

Symptoms of gastric cancer from a patient perspective

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BACKGROUND

- Patients with metastatic gastric cancer (GC) have a poor prognosis, including a 5-year survival rate of ≈4% and a median overall survival (OS) of ≈1 year^{1,2}
- Treatment generally involves multimodal chemotherapy with platinum agents, taxanes, and fluoropyrimidines, or targeted therapies as single agents or in combination with chemotherapy³; clinical trials of anti-PD-L1/PD-1 monoclonal antibodies are ongoing⁴⁻¹⁴
- There is currently a paucity of data surrounding the impact of GC and chemotherapy regimens on patients' health-related quality of life (HRQoL) and the value of collecting these data as part of standard clinical trial practices
- Patient-reported outcome (PRO) measures, such as the European Organization for Treatment of Cancer (EORTC) general module (EORTC QLQ-C30),¹⁵ have historically been limited by trial design characteristics (eg, single-arm or open-label studies)¹⁶
- Here, we present PRO data from a qualitative assessment of patients with locally advanced or metastatic adenocarcinoma of the stomach or the gastroesophageal junction (GC/GEJC) using the traditional EORTC QLQ-C30 questionnaire and the EORTC's disease-specific GC module, the QLQ-STO22,¹⁵ as a framework to understand the key GC/GEJC- and treatment-related symptoms that should be assessed in clinical trials

OBJECTIVES

- Understand the key disease- and treatment-related symptoms that are experienced by patients with GC/GEJC and determine key PRO concepts that should be measured in clinical trials
- Identify EORTC subscales from the EORTC QLQ-C30 and QLQ-STO22 modules that correspond with the key disease- and treatment-related symptoms of importance to patients with GC/GEJC and their clinicians

METHODS

Study design

- RTI Health Solutions (RTI-HS), a nonprofit, independent research organization, conducted individual, in-depth interviews with patients to better understand what key disease- and treatment-related symptoms patients experience and/or key concepts that should be measured in clinical trials of patients with GC/GEJC
 - Eligible patients (**Table 1**) were screened by the recruitment partners and scheduled for a telephone interview with RTI-HS

Table 1. Key patient eligibility criteria

Mandatory inclusion criteria	Desired (optional) inclusion criteria
Unresectable, locally advanced or metastatic GC/GEJC	No prior chemotherapy for unresectable locally advanced GC/GEJC
≥18 years of age	Currently receiving standard-of-care (SOC) chemotherapy as first-line treatment for advanced disease ³
Literacy and fluency in English	Self-reported ECOG PS ≤2
Willing and able to participate in a 1-hour interview	No human epidermal growth factor receptor overexpression and no prior or current first-line treatment with trastuzumab

ECOG, Eastern Cooperative Oncology Group; PS, performance status.

Patient interviews

- Interviews, based on semi-structured, study-specific guides, were co-conducted by 2 experienced RTI-HS interviewers (**Figure 1** and **Table 2**)
 - Patient interviews focused on disease-specific symptoms as well as symptoms experienced as a result of treatments for GC/GEJC
 - Patients were read the items of the EORTC disease-specific module (QLQ-STO22), followed by items from the general cancer module (QLQ-C30), and asked to note whether they had ever experienced the symptom or side effect in question

Figure 1: Interview format

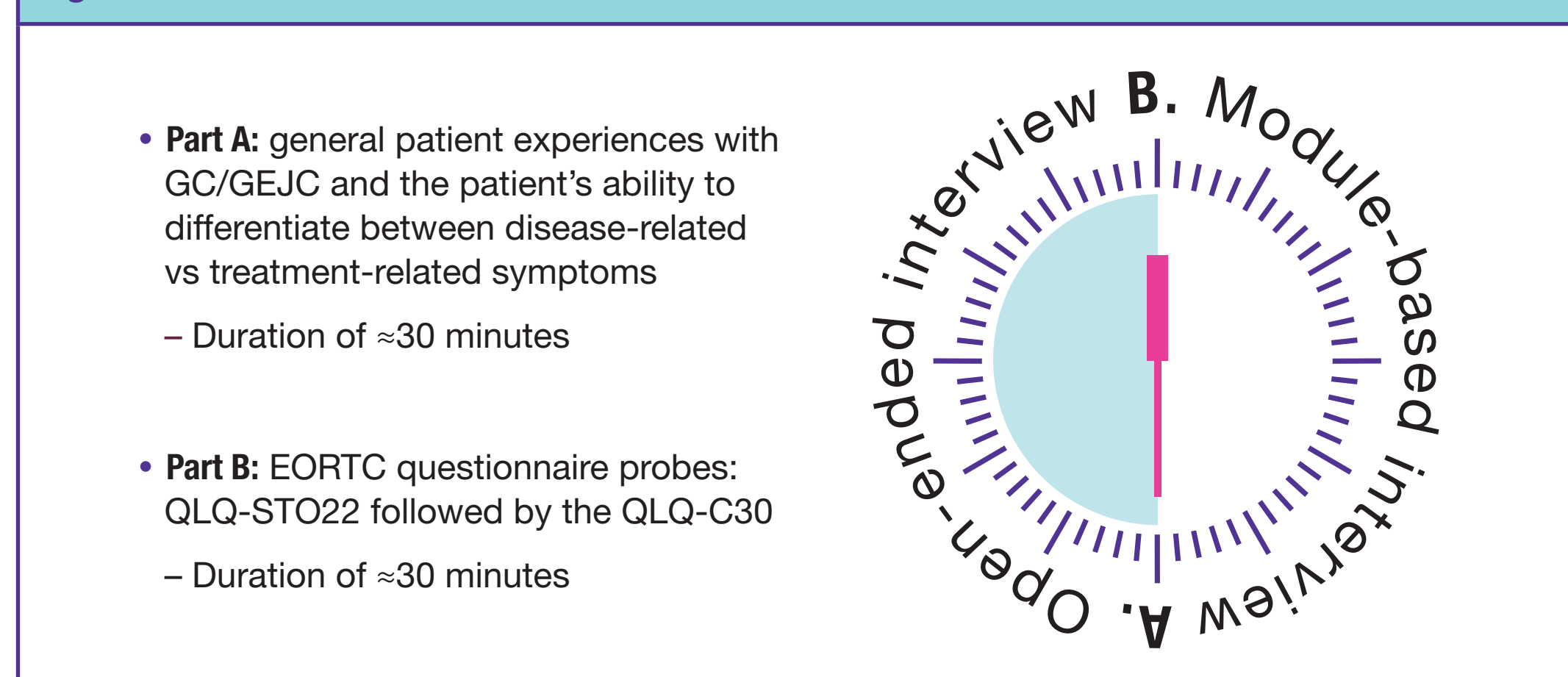


Table 2. PRO instruments

	GC-specific	General cancer
Questionnaire	QLQ-STO22	EORTC QLQ-C30
Purpose	Identify disease symptoms, treatment side-effects, and emotional issues specific to GC	Assess key functional aspects of HRQoL in cancer patients, regardless of tumor type
Items	22	30
Scales	5 scales (dysphagia, chest and abdominal pain, reflux, eating restrictions, and anxieties) and 4 single items (dry mouth, body image, taste problems, and hair loss)	5 functional scales (physical, role, cognitive, emotional, and social), 3 symptom scales (fatigue, pain and nausea, and vomiting), a global health status/QoL scale, and 6 single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties)

RESULTS

Patient population

- Eligible patients (N=12) had self-reported unresectable, locally advanced or metastatic GC/GEJC (**Table 3**)
 - 4 patients were recruited through L&E Research, a qualitative research facility in Raleigh, NC, USA
 - 8 patients were recruited through a patient advocacy group, Debbie's Dream Foundation: Curing Stomach Cancer
 - ≈50% of study participants were diagnosed with GC/GEJC ≥1 year prior to study; the remaining patients were diagnosed within the past 4 years (**Table 3**)

Table 3: Baseline characteristics of study participants

Characteristics	N=12 n (%)
Mean age, years (range)	58.0 (27-74)
Sex, n (%)	
Male	9 (75)
Female	3 (25)
ECOG PS, n (%)	
0	5 (42)
1	5 (42)
2	2 (17)
Race, n (%)	
White	11 (92)
Other	1 (8)
Highest level of education, n (%)	
Some college	3 (25)
College degree	5 (42)
Professional degree	4 (33)
Occupation, n (%)	
Not working/retired	8 (67)
Working (full time/part time)	3 (25)
Homemaker	1 (8)
Current treatment for GC/GEJC, n (%)	
Chemotherapy*	9 (75)
Targeted therapy	1 (8)
Hormone therapy	1 (8)
Immunotherapy (unspecified)	1 (8)

* 2 patients reported current SOC chemotherapy treatment³

Patient-reported symptoms attributed to GC/GEJC vs treatment of GC/GEJC

- 19 symptoms of GC/GEJC were self-reported by patients (**Table 4**), most commonly stomach pain and early satiety (n=6; 50%), constipation (n=5, 42%), tiredness, diarrhea, difficulty swallowing (n=4; 33%), and weakness, flu-like symptoms, and vomiting (n=3; 25%)
- Patients reported 20 symptoms related to treatment of GC/GEJC (**Table 5**), most commonly fatigue/tiredness (n=9; 75%), neuropathy (n=6; 50%), and vomiting (n=5; 42%)

Table 4: Disease-related patient-reported symptoms attributed to GC/GEJC (≥25% of patients)

Symptom	N = 12 n (%)	Patient description of symptoms
Stomach pain	6 (50)	"I had stomach pains that bothered me a lot... seemed like that was a sign that something was not right."
Early satiety	6 (50)	"It seems I couldn't... I ate, but I felt full all the time."
Constipation	5 (42)	"So I was worried I had diverticulitis and [...] maybe the constipation had something to do with that."
Tiredness	4 (33)	"I was tired. So you know, I... Just didn't feel well."
Diarrhea	4 (33)	"A lot of diarrhea and constipation."
Difficulty swallowing	4 (33)	"Having trouble swallowing and getting the food down, digesting it, lots of pain."
Weakness	3 (25)	"The weakness was from not eating."
Flu-like symptoms	3 (25)	"Oftentimes I felt sick [...] often time I got fever and all that."
Vomiting	3 (25)	"I had vomiting. I felt sick every time I ate something."

Table 5: Patient-reported symptoms attributed to GC/GEJC treatment

Symptom	N = 12 n (%)	Patient description of symptoms
Fatigue/tiredness	9 (75)	"Well, the treatment itself, I had a lot of other side effects like really tired, [...] feeling horrible at times..."
Neuropathy	6 (50)	"And the neuropathy is just a constant annoyance."
Vomiting	5 (42)	"I did a lot of vomiting during the time I was on [chemotherapy]."
Nausea	4 (33)	"Well, because I couldn't function when I was nauseous."
Sleep issues	3 (25)	"But I had trouble sleeping."
Flu-like symptoms	3 (25)	"Well, the treatment itself [...] flu-like symptoms, aching..."
Weakness	2 (17)	"I'd say the most important is feeling weak, interfering with family life, and worried and being worried"
Hair loss	2 (17)	"Hair loss, yes, when I went from [chemotherapy]..."
Skin issues (red spots/peeling)	2 (17)	"Dry skin things, so my skin started peeling off on my feet."
Hypersensitivity to cold	2 (17)	"I couldn't drink anything cold after the [chemotherapy] for at least 5 days. I couldn't really step on cold tile, or I would feel it."
Toenails splitting	2 (17)	"My toenails seem to be almost cracking in half, some of them. I don't know if that was from the chemo or not."
Dizziness	2 (17)	"I was dizzy. I mean, it was taking over my body."
Swelling of legs/feet	1 (8)	"... I got this tingling and swelling that went down to my feet and into my hands."
Constipation	1 (8)	"Constipation was a cause of the treatment."
Pain in stomach that moves to back and legs	1 (8)	"The pain is usually in the stomach area and it radiates all around."
No appetite	1 (8)	"My appetite wasn't great at the beginning of chemo..."
Abdominal swelling	1 (8)	"And my stomach was swollen. Whether that was related to the cancer or the treatment, I think it was a combination of both."
Weight loss	1 (8)	"... I was losing that weight and I really felt like I was atrophying..."
Nails separated from nail bed	1 (8)	"... very unusual where the nail was separating from the nail bed..."
Anxiety	1 (8)	"And there's time where you have to talk to yourself from getting anxiety attacks because it's basically poison going into your body."

* Can also be observed as a clinical sign

Patient-endorsed concepts from the EORTC modules

- Of the 12 patients, 8 (66.7%) spontaneously reported experiencing ≥15 of 22 symptoms queried on the QLQ-STO22 questionnaire
 - Most of the participants endorsed 4 of 4 items in the pain subscale as well as 3 of 4 items in the eating restrictions subscale (**Table 6**)
- 8 of 12 patients (66.7%) reported ≥20 of 30 items on the QLQ-C30 questionnaire; most participants endorsed the items included in the fatigue subscale (**Table 7**)

Table 6: Probed results from the GC-specific module, EORTC QLQ-STO22

Items in the EORTC QLQ-STO22	N = 12 n (%)
Problems eating solid foods	9 (75)
Problems eating liquidised or soft foods	3 (25)
Problems drinking liquids	6 (50)
Discomfort when eating*	11 (92)
Stomach pain*	11 (92)
Stomach discomfort*	11 (92)
Bloating*	10 (83)
Acid or bile in mouth	5 (42)
Acid indigestion or heartburn	6 (50)
Belching	6 (50)
Fill up quickly when eating*	10 (83)
Trouble enjoying meals*	12 (100)
Takes a long time to complete meals*	8 (67)
Dry mouth	6 (50)
Food and drink taste different	7 (58)
Trouble eating in front of others*	4 (33)
Thinking about illness	12 (100)
Worried about low weight	8 (67)
Feeling less attractive	6 (50)
Worried about health in future	11 (92)
Hair loss	11 (92)
Upset by hair loss*	5 (42)

Items listed in order of questionnaire. Bold font denotes items endorsed by >65% of participants; * Classified within EORTC pain subscale; † Classified within EORTC eating restriction subscale; ‡ Item applicable only to responders with hair loss.

Table 7: Probed results from the general cancer module (EORTC QLQ-C30)

Items in the EORTC QLQ-C30	N = 12 n (%)
Trouble doing strenuous activity	9 (75)
Trouble taking a long walk	7 (58)
Trouble taking a short walk outside	1 (8)
Need to stay in bed or chair	5 (42)
Need help eating/dressing/washing self/using toilet	3 (25)
Limited in doing work or other daily tasks	8 (67)
Limited in doing hobbies or other leisure tasks	9 (75)
Short of breath	8 (67)
Had pain	9 (75)
Needed rest*	11 (92)
Trouble sleeping	11 (92)
Felt weak*	9 (75)
Lacked appetite	10 (83)
Nauseated	7 (58)
Vomited	5 (42)
Constipated	7 (58)
Diarrhea	8 (67)
Tired*	10 (83)
Pain interfered with daily tasks	6 (50)
Difficulty concentrating	8 (67)
Tense feeling	8 (67)
Worry	9 (75)
Irritable	10 (83)
Depressed	8 (67)
Difficulty remembering things	6 (5)
Condition/treatment interfered with family life	8 (67)
Condition/treatment interfered with social tasks	7 (58)
Condition/treatment caused financial difficulties	6 (50)

Items listed in the order of the questionnaire; Bold text denotes items endorsed by >65% of participants; * Classified within EORTC fatigue subscale.

CONCLUSIONS

- Results from the patient interviews indicated that nearly all spontaneously reported symptoms were assessed in 1 or both EORTC modules, and no significant patient-reported concepts were considered missing across the 2 modules
 - Patients most often associated fatigue and neuropathy with treatment for GC/GEJC; however, patients also reported decreased pain, satiety, difficulty swallowing, constipation, and diarrhea following treatment of GC/GEJC
- The EORTC subscales that assessed the most common patient-reported symptoms were:
 - EORTC QLQ-STO22: pain subscale
 - EORTC QLQ-STO22: eating restrictions subscale
 - EORTC QLQ-C30: fatigue subscale

FUTURE CONSIDERATIONS

- Inclusion of both the QLQ-C30 and the QLQ-STO22 in clinical trials may provide a more complete assessment of HRQoL in patients with GC/GEJC than use of either instrument alone
- PRO measures to assess HRQoL in patients undergoing first-line treatment for stage IV GC are planned^{13,14}

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