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Datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients with pre-treated inoperable/metastatic HR+/HER2– breast cancer: Results from TROPION-Breast01 China cohort

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Declaration of interests

Shusen Wang

- **Consultant or advisor** to AstraZeneca and Daiichi Sankyo
- **Acted as a speaker** for AstraZeneca, Lilly, Novartis, Pfizer, and Roche
- **Received research funding** from AstraZeneca and Pfizer

Background

- Chemotherapy is widely used for the treatment of endocrine resistant HR+/HER2– advanced breast cancer, but is associated with low response rate, poor prognosis, and significant toxicity[1–4]
- Dato-DXd is a TROP2-directed ADC composed of a humanised anti-TROP2 IgG1 mAb attached to a topoisomerase-I inhibitor payload via a plasma-stable, tumour-selective, tetrapeptide-based cleavable linker[5]
- Primary results from the global phase 3, open-label, randomised TROPION-Breast01 study demonstrated:[6]
  - A statistically significant and clinically meaningful improvement in PFS by BICR with Dato-DXd versus ICC: median 6.9 vs 4.9 months (HR 0.63 [95% CI: 0.52–0.76]; p<0.0001)
  - ORR (by BICR): 36.4% in the Dato-DXd arm vs 22.9% in the ICC arm
- Here we present the efficacy and safety data from patients enrolled in mainland China

ADC, antibody-drug conjugate; BICR, blinded independent central review; CI, confidence interval; Dato-DXd, datopotamab deruxtecan; HER2, human epidermal receptor-2; HR, hazard ratio; HR+, hormone receptor positive; ICC, investigator's choice of chemotherapy; IgG1, immunoglobulin G1; mAb, monoclonal antibody; ORR, objective response rate; PFS, progression-free survival; TROP2, trophoblast cell surface antigen-2.

1. Gennari A, et al. Ann Oncol 2021;32:1475–95;
2. Chainitikun S, et al. Breast Cancer Res Treat 202;183:729–29;
3. Tolaney SM, et al. ESMO Open 2024;9:103691;
4. Kuderer NM, et al. Nat Rev Clin Oncol 2022;19:681–97;
5. Okajima D, et al. Mol Cancer Ther 2021;20:2329–40;
6. Bardia A, et al. J Clin Oncol 2024;JCO2400920.

TROPION-Breast01 study design[1,2]

Randomised, phase 3, open-label, global study (NCT05104866)

Key inclusion criteria:

- Patients with HR+/HER2– breast cancer*
- Previously treated with 1–2 lines of chemotherapy (in the inoperable/ metastatic setting)
- Experienced progression on ET and for whom ET was unsuitable
- ECOG PS 0 or 1

N=732

1:1

Dato-DXd
6 mg/kg IV Day 1 Q3W
(Global: n=365; China: n=44)

Investigator's choice of chemotherapy (ICC)
per protocol directions†
(eribulin mesylate; vinorelbine; gemcitabine; capecitabine)
(Global: n=367; China: n=39)

Treatment continued until PD, unacceptable tolerability, or other discontinuation criteria

Endpoints:

- **Dual primary:** PFS by BICR per RECIST v1.1, and OS
- **Secondary endpoints included:** ORR, PFS (investigator assessed), TFST and safety

Here we present the efficacy and safety data from a pre-specified subgroup analysis of the 83 patients recruited in mainland China:‡

Randomisation stratified by:

- **Lines of chemotherapy** in the unresectable/metastatic setting (1 vs 2)
- **Geographic location** (US/Canada/Europe vs other geographic regions)
- **Previous CDK4/6 inhibitor** (yes vs no)

Detailed description of the statistical methods published previously.[1] *Per American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines; HER2– defined as IHC 0/1+/2+; ISH negative; †ICC was administered as follows: eribulin mesylate, 1.4 mg/m^2 IV on Days 1 and 8, Q3W; capecitabine, 1000 or 1250 mg/m^2 orally twice daily on Days 1 to 14, Q3W (dose per standard institutional practice); vinorelbine, 25 mg/m^2 IV on Days 1 and 8, Q3W; or gemcitabine, 1000 mg/m^2 IV on Days 1 and 8, Q3W. ‡44 and 36 patients received treatment with Dato-DXd and ICC, respectively. CDK4/6, cyclin-dependent kinase 4/6; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; IHC, immunohistochemistry; ISH, in situ hybridisation; IV, intravenous; OS, overall survival; PD, progressive disease; Q3W, every 3 weeks; RECIST, Response Evaluation Criteria in Solid Tumors; TFST, time to first subsequent therapy.

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1. Bardia A, et al. Future Oncol 2024;20:423–36;
2. Bardia A, et al. J Clin Oncol 2024;JCO2400920.

Demographics and baseline characteristics: China cohort

- At data cutoff (17 July 2023) median follow-up was 9.7 months in the Dato-DXd arm and 9.2 months in the ICC arm; treatment was ongoing in 10 (22.7%) and 3 (8.3%) patients, respectively

	Dato-DXd		ICC	
	Global (n=365)	China (n=44)	Global (n=367)	China (n=39)
Age, median (range), years	56 (29–86)	50 (30–73)	54 (28–86)	48 (33–70)
Female, n (%)	360 (98.6)	44 (100)	363 (98.9)	39 (100)
Overall disease classification, n (%)				
Metastatic	356 (97.5)	44 (100)	365 (99.5)	39 (100)
Locally advanced/inoperable	9 (2.5)	0	2 (0.5)	0
Metastatic site, n (%)				
Bone	260 (71.2)	32 (72.7)	251 (68.4)	28 (71.8)
Brain	35 (9.6)	8 (18.2)	23 (6.3)	5 (12.8)
Liver	275 (75.3)	31 (70.5)	251 (68.4)	26 (66.7)
Prior lines of chemotherapy, n (%)				
1	229 (62.7)	30 (68.2)	225 (61.3)	23 (59.0)
2	135 (37.0)	14 (31.8)	141 (38.4)	16 (41.0)
Prior CDK4/6 inhibitor, n (%)	304 (83.3)	34 (77.3)	300 (81.7)	24 (61.5)
Prior taxanes/anthracyclines, n (%)	295 (80.8) / 228 (62.5)	43 (97.7) / 38 (86.4)	296 (80.7) / 239 (65.1)	38 (97.4) / 31 (79.5)

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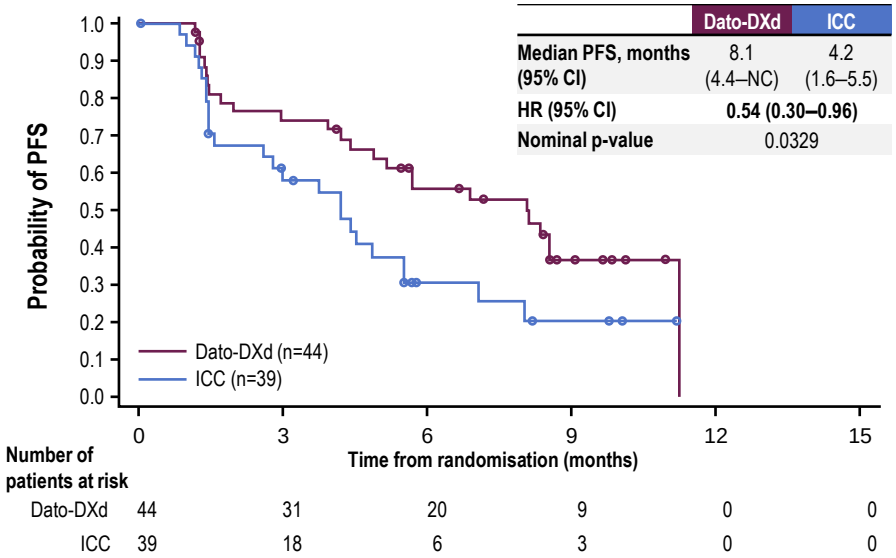
Data taken from the ITT populations.
ITT, intent-to-treat.

Progression-free survival: China cohort

- In the China cohort, Dato-DXd demonstrated improved PFS versus ICC

PFS by BICR: China cohort



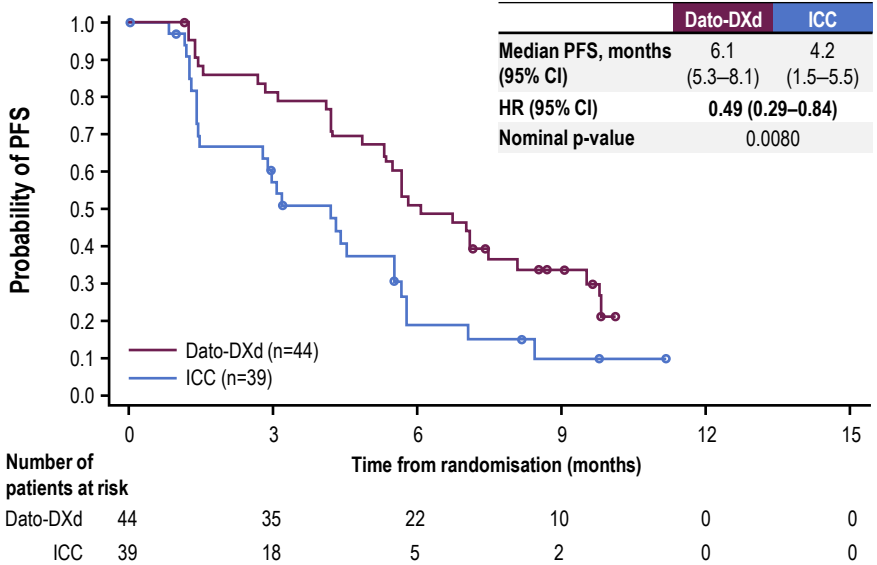
	Dato-DXd	ICC
Median PFS, months (95% CI)	8.1 (4.4–NC)	4.2 (1.6–5.5)
HR (95% CI)	0.54 (0.30–0.96)	
Nominal p-value	0.0329	

Number of patients at risk

Dato-DXd	44	31	20	9	0	0
ICC	39	18	6	3	0	0

- **PFS by BICR – Global:** median 6.9 vs 4.9 months; HR 0.63 (95% CI: 0.52–0.76)

PFS by investigator: China cohort



	Dato-DXd	ICC
Median PFS, months (95% CI)	6.1 (5.3–8.1)	4.2 (1.5–5.5)
HR (95% CI)	0.49 (0.29–0.84)	
Nominal p-value	0.0080	

Number of patients at risk

Dato-DXd	44	35	22	10	0	0
ICC	39	18	5	2	0	0

- **PFS by investigator – Global:** median 6.9 vs 4.5 months; HR 0.64 (95% CI: 0.53–0.76)

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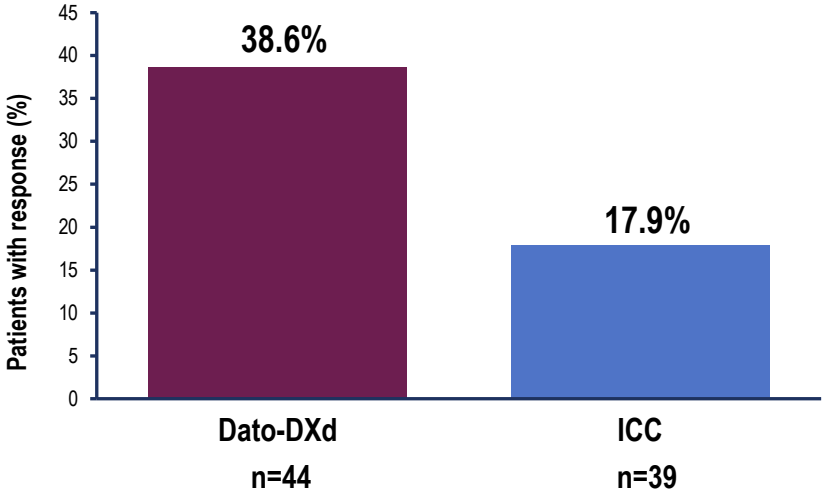
Data cutoff: 17 July 2023. Efficacy analysis was conducted in the ITT populations.
NC, not calculable.

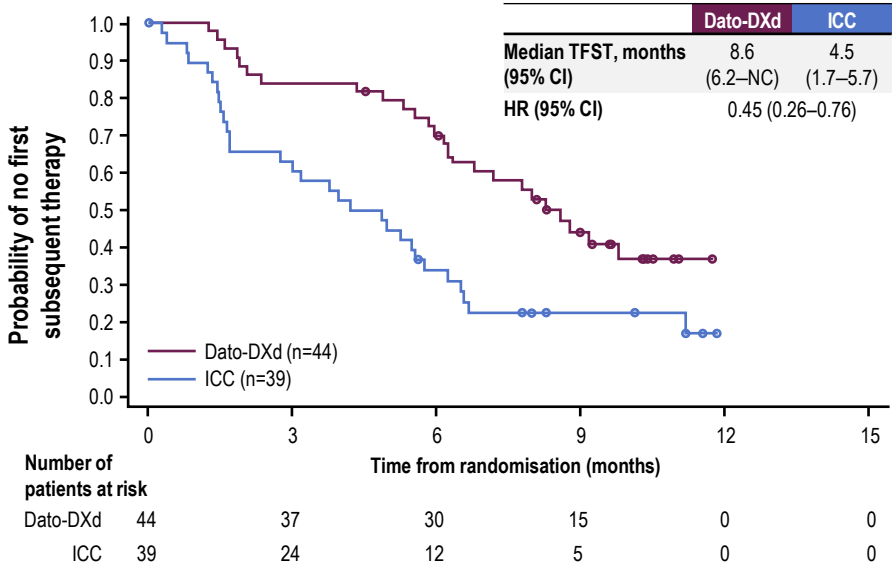
Overall response rate and time to first subsequent therapy: China cohort

- In the China cohort, ORR by BICR was higher for patients in the Dato-DXd arm compared with the ICC arm

Confirmed ORR by BICR



TFST (secondary endpoint)



- **Confirmed ORR – Global:** 36.4% vs 22.9%
- **TFST – Global:** median 8.2 vs 5.0; HR 0.53 (95% CI: 0.45–0.64)

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Data cutoff: 17 July 2023 Efficacy analysis was conducted in the ITT populations.

Overall safety summary: China cohort

- The safety profile was manageable and generally consistent with the global population

Events, n (%)	Dato-DXd (n=44)	ICC (n=36)
TEAEs	43 (97.7)	34 (94.4)
Grade ≥3	14 (31.8)	22 (61.1)
TRAEs	43 (97.7)	30 (83.3)
Grade ≥3	12 (27.3)	20 (55.6)
TEAEs with outcome of:		
Death	0	0
Discontinuation of study drug	1 (2.3)	0
Dose reduction of study drug	6 (13.6)	8 (22.2)
Dose interruption of study drug	13 (29.5)	11 (30.6)
Serious TEAEs	5 (11.4)	9 (25.0)

Median treatment duration:

- **China: 6.4** months with Dato-DXd and **2.8** months with ICC
- **Global: 6.7** months with Dato-DXd and **4.1** months with ICC

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Data cutoff: 17 July 2023. Safety analysis was conducted in the SAS, defined as patients in the ITT population who received at least 1 dose of the study intervention.
SAS, safety analysis set; TEAEs, treatment-emergent adverse events; TRAEs, treatment-related adverse events.

TRAEs occurring in ≥20% of patients and AESIs: China cohort

- Consistent with the global cohort safety results, the majority of AEs were grade 1/2 and were manageable per standard treatment or Dato-DXd toxicity management guidelines

TRAE, n (%)	Dato-DXd (n=44)		ICC (n=36)	
	All-grade	Grade ≥3	All-grade	Grade ≥3
Nausea	21 (47.7)	2 (4.5)	7 (19.4)	0
Aspartate aminotransferase increased	18 (40.9)	1 (2.3)	11 (30.6)	1 (2.8)
Dry eye	16 (36.4)	1 (2.3)	5 (13.9)	0
Vomiting	13 (29.5)	0	3 (8.3)	0
Alopecia	12 (27.3)	-	10 (27.8)	-
Alanine aminotransferase increased	12 (27.3)	1 (2.3)	9 (25.0)	0
Anaemia	11 (25.0)	0	19 (52.8)	2 (5.6)
Neutrophil count decreased	11 (25.0)	1 (2.3)	16 (44.4)	11 (30.6)
Stomatitis	10 (22.7)	3 (6.8)	1 (2.8)	1 (2.8)
Decreased appetite	9 (20.5)	0	7 (19.4)	0
Constipation	9 (20.5)	0	4 (11.1)	0
White blood cell count decreased	7 (15.9)	1 (2.3)	17 (47.2)	6 (16.7)
Fatigue	6 (13.6)	0	9 (25.0)	0
Hypertriglyceridaemia	3 (6.8)	0	9 (25.0)	0

Adverse events of special interest in the China cohort:

- No patients in the China cohort discontinued treatment due to **oral mucositis/stomatitis***
- **Ocular events**† were mostly dry eye; one patient discontinued Dato-DXd due to dry eye
- **Adjudicated drug-related ILD**‡ was reported in one patient in the Dato-DXd group (grade 2)

- In the global population, most frequent TRAEs were nausea (51.1%), stomatitis (50.0%), and alopecia (36.4%) in the Dato-DXd arm, and neutropenia (24.2%), nausea (23.6%), alopecia (20.5%) and decreased neutrophil count (20.5%) in the ICC arm

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Data cutoff: 17 July 2023. Safety analysis was conducted in the SAS, defined as patients in the ITT population who received at least 1 dose of the study intervention. TRAEs are those that were assessed by the investigator as possibly related to study treatment. *Treatment-emergent oral mucositis/stomatitis events included mouth ulceration, oral pain, oropharyngeal pain, stomatitis; all grade: 43.2% with Dato-DXd, 13.9% with ICC; grade ≥3: 6.8% with Dato-DXd, 2.8% with ICC. †Treatment emergent ocular surface events included conjunctivitis, dry eye, keratitis, meibomian gland dysfunction, punctate keratitis, vision blurred and xerophthalmia; all grade: 50% with Dato-DXd, 16.7% with ICC; grade ≥3: 2.3% with Dato-DXd, 0% with ICC. ‡ILD includes events that were adjudicated as ILD and related to the use of Dato-DXd or ICC (includes cases of potential ILD/pneumonitis, based on MedDRA v23.0 for the narrow ILD SMQ, selected terms from the broad ILD SMQ, and PTs of respiratory failure and acute respiratory failure); all grade: 2.3% with Dato-DXd (grade 2), 0% with ICC. AE, adverse event; AESI, adverse event of special interest; ILD, interstitial lung disease; PTs, preferred terms; SMQ, standard MedDRA query; SOC, system organ class.

Conclusions: China cohort

- Dato-DXd demonstrated improved efficacy compared with ICC in Chinese patients enrolled in TROPION-Breast01, consistent with the overall global population; Dato-DXd showed:
  - Improved PFS by BICR and investigator compared with ICC in the China cohort
  - A higher ORR compared with ICC
  - A longer time to first subsequent therapy compared with ICC
- Dato-DXd demonstrated a manageable safety profile in this China cohort, consistent with the overall population
  - Patients receiving Dato-DXd had fewer grade ≥3 TRAEs and fewer serious TEAEs vs ICC
  - Most AESIs were grade 1/2

Results support Dato-DXd as a potential new therapeutic option for Chinese patients with previously treated metastatic HR+/HER2– breast cancer

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Datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients with pre-treated inoperable/metastatic HR+/HER2– breast cancer: Results from TROPION-Breast01 China cohort

Plain Language Summary

Why did we perform this research?

- Hormone receptor-positive (HR+)/human epidermal growth factor 2-negative (HER2–) breast cancer is the most common type of breast cancer. HR+/HER2– breast cancer is usually treated with hormonal therapy (called endocrine therapy); however, if this treatment does not work or patients could not receive it, then chemotherapy is given.
- TROPION-Breast01 was a phase 3 clinical research study in which a new treatment, called datopotamab deruxtecan (Dato-DXd), was compared with chemotherapy. Dato-DXd consists of an antibody (datopotamab) and an anticancer drug payload (DXd), joined via a stable cleavable linker.
- Results from TROPION-Breast01 showed that the time from starting treatment to the cancer getting worse or death (known as progression-free survival) was longer in patients who received Dato-DXd than those who received chemotherapy. The study also showed that the type of side effects seen were typical of Dato-DXd treatment and could be managed.[1]
- This summary focuses on the results from the cohort of patients who enrolled in mainland China.

How did we perform this research?

- Patients enrolled in this study had HR+/HER2– breast cancer that could not be removed by surgery (inoperable) or had spread to other parts of the body (metastatic) and had previously been treated with one or two rounds of chemotherapy. Their cancer had become worse following endocrine therapy or they could not be treated with endocrine therapy.
- In China, 83 patients were randomly assigned to receive either Dato-DXd (n=44) or chemotherapy (n=39).

What were the findings of this research?

- In Chinese patients in TROPION-Breast01, the characteristics and demographics of the patients were generally balanced between those receiving Dato-DXd and chemotherapy.
- The time from starting treatment to the cancer getting worse or death (progression-free survival) was longer in patients who received Dato-DXd than in patients who received chemotherapy, which was consistent with the results from the global population.
- A higher percentage of patients who received Dato-DXd had tumours that got smaller compared with chemotherapy.
- Patients who received Dato-DXd also had a longer time until they received additional treatment after the planned study drugs were finished (time to first subsequent therapy) compared with chemotherapy.
- The side effects seen in Chinese patients receiving Dato-DXd could be managed and were generally consistent with those seen in the global population. Patients receiving Dato-DXd had fewer grade ≥3 side effects (those requiring hospital care/limited basic daily activities, or those that were life threatening and required urgent medical treatment) and had fewer serious side effects.

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What are the implications of this research?

These results support Dato-DXd as a potential new treatment option for Chinese patients with previously treated metastatic HR+/HER2– breast cancer

1. Bardia A, et al. J Clin Oncol 2024;JCO2400920.