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First-line datopotamab deruxtecan (Dato-DXd) vs chemotherapy in patients with locally recurrent inoperable or metastatic TNBC for whom immunotherapy was not an option: Patient-reported outcomes (PROs) from TROPION-Breast02

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Declaration of interests

Peter Schmid, MD, PhD, FRCP

- **Speaker's bureau:**
  Daiichi-Sankyo, Novartis, AstraZeneca, Menarini-Sti, Gilead, MSD, Roche
- **Advisory role:**
  AstraZeneca, Boehringer Ingelheim, Novartis, Seagen, Gilead, Daiichi-Sankyo, MSD, Bicycle Therapeutics, Lilly, Summit Therapeutics, Olema Oncology, Roche, Pfizer
- **Research grant:**
  AstraZeneca, Genentech, Roche

Background

- In the phase 3 **TROPION-Breast02** study, first-line Dato-DXd showed **statistically significant and clinically meaningful improvements in OS and PFS** compared with ICC in patients with locally recurrent inoperable or metastatic TNBC for whom immunotherapy was not an option[1]
  - Median OS: 23.7 vs 18.7 months; HR 0.79 (95% CI 0.64–0.98); P=0.0291
  - Median PFS by BICR: 10.8 vs 5.6 months; HR 0.57 (95% CI 0.47–0.69); P<0.0001
- The Dato-DXd safety profile was **manageable and generally consistent** with the known profile[1]
  - Despite more than double the median duration of treatment (8.5 vs 4.1 months), rates of grade ≥3 and serious TRAEs were similar, and discontinuations were lower, with Dato-DXd vs ICC

Here, we report the impact of treatment on patients' symptoms, functioning and quality of life in TROPION-Breast02

BICR, blinded independent central review; CI, confidence interval; Dato-DXd, datopotamab deruxtecan; HR, hazard ratio; ICC, investigator's choice of chemotherapy; OS, overall survival; PFS, progression-free survival; TNBC, triple-negative breast cancer; TRAEs, treatment-related adverse events.

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1. Dent RA, et al. *Ann Oncol* 2025;36(suppl_2): S1566-7;
2. Dent R, et al. *Ann Oncol* 2026 (in press).

TROPION-Breast02: Study Design

Randomised, phase 3, open-label, global study (NCT05374512)

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 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)

Treatment continued until investigator-assessed RECIST v1.1 progressive disease, unacceptable toxicity, or another discontinuation criterion was met

Endpoints

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

Randomisation 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)¶

*According to ASCO/CAP criteria. †Including patients with PD-L1-low tumours, or patients with PD-L1-high tumours with (a) disease relapse after prior PD-(L)1 inhibitor therapy for early-stage breast cancer, (b) comorbidities precluding PD-(L)1 inhibitor therapy, or (c) no regulatory access to PD-(L)1 inhibitor therapy. ‡DFI defined as time between date of completion of treatment with curative intent and date of first documented local or distant disease recurrence. §Recruitment of patients with PD-L1-high tumours who would otherwise be eligible for pembrolizumab if regulatory access was available was capped at ~10% of randomised patients. ¶Recruitment of patients with DFI 0–12 months was capped at ~20% of randomised patients. #If no prior taxane, or prior taxane in the (neo)adjuvant setting and DFI >12 months: paclitaxel 80 mg/m^2 IV, D1, 8, 15, Q3W, or nab-paclitaxel 100 mg/m^2 IV, D1, 8, 15, Q4W; if prior taxane and DFI 0–12 months: capecitabine 1000 or 1250 mg/m^2 orally twice daily, D1–14, Q3W (dose determined by standard institutional practice), or eribulin mesylate 1.4 mg/m^2 / eribulin 1.23 mg/m^2 IV, Day 1, 8, Q3W, or carboplatin AUC6 IV, D1, Q3W.

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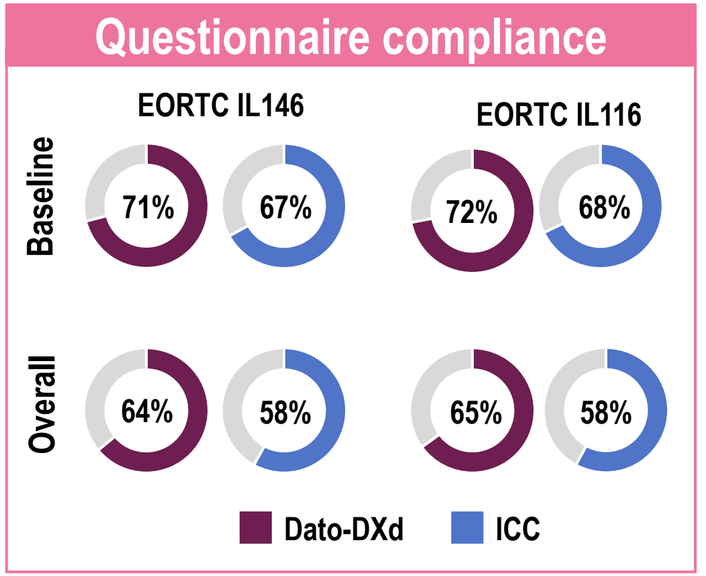
CPS, combined positive score; D, day; DFI, disease-free interval; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenously; ORR, objective response rate; PD-(L)1, programmed cell death (ligand) 1; PROs, patient-reported outcomes; QXW, every X weeks.; RECIST v1.1, Response Evaluation Criteria for Solid Tumours version 1.1.

Patient-reported endpoints and assessments

PROs were assessed at baseline and throughout the study via electronic PRO questionnaires*

- Compliance rates were similar between arms; the most common reasons for missing PROs at baseline were “technical problems with device” and “patient forgot”



Secondary PRO endpoints:

- Time to deterioration (TTD) in GHS/QoL, physical functioning and pain using EORTC IL146 and in breast and arm symptoms using EORTC IL116†
  - Time to first deterioration: the time from date of randomisation to the date of first deterioration based on derived meaningful change thresholds‡
  - Time to confirmed deterioration: required deterioration to be confirmed at a subsequent timepoint

Exploratory PRO endpoints included:

- TTD & change from baseline in symptoms and functioning using EORTC IL146/116
- Patient-reported symptomatic AEs using PRO-CTCAE, EORTC IL147 and Mouth and Throat Symptoms Diary
- Patient-reported treatment tolerability using PGI-TT

*Schedule of assessments: On C1D1, Q3W for the first 48 weeks, Q6W until EoT, at EoT, and then Q6W until 18 weeks after disease progression for EORTC QLQ-C30/IL116, and on C1D1, weekly for the first 12 weeks, then Q3W until EoT for PRO-CTCAE, EORTC IL147 and PGI-TT; †EORTC IL146 contains selected items from the EORTC QLQ-C30. EORTC IL116 is a subset of EORTC QLQ-BR45. Only arm and breast symptom scales were used from the EORTC QLQ-BR45. ‡16.67 for GHS/QoL, pain and breast symptoms, 13.33 for physical functioning and 22.22 for arm symptoms.
AEs, adverse events; C1D1, Cycle 1 Day 1; EORTC, European Organisation for Research and Treatment of Cancer; EoT, end of treatment; GHS/QoL, global health status/quality of life; PGI-TT, Patient’s Global Impression of Treatment Tolerability;
PRO-CTCAE, Patient-reported Outcomes version of the Common Terminology Criteria for Adverse Events; QLQ-BR45, 45-item quality of life questionnaire for breast cancer symptoms; QLQ-C30, 30-item core quality of life questionnaire; TTD, time to deterioration.

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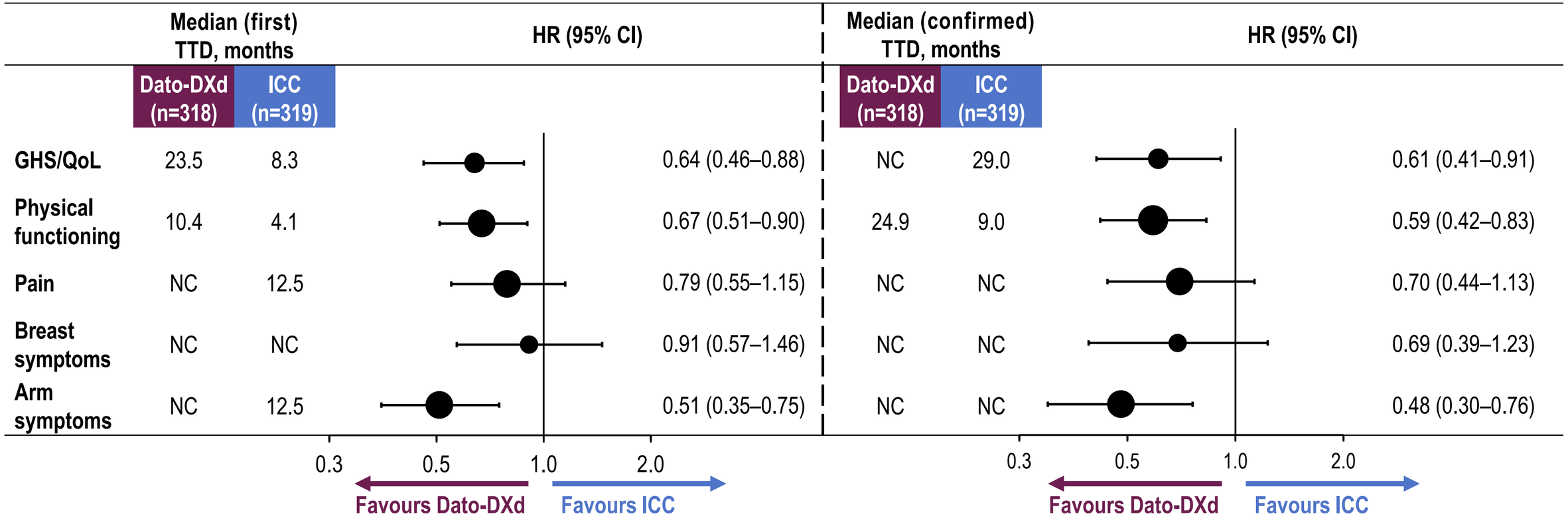
Time to deterioration in secondary endpoints



HRs numerically favoured Dato-DXd, indicating that time to first and confirmed deterioration were delayed in the Dato-DXd arm

For EORTC QLQ-C30 IL146 (GHS/QoL, physical functioning and pain) and IL116 (breast and arm symptoms), deterioration was defined as a change from baseline that reached a clinically meaningful deterioration threshold of 16.67 for GHS/QoL, pain and breast symptoms, 13.33 for physical functioning and 22.22 for arm symptoms. The size of the circles represents the number of events. NC, not calculable.

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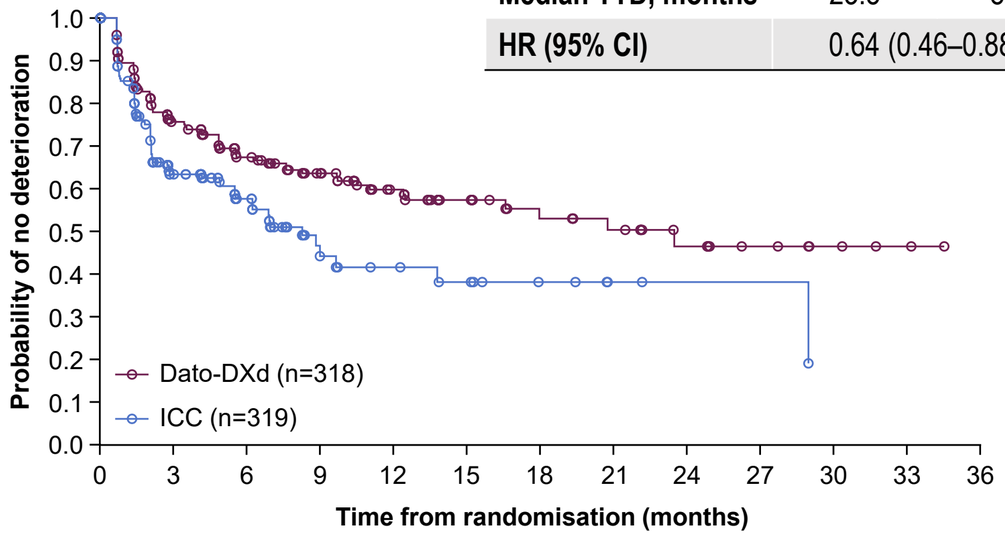
Time to deterioration in GHS/QoL

TTD in GHS/QoL (first instance) – Secondary endpoint

	Dato-DXd	ICC
Median TTD, months	23.5	8.3
HR (95% CI)	0.64 (0.46–0.88)	

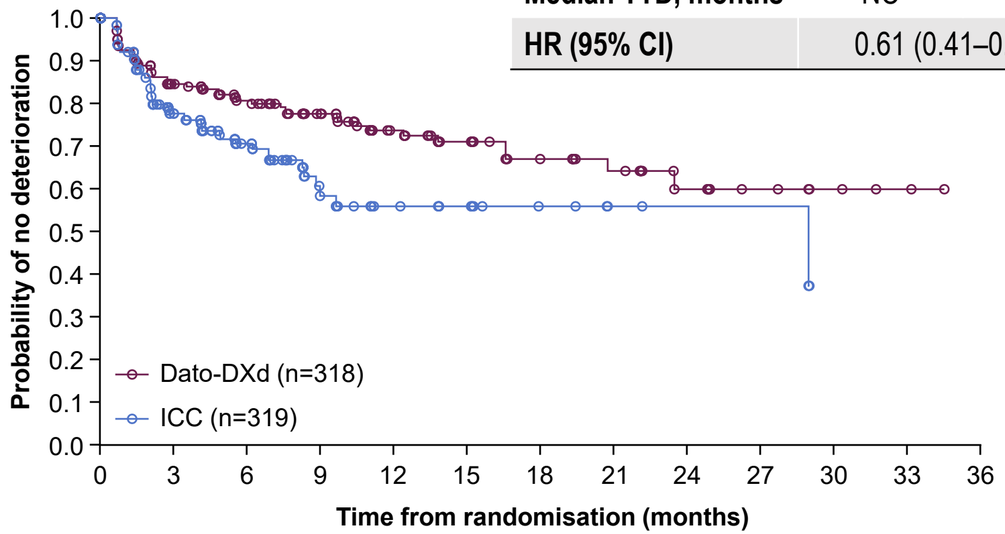


No. at risk

Dato-DXd	318	127	95	75	51	34	23	19	12	7	4	2	0
ICC	319	85	48	19	13	10	6	3	2	2	0	0	0

TTD in GHS/QoL (confirmed) – Secondary endpoint

	Dato-DXd	ICC
Median TTD, months	NC	29.0
HR (95% CI)	0.61 (0.41–0.91)	



No. at risk

Dato-DXd	318	143	111	89	60	42	30	23	13	7	4	2	0
ICC	319	103	59	26	16	12	7	4	3	3	0	0	0

KM curves showed early separation between the arms in favour of Dato-DXd, which was sustained over time

For EORTC QLQ-C30 IL146, deterioration was defined as a change from baseline that reached a clinically meaningful deterioration threshold of 16.67.
KM, Kaplan-Meier.

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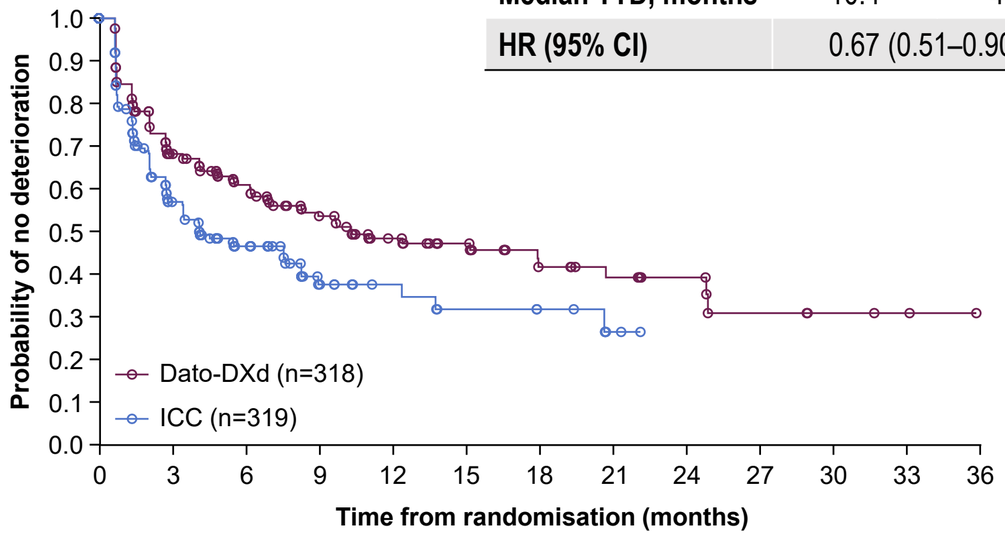
Time to deterioration in physical functioning

TTD in physical functioning (first instance) – Secondary endpoint

	Dato-DXd	ICC
Median TTD, months	10.4	4.1
HR (95% CI)	0.67 (0.51–0.90)	

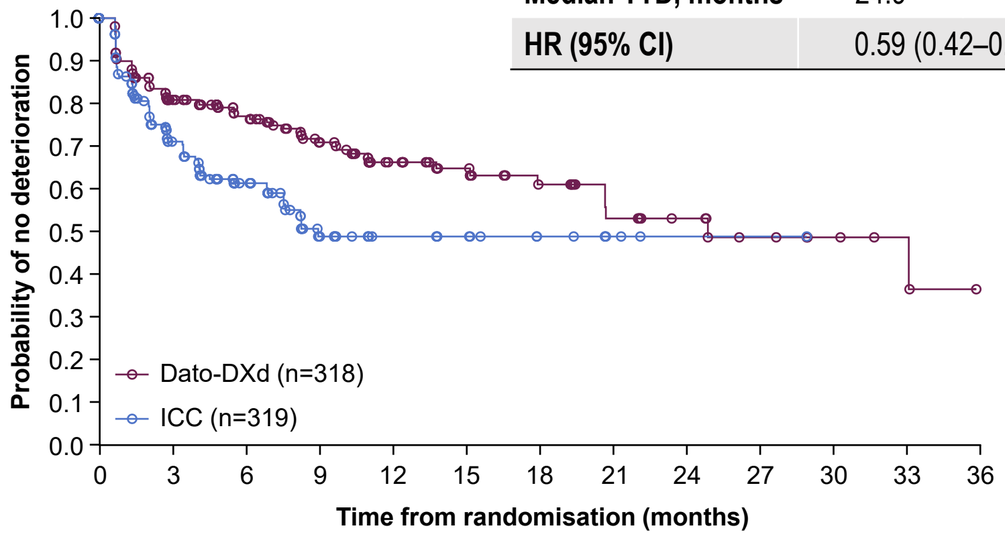


No. at risk

Dato-DXd	318	122	90	67	42	32	22	16	11	6	4	3	1
ICC	319	83	45	21	13	9	7	2	0	0	0	0	0

TTD in physical functioning (confirmed) – Secondary endpoint

	Dato-DXd	ICC
Median TTD, months	24.9	9.0
HR (95% CI)	0.59 (0.42–0.83)	



No. at risk

Dato-DXd	318	146	112	86	54	40	29	20	14	9	6	4	1
ICC	319	102	58	28	15	12	7	3	1	1	0	0	0

KM curves showed early separation between the arms in favour of Dato-DXd, which was sustained over time

For EORTC QLQ-C30 IL146, deterioration was defined as a change from baseline that reached a clinically meaningful deterioration threshold of 13.33.

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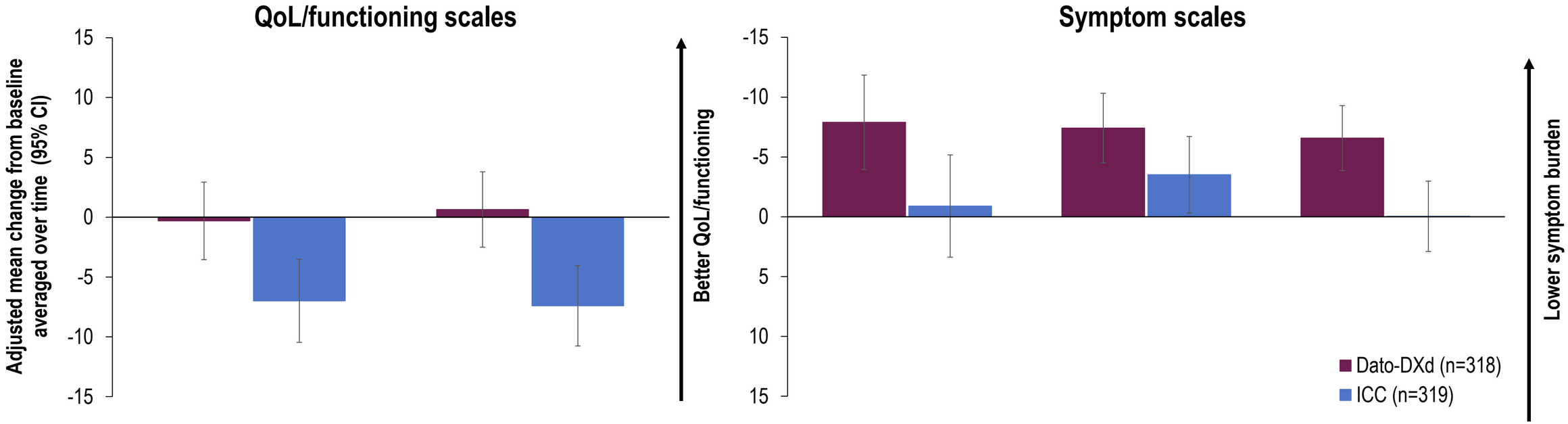
Change from baseline for secondary endpoint scales



	GHS/QoL	Physical functioning	Pain	Breast symptoms	Arm symptoms
Dato-DXd vs ICC (95% CI)	Δ 6.69 (3.26, 10.11)	Δ 8.05 (4.51, 11.58)	Δ −7.0 (−11.38, −2.62)	Δ −3.91 (−7.36, −0.46)	Δ −6.53 (−9.37, −3.69)

Dato-DXd showed numerically greater improvements in secondary symptoms, functioning and GHS/QoL versus ICC

Change from baseline of symptoms and functioning scales was analysed using a mixed-effects model for repeated measures analysis of change from baseline for all post-baseline timepoints with at least 20 patients in at least one treatment group present. The scores shown are the adjusted mean scores from all patients averaged across all timepoints.

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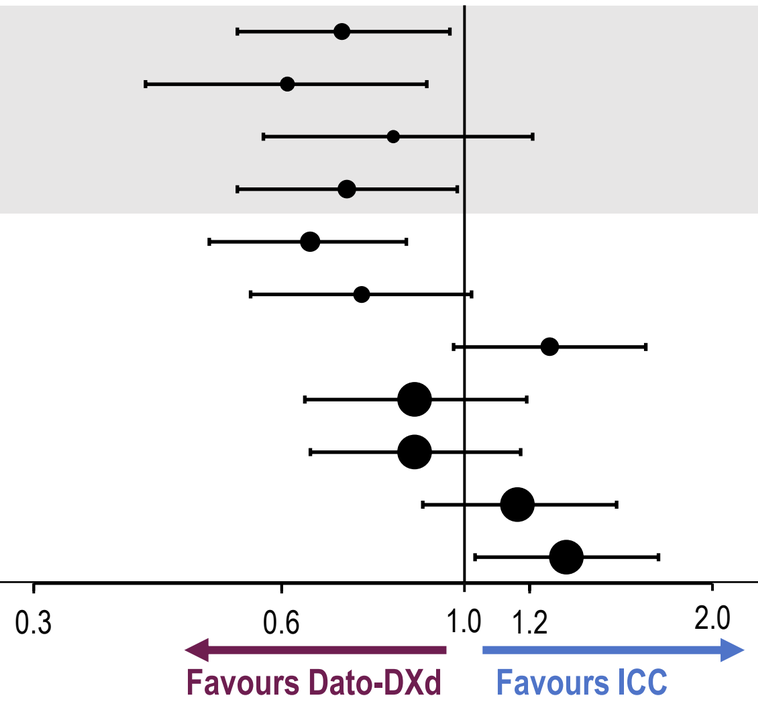
Time to deterioration in other symptoms and functioning

		Median (first) TTD, months		HR (95% CI)
		Dato-DXd (n=318)	ICC (n=319)	
Functioning	Role	11.1	5.6	0.71 (0.53–0.96)
	Emotional	NC	NC	0.61 (0.41–0.90)
	Cognitive	30.4	NC	0.82 (0.57–1.21)
	Social	18.0	5.6	0.72 (0.53–0.98)
Symptoms	Fatigue	8.3	3.4	0.65 (0.49–0.85)
	Diarrhoea	15.2	7.0	0.75 (0.55–1.02)
	Nausea/Vomiting	3.5	5.6	1.27 (0.97–1.66)
	Dyspnoea	15.2	9.0	0.87 (0.64–1.19)
	Insomnia	7.7	4.9	0.87 (0.65–1.17)
	Appetite Loss	4.2	4.2	1.16 (0.89–1.53)
	Constipation	2.8	3.5	1.33 (1.03–1.72)



For most other symptoms and functioning scales, HRs numerically favoured Dato-DXd, indicating that time to first deterioration was delayed in the Dato-DXd arm versus the ICC arm

Per EORTC QLQ-C30 IL146.

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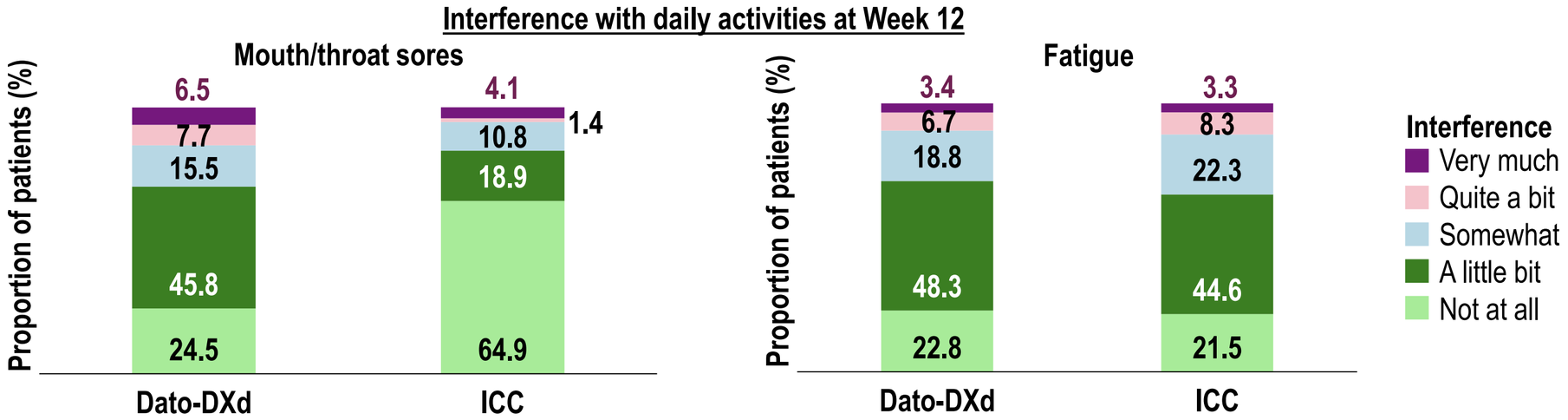
Patient-reported symptomatic AEs

- **Patient-reported symptomatic AEs*** were **generally consistent** with clinician-reported safety data
  - With Dato-DXd vs ICC, fewer patients reported any abdominal pain, shortness of breath, hair loss, numbness/tingling and general pain
  - With ICC vs Dato-DXd, fewer patients reported any nausea, vomiting, constipation, fatigue and dry eye
- **Limited interference**† with patients' daily activities was observed among patients who reported any decreased appetite, abdominal pain, shortness of breath, cough, numbness/tingling, general pain, fatigue and mouth/throat sores for both the Dato-DXd and ICC arms:



- In an analysis of patient-reported treatment tolerability, most patients in both arms were bothered by side effects of treatment 'not at all' or 'a little bit'‡

Patient-reported symptomatic AEs were generally consistent with clinician-reported safety data, with limited interference affecting patients' daily activities

*Patient-reported symptomatic AEs were measured using select items from PRO-CTCAE, EORTC IL147, and the Mouth and Throat Symptoms Diary; †Interference was assessed for symptoms reported with any frequency and severity greater than "None"/"Never" via PRO-CTCAE and EORTC IL147; ‡Patient-reported treatment tolerability was measured using PGI-TT as responses to the question "in the last 7 days, how bothered were you by the side effects of your cancer treatment?".

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Conclusions

In TROPION-Breast02, the improved efficacy observed with Dato-DXd compared with ICC was complemented by **meaningful and sustained improvements in QoL outcomes**

- The impact of Dato-DXd on patients' symptoms, functioning and GHS/QoL was favourable compared with ICC, even though patients received Dato-DXd for longer
- TTD in GHS/QoL, physical functioning, pain, and breast and arm symptoms was delayed with Dato-DXd versus ICC, and mean change from baseline numerically favoured the Dato-DXd arm
- TTD was delayed in the Dato-DXd arm for the majority of other functioning and symptom scales
- Patient-reported symptomatic AEs were generally consistent with clinician-reported safety data, with limited interference affecting patients' daily activities

These PRO data further support Dato-DXd as a new first-line standard of care in patients with locally recurrent inoperable or metastatic TNBC for whom immunotherapy is not an option

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- TROPION-Breast02 investigators and site personnel

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