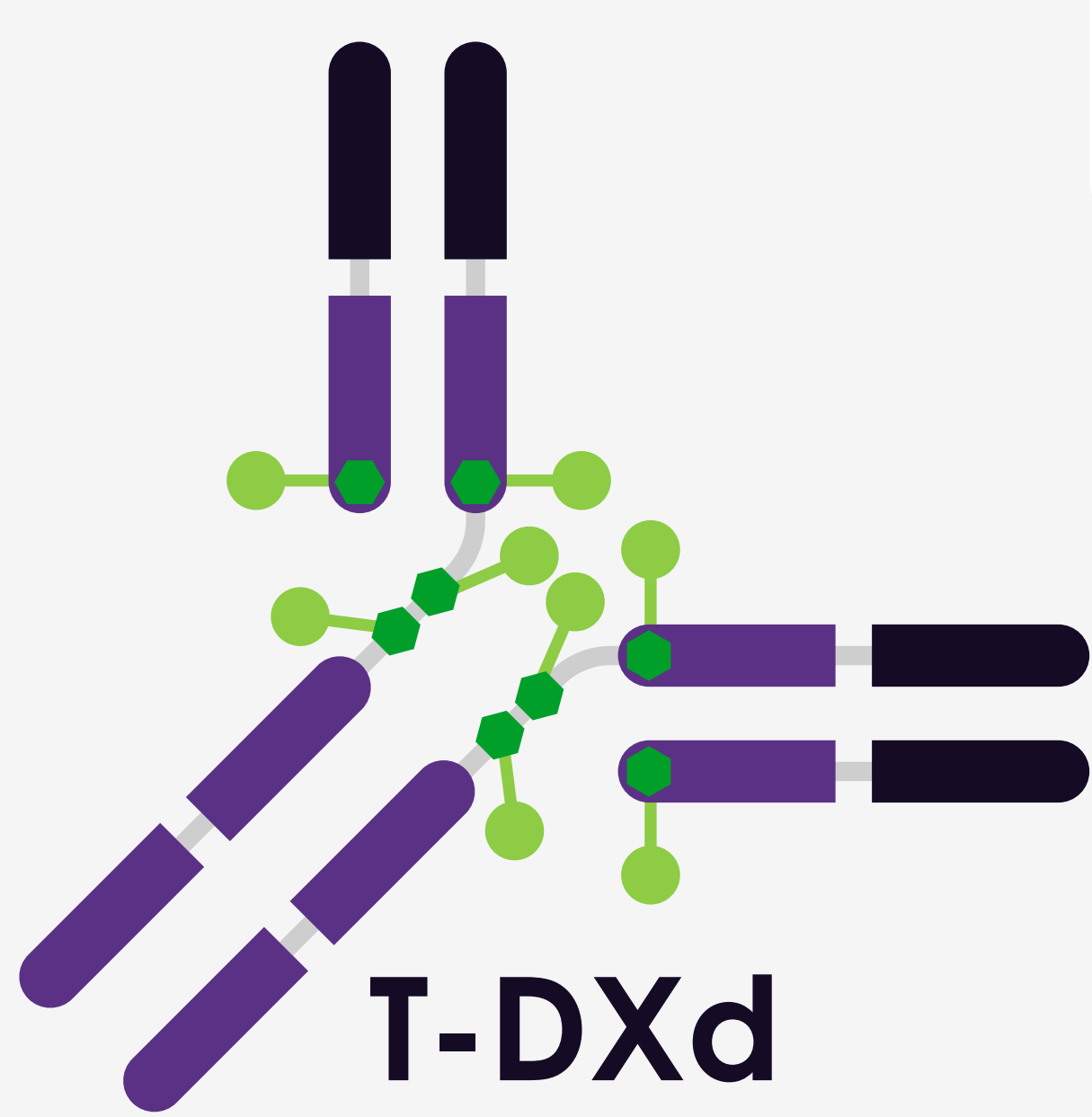


Key highlights

San Antonio Breast Cancer Symposium 2022

DESTINY-Breast



T-DXd

vs TPC in T-DM1
treated HER2+
mBC

1° endpoint
mPFS 17.8 mo
vs 6.9 mo

02
Ph3¹

vs T-DM1 in
HER2+ mBC

1° endpoint
mPFS 28.8 mo
vs 6.9 mo

03
Ph3²

vs TPC in
previously
treated
HER2-low mBC

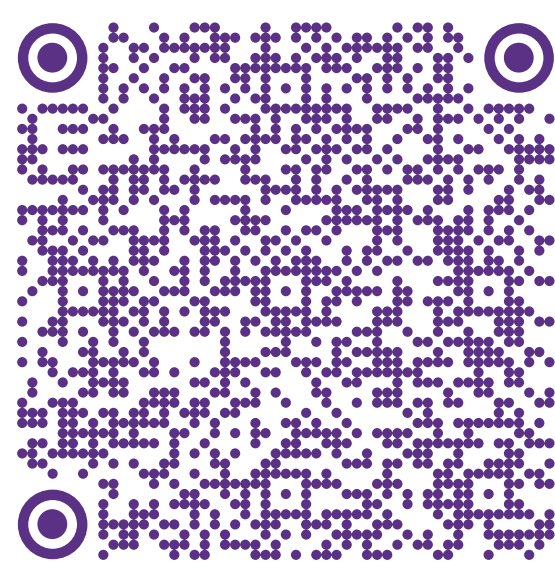
1° endpoint
mPFS 9.9 mo
vs 5.1 mo

04
Ph3³

Debate on HER2-low: Is HER2-low a separate entity?

NO⁴ (IHC)

- Expression lacks stability, concordance, and can change in response to treatment or surgery
- No clear impact on prognosis or benefit of therapy



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HER2-negative

0

1+

2+

3+

HER2-positive

HER2-neg

HER2-Low

HER2-positive

-

+

YES⁵ (ISH)

- Fewer G3 tumours and lower signs of proliferation (Ki67) and tp53 mutations
- Anti-HER2 ADCs, CDK4/6i's or other novel drugs may have clinical benefit
- Expanded trial inclusion of previously HER2-patients who may benefit

PARPi efficacy: Systematic review of *BRCA* 1/2-related BC and prior platinum exposure⁶

Platinum salts: dsDNA breaks

PARPi's: DNA damage in *mBRCA* 1/2 tumours

Cross-resistant DNA-damage mechanism?

Prior platinum exposure	Yes	No
PARPi PFS vs control (HR, 95% CI)	0.72; 0.53–0.97	0.68; 0.52–0.89

PARPi's appear effective even with prior platinum exposure,
decreasing concerns of cross-resistance

Abbreviations: ADC, antibody-drug conjugate; G3, grade 3; HR, hazard ratio; IHC, immunohistochemistry; ISH, in situ hybridisation; mBC, metastatic breast cancer; mo, month; mPFS, median progression-free survival; Ph3, phase 3; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

References: 1. Krop I. SABCS 2022. GS2-01. 2. Hurvitz SA. SABCS 2022. GS2-02. 3. Modi S. NEJM 2022;387:9–20. 4. Tolaney SM. SABCS 2022. Special Session 3. 5. Curigliano G. SABCS 2022. Special Session 3. 6. Marinho AD. SABCS 2022. PD-01-08.

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