First-line datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients with locally recurrent inoperable or metastatic triple-negative breast cancer (TNBC) for whom immunotherapy was not an option: Additional efficacy endpoints from the TROPION-Breast02 study

David W. Cescon,[1] Tiffany A. Traina,[2] Peter Schmid,[3] Javier Cortés,[4] Zhimin Shao,[5] Shigehira Saji,[6] Kyung Hae Jung,[7] Thomas Bachelot,[8] Shouman Wang,[9] Emilio Murillo Ramírez,[10] Gul Basaran,[11] Yee Soo Chae,[12] Agostina Stradella,[13] Rofhiwa Mathiba,[14] Shin-Cheh Chen,[15] Nicola Battelli,[16] Naoki Niikura,[17] Kechen Zhao,[18] Micah J. Maxwell,[19] Rebecca Dent[20]

[1]Princess Margaret Cancer Centre/UHN, Toronto, Ontario, Canada; [2]Memorial Sloan Kettering Cancer Center (MSKCC), New York, NY, USA; [3]Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, London, United Kingdom; [4]International Breast Cancer Center (IBCC), Pangaea Oncology, Barcelona, Spain; [5]Fudan University Shanghai Cancer Center, Shanghai, China; [6]Fukushima Medical University, Fukushima, Japan; [7]Asan Medical Center - University of Ulsan College of Medicine, Seoul, Republic of Korea; [8]Centre Léon Bérard, Lyon, France; [9]Xiangya Hospital of Central South University, Changsha, China; [10]Centro Médico Nacional de Occidente, Zapopan, Mexico; [11]School of Medicine, MAA Acıbadem University, Istanbul, Türkiye; [12]Kyungpook National University Chilgok Hospital, Kyungpook National University School of Medicine, Kyungpook, Republic of Korea; [13]Institut Catala d'Oncologia – IDIBELL (ICO L'Hospitalet), Barcelona, Spain; [14]Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa; [15]Chang Gung Medical Memorial Hospital, Taipei City, Taiwan; [16]Ospedale Generale Provinciale Macerata, Macerata, Italy; [17]Tokai University School of Medicine, Kanagawa, Japan; [18]Biometrics, Late-Stage Development, Oncology R&D, AstraZeneca, Wilmington, DE, USA; [19]Clinical Development, Late-Stage Development, Oncology R&D, AstraZeneca, Gaithersburg, MD, USA; [20]National Cancer Center Singapore and Duke-NUS Medical School, Singapore.

PRESENTED BY: **David W. Cescon, MD, PhD**

Key takeaways

In TROPION-Breast02, improvements in secondary efficacy endpoints (TFST, PFS2, and TSST) were observed with Dato-DXd compared with ICC, consistent with the dual primary endpoints of OS and PFS by BICR

Alongside the manageable safety profile and meaningful and sustained improvements in quality-of-life outcomes vs ICC reported previously, the totality of data support Dato-DXd as a new 1L standard of care for patients with locally recurrent inoperable or metastatic TNBC for whom immunotherapy is not an option

1L, first-line; BICR, blinded independent central review; Dato-DXd, datopotamab deruxtecan; ICC, investigator's choice of chemotherapy; OS, overall survival; PFS, progression-free survival; PFS2, time to second progression or death; TFST, time to first subsequent therapy or death; TNBC, triple-negative breast cancer; TSST, time to second subsequent therapy or death.

TROPION-Breast02: Study design[1]

Key inclusion criteria:

- Patients with histologically or cytologically documented locally recurrent inoperable or metastatic TNBC
- No prior chemotherapy or targeted systemic therapy in the locally recurrent inoperable or metastatic setting
- Immunotherapy not an option
- ECOG PS 0 or 1
- No minimum disease-free interval (DFI)

1:1

Dato-DXd
6 mg/kg IV Day 1 Q3W
(n=323)

Investigator's choice of chemotherapy (ICC)
Paclitaxel, nab-paclitaxel, capecitabine, eribulin mesylate/eribulin, carboplatin
(n=321)

Endpoints

- **Dual primary:** PFS by BICR per RECIST v1.1, and OS
- **Secondary included:** PFS (investigator-assessed), ORR, DoR, DCR at 12 weeks, safety, PROs, TFST, PFS2, and TSST

Randomization stratified by:

- Geographic region (US/Canada/Europe vs other geographic regions)
- PD-L1 status (high [CPS ≥10] vs low [CPS <10])
- DFI history (*de novo* vs prior DFI 0–12 months vs prior DFI >12 months)

Treatment continued until investigator-assessed RECIST v1.1 progressive disease, unacceptable toxicity, or another discontinuation criterion was met; following progression or discontinuation of study treatment, patients could receive subsequent therapies, including approved ADCs or chemotherapy, at the investigator's discretion.

- TROPION-Breast02 enrolled patients who were representative of the real-world TNBC population, including patients with DFI 0–6 months (15%) who are often excluded from clinical trials

PFS2, time to second progression or death; TFST, time to first subsequent therapy or death; TNBC, triple-negative breast cancer; TSST, time to second subsequent therapy or death.

1. Dent R, et al. Oral presentation at ESMO 2025; Abstract LBA21.

Demographics and baseline characteristics

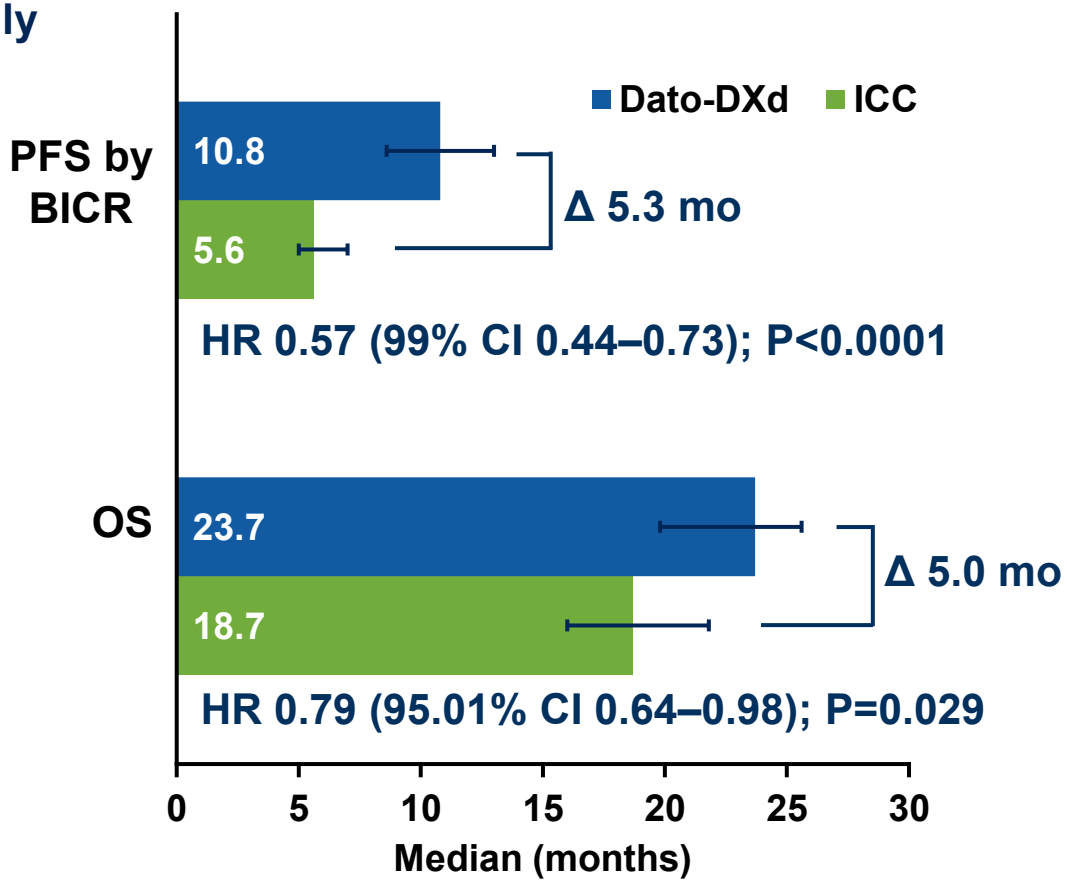
		Dato-DXd (n=323)	ICC (n=321)
Median age (range), years		56 (27–85)	57 (23–83)
Female, n (%)		323 (100)	319 (99)
Race, n (%)	Black or African American	13 (4)	14 (4)
	Asian	151 (47)	131 (41)
	White	131 (41)	153 (48)
	Other*	28 (9)	23 (7)
Geographic region, n (%)	US, Canada, Europe	120 (37)	120 (37)
	Other geographic regions	203 (63)	201 (63)
ECOG PS, n (%)	0	195 (60)	182 (57)
	1	128 (40)	139 (43)
DFI history, n (%)	*De novo*	109 (34)	110 (34)
	Prior DFI 0–12 months‡	67 (21)	66 (21)
	Prior DFI 0–6 months	***47 (15)***	***51 (16)***
	Prior DFI >12 months‡	147 (46)	145 (45)

		Dato-DXd (n=323)	ICC (n=321)
PD-L1 status,† n (%)	Low (CPS <10)	287 (89)	291 (91)
	High (CPS ≥10)	34 (11)	29 (9)
Metastases, n (%)	Visceral	253 (78)	233 (73)
	Liver	93 (29)	98 (31)
	Brain§	36 (11)	28 (9)
Number of metastatic sites, n (%)	<3	207 (64)	215 (67)
	≥3	116 (36)	106 (33)
Pre-selected choice of chemotherapy, n (%)	Nab-paclitaxel	180 (56)	172 (54)
	Paclitaxel	82 (25)	92 (29)
	Eribulin mesylate/eribulin	43 (13)	35 (11)
	Carboplatin	11 (3)	14 (4)
	Capecitabine	7 (2)	8 (2)

*Including not reported. †Based on central laboratory testing, using Agilent PD-L1 IHC 22C3 pharmDx Assay (Agilent Technologies, Santa Clara, CA); PD-L1 status missing/not applicable in 2 patients in the Dato-DXd arm and 1 patient in the ICC arm. ‡Prior (neo)adjuvant cancer therapy was received by 66% of patients, including nitrogen mustards (57%), taxanes (57%), anthracyclines (56%), pyrimidine analogues (27%), platinum compounds (16%), and PD-(L)1 inhibitors (5%). §Patients with asymptomatic, stable brain metastases were permitted in the study.

Background: TROPION-Breast02

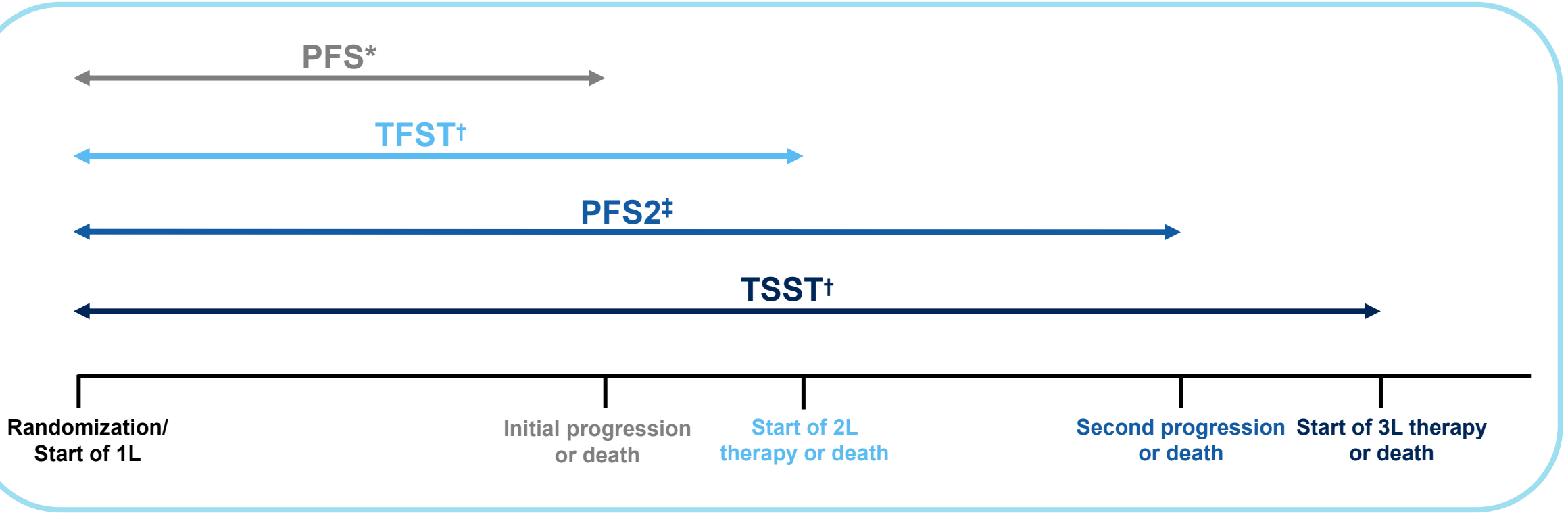
- First-line Dato-DXd showed **statistically significant and clinically meaningful improvements in OS and PFS** compared with ICC[1]
- With Dato-DXd versus ICC, the ORR was more than double (63% vs 29%) and median DoR was approximately 5 months longer (12.3 vs 7.1 months) [1]
- The Dato-DXd safety profile was manageable and generally consistent with the known profile, and treatment-related discontinuations were lower vs ICC[1]
- Improved efficacy outcomes were complemented by meaningful and sustained improvements in QoL outcomes vs ICC[2]
- Median study follow-up was 27.5 months (range: 13.3–38.7)[1]



CI, confidence interval; DoR, duration of response; HR, hazard ratio; ORR, objective response rate; QoL, quality of life.

1. Dent R, et al. Ann Oncol 2026 (in press);
2. Schmid P, et al. Oral presentation at ESMO Breast 2026; 415O.

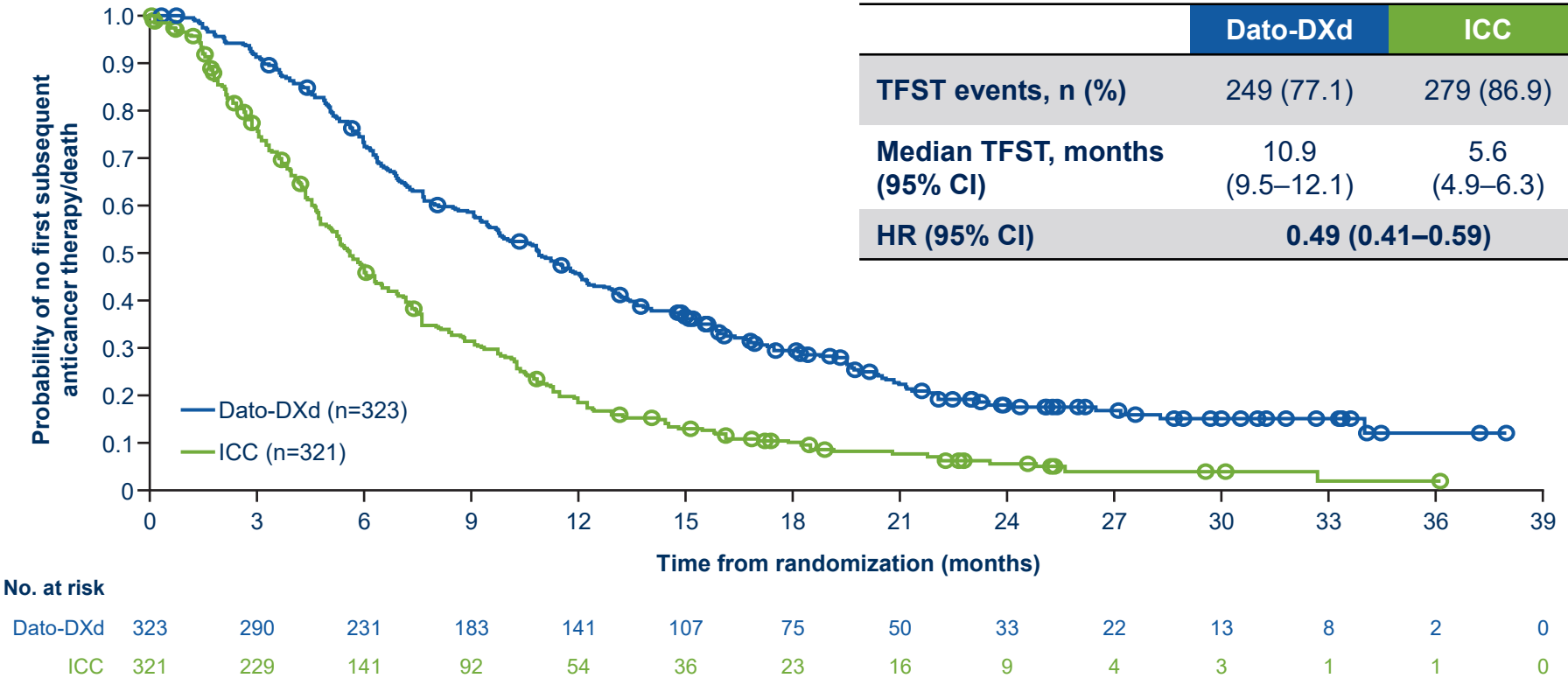
Secondary efficacy endpoints



- Prespecified secondary endpoints of TFST, PFS2, and TSST were analyzed in all randomized patients, using a stratified log-rank test
  - HRs and 95% CI were estimated using a stratified Cox proportional hazards model

*PFS assessed by BICR per RECIST v1.1 was a primary endpoint; investigator-assessed PFS was a secondary endpoint. †Irrespective of progression. ‡Investigator-assessed; regardless of withdrawal from subsequent therapy or missed visits.
PFS, progression-free survival; PFS2, time to second progression or death; TFST, time to first subsequent therapy or death; TNBC, triple-negative breast cancer; TSST, time to second subsequent therapy or death.

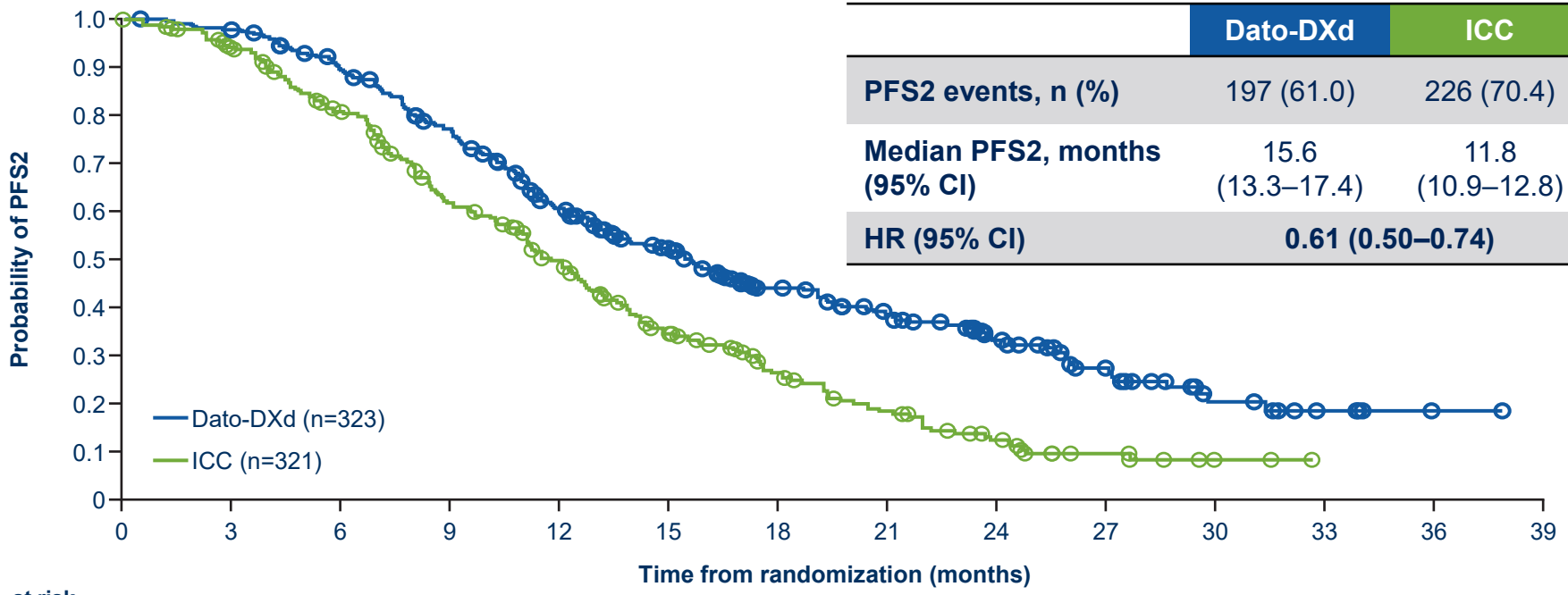
Time to first subsequent therapy or death (TFST)



	Dato-DXd	ICC
TFST events, n (%)	249 (77.1)	279 (86.9)
Median TFST, months (95% CI)	10.9 (9.5–12.1)	5.6 (4.9–6.3)
HR (95% CI)	**0.49 (0.41–0.59)**	

TFST numerically favored Dato-DXd vs ICC, consistent with PFS by BICR, indicating extended disease control on 1L therapy and delayed initiation of subsequent therapy

Time to second progression or death (PFS2)



	Dato-DXd	ICC
PFS2 events, n (%)	197 (61.0)	226 (70.4)
Median PFS2, months (95% CI)	15.6 (13.3–17.4)	11.8 (10.9–12.8)
HR (95% CI)	**0.61 (0.50–0.74)**	

No. at risk

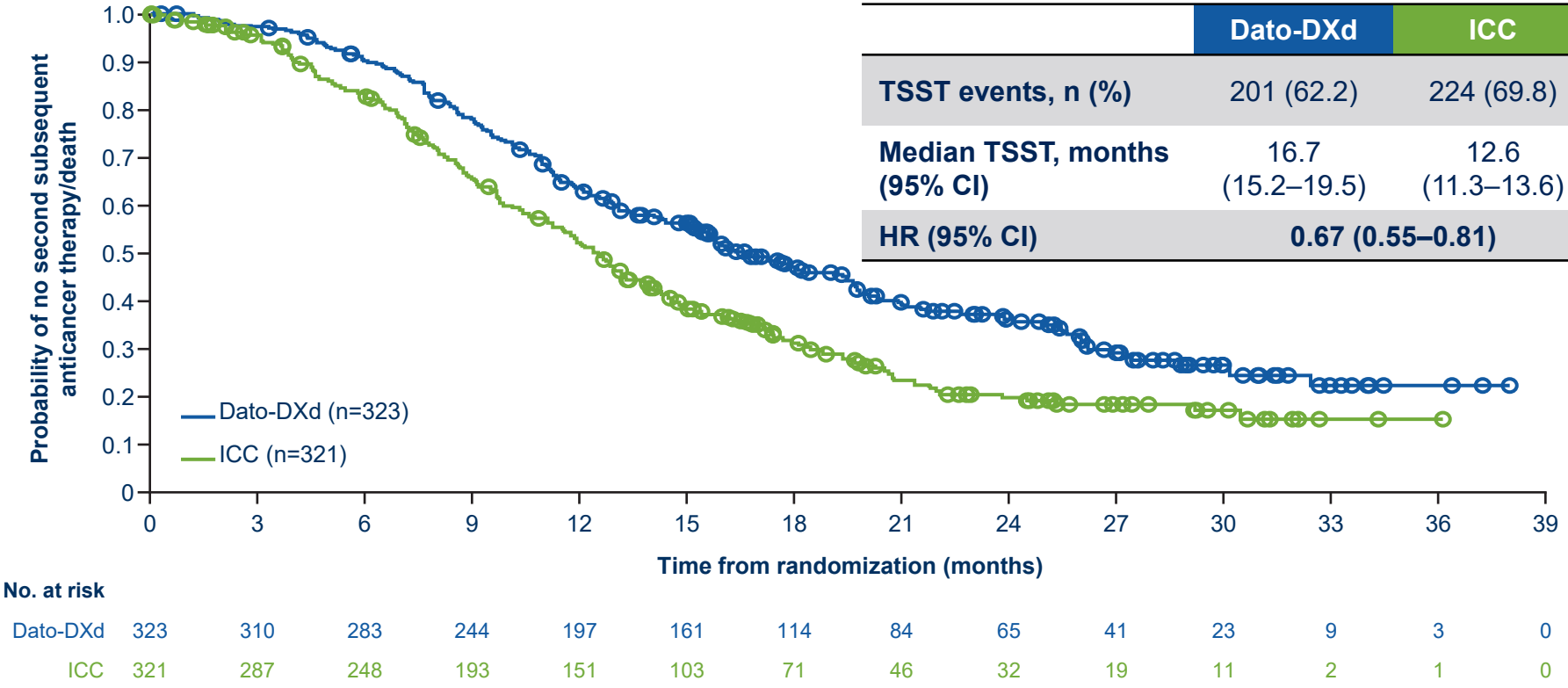
Dato-DXd	323	310	278	235	176	133	91	72	47	31	12	6	1	0
ICC	321	279	230	169	127	80	52	34	19	8	2	0	0	0

Efficacy benefits were sustained through PFS2, consistent with OS results

PFS2 was assessed every 3 months ±14 days after objective progression per local standard clinical practice, defined as radiologic (preferred), symptomatic progression, or death occurring during/after subsequent anticancer therapy.

PRESENTED BY: **David W. Cescon, MD, PhD**

Time to second subsequent therapy or death (TSST)



	Dato-DXd	ICC
TSST events, n (%)	201 (62.2)	224 (69.8)
Median TSST, months (95% CI)	16.7 (15.2–19.5)	12.6 (11.3–13.6)
HR (95% CI)	**0.67 (0.55–0.81)**	

No. at risk

Dato-DXd	323	310	283	244	197	161	114	84	65	41	23	9	3	0
ICC	321	287	248	193	151	103	71	46	32	19	11	2	1	0

TSST numerically favored Dato-DXd vs ICC, consistent with PFS2

PRESENTED BY: **David W. Cescon, MD, PhD**

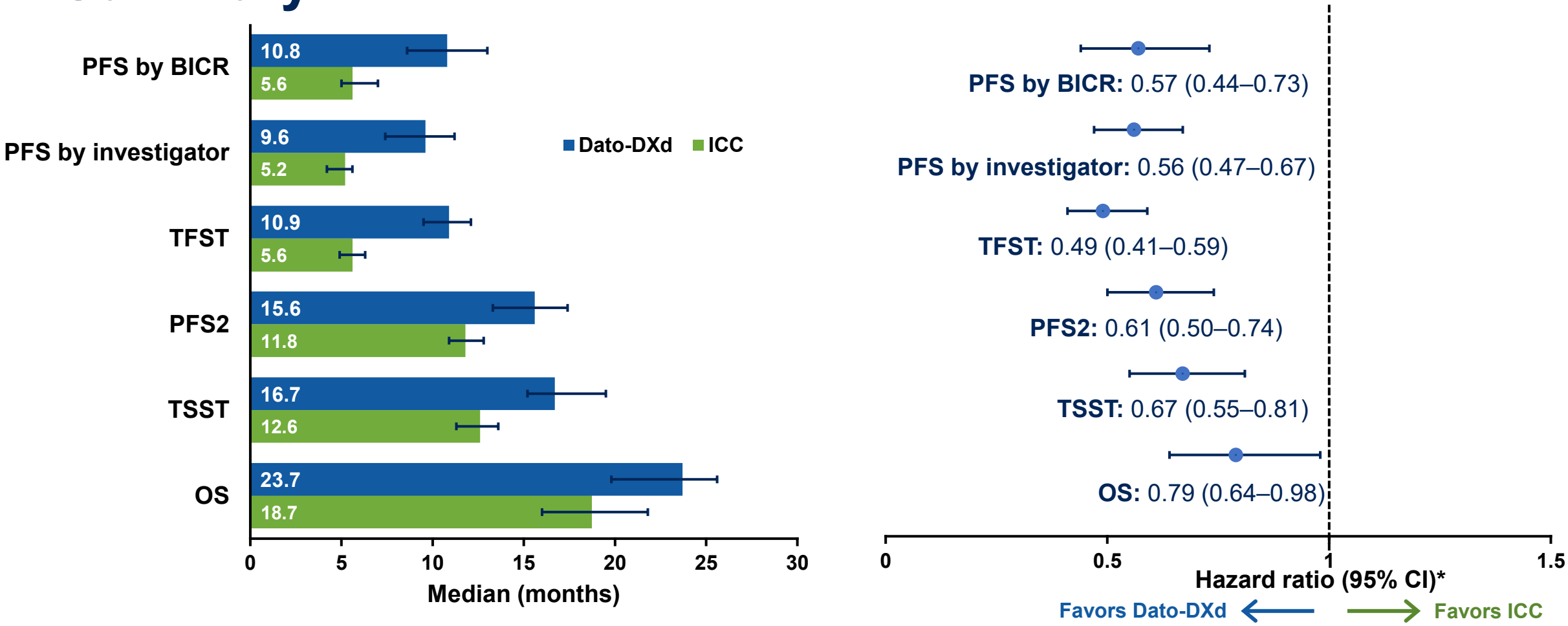
Subsequent ADC therapy

Subsequent therapy (in any treatment line), n (%)	Patients off study treatment at data cutoff	
	Dato-DXd n=278	ICC n=313
Any subsequent therapy*	210 (76)	232 (74)
Any ADC†	44 (21)	95 (41)
Sacituzumab govitecan	33 (16)	76 (33)
Sacituzumab tirumotecan	0	1 (<1)
Trastuzumab deruxtecan	16 (8)	34 (15)

Most patients in both arms received subsequent therapy, including approved ADCs;
the most commonly used ADC was sacituzumab govitecan, followed by trastuzumab deruxtecan

*Percentages are calculated out of the number of patients off study treatment at data cutoff in each treatment group. 100 patients in the Dato-DXd arm and 112 patients in the ICC arm received a second subsequent therapy. †Percentages are calculated out of the number of patients who received any subsequent therapy in each treatment group. Includes sacituzumab govitecan, sacituzumab tirumotecan or trastuzumab deruxtecan only. Two patients in the Dato-DXd arm received disitamab vedotin. Patients could have received more than one ADC and are counted in each row for the ADC they received.
2L, second-line; SoC, standard of care.

Summary



Green and blue bars represent median values; error bars denote the 95% CI, calculated as the difference between the median and the lower bound (lower error) and between the upper bound and the median (upper error). *A 99% CI was used for the PFS by BICR HR and a 95.01% CI was used for the OS HR. BICR, blinded independent central review; CI, confidence interval; Dato-DXd, datopotamab deruxtecan; ICC, investigator's choice of chemotherapy; OS, overall survival; PFS, progression-free survival; PFS2, time to second progression or death; TFST, time to first subsequent therapy or death; TSST, time to second subsequent therapy or death.

Key takeaways / conclusions

In TROPION-Breast02, improvements in TFST, PFS2, and TSST were observed with Dato-DXd compared with ICC, consistent with the dual primary endpoints of OS and PFS by BICR

The totality of data support Dato-DXd as a new 1L standard of care for patients with mTNBC for whom immunotherapy is not an option

1L, first-line; BICR, blinded independent central review; Dato-DXd, datopotamab deruxtecan; ICC, investigator's choice of chemotherapy; OS, overall survival; PFS, progression-free survival; PFS2, time to second progression or death; TFST, time to first subsequent therapy or death; mTNBC, metastatic triple-negative breast cancer; TSST, time to second subsequent therapy or death.

Acknowledgments

The authors would like to particularly thank:

- Patients
- Families and caregivers
- TROPION-Breast02 investigators and site personnel

TROPION-Breast02 (NCT05374512) is sponsored by AstraZeneca. In July 2020, Daiichi-Sankyo entered into a global development and commercialization collaboration with AstraZeneca for Dato-DXd.

Medical writing support for the development of this presentation, under the direction of the authors, was provided by Claire Bellis, PhD, of Ashfield MedComms (Cape Town, South Africa), an Inizio Company, in accordance with Good Publication Practice guidelines (https://www.ismpp.org/gpp-2022), and was funded by AstraZeneca.

ESMO ANNALS OF ONCOLOGY DRIVING INNOVATION IN ONCOLOGY

Scan the QR code to access the manuscript

ORIGINAL ARTICLE · Articles in Press, April 03, 2026 · *Open Access*

Download Full Issue

Datopotamab deruxtecan in patients with untreated, advanced triple-negative breast cancer (TROPION-Breast02): a randomised, open-label, international, phase III trial

R. Dent [1] · Z. Shao [2] · P. Schmid [3] · ... · M.J. Maxwell [26] · T. Traina [27] on behalf of the TROPION-Breast02 investigators * ... Show more

Affiliations & Notes Article Info

PRESENTED BY: **David W. Cescon, MD, PhD**