The effectiveness of post-T-DXd treatments in HER2+ metastatic BC patients: The EN-SEMBLE Study

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Presenting Author Conflict OF Interest Self－Declaration Form

Presenting Author Name: Toru Mukohara

	Applicability	If applicable, company name, etc.
(1) Position as an officer or advisor	No	
(2) Ownership of stock	No	
(3) Royalties or licensing fees	No	
(4) Honoraria, etc.	Yes	Daiichi Sankyo, Eli Lilly Japan
(5) Manuscript fees, etc.	No	
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(7) Donation	Yes	
(8) Consulting fee for litigation, etc.	No	
(9) Accept contract researcher	No	
(10) Endowed course	No	
(11) Other remuneration	No	

Background

- In the DESTINY-Breast01, 02, and 03 clinical trials, T-DXd has shown significant clinical benefits in patients with HER2-positive, metastatic breast cancer (mBC).[1–3]
- Patients discontinue T-DXd treatment mainly due to PD or AEs, such as ILD, in real-world clinical practice.
- However, limited information is available about the efficacy of HER2-directed therapies post T-DXd; more is needed in order to define the optimal treatment strategy for HER2+ mBC previously treated with T-DXd.

Objective

- The aim of the EN-SEMBLE study was to examine the distribution of post-T-DXd regimens, including their effectiveness and the incidence of ILD, in real-world clinical practice in Japan.

AEs, adverse events; HER2, human epidermal growth factor receptor 2; ILD, interstitial lung disease; mBC, metastatic breast cancer; PD, progressive disease; T-DXd, trastuzumab deruxtecan.

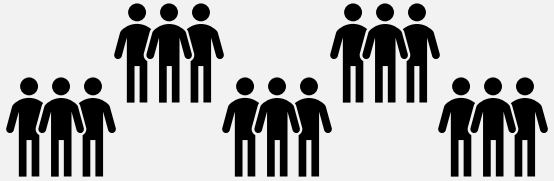
1 Saura C, et al. *Ann Oncol.* 2024;35:302-307. 2 André F, et al. *Lancet.* 2023;401:1773-1785. 3 Cortés J, et al. *N Engl J Med.* 2022;386:1143-1154.

Study design

EN-SEMBLE Study: A nationwide cohort study in real-world settings in Japan

All-patient post-marketing surveillance

(jRCT1080225197)



- Started T-DXd treatment between May 2020 (launch date of T-DXd) and May 2021.
- With HER2-positive metastatic or recurrent BC.

Registration period: May 2020–May 2023

Observation period: May 2020–Nov 2023

Eligibility Criteria

- Enrolled in all-patient PMS
- Have discontinued T-DXd treatment
- Started a post–T-DXd treatment
- Informed consent/opt-out consent
- Age ≥ 18 years

EN-SEMBLE study

(jRCT1030220506)

Endpoints

- Distribution of post–T-DXd treatment regimens
- Effectiveness: rwPFS, rwTTF, rwTTNT, and OS from 1st post–T-DXd treatment
- Incidence of ILD in 1st post–T-DXd treatment

A pre-specified subgroup analysis was planned

BC, breast cancer; HER2, human epidermal growth factor receptor 2; jRCT, Japan registry of clinical trials; PMS, post-marketing surveillance; T-DXd, trastuzumab deruxtecan.

Patient disposition

Patients receiving T-DXd **n = 1,213**
(Patients enrolled in all-patient PMS)

Patients excluded from registration (n = 538)
- Continued T-DXd treatment (n = 173)
- Did not receive next treatment[a] (n = 273)
- Next treatment pending[b] (n = 34)
- Written consent not obtained (n = 4)
- Other (n = 32)
- Unknown/missing (n = 24)

Registered patients **n = 675**

Patients excluded from analysis set (n = 11)
- Did not start T-DXd treatment between May 25, 2020, and Nov 30, 2021 (n = 4)
- Not enrolled in the all-patient PMS (n = 3)
- Did not start a subsequent treatment after discontinuation of T-DXd (n = 3)
- Written consent not obtained, or withdrawal from the study (n = 5)

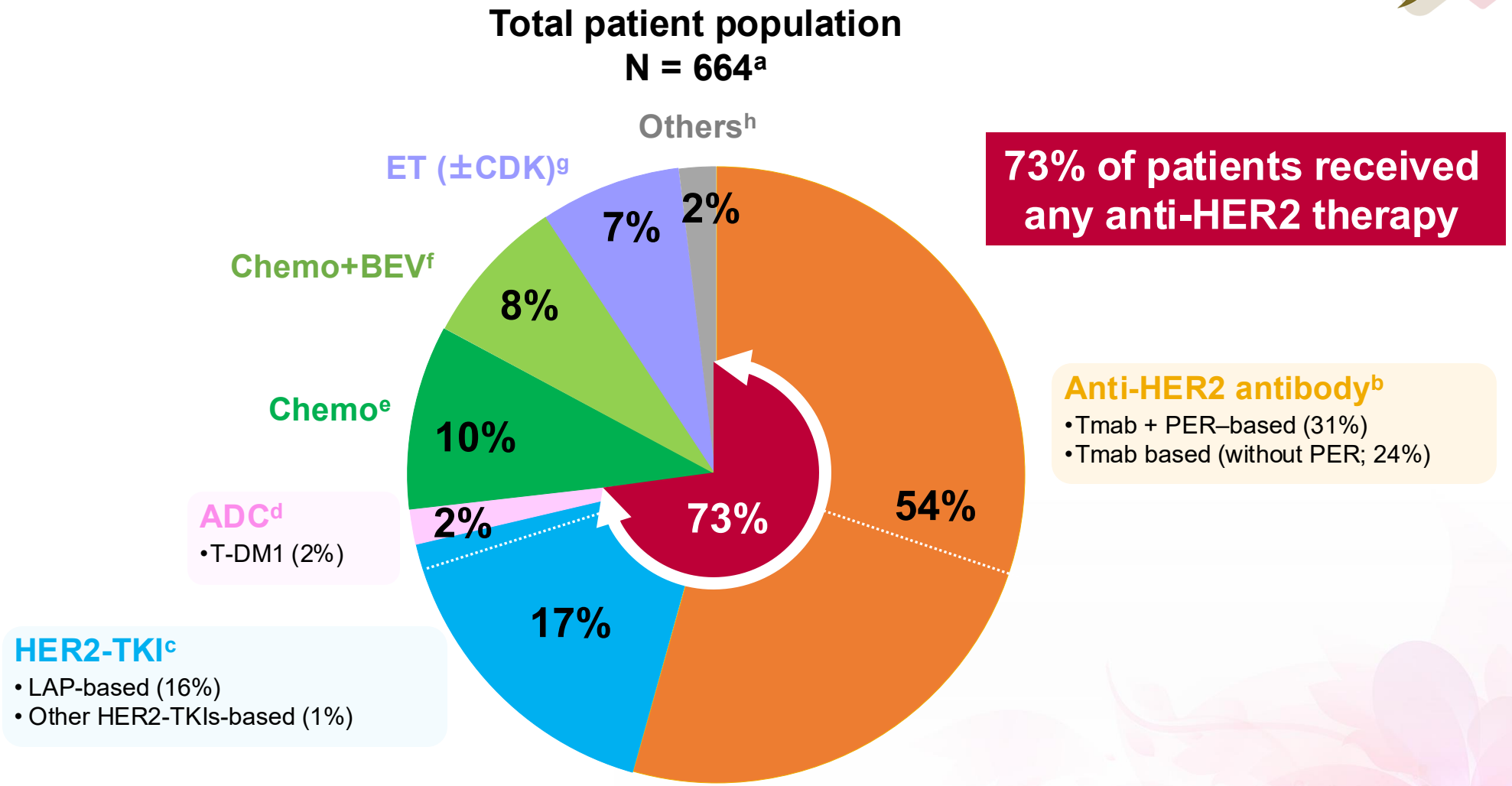
Analysis set **n = 664**

Patients were registered at 222 sites nationwide in Japan;
median follow-up was 12.0 months (range, 0.3–36.2 months)

PMS, post-marketing surveillance; T-DXd, trastuzumab deruxtecan.

[a]Death, palliative care, lost to follow-up, transferred to another hospital after discontinuation of T-DXd. [b]Did not start next treatment after discontinuation of T-DXd.

Distribution of 1st post–T-DXd treatments



ADC, antibody-drug conjugate; BEV, bevacizumab; CDK cyclin-dependent kinase; Chemo, chemotherapy; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; LAP, lapatinib; PER, pertuzumab; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; Tmab, trastuzumab; TKI, tyrosine kinase inhibitor.
[a]Percentages were calculated using the total patient population as the denominator. [b]Tmab + PER + other anticancer therapies, Tmab + other anticancer therapies, Tmab + PER, Tmab alone. [c]LAP + other anticancer therapies or LAP alone. [d]T-DM1 alone. [e]Chemo alone or multiple chemo. [f]BEV + chemo. [g]ET + CDK4/6, ET alone, or multiple ET. [h]Other anticancer therapies that do not fall under other categories listed.

Baseline characteristics

		All patients	1st post–T-DXd treatment regimen		
			Anti-HER2 antibody	HER2-TKI	ADC
		N = 664	n = 361	n = 113	n = 12
At the start of 1st post–T-DXd treatment					
Age	median (range), years	60 (30–89)	61 (35–89)	58 (35–83)	61.5 (48–88)
	<65 years	416 (62.7)	219 (60.7)	75 (66.4)	7 (58.3)
	≥65 years	248 (37.3)	142 (39.3)	38 (33.6)	5 (41.7)
Sex	Female	661 (99.5)	360 (99.7)	112 (99.1)	12 (100.0)
	Male	3 (0.5)	1 (0.3)	1 (0.9)	0 (0.0)
HER2 status	IHC 3+	407 (61.3)	223 (61.8)	78 (69.0)	7 (58.3)
	IHC 2+/ISH +	173 (26.1)	92 (25.5)	31 (27.4)	4 (33.3)
	ISH+ other than the above/ISH-	33 (5.0)	16 (4.4)	1 (0.9)	0 (0.0)
	Unknown/both missing	51 (7.7)	30 (8.3)	3 (2.7)	1 (8.3)
ECOG PS	0	326 (49.1)	185 (51.2)	49 (43.4)	3 (25.0)
	1	251 (37.8)	127 (35.2)	50 (44.2)	8 (66.7)
	>2	57 (8.6)	26 (7.2)	9 (8.0)	1 (8.3)
	Unknown	30 (4.5)	23 (6.4)	5 (4.4)	0 (0.0)
Visceral metastasis	Yes	529 (79.7)	280 (77.6)	91 (80.5)	9 (75.0)
	No	135 (20.3)	81 (22.4)	22 (19.5)	3 (25.0)
Brain metastasis	Yes	153 (23.0)	79 (21.9)	31 (27.4)	4 (33.3)
	No	500 (75.3)	275 (76.2)	80 (70.8)	8 (66.7)
	Unknown	11 (1.7)	7 (1.9)	2 (1.8)	0 (0.0)

Data are shown as n (%) unless otherwise specified

ADC, antibody-drug conjugate; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, *in situ* hybridization; PgR, progesterone receptor; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor.

Median and its 95% CI were calculated using the Kaplan-Meier method.

Baseline characteristics (cont.)

		All patients	1st post–T-DXd treatment regimen		
			Anti-HER2 antibody	HER2-TKI	ADC
		N = 664	n = 361	n = 113	n = 12
Prior cancer therapy for unresectable or recurrent BC before T-DXd treatment					
Number of prior regimens	median (range), line	3 (1–42)	4 (1–25)	3 (1–15)	3 (1–13)
	≤2 lines	190 (28.6)	87 (24.1)	46 (40.7)	5 (41.7)
	≥3 lines	459 (69.1)	265 (73.4)	64 (56.6)	7 (58.3)
Prior regimens	Anti-HER2 therapy	654 (98.5)	355 (98.3)	110 (97.3)	12 (100.0)
	Trastuzumab	620 (93.4)	342 (94.7)	103 (91.2)	11 (91.7)
	Pertuzumab	601 (90.5)	328 (90.9)	102 (90.3)	10 (83.3)
	T-DM1	606 (91.3)	329 (91.1)	107 (94.7)	9 (75.0)
	Chemotherapy	600 (90.4)	328 (90.9)	100 (88.5)	11 (91.7)
	Endocrine therapy	253 (38.1)	127 (35.2)	42 (37.2)	2 (16.7)
T-DXd treatment					
BC status	*De novo* stage IV	250 (37.7)	134 (37.1)	42 (37.2)	4 (33.3)
	Recurrent BC	394 (59.3)	215 (59.6)	67 (59.3)	8 (66.7)
Duration of T-DXd treatment	median (range), month	8.1 (0.03–35.4)	8.3 (0.03–35.4)	9.9 (0.7–29.4)	7.2 (1.4–19.6)
History of ILD in T-DXd treatment	Yes	155 (23.3)	100 (27.7)	22 (19.5)	4 (33.3)
	None	508 (76.5)	261 (72.3)	90 (79.6)	8 (66.7)
	Unknown	1 (0.2)	0 (0.0)	1 (0.9)	0 (0.0)
Reason for T-DXd discontinuation	PD	448 (67.5)	223 (61.8)	84 (74.3)	5 (41.7)
	ILD	146 (22.0)	96 (26.6)	20 (17.7)	3 (25.0)
	AEs other than ILD	34 (5.1)	23 (6.4)	6 (5.3)	1 (8.3)
	Others	36 (5.4)	19 (5.3)	3 (2.7)	3 (25.0)

ADC, antibody-drug conjugate; AEs, adverse events; BC, breast cancer; HER2, human epidermal growth factor receptor 2; ILD, interstitial lung disease; PD, progressive disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor.

Median and its 95% CI were calculated using the Kaplan-Meier method.

Data are shown as n (%) unless otherwise specified

Outcomes for 1st post–T-DXd treatment

median (95% CI), months

	All patients	1st post–T-DXd treatment regimen						
		Anti-HER2 antibody	HER2-TKI	ADC	Chemo	Chemo + BEV	ET ± CDK	Others
	N = 664	n = 361	n = 113	n = 12	n = 64	n = 52	n = 49	n = 13
rwPFS	**4.1** (3.9–4.5)	**4.1** (3.8–4.6)	**4.3** (3.8–6.2)	**2.6** (1.0–4.7)	**2.8** (2.1–3.9)	**4.2** (3.0–5.4)	**6.5** (3.8–7.4)	**2.8** (1.0–7.3)
rwTTF	**3.8** (3.7–4.1)	**3.9** (3.6–4.3)	**4.2** (3.7–5.6)	**2.0** (0.3–3.1)	**2.5** (2.1–3.8)	**3.7** (2.6–4.8)	**5.6** (2.5–6.7)	**2.8** (1.4–7.3)
rwTTNT	**5.0** (4.6–5.5)	**5.1** (4.5–5.7)	**5.3** (4.4–6.8)	**3.0** (1.0–5.9)	**4.0** (3.5–4.5)	**5.5** (3.9–6.2)	**6.7** (4.8–10.1)	**4.4** (1.9–10.2)
OS	**16.2** (13.8–17.2)	**17.2** (15.1–19.8)	**16.3** (12.2–18.7)	**9.3** (4.3–NE)	**11.4** (5.9–19.2)	**8.2** (6.0–10.5)	**21.9** (16.9–NE)	**12.1** (5.1–NE)

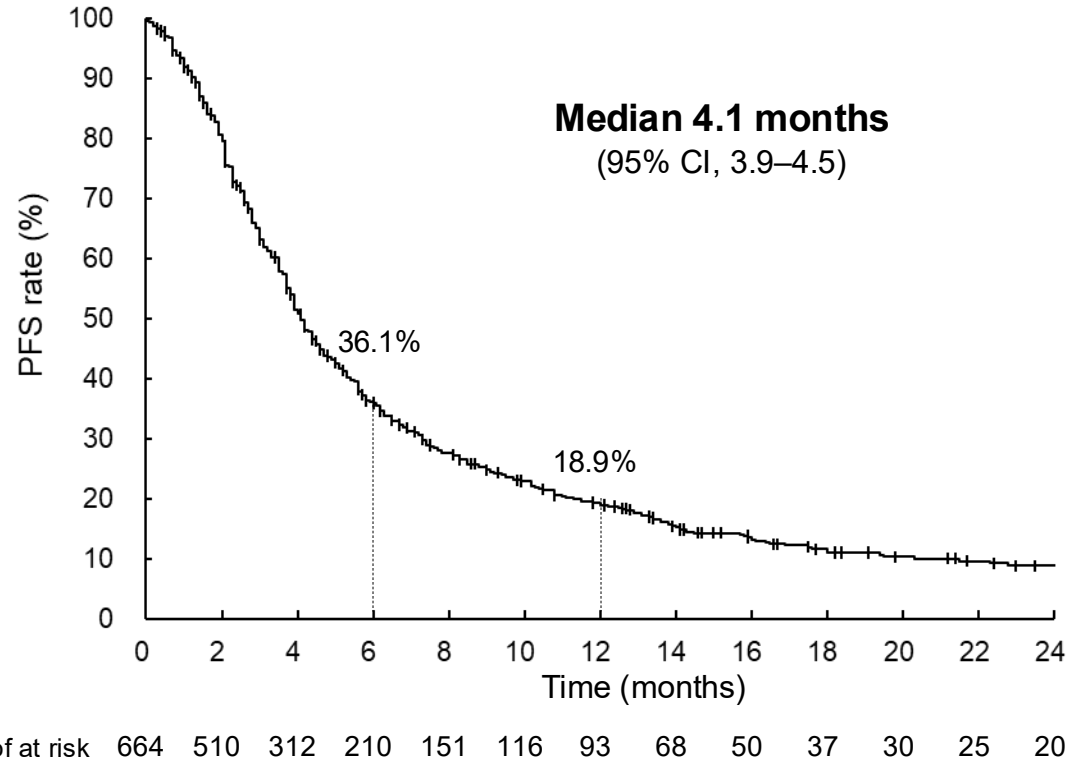
ADC, antibody-drug conjugate; BEV, bevacizumab; CDK, cyclin-dependent kinase; Chemo, chemotherapy; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; NE, not estimable; OS, overall survival; PFS, progression-free survival; rw, real-world; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor; TTF, time to treatment failure; TTNT, time to next treatment.

Median and its 95% CI were calculated using the Kaplan-Meier method

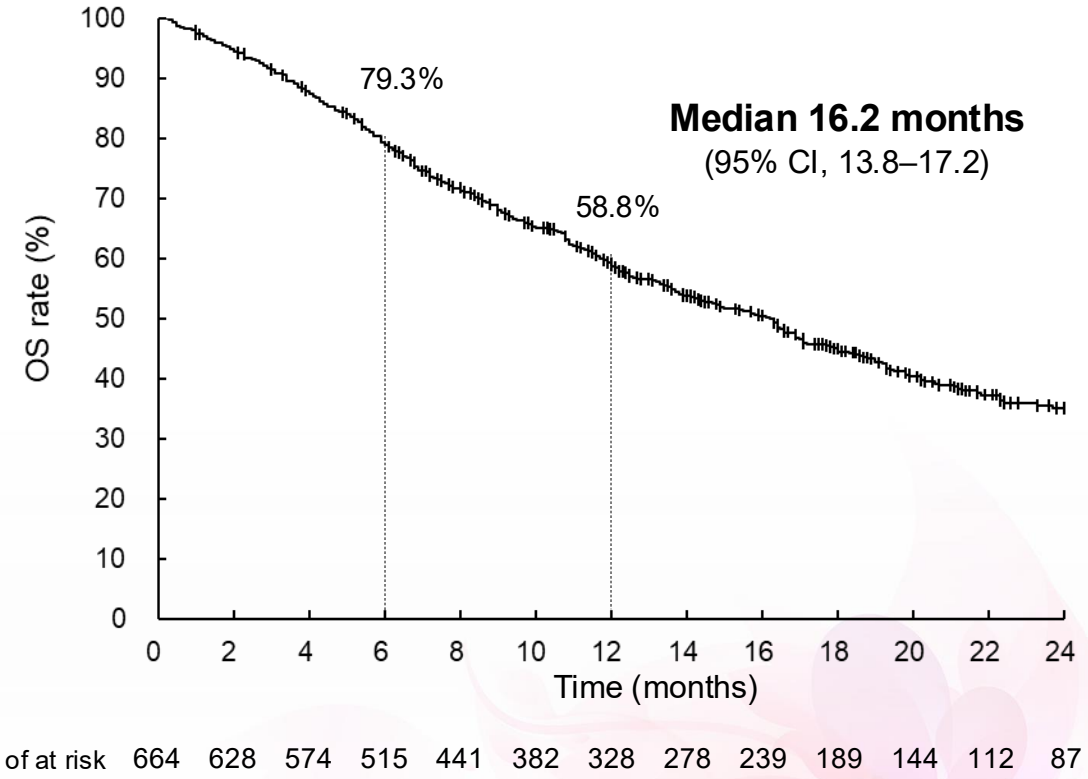
rwPFS and OS in the overall population

Kaplan–Meier curves from the time of the 1st post–T-DXd treatment

rwPFS



OS



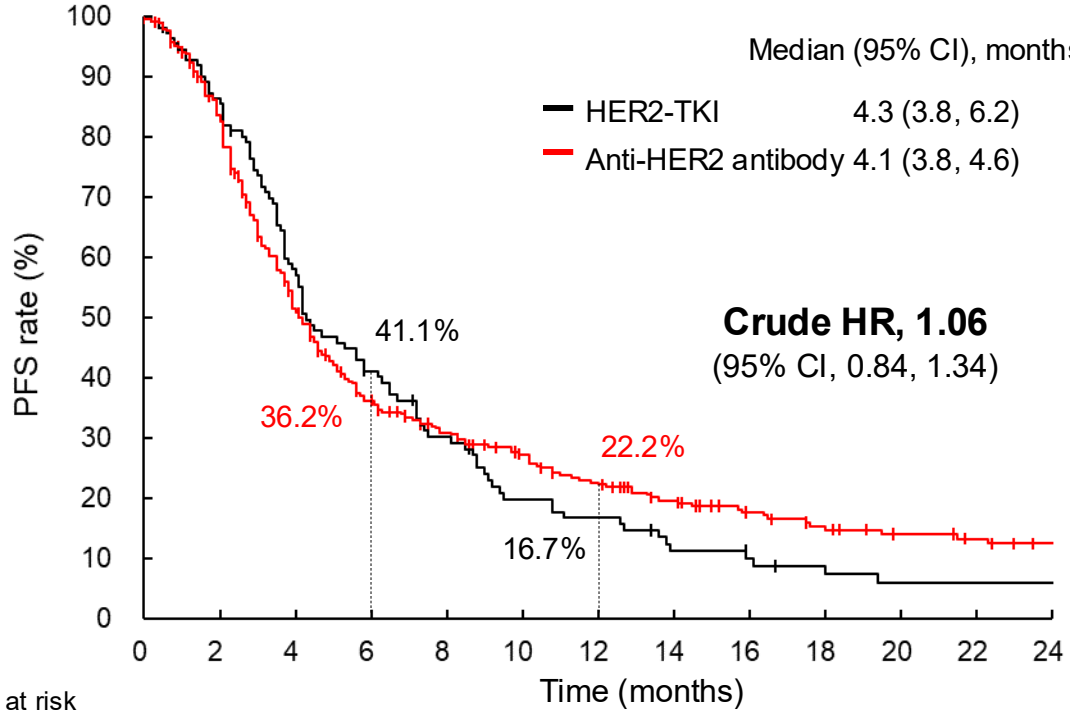
HER2, human epidermal growth factor receptor 2; HR, Hazard ratio; OS, Overall survival; PD, progressive disease; PFS, progression-free survival; pts, patients; rw, real-world; T-DXd, trastuzumab deruxtecan..

Medians and their 95% CIs were calculated using the Kaplan–Meier method. HRs and their 95% CIs were calculated using the Cox proportional hazards model.

rwPFS and OS by subgroup: HER2-TKI vs Anti-HER2 antibody

Kaplan–Meier curves from the time of the 1st post–T-DXd treatment

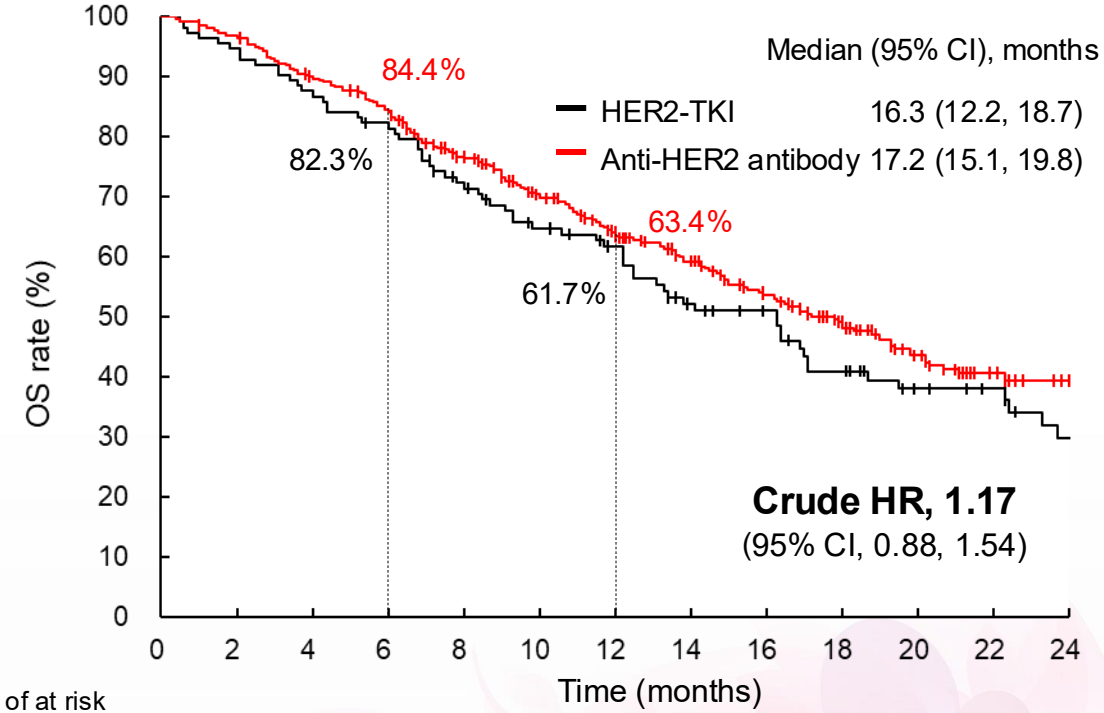
rwPFS



No. of at risk

HER2-TKI	113	94	62	42	30	19	16	10	8	5	4	4	4
Anti-HER2 antibody	361	286	168	114	88	71	56	44	32	25	19	16	12

OS



No. of at risk

HER2-TKI	113	107	98	92	77	66	59	46	41	32	24	21	14
Anti-HER2 antibody	361	349	320	299	254	217	186	162	134	105	80	61	50

HER2, human epidermal growth factor receptor 2; HR, hazard ratio; PFS, progression-free survival;. PER, pertuzumab; rw, real-word; T-DXd, trastuzumab deruxtecan; TKI, tyrosine kinase inhibitor; Tmab, trastuzumab.

Medians and their 95% CIs were calculated using the Kaplan–Meier method. HRs and their 95% CIs were calculated using the Cox proportional hazards model.

Outcomes by subgroup based on reason for T-DXd discontinuation

(95% CI)

Reason for discontinuation of T-DXd	N	rwPFS		rwTTNT		OS	
		Median, months	Crude HR	Median, months	Crude HR	Median, months	Crude HR
PD	448	**3.5** (3.0–3.8)	**0.42** (0.34–0.51)	**4.2** (3.8–4.6)	**0.46** (0.37–0.56)	**12.0** (10.9–13.6)	**0.35** (0.27–0.45)
AEs (ILD/other than ILD)	180	**7.3** (5.7–10.3)		**8.3** (6.2–11.3)		**32.4** (22.3–NE)	
ILD	146	**7.2** (5.4–10.2)	**0.87** (0.54–1.39)	**7.8** (5.9–10.8)	**0.75** (0.48–1.19)	**32.4** (21.3–NE)	**0.79** (0.42–1.51)
AE other than ILD	34	**10.2** (5.1–14.0)		**11.3** (5.1–27.4)		**NR** (19.8–NE)	

AE; adverse event; HR, hazard ratio; ILD, Interstitial lung disease; NE, not estimable; NR, not reached; OS, overall survival; PD, progressive disease; PFS, progression-free survival; rw, real-world; T-DXd, trastuzumab deruxtecan; TTNT, time to next treatment.

Medians and their 95% CIs were calculated using the Kaplan–Meier method. HRs and their 95% CIs were calculated using the Cox proportional hazards model.

ILD in the 1st post–T-DXd treatment

	N	ILD events n (%)	(95% CI)
All patients	664	10 (1.5)	(0.7–2.8)
History of ILD in T-DXd treatment			
Yes	155	5 (3.2)	(1.1–7.4)
No	508	4 (0.8)	(0.2–2.0)
Unknown	1	1 (100)	(2.5–100)

Backgrounds for the patients with ILD

No.	History of ILD in T-DXd treatment			1st post–T-DXd treatment	
	Yes/No	Worst Grade[a]	Outcome[b]	Regimens	Time to onset of ILD (days)
1	Yes	Grade 2	Non-recovery	Tmab + Eribulin	22
2	Yes	Grade 1	Non-recovery	Tmab	255
3	Yes	Grade 3	Recovery	Tmab + PER + Eribulin	23
4	Yes	Grade 3	Recovery	Tmab + PER + Eribulin	39
5	Yes	Grade 1	Recovery	Eribulin	161
6	No	-	-	Tmab + PER + Eribulin	38
7	No	-	-	Tmab + Paclitaxel	108
8	No	-	-	Tmab + PER + Docetaxel	117
9	No	-	-	Abemaciclib + Fulvestrant	134
10	Unknown	-	-	Lapatinib + Capecitabine	100

AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; ILD, Interstitial lung disease; PER, pertuzumab; PD, progressive disease; T-DXd, trastuzumab deruxtecan; Tmab, trastuzumab.
[a]CTCAE grade decided by attending physician. [b]ILD status on the first day of the 1st post–T-DXd treatment.

Incidence of ILD, with the 95%CIs calculated using the Clopper–Pearson method

Limitations

- Inherent risks for bias may have occurred due to:
  - ✓the study being non-blinded, non-randomized, and with no control arm
  - ✓the fact that among the patients who were enrolled in the all-patient PMS, only those who were able to start the post-T-DXd treatment were enrolled in the present study.
- The all-patient PMS for T-DXd was conducted when prior T-DM1 treatment was required. Since T-DXd was administered as different lines of treatment, subsequent therapies were also different lines of treatment and may not be directly comparable.

PMS, post-marketing surveillance; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Conclusion

- In the current study, 73% of patients received anti-HER2 therapy and 54% received anti-HER2 antibody regimens as 1st post–T-DXd treatments.
- The rwPFS and OS results were numerically similar for anti-HER2 antibody and HER2-TKI-based therapies received as 1st post–T-DXd treatments.
- Patients who discontinued T-DXd due to AEs, including ILD, had numerically better outcomes than those who discontinued due to PD.
- The 1st post–T-DXd treatments were generally safe for patients with a history of ILD incidence caused by T-DXd treatment, with a recurrence rate of 3.2%.

AE, adverse event; HER2, human epidermal growth factor receptor 2; ILD, interstitial lung disease; PD, progressive disease; T-DXd, trastuzumab deruxtecan.

Participating Study Sites

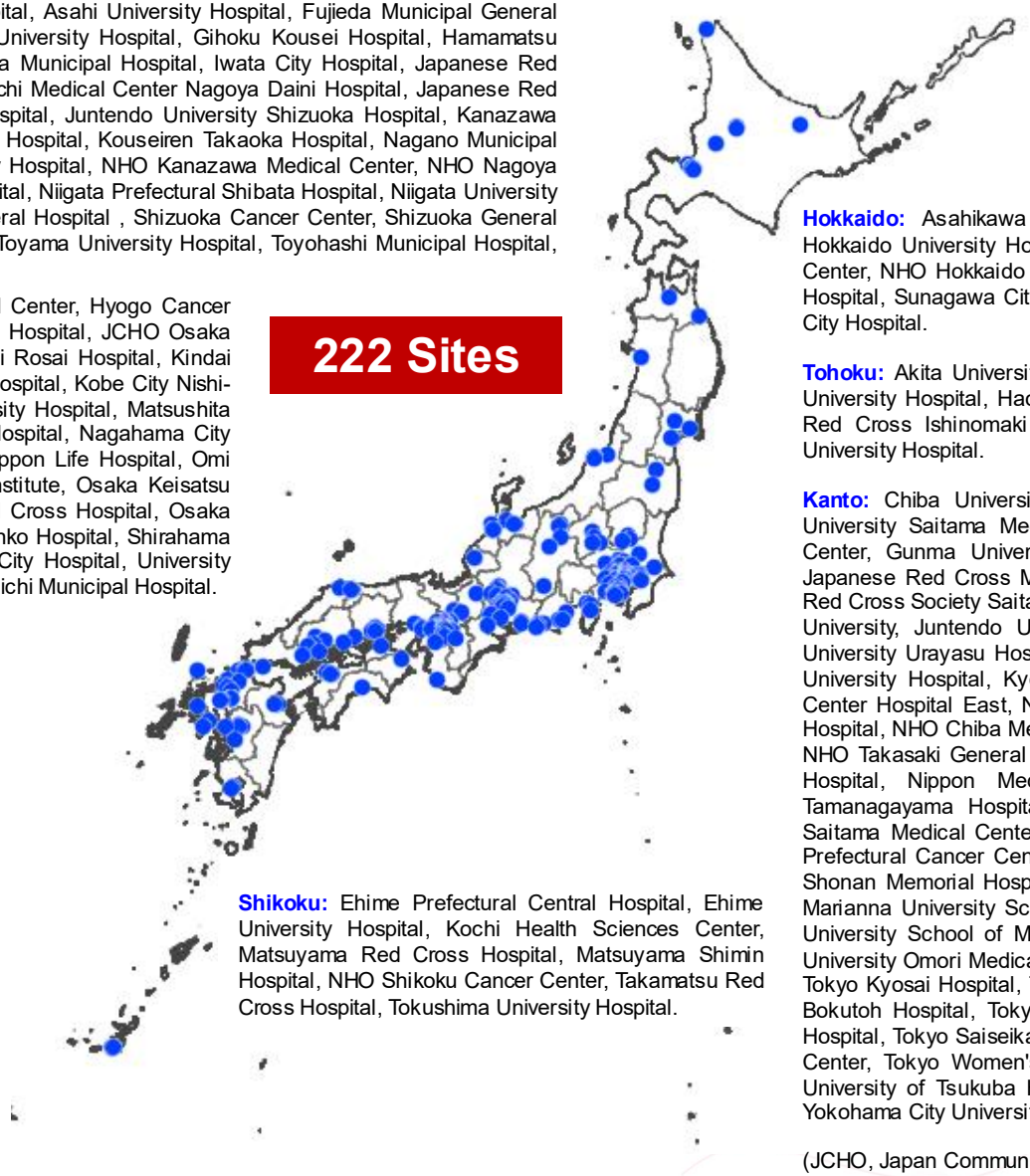
Chubu: Aichi Cancer Center, Aichi Medical University Hospital, Aizawa Hospital, Asahi University Hospital, Fujieda Municipal General Hospital, Fujita Health University Hospital, Fukui Red Cross Hospital, Gifu University Hospital, Gihoku Kousei Hospital, Hamamatsu Medical Center, Hamamatsu University Hospital, Ichinomiyanishi Hospital, Iida Municipal Hospital, Iwata City Hospital, Japanese Red Cross Aichi Medical Center Nagoya Daiichi Hospital, Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital, Japanese Red Cross Nagano Hospital, JCHO Chukyo Hospital, JCHO Mishima General Hospital, Juntendo University Shizuoka Hospital, Kanazawa Medical University Hospital, Kanazawa University Hospital, Kasugai Municipal Hospital, Kouseiren Takaoka Hospital, Nagano Municipal Hospital, Nagoya City University East Medical Center, Nagoya City University Hospital, NHO Kanazawa Medical Center, NHO Nagoya Medical Center, NHO Shinshu Ueda Medical Center, Niigata City General Hospital, Niigata Prefectural Shibata Hospital, Niigata University Medical & Dental Hospital, Ogaki Municipal Hospital, Seirei Hamamatsu General Hospital , Shizuoka Cancer Center, Shizuoka General Hospital, Tajimi City Hospital, Tokoname City Hospital, Toyama City Hospital, Toyama University Hospital, Toyohashi Municipal Hospital, Toyokawa City Hospital, Yaizu City Hospital.

Kinki: Aihara Hospital, Bellland General Hospital, Higashiosaka City Medical Center, Hyogo Cancer Center, Hyogo Medical University Hospital, Japanese Red Cross Kyoto Daini Hospital, JCHO Osaka Hospital, Kakogawa City Hospital, Kansai Medical University Hospital, Kansai Rosai Hospital, Kindai University Nara Hospital, Kitano Hospital, Kobe City Medical Center General Hospital, Kobe City Nishi-Kobe Medical Center, Kobe Minimally invasive Cancer Center, Kyoto University Hospital, Matsushita Memorial Hospital, Mie Prefectural General Medical Center, Mie University Hospital, Nagahama City Hospital, Nara Medical University Hospital, NHO Osaka National Hospital, Nippon Life Hospital, Omi Medical Center, Osaka City General Hospital, Osaka International Cancer Institute, Osaka Keisatsu Hospital, Osaka Medical and Pharmaceutical University Hospital, Osaka Red Cross Hospital, Osaka Rosai Hospital, Osaka University Hospital, Rinku General Medical Center, Shinko Hospital, Shirahama Hamayu Hospital, Suita Municipal Hospital, Sumitomo Hospital, Takarazuka City Hospital, University Hospital Kyoto Prefectural University of Medicine, Yao Municipal Hospital, Yokkaichi Municipal Hospital.

Chugoku: Fukuyama City Hospital, Hiroshima City North Medical Center Asa Citizens Hospital, Hiroshima Prefectural Hospital, JA Hiroshima General Hospital, JA Onomichi General Hospital, Kawasaki Medical School General Medical Center, Kawasaki Medical School Hospital, Matsue Red Cross Hospital, NHO Higashi-Hiroshima Medical Center, NHO Iwakuni Clinical Center, NHO Kure Medical Center, NHO Okayama Medical Center, NHO Yonago Medical Center, Okayama University Hospital, Tottori University Hospital, Yamaguchi University Hospital.

Kyusyu/Okinawa: Fukuoka University Chikushi Hospital, Fukuoka Wajiro Hospital , Hospital of the University of Occupational and Environmental Health,Japan, Iizuka Hospital, JCHO Kurume General Hospital, Kagoshima University Hospital, Kitakyushu Municipal Medical Center, Kokura Memorial Hospital, Kumamoto City Hospital, Kumamoto Rosai Hospital, Kumamoto University Hospital, Kurume University Hospital, Nagasaki Prefecture Shimabara Hospital, Nagasaki University Hospital, Naha City Hospital, NHO Kyushu Cancer Center, NHO Kyushu Medical Center, NHO Nagasaki Medical Center, NHO Saga Hospital, Oita Prefectural Hospital, Oita University Hospital, Saga University Hospital, Sagara Hospital, Saiseikai Kumamoto Hospital, Sasebo City General Hospital, St. Mary's Hospital, Steel Memorial Yawata Hospital, University of the Ryukyus Hospital, Urasoe General Hospital.

222 Sites



Shikoku: Ehime Prefectural Central Hospital, Ehime University Hospital, Kochi Health Sciences Center, Matsuyama Red Cross Hospital, Matsuyama Shimin Hospital, NHO Shikoku Cancer Center, Takamatsu Red Cross Hospital, Tokushima University Hospital.

Hokkaido: Asahikawa Medical University Hospital, Asahikawa-Kosei General Hospital, Hokkaido University Hospital, Japanese Red Cross Kitami Hospital, KKR Sapporo Medical Center, NHO Hokkaido Cancer Center, NTT Medical Center Sapporo, Sapporo City General Hospital, Sunagawa City Medical Center, Teine Keijinkai Hospital, Tonan Hospital, Wakkanai City Hospital.

Tohoku: Akita University Hospital, Aomori Prefectural Central Hospital, Fukushima Medical University Hospital, Hachinohe City Hospital, Hoshi General Hospital Foundation, Japanese Red Cross Ishinomaki Hospital, Osaki Citizen Hospital, Tohoku Rosai Hospital, Tohoku University Hospital.

Kanto: Chiba University Hospital, Dokkyo Medical University Hospital, Dokkyo Medical University Saitama Medical Center, Fujisawa City Hospital, Funabashi Municipal Medical Center, Gunma University Hospital, Higashiyamato Hospital, Isesaki Municipal Hospital, Japanese Red Cross Medical Center, Japanese Red Cross Musashino Hospital, Japanese Red Cross Society Saitama Red Cross Hospital, JCHO Saitama Medical Center, Jichi Medical University, Juntendo University Hospital, Juntendo University Nerima Hospital, Juntendo University Urayasu Hospital, Kanagawa Cancer Center, Kasukabe Medical Center, Kitasato University Hospital, Kyoundo Hospital, National Cancer Center Hospital, National Cancer Center Hospital East, National Center for Global Health and Medicine, Nerima Hikarigaoka Hospital, NHO Chiba Medical Center, NHO Saitama Hospital, NHO Shibukawa Medical Center, NHO Takasaki General Medical Center, NHO Tokyo Medical Center, Nippon Medical School Hospital, Nippon Medical School Musashikosugi Hospital, Nippon Medical School Tamanagayama Hospital, Ofuna Chuo Hospital, Saiseikai Yokohamashi Nanbu Hospital, Saitama Medical Center, Saitama Medical University International Medical Center, Saitama Prefectural Cancer Center, Seirei Yokohama Hospital, Shonan Kamakura General Hospital, Shonan Memorial Hospital, Showa University Hospital, St. Luke's International Hospital, St. Marianna University School of Medicine, The Cancer Institute Hospital Of JFCR, The Jikei University School of Medicine Daisan Hospital, Tochigi Medical Center Shimotsuga, Toho University Omori Medical Center, Tokai University Hachioji Hospital, Tokai University Hospital, Tokyo Kyosai Hospital, Tokyo Medical University Hachioji Medical Center, Tokyo Metropolitan Bokutoh Hospital, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Tokyo Saiseikai Central Hospital, Tokyo Women's Medical University Adachi Medical Center, Tokyo Women's Medical University Yachiyo Medical Center, Toranomon Hospital, University of Tsukuba Hospital, Yatsu Hoken Hospital, Yokohama City University Hospital, Yokohama City University Medical Center, Yokohama Rosai Hospital.

(JCHO, Japan Community Healthcare Organization; NHO, National Hospital Organization)

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