

# **Oncology Today with Dr Neil Love — HER2-Positive Metastatic Breast Cancer**

*A CME/MOC-Accredited Virtual Event*

**Wednesday, May 17, 2023**

**5:00 PM – 6:00 PM ET**

**Faculty**

**Joyce O'Shaughnessy, MD**

**Moderator**

**Neil Love, MD**

# Faculty



**Joyce O'Shaughnessy, MD**

Celebrating Women Chair in Breast Cancer Research  
Baylor University Medical Center  
Director, Breast Cancer Research Program  
Texas Oncology  
US Oncology  
Dallas, Texas



**Moderator**

**Neil Love, MD**  
Research To Practice

# ONCOLOGY TODAY

WITH DR NEIL LOVE

## HER2-Positive Metastatic Breast Cancer



PROFESSOR GIUSEPPE CURIGLIANO  
EUROPEAN INSTITUTE OF ONCOLOGY



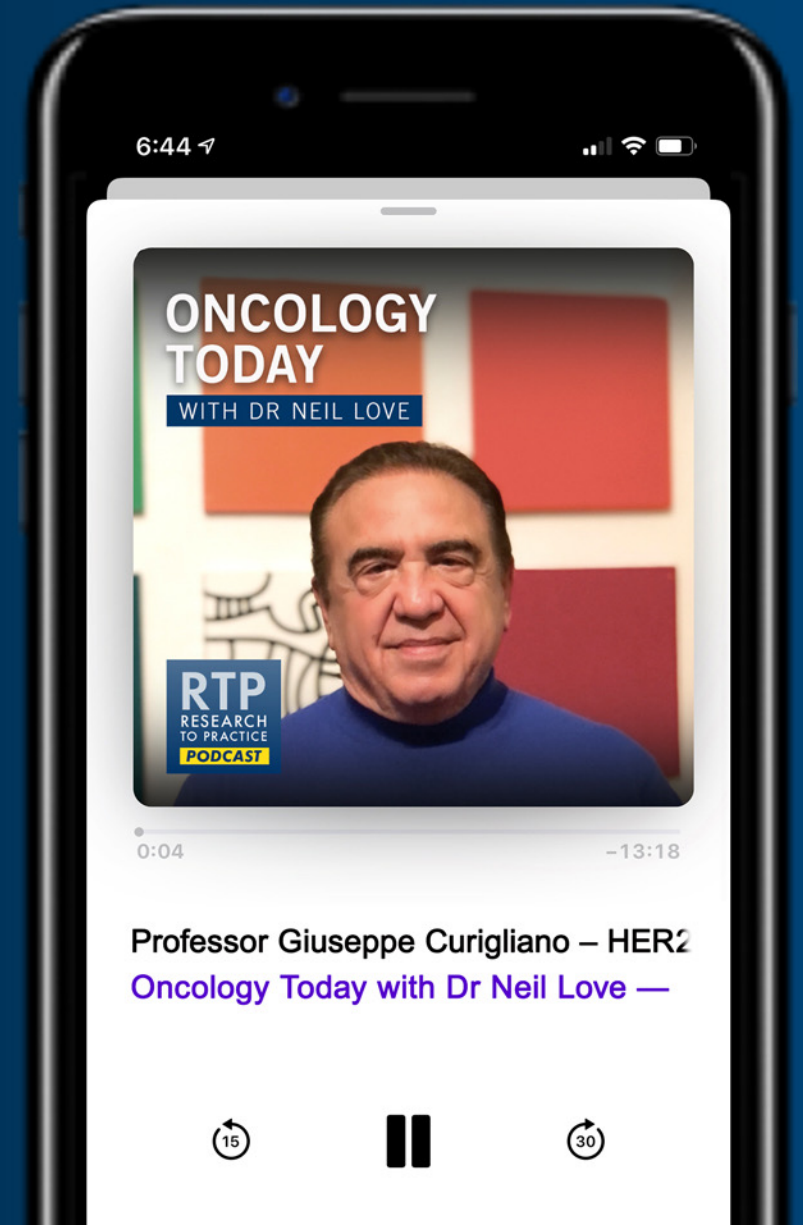
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## Dr Love — Disclosures

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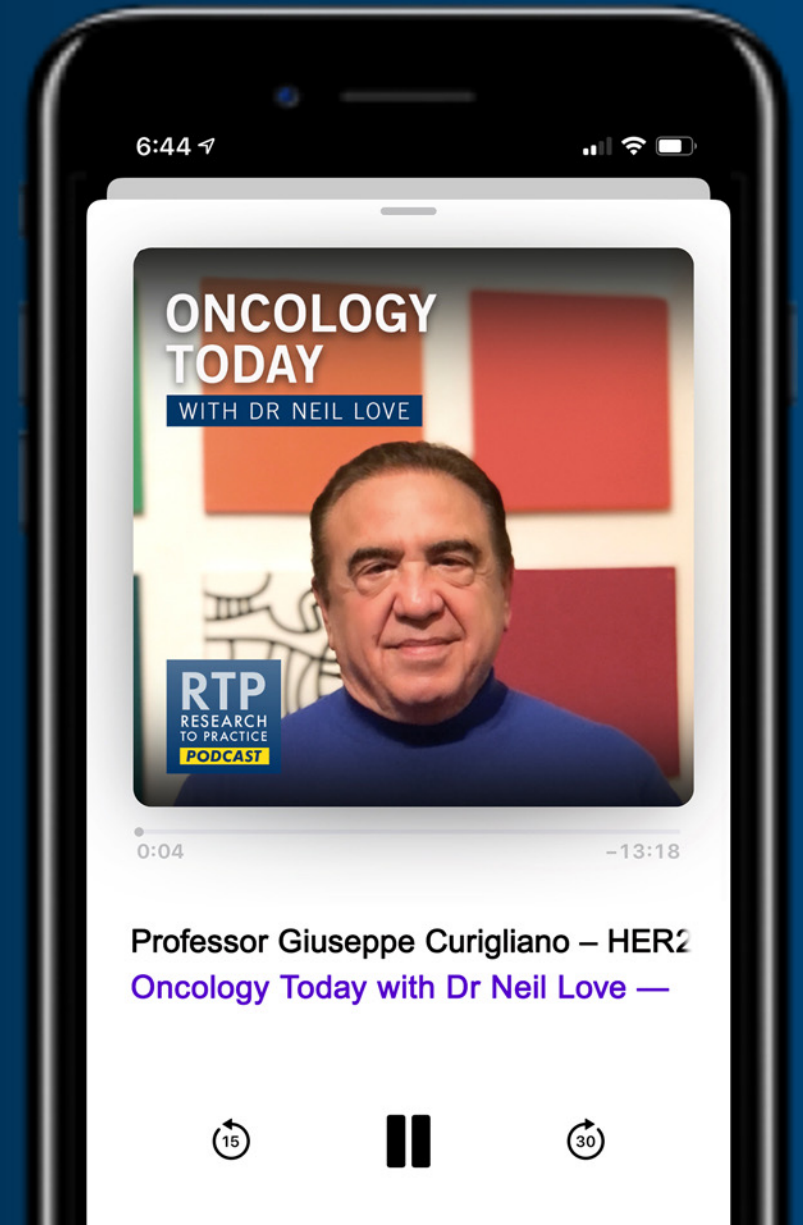
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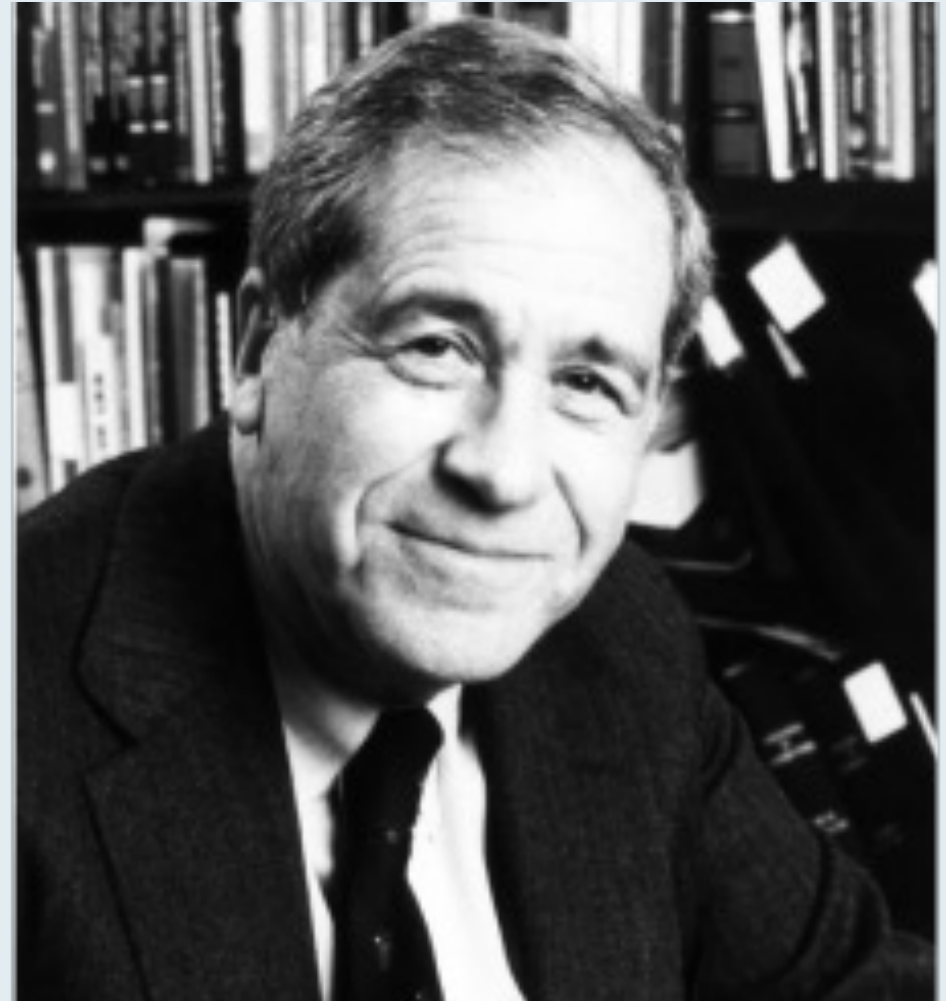
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**Gianni Bonadonna, MD**



**Bernard Fisher, MD**

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## Anti-HER2 Treatment 2 Years from Now





UNIVERSITÀ DEGLI STUDI  
DI MILANO



# HER2 positive metastatic breast cancer

Giuseppe Curigliano, MD, PhD  
University of Milano and Istituto Europeo di Oncologia, IRCCS  
Milano, Italia

# Case 1



# Case 1. Clinical presentation, diagnosis, staging

<b>Patient</b>	<ul style="list-style-type: none"><li>• 45 yo woman, <b>premenopausal</b></li><li>• Comorbidities: none</li><li>• Family history: mother with BC (55 yo) and upper limb STS</li></ul>
<b>Presentation</b>	<ul style="list-style-type: none"><li>• Detection of <b>lump</b> in the right breast and right axillary <b>adenopathy</b> at self-examination</li></ul>
<b>Physical examination</b>	<ul style="list-style-type: none"><li>• Lesion of 70 mm in the right LIQ/LOQ</li><li>• Hard right axillary lymphadenopathy of 25 mm</li><li>• Abdominal PE: negative.</li></ul>
<b>Work-up</b>	<ul style="list-style-type: none"><li>• Mammography + breast and axillary US + breast MRI: right breast lesion of 75x53 mm, multiple right axillary lymphadenopathy</li><li>• <b>PET-CT scan and CT scan: multiple hepatic metastasis</b> <sup>(1)</sup></li></ul>
<b>Breast US-guided biopsy</b>	<ul style="list-style-type: none"><li>• Invasive carcinoma NOS <b>ER: 90%; PgR: 35%; HER2: 0</b>; Ki67: 25%</li></ul>
<b>Genetic testing</b>	<ul style="list-style-type: none"><li>• <b>Pathogenic <i>BRCA2</i> variant c.6405_6409 (p_Asn2135fs)</b></li></ul>

# 1. Clinical presentation, diagnosis, staging

## Patient

- 45 yo woman, **premenopausal**
- Comorbidities: none
- Family history: mother with BC (55 yo) and upper limb STS

***De novo* mBC**  
**ER-positive/HER2-negative**  
**gBRCA mut**

## Breast US-guided biopsy

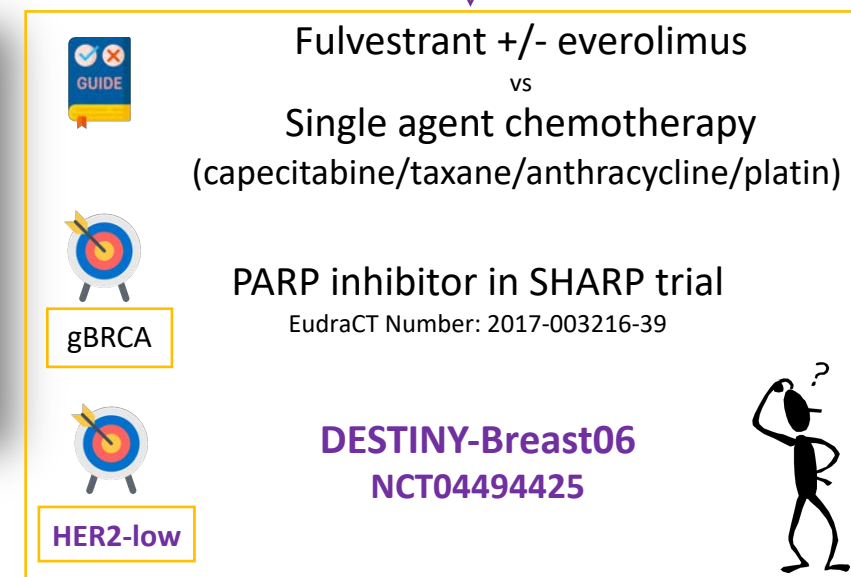
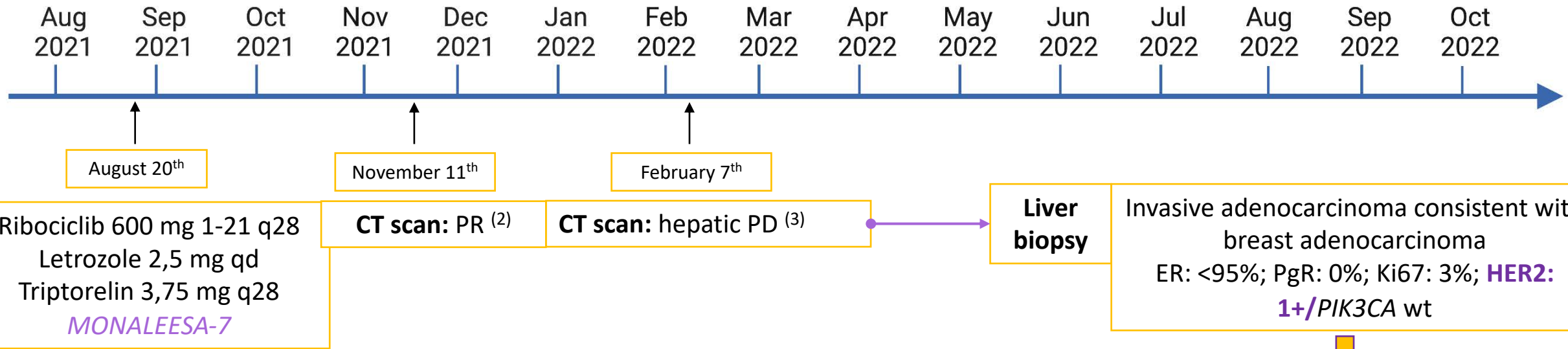
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## Genetic testing

- **Pathogenic *BRCA2* variant c.6405\_6409 (p\_Asn2135fs)**

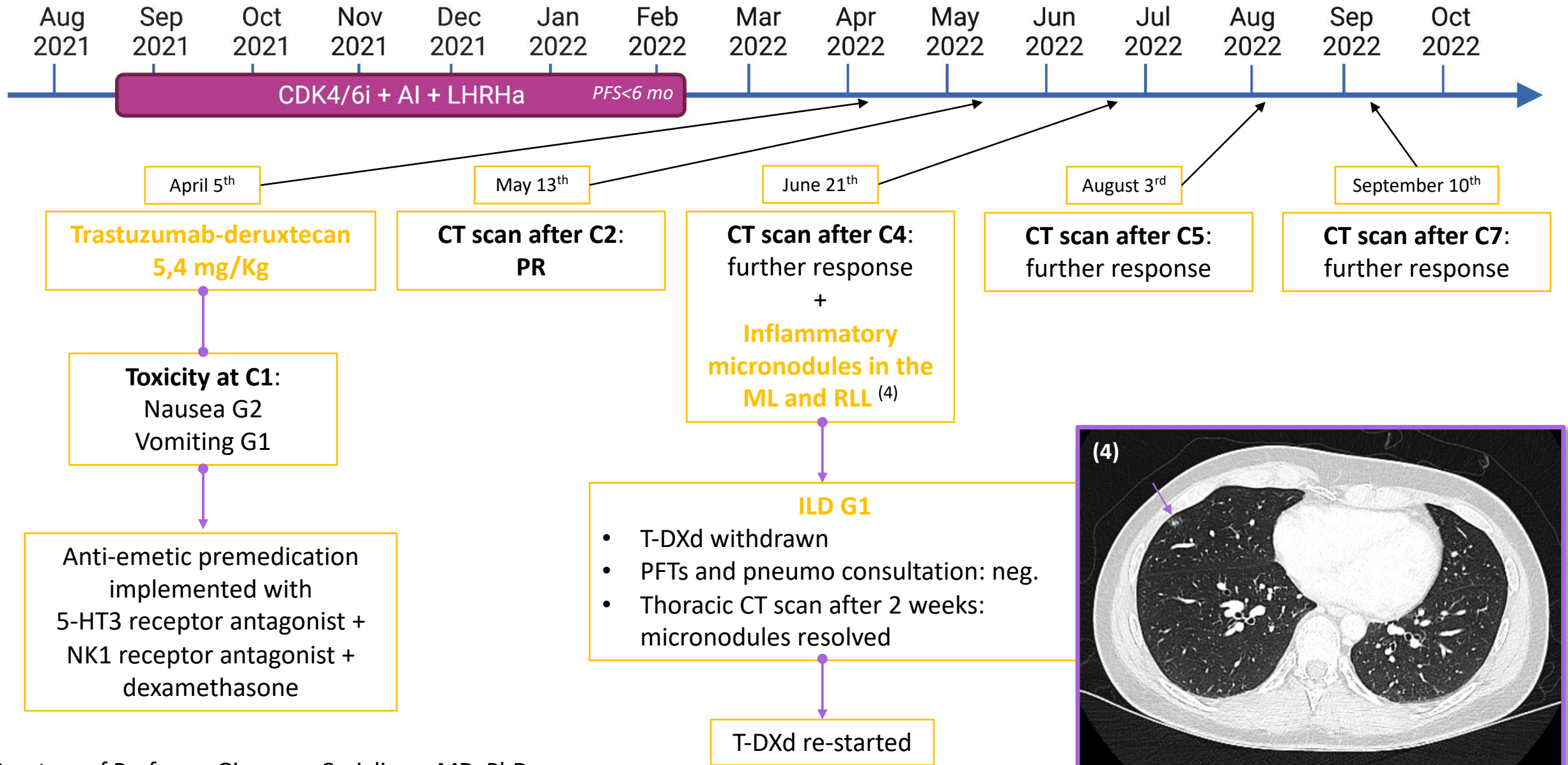


## 2. First line

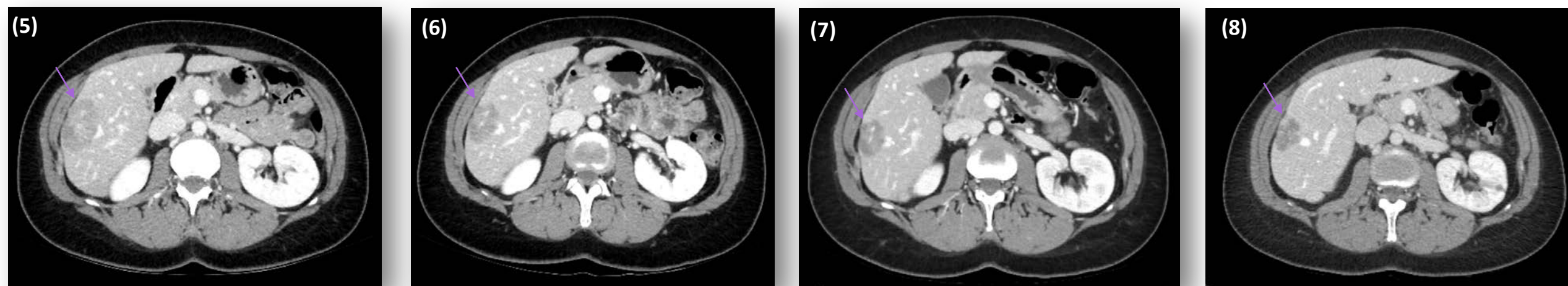
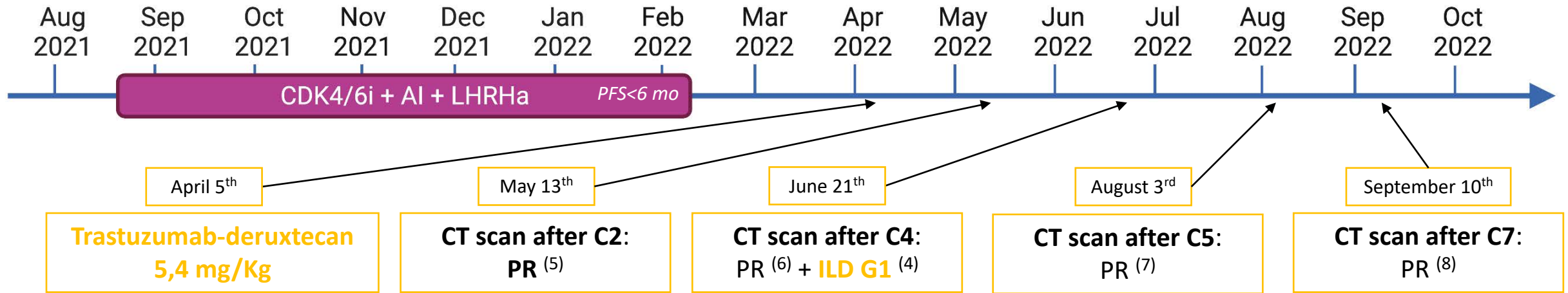




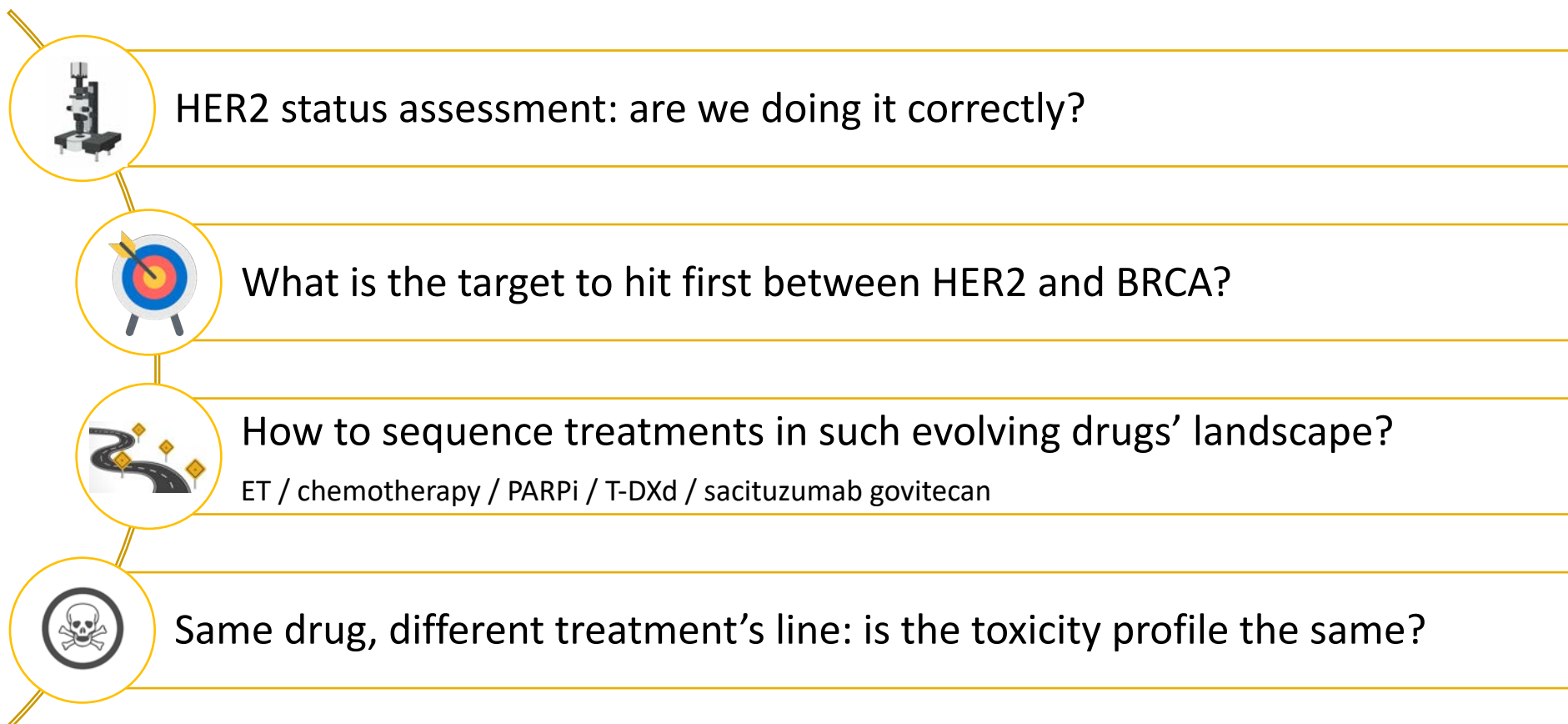
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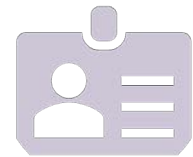
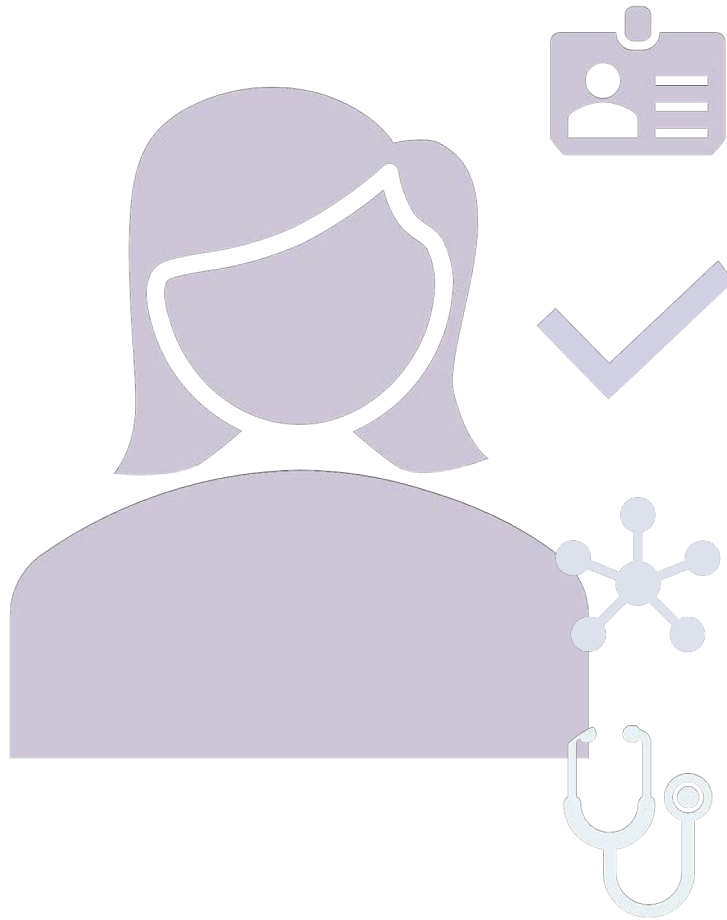
# 4. Points of discussion



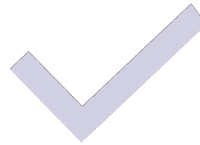
# Case 2



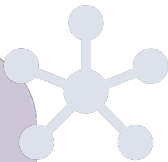
# The patient



MDP, 24 yrs old (pre-menopausal)



PS ECOG 0, 43 kg, 155 cm

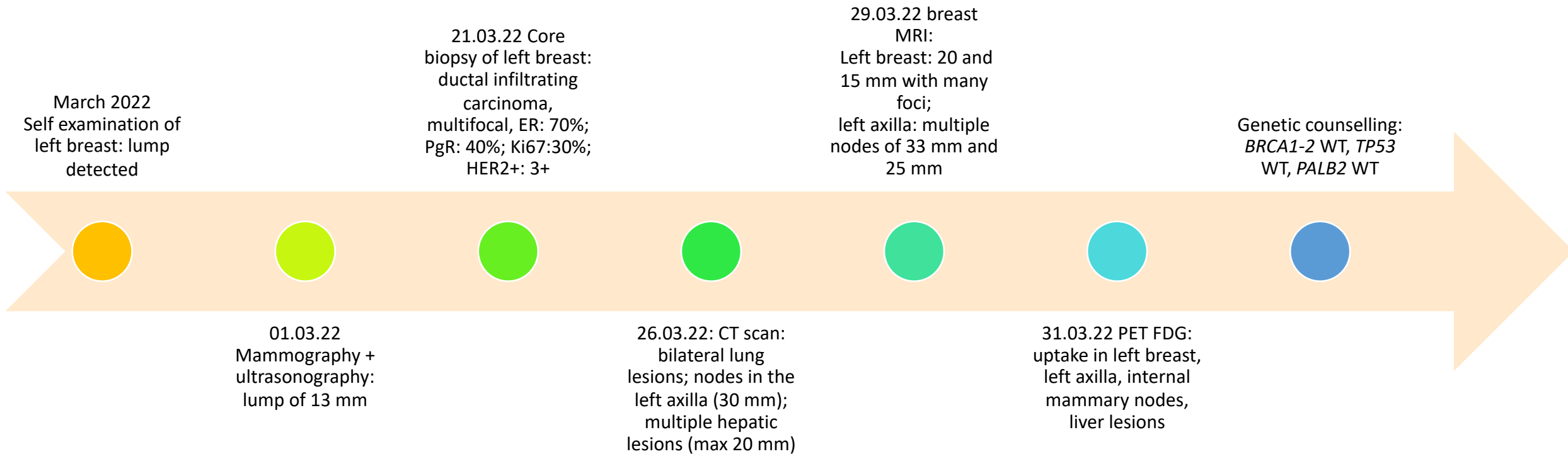


Familiarity: aunt (mother-side), aunt (father-side) with breast cancer



Former smoker, no comorbidities;  
previous fibroadenoma of left breast

# Diagnosis



# First line

- 15.04.22 signed informed consent to **DESTINY-Breast07**
- 22.04.22 Core biopsy left breast: ductal infiltrating carcinoma,  
ER: 90%; PgR: 0%; HER2: 3+
- 11.05.22 start Triptorelin 3.75 mg q4w
- 10.05.22 start Trastuzumab-Deruxtecan 5.4 mg/kg + Pertuzumab q3w

# Evaluation of response

	Left axilla (nodal)	Left breast lump	Liver (S4/S8)	Liver (S4)	Lung lesions (NT)
20.04.22	19	24	12	24	Present
16.06.22	9	13	7	9	Present
27.07.22	7	Not detectable	5	7	Present

10.05.22  
C1

31.05.22  
C2

21.06.22  
C3

12.07.22  
C4

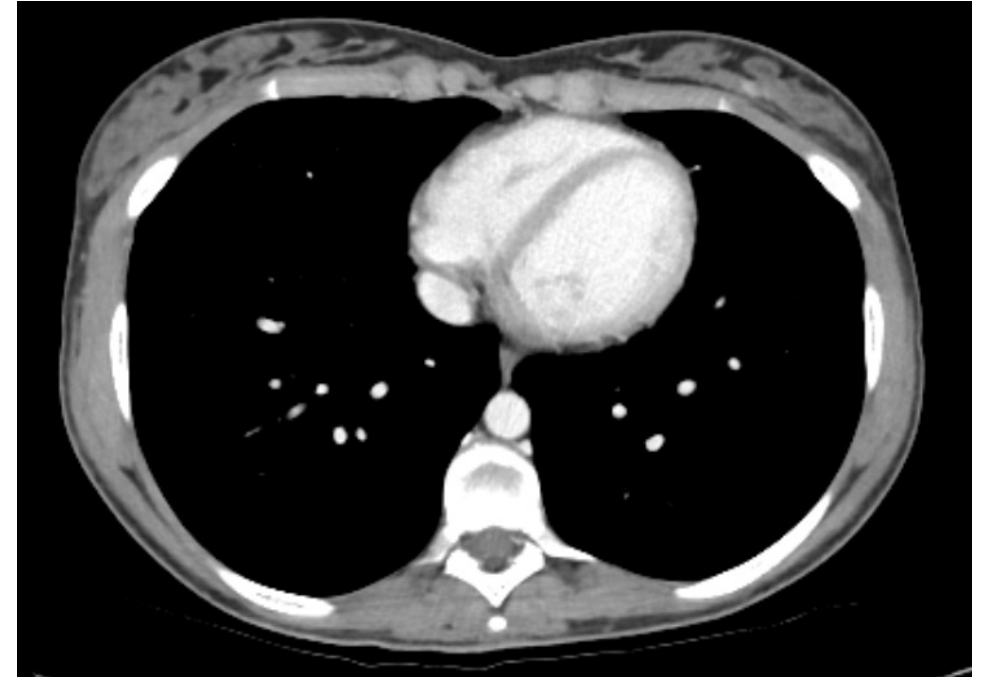
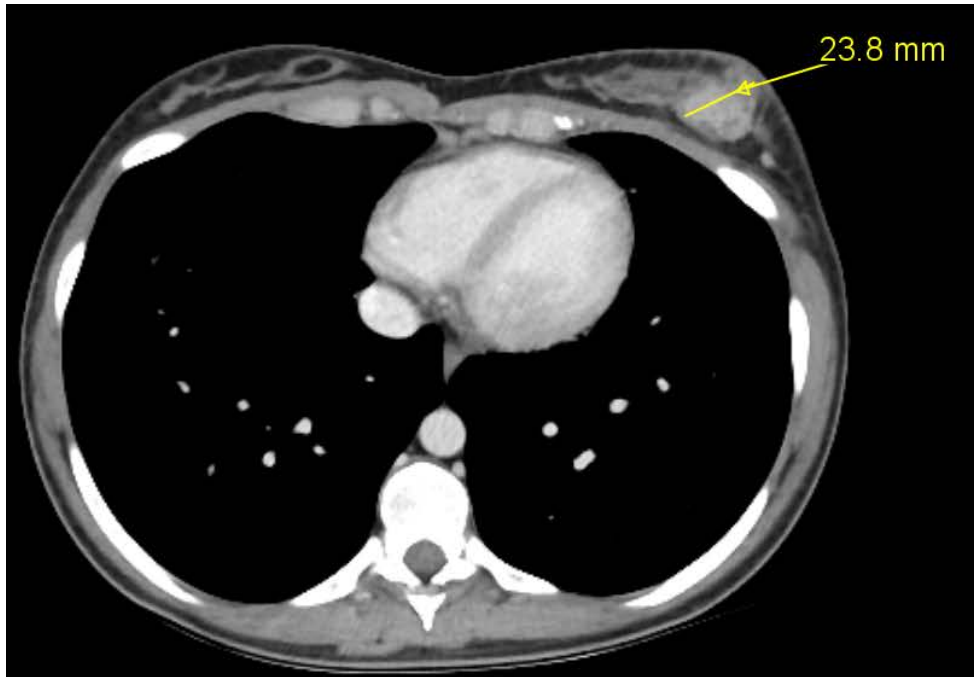
02.08.22  
C5



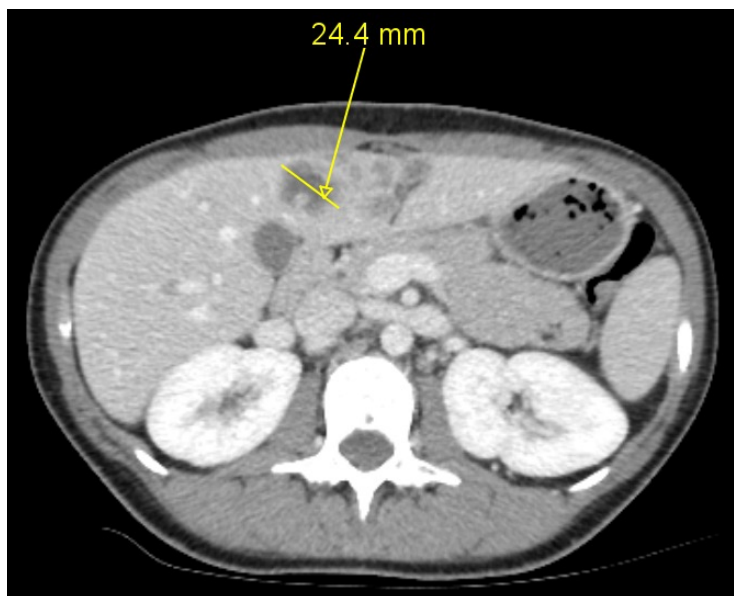
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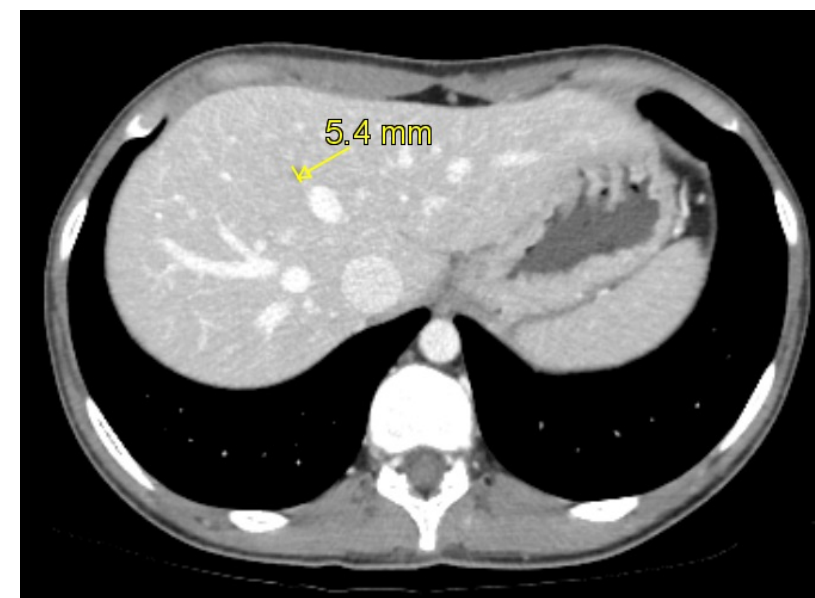
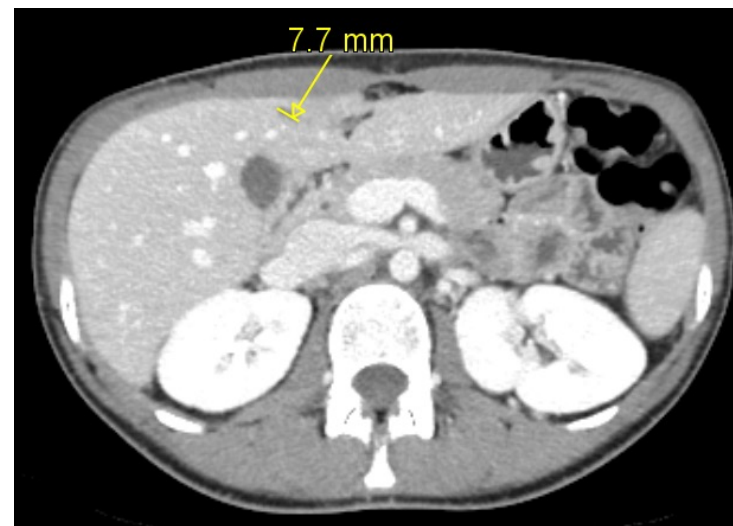
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20.04.22



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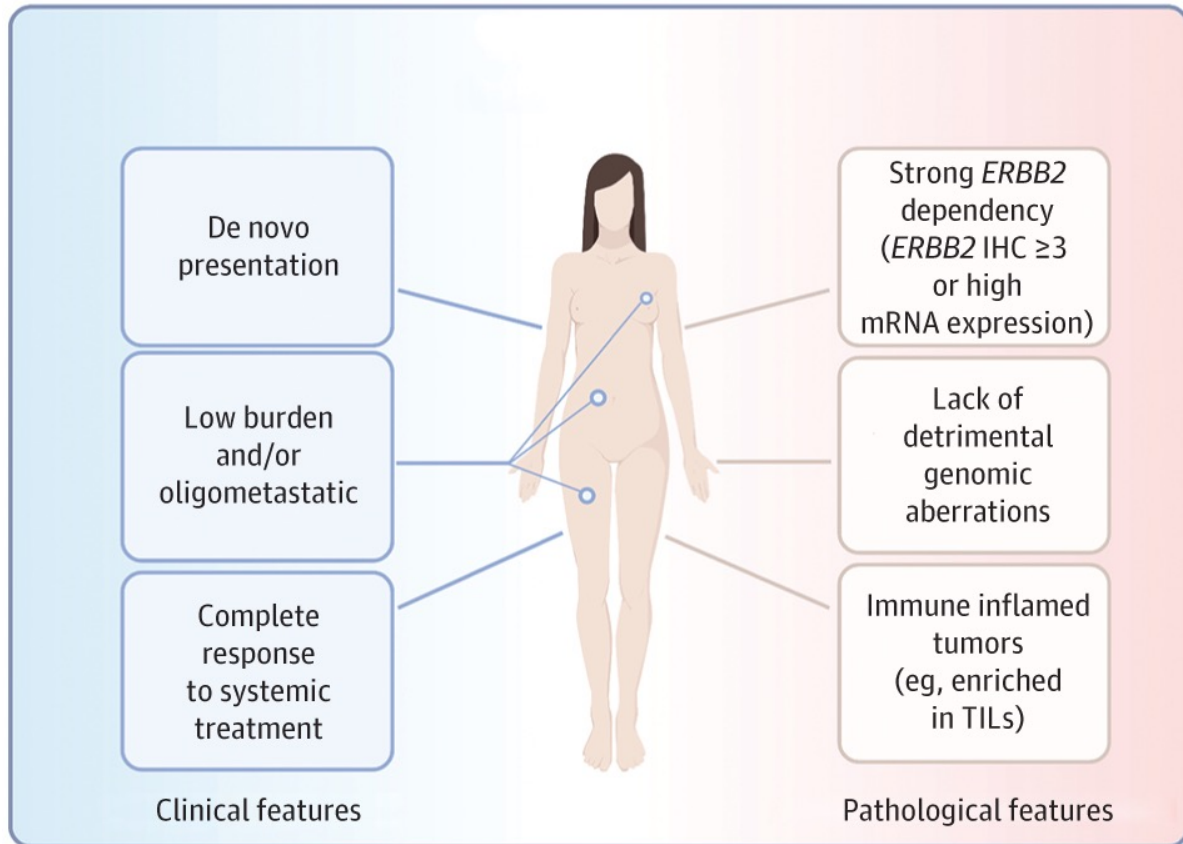


# Evaluation of response

The patient is currently on treatment, with partial response for RECIST 1.1 criteria

T-DXd + pertuzumab is well tolerated with only G1 AEs (anemia, leukopenia, neutropenia, alopecia)

# Discussion



Tarantino et al, JAMA 2022

- Clinical and pathologic features could identify patients with HER2+ MBC who are more likely to experience a long-lasting response to systemic treatment.
- This population may potentially derive benefit from a tailored escalation of frontline treatment with novel anti-HER2 drugs.
- The phase III DESTINY-Breast09 trial is currently testing T-DXd +/- pertuzumab vs standard of care (taxane, trastuzumab and pertuzumab)

# Agenda

## **INTRODUCTION**

**MODULE 1: HER2-positive metastatic breast cancer —  
Professor Giuseppe Curigliano, MD, PhD**

**MODULE 2: ASCO 2023 preview**

**An age-specific pooled analysis of trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-positive (HER2+) metastatic breast cancer (mBC) from DESTINY-Breast01, -02, and -03.**

Krop IE et al.

ASCO 2023;Abstract 1006.

**Dynamic HER2-low status among patients with triple negative breast cancer (TNBC): The impact of repeat biopsies.**

Bar Y et al.

ASCO 2023;Abstract 1005.

**A phase 2 study of HER3-DXd in patients (pts) with metastatic breast cancer (MBC).**

Hamilton EP et al.

ASCO 2023;Abstract 1004.

## **Phase III NATALEE trial of ribociclib + endocrine therapy as adjuvant treatment in patients with HR+/HER2– early breast cancer.**

Slamon DJ et al.

ASCO 2023;Abstract LBA500.

## **Efficacy and safety results by age in monarchE: Adjuvant abemaciclib combined with endocrine therapy (ET) in patients with HR+, HER2-, node-positive, high-risk early breast cancer (EBC).**

Hamilton EP et al.

ASCO 2023;Abstract 501.

# Effects of ovarian ablation or suppression on breast cancer recurrence and survival: Patient-level meta-analysis of 14,993 pre-menopausal women in 25 randomized trials.

Gray RG et al.

ASCO 2023;Abstract 503.

## **Discussion: Thinking Differently About Breast Cancer in Young Women**

Ines Maria Vaz Duarte Luis, MD, PhD | Gustave Roussy



## **Dynamics and type of ESR1 mutations under aromatase inhibitor or fulvestrant combined with palbociclib after randomization in the PADA-1 trial.**

Bidard FC et al.

ASCO 2023;Abstract 1002.

## **Detection of circulating tumor DNA following neoadjuvant chemotherapy and surgery to anticipate early relapse in ER positive and HER2 negative breast cancer: Analysis from the PENELOPE-B trial.**

Turner NC et al.

ASCO 2023;Abstract 502.

## **Randomized trial of fixed dose capecitabine compared to standard dose capecitabine in metastatic breast cancer: The X-7/7 trial.**

Khan QJ et al.

ASCO 2023;Abstract 1007.

# APPENDIX

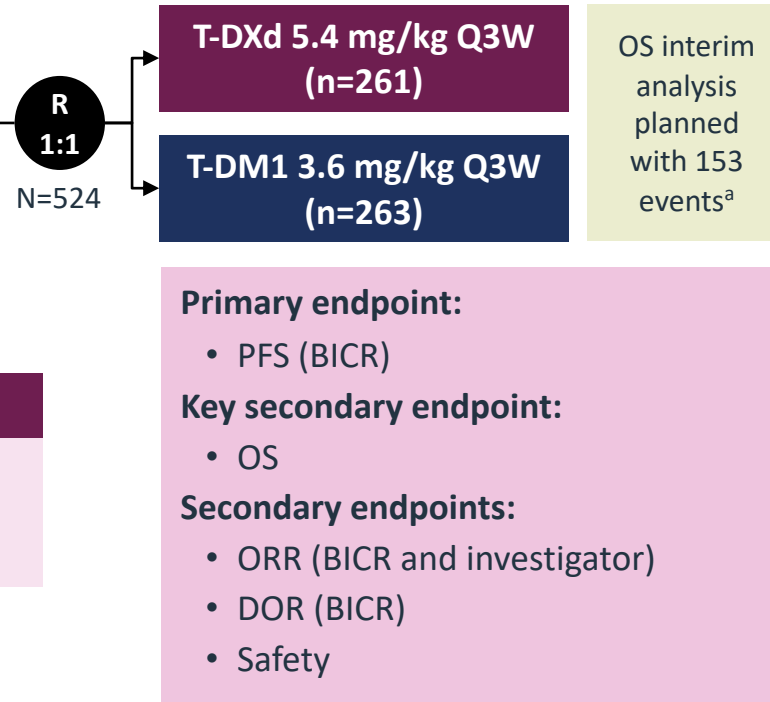
# DESTINY-Breast03 (Phase 3): Updated efficacy of T-DXd vs T-DM1 for patients with HER2+ metastatic BC

## Key eligibility

- Unresectable or metastatic HER2+ BC
- Previous treatment with trastuzumab and a taxane in metastatic or (neo)adjuvant setting with recurrence <6 months' treatment

## Stratification factors

- HR status
- Prior pertuzumab treatment
- History of visceral disease



## Patient disposition

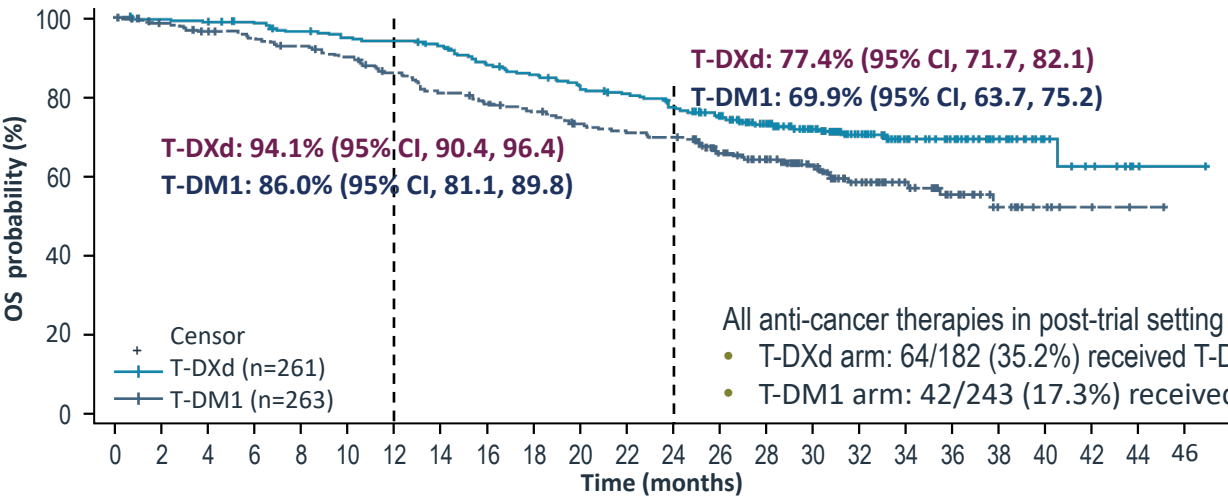
n (%)	T-DXd (n=261)	T-DM1 (n=263)
Randomized but not treated	4 (2)	2 (10)
Treatment status		
Ongoing	75 (29)	18 (7)
Discontinued	182 (71)	243 (93)
Primary reason for discontinuation		
PD	94 (37)	178 (68)
AE	54 (21)	21 (8)
Clinical progression	5 (2)	14 (5)
Death	4 (2)	4 (2)
Patient withdrawal	17 (7)	12 (5)
Physician discretion	2 (1)	8 (3)
Other	6 (2)	6 (2)

<sup>a</sup>At data cutoff (July 2022), 169 OS events had been observed and p-value for statistical significance was 0.013.

BICR, blinded independent central review; DOR, duration of response; PD, progressive disease; T-DXd, trastuzumab deruxtecan; T-DM1, ado-trastuzumab emtansine.












Hurvitz SA, et al. SABCS 2022. Abstract GS2-02


# DESTINY-Breast03 (Phase 3): Updated OS (secondary endpoint) with T-DXd vs T-DM1 for patients with HER2+ metastatic BC



	T-DXd	T-DM1
Median OS (95% CI), months	NR (40.5, NE)	NR (34.0, NE)
HR (95% CI); P-value	0.64 (0.47, 0.87): 0.0037	

## Subgroup OS analysis

		Events, n/N		Median OS, months (95% CI)		HR (95% CI)	
		T-DXd	T-DM1	T-DXd	T-DM1		
All patients		72/261	97/263	NR (40.5, NE)	NR (34.0, NE)		0.64 (0.47, 0.87)
HR status	+ (n=272)	42/133	51/139	NR (NE, NE)	37.7 (34.0, NE)		0.76 (0.50, 1.14)
	– (n=248)	30/126	45/122	NR (40.5, NE)	NR (28.5, NE)		0.55 (0.35, 0.87)
Prior pertuzumab	Yes (n=320)	41/162	50/158	NR (40.5, NE)	NR (37.7, NE)		0.70 (0.46, 1.06)
	No (n=204)	31/99	47/105	NR (NE, NE)	31.5 (22.7, NE)		0.59 (0.38, 0.93)
Baseline visceral disease	Yes (n=384)	64/195	80/189	NR (40.5, NE)	35.4 (29.9, NE)		0.68 (0.49, 0.95)
	No (n=140)	8/66	17/74	NR (NE, NE)	NR (NE, NE)		0.44 (0.19, 1.02)
Prior lines of systemic therapy	<3 (n=379)	44/188	57/191	NR (40.5, NE)	NR (37.7, NE)		0.70 (0.47, 1.04)
	≥3 (n=145)	28/73	40/72	NR (27.4, NE)	22.8 (16.1, 31.5)		0.55 (0.34, 0.89)
Baseline brain metastases	Yes (n=82)	17/43	22/39	NR (23.8, NE)	25.1 (12.6, NE)		0.54 (0.29, 1.03)
	No (n=442)	55/218	75/224	NR (40.5, NE)	NR (37.7, NE)		0.66 (0.47, 0.94)



### Median study follow-up:

- T-DXd: 28.4 months (range, 0.1–46.9)
- T-DM1: 26.5 months (range, 0.0–45.0)

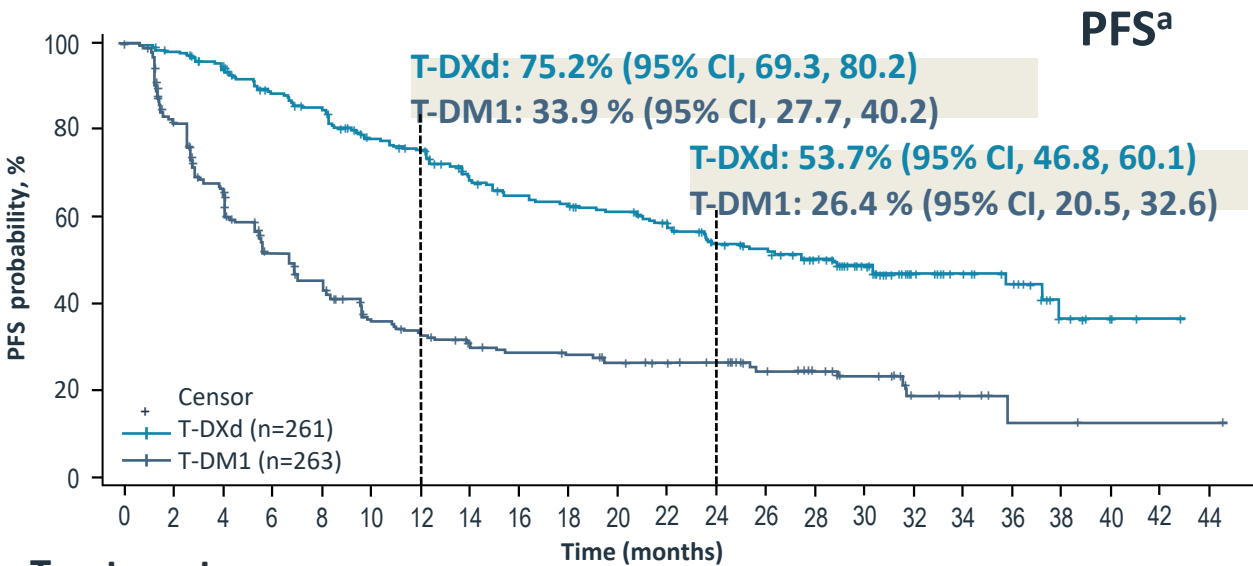
Prespecified OS interim analysis was planned with 153 events

- At data cutoff (July 2022), 169 OS events had occurred

T-DXd, trastuzumab deruxtecan; T-DM1, ado-trastuzumab emtansine.

Hurvitz SA, et al. SABCS 2022. Abstract GS2-02

# DESTINY-Breast03 (Phase 3): Updated PFS<sup>a</sup> (primary endpoint) and response with T-DXd vs T-DM1 for patients with HER2+ metastatic BC



	T-DXd	T-DM1
Median PFS (95% CI), months	28.8 (22.4, 37.9)	6.8 (5.6, 8.2)
HR (95% CI); P-value	0.33 (0.26, 0.43): <0.000001	

• mPFS was x4 longer for T-DXd compared with T-DM1

## Treatment response

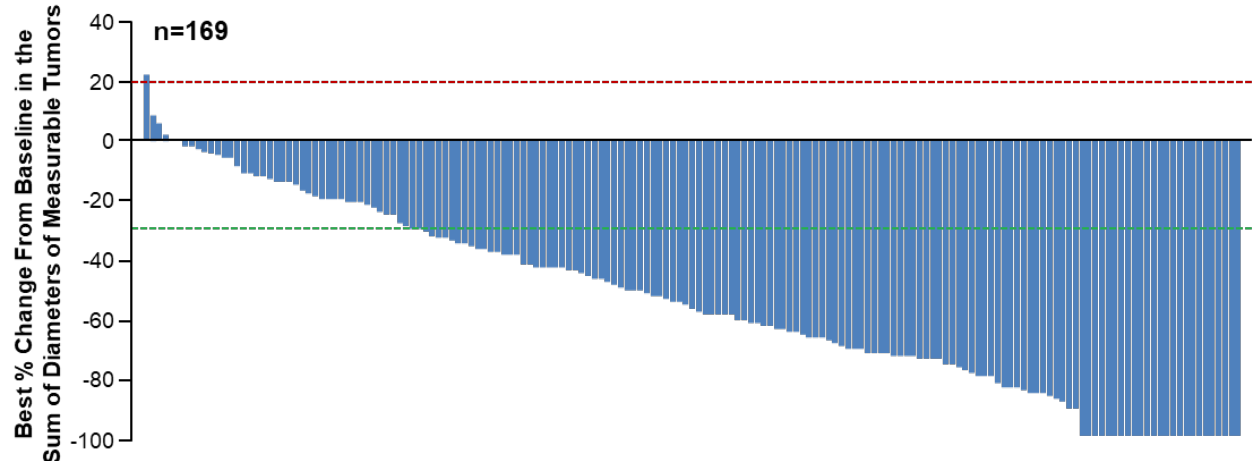
	T-DXd (n=261) <sup>b</sup>	T-DM1 (n=263) <sup>b</sup>
ORR <sup>a</sup> , n (%) [95% CI]; nominal P-value	205 (78.5) [73.1, 83.4]; <0.0001	92 (35.0) [29.2, 41.1]
CR, n (%)	55 (21.1)	25 (9.5)
PR, n (%)	150 (57.5)	67 (25.5)
SD, n (%)	47 (18.0)	110 (41.8)
PD, n (%)	3 (1.1)	47 (17.9)
NE, n (%)	6 (2.3)	14 (5.3)
CBR, n (%) [95% CI]; nominal P-value	233 (89.3) [84.9, 92.8]; <0.0001	122 (46.4) [40.2, 52.6]
mDOR <sup>a</sup> , months [95% CI]	36.6 (2.4, NE)	23.8 (12.6, 34.7)

<sup>a</sup>By BICR. <sup>b</sup>Only patients with measurable disease at baseline and ≥1 postbaseline target lesion assessment were included. CBR, clinical benefit rate; CR, complete response; DOR, duration of response; ORR, objective response rate; NE, not evaluable. PD, progressive disease; PR, partial response. T-DXd, trastuzumab deruxtecan; T-DM1, ado-trastuzumab emtansine; SD, stable disease. Hurvitz SA, et al. SABCS 2022. Abstract GS2-02

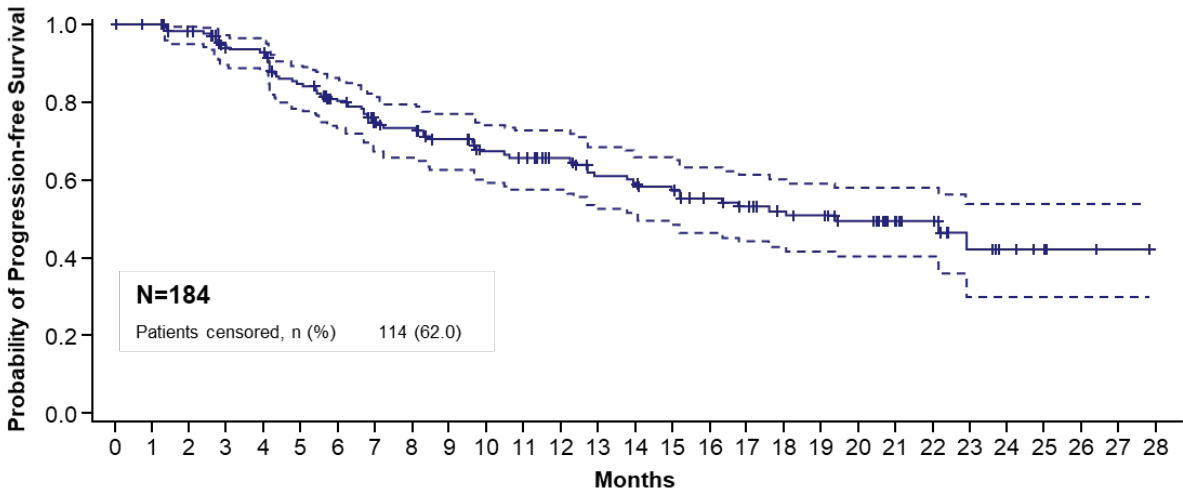
# Trastuzumab-Deruxtecan: DESTINY-Breast01

## Phase II study

ORR



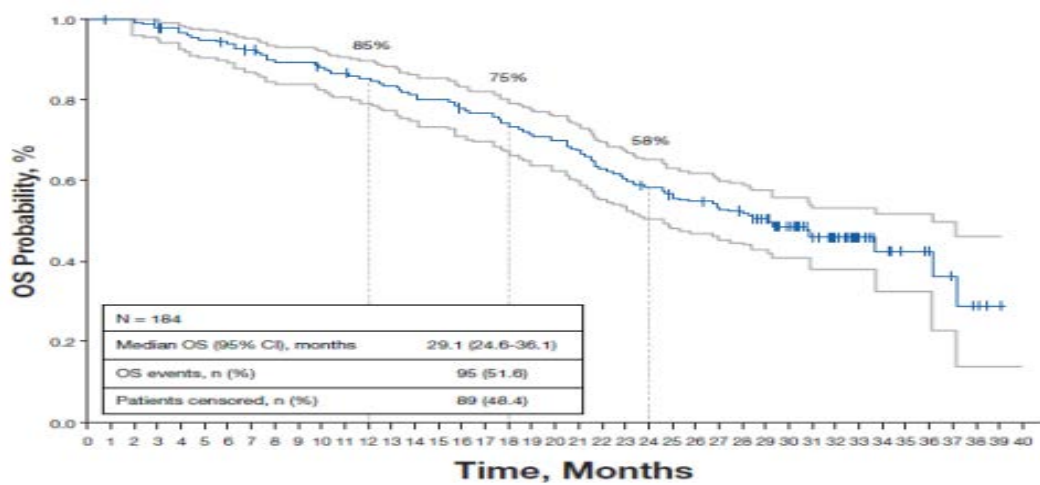
mPFS: 19.4 months



### Intent-to-treat analysis

	August 2019 DCO T-DXd 5.4 mg/kg (N=184)	June 2020 DCO T-DXd 5.4 mg/kg (N=184)	March 2021 DCO T-DXd 5.4 mg/kg (N=184)
Median duration of follow up (range), months	11.1 (0.7-19.9)	20.5 (0.7-31.4)	26.5 (0.7-39.1)
Patients remaining on treatment, n (%)	79 (42.9)	37 (20.1)	28 (15.2)
Confirmed ORR <sup>a</sup> by ICR, n (%)	112 (60.9)	113 <sup>b</sup> (61.4)	114 (62.0)
95% CI	53.4-68.0	54.0-68.5	54.5-69.0
CR	11 (6.0)	12 (6.5)	13 (7.1)
PR	101 (54.9)	101 (54.9)	101 (54.9)
SD	67 (36.4)	66 (35.9)	65 (35.3)
PD	3 (1.6)	3 (1.6)	3 (1.6)
Not evaluable	2 (1.1)	2 (1.1)	2 (1.1)
Median DOR (95% CI), months	14.8 (13.8-16.9)	20.8 <sup>b</sup> (15.0-NE)	18.2 (15.0-NE)
Median time to response (95% CI), months	1.6 (1.4-2.7)	1.6 (1.4-2.7)	1.6 (1.4-2.7)
Median PFS (95% CI), months	16.4 (12.7-NE)	19.4 (14.1-NE)	19.4 (14.1-25.0)
Median OS (95% CI), months	NE (NE-NE)	24.6 (23.1-NE)	29.1 (24.6-36.1)

mOS: 29.1 months



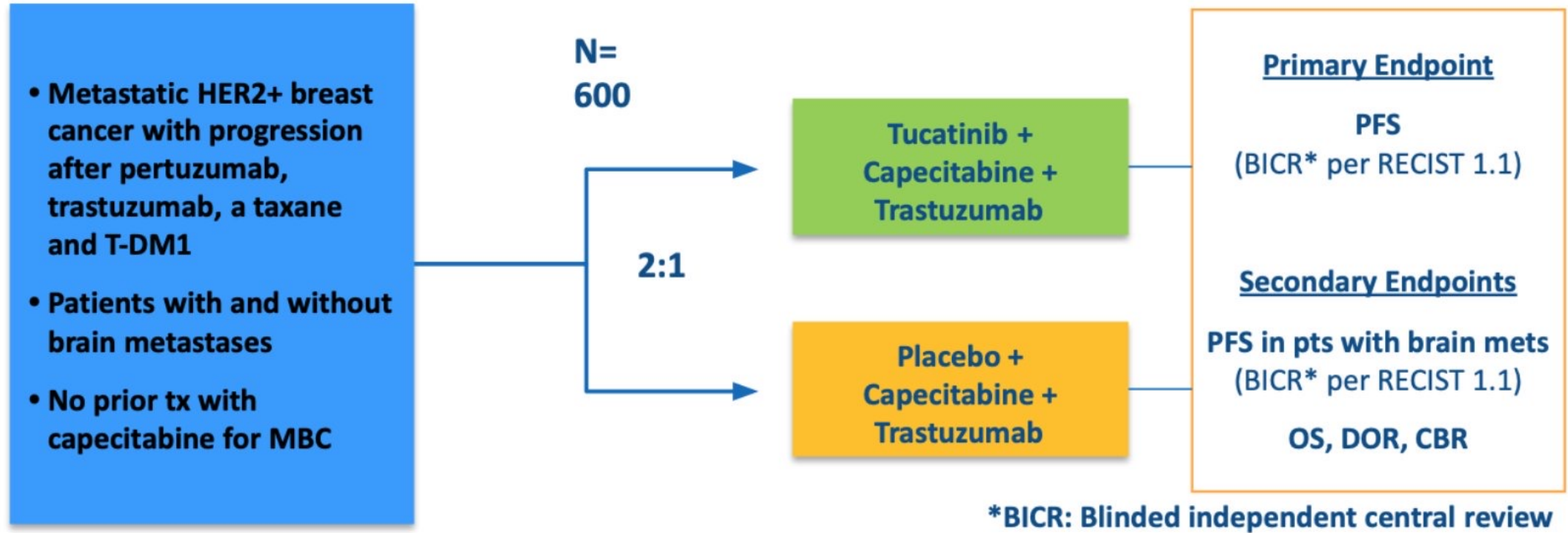
# Adverse Events of Special Interest: Interstitial Lung Disease

Interstitial Lung Disease, n (%) <sup>a</sup>	August 2019 DCO T-DXd 5.4 mg/kg (N=184)	June 2020 DCO T-DXd 5.4 mg/kg (N=184)	March 2021 DCO T-DXd 5.4 mg/kg (N=184)
Grade 1	5 (2.7)	6 (3.3)	7 (3.8)
Grade 2	15 (8.2)	16 (8.7)	16 (8.7)
Grade 3	1 (0.5)	1 (0.5)	1 (0.5)
Grade 4	0	0	0
Grade 5	4 (2.2)	5 (2.7)	5 (2.7)
<b>Any grade/total</b>	<b>25 (13.6)</b>	<b>28 (15.2)</b>	<b>29 (15.8)</b>

Median time from the first infusion of T-DXd to onset of ILD was 27.6 weeks (range, 6-76 weeks)

ILD, interstitial lung disease.

# HER2CLIMB trial: tucatinib, trastuzumab, capecitabine

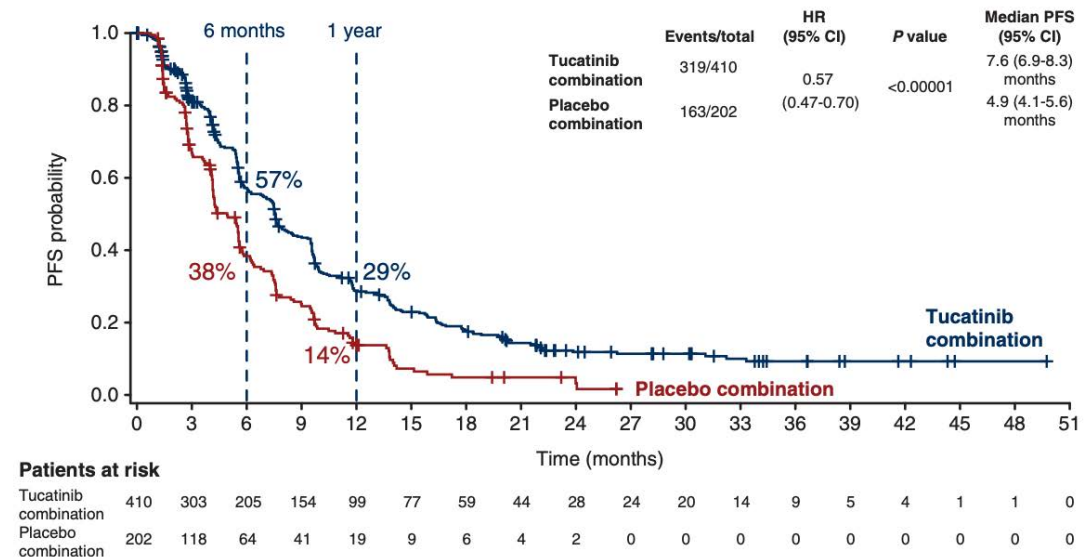
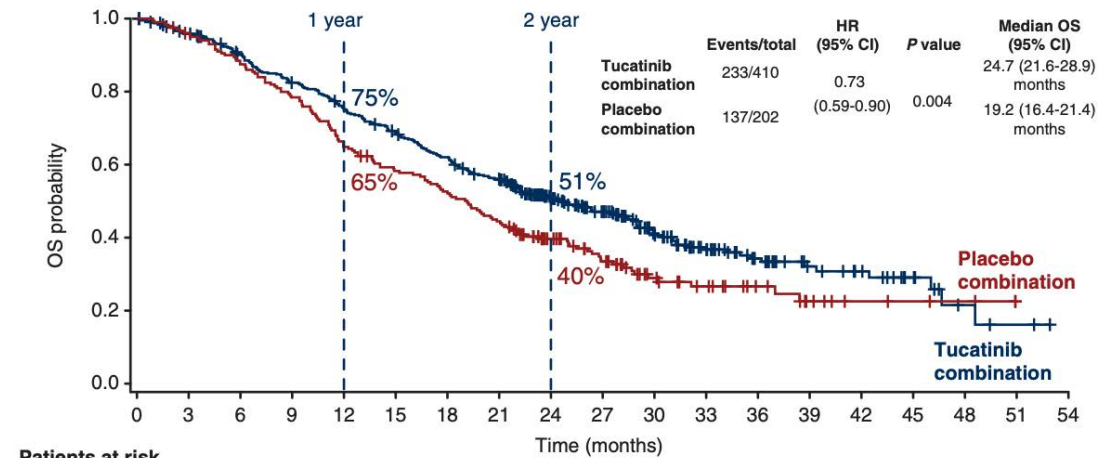




# HER2CLIMB trial: tucatinib, trastuzumab, capecitabine

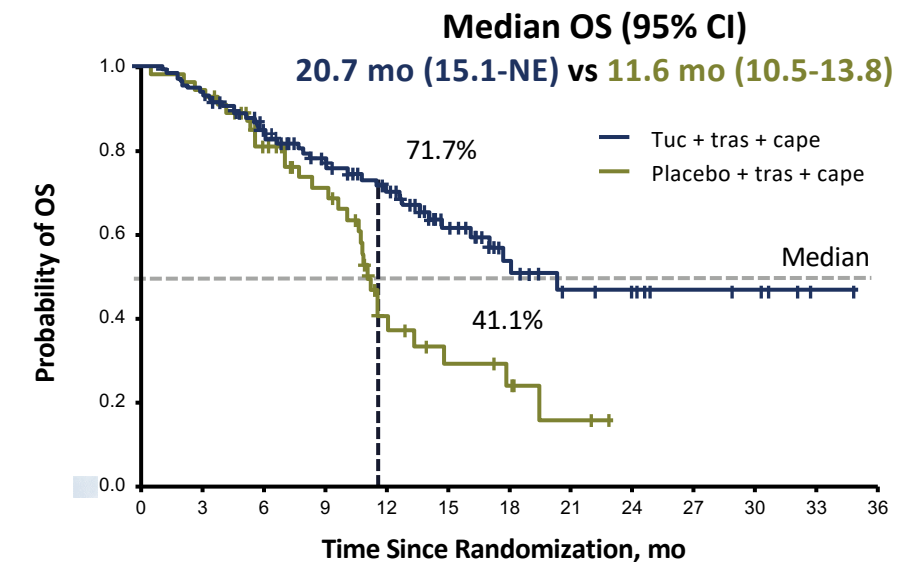
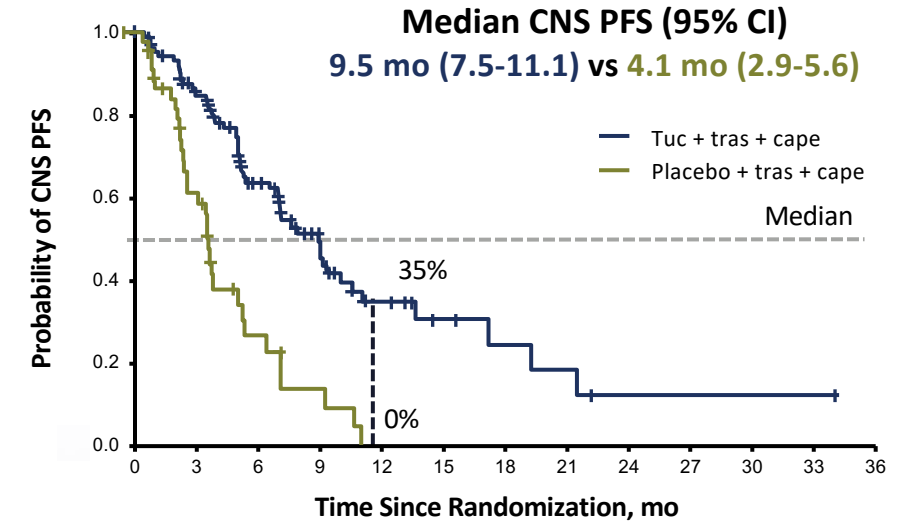
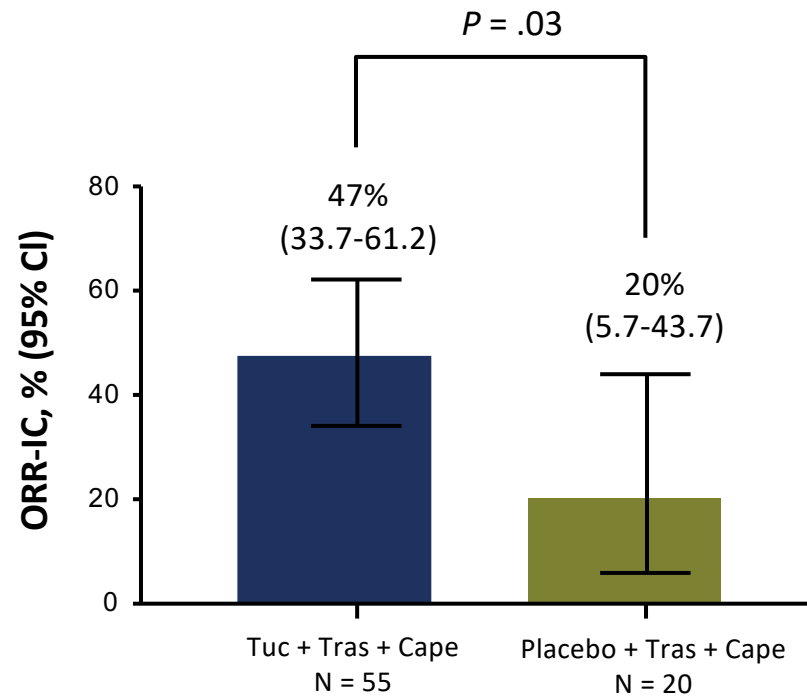
**Improved PFS** at 1 year: 29% vs 14%  
(HR, 0.54; P<0.001)

**Improved OS** at 2 years: 51% vs 40%  
(HR, 0.73, p=0.004)



# HER2CLIMB trial: relevant intracranial activity

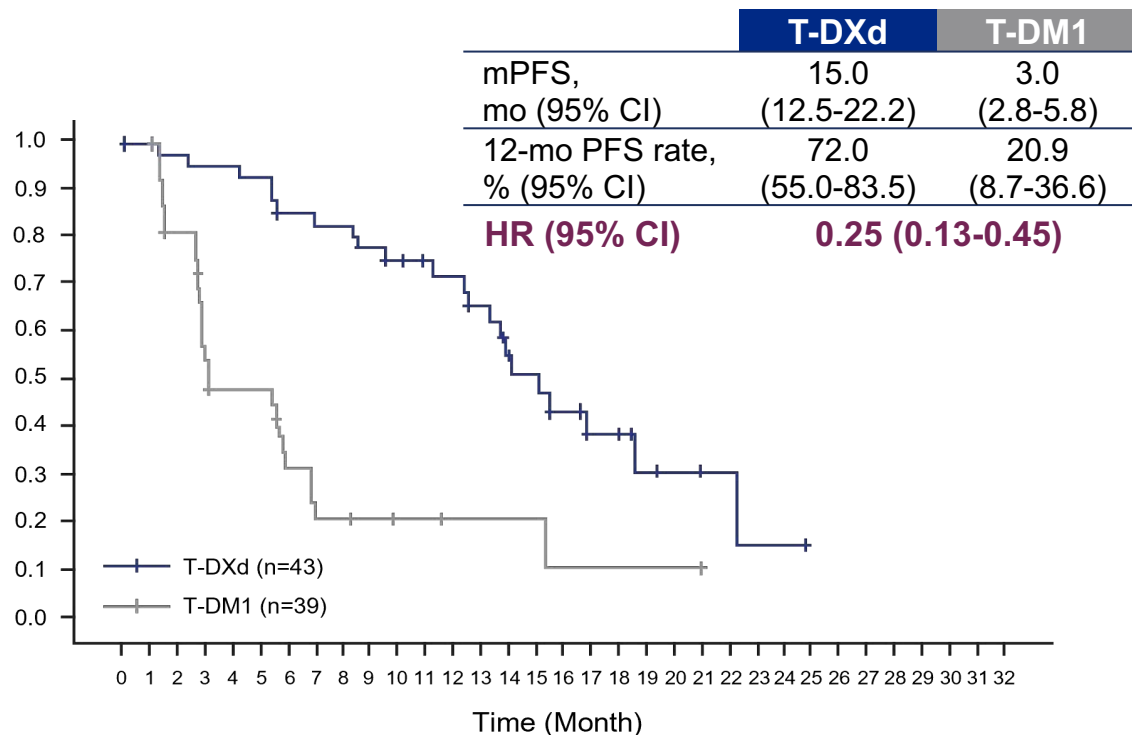
## Confirmed ORR (RECIST 1.1)



# DESTINY-Breast03: PFS KM Curves for Patients With and Without BM

## Brain Metastases at Baseline

Progression-Free Survival Probability, %



Patients Still at Risk:

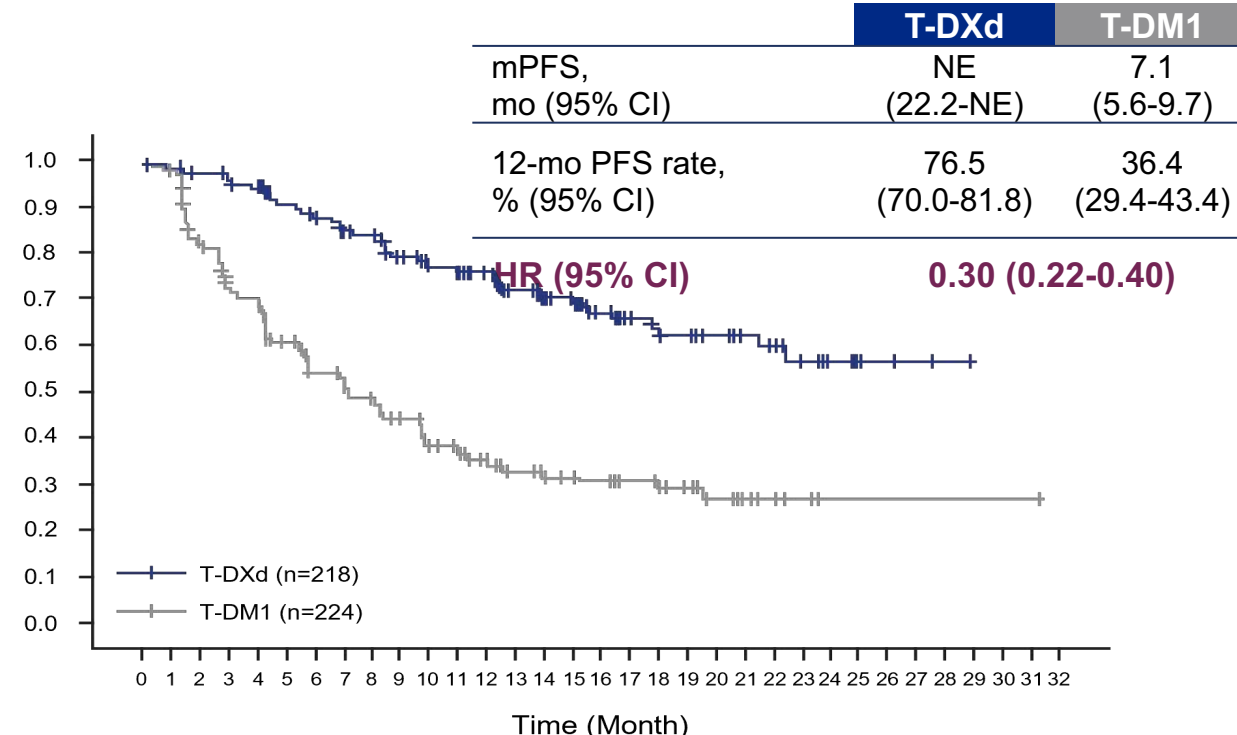
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
<b>T-DXd (43)</b>	43	41	40	39	38	38	34	33	33	29	26	24	23	20	14	13	10	7	6	4	3	2	2	1	1	0	0	0	0	0	0	0	0
<b>T-DM1 (39)</b>	39	38	28	17	15	9	6	6	5	3	3	2	2	2	2	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0

### In patients with BM at baseline, PD was observed:

- In 48.8% (21/43) treated with T-DXd versus 69.2% (27/39) with T-DM1
- In the brain in 42.9% (9/21) treated with T-DXd versus 40.7% (11/27) with T-DM1

## No Brain Metastases at Baseline

Progression-Free Survival Probability, %



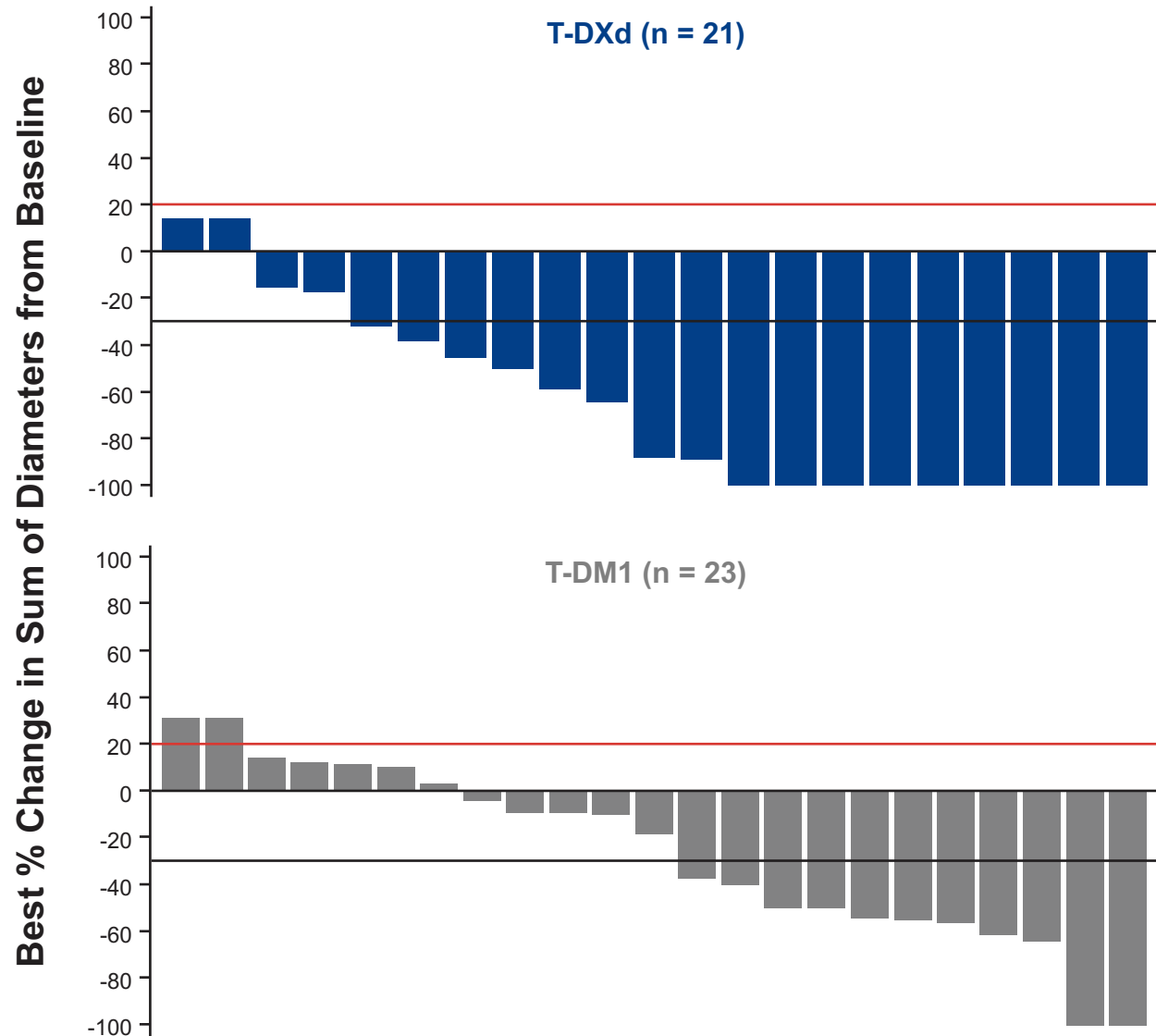
Patients Still at Risk:

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32
<b>T-DXd (218)</b>	218	215	210	205	201	186	180	169	167	154	142	140	127	112	98	92	69	57	47	41	33	27	23	18	9	6	5	3	2	0	0	0	0
<b>T-DM1 (224)</b>	224	214	172	146	140	117	99	90	87	73	62	57	49	41	35	32	28	22	20	15	11	8	6	4	1	1	1	1	1	1	1	1	0

### In patients without BM at baseline, PD was observed:

- In 28.9% (63/218) treated with T-DXd versus 57.1% (128/224) with T-DM1
- In the brain in 6.3% (4/63) treated with T-DXd versus 0.8% (1/128) with T-DM1

# Intracranial Response per BICR using RECIST 1.1



	T-DXd (n = 36)	T-DM1 (n = 36)
<b>Best Overall Response, n (%)<sup>a</sup></b>		
CR	10 (27.8)	1 (2.8)
PR	13 (36.1)	11 (30.6)
Non-CR/non-PD	6 (16.7)	7 (19.4)
SD	4 (11.1)	7 (19.4)
PD	1 (2.8)	8 (22.2)
Not evaluable	0	1 (2.8)
Missing	2 (5.6)	1 (2.8)

CR, complete response; DCR, disease control rate; mDOR, median duration of response; PD, progressive disease; PR, partial response; SD, stable disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

Table includes target and non-target lesions. Only patients with target lesion assessments are eligible for inclusion in waterfall.

Red line at 20% indicates progressive disease; black line at -30% indicates partial response.

<sup>a</sup>Denominator for percentages is the number of subjects in the full analysis set with brain metastases tumor assessment

HER2CLIMB-05 (NCT05132582) is a phase 3, randomized, double-blind study evaluating tucatinib plus T+P as maintenance therapy for HER2+ MBC. Approximately 650 pts will be enrolled.

DESTINY-Breast07 will investigate the safety, tolerability, and anti-tumour activity of trastuzumab deruxtecan (T-DXd) in combination with other anti-cancer agents in patients with HER2-positive Metastatic Breast Cancer. The study will assign patients to different treatment combinations.

Phase III Study of Trastuzumab Deruxtecan (T-DXd) With or Without Pertuzumab Versus Taxane, Trastuzumab and Pertuzumab in HER2-positive, First-line Metastatic Breast Cancer (DESTINY-Breast09)

DESTINY-Breast12 is a Phase IIIb/IV study seeking to better understand the treatment benefit of trastuzumab deruxtecan (T-DXd) in adult patients with or without brain metastases who have unresectable/advanced or metastatic HER2-positive breast cancer.

# ***Meet The Professor***

## **Optimizing the Management of Colorectal Cancer**

**Thursday, May 18, 2023  
5:00 PM – 6:00 PM ET**

**Faculty**

**Michael J Overman, MD**

**Moderator**

**Neil Love, MD**

***Thank you for joining us!***

***Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open up to 5 minutes after the meeting ends.***

***CME and MOC credit information will be emailed to each participant within 5 business days.***