

How I Treat Triple Negative Breast Cancer

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Disclosures

I have the following relevant financial relationships to disclose:

Consultant for: Amgen, Arvinas, Bristol-Myers Squibb, Celgene, Eli Lilly, Genentech/Roche, Immunomedics, Merck, OBI Pharma, Pfizer, Puma, Spectrum Pharmaceuticals, Syndax Pharmaceuticals, Peregrine, Calithera, Daiichi-Sankyo, Seattle Genetics, AstraZeneca and TapImmune.

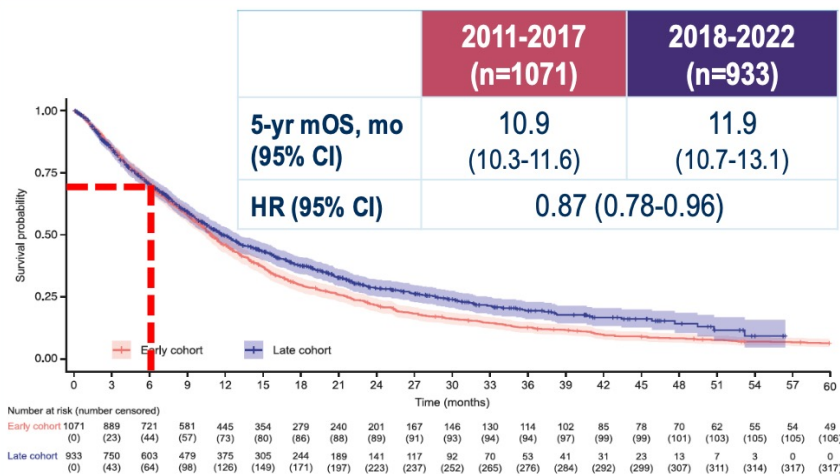
Grant/Research support from: Bristol-Myers Squibb; MedImmune, LLC/AstraZeneca; BTG; and Merck.

Survival outcomes in mTNBC

Real-world data

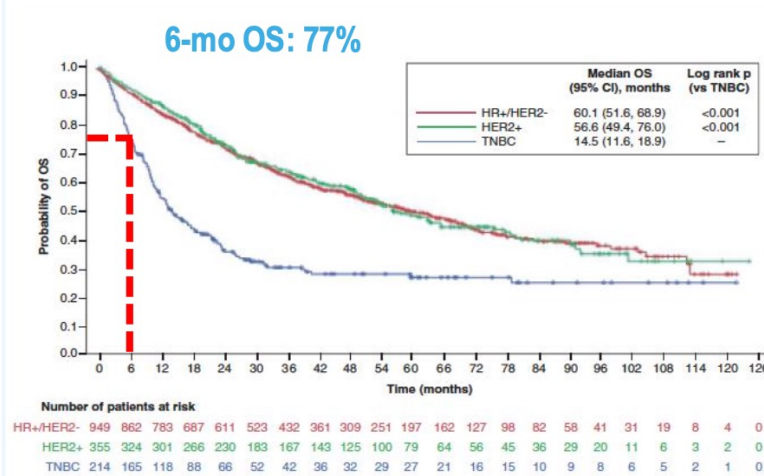
Flatiron (2011-2022) N=2,004

Median OS: 11.3 months (95% CI: 10.7-12.0)
OS at 12 months: 48%



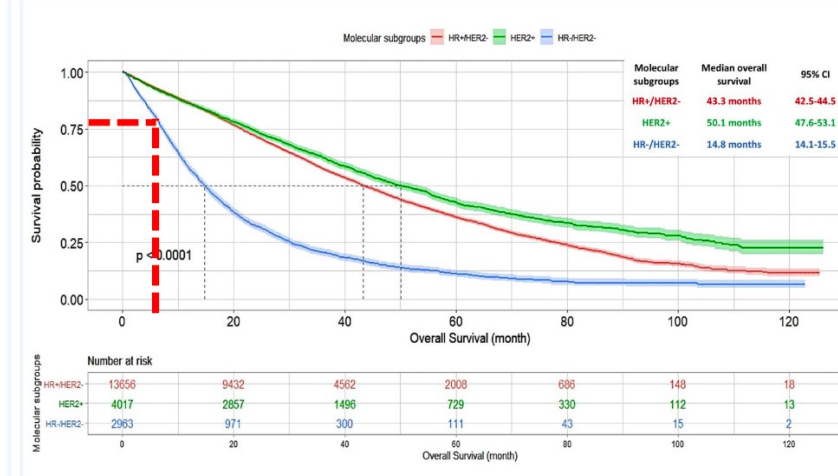
Patient360 (2010-2019) N=214

Median OS: 14.5 mo. (95% CI: 11.6-18.9)
OS at 12 months: 56%



ESME French Cohort (2008-2016) N=2,963

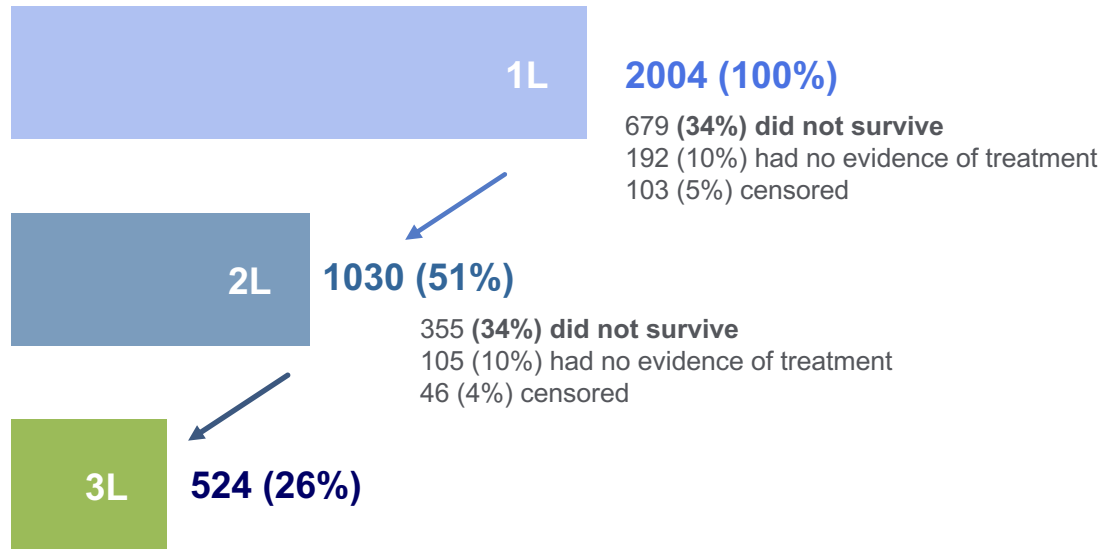
Median OS: 14.8 mo. (95% CI: 14.1-15.5)



Approximately 25%-30% of patients diagnosed with mTNBC do NOT survive past 6 months

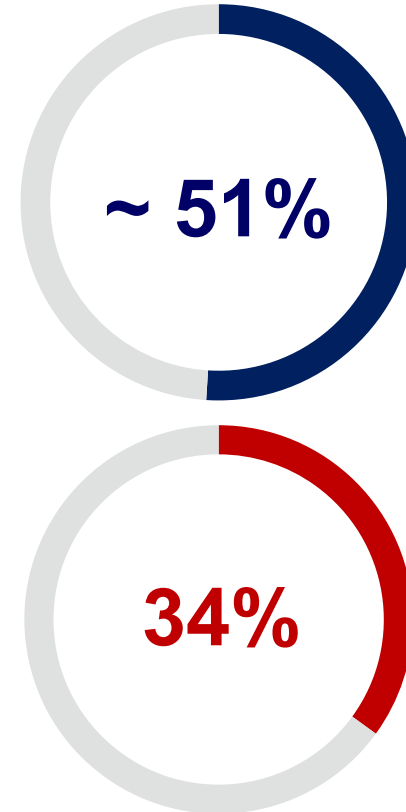
Important to Use Most Effective Therapy First in mTNBC

Patient disposition, n (%)^{1*}



Percentages for 2L and 3L patients are expressed as a proportion of the total patient population (2L: 1030/2004 (51%); 3L: 524/2004 (26%))

*This retrospective observational study used Flatiron Health de-identified electronic health record data from the USA. Punie K, et al.¹



of patients who receive 1L treatment will subsequently get treated with 2L treatment...

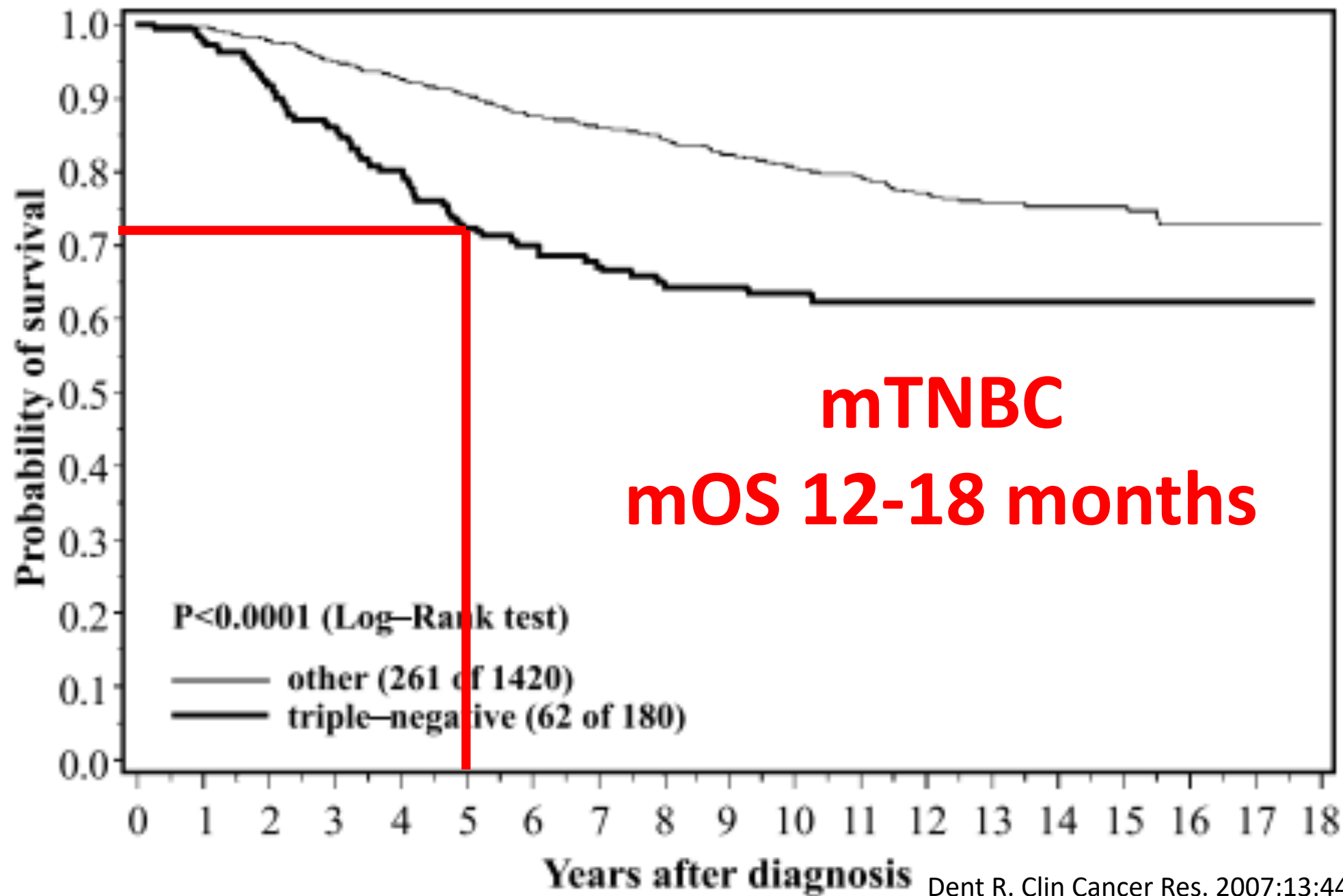
...do not survive to receive a next line of therapy, **confirming the unmet need** for more efficacious treatment options **for previously untreated patients with mTNBC**^{1,2}

Approximately 50% of patients with mTNBC do not receive treatment beyond 1L due to health deterioration, patient preference, or death¹⁻³

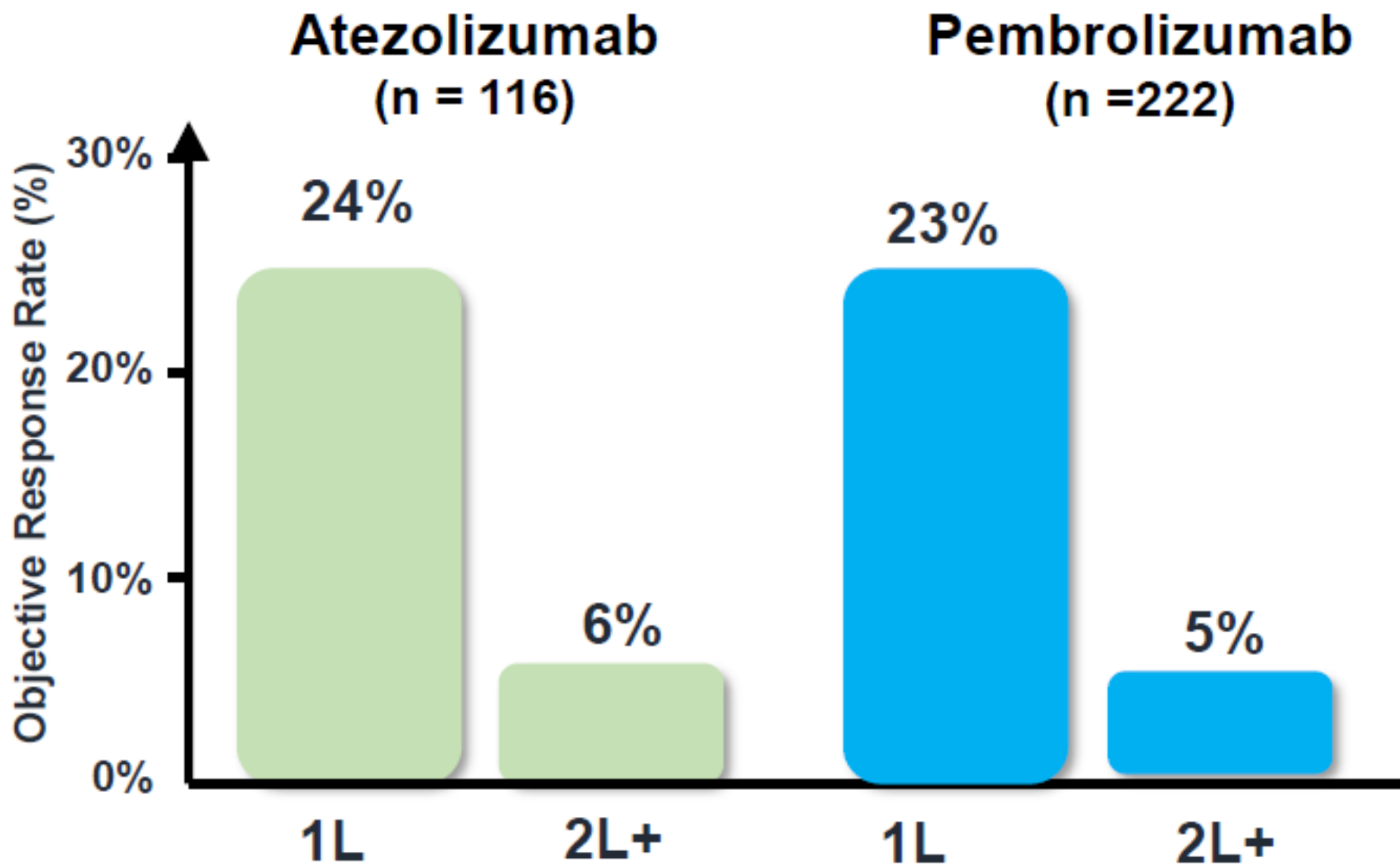
1L/2L/3L, first-/second-/third-line; mTNBC, metastatic triple-negative breast cancer.

1. Punie K, et al. *Oncologist*. 2025;30:oyaf034; 2. Skinner KE, et al. *Future Oncol*. 2021;17(8):931-941; 3. Khankeh HR, et al. *BMC Palliat Care*. 2023;22:10.

Slide courtesy of Dr. Sara Tolaney



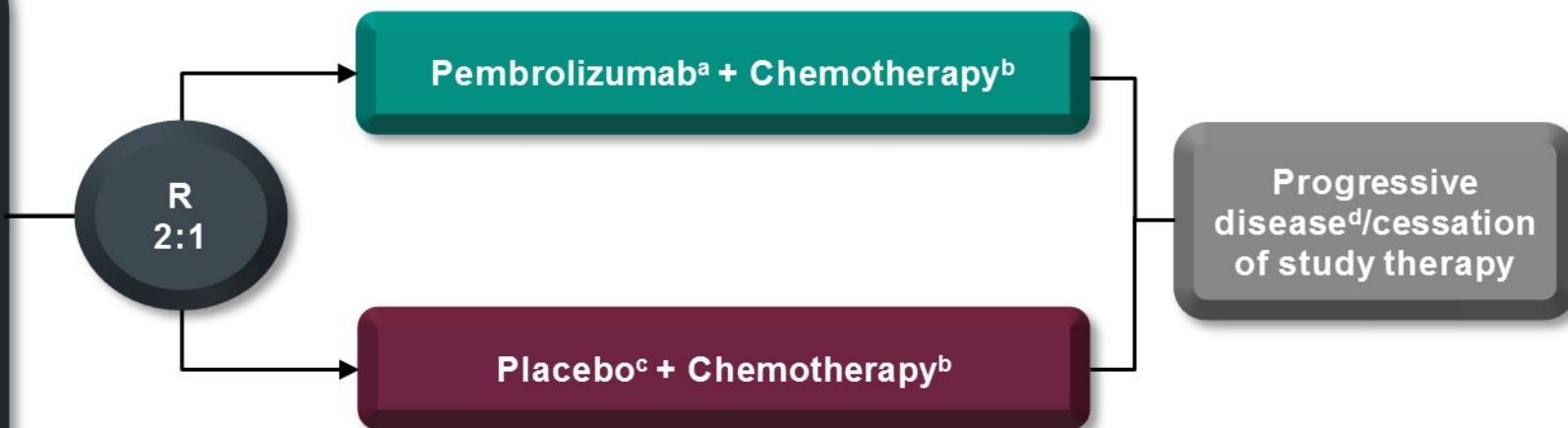
Lesson Learned from IO in mTNBC



KEYNOTE-355 Study Design (NCT02819518)

Key Eligibility Criteria

- Age ≥ 18 years
- Central determination of TNBC and PD-L1 expression
- Previously untreated locally recurrent inoperable or metastatic TNBC
- 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 vs gemcitabine/carboplatin)
- PD-L1 tumor expression (CPS ≥ 1 vs CPS < 1)
- Prior treatment with same class chemotherapy in the neoadjuvant or adjuvant setting (yes vs no)

^aPembrolizumab 200 mg intravenous (IV) every 3 weeks (Q3W)

^bChemotherapy dosing regimens are as follows:

Nab-paclitaxel 100 mg/m² IV on days 1, 8, and 15 every 28 days

Paclitaxel 90 mg/m² IV on days 1, 8, and 15 every 28 days

Gemcitabine 1000 mg/m²/carboplatin AUC 2 on days 1 and 8 every 21 days

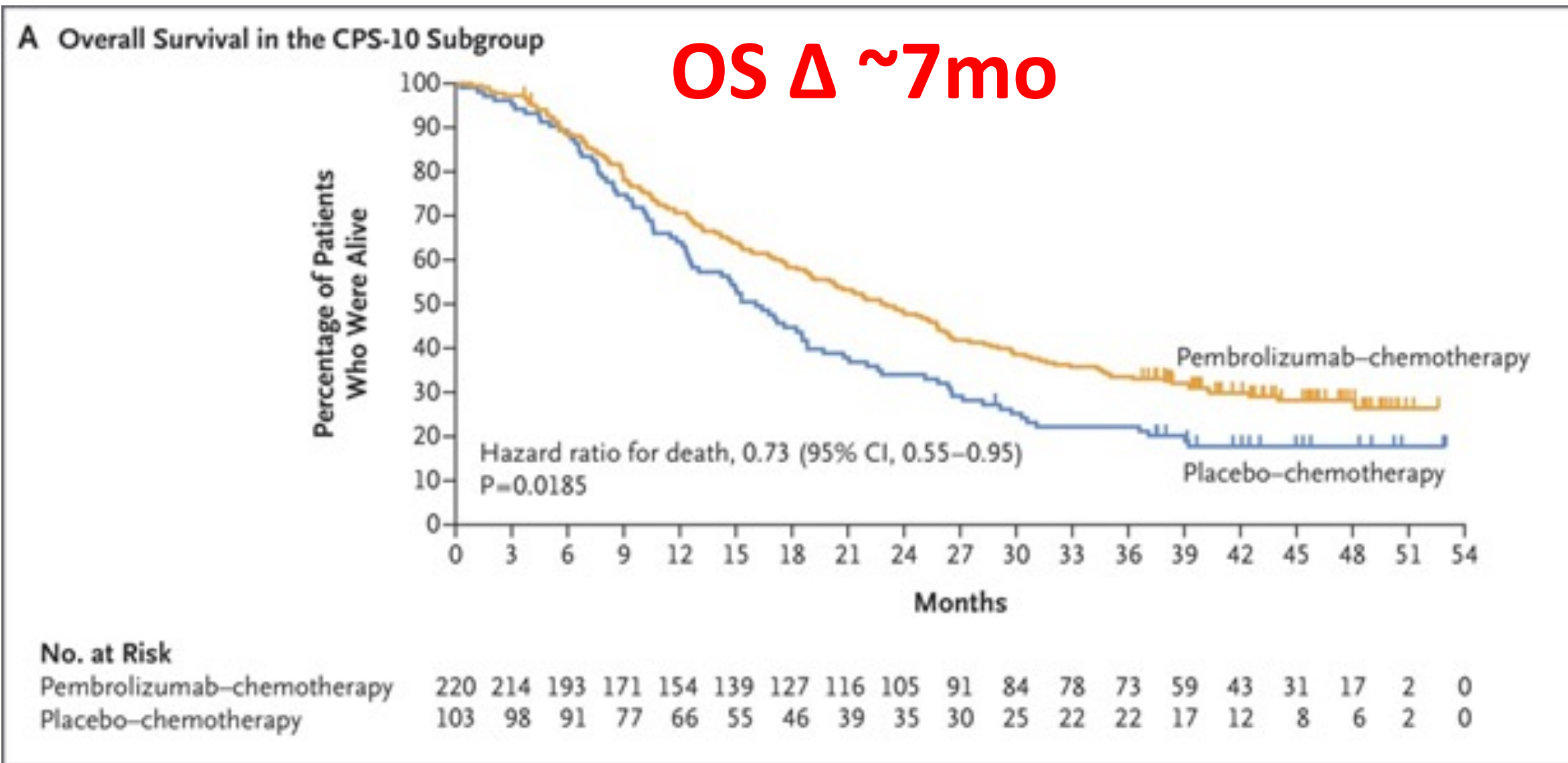
^cNormal saline

^dTreatment may be continued until confirmation of progressive disease

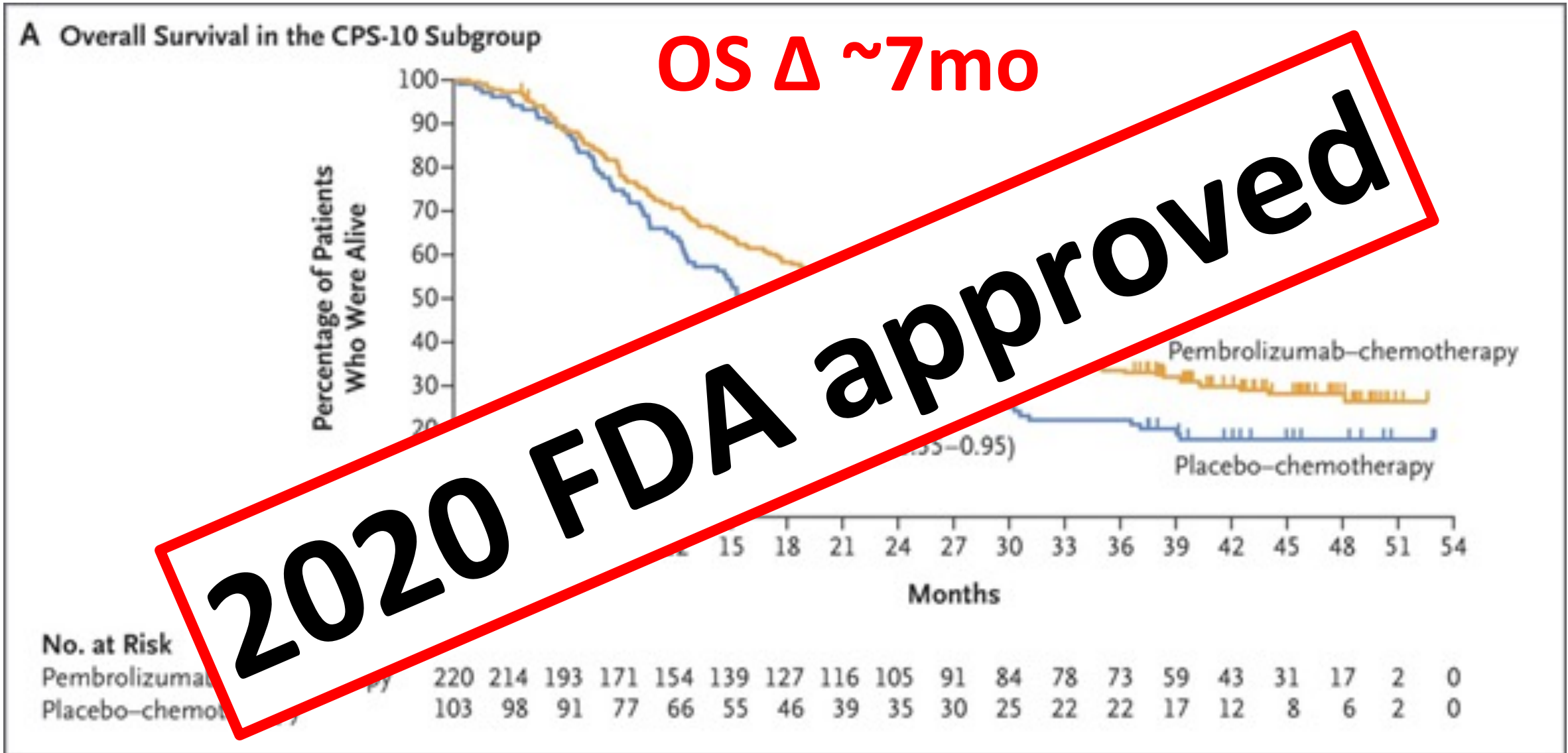
CNS=central nervous system; ECOG=Eastern Cooperative Oncology Group;

PD-L1=programmed death ligand 1; R=randomized; TNBC=triple-negative breast cancer

KEYNOTE-355 OS in CPS $\geq$ 10



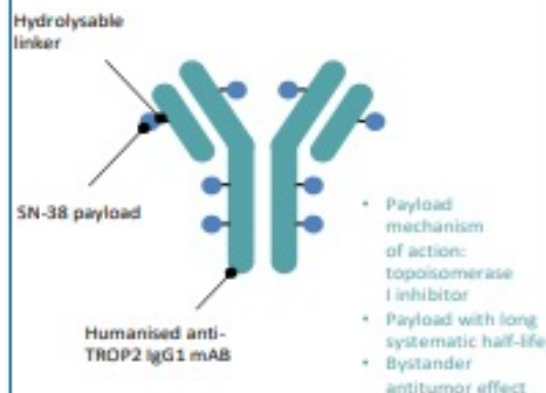
KEYNOTE-355 OS in CPS $\geq$ 10



Targets for ADCs in Breast Cancer

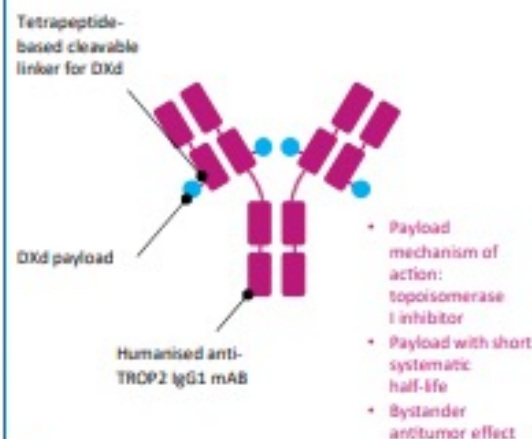
Sacituzumab govitecan

DAR ≈ 8



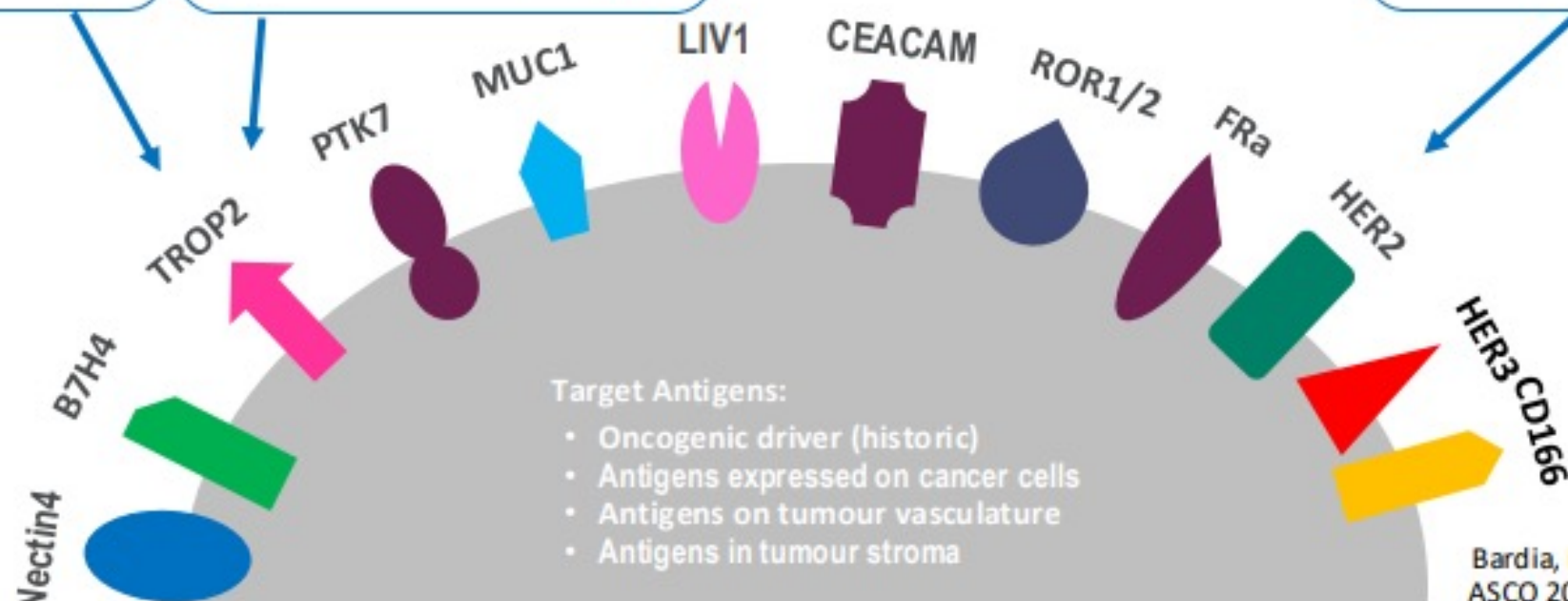
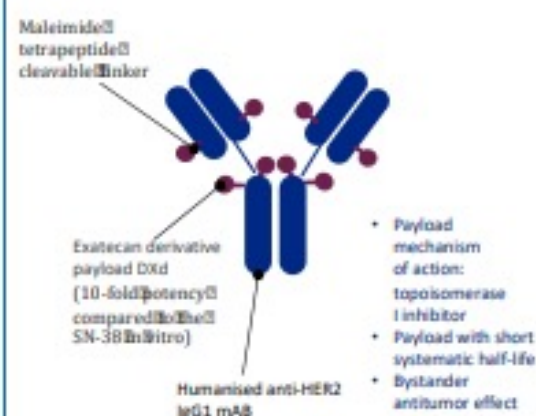
Datopotamab deruxtecan

DAR ≈ 4

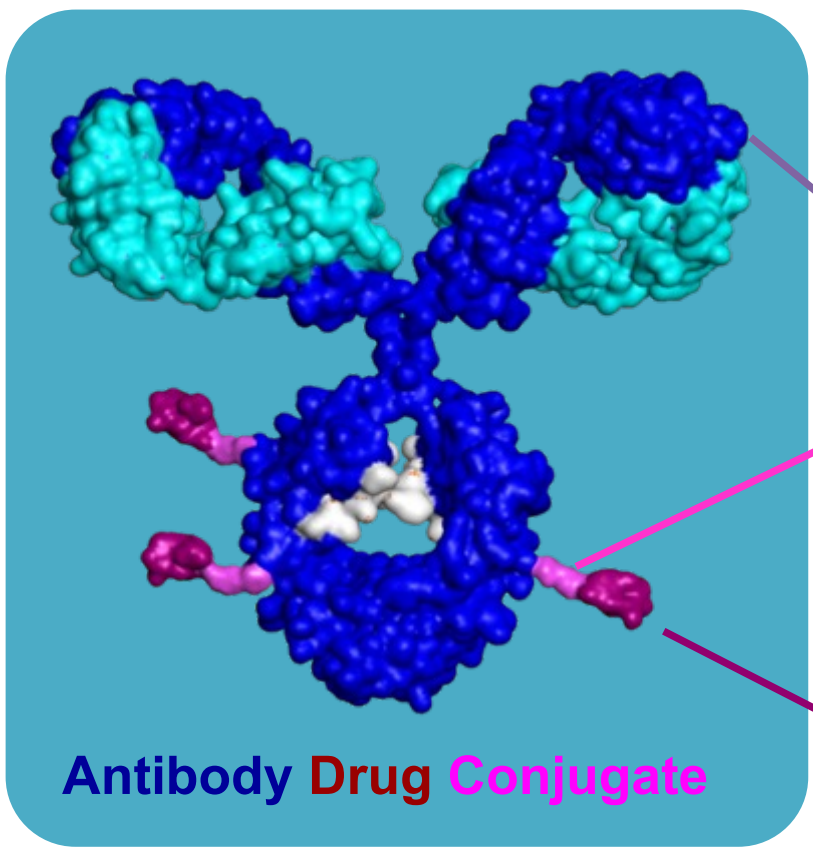


Trastuzumab deruxtecan

DAR ≈ 8



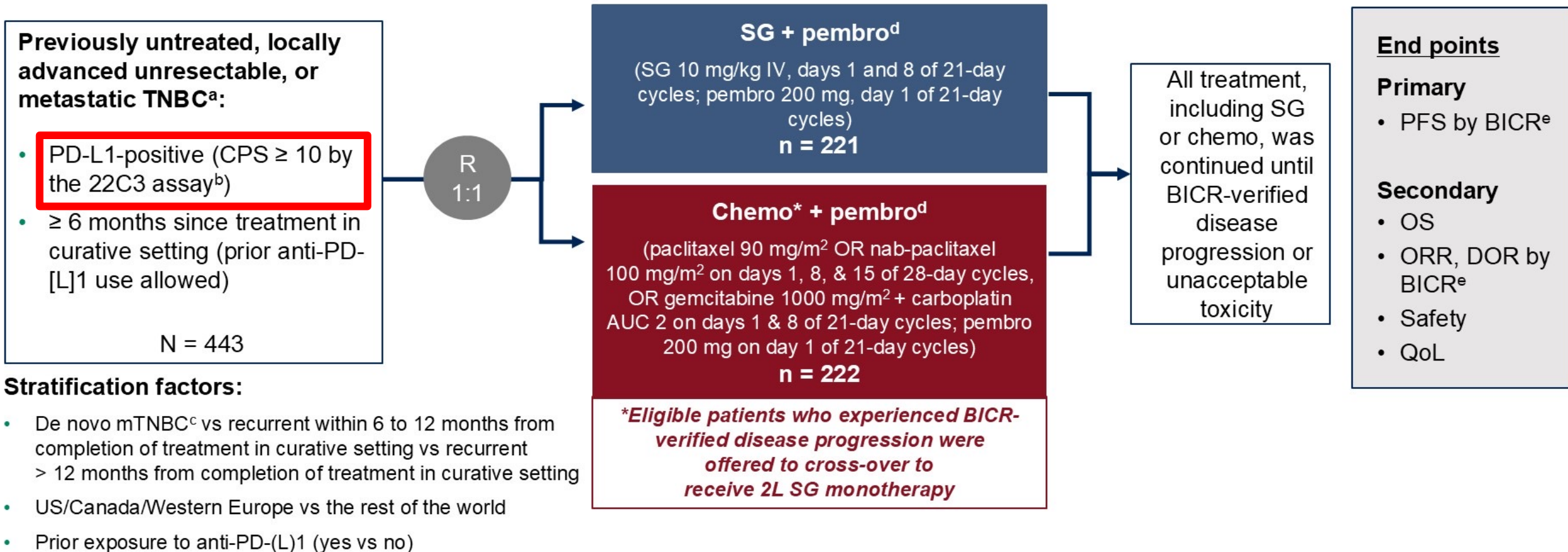
ADCs Have Different Antibodies, Linkers and Payloads



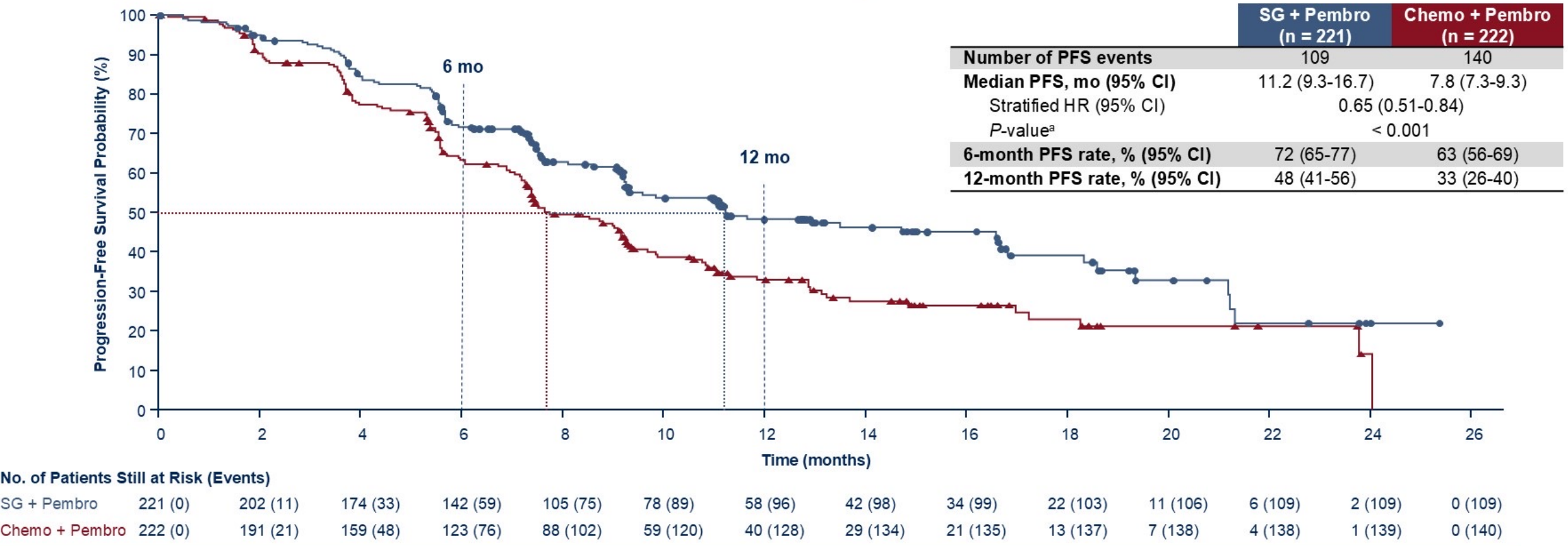
	ADC Attributes	Sacituzumab govitecan (SG)	Datopotamab deruxtecan (Dato-DXd)	Sacituzumab tirumotecan (sac-TMT)
		Target	TROP2	TROP2
		Antibody	hRS7 IgG1k	Datopotamab
Antibody	DAR	~7.6:1	~4:1	hRS7 IgG1
	Linker	Hydrolysable	Tetrapeptide-based	~7.4:1
	Cleavable linker?	Yes	Yes	2-methylsulfonyl pyrimidine
Linker	Payload	SN-38	DXd	Yes
	Payload MoA	Topo1 inhibitor	Topo1 inhibitor	KL610023 (T030)
	Membrane permeable?	Yes	Yes	Topo1 inhibitor
Payload				Yes

ADC, antibody-drug conjugate; DAR, drug to antibody ratio; Dato-DXd, datopotamab deruxtecan; HER2/3, human epidermal growth factor receptor 2/3; IgG, immunoglobulin; MMAE, monomethyl auristatin E; MoA, mechanism of action; SG, sacituzumab govitecan; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TROP, trophoblast cell surface antigen.

ASCENT-04/KEYNOTE-D19 Study Design



Progression-Free Survival by BICR



SG + pembro demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo + pembro by BICR analysis, with a 35% reduction in risk of disease progression or death

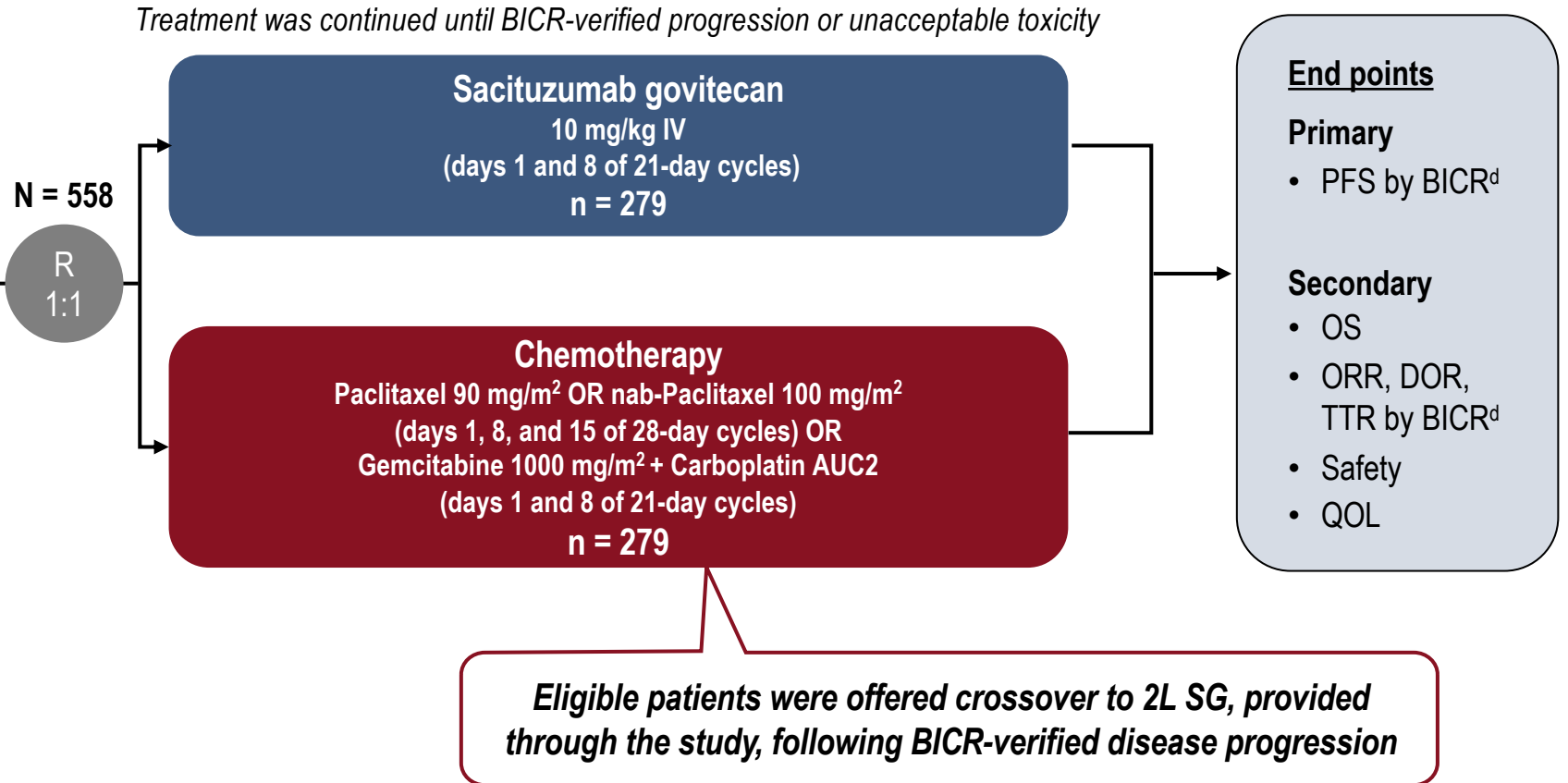
ASCENT-03: Study Design

Patients with previously untreated, locally advanced inoperable or metastatic TNBC^a:

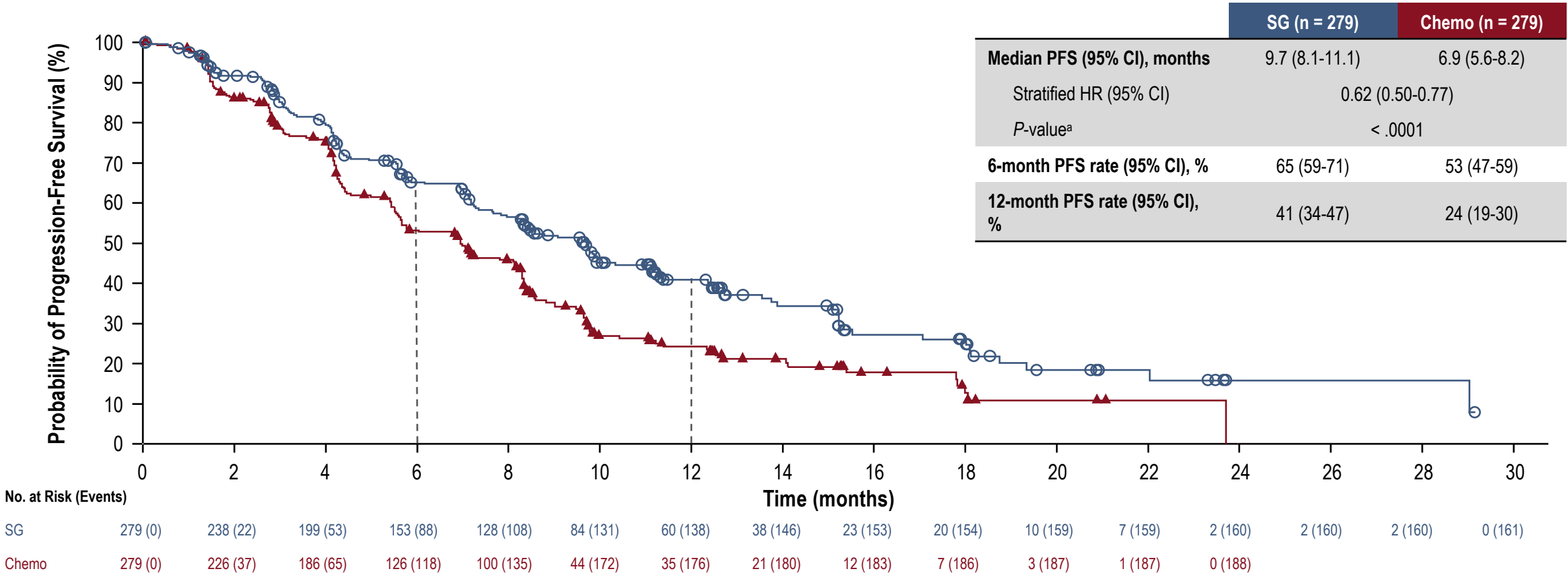
- Not candidates for PD-(L)1 inhibitors:
 - PD-L1 negative^b tumors (CPS < 10)
 - PD-L1 positive^b tumors (CPS ≥ 10) and previously treated with a PD-(L)1 inhibitor in curative setting
 - Ineligible for a PD-(L)1 inhibitor due to a comorbidity
- ≥ 6 months since treatment in curative setting
- Previously treated, stable CNS metastases were allowed

Stratification factors:

- US/Canada/Western Europe vs rest of the world
- De novo mTNBC^c vs recurrent within 6 to 12 months of treatment vs recurrent after > 12 months from treatment in curative setting



Progression-Free Survival by BICR



SG demonstrated statistically significant and clinically meaningful improvement in PFS vs chemo by BICR analysis, with a 38% reduction in risk of disease progression or death

TROPION-Breast02: Study Design

Randomised, phase 3, open-label, global study (NCT05374512)

Key inclusion criteria:

- Patients with histologically or cytologically documented locally recurrent inoperable or metastatic TNBC*
- No prior chemotherapy or targeted systemic therapy in the locally recurrent inoperable or metastatic setting
- Immunotherapy not an option[†]
- ECOG PS 0 or 1
- No minimum DFI[‡]

1:1

Dato-DXd

6 mg/kg IV Day 1 Q3W
(n=323)

Investigator's choice of chemotherapy (ICC)[#]

Paclitaxel, nab-paclitaxel, capecitabine,
eribulin mesylate/eribulin, carboplatin
(n=321)

Endpoints

Dual primary:

- OS
- PFS by BICR per RECIST v1.1

Secondary included:

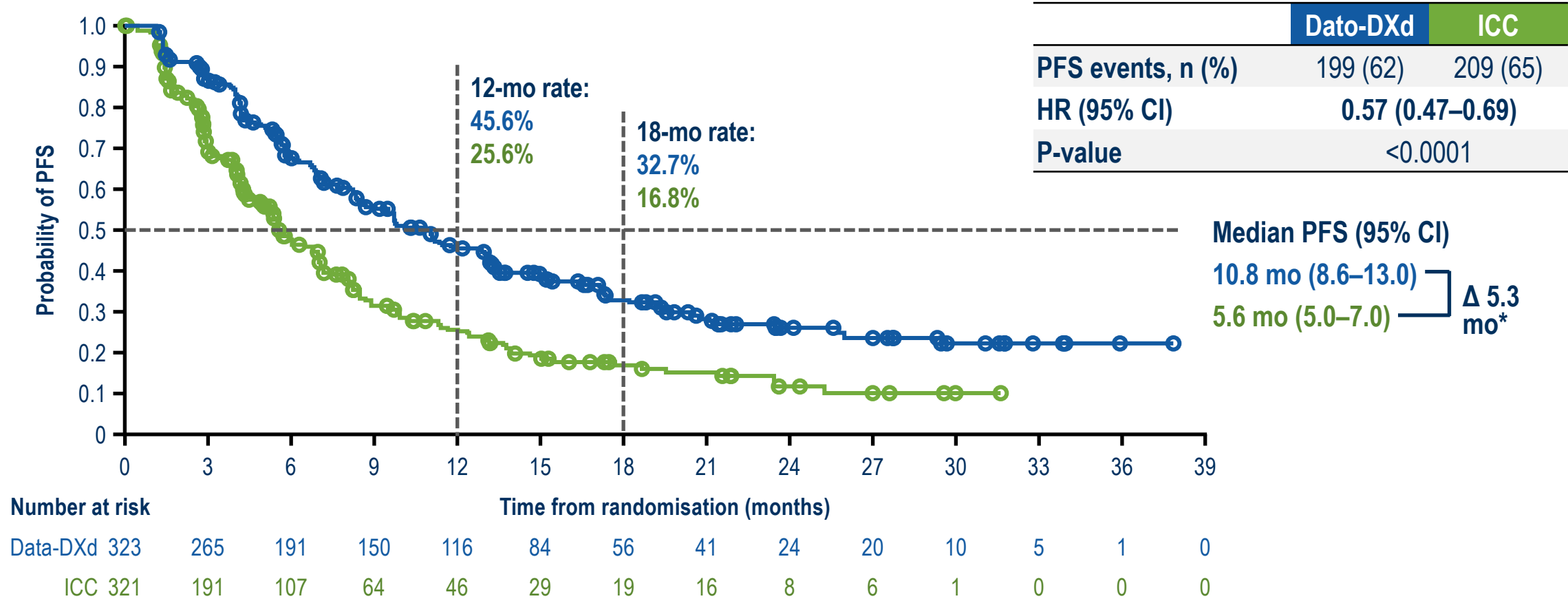
- PFS (investigator-assessed)
- ORR, DoR
- Safety

Randomisation stratified by:

- Geographic region (US/Canada/Europe vs other geographic regions)
- PD-L1 status (high [CPS ≥10] vs low [CPS <10])[§]
- DFI history (*de novo* vs prior DFI 0–12 months vs prior DFI >12 months)^{||}

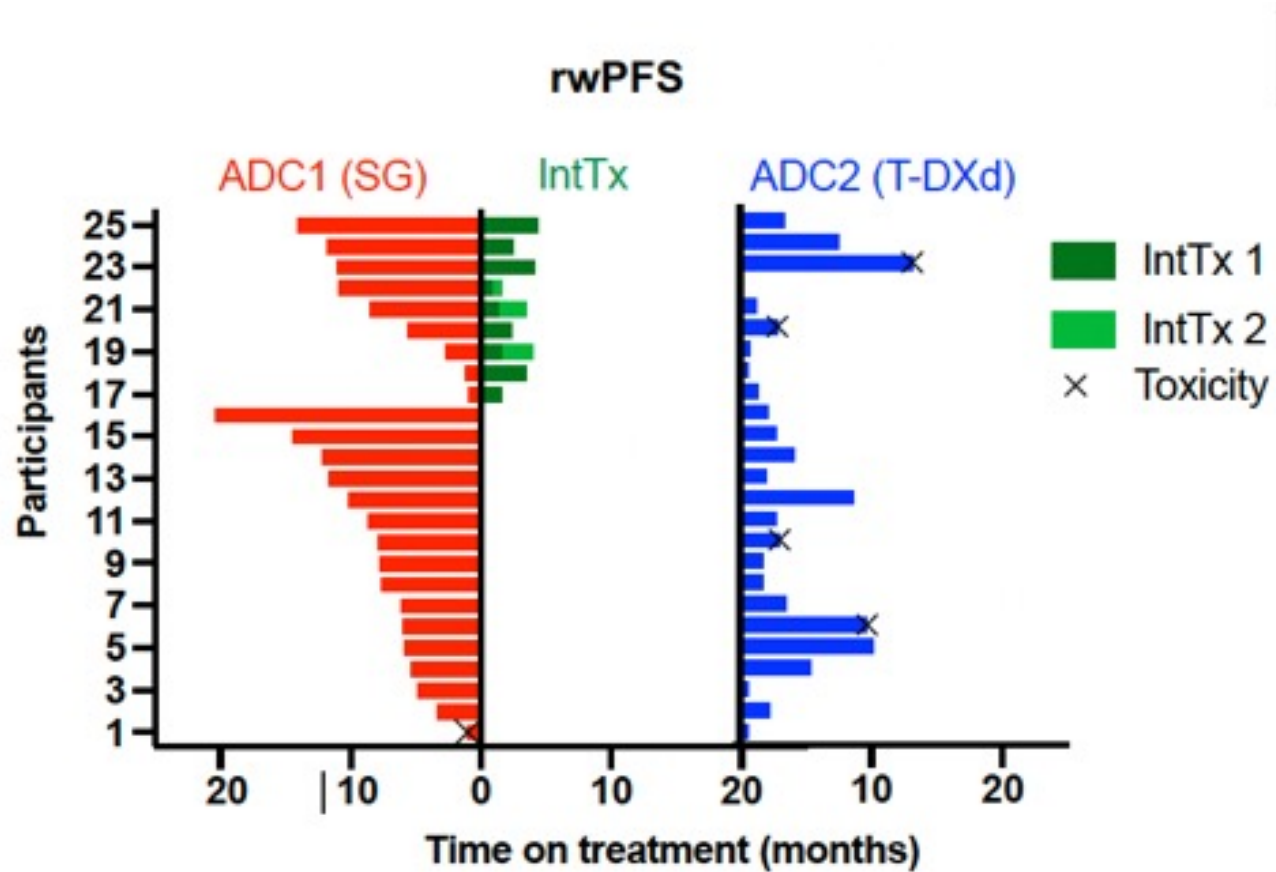
- Treatment continued until investigator-assessed RECIST v1.1 progressive disease, unacceptable toxicity, or another discontinuation criterion was met
- Following progression or discontinuation of study treatment, patients could receive subsequent therapies, including approved ADCs or chemotherapy, at the investigator's discretion^{||}

Progression-Free Survival by BICR



Dato-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with ICC, reducing the risk of progression or death by 43%

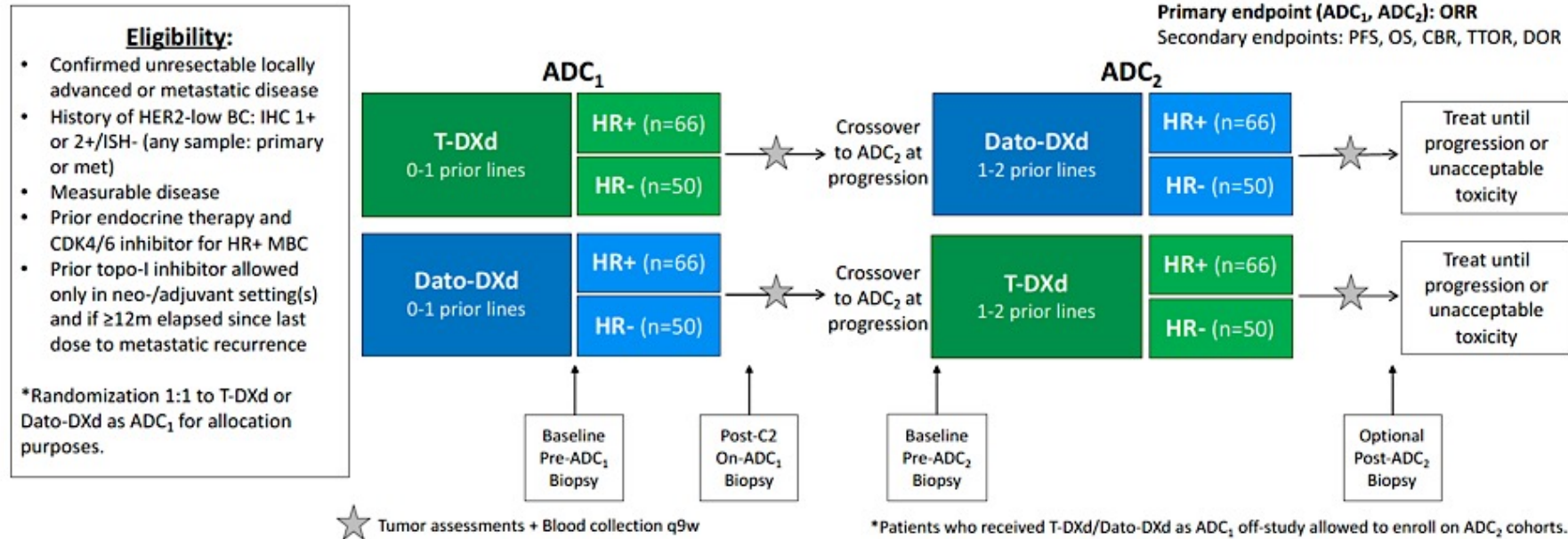
Sequential T-DXd Post Sacituzumab Govitecan in mTNBC



	ADC1 (SG)	ADC2 (T-DXd)
Median rwPFS from time of each ADC start, months	7.7	2.8
Median rwOS from time of each ADC start, months	16.2	6.5

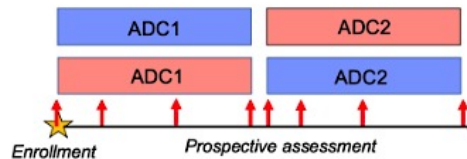
On average, shorter PFS with ADC2

TBCRC 064: Treatment of ADC-Refractory Breast Cancer with Dato-DXd or T-DXd (TRADE DXd). PI: Ana Garrido-Castro



TBCRC-067 ENCORE: Multicenter Prospective Registry of Sequential ADCs in HER2- mBC PI: Laura Huppert

Cohorts 1 & 2: Enrollment Prior to ADC1



- Cohort 1: HR+/HER2- MBC (~35 patients)
- Cohort 2: mTNBC (~25 patients)

Cohorts 3 & 4: Enrollment Prior to ADC2



- Cohort 3: HR+/HER2- MBC (~25 patients)
- Cohort 4: mTNBC (~15 patients)

For all cohorts:

- ADCs and imaging at least q12wk per SOC
- PRO data collection
- Research blood collection: Prior to C1D1, C2D1, C5D1, q4 cycles, end of treatment
- Archival tissue collection and research biopsy if SOC biopsy planned
- Intervening therapies between ADCs is allowed

Primary Endpoints:

- Real-world progression free survival of ADC1 (rwPFS1)
- Real-world progression free survival of ADC2 (rwPFS2)

Secondary Endpoints (for each ADC):

- Overall response rate (ORR), duration of response (DOR), best overall response (BOR), disease control rate (DCR)
- Real-world overall survival (rwOS)
- Safety

Exploratory Endpoints:

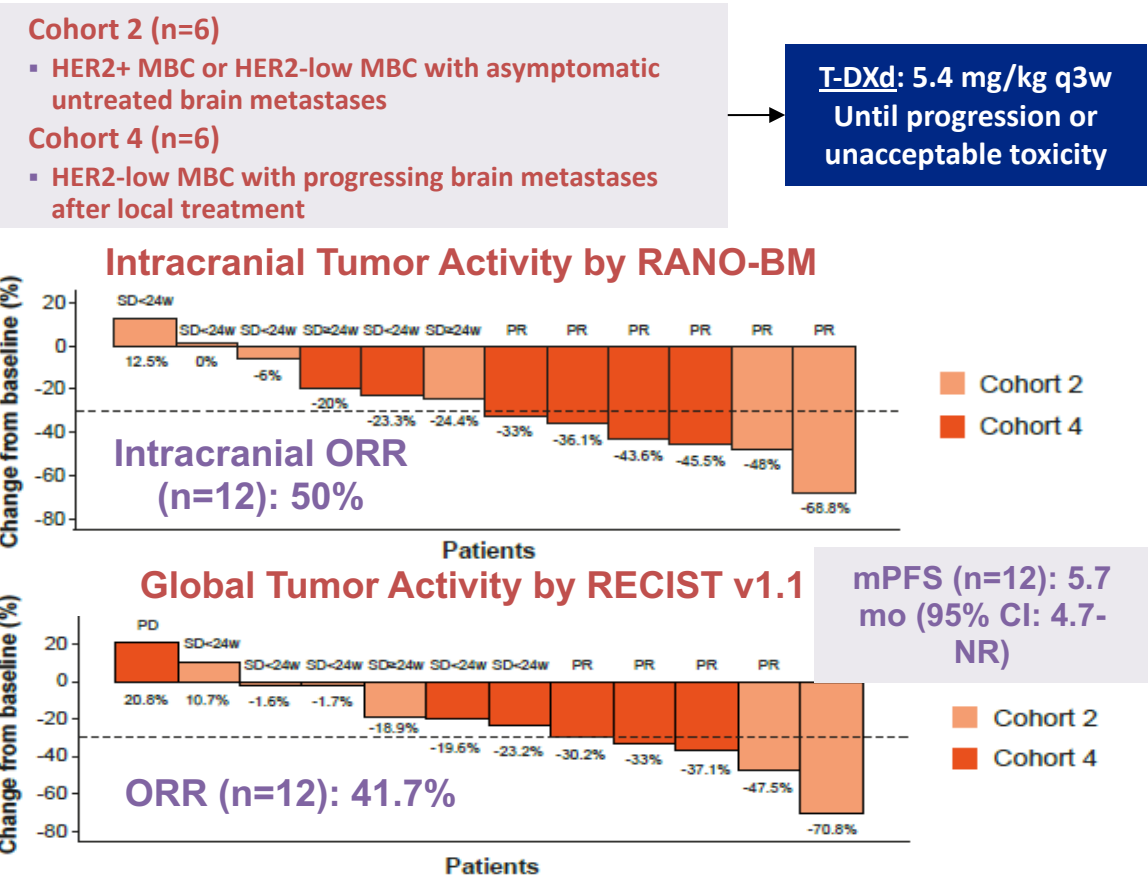
- Translational correlates of ADC response/resistance (see below)

↑ = Study Blood Draw (20ml)

T-DXd and SG in Patients With HER2-Low and Treatment-Naive MBC With Brain Metastases

T-DXd in Patients With HER2-Low MBC and Brain Metastases: the Phase 2 DEBBRAH Trial¹

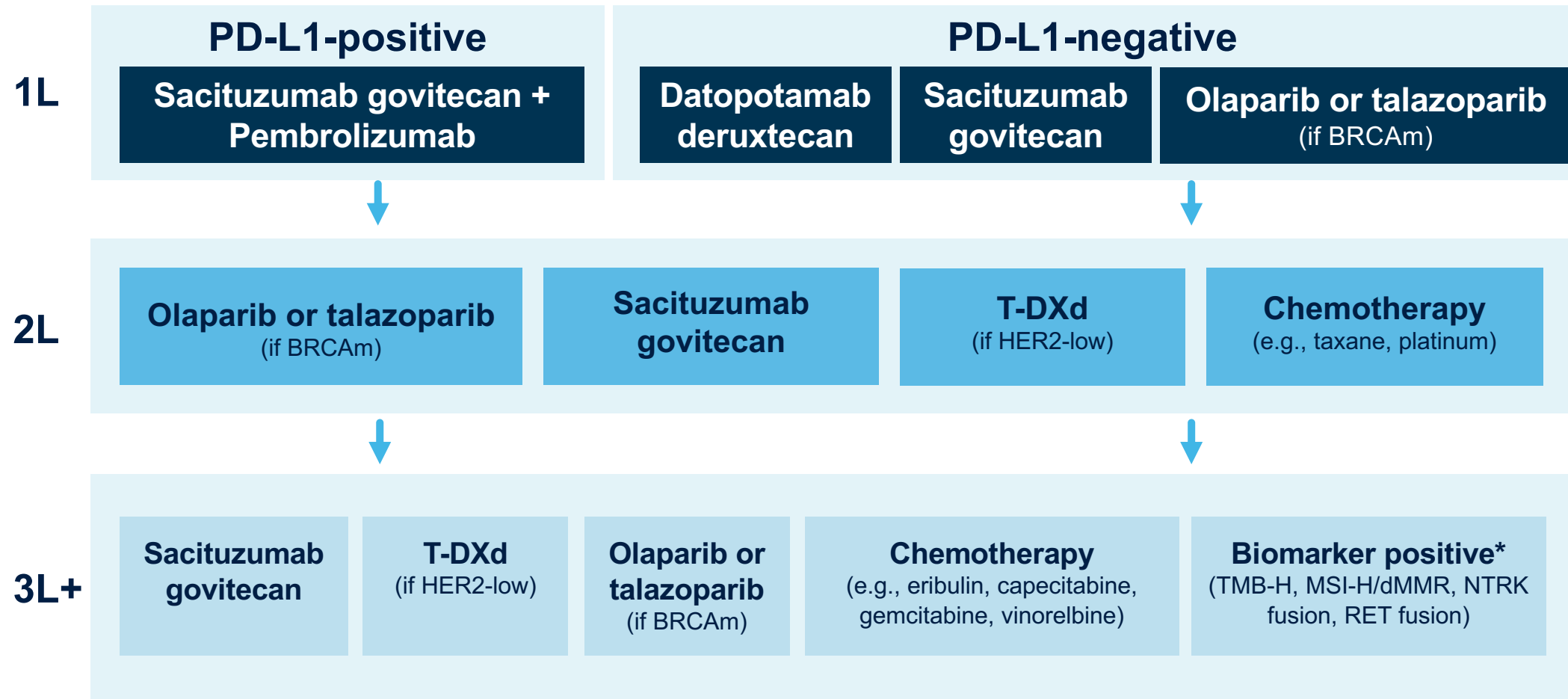
Sacituzumab Govitecan in Patients With mTNBC and Brain Metastases: Subgroup Analysis From the ASCENT Trial²



Efficacy		SG (n=32)	TPC (n=29)
PFS	Events, n	24	21
	Median (95% CI), months	2.8 (1.5-3.9)	1.6 (1.3-2.9)
	HR (95% CI)	0.65 (0.35-1.22)	
OS	Events, n	24	21
	Median (95% CI), months	6.8 (4.7-14.1)	7.5 (4.7-11.1)
	HR (95% CI)	0.87 (0.47-1.63)	
ORR, n (%)		1 (3)	0
Best overall response, n (%)	CR	0	0
	PR	1 (3)	0
	SD	15 (47)	9 (31)
	SD >6 months	2 (6)	1 (3)
	PD	11 (34)	11 (38)
Not evaluable		5 (16)	9 (31)
CBR, n (%)		3 (9)	1 (3)

1. Perez-Garcia JM, et al. SABCs 2022. Abstract PD7-02. 2. Dieras V, et al. SABCs 2020. Abstract PD13-07.

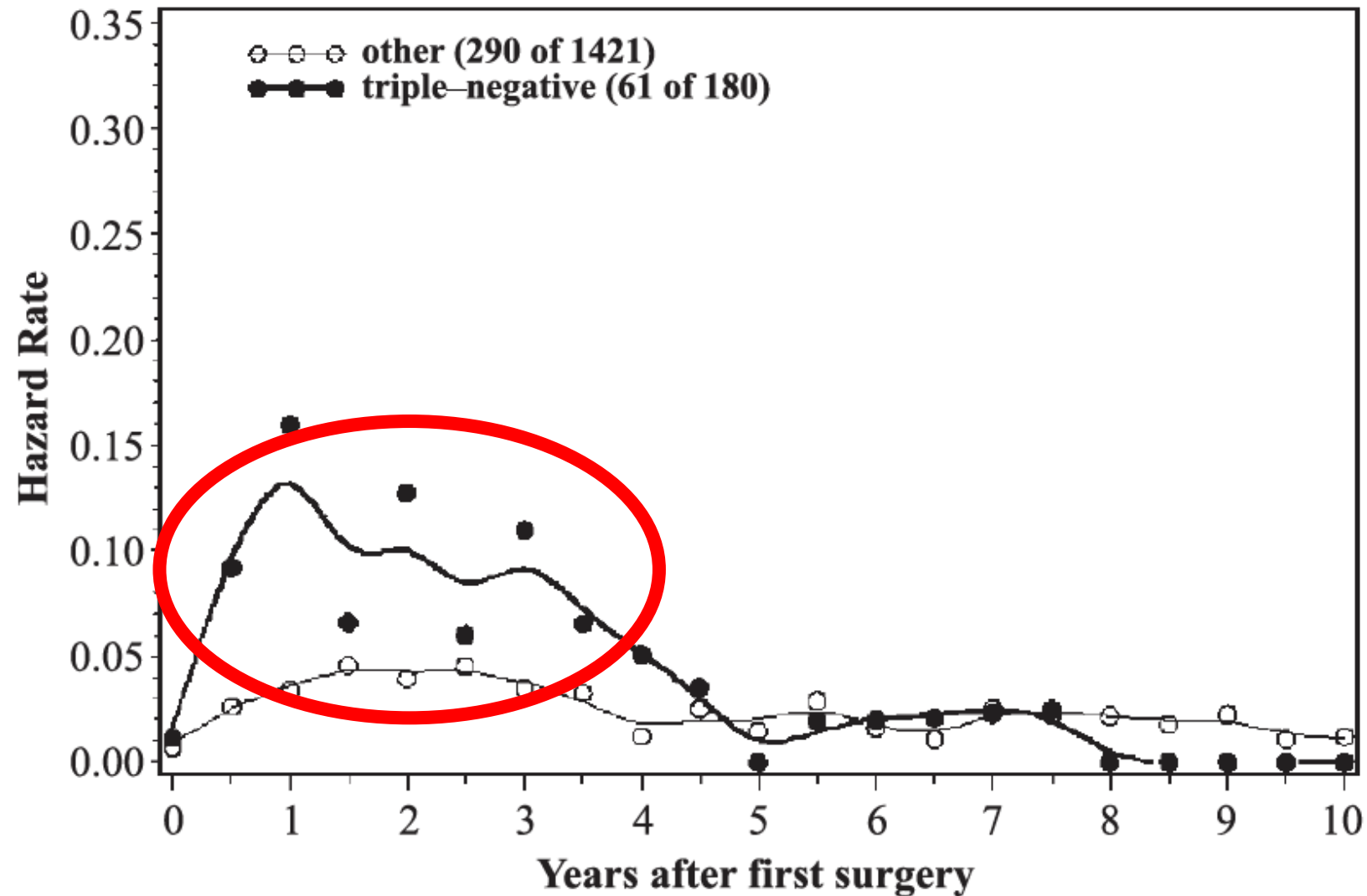
Treatment Algorithm for mTNBC



*TMB-H: Pembrolizumab; MSI-H: Pembrolizumab, Dostarlimab; NTRK fusion: Larotrectinib, Entrectinib, Repotrectinib; RET fusion: Selpercatinib. Slide courtesy of Ana Garrido-Castro

Slide courtesy of S. Tolaney

“Triple Negative Breast Cancer” Risk of Recurrence Occurs Early



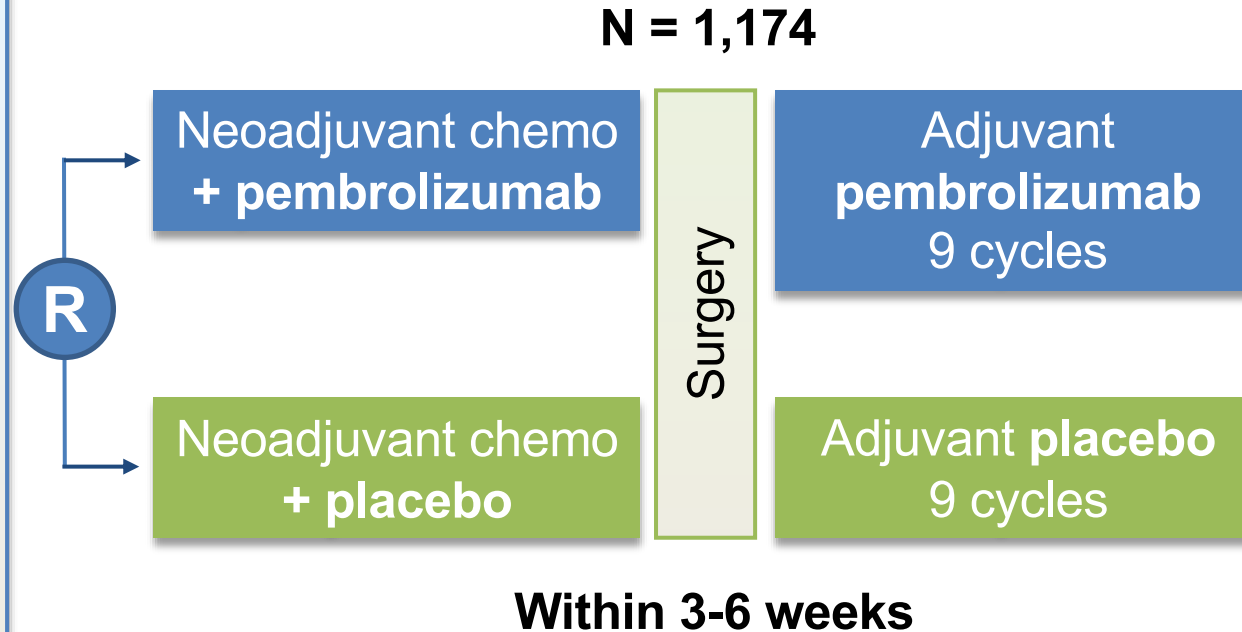
KEYNOTE-522

Eligibility

- Newly diagnosed TNBC (central confirmation)
- T1c N+ or T $\geq$ 2 N0-2
- PD-L1+ or PD-L1-

Stratification

- T1/T2 vs T3/T4
- N0 vs N+
- Carboplatin Q1W vs Q3W



Primary endpoints

- pCR rate (ypT0/Tis ypN0)
- EFS

Secondary endpoints

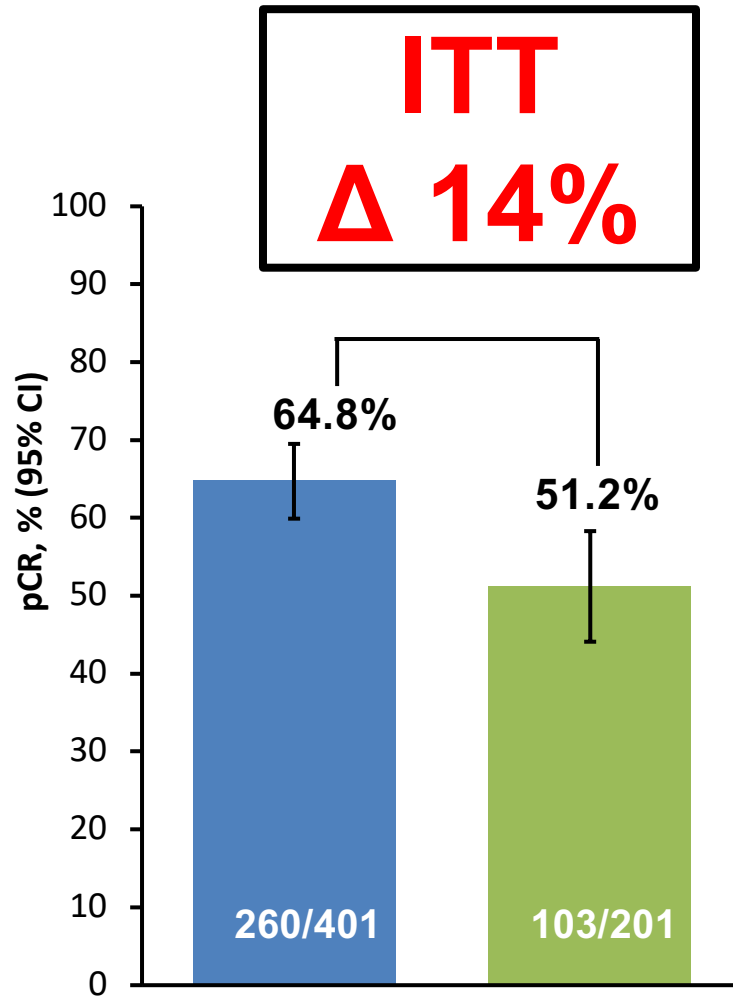
- Alternative pCR rate (ypT0 ypN0)
- pCR rate in PD-L1+
- EFS in PD-L1+
- OS

Study Treatment

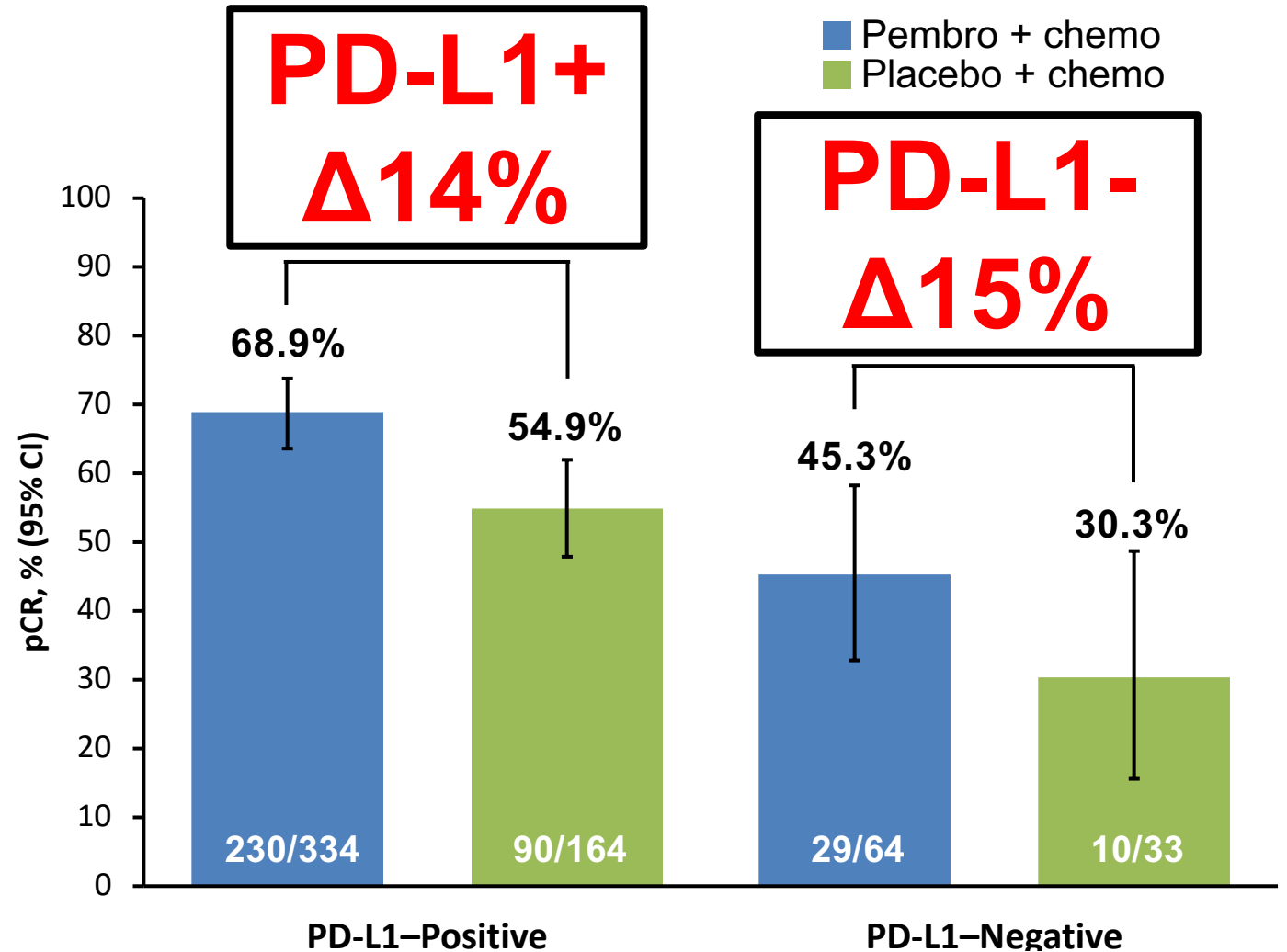


Paclitaxel 80 mg/m² IV weekly
Carboplatin weekly (AUC 1.5) or Q3W (AUC5)
Doxorubicin 60 mg/m² IV Q3W
(Epirubicin 90 mg/m² IV Q3W)
Cyclophosphamide 600 mg/m² IV Q3W
Pembrolizumab 200 mg IV Q3W

KEYNOTE-522: pCR at IA1



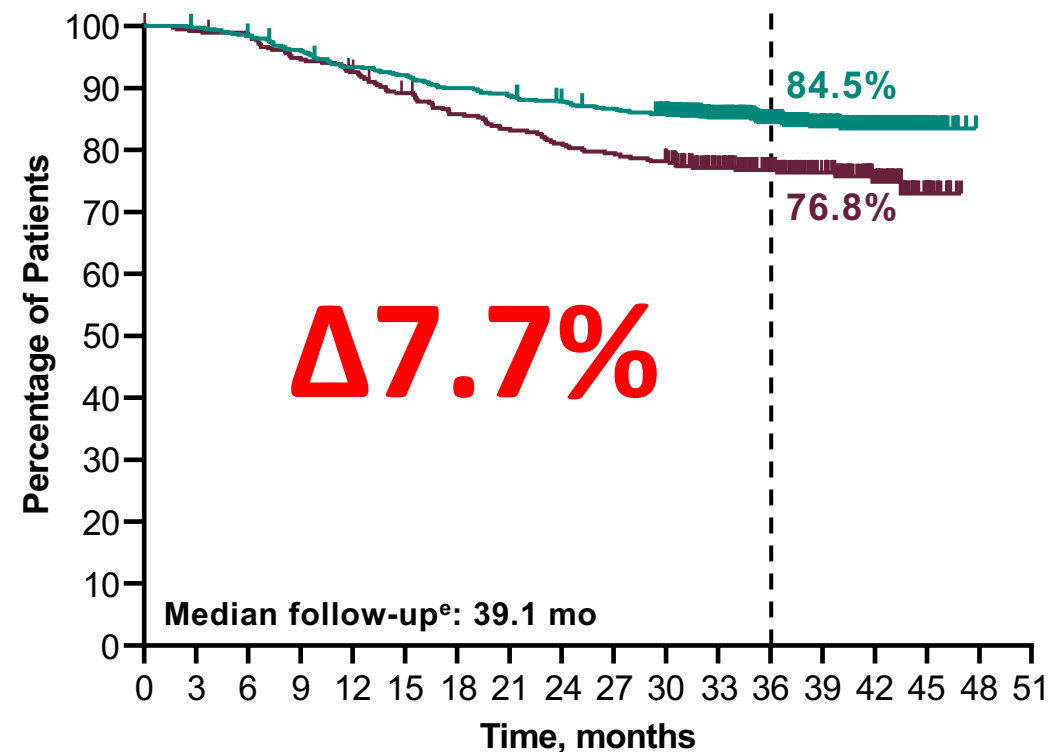
Heather L. McArthur



Schmid P et al. NEJM 2019.

EFS at IA4 and IA6

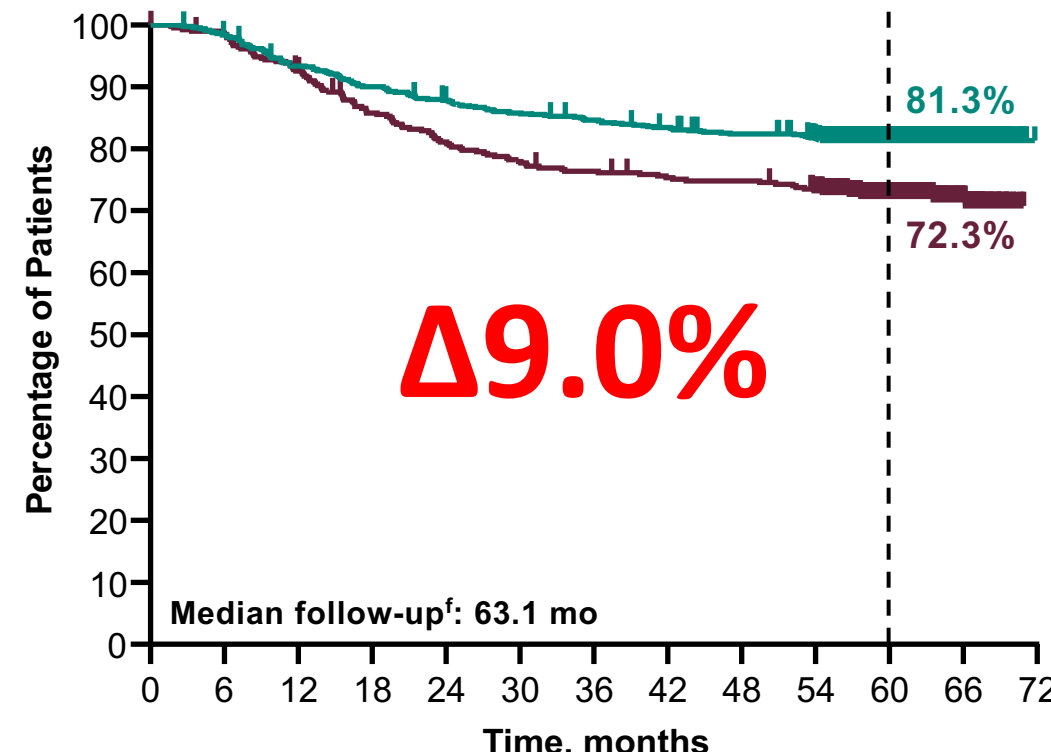
IA4 ^a	Events	HR (95% CI)	P value
Pembro + Chemo/Pembro	15.7%	0.63 ^c (0.48–0.82)	0.00031 ^d
Placebo + Chemo/Placebo	23.8%		



No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51
Pembro + Chemo/Pembro	784	781	769	751	728	718	702	692	681	671	652	551	433	303	165	28	0	0
Placebo + Chemo/Placebo	390	386	382	368	358	342	328	319	310	304	297	250	195	140	83	17	0	0

Heather. L. McArthur

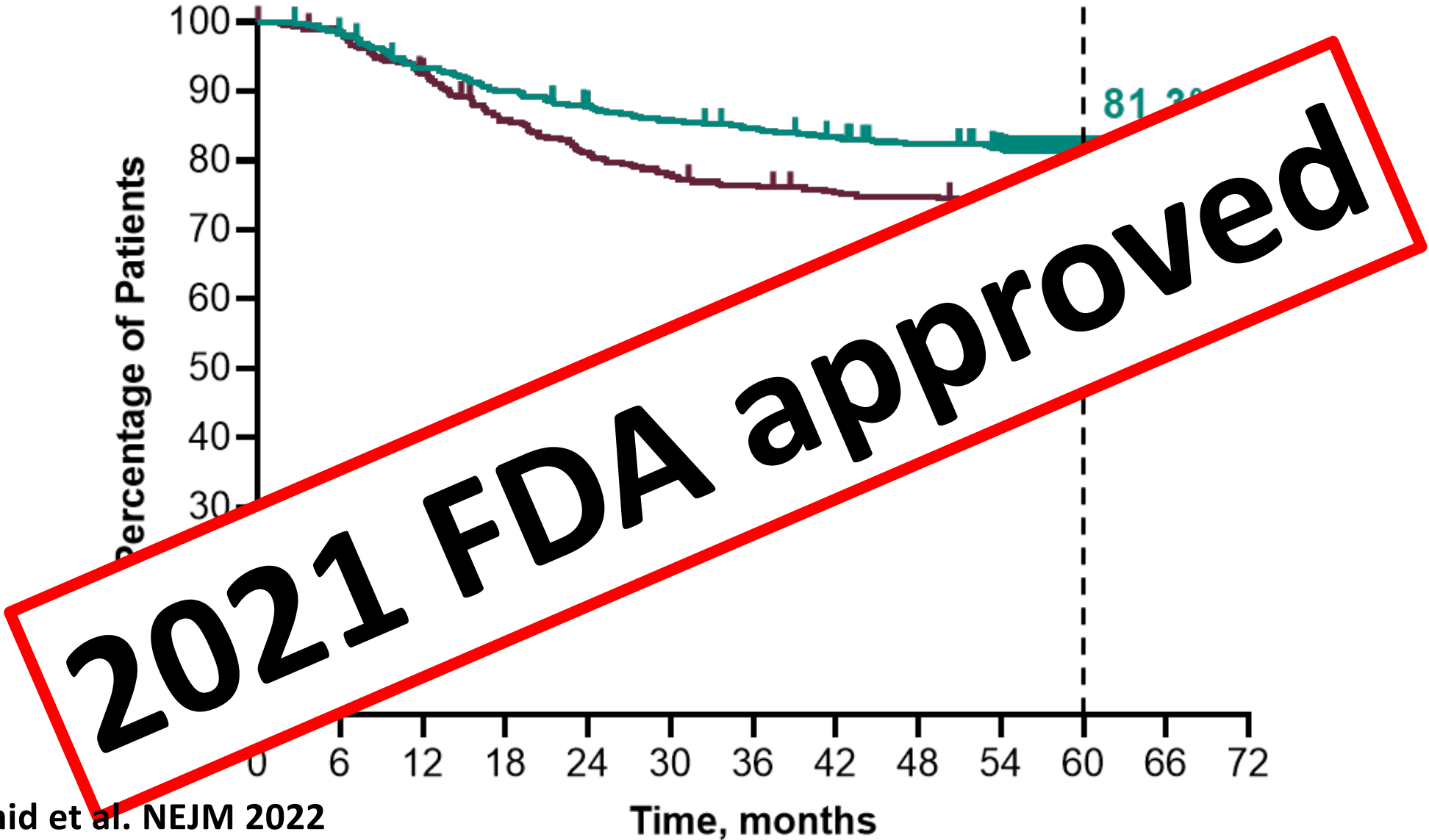
IA6 ^b	Events	HR (95% CI)
Pembro + Chemo/Pembro	18.5%	0.63 ^c (0.49–0.81)
Placebo + Chemo/Placebo	27.7%	



No. at risk	0	6	12	18	24	30	36	42	48	54	60	66	72
Pembro + Chemo/Pembro	784	769	728	702	681	665	654	643	631	612	411	162	0
Placebo + Chemo/Placebo	390	382	358	329	311	299	292	286	284	274	189	79	0

Schmid et al. NEJM 2020; Schmid et al. NEJM 2022

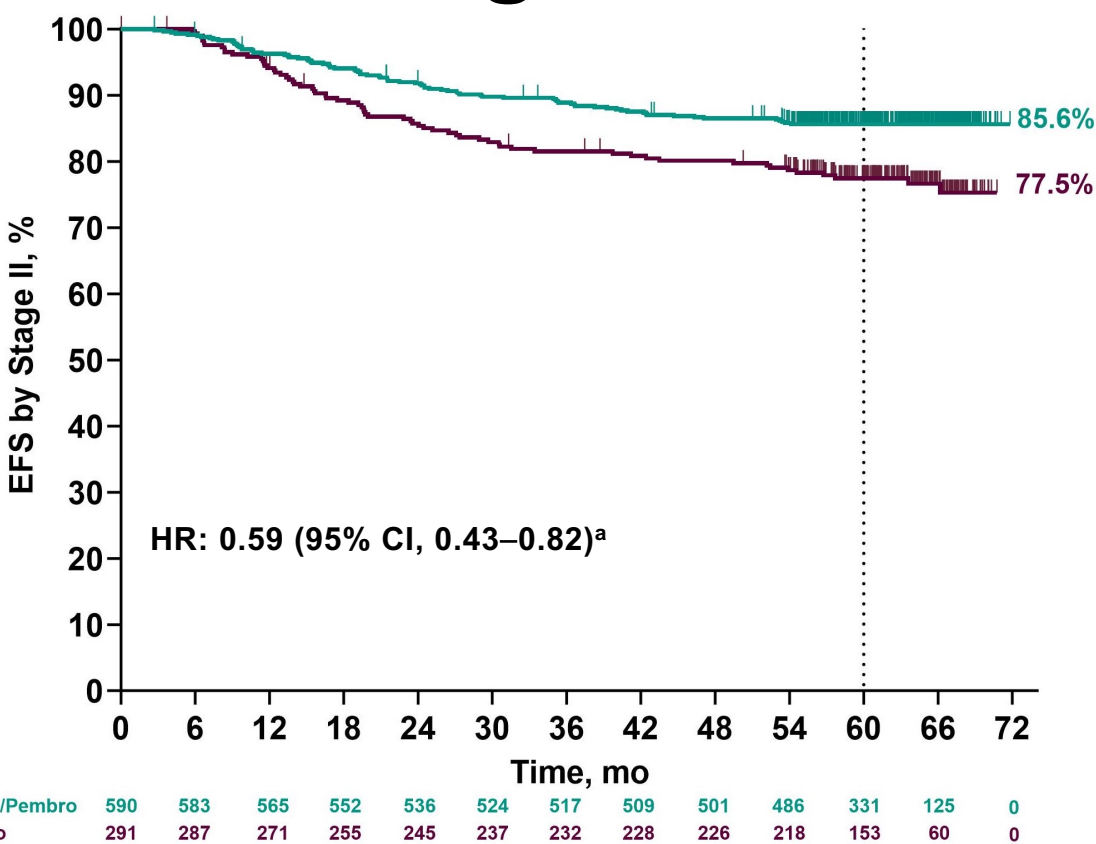
Applying Wins From Late-Stage Cancer to Cure More Early-Stage Cancers



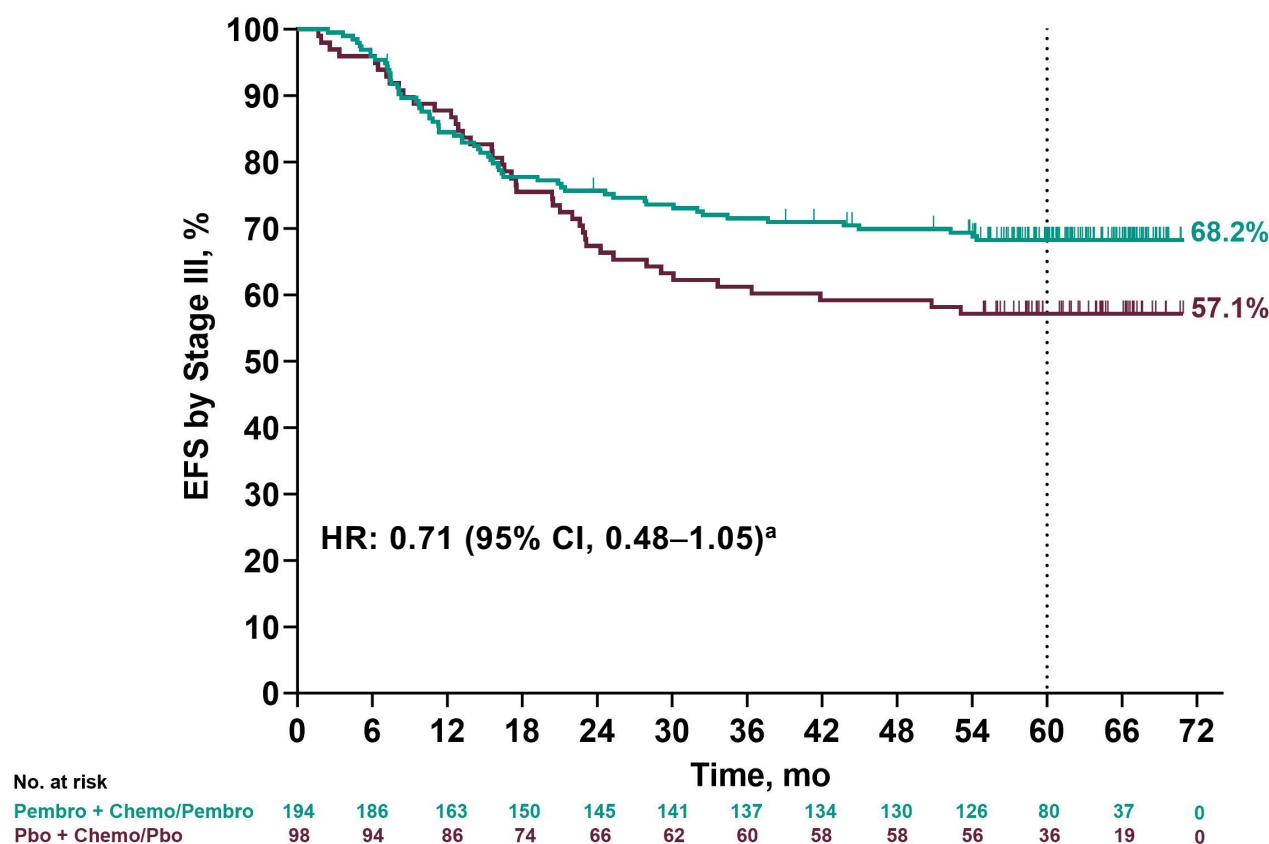
Schmid et al. NEJM 2022

K522 EFS by Stage

Stage II

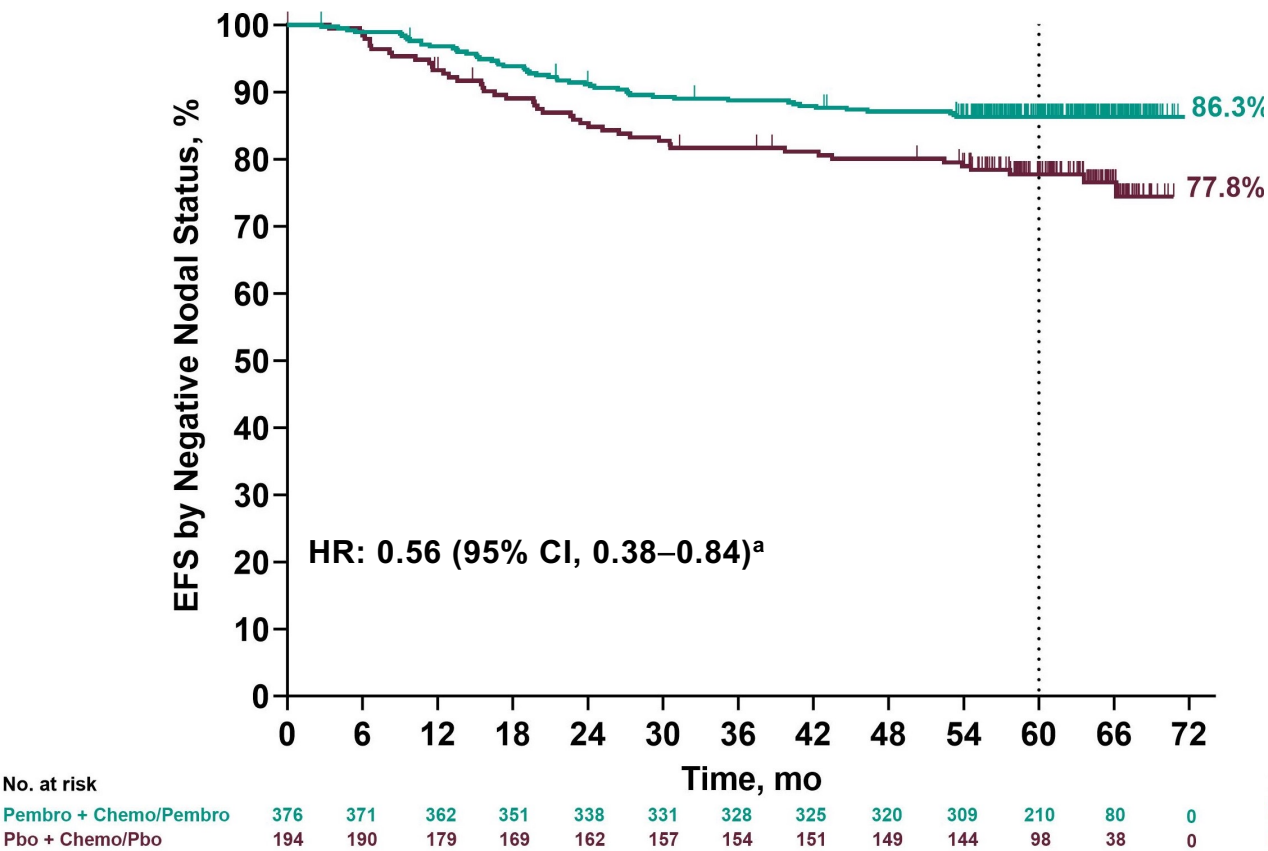


Stage III

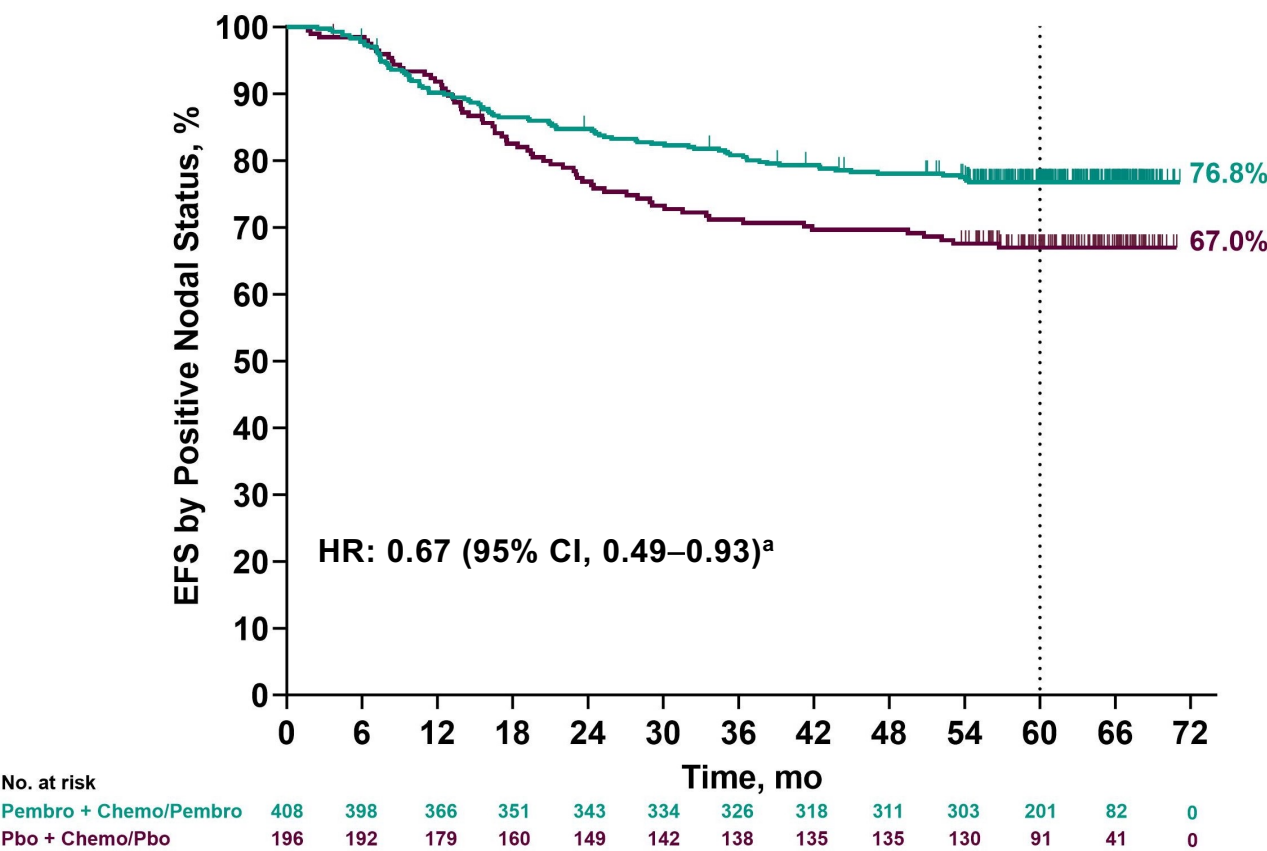


EFS by Nodal Status

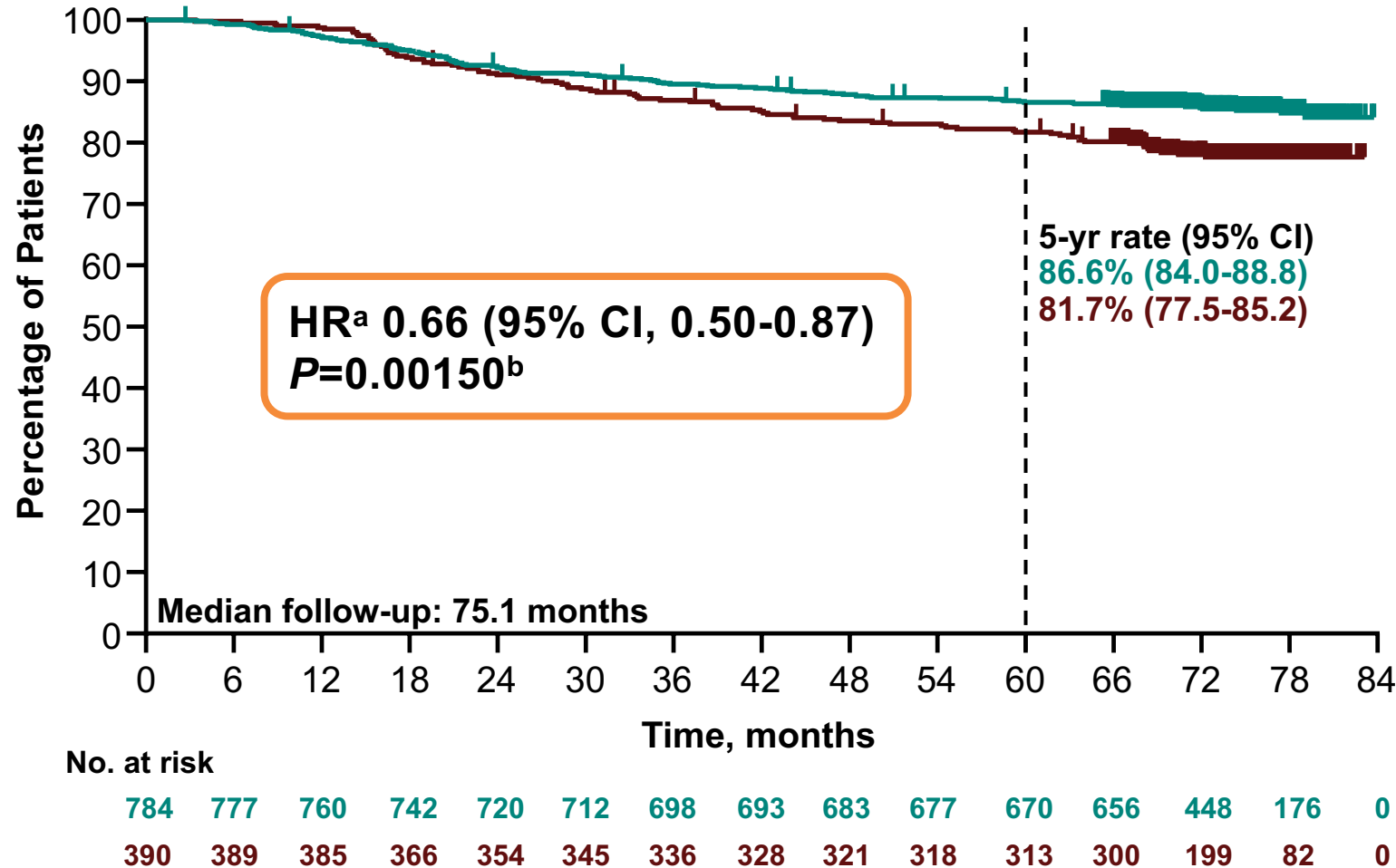
Negative Nodal Status



Positive Nodal Status



Key Secondary Endpoint: Overall Survival



Δ4.9%

	Pts w/ Event
Pembro + Chemo/Pembro	14.7%
Placebo + Chemo/Placebo	21.8%



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Overall Survival with Pembrolizumab in Early-Stage Triple-Negative Breast Cancer

Peter Schmid, M.D., Javier Cortes, M.D., Rebecca Dent, M.D.,
Heather McArthur, M.D., Lajos Pusztai, M.D., Sherko Kümmel, M.D.,
Carsten Denkert, M.D., Yeon Hee Park, M.D., Rina Hui, Ph.D.,
Nadia Harbeck, M.D., Masato Takahashi, M.D., Seock-Ah Im, M.D.,
Michael Untch, M.D., Peter A. Fasching, M.D., Marie-Ange Mouret-Reynier, M.D.,
Theodoros Foukakis, M.D., Marta Ferreira, M.D., Fatima Cardoso, M.D.,
Xuan Zhou, Ph.D., Vassiliki Karantza, M.D., Konstantinos Tryfonidis, M.D.,
Gursel Aktan, M.D., and Joyce O'Shaughnessy, M.D.,
for the KEYNOTE-522 Investigators*

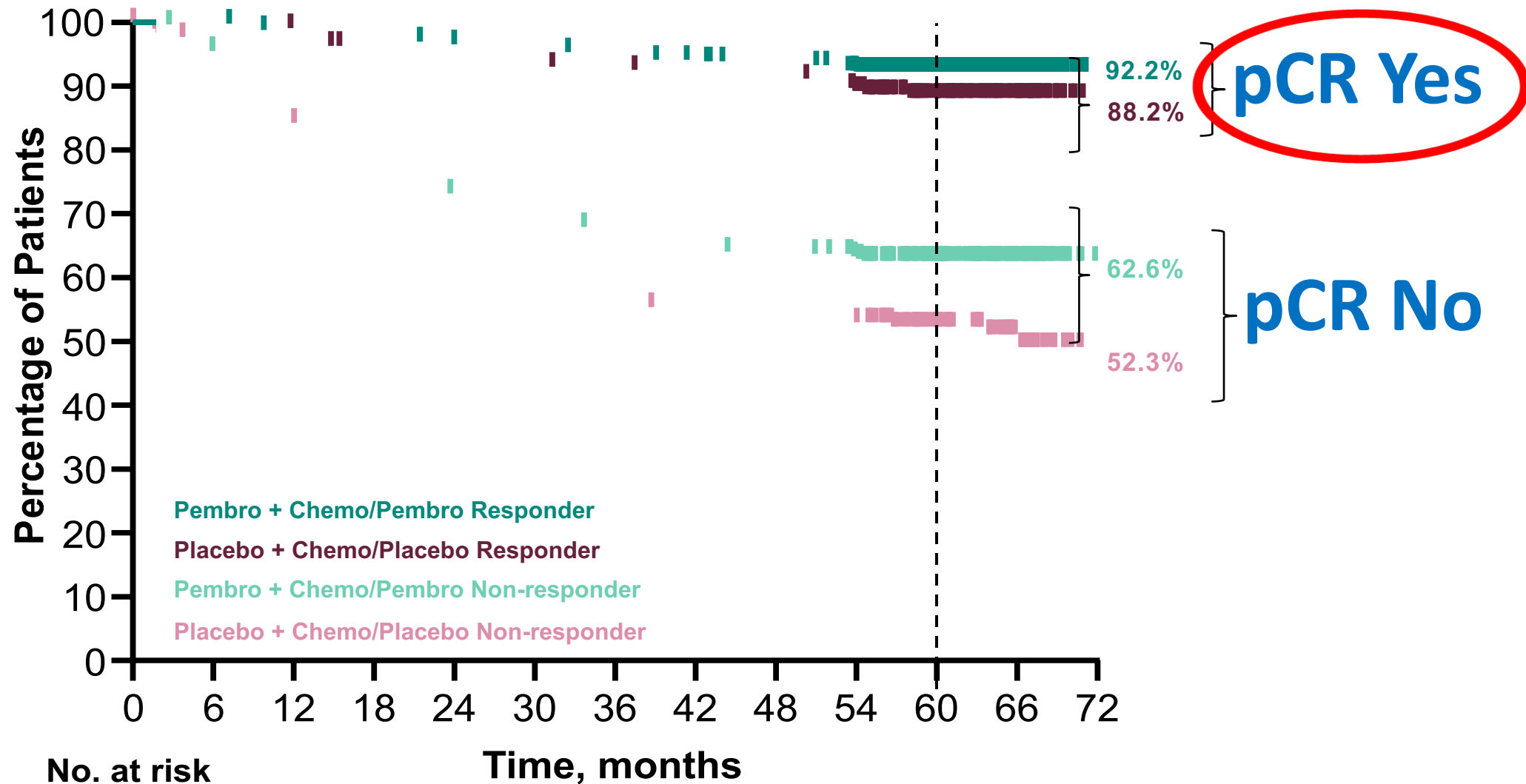
ORIGINAL ARTICLE – BREAST ONCOLOGY

Surgical Outcomes After Neoadjuvant Pembrolizumab Plus Chemotherapy for Triple-Negative Breast Cancer: Results from the Randomized, Placebo-Controlled Phase 3 KEYNOTE-522 Study

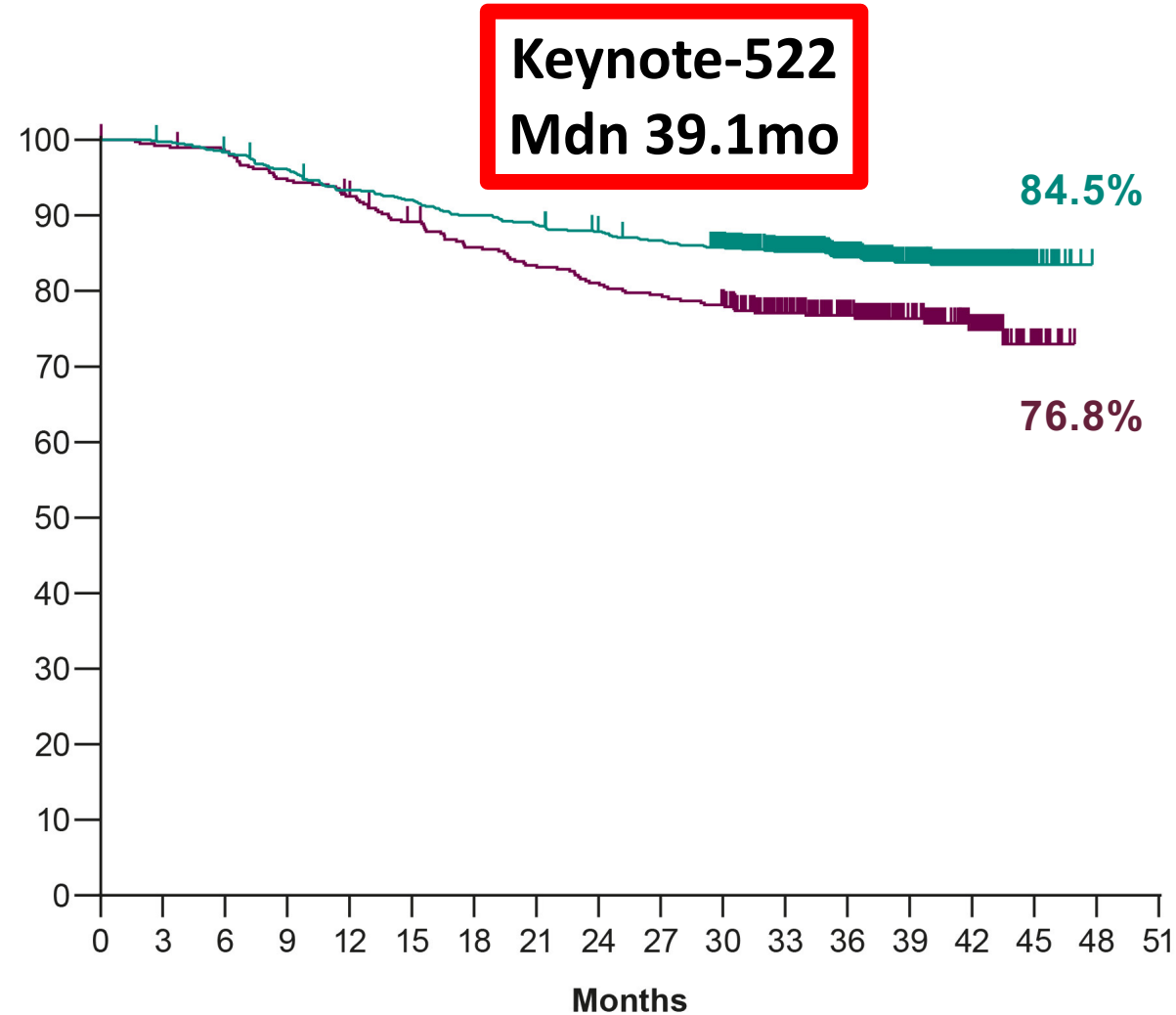
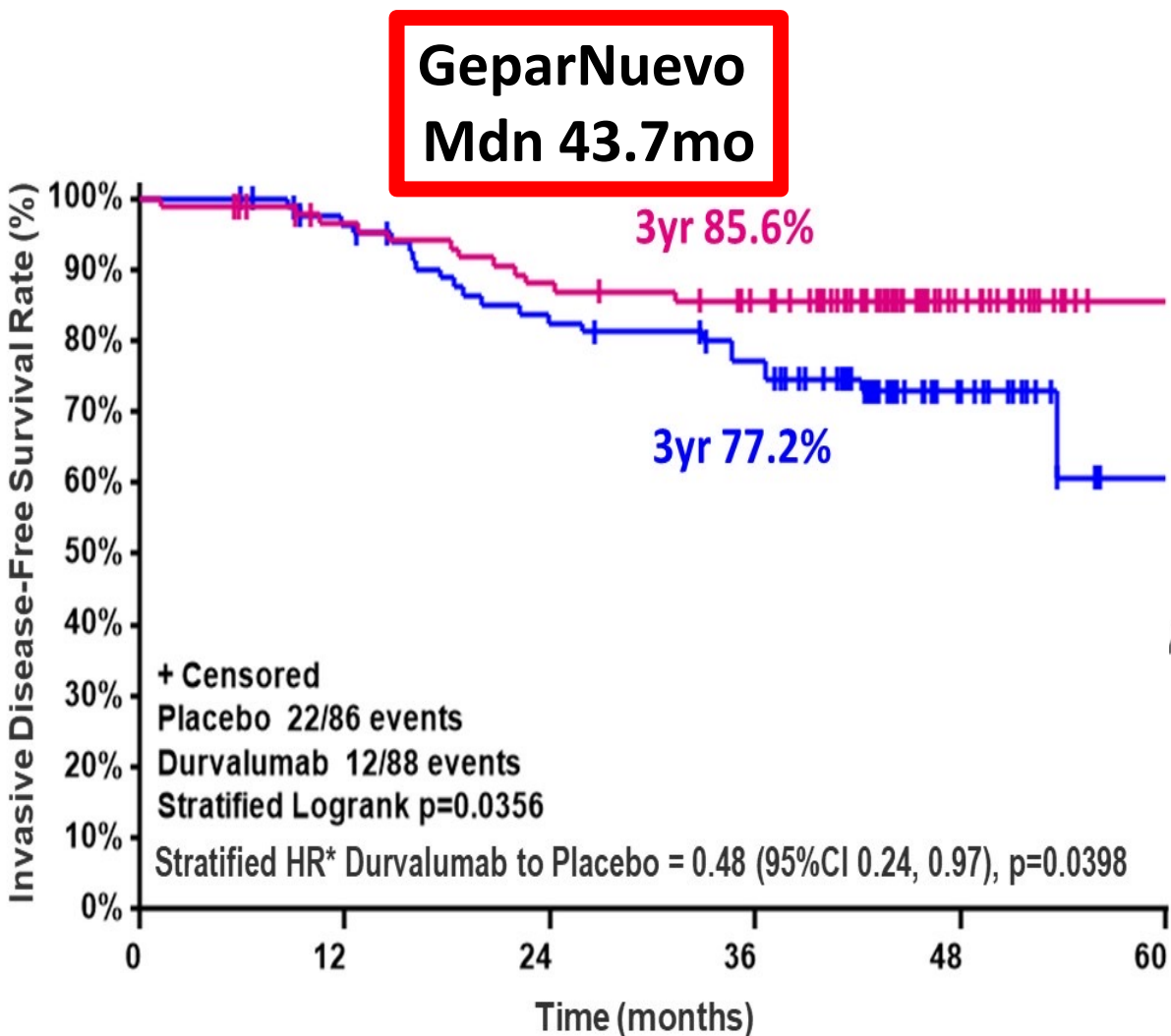
Sherko Kuemmel, MD, PhD^{1,2}, Peter A. Fasching, MD³, Peter Schmid, MD, PhD⁴, Nadia Harbeck, MD⁵, Masato Takahashi, MD⁶, Michael Untch, MD, PhD⁷, Jean-Francois Boileau, MD⁸, Javier Cortes, MD, PhD^{9,10,11}, Rebecca Dent, MD¹², Joyce O'Shaughnessy, MD¹³, Lajos Pusztai, MD, PhD¹⁴, Theodoros Foukakis, MD, PhD¹⁵, Yeon Hee Park, MD, PhD¹⁶, Rina Hui, MBBS, PhD^{17,18}, Fatima Cardoso, MD¹⁹, Carsten Denkert, MD²⁰, Liyi Jia, PhD²¹, Wilbur Pan, MD, PhD²¹, Vassiliki Karantza, MD, PhD²¹, and Heather McArthur, MD, MPH²²

What Subset Derives Benefit?

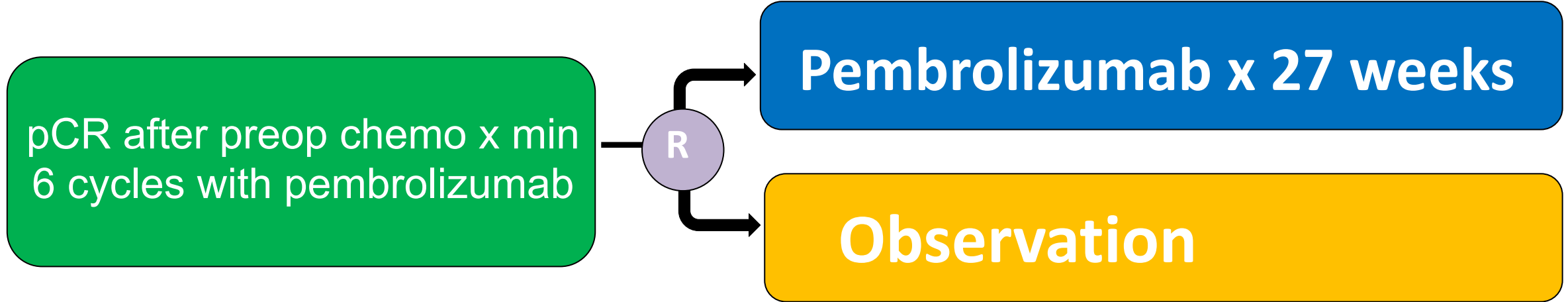
EFS by pCR at IA6



Is the benefit of IO conferred with neoadjuvant administration?



OptimelCE-PCR study: For patients with pCR



N = 1956 (56month accrual estimated)

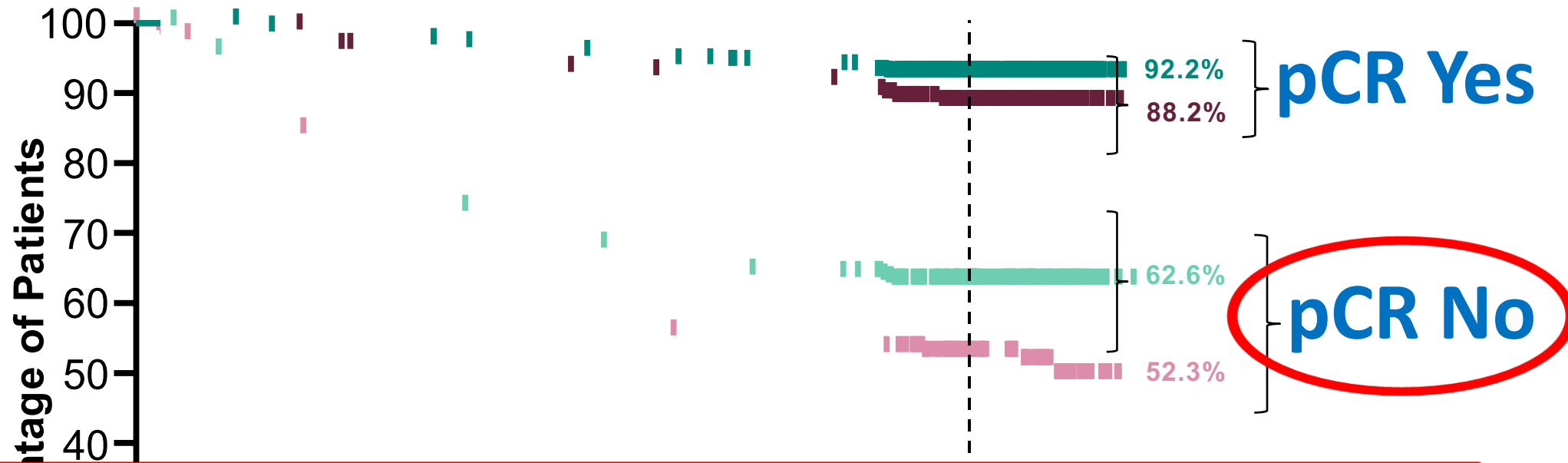
Stratification Factors:

- Baseline nodal status
- Receipt of anthracycline chemotherapy: yes vs no

1^oEndpoints: RFS and QOL at 27weeks

What Subset Derives Benefit?

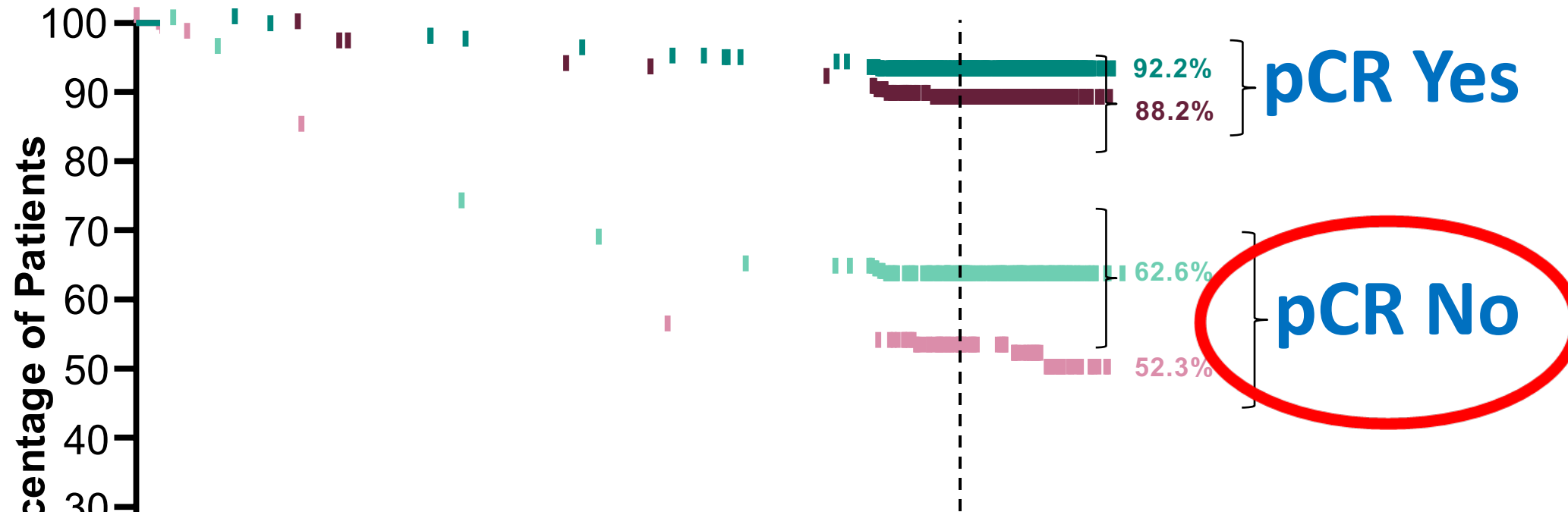
EFS by pCR at IA6



>1/3 RD patients
experience an event within 5y

What Subset Derives Benefit?

EFS by pCR at IA6



30% of RD patients
DIE within 5y

ALEXANDRA/IMpassion030 phase 3 Open-label Study Design

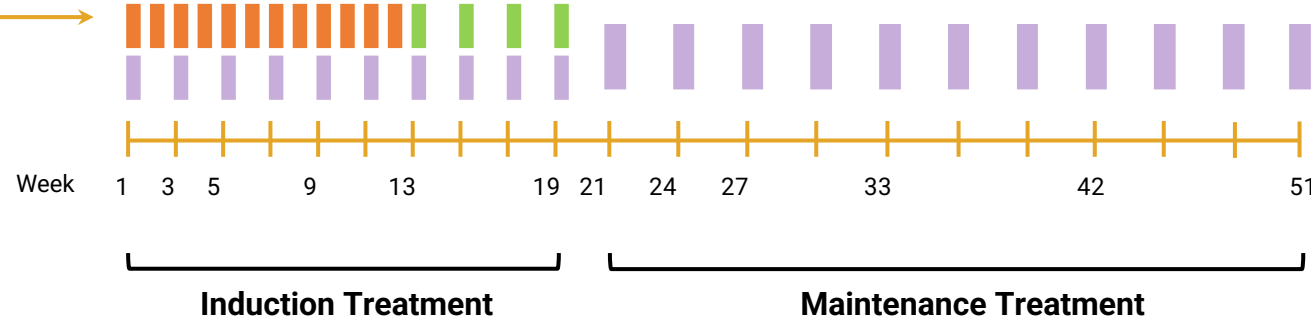
SURGERY

Early TNBC

- Stage II-III
- At least 50% node-positive
- N=2300

(R)

Arm A: Atezolizumab + Chemotherapy experimental arm



Arm B: Chemotherapy only control arm



Stratification factors:

Axillary nodal status

(0 vs. 1-3 vs. ≥ 4 positive lymph nodes)

Surgery

(breast conserving vs. mastectomy)

Tumor PD-L1 status

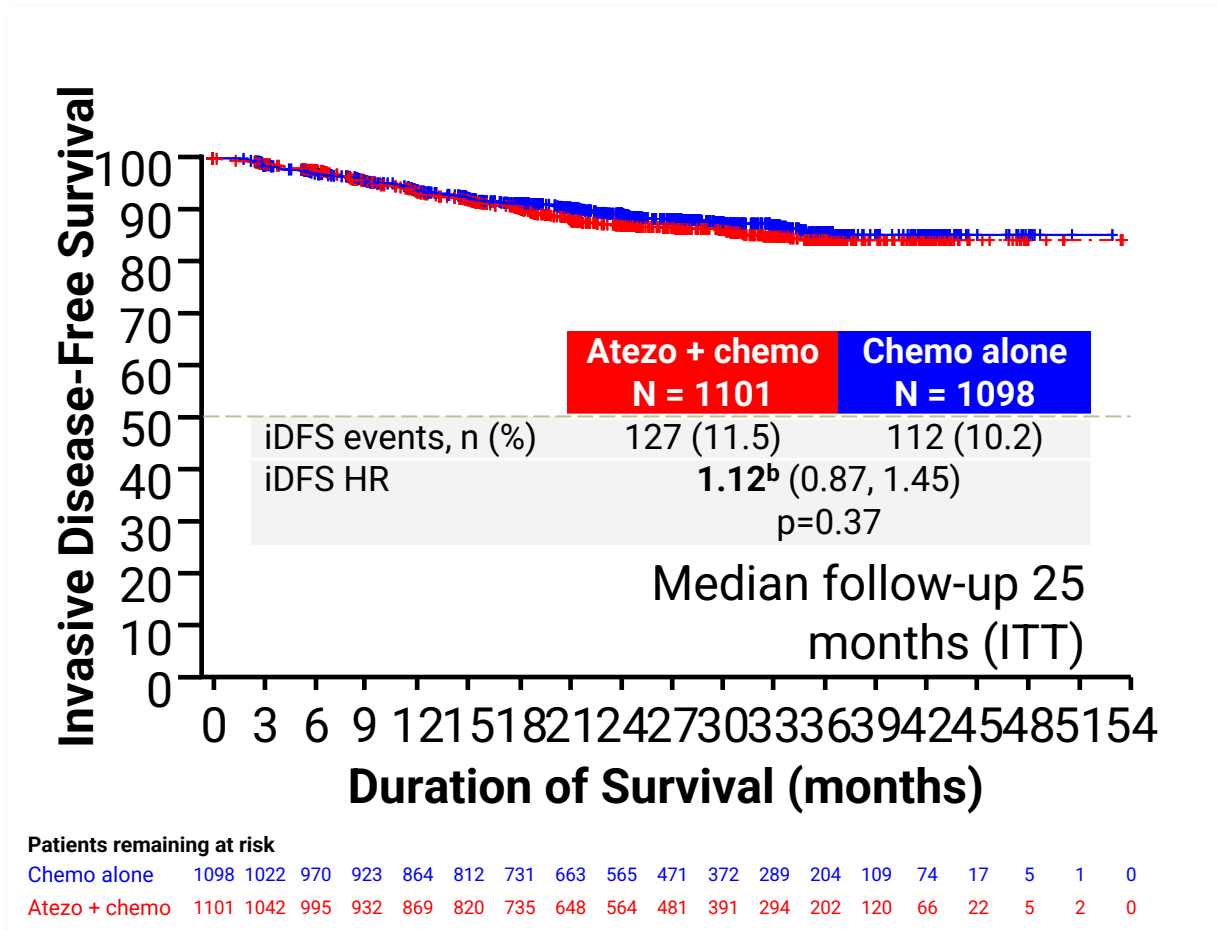
(IC0 vs. IC1/2/3)

- Paclitaxel qw for 12 weeks
- ddAC/EC q2w for 4 doses supported with G-CSF/GM-CSF
- Atezolizumab
 - Induction: 840 mg q2w for up to 10 doses
 - Maintenance: 1200 mg q3w to complete 1 year
- Monitoring visit Arm B

End of
30-day safety
reporting period
after last study
treatment

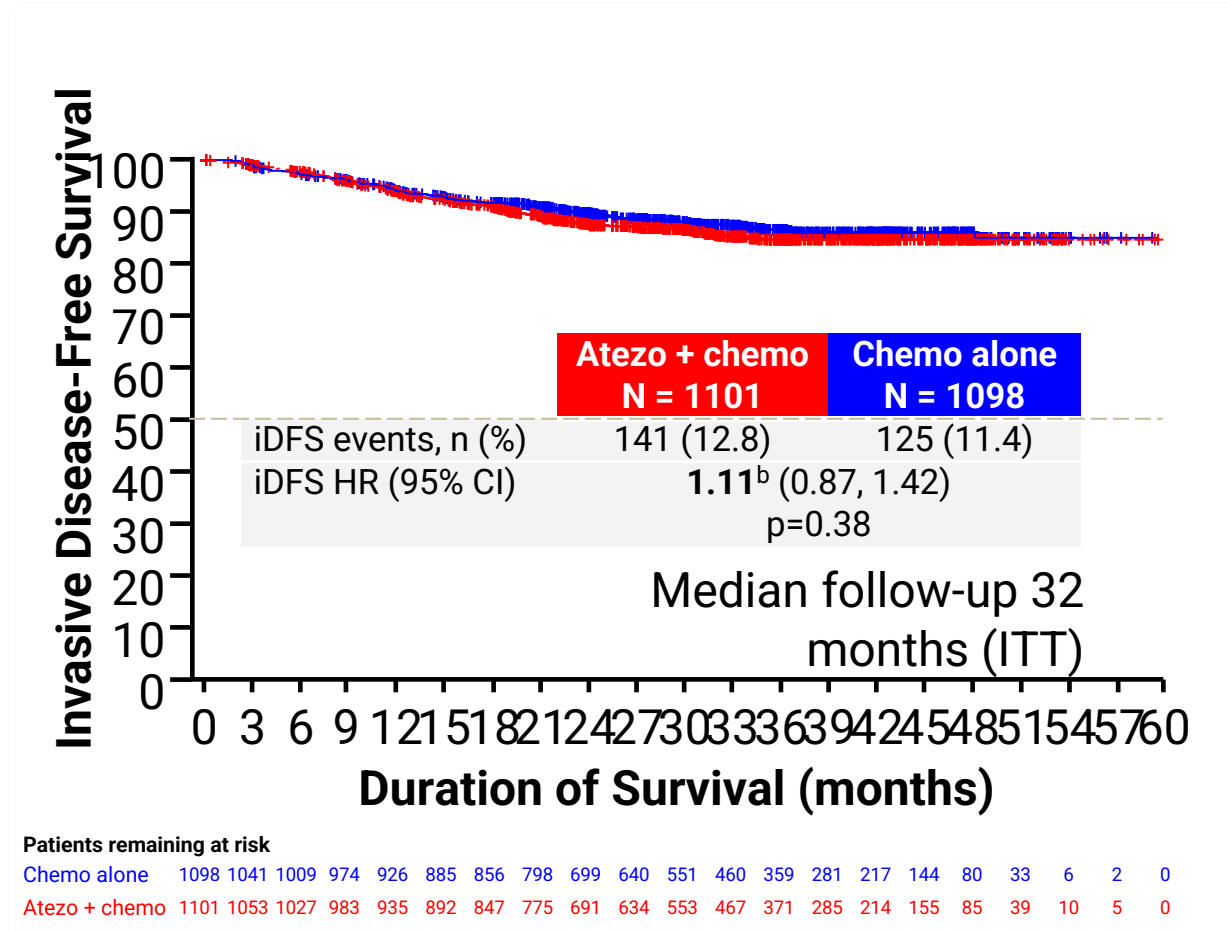
iDFS IA and Final Analysis

Interim Analysis



Heather L. McArthur

Final Analysis



Ignatiadis et al. SABCS 2023

McArthur et al. EBCC 2024

Ignatiadis, Bailey McArthur et al. JAMA 2025

SWOG 1418/NRG BR006

TNBC with ≥ 1 cm residual
invasive breast cancer or any +
LN after neoadjuvant
chemotherapy
N=1000

1:1

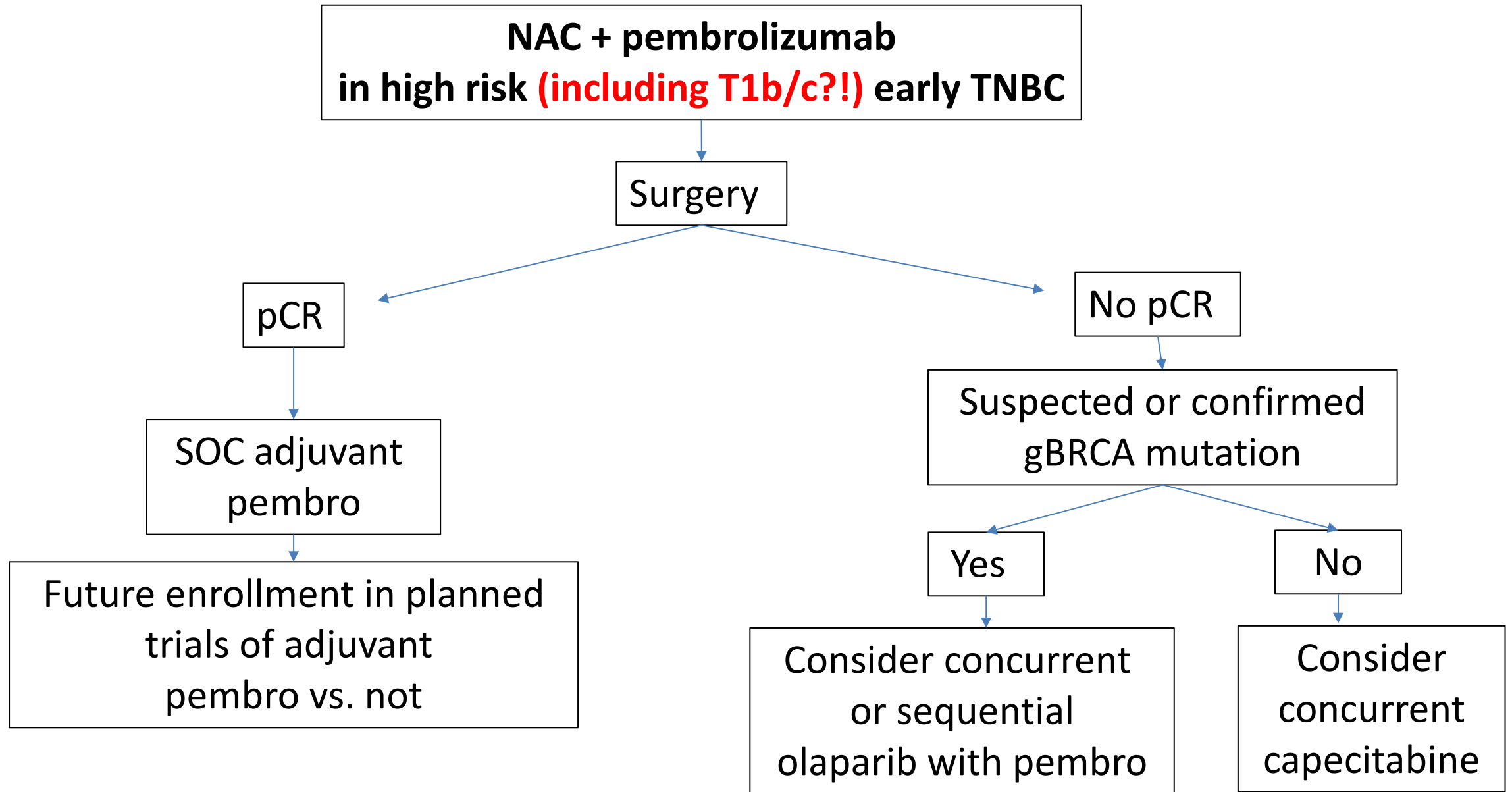
Pembrolizumab 200 mg IV q 3 weeks x 1y

Observation

- **Registration:**
 - Central PD-L1 testing
- **Stratification:**
 - Nodal stage ypNo vs ypN+
 - Residual tumor ≥ 2 vs < 2 cm
 - PD-L1 pos vs neg
 - Prior adjuvant chemo yes vs no

- **Hypothesis:**
 - Pembrolizumab reduces IDFS by 33% c/w observation alone
- **Primary Endpoint:**
 - Invasive DFS in PD-L1-positive and overall cohort
- **Secondary Endpoints:**
 - Toxicity
 - OS
 - DRFS
 - QOL (PROMIS, PRO-CTCAE forms, inflammatory markers)
 - Tissue banking

Activated in 2016 and closed in 2021



Consider concurrent pembro with radiation

TroFuse-012 (sac-TMT for RD)

- Centrally confirmed TNBC (ER<1%, PR<1%, HER2-)
- Non-pCR after at least 5 cycles of pembrolizumab and chemotherapy, including 1 cycle of anthracycline-based neoadjuvant therapy
- Randomization within 12 weeks of definitive surgery
- Adjuvant RT if indicated, completed before randomization

N=1530

RANDOMIZATION 1:1

Arm 1

Pembrolizumab 400 mg q6w x 5 doses
+
sac-TMT 4 mg/kg q2w x 12 doses

Arm 2

Treatment of Physician's Choice (TPC)
Pembrolizumab 400 mg q6w x 5 doses
or
Pembrolizumab 400 mg q6w x 5 doses and
capecitabine 1000 mg/m² to 1250 mg/m² BID on Days
1-14 and Days 22-35 every 42 days x 4 (2 weeks on, 1
week off)

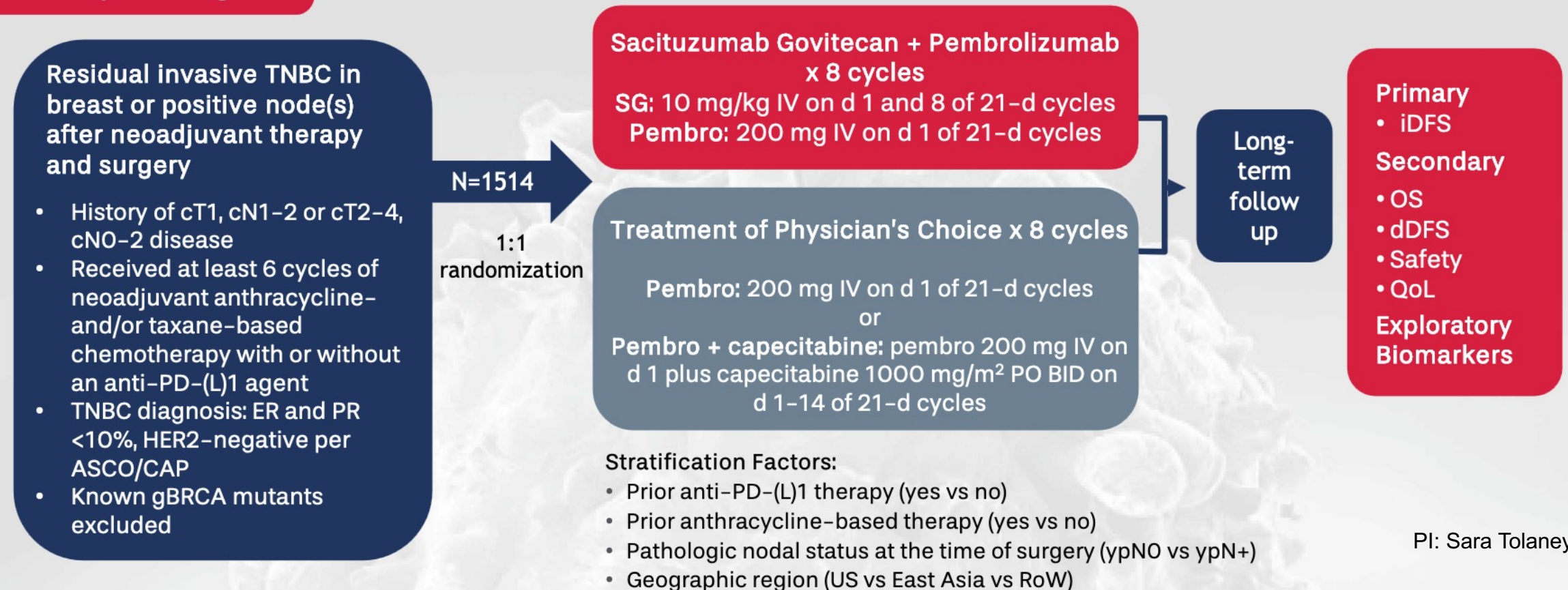
Stratification factors

1. Residual tumor and lymph node status:
 - a. [Tumor < 1 cm (ypT1mi – T1b), ypN0] (capped at ~15%)
vs
 - b. [Tumor ≥ 1 cm (ypT1c+), ypN0] or [No tumor or tumor < 1 cm (ypT0 – T1b), ypN1]
vs
 - c. [Tumor ≥ 1 cm (ypT1c+), ypN1] or [No tumor or any tumor size (ypT0+), ypN2+]
2. TROP2 expression per IHC (low vs medium vs high).
3. Intention to use capecitabine (yes [capped at ~60%] vs no)

A Randomized, Open-label, Phase 3 Study of Adjuvant Sacituzumab Govitecan + Pembrolizumab Versus Treatment of Physician's Choice in Patients With TNBC Who Have Residual Disease After Neoadjuvant Therapy and Surgery (ASCENT-05 / OptimICE-RD)

Study Design^{1,2}

Trial registration number: NCT05633654



TROPION-Breast03 (Dato-DXd for RD)

Patients with Stage I-III TNBC without pathological CR (N≈1075)

- Histologically confirmed invasive TNBC (ER <1%, PR <1%, HER2 negative)^{3,4,a}
- Completed at least 6 cycles of neoadjuvant therapy containing an anthracycline and/or a taxane with or without carboplatin, with or without pembrolizumab
- Residual invasive disease after neoadjuvant therapy
- No evidence of locoregional or distant relapse
- Radiotherapy^b delivered before the start of study treatment
- No adjuvant systemic therapy
- ECOG PS 0–1
- Adequate bone marrow reserve and organ function
- No known germline BRCA1 or BRCA2 mutation

Locations: North America, South America, Asia, Europe
ClinicalTrials.gov Identifier: [NCT05629585](https://clinicaltrials.gov/ct2/show/study/NCT05629585)

Randomization
(2:1:2)²

**Dato-DXd 6 mg/kg IV Q3W × 8 cycles
+
Durvalumab 1120 mg IV Q3W × 9 cycles**

Dato-DXd
6 mg/kg IV Q3W × 8 cycles

Investigator's Choice of Therapy^c
(capecitabine, pembrolizumab, or
capecitabine + pembrolizumab)

Stratification Factors²:

- Prior neoadjuvant pembrolizumab (yes vs no); cap no at 40%
- Residual disease (<1 cm vs ≥1 cm)^d; cap <1 cm at 20%
- Prior neoadjuvant platinum CT (yes vs no)

Primary Endpoint

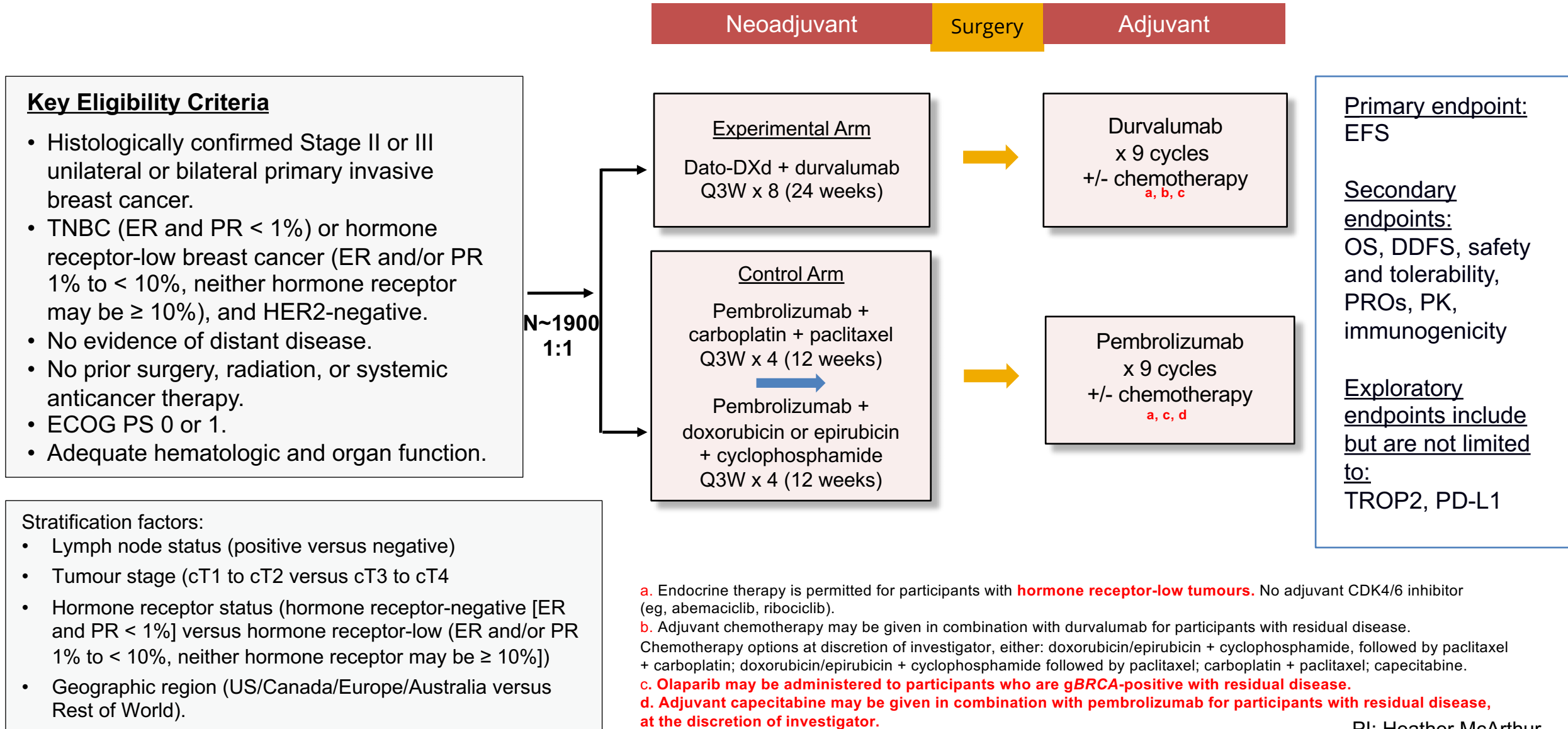
- **Dato-DXd + durvalumab vs ICT:** iDFS

Secondary Endpoints

- **Dato-DXd + durvalumab vs ICT:** DDFS, OS
- **Dato-DXd vs ICT:** iDFS, DDFS, OS
- **Dato-DXd + durvalumab vs Dato-DXd:** iDFS, DDFS
- PROs, PK, immunogenicity, safety

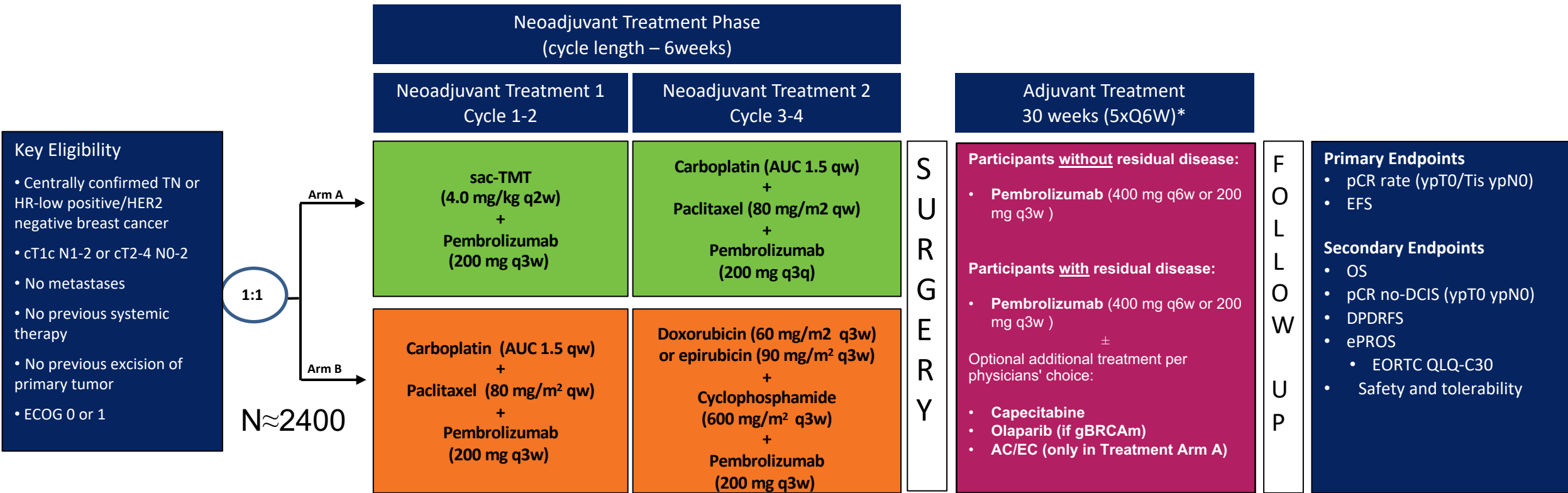
TROPION-Breast04

Dato-DXd + Durva in Neoadjuvant/Adjuvant TNBC



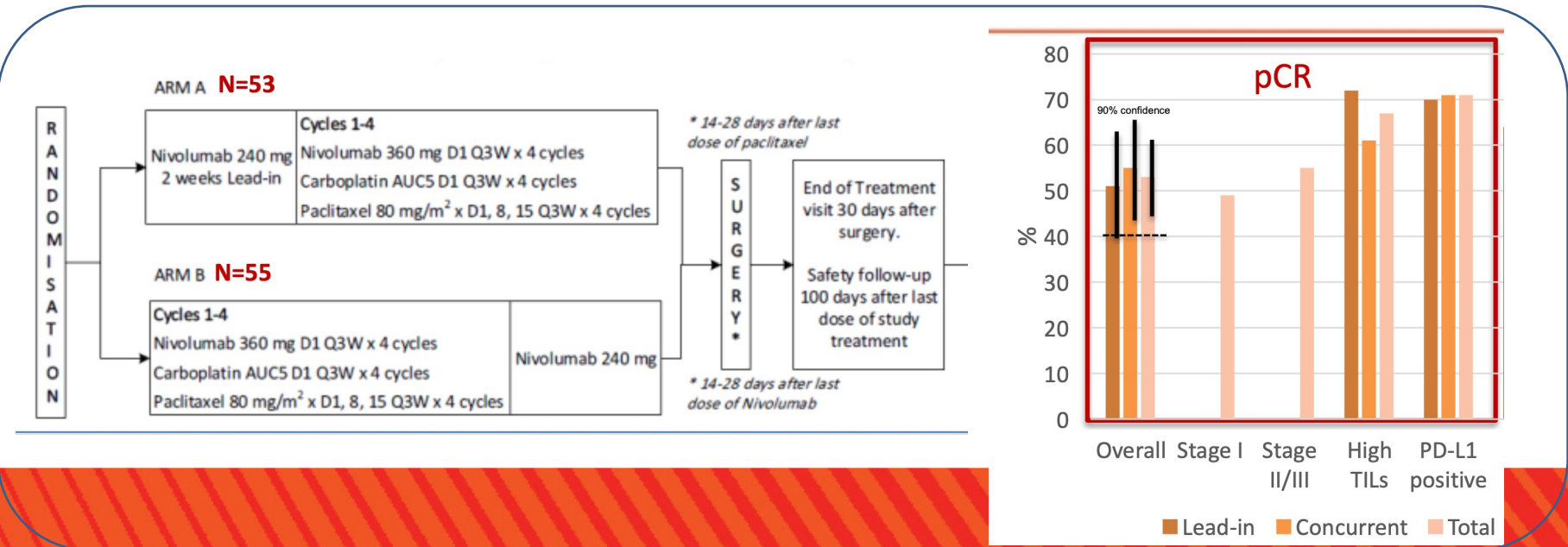
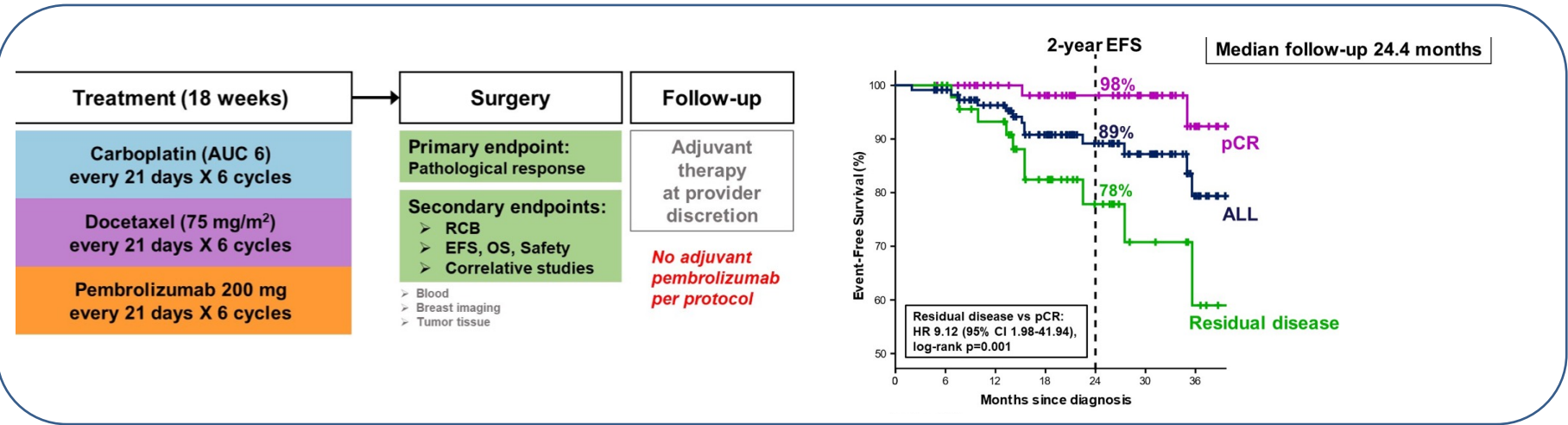
TroFuse-032

Sac-TMT + Pembro in Neoadjuvant/Adjuvant TNBC



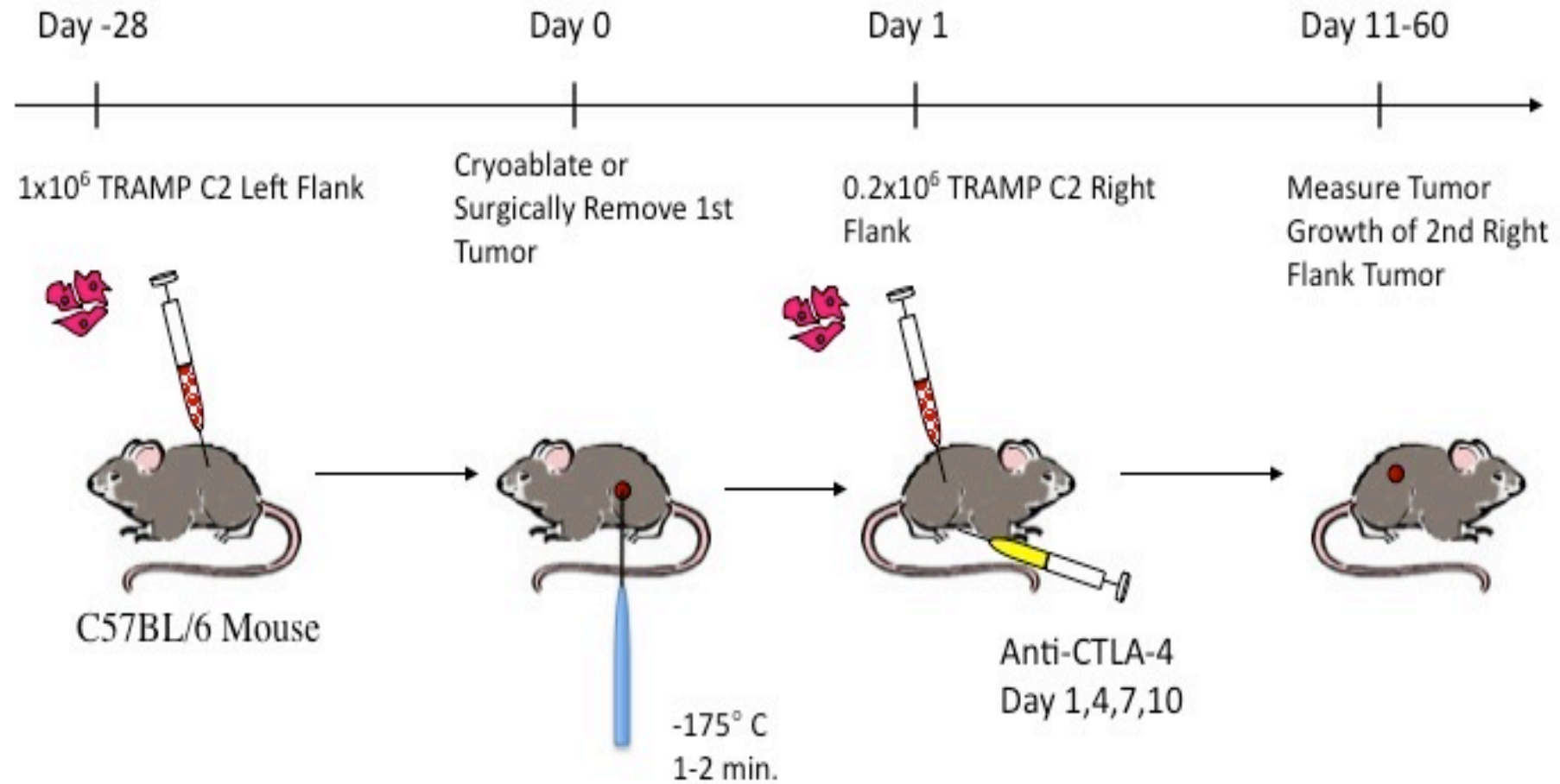
Adjuvant radiotherapy is permitted after surgery concurrently with pembrolizumab.
XRT must be completed before optional additional TPC (if used).

Anti-PD1 with anthracycline-free chemo

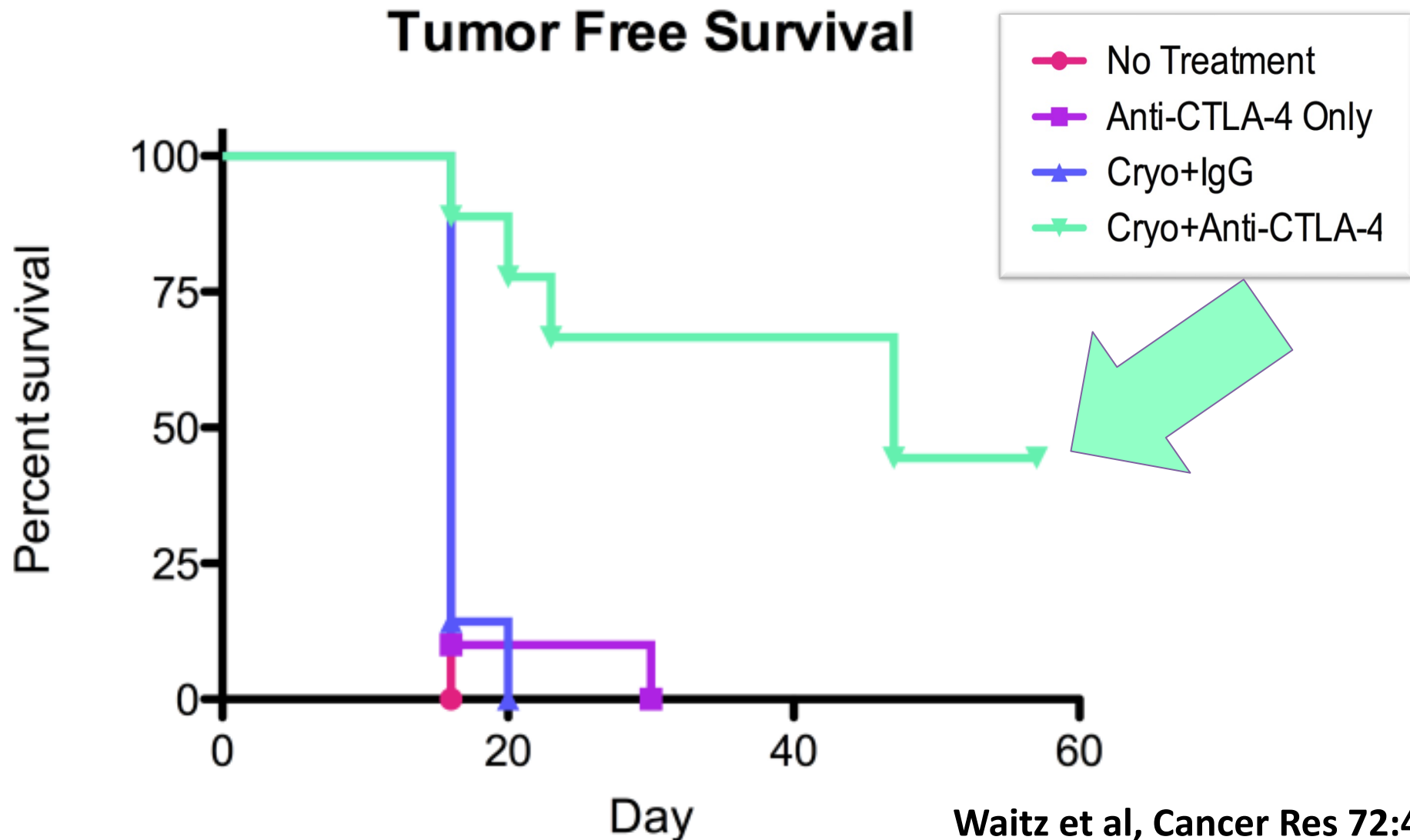


S22I 2: Shorter Anthracycline-free Chemoimmunotherapy Adapted to pathological Response in Early TNBC (SCARLET), n=2,400
PI: P. Sharma

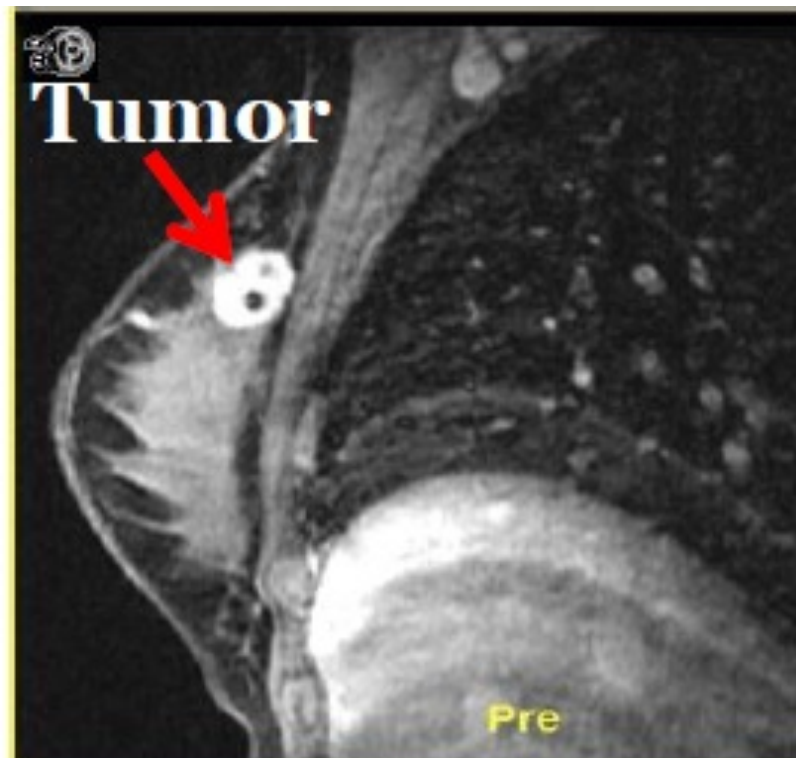
Can We Improve Immune Therapy Responses?



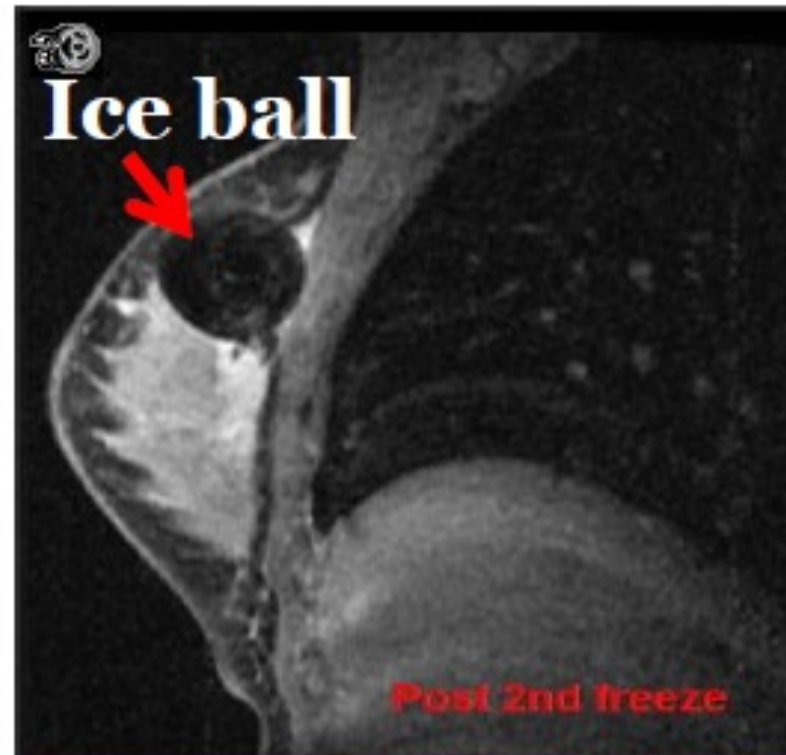
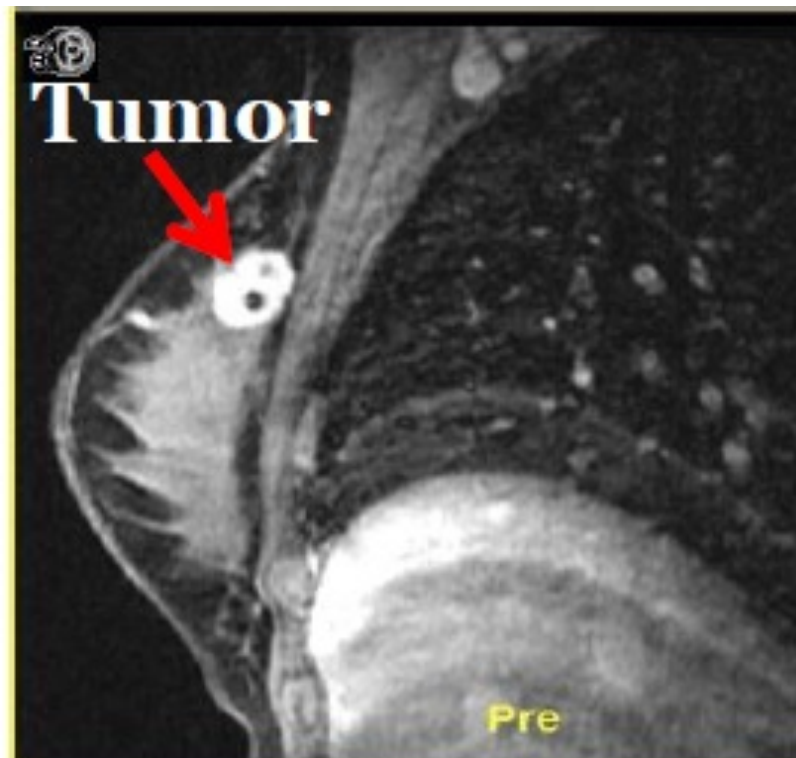
Immune stimulation with tumor freezing protects from tumor re-challenge



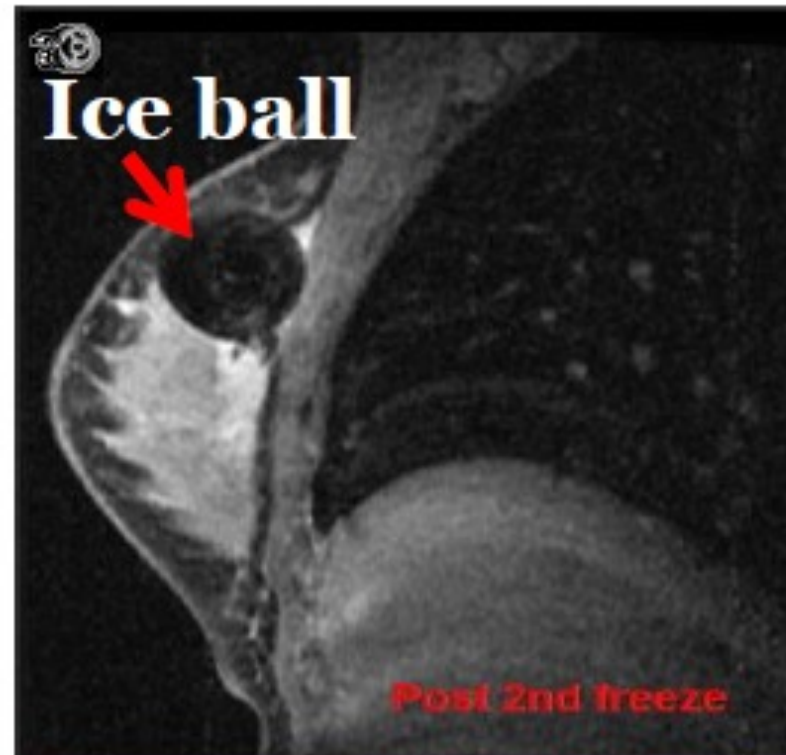
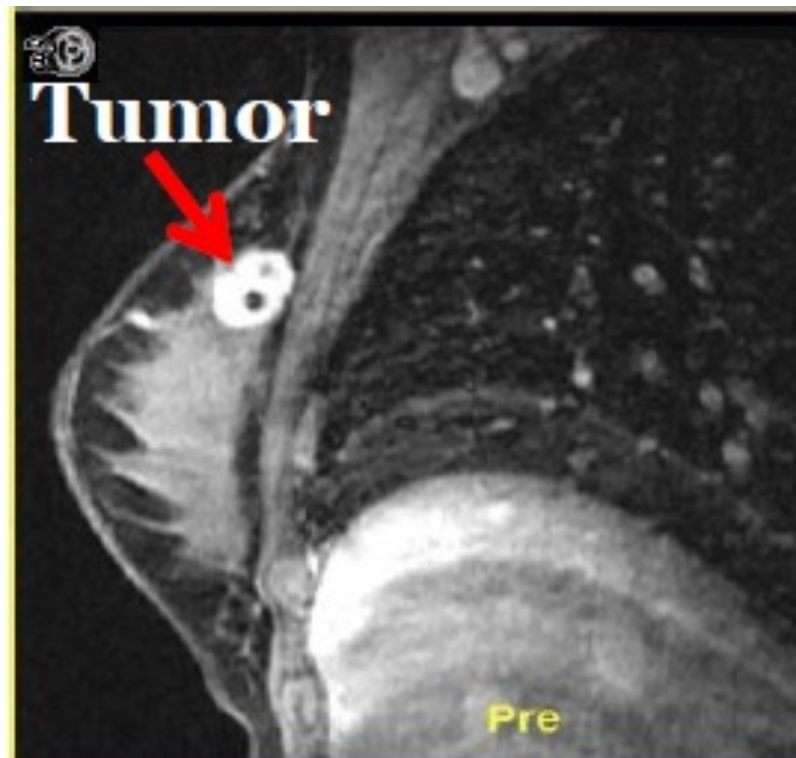
Tumor Freezing



Tumor Freezing

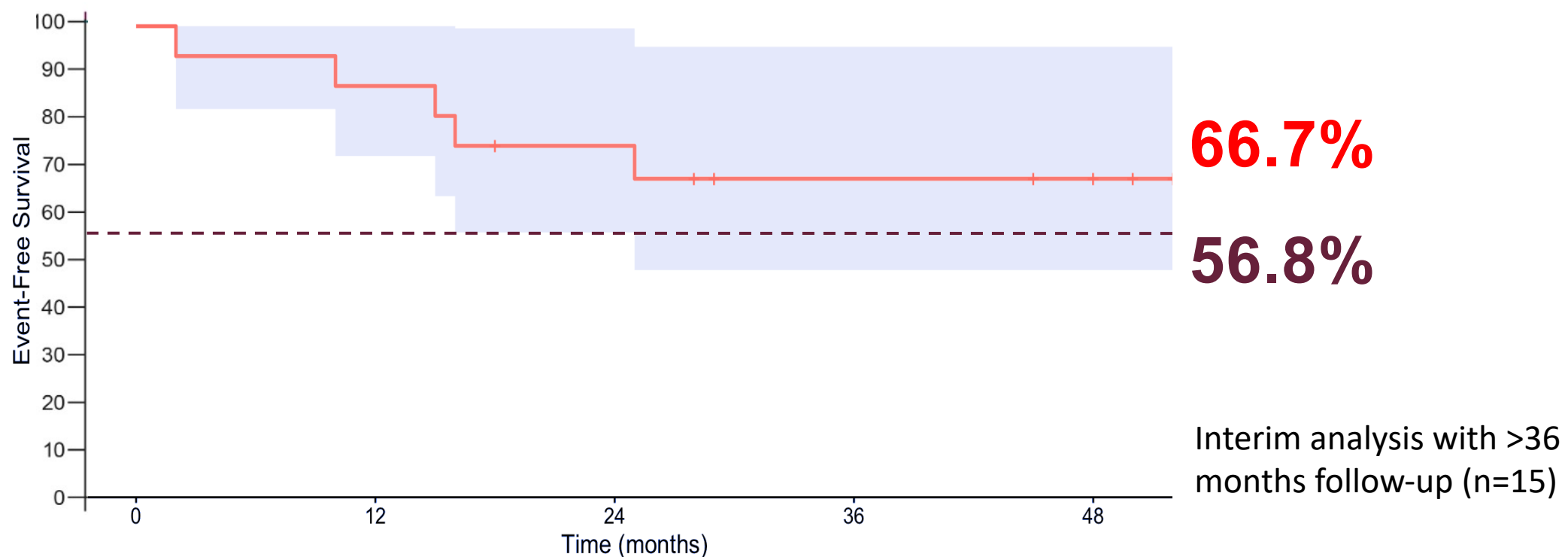


Tumor Freezing



Tumor Freezing: Cohort 1 results

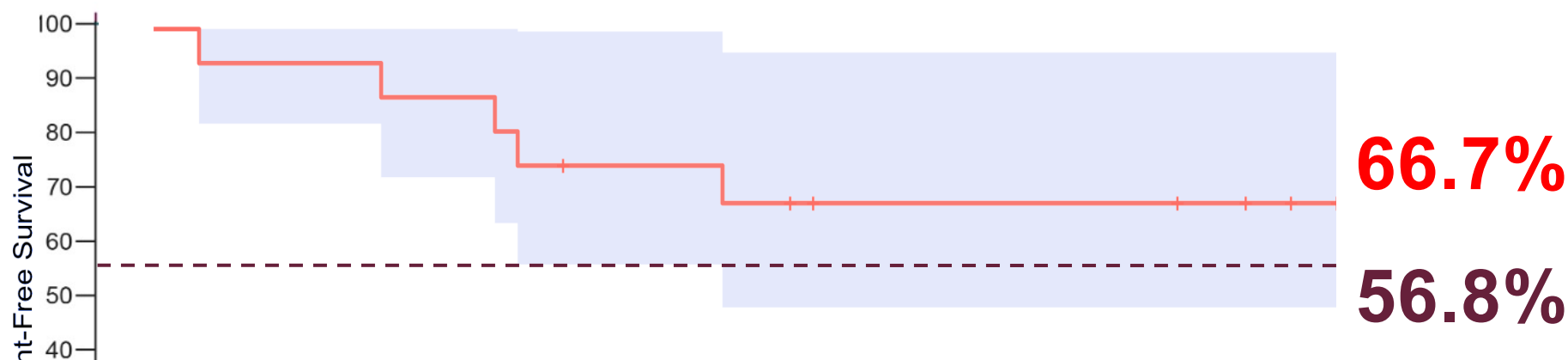
Improved Cure Rates by 9.9%!



Recently completed phase 2 trial at UTSW, Cedars-Sinai, Providence

Tumor Freezing: Cohort 1 results

Improved Cure Rates by 9.9%!



Abstract Number: 3064

Presentation Number: RF6-1

Presentation Title: Interim event-free survival with peri-operative immune checkpoint inhibition and cryoablation in residual triple-negative breast cancer

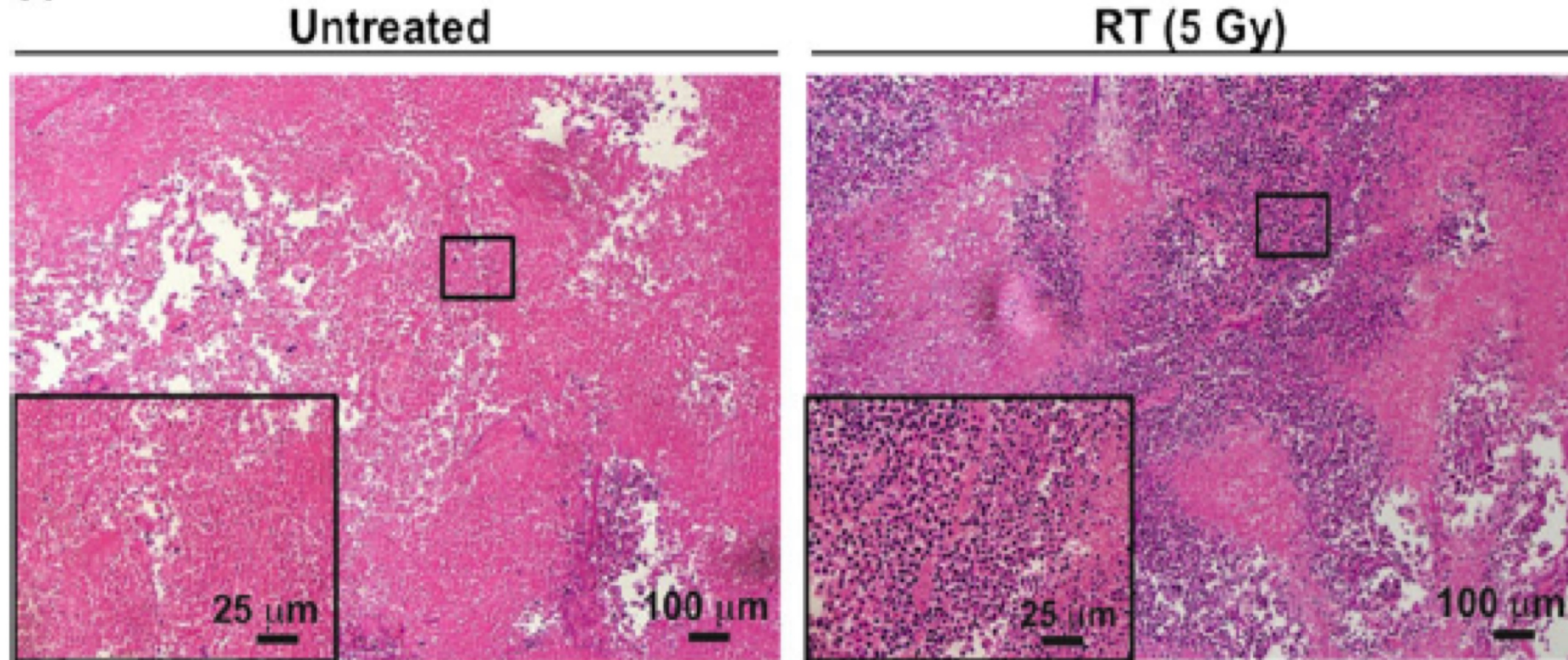
Presentation Date/Time: Thursday, December 10, 2026, 5:30 PM - 6:30 PM

Location: Stars at Night 1-2

Radiation Therapy is Immunogenic

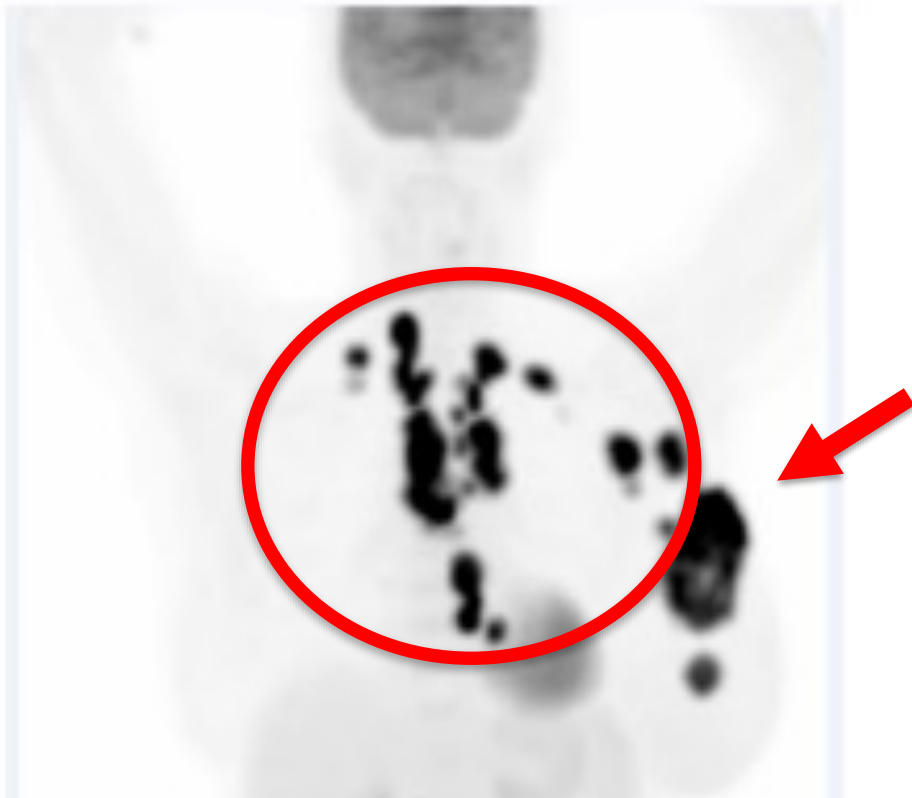
TILs after RT

A



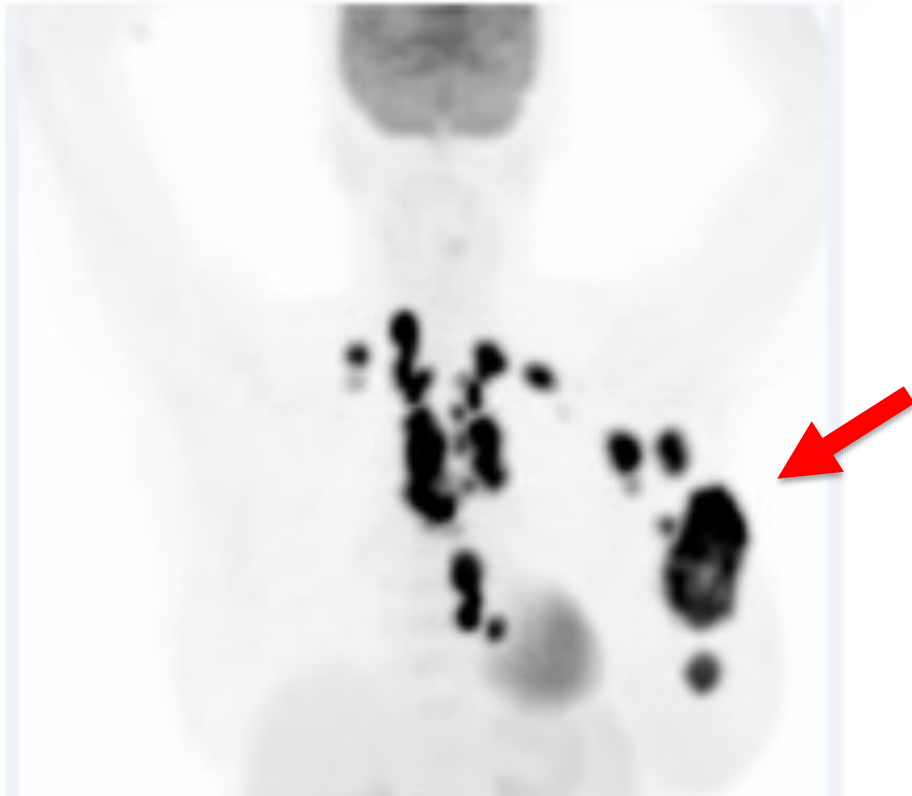
Murine mammary Carcinoma
96 h after 5 Gy RT

Baseline PET MIP

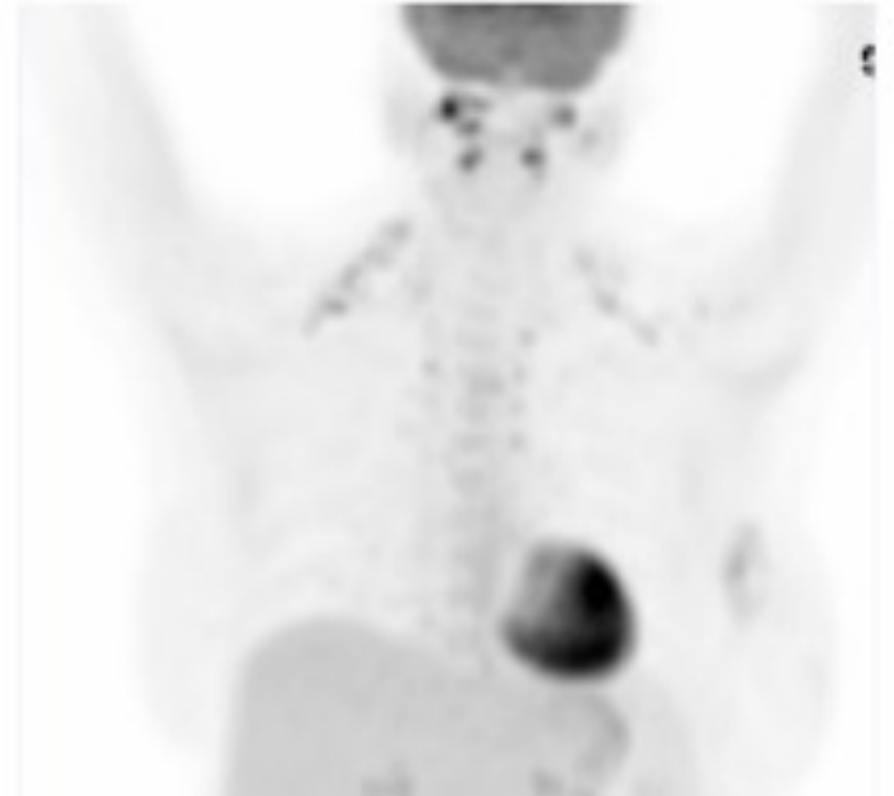


McArthur et al, ASCO 2018; Ho et al, Cancer 2019

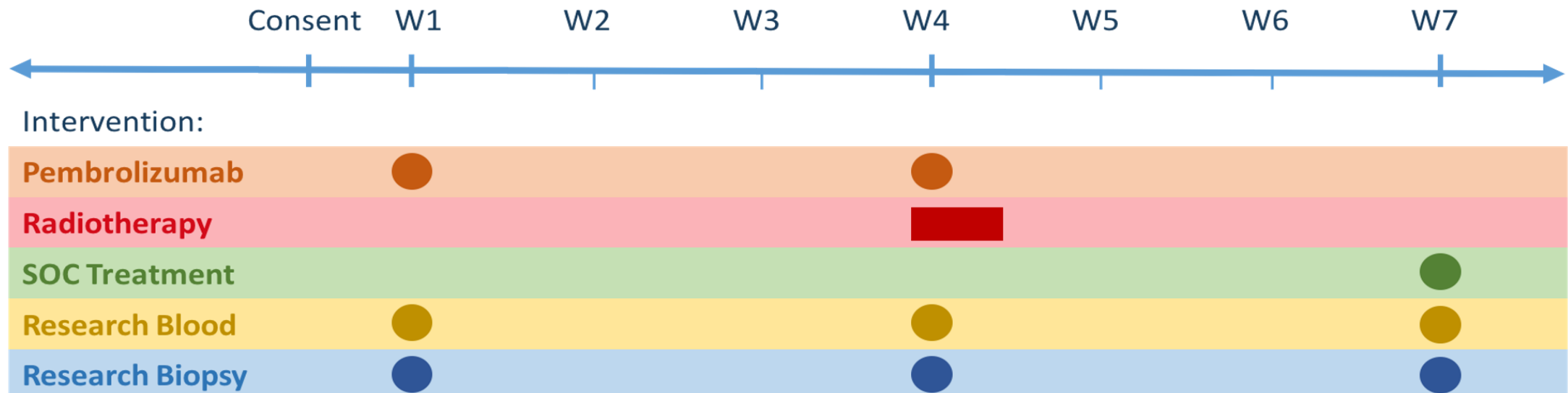
Baseline PET MIP



19 Wk PET MIP

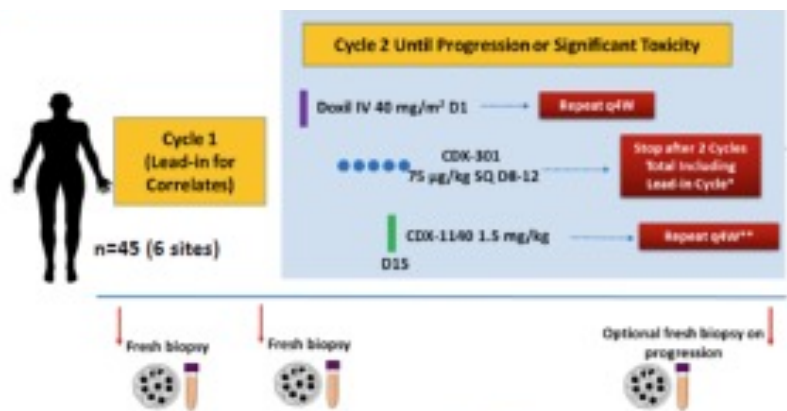


The **PEARL** trial: **P**re-operative pembrolizumab with **r**adiation therapy in early stage TNBC¹



- 50 patients enrolled between 12/2017 to 04/2021
- 28/50 (56%) achieved a pCR
- 13/17 (76%) with node-positive disease became node-negative

Breast Cancer Program: Focus on the Tumor Immune Microenvironment



- B-cell
- Dendritic cell
- CD4 T-cell
- CD8 T-cell
- Monocyte/Macrophage
- Mast cell
- NK-cell



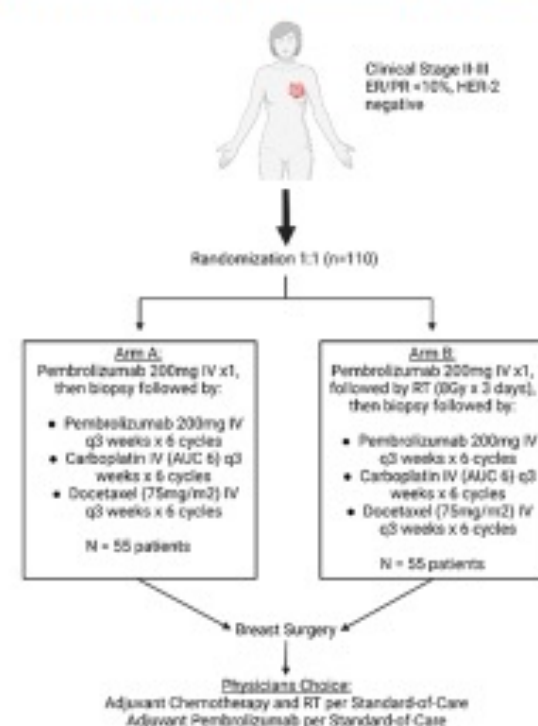
Alluri
(ET)



McArthur
(ET)



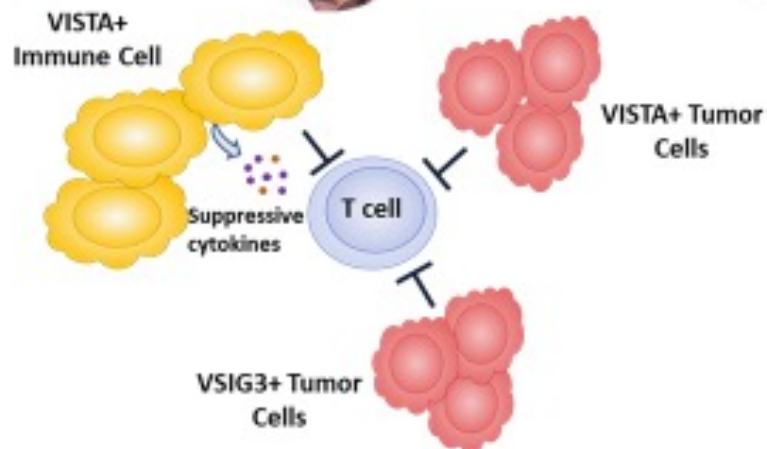
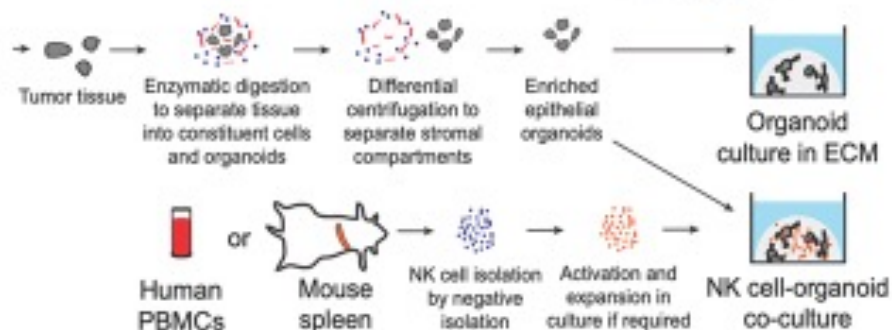
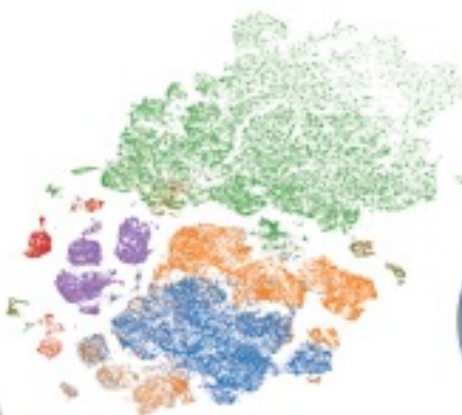
Gruber
(CC)



Reddy
(ET)



Chan
(CNC)



K08CA245024
 K08CA267189
 CPRIT RR200090
 CPRIT RR190020
 ASCO ACRA
 Damon Runyon 112-21
 V Foundation
 DOD W81XWH-21-1-0112

Thank you!