus AI, Inc., which received funding from Astellas Pharma Global Development, Inc. to conduct this study.

RM reports receiving consulting fees from Merck, Bristol Myers Squibb, Eli Lilly, Novartis, Astellas Pharma, Seagen, Guardant Health, BostoGene, Eisai, AstraZeneca, Arcus Biosciences, GSK, and Natera for participation on data safety monitoring or advisory boards.

Click or scan this quick response (QR) code to download this poster, along with its supplementary material. Copies of this poster obtained through the QR code are for personal use only and may not be reproduced without written permission of the authors.

For more information, please direct comments or inquiries to: Samuel J. Klempner, **email:** sklempner@mgb.org

Poster presented at the European Society for Medical Oncology Gastrointestinal Cancers (ESMO GI) Congress; June 26–29, 2024; Munich, Germany