Real-World Unmet Needs in Patients with HER2-negative Advanced Gastric, Gastroesophageal or Esophageal Adenocarcinoma Receiving First-Line Treatment Globally

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Conclusion

- Novel treatments with higher response rates and comparable or better safety profiles are needed for patients with advanced HER2-negative gastric, gastroesophageal junction or esophageal adenocarcinoma (GC/GEJ/EAC).
- Half of the patients receiving first line (1L) chemotherapy or chemotherapy combined with immune checkpoint inhibitors (ICI [standard of care]) had not experienced a partial or complete response.
- In this convenience sample, the adverse event (AE) profile was comparable between patients receiving 1L chemotherapy alone or chemotherapy+ICI, suggesting that the addition of ICI didn't lead to an increase in AEs from both physician reported and patient self-reported data. The physician- patient differences in the reporting of AEs suggests that AEs may be perceived differently by physicians and patients.

Plain Language Summary

- Patients with cancer of the stomach or esophagus can be treated with chemotherapy with or without medication that helps the immune system attack the cancer. However, it is not known how these medications make patients feel in a real-world environment, or how the cancer responds to treatment.
- We surveyed patients and doctors to understand any side effects of these medications along with how the cancer responded to the treatment.
- About half of patients on any treatment (chemotherapy or chemotherapy+immune system medication) did not have their cancer respond to the treatment.
- The most common side effects reported by doctors was feeling nauseous and having numb hands and feet. The side effects were similar for patients receiving chemotherapy only and chemotherapy alongside immune system medication.
- Patients often reported appetite loss and trouble sleeping.
- There is a need for more effective medicines to treat cancer of the stomach or esophagus. These new medicines should not have worse side effects than current treatments.

Limitations

- Patients were required to be living at the time of data collection; therefore, in this convenience sample, patients who died during treatment are not included in the DSP.
- While minimal inclusion criteria governed the selection of the participating physicians, who were recruited in order to provide a diverse and pragmatic sample, participation was influenced by willingness to complete the survey.
- This was a convenience sample of physicians and patients; hence further research is needed to generalize the results.

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Introduction

- The incidence and mortality rate of advanced gastric, gastroesophageal junction or esophageal adenocarcinoma (GC/GEJC/EAC) remains high despite the recent monotherapy use of immune checkpoint inhibitors (ICI) in the first-line (1L) setting.
- 1L ICIs in combination with chemotherapy have been shown to benefit patients in the clinical setting [1, 2], with additional treatment options such as STAR-221 [3], aiming to further improve patient outcomes.
- There is currently limited information on the real-world impact of 1L ICI in a heterogenous population of patients with advanced or metastatic HER2-GC/GEJC/EAC. Adverse event (AE) reporting by both patients and physicians has not been well studied, with a further need to understand response to treatment in patients receiving 1L ICI plus chemotherapy (fluorouracil + leucovorin + oxaliplatin, or capecitabine + oxaliplatin) or 1L chemotherapy alone.
- This study assessed real-world unmet needs and treatment-related AEs among patients with advanced HER2- GC/GEJC/EAC in Europe, the United States (US) and Asia who received 1L chemotherapy alone or in combination with ICI.

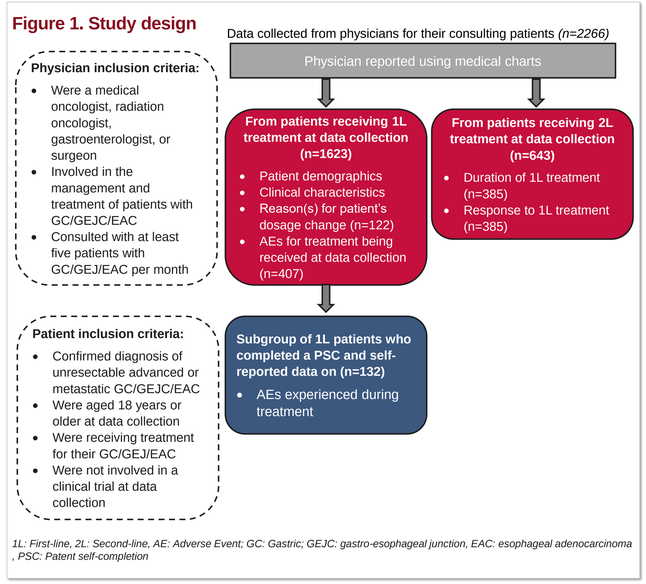
Objectives

- To describe the real-world AEs of 1L treatment with chemotherapy (alone or in combination with ICI), as reported by both GC/GEJC/EAC patients and their treating physicians.
- To understand 1L treatment duration and response in the real-world setting.

Methods

- Data were extracted from the Adelphi Real World gastric cancer Disease Specific Programme™ (DSP).This is a cross-sectional survey that includes retrospective data collected by physicians via medical chart review for their next consecutively consulting patients with advanced or metastatic HER2-negative GC/GEJC/EAC, who are receiving 1L or 2L+ treatment and alive at the time of data collection.
- Data were collected across Europe (France, Germany, Spain and the United Kingdom), the United States and Asia (China, Japan, South Korea) between October 2022 and September 2024.
- The DSP methodology has been described [4, 5], validated [6] and shown to be representative and consistent over time [7]. The design and inclusion criteria of the Adelphi Real World gastric cancer DSP is shown in **Figure 1**.
- Physicians reported patient demographics, clinical characteristics, reasons for dosage change and any AEs for patients receiving 1L treatment at data collection. Additionally, the response to 1L treatment of patients receiving 2L+ at data collection was also reported by physicians. Patients voluntarily completed a patient self-completion (PSC) questionnaire reporting AEs.
- Analyses were descriptive.

Figure 1. Study design



1L: First-line, 2L: Second-line, AE: Adverse Event; GC: Gastric; GEJC: gastro-esophageal junction, EAC: esophageal adenocarcinoma , PSC: Patent self-completion

Results

- Overall, 450 physicians reported on 1623 patients receiving 1L treatment and 643 patients receiving 2L+ treatment at the time of data collection. In total, 132 patients self-reported data. 1L patient demographics and clinical characteristics can be found in **Table 1**.

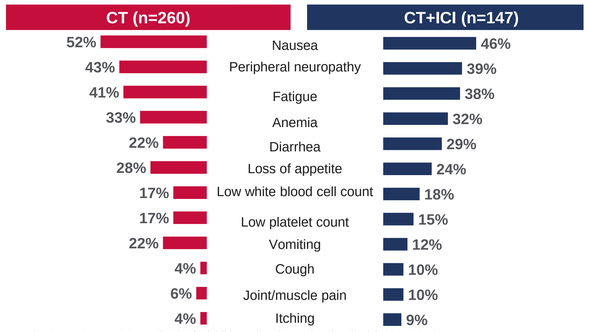
Table 1. Demographics and clinical characteristics of patients with HER2- GC/GEJC/EAC receiving 1L treatment at the time of data collection

	All patients (n=1623)	Treatment type			Region		
		CT (n=551)	CT + ICI (n=389)	Other (n=683)	Europe (n=977)	US (n=154)	Asia (n=492)
Age in years, median (IQR)	67 (59–71)	67 (60–71)	65 (58–70)	67 (59-72)	67 (61–72)	66 (58–70)	65 (57–71)
Biological males, n (%)	1173 (72)	396 (72%)	275 (71)	502 (73)	702 (72)	116 (75)	355 (72)
Ethnicity, n (%) [a]							
White	729 (89)	319 (92)	144 (84)	266 (88)	629 (94)	100 (65)	
Non-White	92 (11)	29 (8)	27 (16)	36 (12)	39 (6)	53 (35)	
PD-L1 CPS score where known, n (%)							
<5	517 (32)	279 (51)	21 (5)	217 (32)	306 (31)	27 (18)	184 (37)
≥5	544 (34)	37 (6)	312 (80)	195 (29)	333 (34)	63 (41)	148 (30)
Disease status at latest diagnosis, n (%)							
De novo	474 (29)	108 (20)	68 (17)	298 (44)	227 (23)	73 (47)	174 (35)
Relapsed	1144 (70)	440 (80)	319 (82)	385 (56)	748 (77)	81 (53)	315 (64)
ECOG score at 1L treatment initiation, n (%)							
0–1	1300 (80)	434 (79)	333 (86)	540 (79)	761 (78)	128 (83)	411 (84)
2–4	322 (20)	116 (21)	56 (14)	142 (21)	215 (22)	26 (17)	81 (16)
Practice setting, n (%)							
Academic	1143 (70)	446 (81)	278 (71)	419 (61)	263 (76)	51 (56)	280 (78)
Community	480 (30	105 (19)	111 (29)	264 (39)	85 (24)	40 (44)	81 (22)

[a] non-white categories include Hispanic/Latino/Latina, Afro-Caribbean, Asian, South-East Asian, Asian, Middle Eastern, Other, African American, Native American; CT: Chemotherapy; CPS, Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; GC/GEJC/EAC: Gastric, gastro-esophageal junction and esophageal adenocarcinoma; ICI: Immune checkpoint inhibitor; US: United States; 1L: First-line; <: less than; ≥greater than or equal to. Please note that Asia consists of China, South Korea and Japan. Europe consists of the United Kingdom, France, Germany and Spain. Ethnicity data were not collected in Asia or France. There is one US patient for which ethnicity data were not available.

- Among the 1623 patients receiving 1L treatment at data collection, 34% (n=551) received chemotherapy alone and 24% (n=389) of patients received chemotherapy+ICI.
- Of these, physician-reported AEs information was available for 47% (n=260) and 38% of patients (n=147), respectively.
  - The most common AEs in patients who received chemotherapy alone or chemotherapy+ICI at 1L were nausea and peripheral neuropathy. Notably, the incidence of diarrhoea and vomiting in patients receiving chemotherapy alone at 1L was 22% and 22%, respectively, compared to 29% and 12% for those receiving chemotherapy+ICI (**Figure 2**).

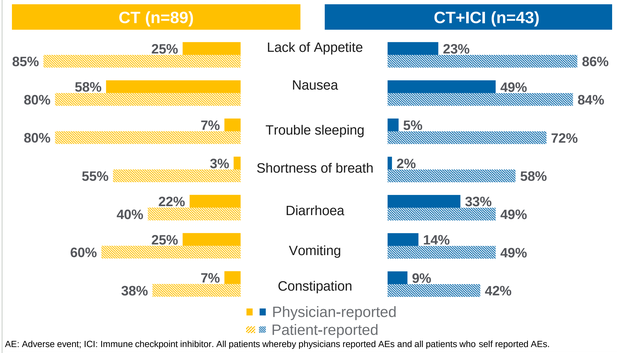
Figure 2. The most common AEs in patients treated with chemotherapy or chemotherapy+ICI



AE: Adverse event; ICI: Immune checkpoint inhibitor. All patients whereby physicians reported AEs .

- Of patients from this convenience sample who received 1L chemotherapy or chemotherapy+ICI, 89 and 43 patients, respectively, also self-reported AEs. Self-reported AEs were compared to those reported by physicians (**Figure 3**). Notably, 80% of patients on chemotherapy and 72% on chemotherapy+ICI reported trouble sleeping compared to 7% and 5% of their physicians, respectively. For shortness of breath this was 55% and 58% of patients, respectively, compared to 3% and 2% of their physicians.

Figure 3. Reporting of AEs by physicians and patients treated with chemotherapy or chemotherapy+ICI



AE: Adverse event; ICI: Immune checkpoint inhibitor. All patients whereby physicians reported AEs and all patients who self reported AEs.

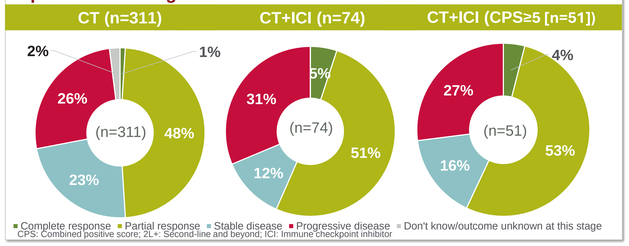
- Of the 69 and 53 patients receiving 1L chemotherapy alone or chemotherapy+ICI, respectively, who required a dose change, 90% (n=62) and 89% (n=47) of patients changed due to unacceptable tolerability and 7% (n=5) and 6% (n=3) due to patient request.
- Data were also collected from patients who were on 2L+ at data collection but received chemotherapy (n=311) or chemotherapy+ICI (n=74) at 1L (**Table 2**). Around half of patients who received 1L chemotherapy or chemotherapy+ICI experienced a partial or complete response, respectively (**Figure 4**). Mean (standard deviation) treatment duration for those who received chemotherapy or chemotherapy+ICI at 1L was 6.2 (3.2) and 7.5 (5.8) months.

Table 2. Demographics and clinical characteristics of patients with HER2-GC/GEJC/EAC who received 1L chemotherapy or chemotherapy+ICI and were receiving 2L+ treatment at the time of data collection

	Treatment type	
	CT (n=311)	CT+ICI (n=74)
Age in years, median (IQR)	69 (63–73)	66 (58–71)
Biological males, n (%)	202 (65)	56 (76)
Ethnicity, n (%)[a]		
White	155 (91)	20 (77)
Non-white	16 (9)	6 (33)
Disease staging at initiation of 1L treatment, n (%)		
Stage III	31 (10)	2 (3)
Stage IV	280 (90)	72 (97)
ECOG score at initiation of 1L treatment, n (%)		
0–1	258 (83)	66 (89)
2–4	53 (17)	8 (11)

[A] Non-white categories include Hispanic/Latino/Latina, Afro-Caribbean, Asian, South-East Asian, Asian, Middle Eastern, Other, African American, Native American; CT: Chemotherapy; ECOG: Eastern Cooperative Oncology Group; GC/GEIC/EAC: Gastric, gastro-esophageal junction and esophageal adenocarcinoma; ICI: Immune checkpoint inhibitor; 1L: First-line;2L+ second-line and beyond.

Figure 4. Response to 1L chemotherapy or chemotherapy+ICI treatment in patients receiving 2L+ at data collection



CPS: Combined positive score; 2L+: Second-line and beyond; ICI: Immune checkpoint inhibitor

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