Poster 1586P

Characteristics, treatment patterns, and outcomes of patients with advanced/metastatic gastric cancer or gastro-esophageal junction adenocarcinoma previously treated with anti-HER2 therapy in an English national registry

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Objective

- To describe characteristics, treatment patterns, and outcomes of patients with advanced/metastatic gastric cancer (GC) or gastro-esophageal junction (GEJ) adenocarcinoma who received anti-human epidermal growth factor receptor (HER2) therapy (trastuzumab) as first line of treatment (1st LoT), based on an English national registry.

Conclusions

- Treatments following 1st LoT anti-HER2 regimens were mainly limited to chemotherapy. More than half of patients in the study cohort died without receiving any subsequent systemic anti-cancer therapy (SACT).
- Overall survival for patients in England with advanced/metastatic GC/GEJ adenocarcinoma previously treated with 1st LoT anti-HER2 regimens remains poor, reflecting a high unmet need for more effective 2nd LoT-onward HER2-directed treatment.

Plain language summary

Why did we perform this research?
To gain a better understanding of how anti-cancer treatment is prescribed to patients with advanced stomach cancer and how these treatments affect survival.

How did we perform this research?
This was a retrospective study using data from an NHS database. The database contains over 140 million patient records, which represents the majority of cancer patients in England. Database entries from January 2010 to December 2019 were included in the study.

What were the findings of this research?
In the database, we identified 948 patients who had started their first treatment for advanced stomach cancer. Of these 948 patients:
- just over 3 in 10 patients were prescribed a 2nd treatment after failing their first-line treatment
- less than 1 in 10 patients continued to receive a 3rd treatment.

Second-line treatments are largely limited to taxanes and irinotecan. Even after receiving 2nd or 3rd treatments, patients only survived for approximately 6 months.

What are the implications of this research?
This research shows that there is an urgent need for more effective 2nd and 3rd LoT options for patients with advanced stomach cancers.

Where can I access more information?
Clinical practice guideline for the treatment of gastric cancer can be found here: https://www.esmo.org/guidelines/guidelines-by-topic/gastrointestinal-cancers/clinical-practice-guideline-gastric-cancer

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Introduction

- GC is often diagnosed at an advanced stage due to insidious disease onset and a lack of screening programmes in England.[1]
- HER2-positive tumours account for approximately 20–30% of GC and GEJ adenocarcinomas. HER2-positivity is a marker of poor prognosis and associated with reduced survival compared with HER2-negative tumours.[2,3]
- There is no approved HER2-directed treatment for GC or GEJ adenocarcinoma after 1st LoT with trastuzumab in England.[3]
- The aim of this observational, non-interventional, retrospective registry study was to describe real-world (rw) treatment patterns and outcomes for patients with GC/GEJ adenocarcinoma receiving SACT.
- A better understanding of the patient journey can help in developing more effective management strategies.

Methods

Study population

The study population was defined as patients in the CAS dataset aged ≥18 years who had:
- pathologically documented inoperable, locally advanced or metastatic (de novo or relapsed/progressed) GC or GEJ adenocarcinoma, and
- initiated physician's choice of 1st LoT in palliative settings with a trastuzumab-containing regimen.

Receipt of a trastuzumab-containing regimen was used as a proxy for HER2 status.

Patients meeting any of the following exclusion criteria were not eligible:
- any other type of primary malignancy,
- any systemic chemotherapy treatment more than 30 days before GC or GEJ adenocarcinoma diagnosis,
- missing vital status, or
- actively treated with the Cancer Drugs Fund registry.

The **Cancer Analysis System (CAS)** is a registry managed by England's National Health Service (NHS), containing 141 million patient records and representing >98% of cancer patients in England.

- **Eligible patients** were identified in the CAS English Cancer Outcomes Services Dataset (Jan 2010–Dec 2019).
- **Treatment pathways and outcomes** were obtained from the Systemic Anti-Cancer Therapy Dataset (Jan 2014–May 2021).
- A novel, regimen-based algorithm was developed to report treatment sequencing and analyse outcomes by LoT.

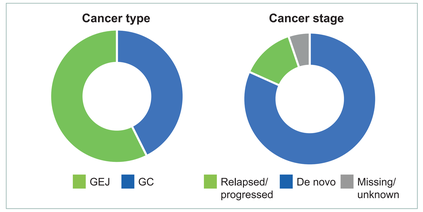
Upon demonstration that this study was for the general benefit of healthcare, no further ethical approval was required.

Analysis methods
- All variables were analysed descriptively.
  - Numbers and percentages were provided for categorical variables.
  - Means, medians, standard deviations, and quartiles were provided for continuous variables.
- Time-to-event outcomes (rwOS and rwTTD) were analysed using Kaplan–Meier estimation.
  - rwOS (overall survival) was defined as the length of time between the start date of a given LoT and the date of death due to any cause.
  - rwTTD (time to discontinuation or death) was defined as the length of time from the start date of a given LoT and the end date of that LoT or death, whichever came first.
  - Patients were censored at the study end date or at the last available record (if lost to follow-up).

Results and interpretation

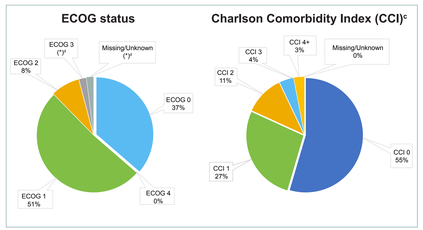
1. Patient demographics and clinical characteristics[a]

A total of 948 patients fulfilled all eligibility criteria and were included in the study cohort.
- Of these 948 patients, 82.1% were male and 90.4% were from a White ethnic group.
- The median age at the start of 1st LoT was 67.0 years (interquartile range [IQR] 57.0–73.0).
- In the overall cohort, 57.4% of the patients had GEJ adenocarcinoma.
- Most patients (81.8%) had a de novo advanced/metastatic disease diagnosis.



Demographics and clinical characteristics were comparable between patients with GC and GEJ adenocarcinoma.

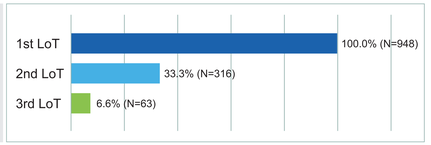
In the overall cohort[b], the most common sites for metastases at 1st LoT index date were **liver** and **lung**, followed by bone and brain:



[a]Baseline characteristics are based on information collected at 1st LoT as the date of advanced/metastatic disease was missing for the relapsed patients group.
[b]As only 54.6% of patients in the overall cohort had confirmed metastases at 1st LoT, metastasis frequency may be under-reported.
[c]The Quan *et al.*[4] CCI calculation was modified by exclusion of the primary GC/GEJ cancer codes and associated metastases.
[d]As a result of data masking, numbers ≤5 and ≥1 are replaced with a suppression symbol (*).

2. Treatment patterns

Out of 948 patients, 316 (33.3%) received 2nd LoT and **only 63 (6.6%)** received 3rd LoT.



The most common regimen for 1st LoT was capecitabine + cisplatin + trastuzumab (54.9%), which is in alignment with the guidelines from the National Institute for Health and Care Excellence (NICE).[5]

Regimens prescribed from 2nd LoT onward were largely limited to taxanes and irinotecan. The most common regimen administered as 2nd LoT was paclitaxel (36.4%), while fluorouracil + irinotecan was most common as 3rd LoT (19.1%).

Most common regimens for 2nd LoT[a]

Regimen	N	%
Paclitaxel	115	36.4%
Docetaxel	98	31.0%
Fluorouracil + irinotecan	19	6.0%

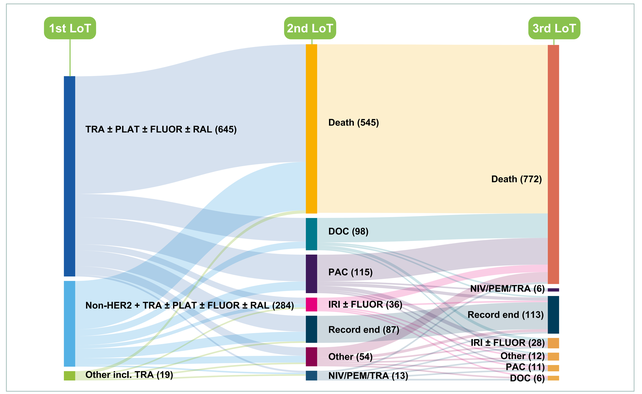
Most common regimens for 3rd LoT[a]

Regimen	N	%
Fluorouracil + irinotecan	12	19.1%
Paclitaxel	11	17.5%
Capecitabine + irinotecan	10	15.9%
Docetaxel	6	9.5%
Irinotecan	6	9.5%
Nivolumab[b]	6	9.5%

[a]Only regimens administered to >5% of the total cohort are shown.
[b]Nivolumab was given a positive scientific opinion to be part of the UK Early Access to Medicines Scheme for metastatic GC and GEJ in 2020.

Treatment-sequencing results

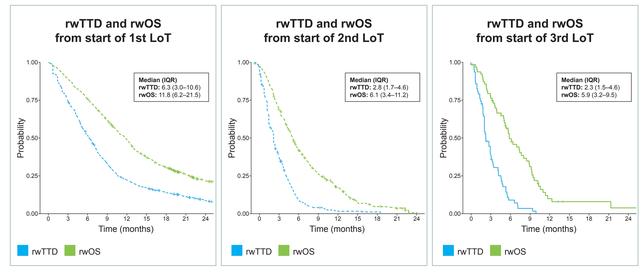
The Sankey diagram illustrates treatment sequencing from 1st to 3rd LoTs for the overall cohort (N=948), based on pre-determined treatment groups.

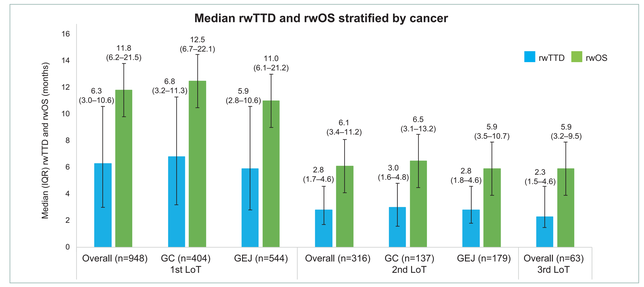


[a]"Death" was defined as patients who died after receiving a specified recorded LoT and before the end of the study time period. "Record end" was defined as patients who did not die or receive any further systemic anti-cancer treatment after a specified LoT before the end of the study time period.
DOC, docetaxel; **FLUOR**, fluoropyrimidine (5-fluorouracil/capecitabine); **IRI**, irinotecan; **NIV**, nivolumab; **Non-HER2**, oxaliplatin ± epirubicin; **PAC**, paclitaxel; **PEM**, pembrolizumab; **PLAT**, platinum compound (carboplatin/cisplatin); **RAL**, raltitrexed; **TRA**, trastuzumab.

3. Treatment outcomes

Shown below are rwTTD and rwOS for the overall cohort, together with corresponding median values. Consistent results were observed for GC and GEJ adenocarcinoma when data were stratified.





Key takeaways

HER2-overexpressing GC/GEJ adenocarcinoma has limited effective, targeted treatment options beyond 1st LoT, and outcomes for GC/GEJ adenocarcinoma remain poor.

As such, there is a high unmet need for HER2-directed treatments with the potential to improve quality of life and survival in this patient population.

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Disclosures
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