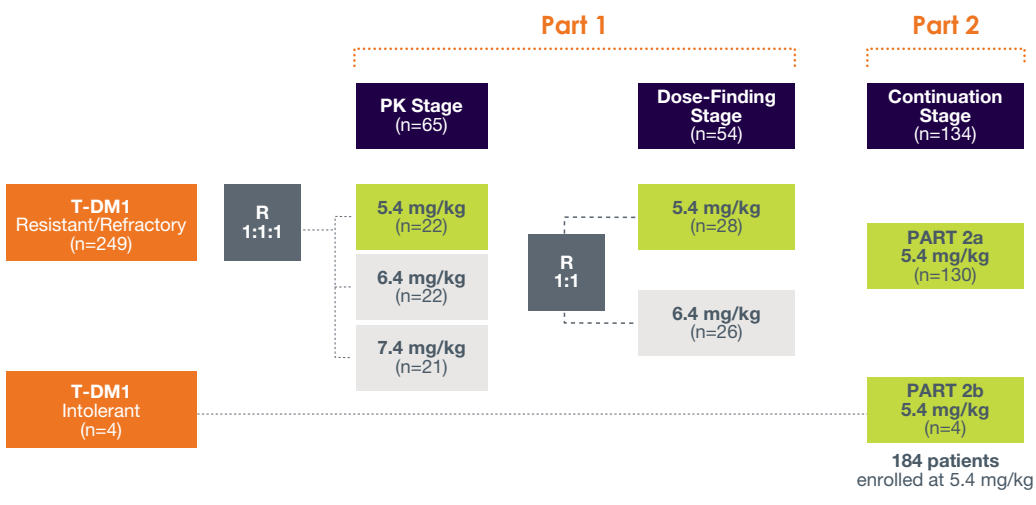
ENHERTU®
trastuzumab deruxtecan

EXTEND HER2+ EXPECTATIONS

DESTINY-Breast01: Study Design

An Open-Label Multicenter Phase 2 Study of ENHERTU[1-3]

Population
- ≥18 years of age
- Unresectable and/or metastatic BC
- HER2 positive (centrally confirmed in archival tissue)
- Prior T -DM1
- Excluded patients with history of significant ILD
- Pretreated and stable brain metastases were allowed



184 patients enrolled at 5.4 mg/kg

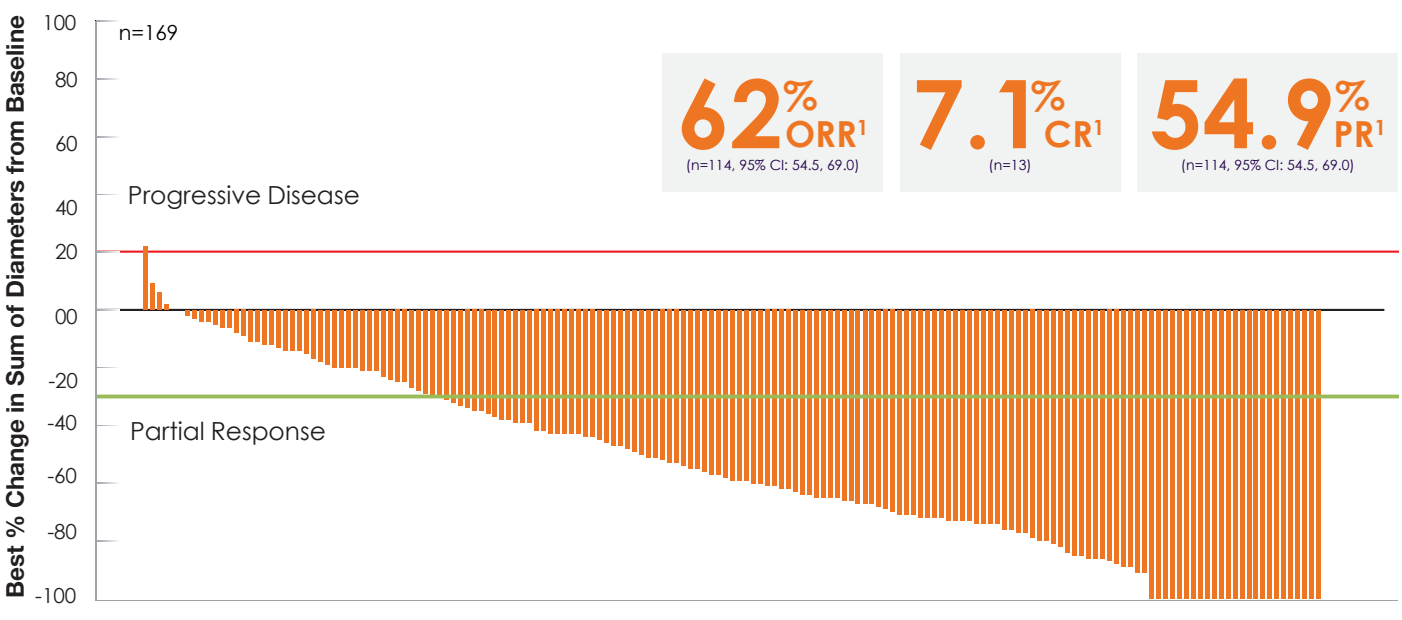
Endpoints
- **Primary:** confirmed ORR by independent central imaging facility review per RECIST v1.1
- **Secondary:** investigator-assessed ORR, DCR, DOR, CBR, PFS, OS, PK and safety

Median Duration of Follow-Up
- **August 1, 2019 data cutoff:** 11.1 months (range, 0.7-19.9 months)[2]
- **June 8, 2020 data cutoff:** 20.5 months (range, 0.7-31.4 months)[3]
- **March 26, 2021 data cutoff:** 26.5 months (range, 0.7-39.1 months)[1]

DESTINY-Breast01: Objective Response Rate

Nearly all patients treated with ENHERTU had their tumors shrink or stabilize[1]

Best percent change from baseline in sum of diameters of target lesions by ICR[1]



By independent central review. A total of 169 patients from the enrolled analysis set (N=184) had both baseline and postbaseline target lesion assessments by independent central review and are included in this analysis.

DESTINY-Gastric01: Study Design[4]

A Phase 2, multicenter, open-label, randomized trial[4]

Adult patients in Japan and South Korea with HER2-expressing, locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma
- **Primary cohort consisted of patients who were HER2+ (IHC3+ or IHC2+/ISH+)**
  - **Had progressed on trastuzumab-based regimen**
  - **Had received ≥2 prior regimens, including fluoropyrimidine and platinum chemotherapy**

Randomized 2:1
N=188

- **ENHERTU** 6.4 mg/kg once every 3 weeks (21-day cycle) (n=126)
- Physician's choice of irinotecan (n=55) or paclitaxel (n=7)

Patients were treated until unacceptable toxicity or disease progression

Primary endpoint
- Objective response rate (ORR), based on an independent central review (ICR)

Secondary endpoints
- Overall survival (OS), progression-free survival (PFS), duration of response (DOR), and disease control rate (DCR)

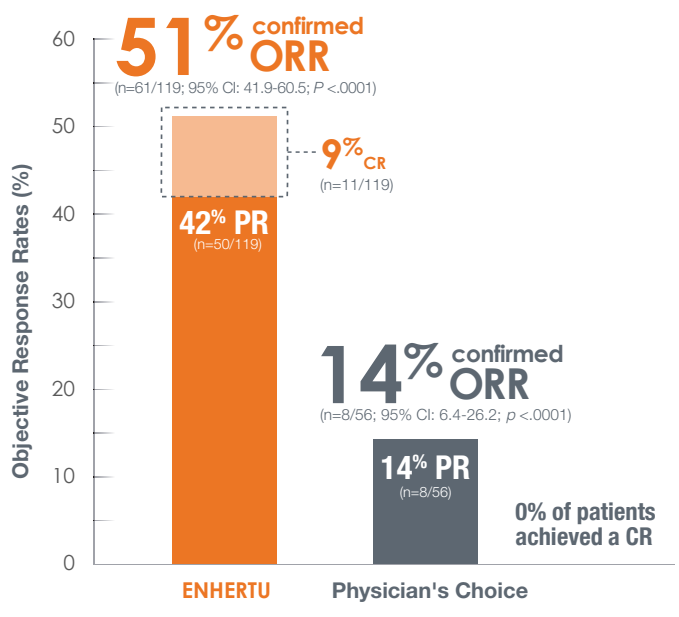
Baseline Demographics and Clinical Characteristics[4]

Characteristic	ENHERTU (n = 125)	Physician's Choice (n = 62)
Age, median (range), years[a]	65.0 (34.0-82.0)	66.0 (28.0-82.0)
Female, %	24.0	24.2
Region, %		
Japan / South Korea	79.2/20.8	80.6/19.4
ECOG PS score, %		
0 / 1	49.6/50.4	48.4/51.6
Primary site, %		
Gastric	86.4	88.7
Gastroesophageal junction	13.6	11.3
Histologic subtype, %		
Intestinal / Diffuse / Other	71.2/22.4/6.4	61.3/29.0/9.7
HER2 expression, %[b]		
IHC 3+	76.8	75.8
IHC 2+, ISH+	23.2	24.2
Prior systemic therapies for advanced/metastatic disease, %[c]		
2	52.8	61.3
3	27.2	29.0
≥4	20.0	9.7
Prior treatment , %		
Therapy containing trastuzumab	100.0	100.0
Therapy containing taxane	84.0	88.7
Therapy containing ramucirumab	75.2	66.1
Irinotecan or other topoisomerase I inhibitors	6.4	8.1
Immune checkpoint inhibitor	35.2	27.4

[a]Median age at informed consent.
[b]HER2 expression was centrally confirmed prospectively by analysis of the most recent archival tissue according to the guidelines from the American Society of Clinical Oncology–College of American Pathologists. According to these guidelines, HER2 positivity was defined as HER2 IHC 3+ or 2+/ISH+.
[c]Therapies intended for "locally advanced/metastatic" or as "neoadjuvant" or "adjuvant" if progressive disease occurred within 6 months since the end of therapy.

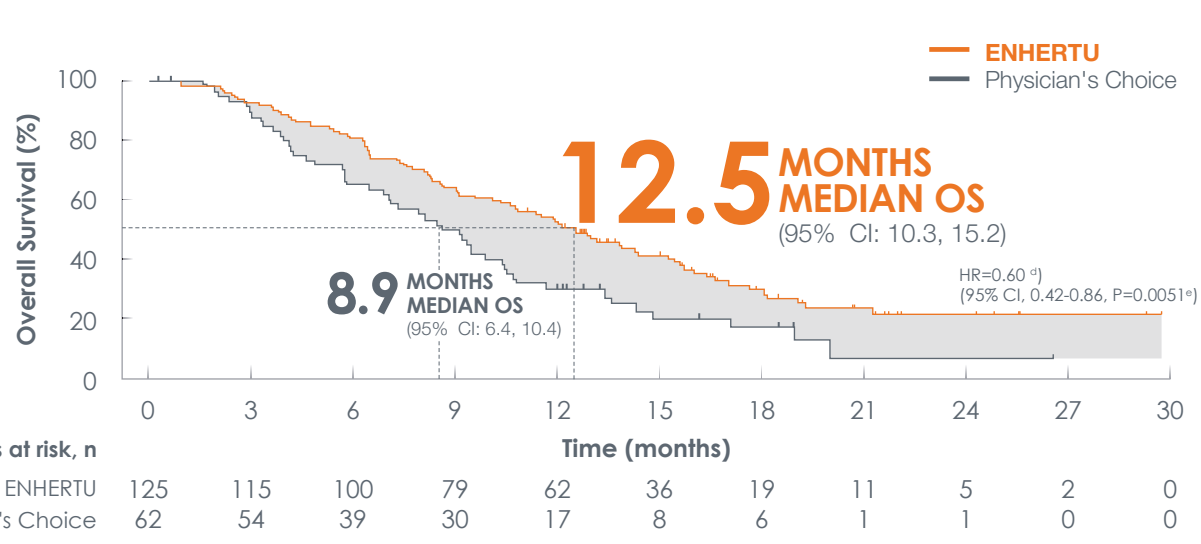
DESTINY-Gastric01: Efficacy

Primary Endpoint: Objective Response Rate (ORR) by ICR[5]



Secondary Endpoint: Overall Survival (OS)

Median OS was 12.5 months (95% CI, 10.3-15.2) with ENHERTU[5]



CI = confidence interval; HR = hazard ratio; OS = overall survival; PC = physician's choice; T-DXd = trastuzumab deruxtecan.
[a] In the T-DXd arm, 41 patients (32.8%) were censored.
[b]In the PC arm, 13 patients (21.0%) were censored.
[c]One patient in the PC arm received crossover treatment of T-DXd.
[d] HR and corresponding 95% CI were estimated using Cox proportional hazards model stratified by region.
[e]Comparison between T-DXd and PC overall using a stratified log-rank test with region as a stratification factor.

ENHERTU MOA Video

References:
1. Saura C, et al. ESMO 2021. Poster 279P
2. Modi S, et al. N Engl J Med. 2020; 382(7):610-621
3. Modi S, et al. SABCS 2020. Poster PD3-06.
4. Shitara K, Bang YJ, Iwasa S, et al. Trastuzumab deruxtecan in previously treated HER2-positive gastric cancer. N Engl J Med. 2020;382(25):2419-2430.
5. Yamaguchi K et al. Presented at: ASCO Virtual Congress 2021; June 4-8, 2021.

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SG-5172_ENH_23MAY2022