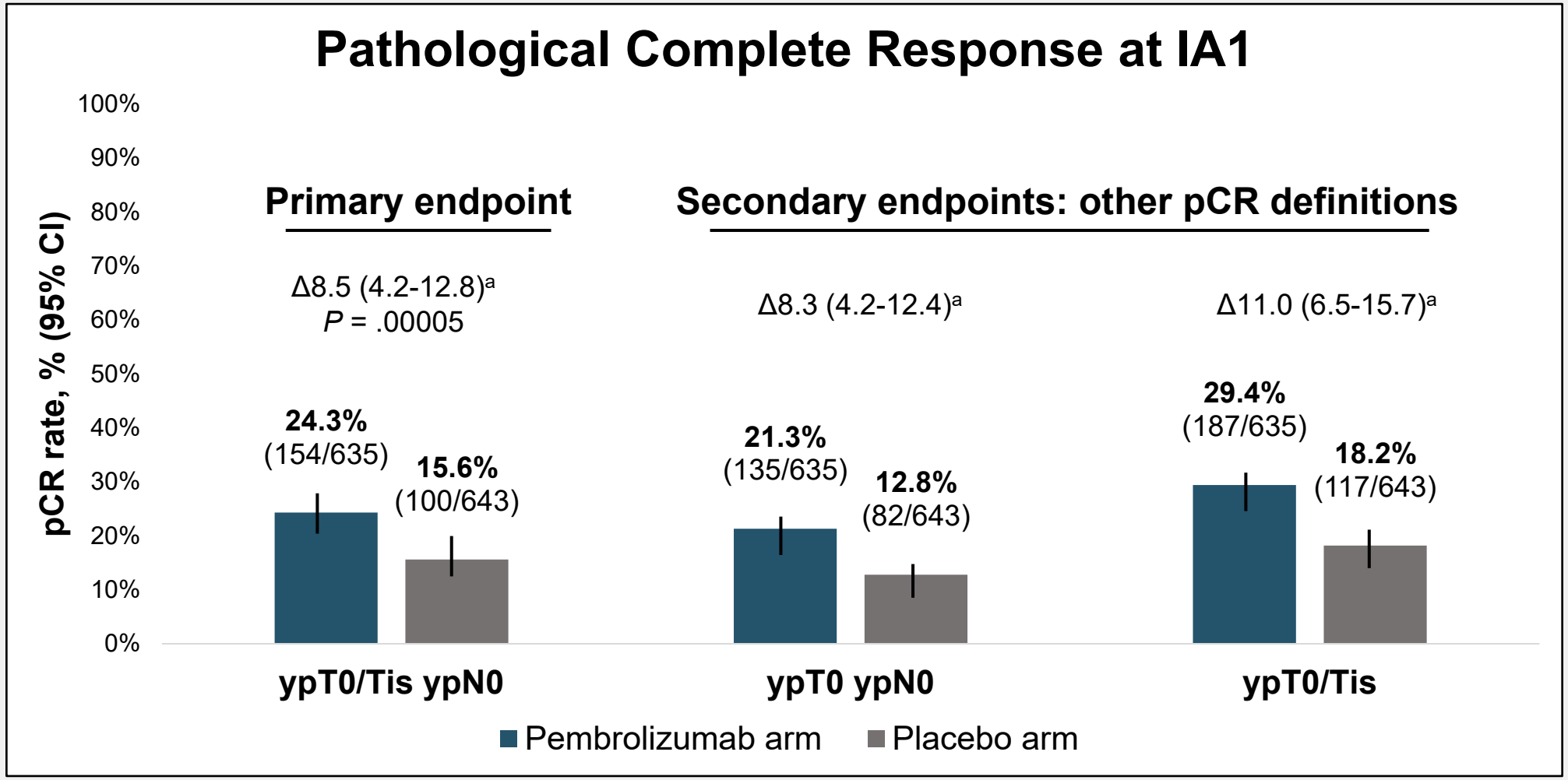
INTEGRITY
CONTINUING EDUCATION

Breast Cancer

Clinical Updates from Madrid

LBA21, Phase 3 Study of Neoadjuvant Pembrolizumab or Placebo + Chemotherapy, Followed by Adjuvant Pembrolizumab or Placebo + Endocrine Therapy for Early-Stage, High-Risk ER+/HER2- Breast Cancer: KEYNOTE-756 Results

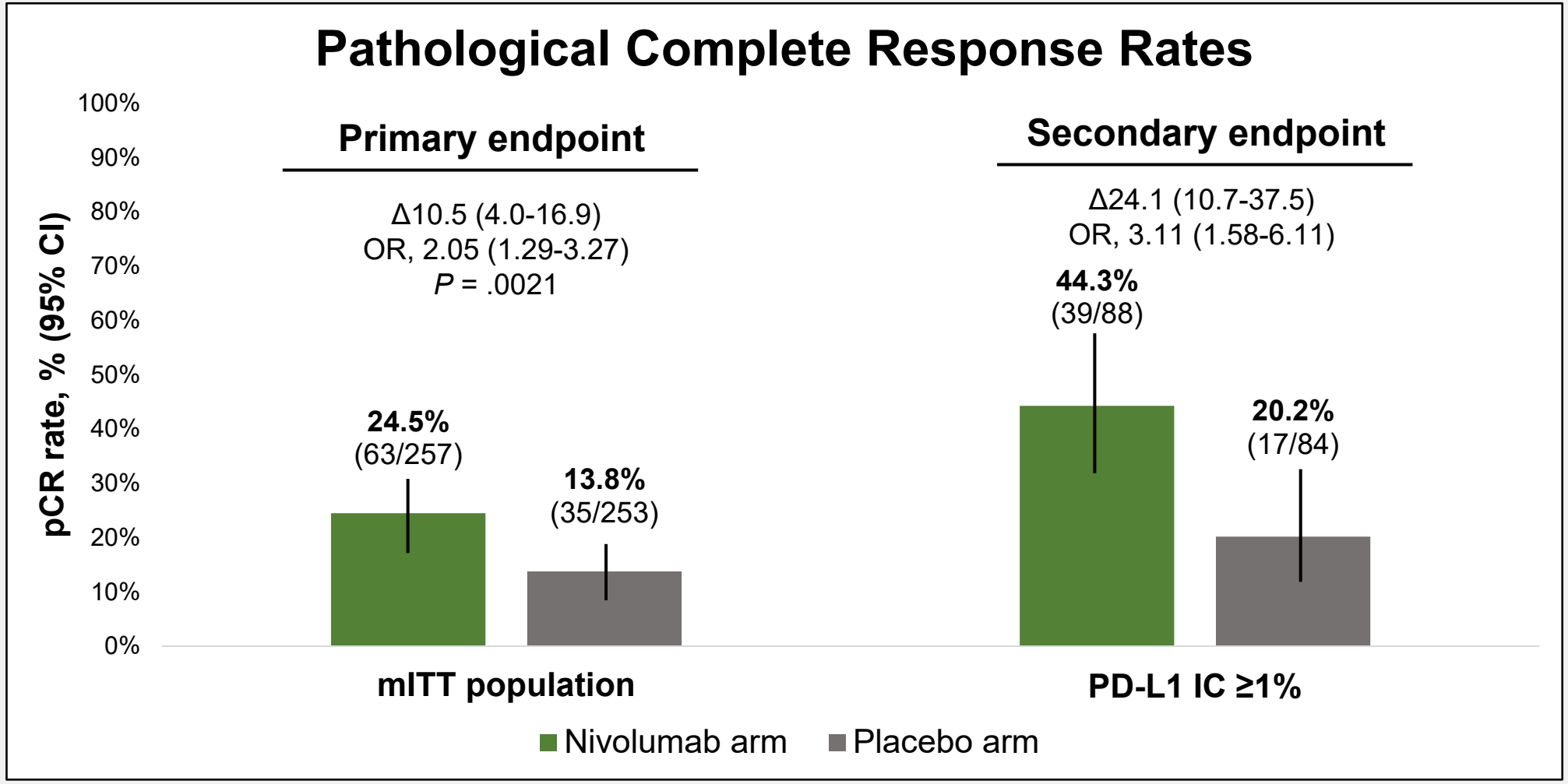


[a]Estimated treatment difference based on Miettinen and Nurminen method stratified by the analysis randomization stratification factors. Data cutoff date: May 25, 2023.

ER+, estrogen receptor positive; HER2-, human epidermal growth factor receptor 2 negative; IA1, interim analysis 1; pCR, pathological complete response.

Cardosa F, et al. ESMO 2023. Abstract LBA21. ClinicalTrials.gov ID: NCT03725059.

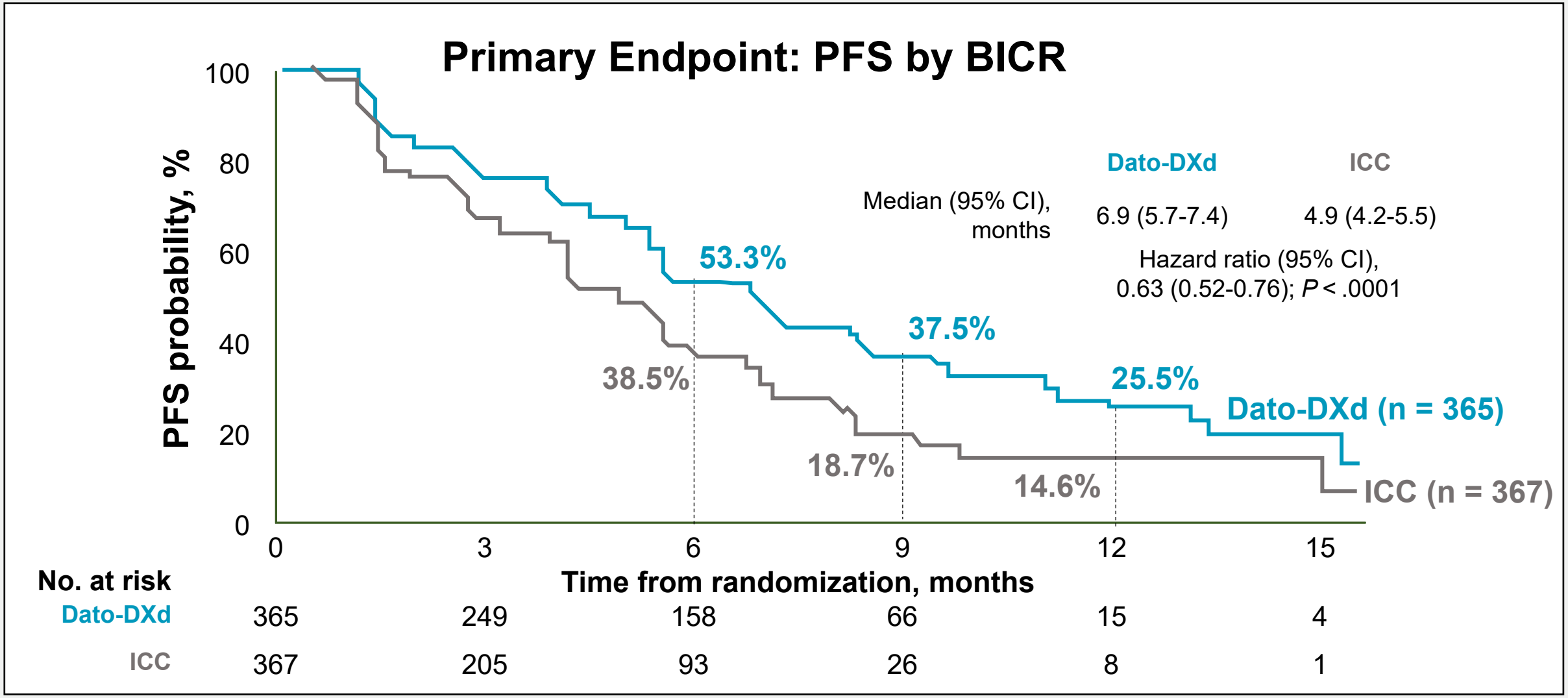
LBA20, A Randomized, Double-Blind Trial of Nivolumab vs Placebo With Neoadjuvant Chemotherapy Followed by Adjuvant Endocrine Therapy ± Nivolumab in Patients With High-Risk, ER+/HER2- Primary Breast Cancer: Pathological Complete Response



ER+, estrogen receptor positive; HER2-, human epidermal growth factor receptor 2 negative; IC, immune cell; mITT, modified intent-to-treat; OR, odds ratio; pCR, pathological complete response; PD-L1, programmed death ligand 1.

Loi S, et al. ESMO 2023. Abstract LBA20. ClinicalTrials.gov ID: NCT04109066.

LBA11, Dato-DXd vs Chemotherapy in Previously Treated Inoperable or Metastatic HR+/HER2- Breast Cancer: Primary Results From the Randomized Phase 3 TROPION-Breast01 Trial: PFS



BICR, blinded independent committee review; Dato-DXd, datopotamab deruxtecan; HER2-, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; ICC, investigator's choice of chemotherapy; PFS, progression-free survival.

Bardia A, et al. ESMO 2023. Abstract LBA11. ClinicalTrials.gov ID: NCT05104866.

377O, A Pooled Analysis of T-DXd in Patients With HER2+ Metastatic Breast Cancer With Brain Metastases From DESTINY-Breast01, 02, and 03: Study Plan

Retrospective Exploratory Pooled Analysis Plan

DESTINY-Breast01 (N = 253)
- Phase 2 study
- Patients previously treated with T-DM1
- Patients with asymptomatic and previously locally treated brain metastases eligible
- Prior brain metastasis therapy within 60 days prohibited

→ **T-DXd**
(Total, n = 184)
(With brain metastases, n = 19)

DESTINY-Breast02 (N = 608)
- Phase 3 study
- Patients previously treated with T-DM1
- Patients with asymptomatic and previously treated/untreated brain metastases eligible
- Prior brain metastasis therapy within 14 days prohibited

2:1 R →
- **T-DXd**
(Total, n = 406)
(With brain metastases, n = 83)
- **TPC per label**
(trastuzumab/capecitabine or lapatinib/capecitabine)
(Total, n = 202)
(With brain metastases, n = 41)

DESTINY-Breast03 (N = 524)
- Phase 3 study
- Patients previously treated with trastuzumab and a taxane in metastatic or (neo)adjuvant setting with recurrence within 6 months of therapy
- Patients with asymptomatic and previously treated/untreated brain metastases eligible
- Prior brain metastasis therapy within 14 days prohibited

1:1 R →
- **T-DXd**
(Total, n = 261)
(With brain metastases, n = 46)
- **T-DM1**
(Total, n = 263)
(With brain metastases, n = 42)

T-DXd pools
(Total, n = 851)
(With brain metastases, n = 148)
(Without brain metastases, n = 703)

Comparator pools
(Total, n = 465)
(With brain metastases, n = 83)
(Without brain metastases, n = 382)

Endpoints:
- IC-ORR (CR + PR in brain) by BICR per RECIST v1.1
- IC-DOR per BICR
- CNS-PFS per BICR
- Safety and tolerability

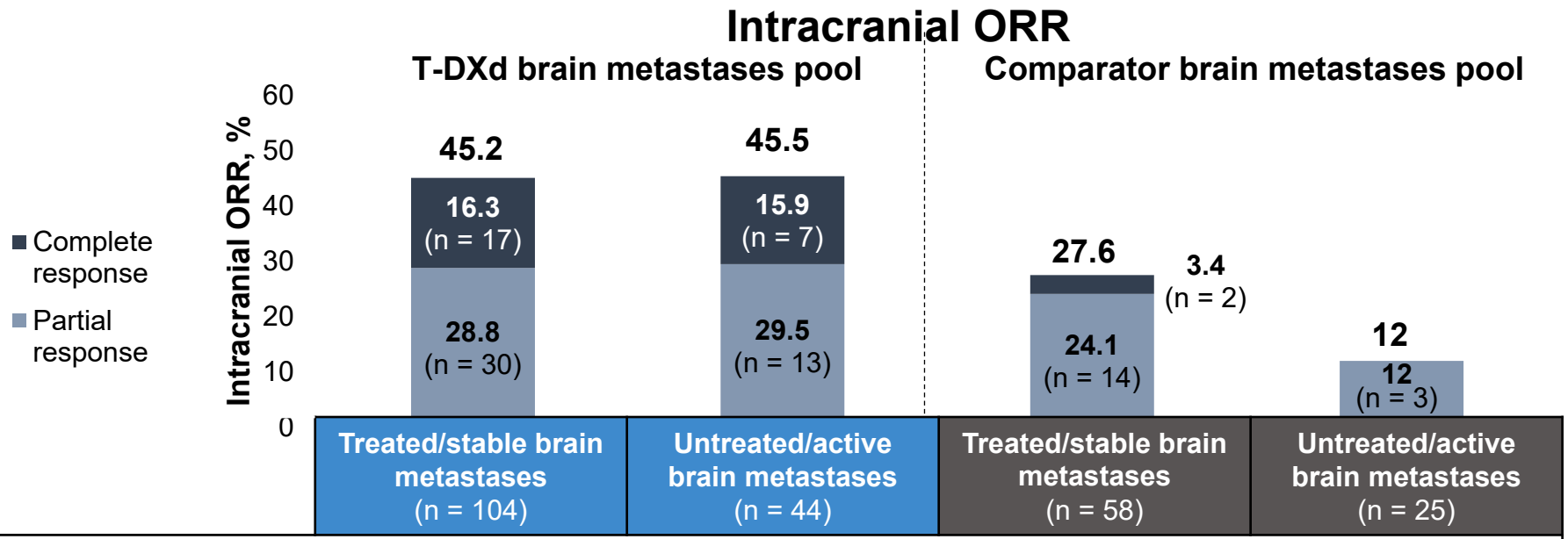
Brain metastasis and non–brain metastasis pools were determined by BICR at baseline among all patients based on mandatory brain CT/MRI screening.

BICR, blinded independent central review; CNS-PFS, central nervous system progression-free survival; CR, complete response; HER2, human epidermal growth factor receptor 2; IC-DOR, intracranial duration of response; IC-ORR, intracranial overall response rate; PR, partial response; R, randomization; RECIST v1.1, Response Evaluation Criteria in Solid Tumours version 1.1; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

Hurvitz S, et al. ESMO 2023. Abstract 377O. CliinicalTrial.gov IDs: NCT03248492; NCT03523585; NCT03529110.

377O, A Pooled Analysis of T-DXd in Patients With HER2+ Metastatic Breast Cancer With Brain Metastases from DESTINY-Breast01, -02, and -03: Intracranial Response

Exploratory Best IC Response, ORR, and DOR per BICR



Best overall IC response, n (%)				
Stable disease	48 (46.2)	15 (34.1)	28 (48.3)	15 (60.0)
Progressive disease	3 (2.9)	1 (2.3)	7 (12.1)	5 (20.0)
NE/missing	6 (5.8)	8 (18.2)	7 (12.1)	2 (8.0)
Median (95% CI) IC-DOR, months	12.3 (9.1-17.9)	17.5 (13.6-31.6)	11.0 (5.6-16.0)	NA

- T-DXd consistently demonstrated superior rates of IC responses over comparator in patients with treated/stable and untreated/active brain metastases
- A trend in prolonged median IC-DOR was most pronounced in the untreated/active brain metastases group

BICR, blinded independent central review; HER2+, human epidermal growth factor receptor 2 positive; IC, intracranial; IC-DOR, intracranial duration of response; NA, not applicable; NE, not evaluable; ORR, overall response rate; T-DXd, trastuzumab deruxtecan.

Hurvitz S, et al. ESMO 2023. Abstract 377O. ClinicalTrials.gov IDs: NCT03248492; NCT03523585; NCT03529110.