CO226

Systematic Literature Review of First-Line Treatments of Patients With Advanced or Metastatic HER2-Positive Gastroesophageal Adenocarcinoma

John Bridgewater, PhD[1]; Javier Sabater, BPharm[2]; Junji Lin, PhD[3]; Tanya Madan, MPharm[4]; Paranjoy Saharia, MSc[4]; Michelle Smith, MSc[5]; Wayne Su, MSc[3]*

*Presenting author

[1]University College London Cancer Institute, London, UK; [2]Jazz Pharmaceuticals, Oxford, UK; [3]Jazz Pharmaceuticals, Philadelphia, PA, USA; [4]Lumanity, Gurugram, India; [5]Lumanity, London, UK

Background

- Gastroesophageal adenocarcinoma (GEA) is a subset of gastroesophageal carcinoma (GEC) that comprises adenocarcinomas arising in the stomach (gastric), esophagus, and gastroesophageal junction (GEJ). By anatomical subtype, an estimated 95% of gastric cancers and 65% of esophageal/GEJ cancers are adenocarcinomas[1,2]
- At an advanced or metastatic stage, they are considered sufficiently similar to be grouped together for treatment recommendations in clinical guidelines[3]
- Approximately 20% of patients with GEA have human epidermal growth factor receptor 2 (HER2)-positive tumors. Since 2010, the first-line treatment of choice for HER2-positive GEA has been a combination of platinum-based chemotherapy and trastuzumab/pembrolizumab
- The increasing incidence of GEA over time, along with recent developments in HER2-positive GEA, makes it pertinent to assess the clinical evidence and inform future comparative effectiveness research for innovative treatments in patients with this disease

Objective

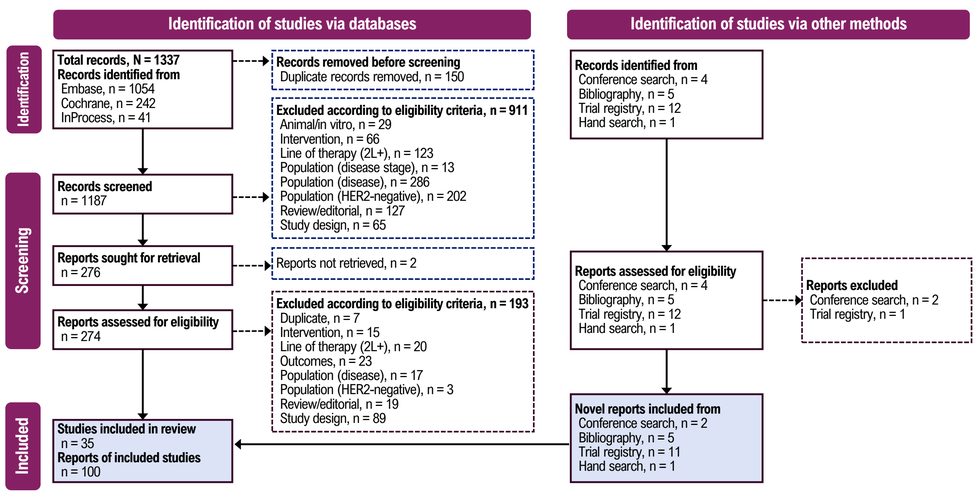
- To summarize the available evidence on clinical efficacy and safety among treatment-naïve patients with unresectable/inoperable advanced or metastatic HER2-positive GEA to inform future pharmacoeconomic research

Methods

- The systematic literature review (SLR) followed the Cochrane and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards[4]
- A systematic literature search was conducted from the start of the database to the cutoff date of August 16, 2024, covering Embase, MEDLINE, MEDLINE In-Process, and the Cochrane Library. Additionally, bibliographic searching, hand searching of conference proceedings (2022–2024), and registry searches were also conducted
- The literature search results were screened according to the predefined inclusion criteria, first by title and abstract, and then by full text
- Screening (both title/abstract and full text) was performed by two independent reviewers, and any discrepancies were resolved by a third independent reviewer
- Studies included from the full-text screening were extracted into predefined extraction grids by a single reviewer, and all extractions were verified against the original sources by a second reviewer

Results

Figure 1. PRISMA Flow Diagram for Clinical Studies of Patients With HER2-Positive GEA



2L+, second-line or later; GEA, gastroesophagesal adenocarcinoma; HER2, human epidermal growth factor receptor 2; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

- Database searches identified 1337 potentially relevant records. Additionally, 19 records were included from bibliographic searching, hand-searching of conference proceedings, and registry searches. After screening, 100 publications reporting data from 35 studies in patients with HER2-positive GEA were included in the SLR
- Among the 35 included studies, only 2 studies included patients with programmed death-ligand 1 (PD-L1) overexpression[5,6]
- A total of 10 randomized controlled trials (RCTs), 22 single-arm studies, and 3 non-RCTs (nRCTs) were included, with most being phase 2 trials (26 studies)
- The median age of study participants ranged from 57 years[7,8] to 68 years.[9] The study participants were predominantly male in all reported studies, with the percentage of male participants varying from 66%[10] to 100%[11]

Table 1. OS and PFS Data for Patients With HER2-Positive GEA in RCTs

Study	Study Setting	Intervention	Median Follow-Up, Months	Evaluable N	OS Estimates		PFS Estimates	
					Median OS (95% CI) Months	HR (95% CI)	Median PFS (95% CI) Months	HR (95% CI)
Li 2024[8]	Phase 2, double-blind, multicenter	HLX22 25 mg/kg + HLX02 + CAPOX	14.3	18	Not reached (12.4–NE)	0.4 (0.13–1.45)	15.1 (6.8–NE)	0.50 (0.17–1.27)
		HLX22 15 mg/kg + HLX02 + CAPOX	14.3	17	Not reached (NE–NE)	0.3 (0.09–1.26)	Not reached (9.8–NE)	0.10 (0.04–0.52)
		Placebo + HLX02 + CAPOX	14.3	18	Not reached (6.4–NE)	Reference	8.2 (5.7–12.7)	Reference
Janjigian 2023 (KEYNOTE-811)[5]	Phase 3, double-blind, multicenter international	Pembrolizumab + trastuzumab + chemo	56	350	20 (17.8–22.1)	0.80 (0.67–0.94)	10 (8.6–12.2)	0.73 (0.61–0.87)
		Placebo + trastuzumab + chemo	56	348	16.8 (14.9–18.7)		8.1 (7.0–8.5)	
Tabernero 2023 (JACOB)[12]	Phase 3, double-blind, multicenter international	Pertuzumab + trastuzumab + chemo	OS: 46.1 PFS: 50.4	388	18.1 (16.2–19.5)	0.85 (0.72–0.99)	8.5 (8.3–9.7)	0.73 (0.62–0.85)
		Placebo + trastuzumab + chemo	OS: 44.4 PFS: 47.4	392	14.2 (12.9–15.7)		7.2 (6.4–8.2)	
Stein 2022 (INTEGA)[6]	Phase 2, open-label, multicenter	Trastuzumab + nivolumab + ipilimumab	18.8	44	23.3	NR	3.2	NR
		Trastuzumab + nivolumab + FOLFOX	18.8	44	22.1		10.7	
Zhao 2022 (SYLT/FNF-004)[13]	Phase 2, open-label, multicenter	ivPOF	41	3	NR	0.50 (0.11–2.31)	NR	0.50 (0.11–2.31)
		ipPOF	41	4	NR	0.17 (0.03–1.06)	NR	0.10 (0.02–0.66)
		mFOLFOX6P	41	3	NR	Reference	NR	Reference
Shah 2017 (HELOISE)[14]	Phase 2, double-blind, multicenter international	High-dose trastuzumab + capecitabine + cisplatin	NR	124	10.61 (9.4–12.42)	1.24 (0.86–1.78)	5.6	1.04 (0.76–1.40)
		SoC trastuzumab + capecitabine + cisplatin	NR	124	12.48 (10.8–13.86)		5.7	
Hecht 2016 (TRIO-013/ LOGiC)[15]	Phase 3, double-blind, multicenter	CAPOX + lapatinib	23	272	11.9 (10.4–13.8)	0.91 (0.74–1.10)	6 (5.6–7.0)	0.82 (0.68–1.00)
		CAPOX + placebo	23	273	10.4 (9.1–11.3)		5.4 (4.4–5.7)	
Bang 2010 (ToGA)[16]	Phase 3, open-label, multicenter international	Trastuzumab + fluoropyrimidine + cisplatin	18.6	294	13.8 (12–16)	0.74 (0.60–0.91)	6.7 (6–8)	0.71 (0.59–0.85)
		Chemo	18.6	290	11.1 (10–13)		5.5 (5–6)	

CAPOX, capecitabine and oxaliplatin; chemo, chemotherapy; FOLFOX, folinic acid, 5-fluorouracil, oxaliplatin; GEA, gastroesophageal adenocarcinoma; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; ipPOF, intraperitoneal paclitaxel + folinic acid, 5-fluorouracil, oxaliplatin; ivPOF, intravenous paclitaxel + folinic acid, 5-fluorouracil, oxaliplatin; mFOLFOX6, modified FOLFOX regimen; NE, not estimable; NR, not reported; OS, overall survival; PFS, progression-free survival; RCT, randomized controlled trial; SoC, standard of care.

- A summary of overall survival (OS) and progression-free survival (PFS) data was reported in 8 of the 10 included RCTs
- Since the pivotal trastuzumab trial (ToGA), only 1 RCT has met its primary endpoint, for the combination of pembrolizumab, trastuzumab, and chemotherapy compared to placebo, trastuzumab, and chemotherapy[5]
- Among the included single-arm studies or nRCTs, 23 studies reported data for OS evaluating trastuzumab in combination with chemotherapy or other targeted agents
  - A study of chemotherapy-only regimens reported the median OS of patients receiving modified docetaxel, cisplatin, and 5-fluorouracil (mDCF) to be 24.9 months[17]
  - Among the studies investigating HER2-targeted therapies without immuno-oncology (IO) products, median OS ranged from 6.3 months with lapatinib + capecitabine[18] to 36.5 months with zanidatamab + standard chemotherapy[19]
    - The OS rates were also particularly high for zanidatamab + standard chemotherapy, reaching 87% at 12 months, 65% at 24 months, and 59% at 30 months[19]
  - Among 3 studies that assessed IO-containing regimens + HER2-targeted therapy, median OS ranged from 19.3 months (global phase 3)[20] to 27.3 months (phase 1b/2 in Korea)[21] for pembrolizumab + trastuzumab with chemotherapy while the OS was not reached for the third study, as of December 20, 2021, with the combination of nivolumab, trastuzumab, oxaliplatin and the fluoropyrimidine derivative S1 (tegafur, gimeracil, oteracil potassium)/capecitabine[22]
- Among single-arm studies or nRCTs, 24 reported data for PFS evaluating trastuzumab with chemotherapy or other targeted agents
  - A study of chemotherapy-only regimens reported the median PFS of patients receiving mDCF to be 13 months[17]
  - Among the studies investigating HER2-targeted therapies without an IO product, median PFS ranged from 4.3 months with lapatinib + capecitabine[18] to 14 months with capecitabine and oxaliplatin (CAPOX) + bevacizumab + trastuzumab.[23] A median PFS of 12.5 months was reported for zanidatamab + standard chemotherapy over a median follow-up of 48 months[19]
  - In IO-containing regimens, often combined with HER2-targeted therapy, median PFS ranged from 8.6 months for pembrolizumab + trastuzumab with capecitabine and cisplatin[20] to 16.7 months with the combination of zanidatamab, tislelizumab (an anti-programmed cell death protein 1 [PD-1] immune checkpoint inhibitor), and CAPOX[24]
- Overall response rate (ORR) was reported in 9 RCTs and ranged from 34% with trastuzumab + nivolumab + ipilimumab[6] to 82.4% with HLX22 + HLX02 + CAPOX[8]
- ORR was also reported in 23 single-arm studies and nRCTs, with results varying across different treatment combinations from 13% with lapatinib + capecitabine[18] to 93.8% observed with trastuzumab + docetaxel/cisplatin/S1[25]
- Duration of response (DOR) was reported in 6 RCTs and ranged from 5.8 months with trastuzumab + nivolumab + ipilimumab[6] to 12.4 months with 25 mg/kg HLX22 + HLX02 + CAPOX[8]
- DOR was reported in 10 single-arm studies and nRCTs, with results varying across different treatment combinations
  - Among the studies investigating HER2-targeted therapies without IO, DOR ranged from 7.3 months with trastuzumab + S1 + cisplatin[26] to 20.4 months with zanidatamab + CAPOX[19]
  - Among the IO-containing regimens, combined with HER2-targeted therapy, the DOR ranged from 9.4 months with pembrolizumab + trastuzumab + chemotherapy[21] to 22.8 months for zanidatamab combined with tislelizumab and CAPOX[24]

Table 2. OS and PFS Data in Patients With HER2-Positive GEA and PD-L1 Overexpression

Study	Population	Intervention	Median Follow-Up, Months	Evaluable N	OS Estimates			PFS Estimates		
					Median OS (95% CI) Months	n (%)	HR (95% CI)	Median PFS (95% CI) Months	n (%)	HR (95% CI)
Janjigian 2023 (KEYNOTE-811)[5]	PD-L1 CPS ≥1	Pembrolizumab + trastuzumab + chemo	56	298	20.1 (17.9–22.9)	NR	0.79 (0.66–0.95)	10.9 (8.5–12.5)	NR	0.72 (0.60–0.87)
		Placebo + trastuzumab + chemo	56	296	15.7 (13.5–18.5)	NR		7.3 (6.8–8.4)	NR	
	PD-L1 CPS ≥5	Pembrolizumab + trastuzumab + chemo	NR	186	20.8 (18.1–24.5)	NR	0.76 (0.59–0.96)	10.9 (8.3–13.0)	NR	0.72 (0.57–0.92)
		Placebo + trastuzumab + chemo	NR	171	16.0 (13.7–19.9)	NR		8.1 (6.8–9.7)	NR	
Stein 2022 (INTEGA)[6]	HER2-positive and PD-L1 CPS ≥1	Trastuzumab + nivolumab + ipilimumab	14.3	31	16.4	17 (54)	NR	2.2	4 (14)	NR
		Trastuzumab + nivolumab + FOLFOX	14.3	28	21.6	20 (71)		10.7	9 (33)	
	HER2-positive and PD-L1 CPS ≥5	Trastuzumab + nivolumab + ipilimumab	14.3	24	12.6 (7.7–NE)	NR	NR	NR	NR	NR
		Trastuzumab + nivolumab + FOLFOX	14.3	22	21.9 (12.9–NE)	NR		NR	NR	

Chemo, chemotherapy; CPS, combined positive score; FOLFOX, folinic acid, 5-fluorouracil, and oxaliplatin; GEA, gastroesophagesal adenocarcinoma; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; NE, not estimable; NR, not reported; OS, overall survival; PD-L1, programmed death-ligand 1; PFS, progression-free survival.

- Only 2 RCTs (and no other studies) reported subgroup data in patients with HER2-positive GEA and PD-L1 overexpression[5,6]
- A phase 3 RCT demonstrated that the anti–PD-1 antibody pembrolizumab + trastuzumab and chemotherapy significantly improved OS and PFS vs trastuzumab and chemotherapy alone in the subset of patients with HER2-positive gastric/GEJ cancer and a PD-L1 combined positive score (CPS) ≥1 as well as ≥5[5]
- The INTEGA study showed that in the population with CPS ≥1, significantly prolonged OS and PFS were observed with trastuzumab + nivolumab and FOLFOX vs trastuzumab + nivolumab and ipilimumab[6]

Table 3. OS and PFS Data in Patients With HER2 IHC 2+ vs IHC 3+ Scores in RCTs

Study	Population	Intervention	Median Follow-Up, Months	Evaluable N	OS Estimates		PFS Estimates	
					Median OS (95% CI) Months	HR (95% CI)	Median PFS (95% CI) Months	HR (95% CI)
Tabernero 2023 (JACOB)[12]	HER2-positive (IHC 2+/ISH+)	Pertuzumab + trastuzumab + chemo	46.1	129	13.0	0.85 (0.65–1.11)	NR	NR
	HER2-positive (IHC 3+)	Placebo + trastuzumab + chemo	44.4	130	11.9		NR	
Stein 2022 (INTEGA)[6]	HER2-positive (IHC 2+)	Trastuzumab + nivolumab + ipilimumab	14.3	40	NR	NR	3.4	NR
		Trastuzumab + nivolumab + FOLFOX	14.3	36	NR		10.7	
	HER2-positive (IHC 2+/ISH+)	Trastuzumab + nivolumab + ipilimumab	14.3	7	6.4 (1.8–NE)	NR	1.4 (1.2–NE)	NR
		Trastuzumab + nivolumab + FOLFOX	14.3	6	NE (NE–NE)		5.2 (1.6–NE)	
	HER2-positive (IHC 2+/ISH+)	Trastuzumab + nivolumab + ipilimumab	18.8	7	6.4	NR	NR	NR
		Trastuzumab + nivolumab + FOLFOX	18.8	7	34.1		NR	
	HER2-positive (IHC 3+)	Trastuzumab + nivolumab + ipilimumab	14.3	33	26.2 (11.5–NE)	NR	4.4 (2.1–9.3)	NR
		Trastuzumab + nivolumab + FOLFOX	14.3	30	22.7 (21.9–NE)		11.3 (9.2–14.6)	
	HER2-positive (IHC 3+)	Trastuzumab + nivolumab + ipilimumab	18.8	33	32.2	NR	NR	NR
		Trastuzumab + nivolumab + FOLFOX	18.8	30	23		NR	
Hecht 2016 (TRIO-013/ LOGiC)[15]	HER2-positive (IHC 2+/FISH+)	CAPOX + lapatinib	24	58	NR	0.79 (0.50–1.25)	NR	NR
		CAPOX + placebo	24	50	NR		NR	
	HER2-positive (IHC 2–3+/FISH+)	CAPOX + lapatinib	24	201	NR	0.86 (0.68–1.09)	NR	NR
		CAPOX + placebo	24	204	NR		NR	
	HER2-positive (IHC 3+/FISH+)	CAPOX + lapatinib	24	143	NR	0.90 (0.69–1.18)	NR	NR
		CAPOX + placebo	24	154	NR		NR	
Bang 2010 (ToGA)[16]	HER2-positive (IHC 0/FISH+ or IHC 1+/FISH+)	Trastuzumab + fluoropyrimidine + cisplatin	18.6	61	10.0	1.07 (0.70–1.62)	5.3	1.00 (0.69–1.45)
		Chemo	18.6	70	8.7		4.8	
	HER2-positive (IHC 2+/FISH+ or IHC 3+)	Trastuzumab + fluoropyrimidine + cisplatin	18.6	228	16.0	0.65 (0.51–0.83)	7.6	0.64 (0.51–0.79)
		Chemo	18.6	218	11.8		5.5	

CAPOX, capecitabine and oxaliplatin; chemo, chemotherapy; FISH, fluorescence ISH; FOLFOX, folinic acid, 5-fluorouracil, and oxaliplatin; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IHC, immunohistochemistry; ISH, in situ hybridization; NE, not estimable; NR, not reported; OS, overall survival; PFS, progression-free survival; RCT, randomized controlled trial.

Table 4. OS and PFS Data in Patients With IHC 2+ vs IHC 3+ Scores in Single-Arm Studies and nRCTs

Study	Population	Intervention	Median Follow-Up, Months	Evaluable N	OS Estimates		PFS Estimates	
					Median OS (95% CI) Months	HR (95% CI)	Median PFS (95% CI) Months	HR (95% CI)
Lee 2022 (PANTHERA)[20]	HER2-positive (IHC 2+/SISH+)	Pembrolizumab + trastuzumab + capecitabine + cisplatin	18.2	13	21.1	NR	9.0	NR
	HER2-positive (IHC 3+)		18.2	30	19.3		8.5	
Takahari 2019 (HIGHSOX)[27]	HER2-positive (IHC 2+/ISH+)	Trastuzumab + oxaliplatin + S1	20.6	75	16.3	NR	NR	NR
	HER2-positive (IHC 3+)		20.6	75	25.9		NR	

HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IHC, immunohistochemistry; ISH, in situ hybridization; nRCT, non-randomized controlled trial; NR, not reported; OS, overall survival; PFS, progression-free survival; S1, tegafur, gimeracil, oteracil potassium; SISH, silver ISH.

- The SLR identified subgroup data for patients with different immunohistochemistry (IHC) scores in 4 RCTs[6,12,15,16] and 2 single-arm studies[20,27]
- Patients with HER2 positivity confirmed via IHC 3+ score demonstrated prolonged median OS[6,12] and median PFS[6] compared with patients with HER2 positivity confirmed by an IHC 2+ and in situ hybridization positivity. Similar improvements in median OS and PFS were observed in lower (IHC 0 to 1+) versus higher (IHC 2+) HER2 expression subgroups, with statistically significant results being observed in comparison with standard chemotherapy in the higher HER2 expression subgroup that received trastuzumab + fluoropyrimidine + cisplatin[27]

- The incidence of any treatment-related adverse events (TRAEs) was high across RCTs, single-arm studies, and nRCTs, with TRAEs reported in more than 85% of patients across all reported studies
- Neutropenia and nausea were the most commonly reported TRAEs among patients receiving trastuzumab combinations[12,14,16]
- Serious TRAEs were reported in 2 RCTs[8,14] and 6 single-arm studies/nRCTs. Seven studies reported serious TRAEs in less than one-third of their study population; however, only 1 single-arm study reported a high serious TRAEs incidence rate of 60% in patients receiving bevacizumab + trastuzumab + docetaxel + oxaliplatin + capecitabine[28]

Conclusions

- No new HER2-targeted treatment since trastuzumab has demonstrated OS benefits in combination regimens for first-line HER2-positive GEA as per RCT evidence
- Dual blockade of HER2 and PD-L1, with the addition of IO to trastuzumab plus chemotherapy, has been shown to improve survival for the subset of patients with confirmed PD-L1 overexpression
- Following treatment with HER2-targeted agents, patients with higher HER2 expression (ie, higher IHC score) generally demonstrated improved survival outcomes when compared with patients with lower HER2 expression
- Multiple trials investigating novel regimens and combinations, including IO therapies and/or targeted agents such as zanidatamab, have demonstrated the potential for improved survival outcomes and durable response for patients with HER2-positive GEA in early phase studies; confirmatory phase 3 trials are currently underway in first-line HER2-positive GEA

References: 1. American Cancer Society. 2021. Accessed 29 January 2025. Available at: https://www.cancer.org/cancer/types/stomach-cancer/about/what-is-stomach-cancer.html. **2.** Arnold M, et al. *Gut*. 2020;69(9):1564. **3.** Tabernero J, et al. *Future Oncol*. 2022;18(29):3255-66. **4.** Moher D, et al. *Syst Rev*. 2015;4(1):1. **5.** Janjigian YY, et al. *Lancet*. 2023;402(10418):2197-208. **6.** Stein A, et al. *JAMA Oncol*. 2022;8(8):1150-8. **7.** Gong J, et al. *BMC Cancer*. 2016;6:68. **8.** Li N, et al. *Med*. 2024;5(10):1255-65.e2. **9.** Mori Y, et al. *J Gastrointest Cancer*. 2022;53(4):930-8. **10.** Ryu MH, et al. *Eur J Cancer*. 2015;51(4):482-8. **11.** Park H, et al. *JAMA Oncol*. 2020;6(8):1231-40. **12.** Tabernero J, et al. *Gastric Cancer*. 2023;26(1):123-31. **13.** Zhao S, et al. *Front Oncol*. 2022;12:850242. **14.** Shah MA, et al. *J Clin Oncol*. 2017;35(22):2558-67. **15.** Hecht JR, et al. *J Clin Oncol*. 2016;34(5):443-51. **16.** Bang YJ, et al. *Lancet*. 2010;376(9742):687-97. **17.** Mondaca S, et al. *Gastric Cancer*. 2019;22(2):355-62. **18.** LaBonte MJ, et al. *Mol Cancer Ther*. 2016;15(9):2251-8. **19.** Elimova E, et al. *J Clin Oncol*. 2025;43(16_suppl):4013. **20.** Lee CK, et al. *Nat Commun*. 2022;13(1):6002. **21.** Janjigian YY, et al. *Lancet Oncol*. 2020;21(6):821-31. **22.** Takahari D, et al. *J Clin Oncol*. 2022;40(4_suppl):276. **23.** Singh H, et al. *Cancer Res*. 2023;83(8_suppl):CT155. **24.** Lee K, et al. *Ann Oncol*. 2023;34:S855-S6. **25.** Mitsui Y, et al. *Cancer Chemother Pharmacol*. 2015;76(2):375-82. **26.** Chua C, et al. *Cancer Chemother Pharmacol*. 2015;76(2):397-408. **27.** Takahari D, et al. *Gastric Cancer*. 2019;22(6):1238-46. **28.** Meulendijks D, et al. *Invest New Drugs*. 2016;34(1):119-28.

Support and Acknowledgements: This analysis was supported by Jazz Pharmaceuticals. Under the direction of the authors, medical writing was provided by Lumanity (Morristown, NJ, USA) and editorial and graphic design support were provided by Red Nucleus (Yardley, PA, USA), which was funded by Jazz Pharmaceuticals, in accordance with Good Publication Practice (GPP 2022) guidelines (https://www.ismpp.org/gpp-2022). Jazz Pharmaceuticals also reviewed and edited the poster for scientific accuracy.

Disclosures: JB has consulted for Bristol Myers Squibb, Incyte, Servier, and Taiho; has received funding from Incyte; and has received honoraria from Incyte and Servier; **JS, JL,** and **WS** are employees of Jazz Pharmaceuticals and own stock or stock options in Jazz Pharmaceuticals; and **TM, PS,** and **MS** are employees of Lumanity.

Corresponding author: Wayne Su
wayne.su@jazzpharma.com

Poster presented at the International Society for Pharmacoeconomics and Outcomes Research Europe (ISPOR EU) 2025, November 9–12, Glasgow, Scotland, UK