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Real-world treatment patterns in patients with HER2-positive locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma (HER2+ aGC/GEJC) in East Asia (HER2+ GASTA)

Do-Youn Oh[1], Winnie Yeo[2], Jen-Shi Chen[3], Yi Ba[4], Wendy Wing Lok Chan[5], Ming Jen Chen[6], Yen-Hao Chen[7], Kangsheng Gu[8], Yi-Ping Hung[9], Jong Gwang Kim[10], Jeeyun Lee[11], Xinjun Liang[12], Suxia Luo[13], Sun Young Rha[14], Ying Yuan[15], Taeheon Kim[16], Momoko Yanagida[17], Risa Sato[17], Rui-Hua Xu[18]

[1]Seoul National University Hospital, Seoul, South Korea, [2]Prince of Wales Hospital, Sha Tin, Hong Kong, [3]Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan, [4]Tianjin Medical University Cancer Hospital, Tianjin, China, [5]Queen Mary Hospital, Pok Fu Lam, Hong Kong, [6]MacKay Memorial Hospital, Taipei, Taiwan, [7]Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan, [8]The First Affiliated Hospital of Anhui Medical University, Hefei, China, [9]Taipei Veterans General Hospital, Taipei, Taiwan, [10]Kyungpook National University Chilgok Hospital, Daegu, South Korea, [11]Samsung Medical Center, Seoul, South Korea, [12]Hubei Cancer Hospital, Wuhan, China, [13]Henan Cancer Hospital, Zhengzhou, China, [14]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea, [15]The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China, [16]Linical Korea, Seoul, South Korea, [17]Daiichi Sankyo Co., Ltd., Tokyo, Japan, [18]Sun Yat-sen University Cancer Center, Guangzhou, China

Introduction

- Gastric cancer (GC) is the fifth most common cancer with more than 968,000 new cases and 659,000 deaths worldwide in 2022.[1] The highest incidence and mortality rates of GC are observed in East Asia.[1]
- There are few treatment options for human epidermal growth factor receptor 2-positive (HER2+) aGC/GEJC beyond the 1st line of treatment (LOT), and treatment options differ by country/region.[2-11]
- Understanding the current treatment patterns with their outcomes helps to guide treatment decisions.

Objectives

Primary	• To describe treatment patterns.
Secondary	• To describe demographics and clinico-pathological characteristics. • To evaluate the clinical outcomes and selected adverse effects.
Exploratory	• To explore the occurrence of hospitalization associated with selected adverse effects.

Methods

Inclusion Criteria

- Adult patients ≥18 years old who were pathologically and/or clinically diagnosed with aGC/GEJC since 01 Jan 2016.
- Patients whose HER2 status was pathologically confirmed HER2+ [immunohistochemistry 3-positive or immunohistochemistry 2-positive and in situ hybridization-positive (IHC3+ or IHC2+/ISH+)] before or at the initiation of 2nd LOT.
- Patients who received at least one LOT and who had at least 6 months of follow-up data from the date of 2nd LOT initiation unless the patient died within the first 6 months from 2nd LOT initiation.

Exclusion Criteria

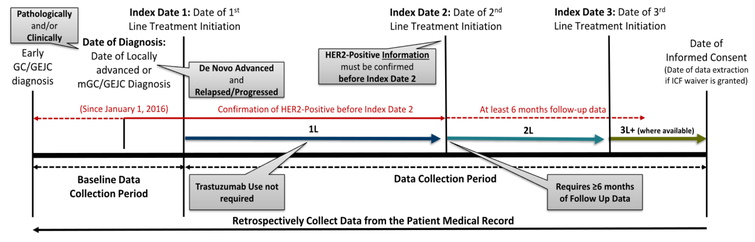
- Patients with a change in HER2 status from positive to negative at progression from early-stage† to advanced-stage disease.
- Patients who had multiple cancers within 3 years of 1st LOT initiation.

†Only if the HER2-positive status was confirmed using archived tumor tissue sample from an early-stage GC/GEJC (before the date of aGC/GEJC diagnosis).

Study design

- A multinational, retrospective study conducted in East Asia at 31 centers from South Korea (KR), China (CN), Taiwan (TW), and Hong Kong (HK). The study design is presented in Figure 1. The data from the medical records of the patients were collected from 01 Jan 2016 until the dates specified in Table 1.

Figure 1: Study design



Analyses

- Number of patients was not determined based on statistical power.
- Efficacy analysis was conducted in HER2+ [IHC3+ or IHC2+/ISH+] population.
- All statistical comparisons were not pre-planned or adjusted.
- Survival distributions were analyzed using the log-rank test, and the hazard ratio with 95% confidence interval (CI) was calculated using the Cox proportional hazards model.
- If the P-value is <0.05, it is marked with '*'.

Conclusion

- This retrospective study from East Asia portrays the real-world treatment patterns for HER2+ aGC/GEJC. All eligible patients had initiated the 2nd LOT with at least 6 months follow-up data unless the patients were deceased after 2nd LOT initiation.
- In the later LOTs, various regimens were used, and it was observed that there was no unified standard of care for HER2+ aGC/GEJC.
- Although the statistical comparisons were not pre-planned or adjusted, the study suggested that the use of trastuzumab in several LOTs may not prolong survival and the use of several types of HER2-targeted therapy may contribute to survival benefit.
  - The median rwOS in 1st LOT was 29.5 months (95% CI: 26.1, 33.7), with the condition that all patients had ≧2 LOTs in this study.
- The availability of HER2-targeted inhibitor with different types of mechanisms of action and its accessibility in later line of therapy seem to be a key for better clinical outcomes.

Results

Number of patients and data collection period

Table 1: Number of patients and data collection period by country/region

Country/Region	No. of patients	Data collection period
South Korea (KR)	119	Jan 2016 to Dec 2022
China (CN)	137	Jan 2016 to Nov 2023
Taiwan (TW)	75	Jan 2016 to Sep 2022
Hong Kong (HK)	25	Jan 2016 to Nov 2023

Demographics and clinico-pathological characteristics

Table 2: Demographics and clinico-pathological characteristics

	KR (n=119)	CN (n=137)	TW (n=75)	HK (n=25)	All (N=356)
Median age at the time of aGC/GEJC diagnosis (years)	61.0	60.0	64.0	65.0	62.0
Comorbidity, n (%)[a]					
Hypertension	29 (24.4)	26 (19.0)	35 (46.7)	12 (48.0)	102 (28.7)
Diabetes	18 (15.1)	13 (9.5)	17 (22.7)	5 (20.0)	53 (14.9)
Others	27 (22.7)	20 (14.6)	23 (30.7)	12 (48.0)	82 (23.0)
Cancer type, n (%)[a]					
GC	113 (95.0)	115 (83.9)	58 (77.3)	19 (76.0)	305 (85.7)
GEJC	7 (5.9)	22 (16.1)	17 (22.7)	6 (24.0)	52 (14.6)
De novo advanced disease or recurrent, n (%)					
De novo advanced disease	97 (81.5)	99 (72.3)	62 (82.7)	13 (52.0)	271 (76.1)
Recurrent	21 (17.6)	37 (27.0)	12 (16.0)	7 (28.0)	77 (21.6)
Unknown	1 (0.8)	1 (0.7)	1 (1.3)	5 (20.0)	8 (2.2)
Type of tumor stage (TNM stage), n (%)[a, b]					
Pathological stage	13 (13.3)	21 (21.0)	12 (19.0)	11 (61.1)	57 (20.4)
Clinical stage	84 (85.7)	76 (76.0)	51 (81.0)	7 (38.9)	218 (78.1)
Unknown	1 (1.0)	4 (4.0)	0 (0.0)	0 (0.0)	5 (1.8)
Clinical stage, n (%)[c]					
IIA, III, IIIA, IIIB, IIIC	1 (1.2)	0 (0.0)	4 (7.8)	0 (0.0)	5 (2.3)
IV, IVA, IVB	83 (98.8)	74 (97.4)	47 (92.2)	7 (100)	211 (96.8)
Unknown	0 (0.0)	2 (2.6)	0 (0.0)	0 (0.0)	2 (0.9)
Metastatic sites, n (%)[d]					
Lymph nodes	65 (54.6)	75 (54.7)	30 (40.0)	13 (52.0)	183 (51.4)
Liver	46 (38.7)	63 (46.0)	29 (38.7)	9 (36.0)	147 (41.3)
Peritoneum	21 (17.6)	23 (16.8)	21 (28.0)	3 (12.0)	68 (19.1)
Lung	13 (10.9)	17 (12.4)	14 (18.7)	5 (20.0)	49 (13.8)
Other	26 (21.8)	28 (20.4)	19 (25.3)	1 (4.0)	74 (20.8)
Gastrectomy conducted before 1st LOT initiation, n (%)					
Yes	36 (30.3)	51 (37.2)	22 (29.3)	8 (32.0)	117 (32.9)
No	83 (69.7)	86 (62.8)	52 (69.3)	17 (68.0)	238 (66.9)
Unknown	0 (0.0)	0 (0.0)	1 (1.3)	0 (0.0)	1 (0.3)
Eastern Cooperative Oncology Group Performance Status (ECOG PS), n (%)[e]					
0	26 (33.8)	17 (43.6)	22 (36.1)	2 (11.8)	67 (34.5)
1	46 (59.7)	22 (56.4)	34 (55.7)	15 (88.2)	117 (60.3)
≥ 2	5 (6.5)	0 (0.0)	5 (8.2)	0 (0.0)	10 (5.2)
HER2-positive status before 2nd LOT, n (%)					
IHC3+ or IHC2+/ISH+	115 (96.6)	129 (94.2)	66 (88.0)	20 (80.0)	330 (92.7)
Other[f]	4 (3.4)	8 (5.8)	9 (12.0)	5 (20.0)	26 (7.3)
Survival status at informed consent date/first data extraction date, n (%)					
Deceased	61 (51.3)	36 (26.3)	63 (84.0)	21 (84.0)	181 (50.8)
Alive	41 (34.5)	31 (22.6)	11(14.7)	4 (16.0)	87 (24.4)
Lost to follow-up	17 (14.3)	70 (51.1)	1 (1.3)	0 (0.0)	88 (24.7)

[a]The percentage exceeded 100% due to double counting. [b]The percentages were calculated based on patients evaluated for TNM stage (patients with de novo advanced disease and unknown were evaluated for TNM stage). [c]The percentage was calculated for patients who had clinical stage (n=218). [d]Some patients had more than one metastatic site. [e]The percentage was based on patients evaluated for ECOG PS [n=194]. [f]HER2-positive other than [IHC3+ or IHC2+/ISH+].

Duration of therapy

Table 4: Median duration of therapy (DoT) in months [95% CI]

	1st LOT	2nd LOT	3rd LOT	4th LOT	Overall DoT from 1st LOT
KR	7.7 [8.3, 10.6]	5.9 [5.7, 7.9]	2.8 [2.9, 5.1]	1.4 [1.7, 3.5]	19.4 [20.8, 25.7]
CN	6.1 [6.6, 8.7]	3.4 [3.6, 5.0]	2.1 [3.0, 5.4]	1.7 [2.0, 4.3]	18.2 [18.3, 22.2]
TW	4.6 [4.5, 6.9]	2.2 [2.9, 5.5]	2.3 [1.8, 5.6]	2.8 [2.0, 4.5]	11.7 [11.5, 16.7]
HK	5.7 [4.7, 8.5]	3.7 [2.6, 5.6]	1.9 [0.9, 2.7]	2.5 [-0.8, 5.4]	15.4 [12.9, 19.1]
All	6.3 [7.1, 8.4]	3.6 [4.5, 5.6]	2.3 [3.2, 4.6]	1.8 [2.3, 3.5]	16.9 [18.4, 21.0]

Selected adverse effects

The selected adverse effects were interstitial lung disease (ILD)/pneumonitis and left ventricular dysfunction.
The drugs associated with ILD/pneumonitis were HER2-targeted ADC monotherapy (n=7), Chemotherapy + HER2-targeted mAb + ICI (n=3), Chemotherapy + HER2-targeted mAb (n=1), Chemotherapy only (n=3), ICI monotherapy (n=1), HER2-targeted mAb + VEGF-TKI (n=1), Other (n=2), and not associated with any LOT (n=4). The drugs associated with left ventricular dysfunction was Chemotherapy + VEGF-targeted mAb (n=1).

Table 6: Selected adverse effects

Selected adverse effects	KR (N=119)	CN (N=137)	TW (N=75)	HK (N=25)	All (N=356)
Proportion of patients with selected adverse effects					
ILD/pneumonitis	4 (3.4)	15 (10.9)	2 (2.7)	1 (4.0)	22 (6.2)
Left ventricular dysfunction	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)
Occurrence of hospitalization associated with selected adverse effects					
ILD/pneumonitis	1 (0.8)	6 (4.4)	2 (2.7)	1 (4.0)	10 (2.8)
Left ventricular dysfunction	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death due to selected adverse effects†					
ILD/pneumonitis	0.0	1 (0.7)	0.0	1 (4.0)	2 (0.6)
Left ventricular dysfunction	0.0	0.0	0.0	0.0	0.0

†For one more patient, the cause of death was selected adverse effect as per survival/follow-up status, but there is no data that mentions "did event result in death=Yes" in selected adverse effects.

Poster

Supplementary material

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials. Alternatively, please visit: bit.ly/DS24ESMOASIA.

This study is sponsored by Daiichi Sankyo and AstraZeneca. In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201).

Poster presented at ESMO Asia Congress 2024 by Do-Youn Oh. Corresponding author email address: ohdoyoun@snu.ac.kr

Treatment

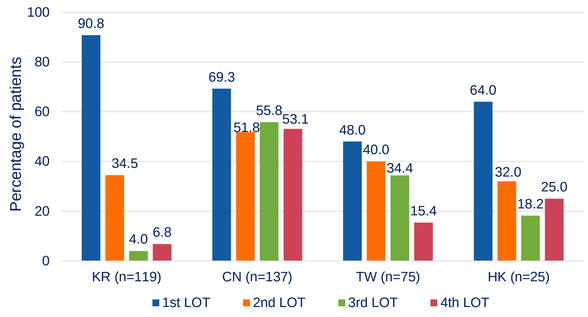
Table 3: Proportion of patients receiving top 3 regimens in each LOT in East Asia

LOT	Treatment regimens	n (%)
1st LOT	Chemotherapy + HER2-targeted mAb	217 (61.0)
	Doublet chemotherapy	65 (18.3)
	Chemotherapy + HER2-targeted mAb + ICI	31 (8.7)
2nd LOT	Chemotherapy + HER2-targeted mAb	85 (23.9)
	Chemotherapy + VEGF-targeted mAb	72 (20.2)
	Mono chemotherapy	46 (12.9)
3rd LOT	Mono chemotherapy	50 (23.5)
	Doublet chemotherapy	33 (15.5)
	HER2-targeted ADC monotherapy	25 (11.7)
4th LOT	Doublet chemotherapy	17 (15.5)
	ICI monotherapy	16 (14.5)
	Mono chemotherapy	16 (14.5)

ADC = antibody-drug conjugates; ICI = immune checkpoint inhibitors; mAb = monoclonal antibodies; TKI = tyrosine kinase inhibitors; VEGF = vascular endothelial growth factor. HER2-targeted mAb, HER2-targeted ADC, and HER2-targeted TKI were included under HER2-targeted therapy. The percentage was based on the number of patients in each LOT (1st LOT: 356, 2nd LOT: 356, 3rd LOT: 213, 4th LOT: 110). Note: Country/region level information is available in supplementary material.

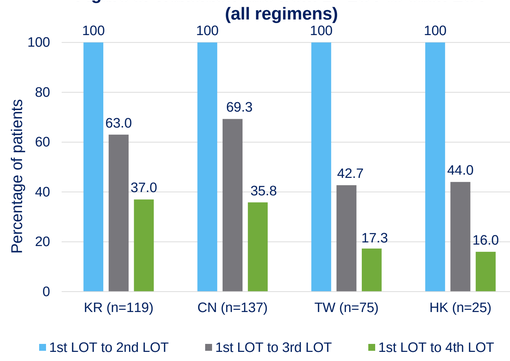
The median number of LOTs in KR and CN was 3.0 (range: 2.0 to 7.0), TW was 2.0 (range: 2.0 to 7.0), and HK was 2.0 (range: 2.0 to 6.0).

Figure 2: Patients who received HER2-targeted therapy (monoclonal antibodies and antibody-drug conjugates)



The percentage is based on the number of patients in each country/region and in each LOT.

Figure 3: Transition rate from 1st LOT to each LOT (all regimens)



Treatment Sequencing from 1st LOT to 4th LOT – HER2-targeted therapy

- In 1st LOT: HER2-targeted therapy (HER2-targeted mAb, HER2-targeted ADC, HER2-targeted TKI) was more predominantly used than Non-HER2-targeted therapy in KR, CN, and HK. In TW, proportion of use of HER2-targeted therapy and Non-HER2-targeted therapy was similar.
- In 2nd and later LOTs: Non-HER2-targeted therapy was more frequently used than HER2-targeted therapy in KR, TW, and HK. In CN, HER2-targeted therapy was more dominantly used than Non-HER2-targeted therapy (Figure 4, Figure 5, Figure 6, Figure 7).

Figure 4: South Korea

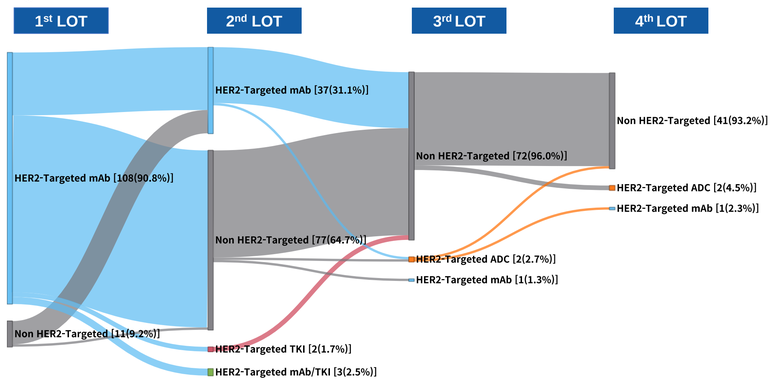


Figure 6: Taiwan

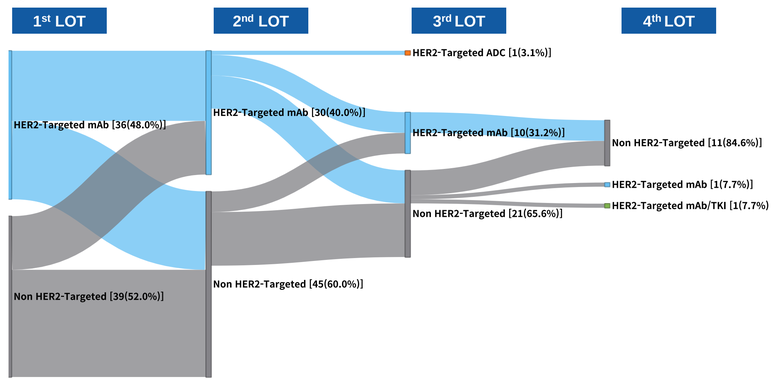


Figure 5: China

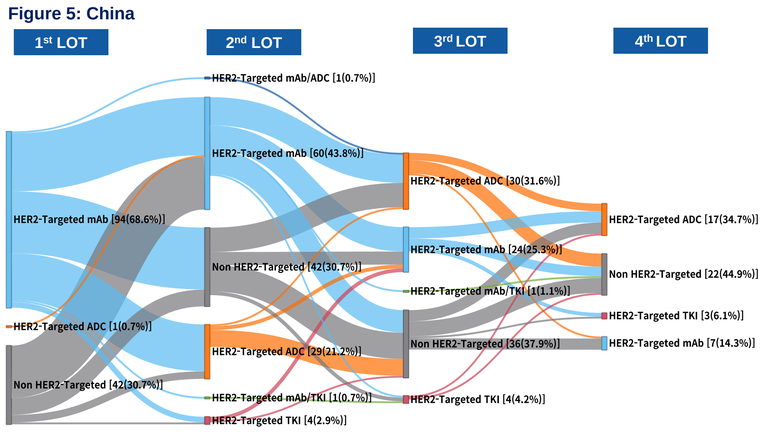
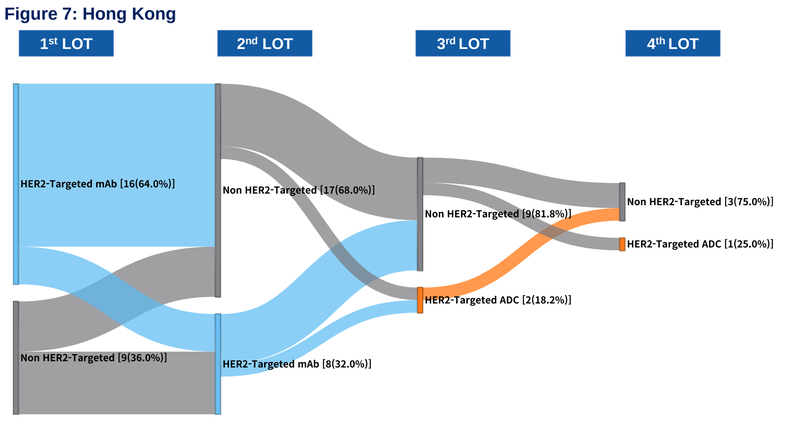


Figure 7: Hong Kong



Real-world time to treatment failure (rwTTF) in each LOT in HER2-positive [IHC3+ or IHC2+/ISH+] patients

Patients on HER2-targeted therapy in 1st, 2nd, and/or 3rd LOTs had significantly longer rwTTF. The statistical comparison was not pre-planned or adjusted.

Table 5: rwTTF - HER2-targeted therapy used (Yes / No)

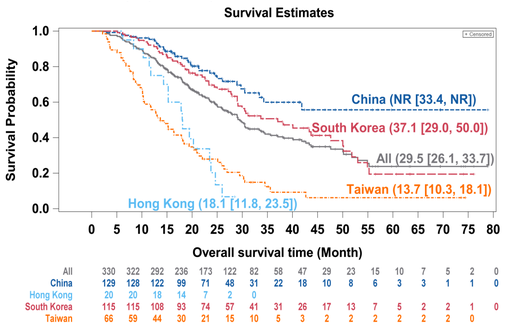
HER2- targeted therapy	n	Median (months)	95% CI	HR [95% CI]#	P-value#
1st LOT					
All	327	6.2	5.7, 6.9		
Yes	242	7.4	6.6, 8.0	0.5 [0.4, 0.6]	<0.0001*
No	85	3.2	2.4, 4.9		
2nd LOT					
All	310	3.6	3.3, 4.0		
Yes	149	4.1	3.4, 5.3	0.7 [0.6, 0.9]	0.0037*
No	161	3.3	2.4, 3.7		
3rd LOT					
All	182	2.2	1.9, 2.9		
Yes	64	2.8	1.6, 4.3	0.7 [0.5, 1.0]	0.0354*
No	118	2.1	1.6, 2.8		
4th LOT					
All	96	1.8	1.3, 2.7		
Yes	29	1.7	0.8, 3.6	1.0 [0.7, 1.6]	0.8698
No	67	2.0	1.1, 3.1		

#log-rank test, HER2-targeted therapy - Yes vs No. *Statistically significant.

Real-world overall survival (rwOS) in 1st LOT in HER2-positive [IHC3+ or IHC2+/ISH+] patients

Figure 8: rwOS by country/region (median rwOS [95% CI])

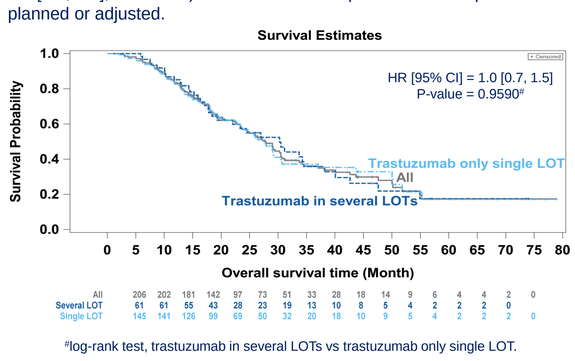
In this study, all patients used ≧2 LOTs. The median rwOS in 1st LOT in East Asia was 29.5 months [95% CI: 26.1, 33.7]. Number of events were different in each country/region. In CN, median rwOS was not reached (NR) due to high proportion of "loss to follow-up" (Table 2).



NR = not reached.

Figure 9: rwOS – Trastuzumab in single LOT use or multiple LOTs use

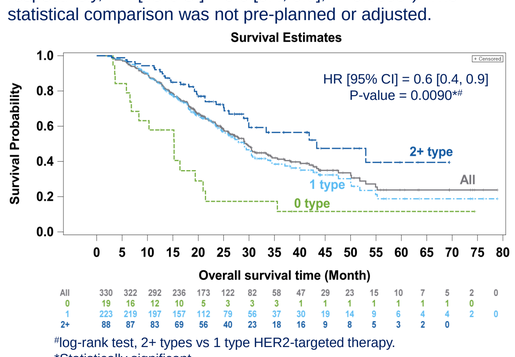
In East Asia, the median rwOS was not statistically different between patients who used trastuzumab in several LOTs vs. trastuzumab in single LOT (30.3 months vs. 27.2 months, hazard ratio (HR) [95% CI] = 1.0 [0.7, 1.5], P=0.9590). The statistical comparison was not pre-planned or adjusted.



#log-rank test, trastuzumab in several LOTs vs trastuzumab only single LOT.

Figure 10: rwOS – 1 type vs 2+ types of HER2-targeted therapy

In East Asia, the median rwOS was longer in patients who used more than 2 types of HER2-targeted therapy vs. only 1 type of HER2-targeted therapy (43.3 months vs. 29.0 months, respectively, HR [95% CI] = 0.6 [0.4, 0.9], P=0.0090*). The statistical comparison was not pre-planned or adjusted.



#log-rank test, 2+ types vs 1 type HER2-targeted therapy.
*Statistically significant.

Conflict of interest

Do-Youn Oh: Advisory board/Consultant: AstraZeneca, Novartis, Genentech/Roche, Merck Serono, Bayer, Taiho, ASLAN, Halozyme, Zymeworks, BMS/Celgene, BeiGene, Basilea, Turning Point, Yuhan, Arcus Biosciences, IQVIA, MSD, LG Chem, Astellas, AbbVie, J-Pharma, Mirati Therapeutics, Eutilex, Moderna, Idience, Alligator Bioscience AB, Hana pharm.
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