Approaching Metastatic Triple-Negative Breast Cancer (TNBC)

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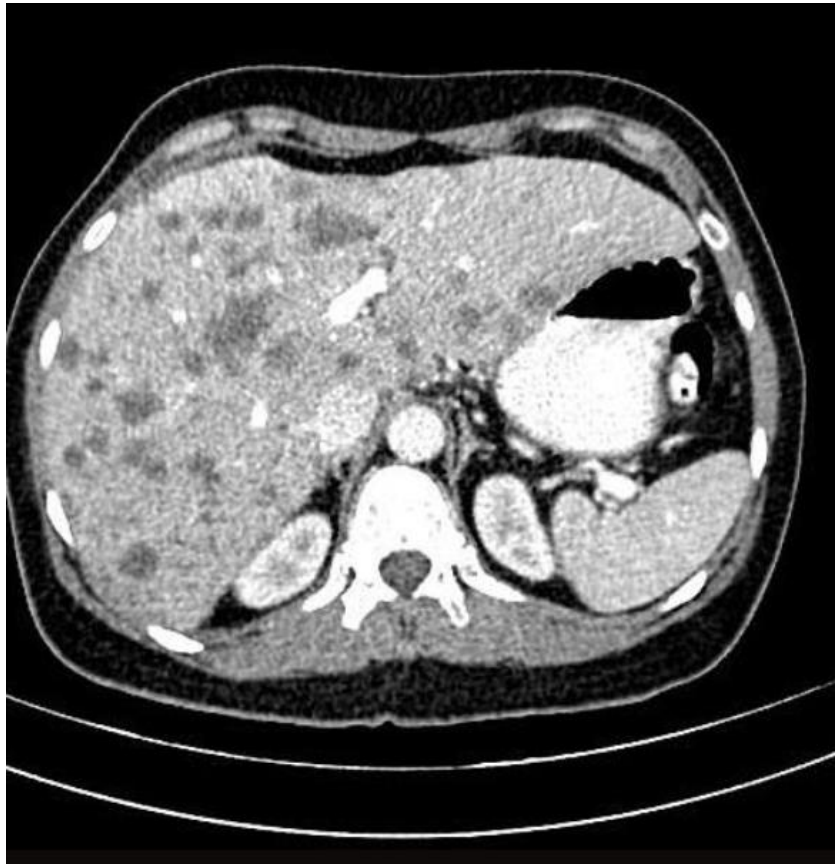
First, a case

56 year-old female

- Initial diagnosis **February 2023** with a cT2N(+) right breast TNBC
  - Neoadjuvant treatment: CT → AC + Pembrolizumab (**end September 2023**)
  - At surgery: ypT1miN0M0
  - Adjuvant treatment: Pembrolizumab x9 cycles (**end June 2024**)
- Clinical follow-up → Jaundice 1 month ago
  - Treatment-free interval: **17m (from chemo) or 8m (from pembro)**
  - EOD: Multiple hepatic metastases, bone metastases, para-aortic and mediastinal adenopathy; subcm pulmonary lesions



Questions

- What is the natural history of TNBC?
- Should she have gotten more adjuvant treatment?
- Should we have followed ctDNA?
- Is there a role for biopsy? What about NGS?
- What are her options now?

Epidemiology

- DEFINITION: Tumors that are ER, PR and HER2 negative
  - ER expression <1% by IHC
    - <10% sometimes included
- 15% of all breast cancers
  - More common in younger ages
    - Age <40 is at 2x higher risk vs age >50
  - **Up to 20% associated with mBRCA**

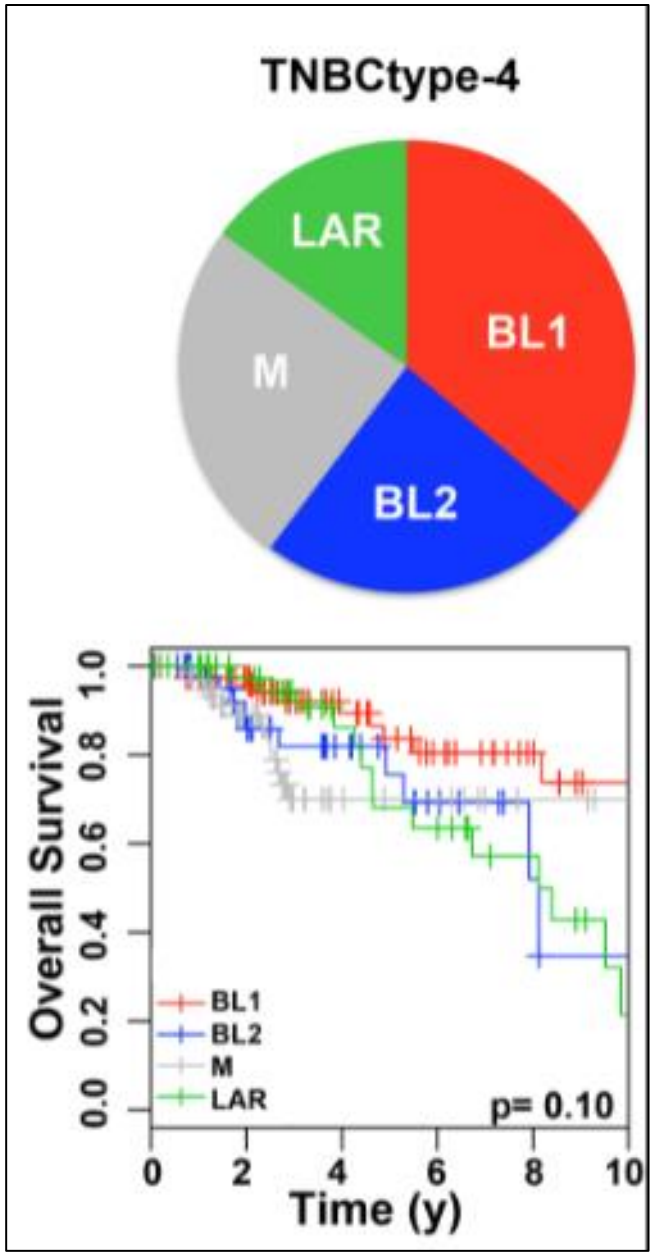
Epidemiology

- Global prevalence:
  - Two times more common in Black women
    - West African ancestry and Ghanian women have high prevalence (34 and 51%, respectively)
  - Limited data in Bangladesh, but suggests >20% prevalence

Bhattacharjee, Hossain, Yeasmin, and Akter. Delta Med J 2018; 6https://doi.org/10.3329/dmcj.v6i1.35962

TNBC: Molecular Subtypes

Subtype	TNBC %	Clinical observations
Basal-like 1 (BL1)	35%	- Associated with best prognosis - High response rate to NAC
Basal-like 2 (BL2)	22%	- Worst survival outcomes noted (median OS, 2.4y)
Mesenchymal (M)	25%	- Highest rate of lung metastases (46%) - Lacks lymphocytic infiltration
Luminal androgen receptor (LAR)	16%	- Lower grade tumors - Highest frequency of N+ disease - Highest rate of bone mets (46%) - Nearly all were ILC

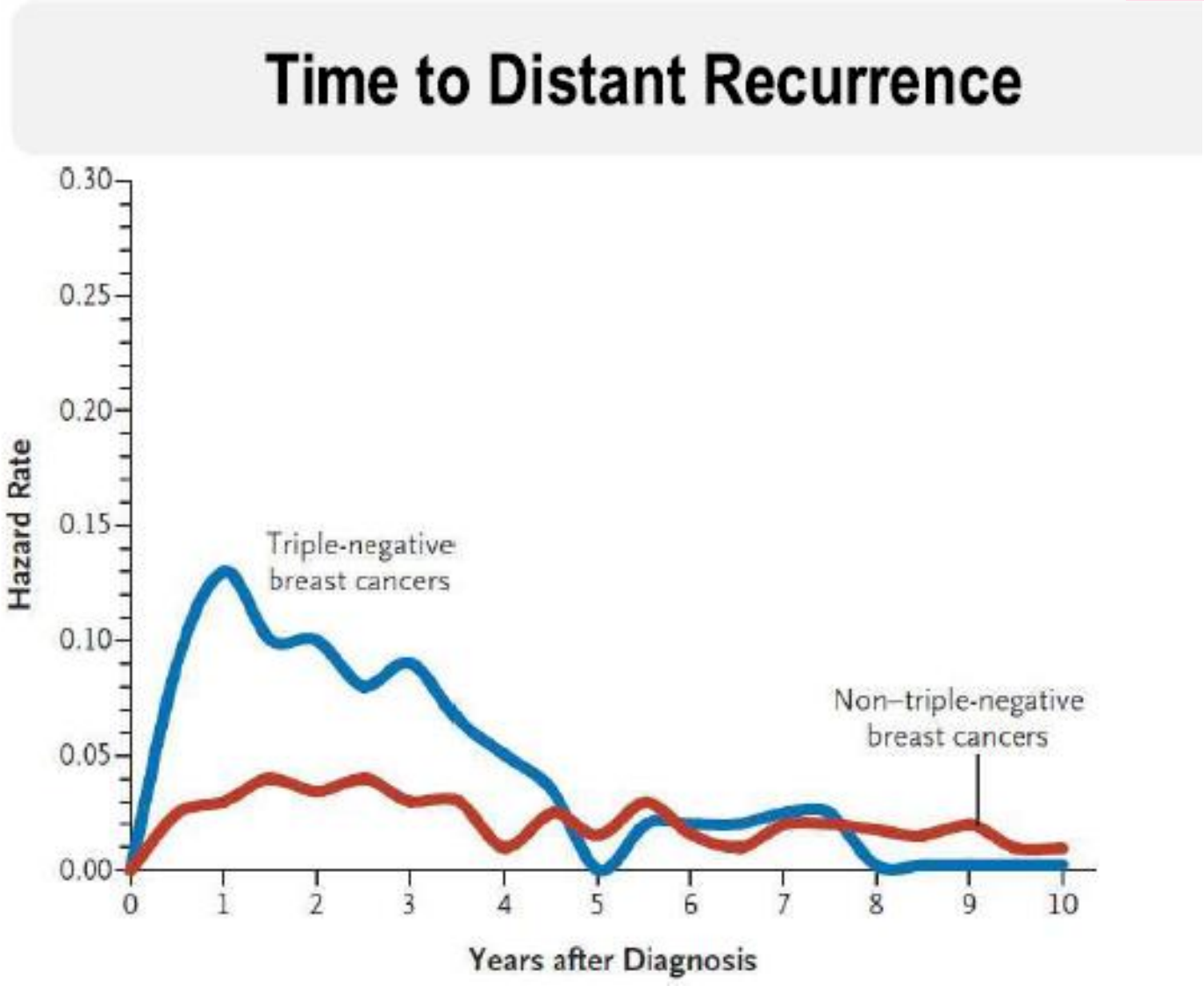


Lehmann BD, Jovanović B, Chen X, et al. PLoS One 2016; 11:e0157368

TNBC is associated with earlier relapse

Mean time to **distant recurrence:**

- TNBC → 2.4y
- HR+ → 4.4y



Dent R, et al. Clin CA Res 2007; 13:4429-34; Gaedcke J, et al. Mod Pathol 2007; 20:864-70;
Foulkes WD, et al. New Engl J Med 2010; 363:1938-48; Nofech-Mozes, et al. Breast Ca Res Treat 2009; 118:131-37.

IMPROVING OUTCOMES IN TNBC

Approach to residual disease (RD) after NACT

Managing residual disease: Capecitabine

Trial	Volunteers	Intervention	Comparator	Outcomes
CREATE-X (Japan)	All with residual disease after anthracycline and taxane containing NACT	Capecitabine x 9	No further treatment	At 5y: capecitabine resulted in: - Higher RFS (69.8 vs 56.1%, HR 0.58 [0.39-0.87]) - Higher OS (78 vs 70%, HR 0.52 [95%CI 0.30-0.90])
CIBOMA/2004-01_GEICAM/ 2003-11	TNBC with residual disease - Stratified by whether basal-like (IHC+ for EGFR and CK 5/6)	Capecitabine x 8	Observation	At 5y: - DFS similar (79.6 vs 76.8%) - OS similar (86.2 vs 85.8%) - Non-basal like TNBC had advantage (DFS 82.6 vs 72.9%, p=.02) and OS 89.5 vs 79.6%, p=.007)
EA1131	TNBC with residual disease	Carboplatin x 4	Capecitabine x 6	At 3y: - DFS similar (42 vs 49%, HR 1.06 [95%CI 0.62-1.81)

Masuda, et al. NEJM 2017;376:2147-2159; Lluch, et al. J Clin Oncol 2020; 38:203-213; Mayer, et al. 2021; 39:2539-51.

Managing residual disease: Capecitabine

Trial	Volunteers	Intervention	Comparator	Outcomes
	All with residual			At 5y: capecitabine resulted in:
EA1131	residual disease	x 4	6	- DFS similar (42 vs 49%, HR 1.06 [95%CI 0.62-1.81)

The data establishing Capecitabine as a standard option for people with residual disease after NACT is weak.

- Studies done **prior** to incorporation of I/O (KN522)

It is best to be treated as a **suggestion**, but not a **recommendation.**

Masuda, et al. NEJM 2017;376:2147-2159; Lluch, et al. J Clin Oncol 2020; 38:203-213; Mayer, et al. 2021; 39:2539-51.

Managing residual disease: mBRCA

Trial	Volunteers	Intervention	Comparator	Outcomes
OlympiA	- Pathogenic or likely pathogenic mutation present - RD after NACT required - TNBC, at least 2cm OR node-positive	Olaparib x 1y	Placebo	At 3 years, compared to placebo: - Improved Invasive DFS (85.9 vs 77.1%, HR 0.58 [95%CI 0.41-0.82]) - Improved distant DFS (87.5 vs 80.4%, HR 0.57 [95%CI 0.39-0.83]) - **In subgroup with TNBC treated with NACT: invasive** DFS improved (90.3 vs 84.8%, HR 0.54 [95%CI 0.34-0.83])

Tutt, et al. N Engl J Med 2021; 384:2394-2405

Managing residual disease: mBRCA

Trial	Volunteers	Intervention	Comparator	Outcomes

The availability of PARP inhibitors is an important breakthrough for people with BRCA mutation associated breast cancer. The use after NACT is a **recommendation.**

Tutt, et al. N Engl J Med 2021; 384:2394-2405

IMPROVING OUTCOMES IN TNBC

Will earlier detection of metastatic disease improving outcomes?

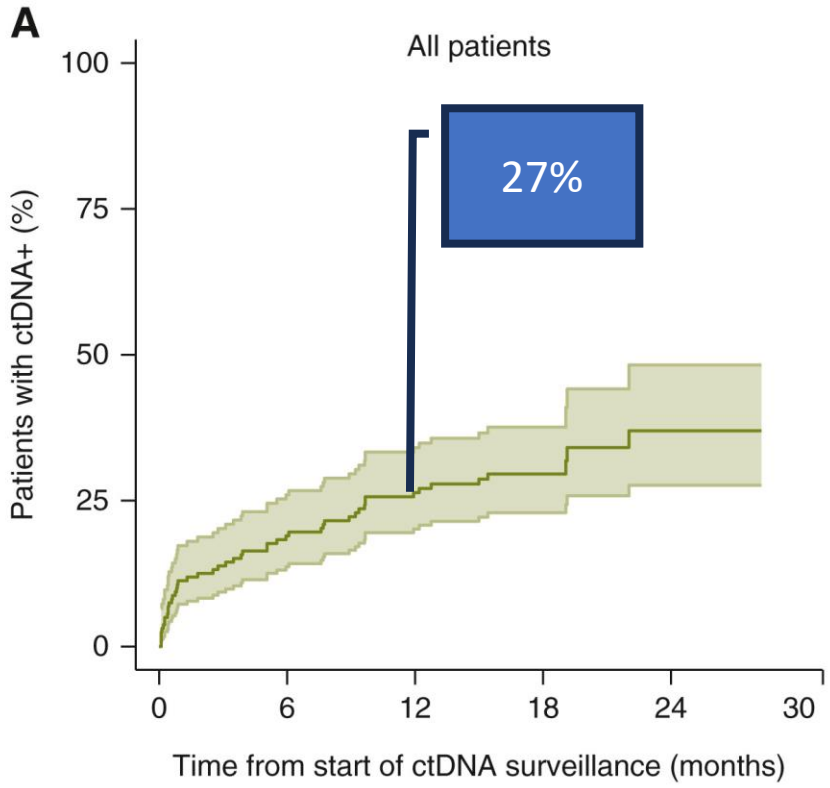
Is there a role for ctDNA tracking for TNBC?

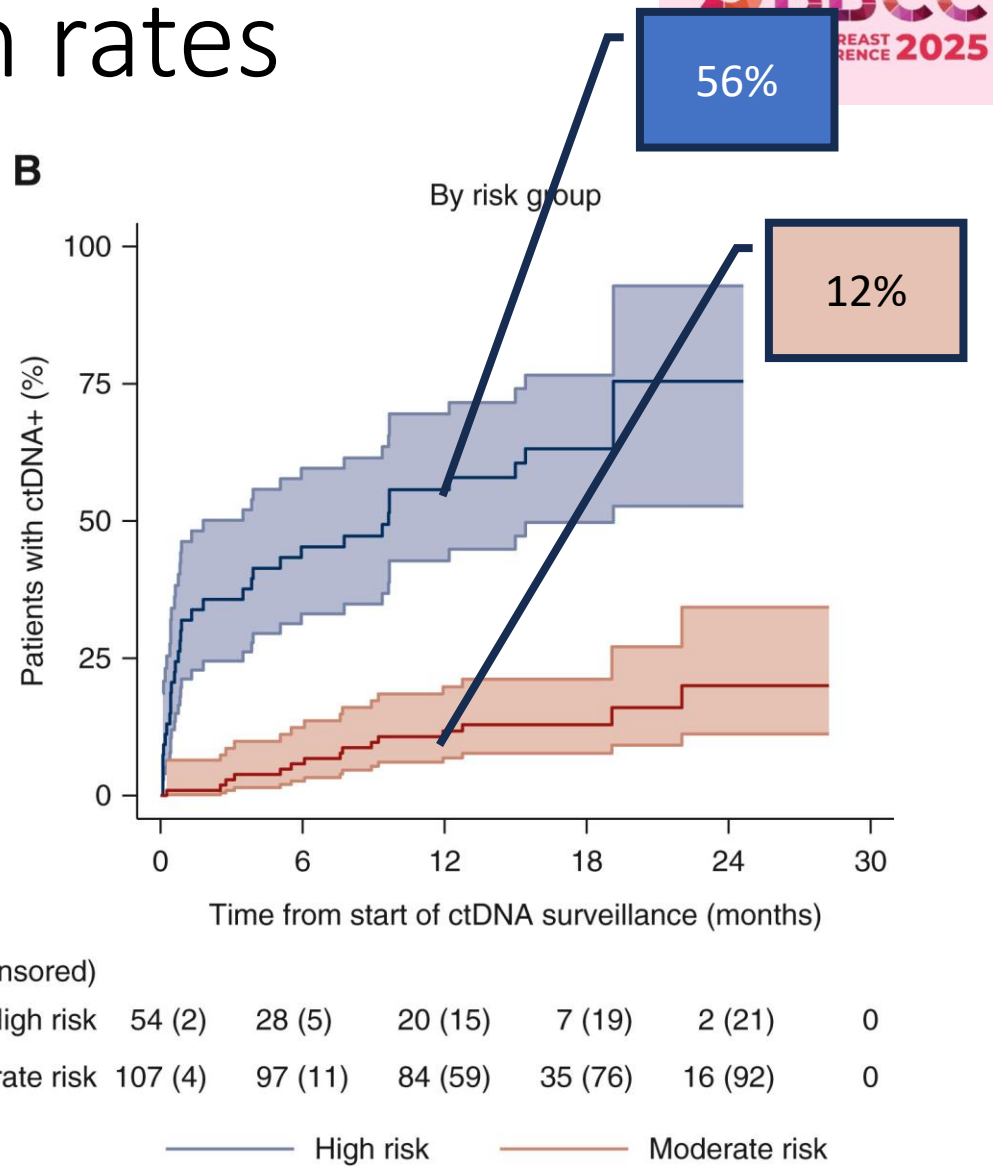
cTRAK

- Patients: People with newly diagnosed TNBC
  - Moderate risk (n=131)
    - After NACT: RD in breast, but N0
    - Postop: T>20mm, N+
  - High risk (n=77)
    - After NACT: N+
    - Postop: T>50mm/N+ or ≥4 nodes involved
- Intervention: ctDNA collection every 3 months up to one year
- Comparator: Observation

Turner NC, et al. Ann Oncol 2023; 34:200-11

ctDNA detection rates





Turner NC, et al. Ann Oncol 2023; 34:200-11

Major findings of cTRAK

- 72% had overt metastatic disease on imaging t time ctDNA+
  - Nearly 20% of patients given adjuvant capeciabine were ctDNA+
- Almost 30% of those with high-risk TNBC had metastatic disease at baseline ctDNA assessment (only 1.4% with moderate risk)

Turner NC, et al. Ann Oncol 2023; 34:200-11

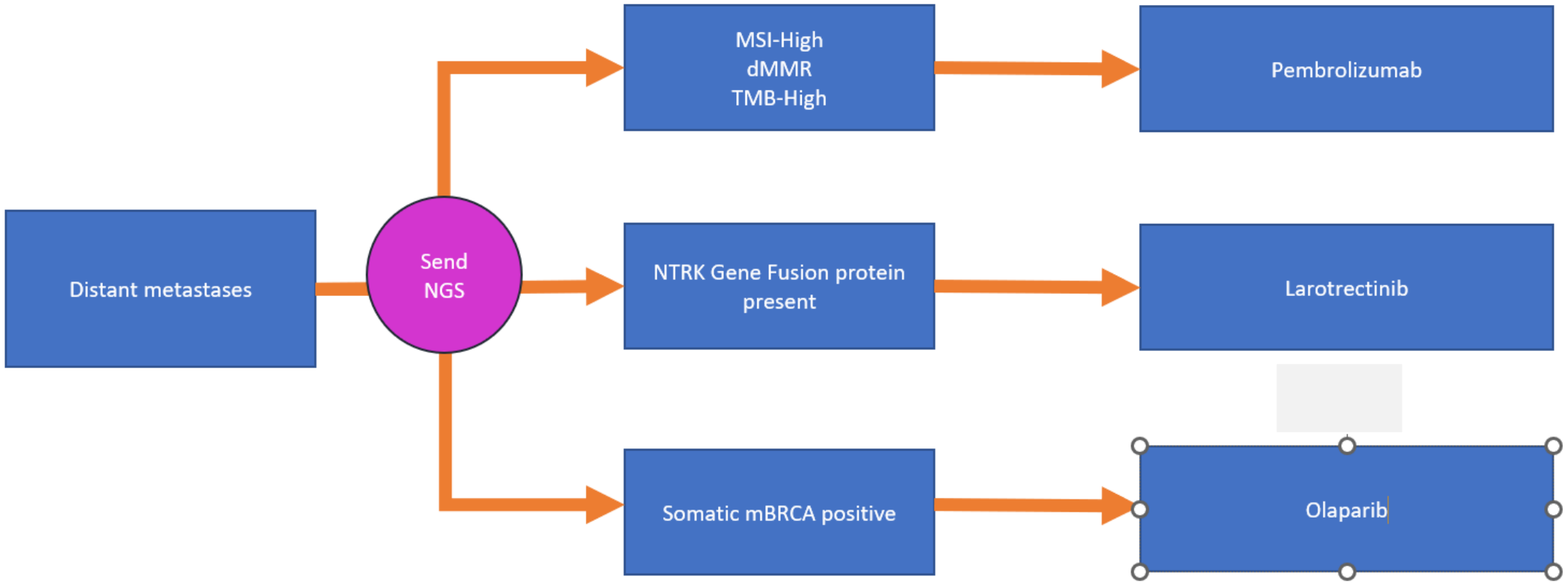
Major findings of cTRAK

While you can follow ctDNA, it remains unclear if it impacts survival

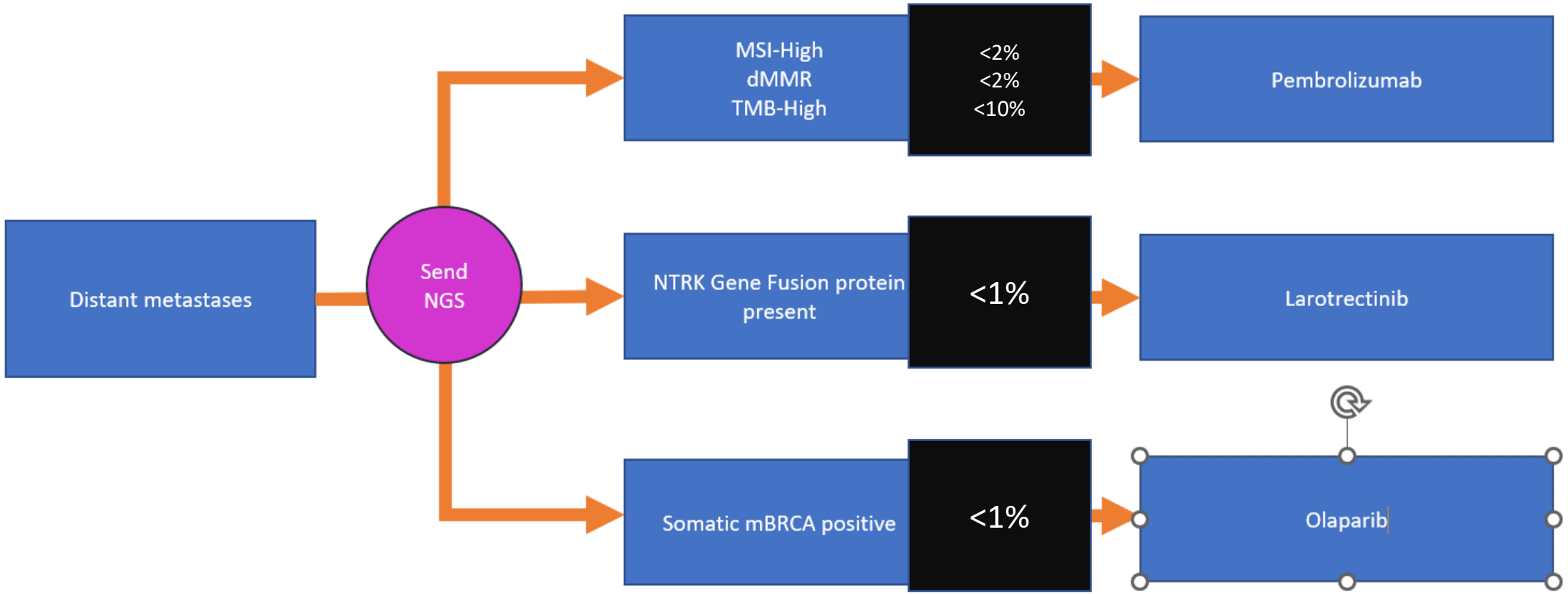
Turner NC, et al. Ann Oncol 2023; 34:200-11

Approaching recurrent and metastatic disease

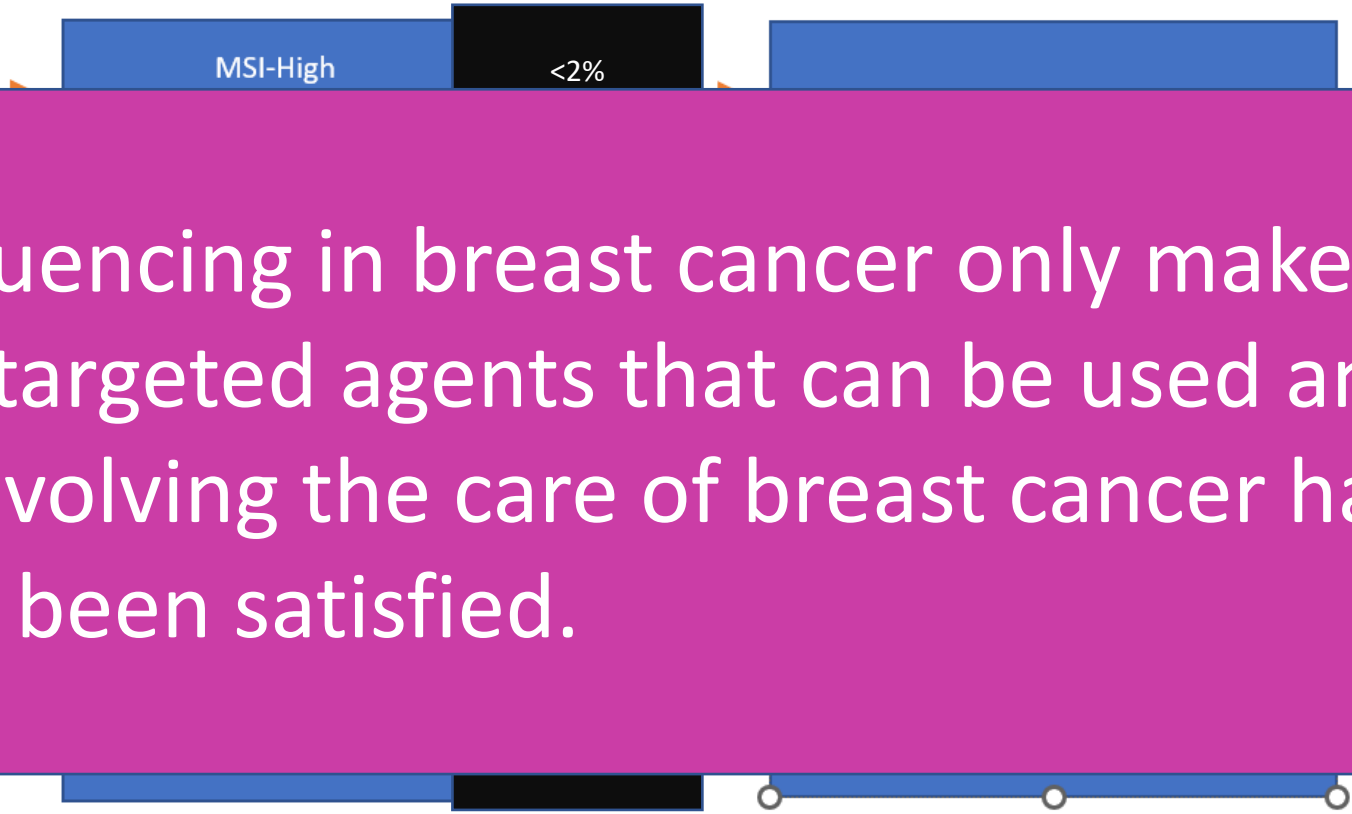
Pathway approach to metastatic TNBC:



Pathway approach to metastatic TNBC: Distant metastatic disease



Pathway approach to metastatic TNBC: Distant metastatic disease

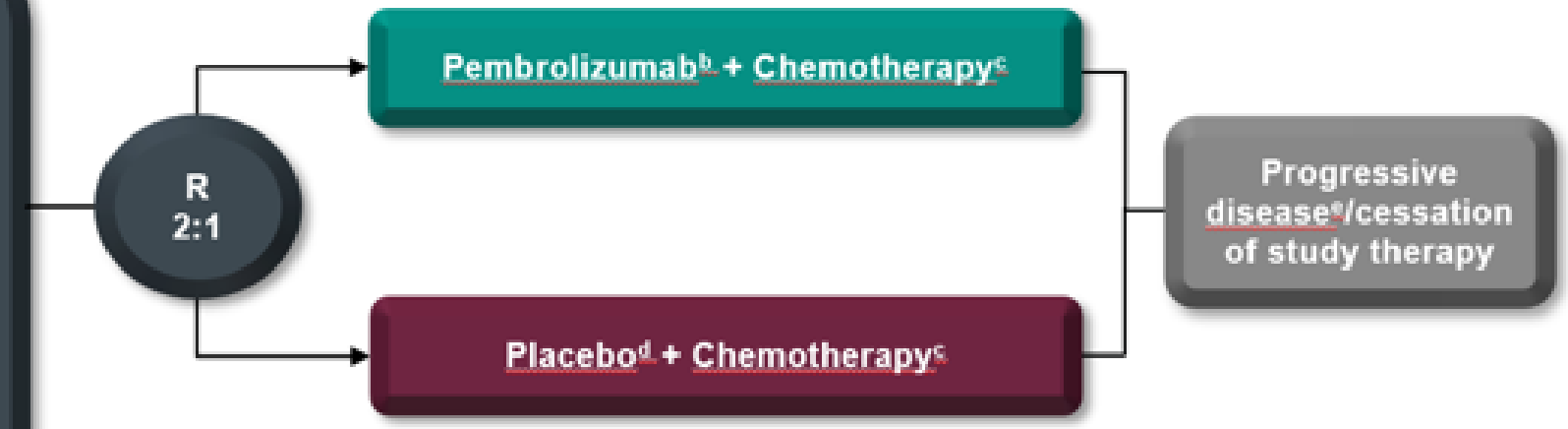


Next generation sequencing in breast cancer only makes sense if (1) there are targeted agents that can be used and (2) if other priorities involving the care of breast cancer have been satisfied.

Keynote 355: Pembrolizumab for MBC

Key Eligibility Criteria

- Age ≥18 years
- Central determination of TNBC and PD-L1 expression[a]
- Previously untreated locally recurrent inoperable or metastatic TNBC
- De novo metastasis or completion of treatment with curative intent ≥6 months prior to first disease recurrence
- ECOG performance status 0 or 1
- Life expectancy ≥12 weeks from randomization
- Adequate organ function
- No systemic steroids
- No active CNS metastases
- No active autoimmune disease



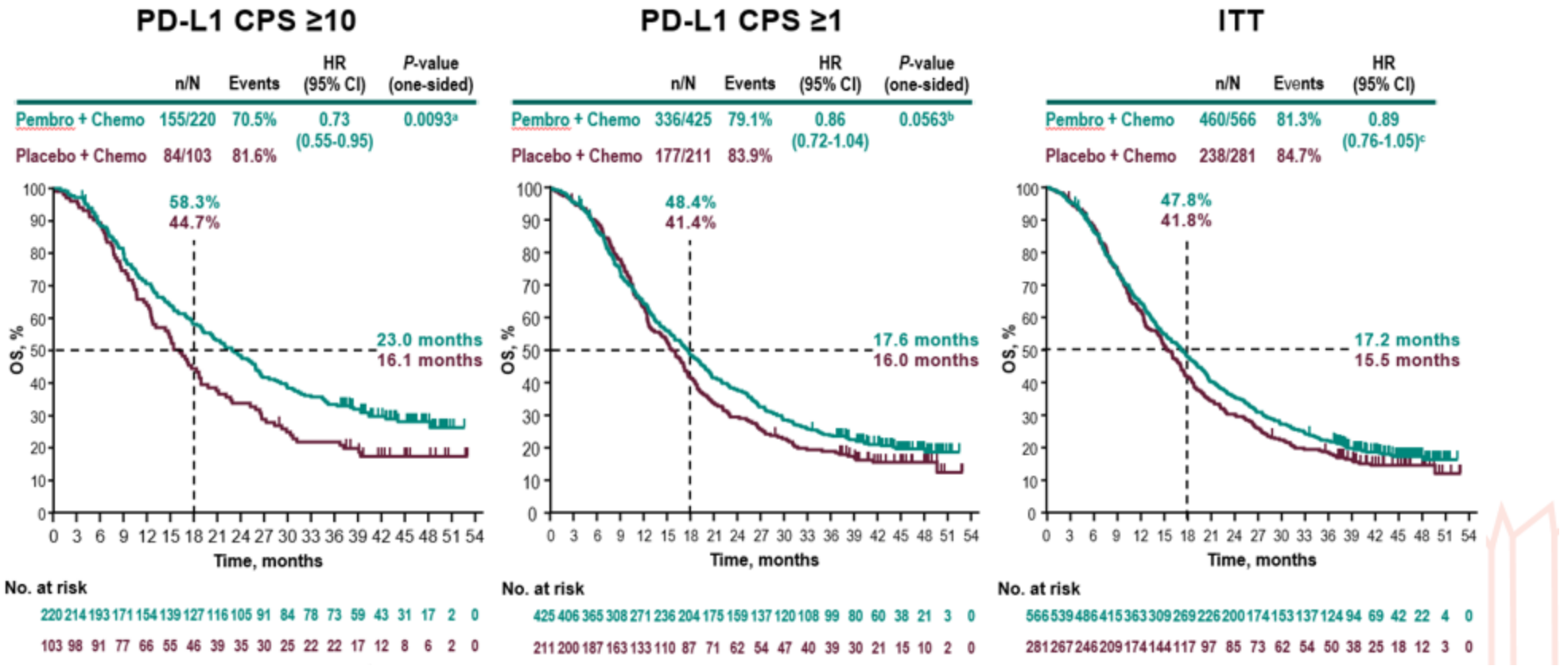
Stratification Factors:

- Chemotherapy on study (taxane or gemcitabine-carboplatin)
- PD-L1 tumor expression (CPS ≥1 or CPS <1)[f]
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes or no)

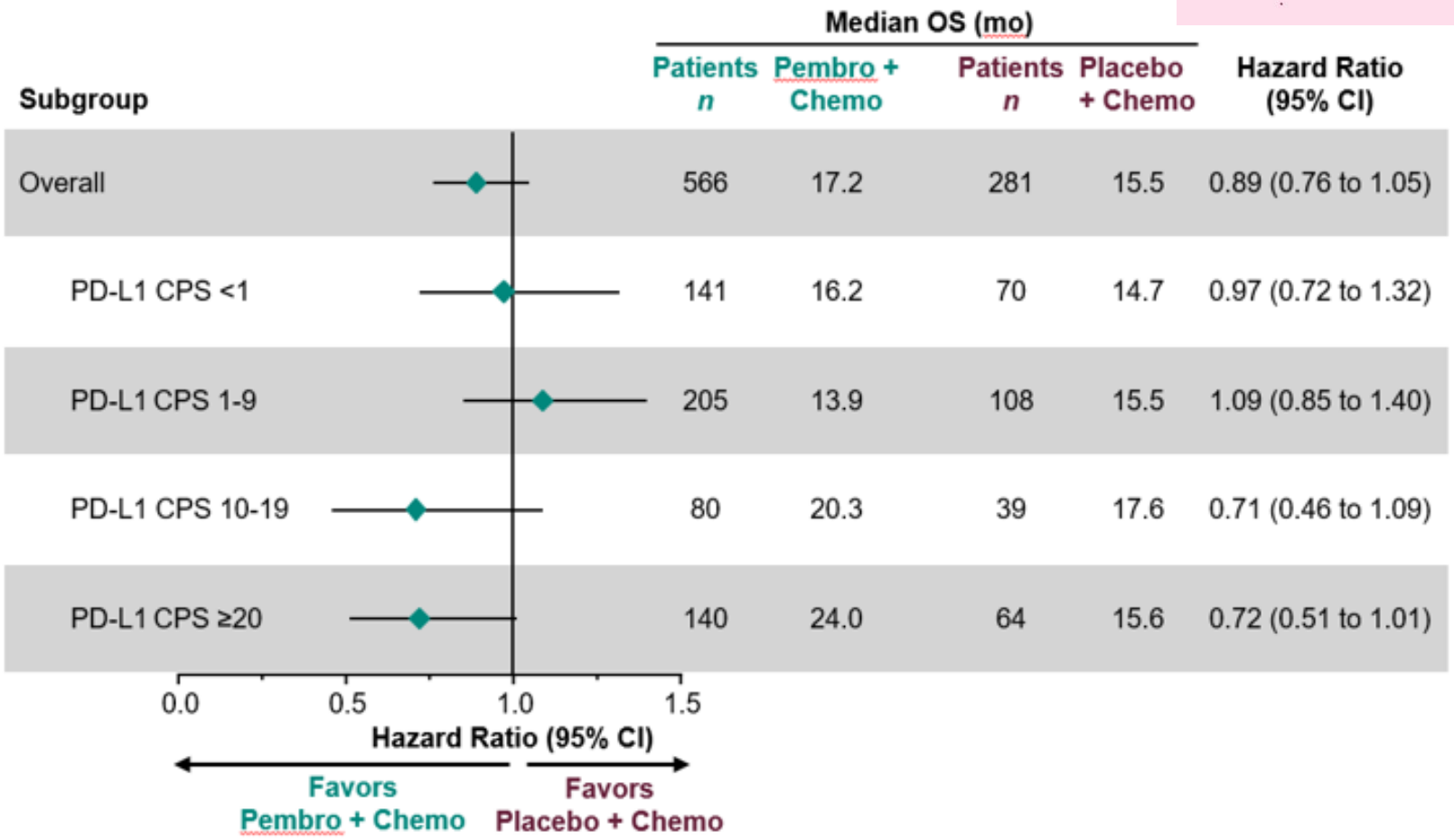
Cortes, et al. N Engl J Med. 2022 Jul 21;387(3):217-226.

Keynote 355: Overall Survival

Cortes, et al. N Engl J Med. 2022 Jul 21;387(3):217-226.

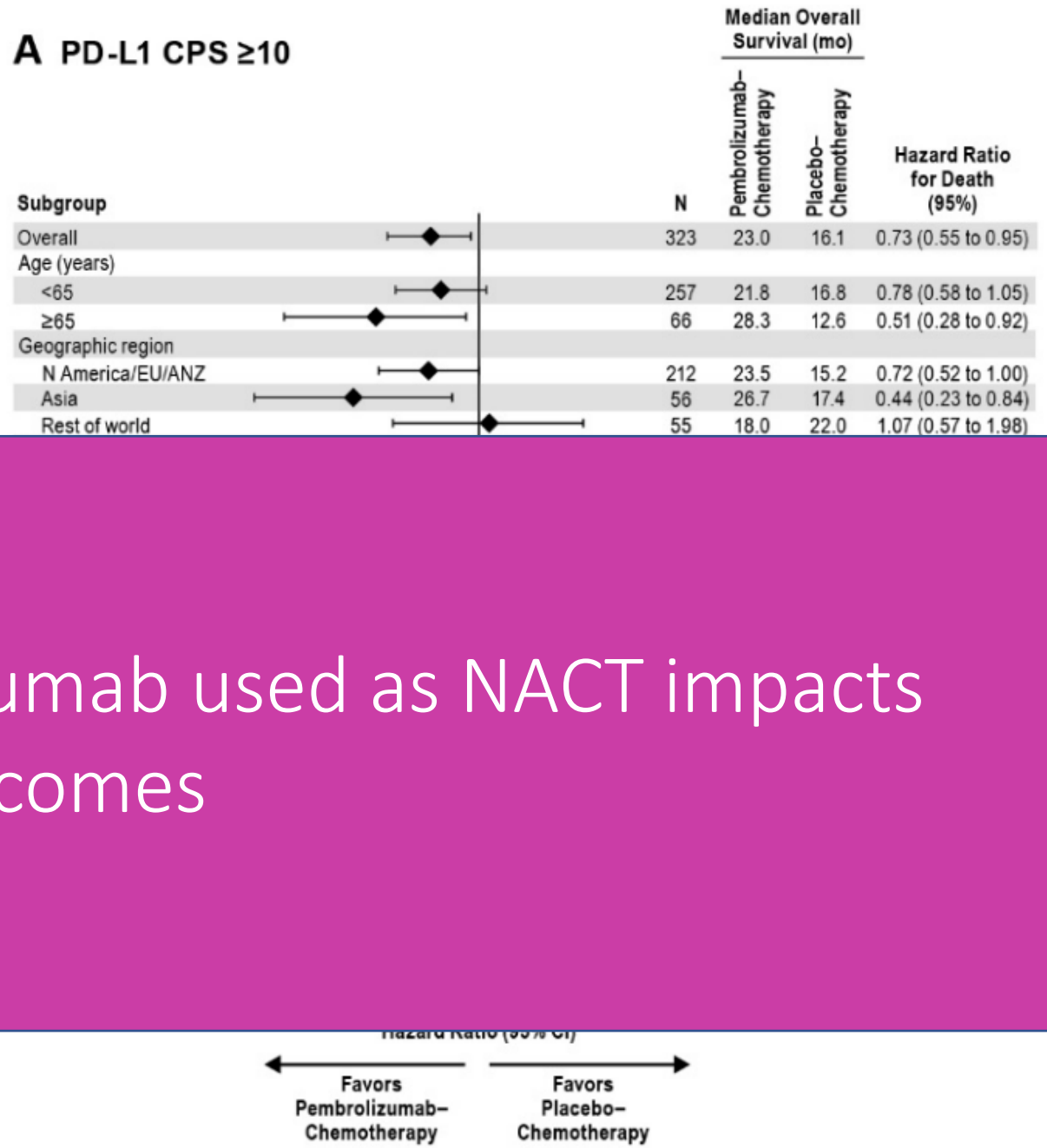


Keynote 355: Overall Survival



Cortes, et al. N Engl J Med. 2022 Jul 21;387(3):217-226.

KN355: Benefit of



Not clear how pembrolizumab used as NACT impacts outcomes

Cortes J, et al. New Engl J Med 2022; 387:217-26

ASCENT:

Sacituzumab Govitecan

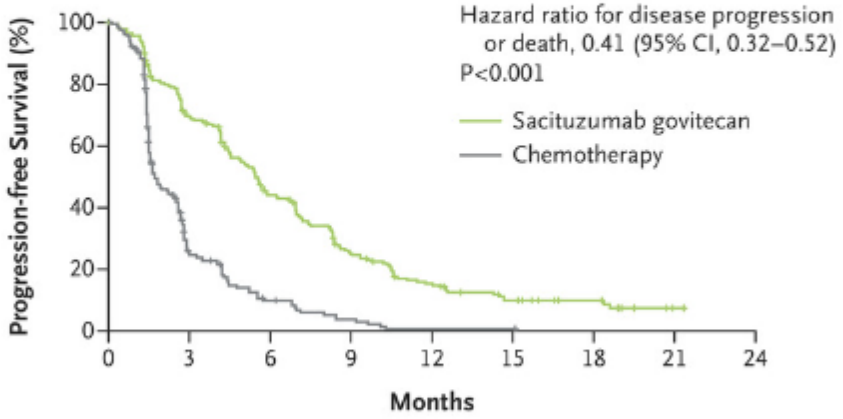
- Antibody-drug conjugate
- Target: Trophoblast cell surface antigen-2 (Trop-2)
- Payload: SN-38 (active metabolite of irinotecan)
- Evaluated against standard chemotherapy in the ASCENT trial
  - Volunteers: Metastatic TNBC (stable brain metastases allowed), no line limit
  - Intervention: SG
  - Comparator: Single agent chemotherapy (Eribulin, vinorelbine, capecitabine, gemcitabine)

Bardia et al. N Engl J Med. 2021 Apr 22;384(16):1529-1541.

ASCENT Trial: Survival results

A Progression-free Survival among Patients without Brain Metastases

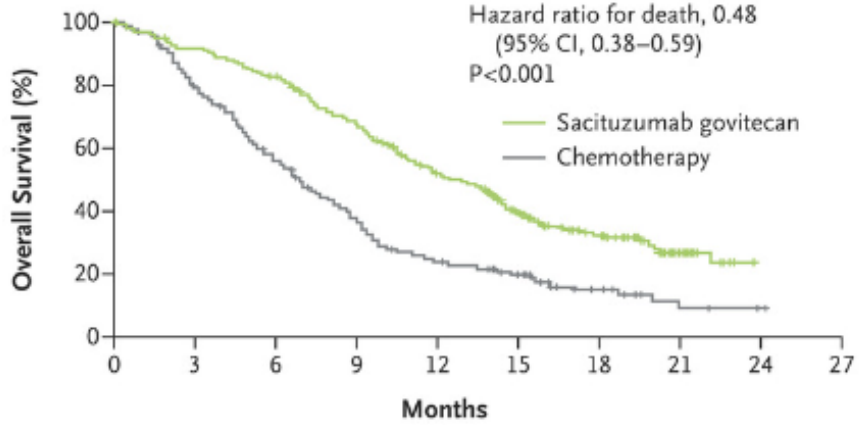
	No. of Patients	No. of Events	Median Progression-free Survival (mo (95% CI))
Sacituzumab Govitecan	235	166	5.6 (4.3–6.3)
Chemotherapy	233	150	1.7 (1.5–2.6)



No. at Risk								
Sacituzumab govitecan	235	154	91	49	28	15	9	1
Chemotherapy	233	39	14	5	1	1	0	0

B Overall Survival among Patients without Brain Metastases

	No. of Patients	No. of Events	Median Overall Survival (mo (95% CI))
Sacituzumab Govitecan	235	155	12.1 (10.7–14.0)
Chemotherapy	233	185	6.7 (5.8–7.7)



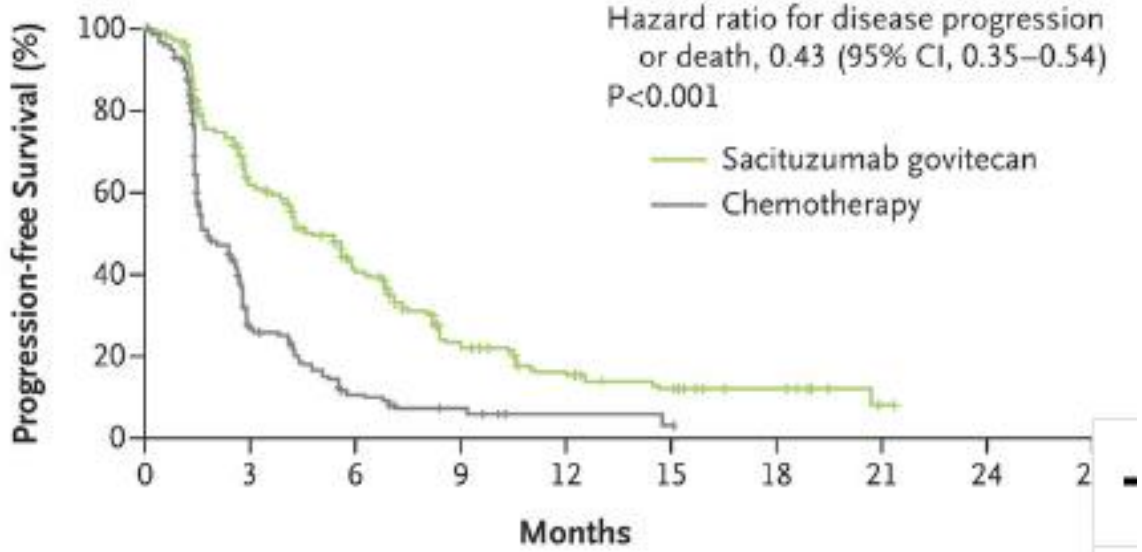
No. at Risk									
Sacituzumab govitecan	235	214	190	153	107	70	37	13	0
Chemotherapy	233	173	117	74	45	30	11	3	1

Bardia et al. N Engl J Med. 2021 Apr 22;384(16):1529-1541.

ASCENT Trial: Survival results

D Progression-free Survival in the Full Population

	No. of Patients	No. of Events	Median Progression-free Survival *mo (95% CI)*
Sacituzumab Govitecan	267	190	4.8 (4.1–5.8)
Chemotherapy	262	171	1.7 (1.5–2.5)



No. at Risk								
Sacituzumab govitecan	267	145	82	38	23	14	8	1
Chemotherapy	262	41	13	6	2	1	0	0

Bardia et al. N Engl J Med. 2021 Apr 22;384(16):1529-1541.

ASCENT Trial: Summary of Efficacy results

Variable	Patients without Brain Metastases		Full Population†	
	Sacituzumab Govitecan (N=235)	Chemotherapy (N=233)	Sacituzumab Govitecan (N=267)	Chemotherapy (N=262)
Median progression-free survival (95% CI) — mo	5.6 (4.3–6.3)	1.7 (1.5–2.6)	4.8 (4.1–5.8)	1.7 (1.5–2.5)
Hazard ratio for disease progression or death (95% CI)	0.41 (0.32–0.52)‡		0.43 (0.35–0.54)	
Median overall survival (95% CI) — mo	12.1 (10.7–14.0)	6.7 (5.8–7.7)	11.8 (10.5–13.8)	6.9 (5.9–7.7)
Hazard ratio for death (95% CI)	0.48 (0.38–0.59)‡		0.51 (0.41–0.62)	
Objective response — no. of patients (%)§	82 (35)	11 (5)	83 (31)	11 (4)
Complete response	10 (4)	2 (1)	10 (4)	2 (1)
Partial response	72 (31)	9 (4)	73 (27)	9 (3)
Clinical benefit — no. of patients (%)¶	105 (45)	20 (9)	108 (40)	21 (8)
Stable disease — no. of patients (%)	81 (34)	62 (27)	96 (36)	71 (27)
Stable disease for ≥6 mo	23 (10)	9 (4)	25 (9)	10 (4)
Progressive disease — no. of patients (%)	54 (23)	89 (38)	65 (24)	100 (38)
Response could not be evaluated — no. of patients (%)‖	18 (8)	71 (30)	23 (9)	80 (31)
Median time to response (95% CI) — mo	1.5 (0.7–10.6)	1.5 (1.3–4.2)	1.5 (0.7–10.6)	1.5 (1.3–4.2)
Median duration of response (95% CI) — mo	6.3 (5.5–9.0)	3.6 (2.8–NE)	6.3 (5.5–9.0)	3.6 (2.8–NE)
Hazard ratio (95% CI)	0.39 (0.14–1.07)			

Bardia et al. N Engl J Med. 2021 Apr 22;384(16):1529-1541.

ASCENT Trial: Adverse Events

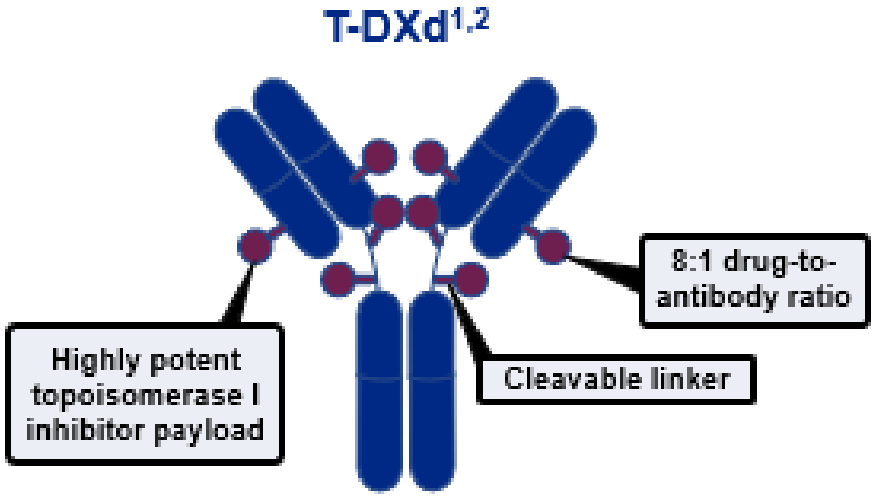
Adverse Event	Sacituzumab Govitecan (N=258)			Chemotherapy (N=224)		
	Any Grade	Grade 3	Grade 4	Any Grade	Grade 3	Grade 4
	number of patients (percent)					
Any adverse event	252 (98)	117 (45)	48 (19)	192 (86)	71 (32)	33 (15)
Hematologic event						
Neutropenia†	163 (63)	88 (34)	44 (17)	96 (43)	45 (20)	29 (13)
Anemia‡	89 (34)	20 (8)	0	54 (24)	11 (5)	0
Leukopenia§	41 (16)	23 (9)	3 (1)	25 (11)	10 (4)	2 (1)
Thrombocytopenia¶	14 (5)	2 (1)	2 (1)	25 (11)	3 (1)	0
Febrile neutropenia	15 (6)	12 (5)	3 (1)	5 (2)	4 (2)	1 (<1)
Gastrointestinal event						
Diarrhea	153 (59)	27 (10)	0	27 (12)	1 (<1)	0
Nausea	147 (57)	6 (2)	1 (<1)	59 (26)	1 (<1)	0
Vomiting	75 (29)	2 (1)	1 (<1)	23 (10)	1 (<1)	0
Constipation	44 (17)	0	0	32 (14)	0	0
Abdominal pain	29 (11)	3 (1)	0	9 (4)	1 (<1)	0
General disorders and administration-site conditions						
Fatigue	115 (45)	8 (3)	0	68 (30)	12 (5)	0
Asthenia	31 (12)	2 (1)	0	23 (10)	3 (1)	0
Skin and subcutaneous disorders: alopecia‖	119 (46)	0	0	35 (16)	0	0
Metabolism and nutrition disorders: decreased appetite	51 (20)	4 (2)	0	32 (14)	1 (<1)	0
Nervous system disorders**††	64 (25)	1 (<1)	0	53 (24)	5 (2)	0
Respiratory, thoracic, and mediastinal disorders††	41 (16)	5 (2)‡‡	0	17 (8)	1 (<1)	0
Musculoskeletal and connective-tissue disorders††	32 (12)	0	0	28 (12)	3 (1)	0
Infections and infestations††	30 (12)	6 (2)	1 (<1)	22 (10)	4 (2)	3 (1)

Bardia et al. N Engl J Med. 2021 Apr 22;384(16):1529-1541.

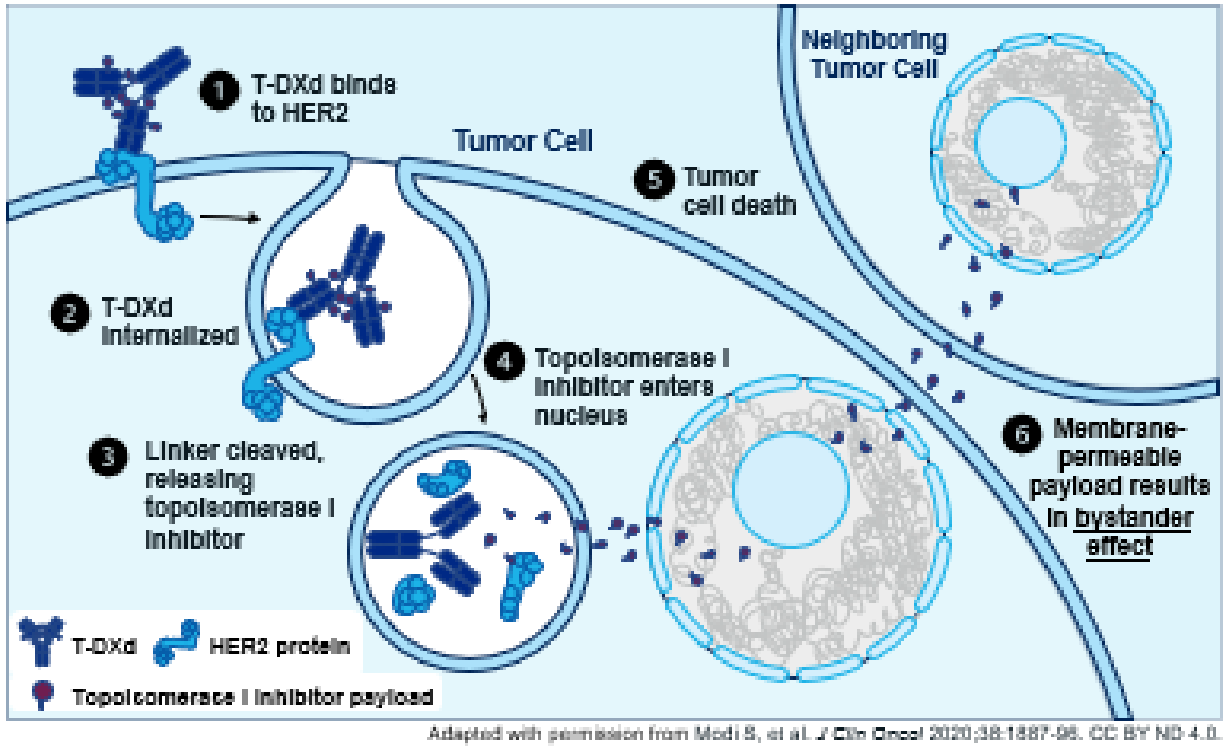
TROP2-directed ADCs

	Sacituzumab govitecan (IMMU-132)	Datopotamab deruxtecan (DS-1062a)	Sacituzumab tirumotecan (MK-2870)
Antibody	hRS7 Humanized IgG1 mAb	MAAP-9001a Humanized IgG1 mAb	hRS7 Humanized IgG1 mAb
Payload	SN38 (DNA Topoisomerase I inhibitor)	DXd (DNA Topoisomerase I inhibitor)	KL610023 (DNA Topoisomerase I inhibitor)
Linker cleavage	Enzymatic and pH-dependent	Enzymatic	Enzymatic and pH-dependent
Bystander effect	Yes	Yes	Yes
DAR	7.6	4	7.4
Half-life	11-14h	~5 days	57h
Dosing	D1, D8 of Q3W schedule	Q3W	Q2W

Trastuzumab Durextecan (T-DXd)



Internalization of T-DXd leads to release of the DXd ayload and subsequent cell death in the target tumor cell nd neighboring tumor cells through the bystander effect[1,2]



Adapted with permission from Modi S, et al. J Clin Oncol 2020;38:1887-98. CC BY ND 4.0.

- **Results from a phase 1b study have reported efficacy of T-DXd in heavily pretreated patients (N = 54) with HER2-low mBC, with a mPFS of 11.1 months and an ORR of 37.0%[3]**

Nakada T, et al. Chem Pharm Bull. 2019;67:173-185. 2. Ogitani Y, et al. Clin Cancer Res. 2016;22:5097-5108. 3. Modi S, et al. J Clin Oncol. 2020;38:1887-1896.

DESTINY-Breast04

Patients[a]
- HER2-low (IHC 1+ vs IHC 2+/ISH−), unresectable, and/or mBC treated with 1-2 prior lines of chemotherapy in the metastatic setting
- HR+ disease considered endocrine refractory

R 2:1

T-DXd
5.4 mg/kg Q3W
(n = 373)

HR+ ≈ 480
HR− ≈ 60

TPC
Capecitabine, eribulin, gemcitabine, paclitaxel, nab-paclitaxel[c]
(n = 184)

Primary endpoint
- PFS by BICR (HR+)

Key secondary endpoints[b]
- PFS by BICR (all patients)
- OS (HR+ and all patients)

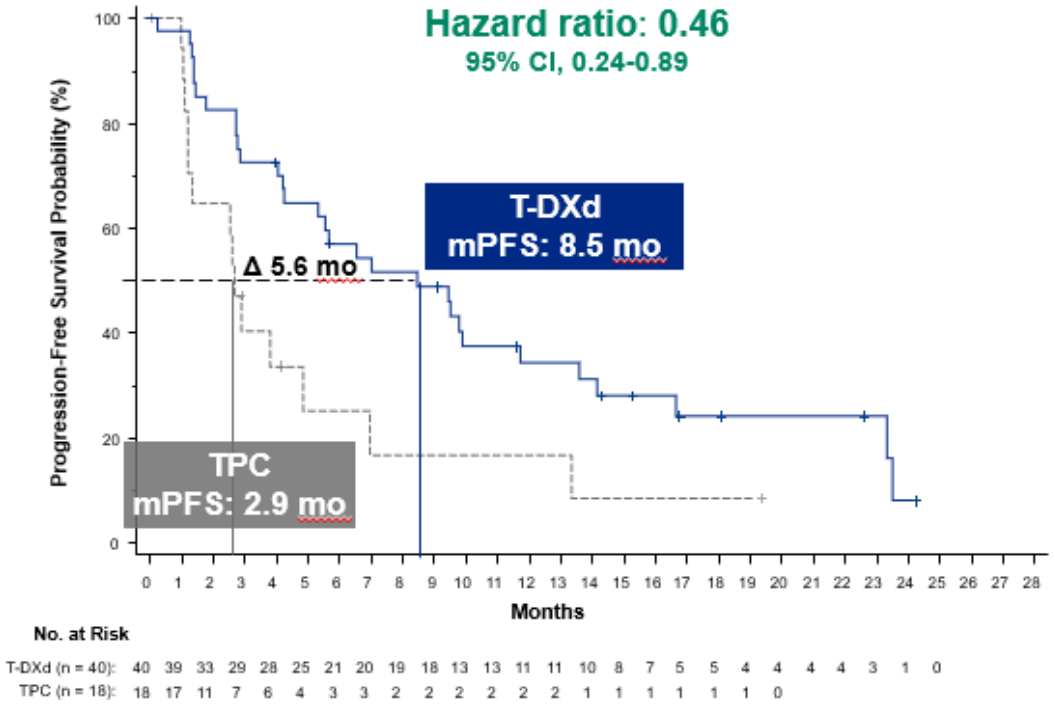
Stratification factors
- Centrally assessed HER2 status[d] (IHC 1+ vs IHC 2+/ISH−)
- 1 versus 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6 inhibitor) versus HR−

10% of population had ER negative disease

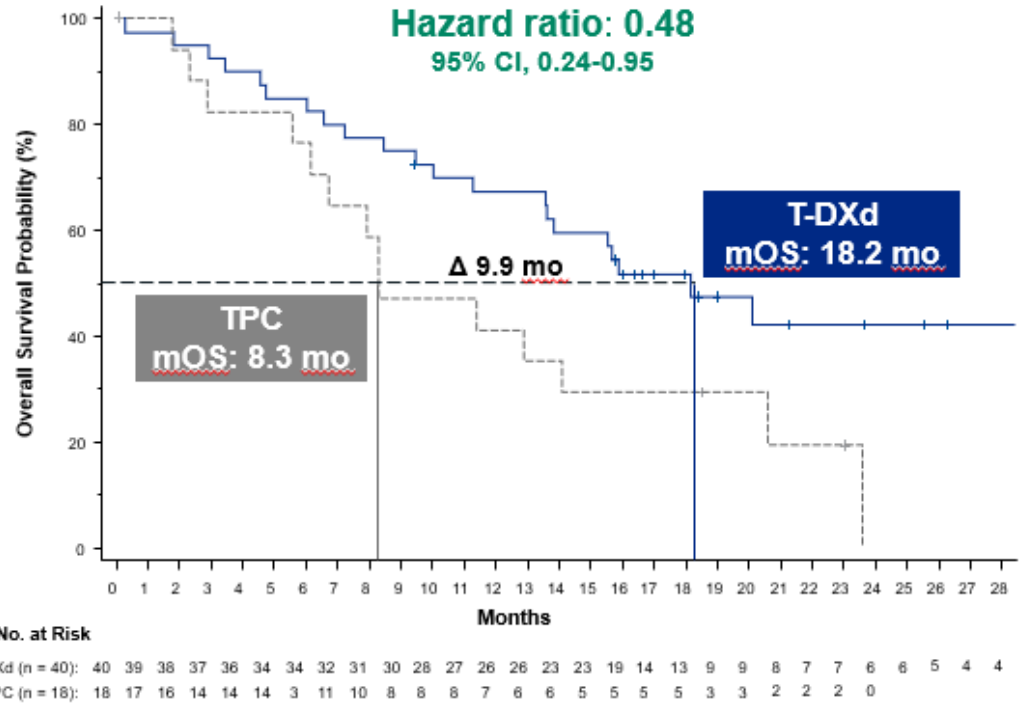
Modi, et al. N Engl J Med. 2022 Jul 7;387(1):9-20.

DESTINY-04: Results in ER-negative disease

PFS

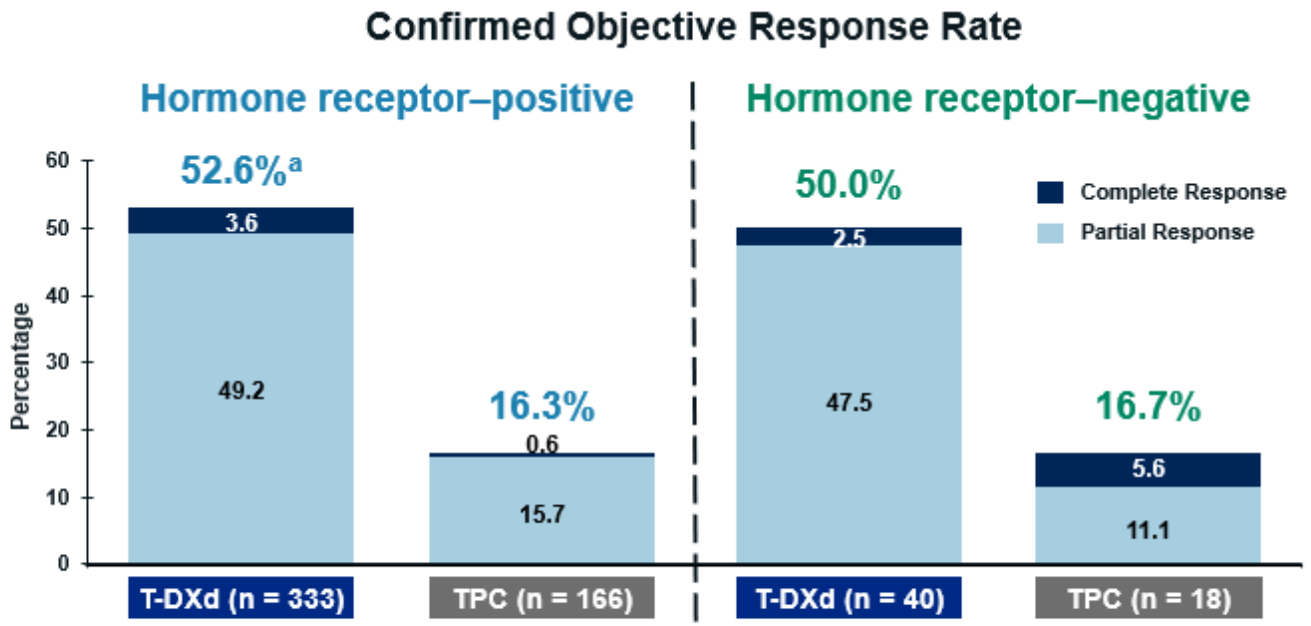


OS



Modi, et al. N Engl J Med. 2022 Jul 7;387(1):9-20.

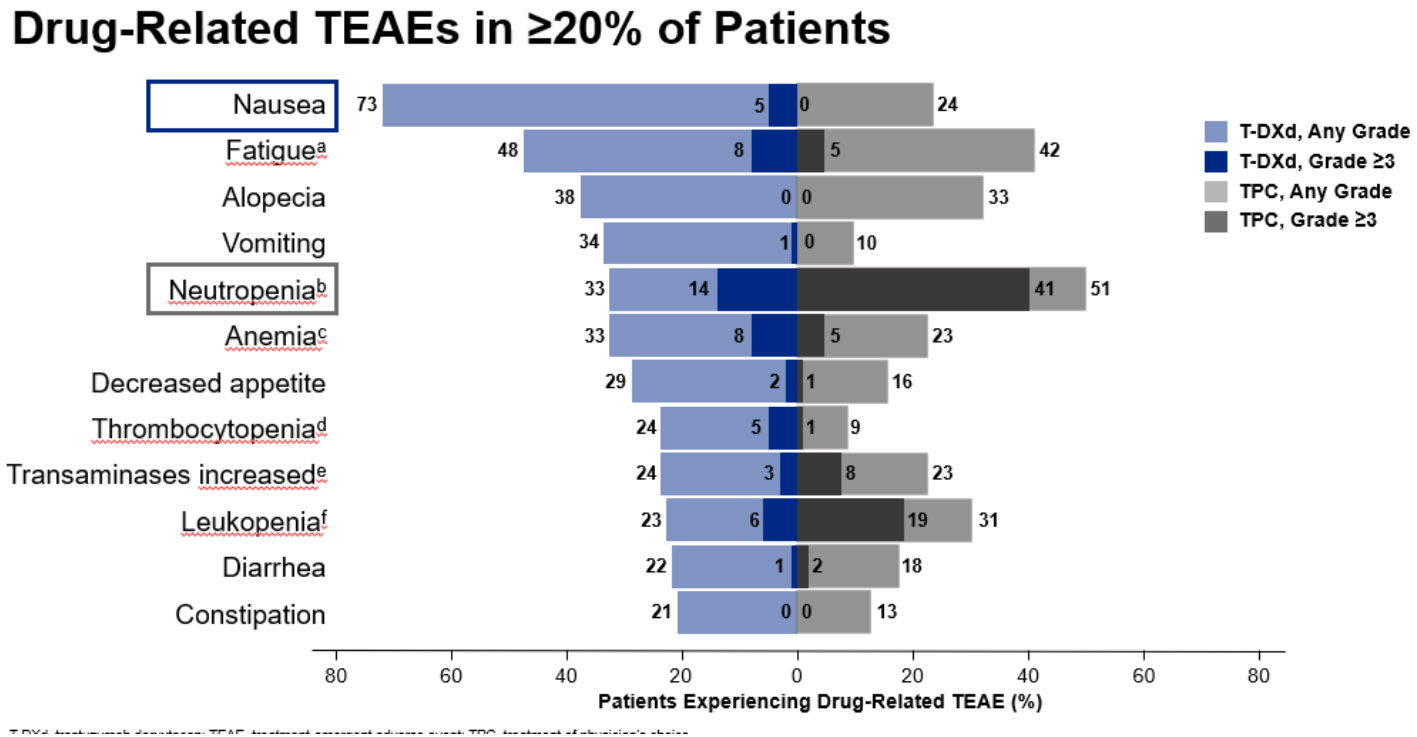
DESTINY-04: Overall Response Rate



	T-DXd (n = 333)	TPC (n = 166)	T-DXd (n = 40)	TPC (n = 18)
Progressive disease, %	7.8	21.1	12.5	33.3
Not evaluable, %	4.2	12.7	7.5	5.6
Clinical benefit rate,[b] %	71.2	34.3	62.5	27.8
Duration of response, months	10.7	6.8	8.6	4.9

Modi, et al. N Engl J Med. 2022 Jul 7;387(1):9-20.

DESTINY-04: Treatment-related adverse events



Modi, et al. N Engl J Med. 2022 Jul 7;387(1):9-20.

DESTINY-04: Special adverse events

Adjudicated as drug-related ILD/pneumonitis[a]

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
T-DXd (n = 371)	13 (3.5)	24 (6.5)	5 (1.3)	0	3 (0.8)	45 (12.1)
TPC (n = 172)	1 (0.6)	0	0	0	0	1 (0.6)

Left ventricular dysfunction[b]

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade
Ejection fraction decreased						
T-DXd (n = 371)	1 (0.3)	14 (3.8)	1 (0.3)	0	0	16 (4.3)
TPC (n = 172)	0	0	0	0	0	0
Cardiac failure[c]						
T-DXd (n = 371)	0	1 (0.3)	1 (0.3)	0	0	2 (0.5)
TPC (n = 172)	0	0	0	0	0	0

Modi, et al. N Engl J Med. 2022 Jul 7;387(1):9-20.

Datopotamab deruxtecan

Antibody drug conjugate, uses Trophoblast cell-surface antigen 2 (TROP2) as target; expressed in approx. 80% of TNBC

ESMO 2021: TROPION-Pan Tumor01 clinical trial

- Volunteers: People with refractory or relapsed solid tumors, including 44 with TNBC
- Outcomes:
  - ORR 34%
  - Disease control rate: 77%
  - Most common AE: nausea, mucositis, fatigue, anemia, and hair loss

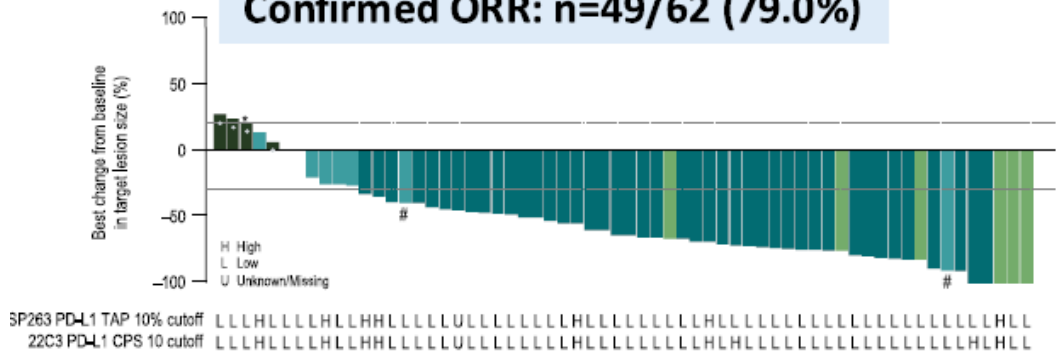
Krop, et al. : 2021 San Antonio Breast Cancer Symposium; December 7-10, 2021; San Antonio, TX. Abstract GS1-05.

Combination therapy: Emerging results

BEGONIA: ADC + ICI in 1L mTNBC

Dato-DXd + Durvalumab in mTNBC

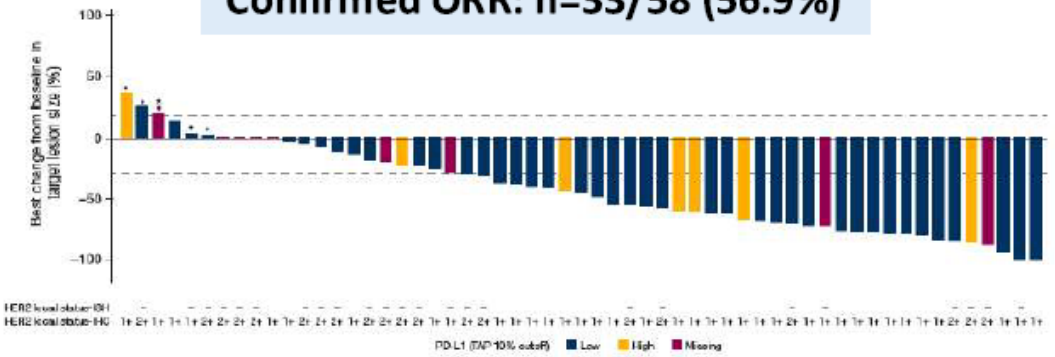
Confirmed ORR: n=49/62 (79.0%)



- Responses observed regardless of PD-L1
- No DLTs
- TRAE ILD/pneumonitis: G1, n=1; G2, n=2
- Stomatitis: most common AE leading to dose reduction (n=11)

T-DXd + Durvalumab in HER2-low mTNBC

Confirmed ORR: n=33/58 (56.9%)



- Responses regardless of PD-L1 or HER2-low category
- No DLTs
- TRAE ILD/pneumonitis: G1, n=3; G2, n=3; G3, n=1, G5, n=1 (COVID-associated pneumonitis)

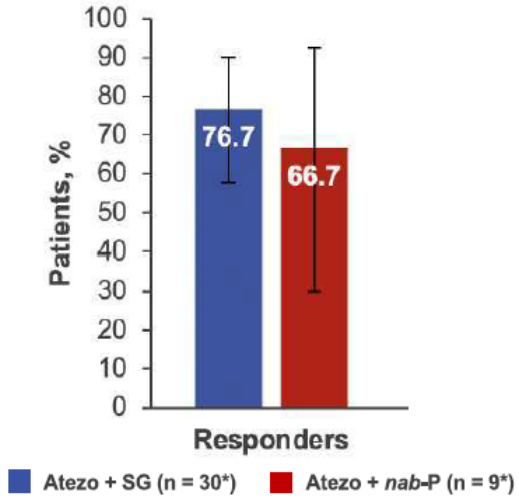
Schmid P et al. ESMO 2023; Schmid P et al. SABCS 2022.

Combination therapy: Emerging results

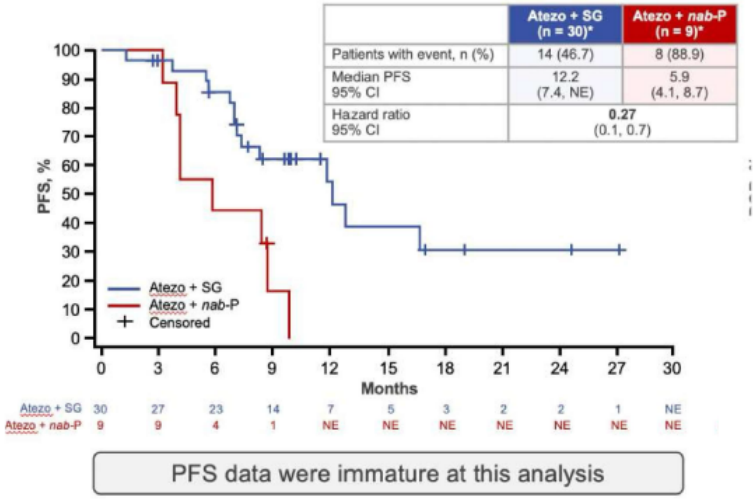
MORPHEUS: SG + ICI in 1L mTNBC

SG + Atezolizumab in 1L PD-L1+ mTNBC

Confirmed ORR = 76.7% (17% CR)



Median PFS: 12.2 mo

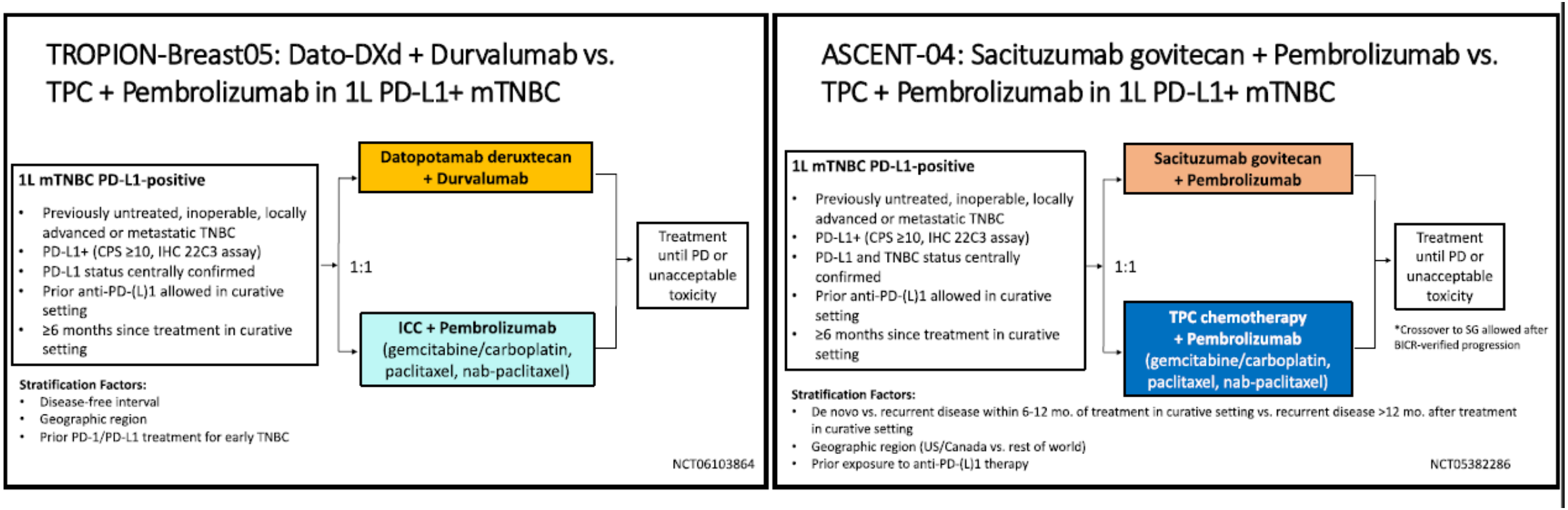


	Atezo + SG (n = 30)*	Atezo + nab-P (n = 9)*
Patients with event, n (%)	14 (46.7)	8 (88.9)
Median PFS 95% CI	12.2 (7.4, NE)	5.9 (4.1, 8.7)
Hazard ratio 95% CI	0.27 (0.1, 0.7)	

PFS data were immature at this analysis

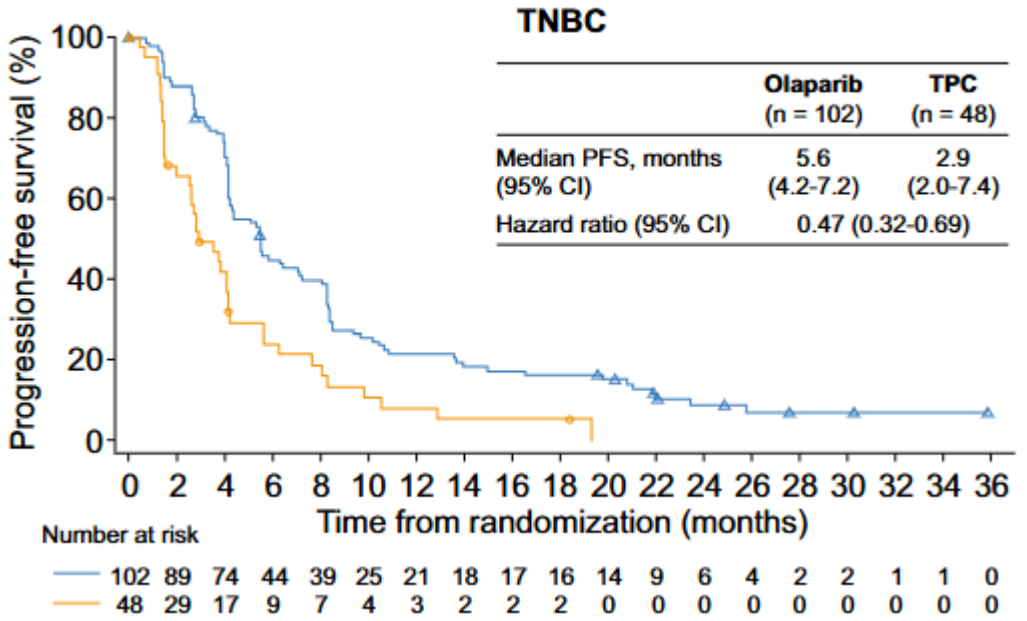
Schmid P et al. ESMO Breast 2024.

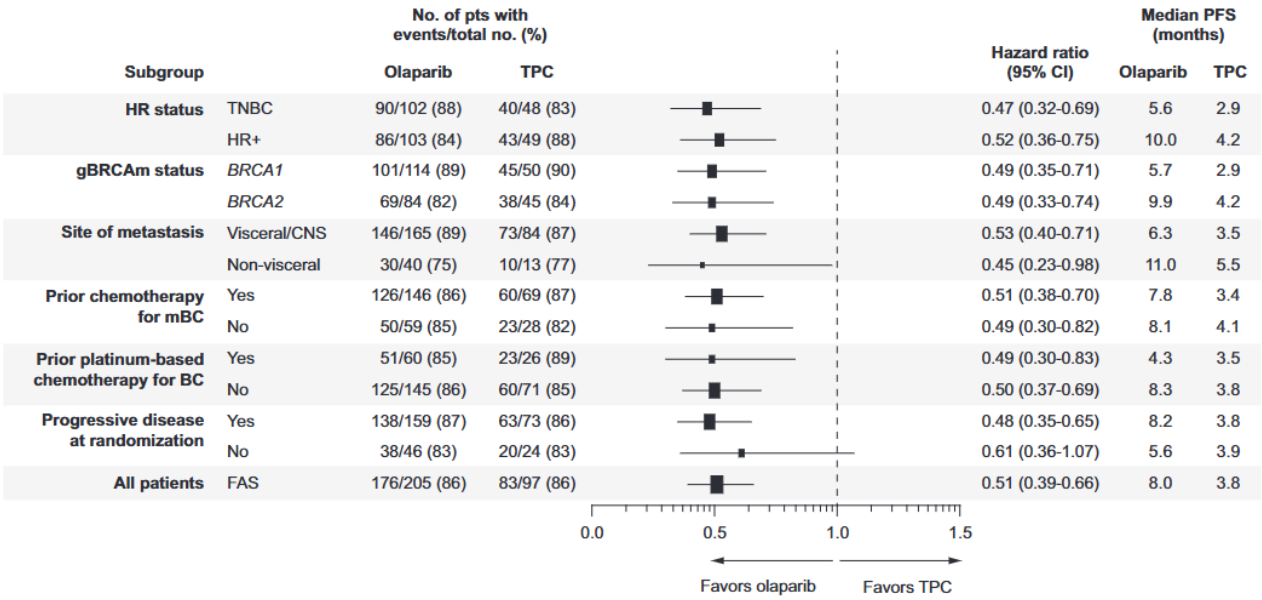
Ongoing trials



PARP Inhibitors: Olaparib

- OLYMPIAD OS results in TNBC cohort
- Allowed up to 2 prior lines
- **Significant improvement** in PFS (median, 5.6 v 2.9m, HR 0.47, 95%CI 0.32-0.69)



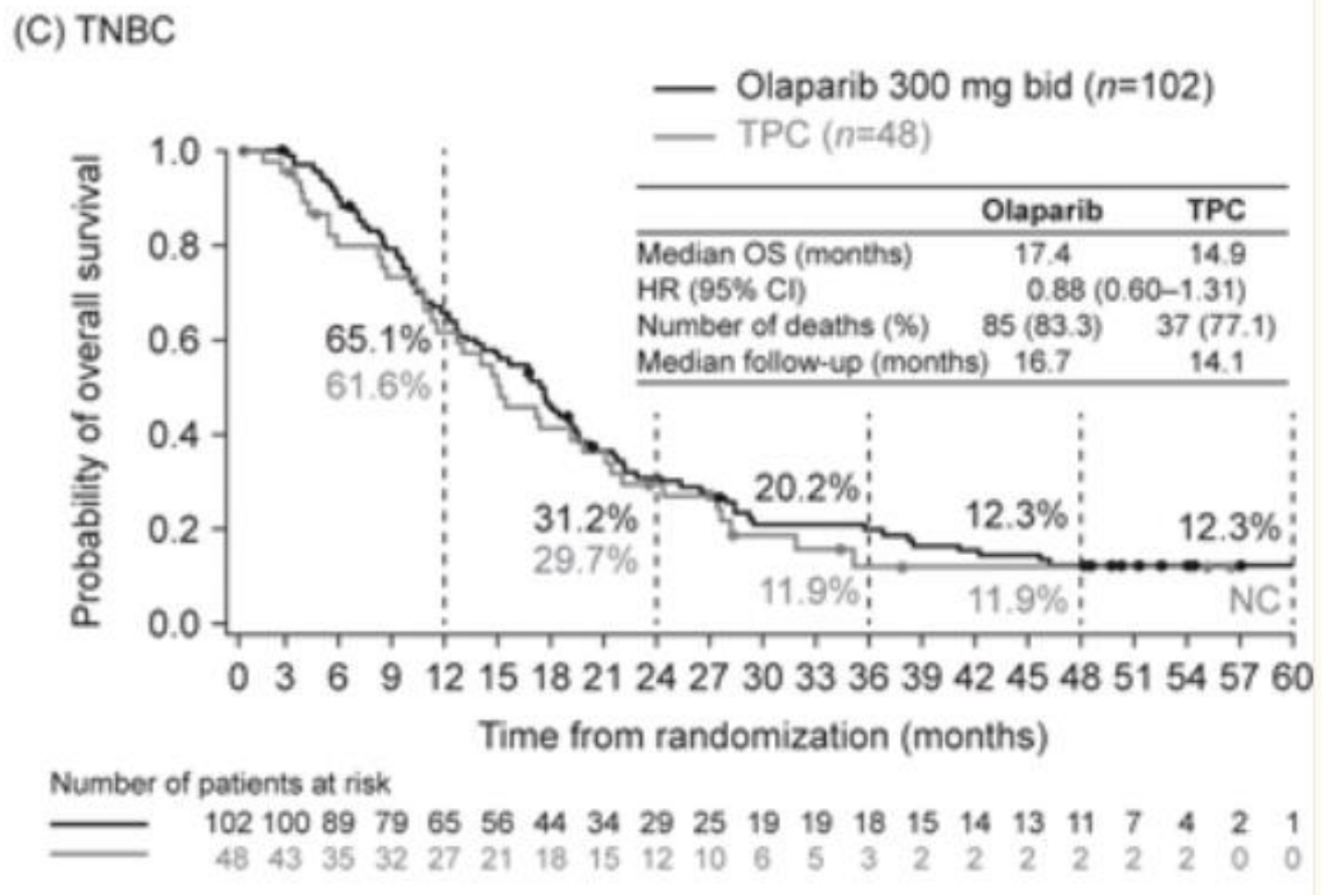


Senkus E, et al. Int J Cancer 2023; 153:803-14

PARP Inhibitors: Olaparib

OLYMPIAD OS results

- Allowed up to 2 prior lines
- 2023 OS Analysis:
  - No significant difference in OS (median, 19.3 v 17m for TPC, HR 0.89, 95%CI 0.67-1.18)
  - Given as 1L: significant benefit seen (median OS 22.6 v 14.7m, HR 0.55, 95%CI 0.33-0.95)
  - OS **not improved** in TNBC

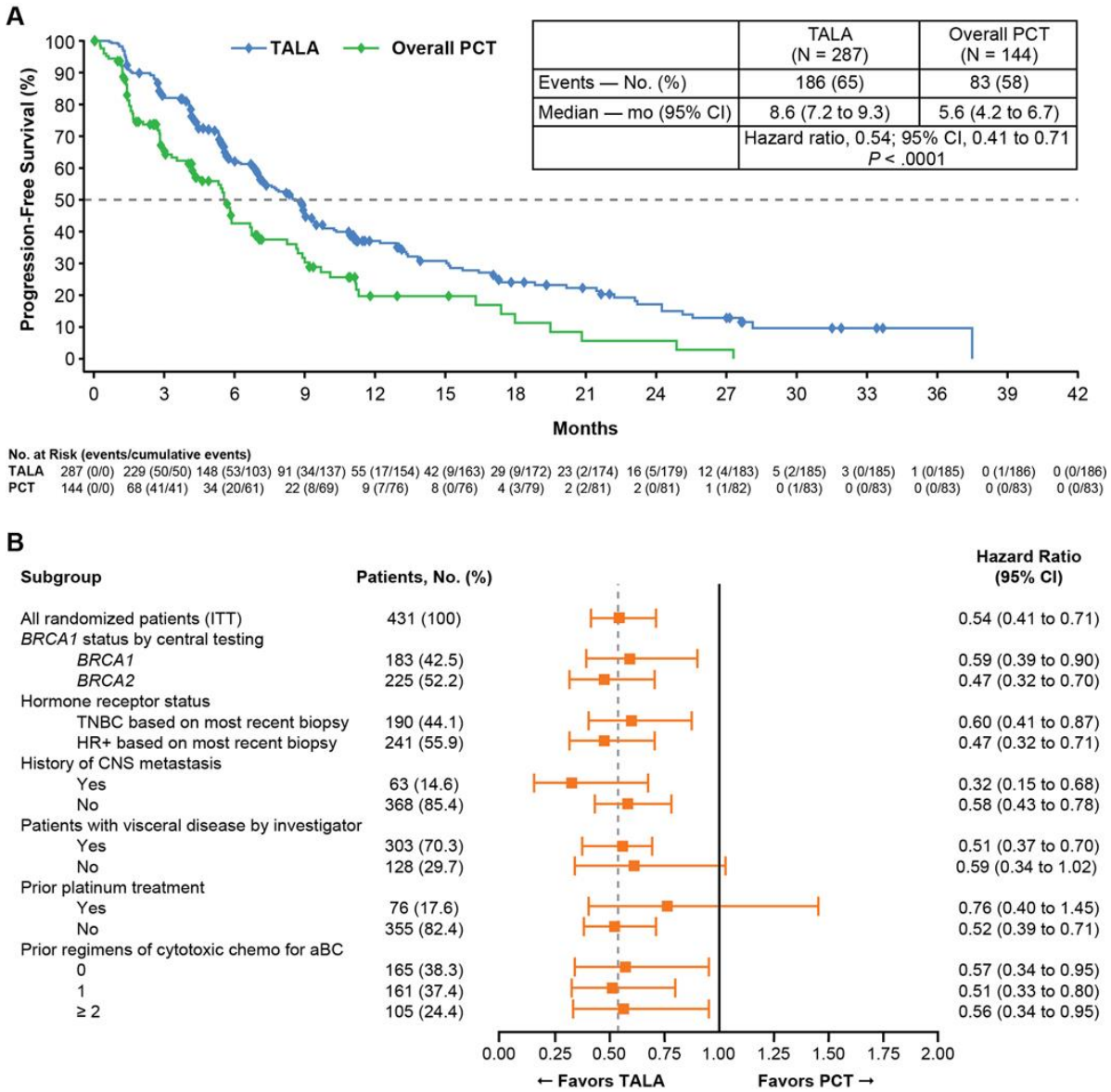


Robson ME, et al. Eur J Cancer 2023; 184:39-47

PARP Inhibitors: Talazoparib

EMBRACA

- TNBC (n=190/432)
- Allowed up to 3 prior lines
- Statistically significant improvement in PFS
- Subgroup analysis showed benefit to both TNBC and HR+

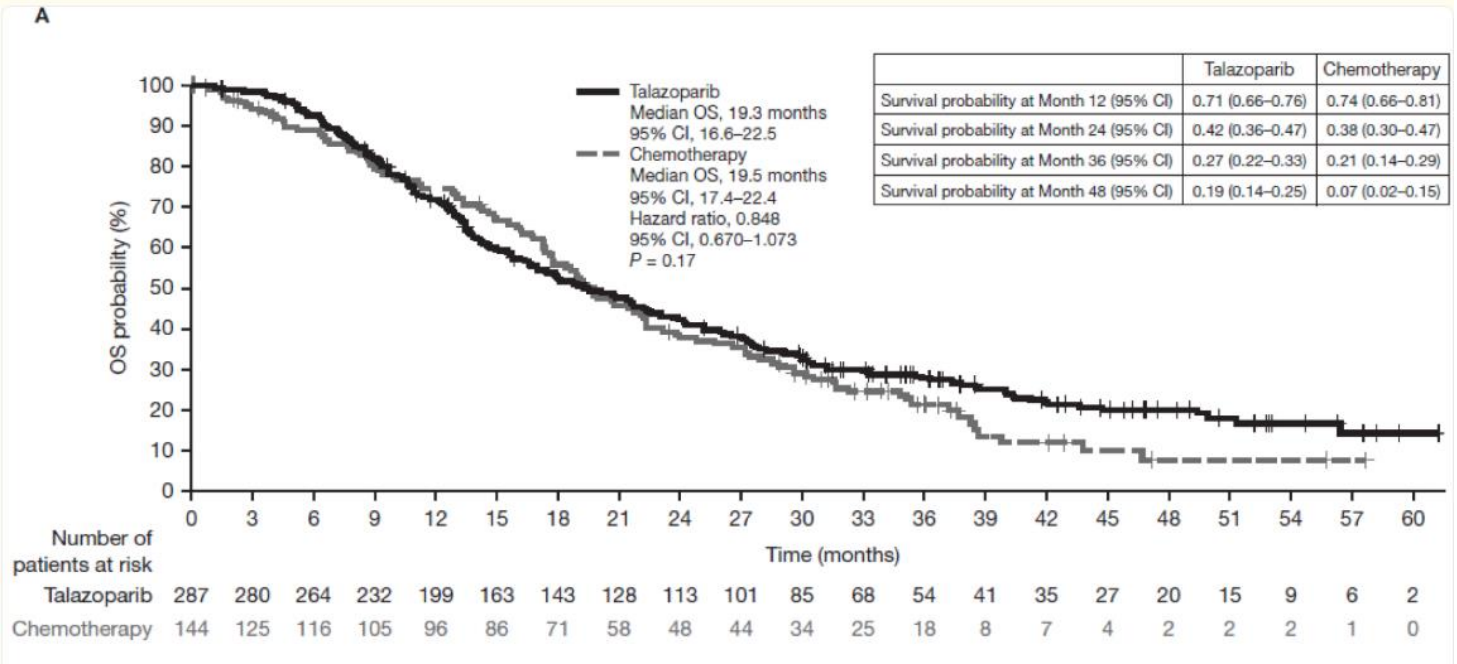


Litton JK, et al. New Engl J Med 2018; 379:753-63

PARP Inhibitors: Talazoparib

EMBRACA

- 2020: No significant improvement in OS among those with TNBC vs chemotherapy (HR 0.899, 95%CI 0.634-1.276)



	Talazoparib	Chemotherapy
Survival probability at Month 12 (95% CI)	0.71 (0.66–0.76)	0.74 (0.66–0.81)
Survival probability at Month 24 (95% CI)	0.42 (0.36–0.47)	0.38 (0.30–0.47)
Survival probability at Month 36 (95% CI)	0.27 (0.22–0.33)	0.21 (0.14–0.29)
Survival probability at Month 48 (95% CI)	0.19 (0.14–0.25)	0.07 (0.02–0.15)

Litton JK, et al. Ann Oncol 2020; 31:1526-35

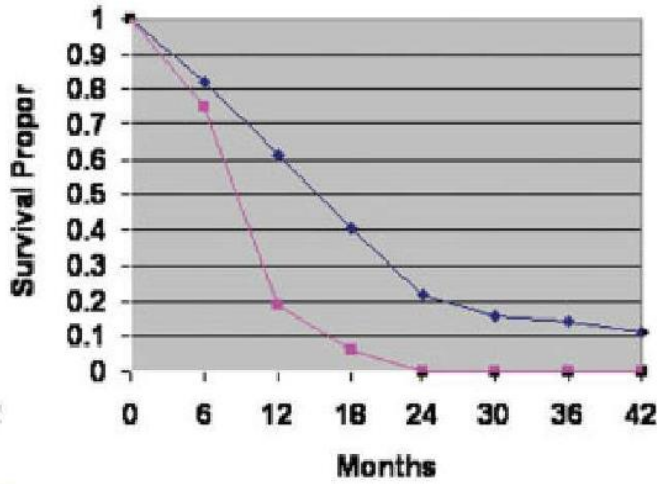
CNS Involvement in TNBC

CNS METASTASES AND TNBC

Special Considerations

Incidence of BM in metastatic TNBC resembles metastatic HER2-positive BC[1]
Shorter BMFS[2]
Higher rate of LMD
Different progression patterns:
- HER2-positive mBC: stable extracranial disease at brain metastases diagnosis common
- SD/PR: 50%[3]
- mTNBC: parallel progression of extra- and intracranial disease

Poor prognosis of mTNBC with BM[4]



OS in mTNBC pts. with/without BM

1 Bansal R et al. Clin Breast Cancer 2023;23:825-831.; 2 Berghoff A et al. Br J Cancer 2012;106:440-446.; 3 Bendell JC et al. Cancer 2003;97:2972-2977.; 4 Lin NU et al. Cancer 2008;113:2638-2645

Novel agents and brain metastases associated with TNBC

Agent	Trial	CNS Eligibility	Primary Results	Comment
T-DxD	DESTINY-Breast 04	Baseline BM	IC-ORR 25% (vs 0% with TPC)	HER2-low disease
Sacituzumab Govitecan	ASCENT (SG vs TPC)	Stable BM ≥4 weeks	PFS 2.8 v 1.6m ORR 3 vs 0% OS 7 months	N=60
Datopotomab durextecan	TROPION-PanTumor 01	Clinically inactive BM or Prior Treated >2w	ORR 32% PFS 4.4m	TNBC cohort (n-44)
	TUXEDO-2	Active BM	IC-ORR 37.5%	First-stage (n=8) - 6 newly dx - 2 progressive dz

Pan S, et al. Therap Adv in Med Oncol 2024; 16: https://doi.org/10.1177/17588359241292266

Conclusions

- What is the natural history of TNBC?
  - **Prone to earlier relapse vs HR+ disease by about 2 years**
- Should she have gotten more adjuvant treatment?
- Should we have followed ctDNA?
- Is there a role for biopsy? What about NGS?
- What are her options now?

Conclusions

- What is the natural history of TNBC?
- Should she have gotten more adjuvant treatment?
  - **Standard of care would have been to suggest use; should be guided by tumor biology.**
- Should we have followed ctDNA?
- Is there a role for biopsy? What about NGS?
- What are her options now?

Conclusions

- What is the natural history of TNBC?
- Should she have gotten more adjuvant treatment?
- Should we have followed ctDNA?
  - **Not ready for routine use; should be done only in setting of a clinical trial**
- Is there a role for biopsy? What about NGS?
- What are her options now?

Conclusions

- What is the natural history of TNBC?
- Should she have gotten more adjuvant treatment?
- Should we have followed ctDNA?
- Is there a role for biopsy? What about NGS?
  - **Biopsy of first recurrence is suggested.**
  - **NGS recommended, but only if options for treatment are available.**
- What are her options now?

Conclusions

- What is the natural history of TNBC?
- Should she have gotten more adjuvant treatment?
- Should we have followed ctDNA?
- Is there a role for biopsy? What about NGS?
- What are her options now?
  - **Multiple new agents available; sequence of use is not entirely clear.**

Conclusions

- Biology drives treatment → TNBC is not one disease
- One in five people with TNBC harbors a BRCA mutation → implications for treatment and for identifying family at risk
- Therapy in the US and Europe requires use of somatic testing → Driver mutations to predict therapy is a reality
- Immunotherapy plays a role in management
- HER2 low is a targetable subtype in all breast cancer subtypes
- Global access is essential to achieve equity


Thank you so much for having me.
On Twitter, Instagram, and TikTok @drdonsdizon