6th Annual

LEAD2024

Enriching Experiences for Women in Hematology & Oncology

Updates in Breast Medical Oncology

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Bio Ascend™
A Vaniam Group Company

University of Nebraska Medical Center
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Early Breast Cancer

Pivotal Clinical Trial Updates from 2024

LEAD2024: Leadership, Empowerment, and Development

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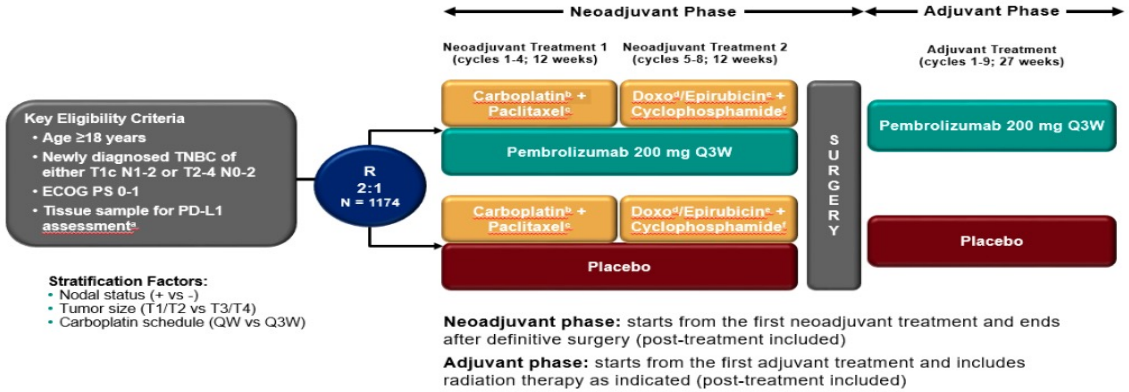
Overall Survival Benefit with addition of Pembrolizumab in Early TNBC

Keynote-522 5y overall survival

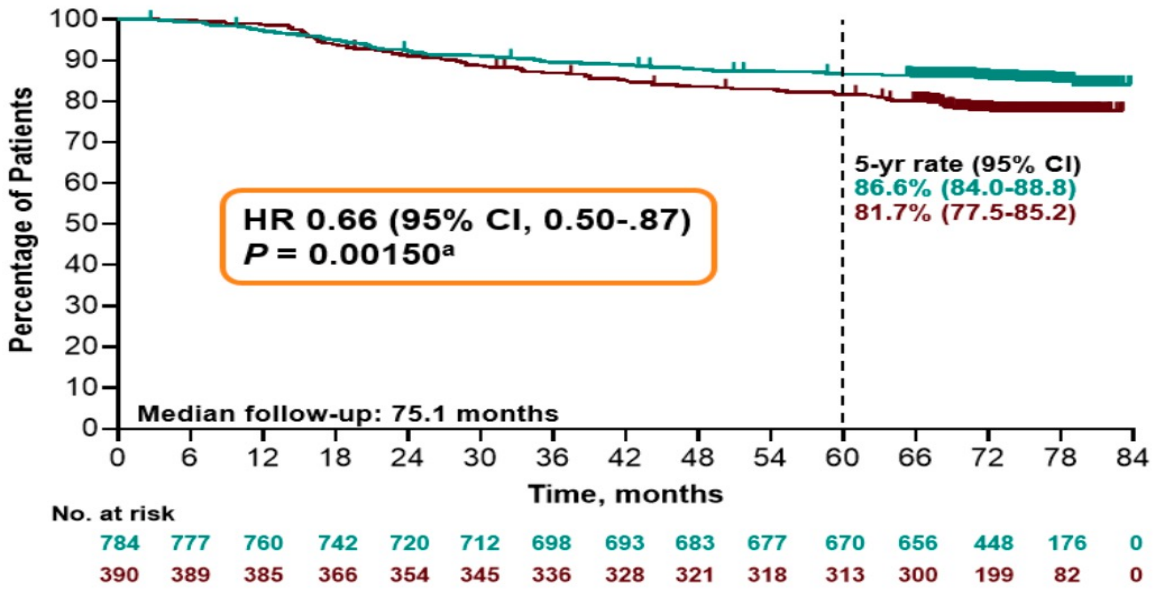


Addition of pembrolizumab to neoadj. chemotherapy:

- Absolute pCR gain: +13.6%
- Most recent event-free survival: HR=0.63
- **Translation into an OS gain ?**
- Prespecified analysis, median FU = ~6y

BARCELONA 2024 ESMO congress

Schmid *et al.*, LBA4



~5% cured by pembrolizumab added to chemo

~15 % died of TNBC despite pembrolizumab

~80% cured by CHI/RT+chemotherapy alone

Schmid et al, ESMO 2024 Annual Congress

Benefit of Ribociclib in Early High-Risk HR+/Her2- Breast Cancer

Adjuvant ribociclib – NATALEE 4y data

Fasching *et al.*, LBA4

4y landmark analysis

- Adult patients with HR+/HER2– EBC
- Prior ET allowed ≤12 mo prior to randomization
- **Anatomical stage IIA**[a]
  - **N0** with:
    - Grade 2 and evidence of high risk:
      - Ki-67 ≥20%
      - Oncotype DX Breast Recurrence Score ≥26 ***or***
      - High risk via genomic risk profiling
    - Grade 3
  - **N1**
- **Anatomical stage IIB**[a]
  - N0 or N1
- **Anatomical stage III**
  - N0, N1, N2, or N3

N = 5101[b]

R 1:1[c]

RIB
400 mg/day
3 weeks on/1 week off
for 3 years

+

NSAI
Letrozole or anastrozole[d]
for ≥5 years
+ goserelin in men and premenopausal women

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Increasing Invasive Disease-Free Survival with Adjuvant Ribociclib x 3yrs in HR+ EBC

Adjuvant ribociclib – NATALEE 4y data

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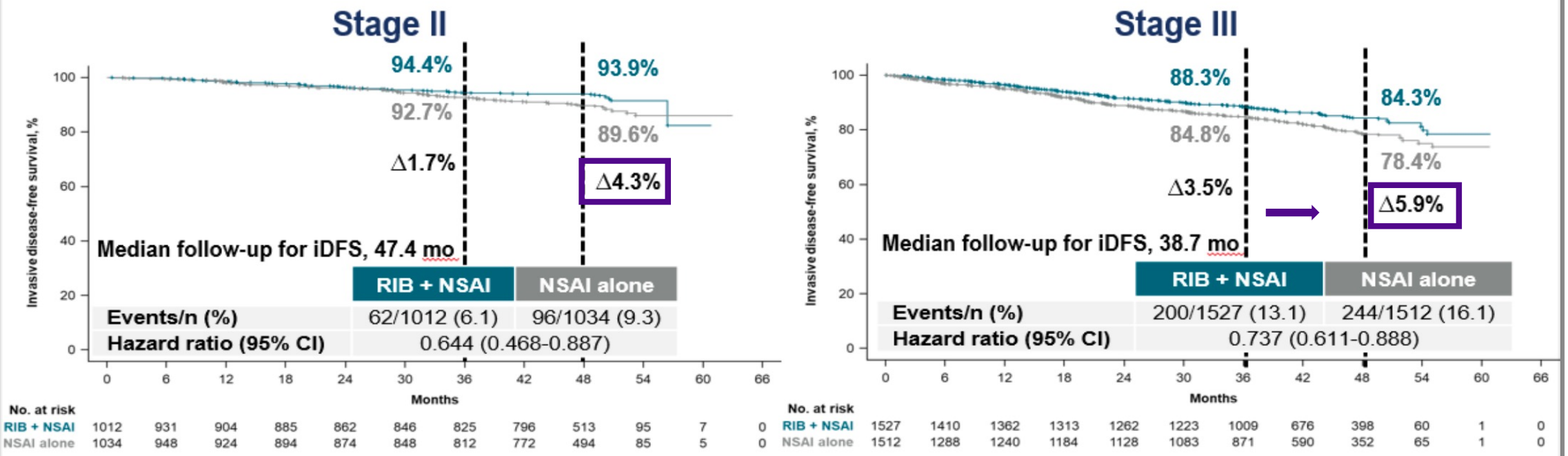
4y landmark analysis



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Fasching et. al, ESMO 2024 Annual Congress

Increasing Invasive Disease-Free Survival with Adjuvant Ribociclib x 3yrs in HR+ EBC

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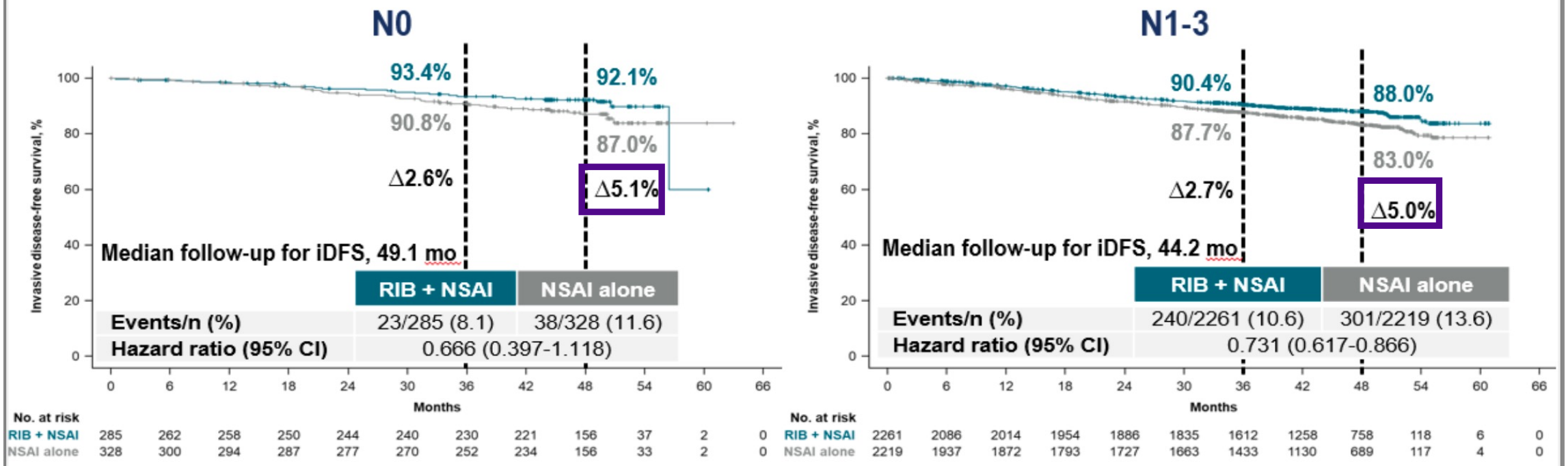

- FDA approved adjuvant ribociclib for use in high-risk early HR+ EBC on Sept 17th, 2024!

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Fasching et. al, ESMO 2024 Annual Congress

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Metastatic Breast Cancer

Sub Text

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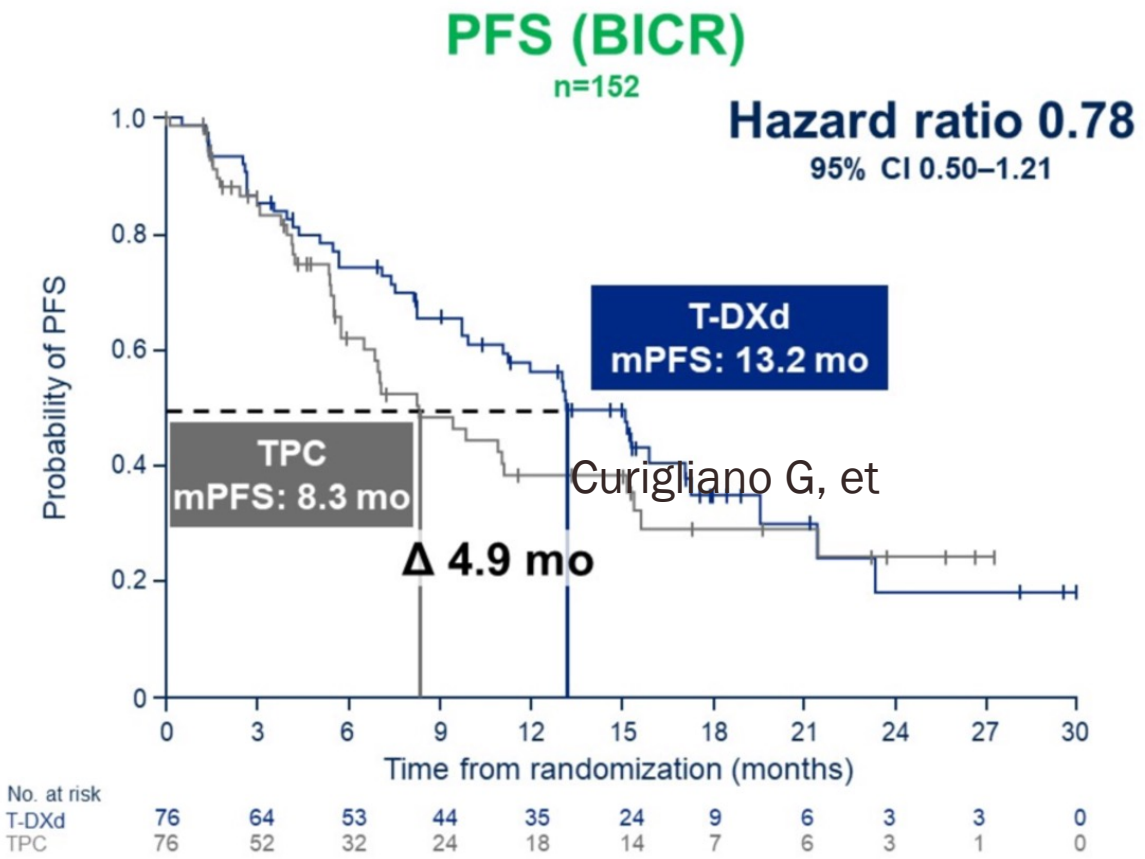
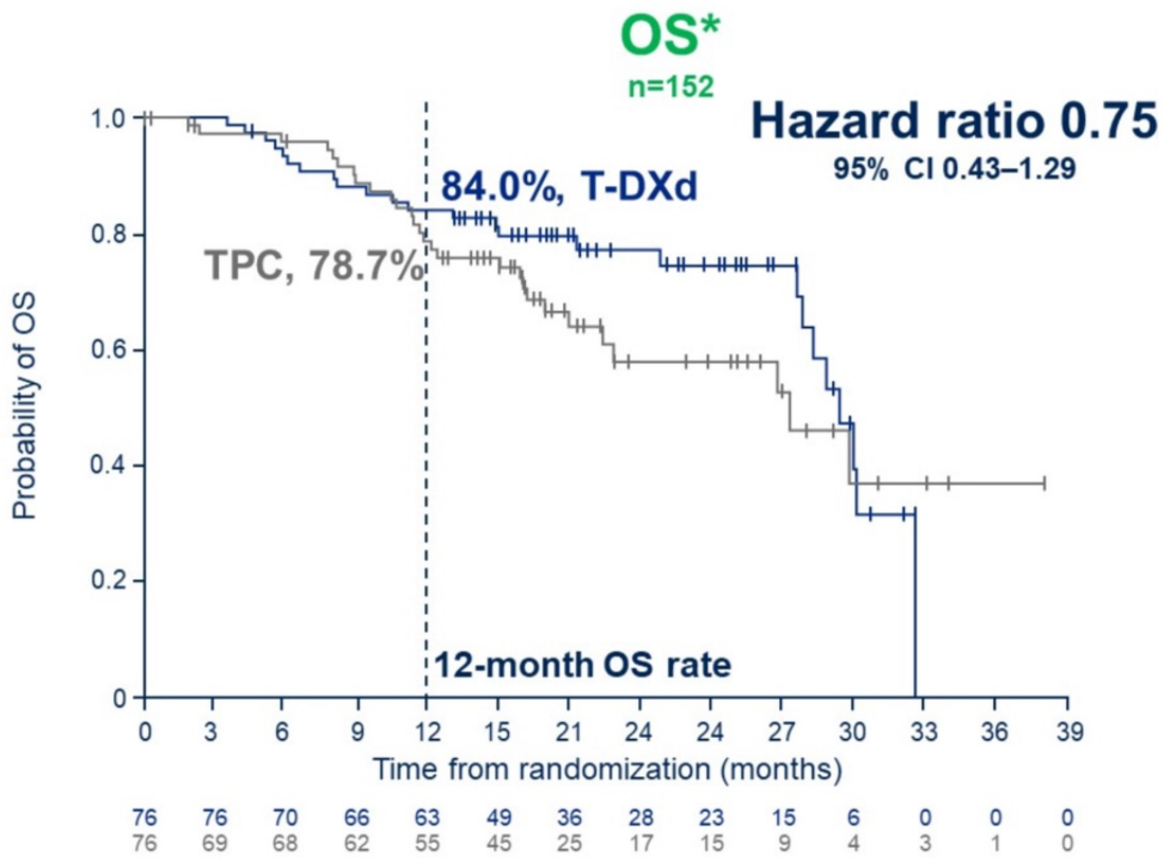
DESTINY-Breast06: PFS and OS in HER2-ultralow





Curigliano G, et

- PFS improvement with T-DXd vs TPC in HER2-ultralow was consistent with results in HER2-low

*34.9% maturity (of total N for population) at this first interim analysis; median duration of follow up was 16.8.

Curigliano G, et. al, ASCO 2024

Introduction of Her2 UltraLow as an option!! DB-06

DESTINY-Breast06: Trial Design

- HR+ mBC
- HER2-low (IHC1+ or IHC2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining)*
- Chemotherapy naïve in the mBC setting

Prior lines of therapy

- ≥2 lines of ET ± targeted therapy for mBC
  OR
- 1 line for mBC **AND**
  - Progression ≤6 mo of starting 1L ET + CDK4/6i
    OR
  - Recurrence ≤24 mo of starting adjuvant ET

R 2:1

- Trastuzumab Deruxtecan (T-DXd) 5.4 mg/kg Q3W (n=436)
  - HER2-low = 713
  - HER2-ultralow = 153†
- Physician's Choice Chemotherapy‡ (n=430)

Stratification

- Prior CDK4/6i use (yes vs no)
- HER2 expression (IHC 1+ vs IHC2+/ISH- vs IHC 0 with membrane staining)
- Prior taxane in the non-metastatic setting (yes vs no)

Primary endpoint:

- PFS (BICR) in HER2-low

Key secondary endpoints:

- PFS (BICR) in ITT (HER2-low + ultralow)
- OS in HER2-low
- OS in ITT (HER2-low + ultralow)

*Study enrollment was based on central HER2 testing. HER2 status was determined based on the most recent evaluable HER2 IHC sample prior to randomization; HER2-ultralow was defined as faint, partial membrane staining in ≤10% of tumor cells (also known as IHC > 0 < 1+); †HER2-ultralow status as determined per IRT data (note: efficacy analyses in the HER2-ultralow subgroup were based on n=152 as determined per central laboratory testing data); ‡Capecitabine, nab-paclitaxel, or paclitaxel.

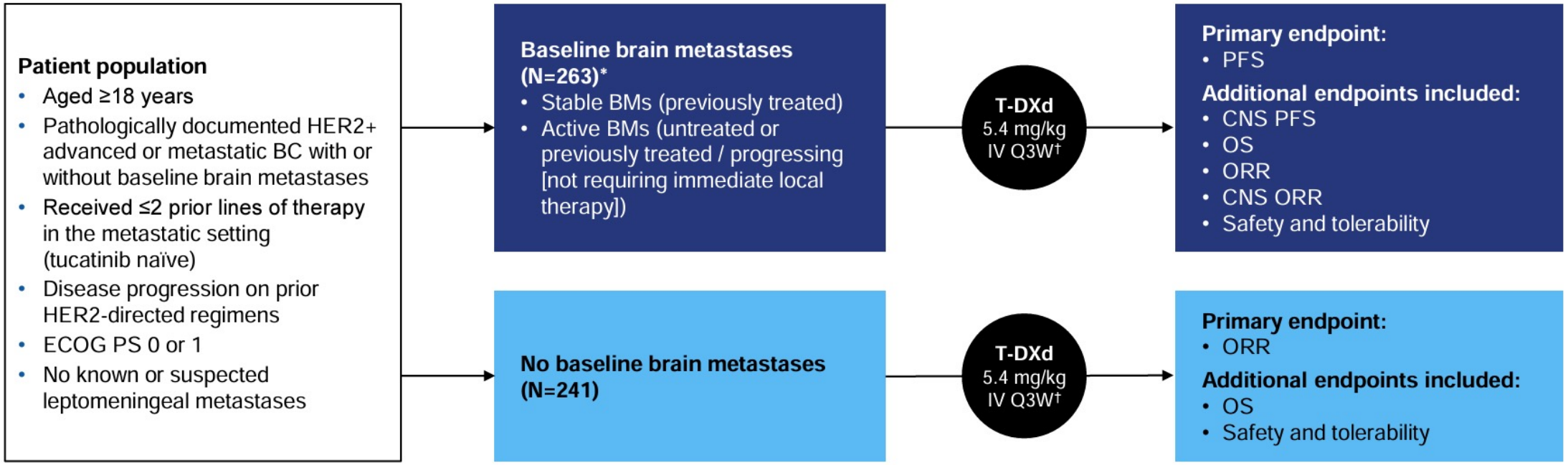
Curigliano G, et al. ASCO 2024

Efficacy of Trastuzumab deruxtecan in Brain Metastases

DESTINY-Breast12

DESTINY-Breast12 study design

Phase 3b/4, multicenter, single-arm, two-cohort, open-label study of T-DXd in previously treated HER2+ mBC with and without brain metastases (BMs); the largest prospective study of T-DXd in patients with stable or active BMs

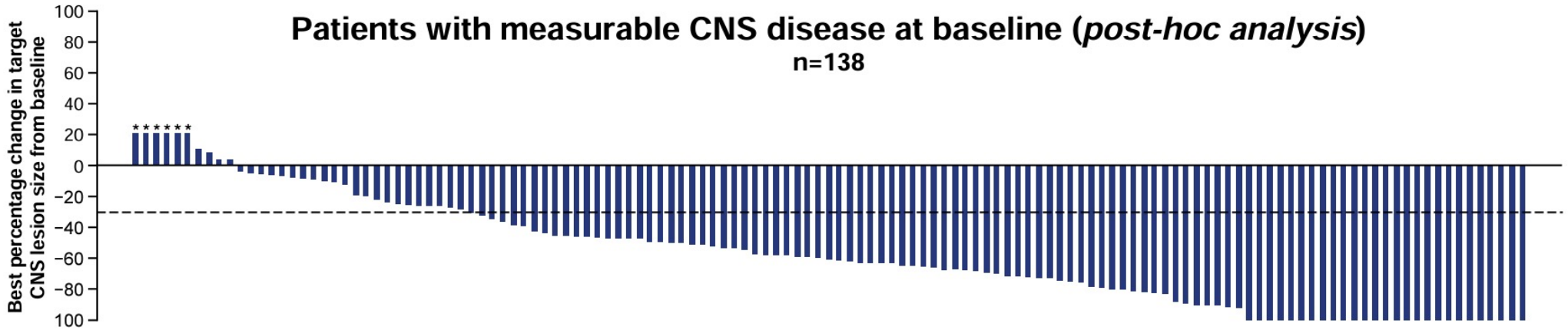


Destiny Breast 12

Trastuzumab deruxtecan CNS response in Her2+ patients with brain metastases

DESTINY-Breast12

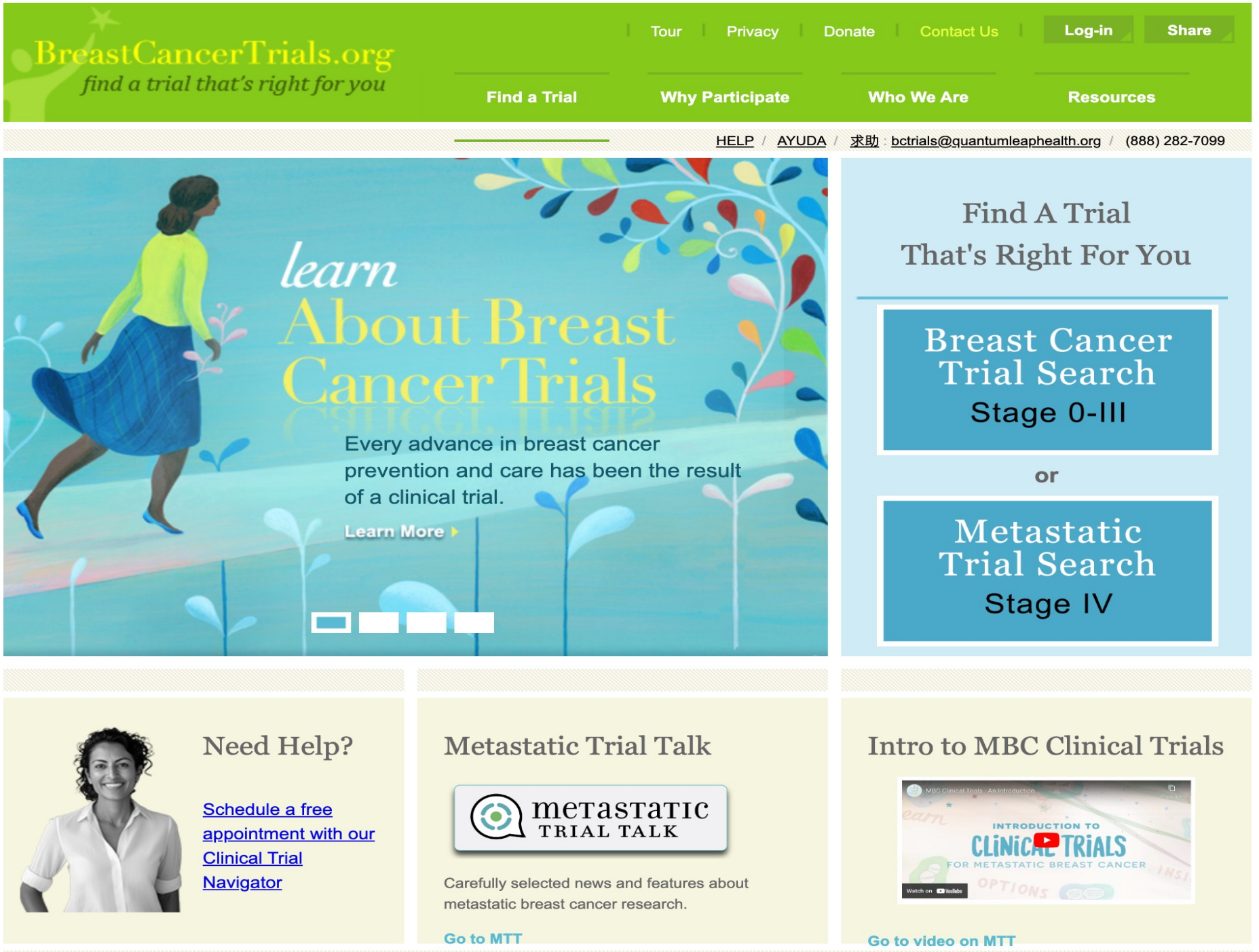
Baseline BMs: CNS ORR



Measurable CNS disease at baseline	All patients (n=138)	Stable BMs (n=77)	Active BMs (n=61)	Active BM subgroups: Untreated (n=23) *Post-hoc analysis*	Active BM subgroups: Previously treated / progressing (n=38) *Post-hoc analysis*
Confirmed CNS ORR, % (95% CI)	**71.7 (64.2, 79.3)**	79.2 (70.2, 88.3)	62.3 (50.1, 74.5)	82.6 (67.1, 98.1)	50.0 (34.1, 65.9)

T-DXd showed substantial CNS responses in the overall BMs population, including patients with stable and active BMs

Dashed line indicates a 30% decrease in target tumor size (PR)
*Imputed values: a value of +20% was imputed if best percentage change could not be calculated because of missing data if: a patient had a new lesion or progression of non-target lesions or target lesions, or had withdrawn because of PD and had no evaluable target lesion data before or at PD
BM, brain metastasis; CI, confidence interval; CNS, central nervous system; ORR, objective response rate; PD, progressive disease; PR, partial response; T-DXd, trastuzumab deruxtecan



Breastcancertrials.org

Thank you!!!