

Real-world (United States) first-line treatment patterns and overall survival of patients with unresectable advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma by HER2 status

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Background

- Human epidermal growth factor receptor 2 (HER2) status is a key determinant of first-line (1L) treatment options in gastric cancer¹
 - However, in certain clinical scenarios, the treating physician may not recommend HER2 testing prior to treatment initiation
- In gastric cancer, the reported level of HER2 overexpression and amplification varies widely from 7% to 27%²⁻⁶
- Treatment patterns and survival outcomes in patients with advanced/metastatic gastric, gastroesophageal junction, or esophageal adenocarcinoma (GC/GEJC/EAC) with unknown HER2 status remain unclear
- This study investigated real-world treatment patterns and clinical outcomes by HER2 status in patients with advanced/metastatic GC/GEJC/EAC in the United States (US), including those with unknown HER2 status

Objectives

Primary

- To describe patient characteristics and 1L treatment patterns in patients with advanced/metastatic GC, GEJC, or EAC in the real-world setting in the US

Secondary

- To estimate overall survival (OS) and progression-free survival (PFS) in patients with advanced/metastatic GC, GEJC, or EAC

Methods

- This retrospective analysis included patients from the US Flatiron Health database, which compiles data collected from > 280 community oncology practices across the US, representing more than 3 million patients with cancer annually
 - Adult patients diagnosed with advanced/metastatic GC, GEJC, or EAC between January 1, 2011 and December 30, 2020, who received at least one line of therapy, were included in the study
 - Patients had medical data for at least 1 month following the index date (date of initial diagnosis of advanced/metastatic disease)
 - Patients with other primary cancers before the index date and who received clinical trial study medications at any time during the study period were excluded
 - Patients with HER2- status who received trastuzumab on any line of treatment were excluded
- Baseline demographic and clinical characteristics and 1L treatment patterns were described
- Treatment patterns were compared between patients with HER2- and HER2-unknown status using Kendall's test
- OS, defined as time from 1L treatment initiation to death or loss of follow-up, was analyzed by Kaplan-Meier methods with log-rank test and a Cox proportional hazards model

Results

Patients

- Among all study patients (N = 3643), 19%, 57%, and 24% of patients had HER2+, HER2-, and HER2-unknown status, respectively (Figure 1)
 - Most patients in the HER2+ subgroup (65%) received 1L trastuzumab
 - Only 5% of patients with HER2-unknown status received 1L trastuzumab; most patients received fluoropyrimidine and platinum-based chemotherapy

Baseline characteristics

- Baseline demographic and clinical characteristics were generally similar between the 3 HER2 subgroups (Table 1)
 - Median age was 65 years in the HER2+ and HER2- subgroups, and 67 years in the HER2-unknown subgroup
 - Most patients were male (HER2+: 82%, HER2-: 73%, HER2-unknown: 76%), White (HER2+: 68%, HER2-: 62%, HER2-unknown: 61%), and treated in a community-practice setting (93%)
 - A lower proportion of patients in the HER2-unknown subgroup (48%) had known Eastern Cooperative Oncology Group performance status (ECOG PS) at 1L treatment initiation compared with patients in the HER2+ (56%) or HER2- (58%) subgroups
 - Most patients had stage IV disease at initial diagnosis (HER2+: 82%, HER2-: 75%, HER2-unknown: 74%)

Figure 1. Distribution of all patients and patients who received 1L trastuzumab treatment by HER2 status, n (%)

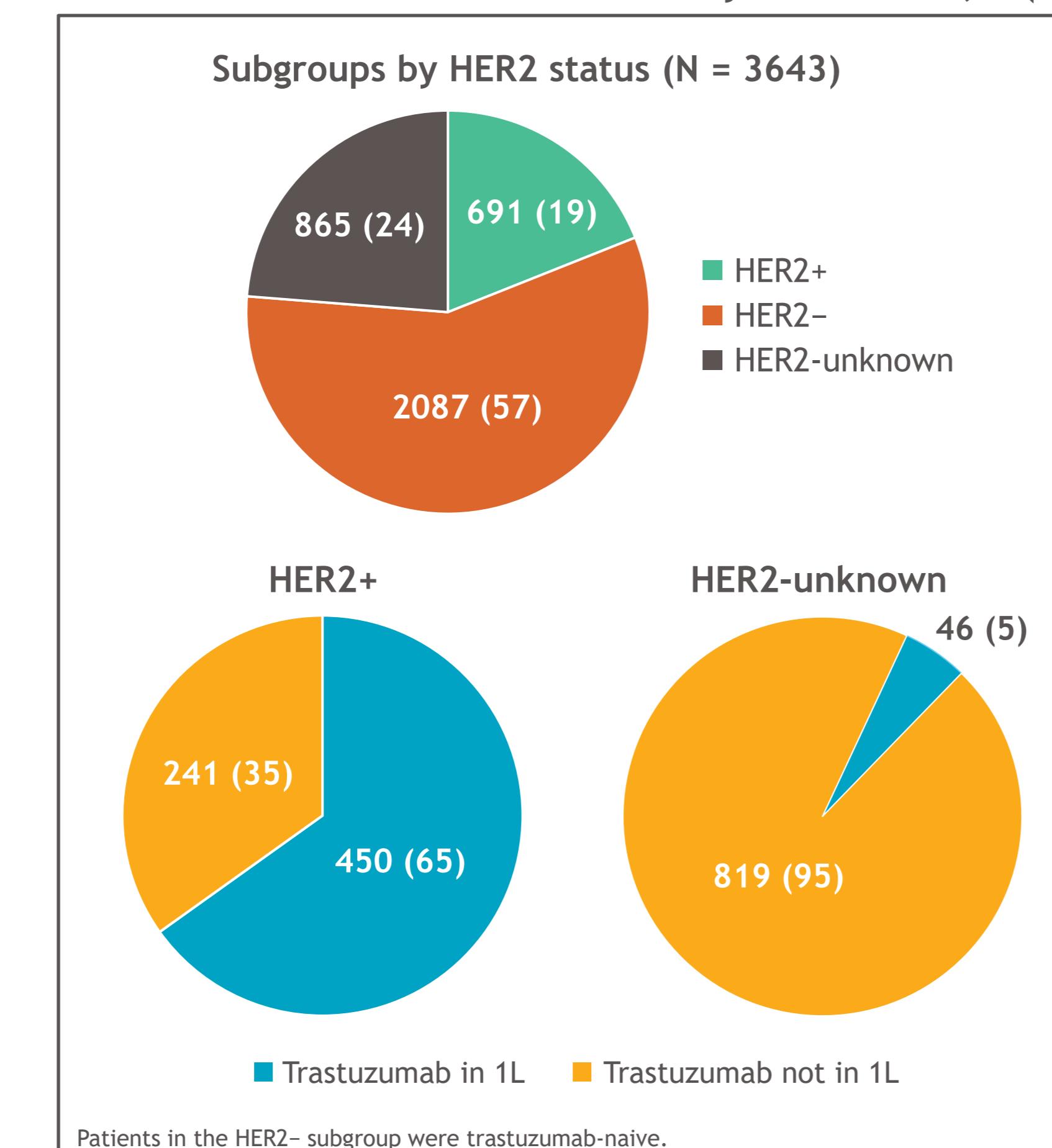


Table 1. Baseline demographic and clinical characteristics of patients (N = 3643) by HER2 status

Characteristic, n (%)	HER2+ (n = 691)	HER2- (n = 2087)	HER2-unknown (n = 865)
Age at index, median (range), years	65 (23–84)	65 (22–84)	67 (29–83)
Male	566 (82)	1517 (73)	660 (76)
Race			
White	469 (68)	1301 (62)	530 (61)
Black	44 (6)	152 (7)	53 (6)
Asian	15 (2)	94 (5)	36 (4)
Other	81 (12)	292 (14)	132 (15)
Missing	82 (12)	248 (12)	114 (13)
Community practice	646 (93)	1949 (93)	804 (93)
History of smoking	476 (69)	1298 (62)	536 (62)
ECOG PS at 1L treatment initiation ^a	390 (56)	1205 (58)	418 (48)
0 ^b	169 (43)	562 (47)	200 (48)
1 ^b	221 (57)	643 (53)	218 (52)
Disease stage at initial diagnosis			
Stage I	6 (1)	38 (2)	18 (2)
Stage II	38 (6)	133 (6)	47 (5)
Stage III	46 (7)	242 (12)	88 (10)
Stage IV	568 (82)	1566 (75)	641 (74)
Unknown/ND	33 (5)	108 (5)	71 (8)
Length of follow-up from index date, median (range), months	12 (1–118)	10 (0–120)	8 (1–80)
Length of follow-up from 1L treatment initiation, median (range), months	10 (0–105)	8 (0–105)	6 (0–71)

^aData represent n (%) of tested patients; ^bData are indicated as a proportion of tested patients. ND, not documented.

Figure 2. 1L systemic treatment patterns in HER2- versus HER2-unknown subgroups

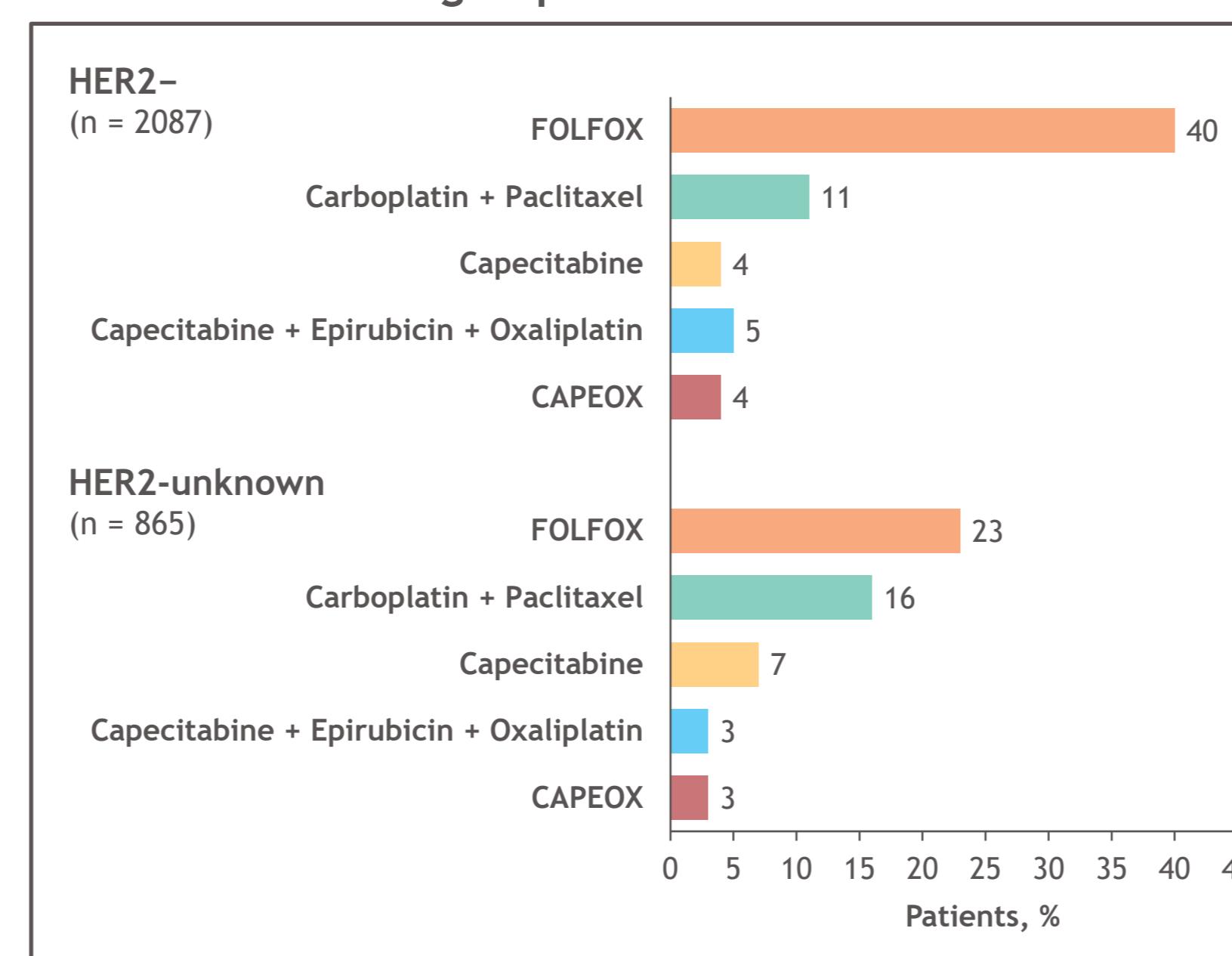
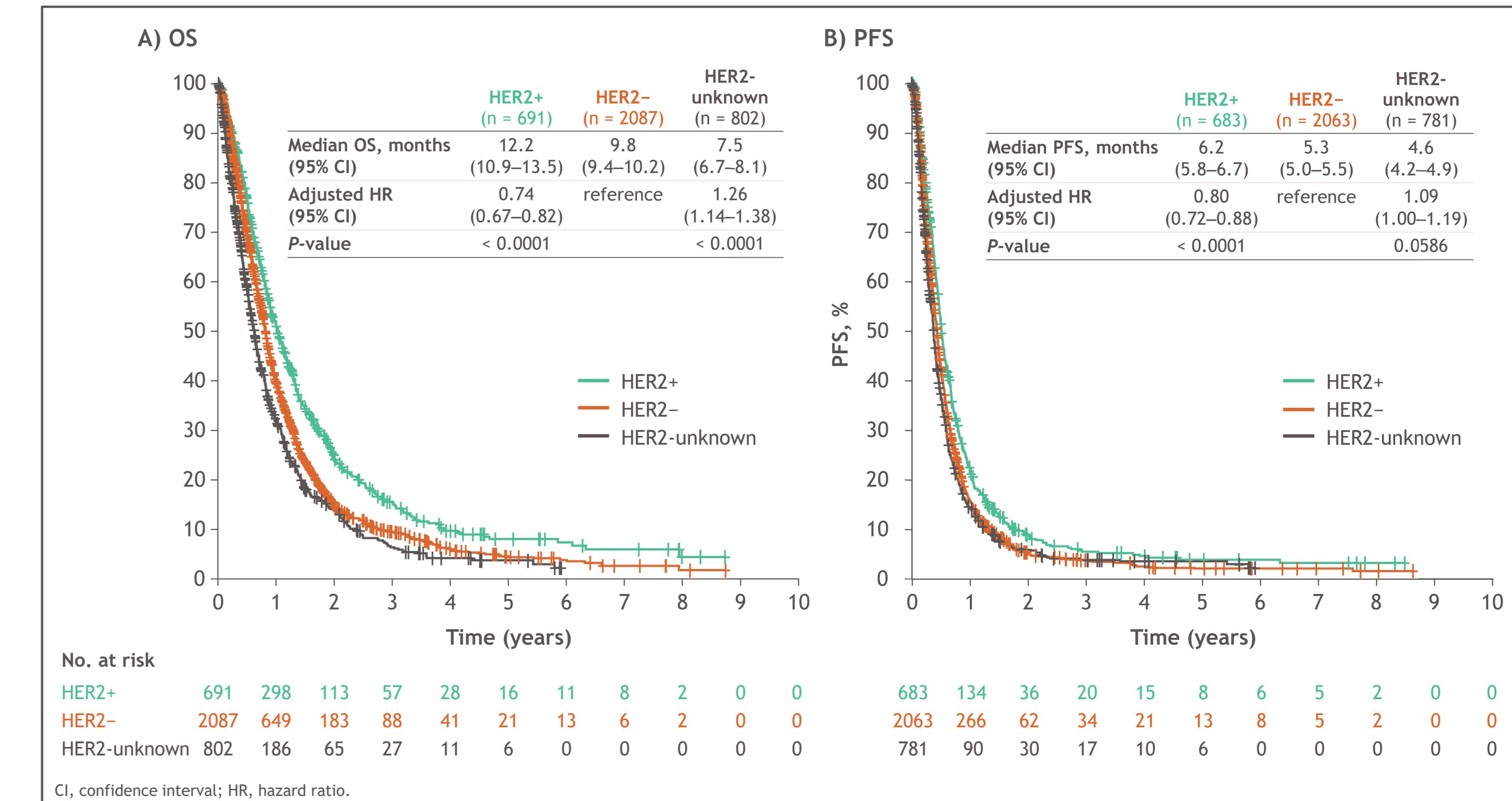


Figure 3. OS and PFS by HER2 status



Treatment patterns

- Patients with HER2-unknown status were less likely to receive 1L treatment compared with those with HER2- status (63% vs 82%; Chi-square P < 0.0001)
- Kendall's test showed that the top 5 1L treatments were similar in patients with HER2- and HER2-unknown status (Figure 2)
 - FOLFOX was the most common 1L treatment regimen in both HER2- (40%) and HER2-unknown (23%) subgroups
- Median duration of 1L therapy was 3.5 months in the HER2+ subgroup, and 2.8 months and 1.8 months in patients who only received chemotherapy in the HER2- and HER2-unknown subgroups, respectively (Table 2)

Table 2. 1L treatment duration by HER2 status

Median (range), months	HER2+ (n = 691)	HER2- (n = 2087)	HER2-unknown (n = 802)
Time from index date to 1L initiation date	0.9 (0.0–95.0)	1.0 (0.0–90.0)	1.1 (0.0–63.0)
Duration of 1L therapy	3.5 (0.0–93.0)	2.8 (0.0–50.0)	1.8 (0.0–36.0)

OS and PFS

- Median OS in the HER2+, HER2-, and HER2-unknown subgroups was 12.2, 9.8, and 7.5 months, respectively (Figure 3A)
- Patients in the HER2- subgroup were 26% less likely and patients who received 1L chemotherapy in the HER2-unknown subgroup were 26% more likely to die from the disease compared with patients in the HER2- subgroup (P < 0.0001)
- Median PFS in the HER2+, HER2-, and HER2-unknown subgroups was 6.2, 5.3, and 4.6 months, respectively (Figure 3B)

Conclusions

- Patients with HER2-unknown status had poorer OS outcomes compared with those with HER2+ or HER2- disease
- 1L treatment patterns were similar in the HER2- and HER2-unknown patient subgroups

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