How I Treat Triple-Negative Breast Cancer in 2023

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HARVARD
MEDICAL SCHOOL

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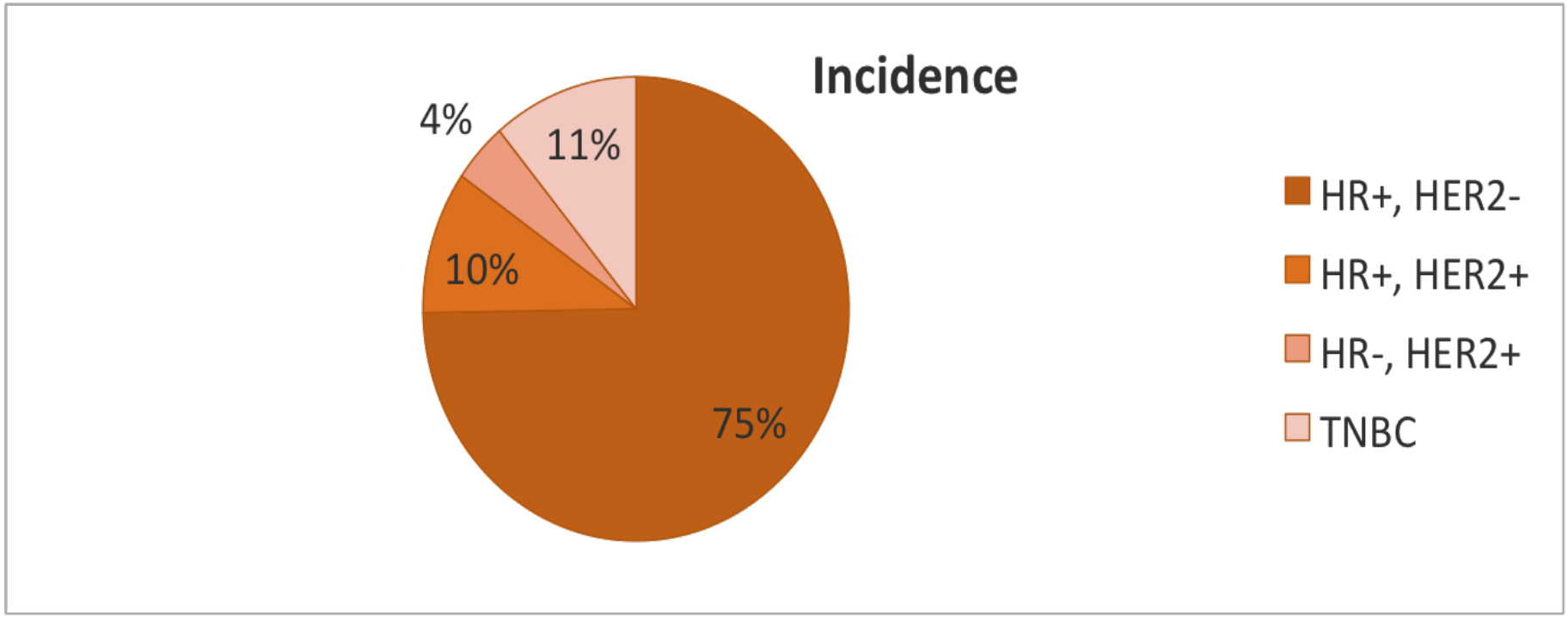
Cancer Institute

Incidence by Hormone Receptor and HER2 Status

Data of 321,958 patients from Surveillance, Epidemiology, and End Results (SEER) database, 2010-2015



HR: hormone receptor; HER2: human epidermal growth factor receptor 2; TNBC: triple-negative breast cancer.

Hwang KT et al. *Clin Cancer Res*. 2019

TNBC: Poorer Prognosis Than Other Subtypes

- High initial sensitivity to chemotherapy
- High relapse rates and higher likelihood of distant disease progression[1]
  - More aggressive visceral disease (liver, lung) [1]
  - Higher frequency of brain metastases[2]
- TNBC recurrence peaks within the first 3 years after treatment[1,3]
  - The likelihood of distant recurrences declines after 5 years
- The mean time to distant recurrence is approximately 2.4 years for TNBC compared with 4.4 years for ER+ patients[4]
- Most deaths occur in the first 3-5 years[1,3]

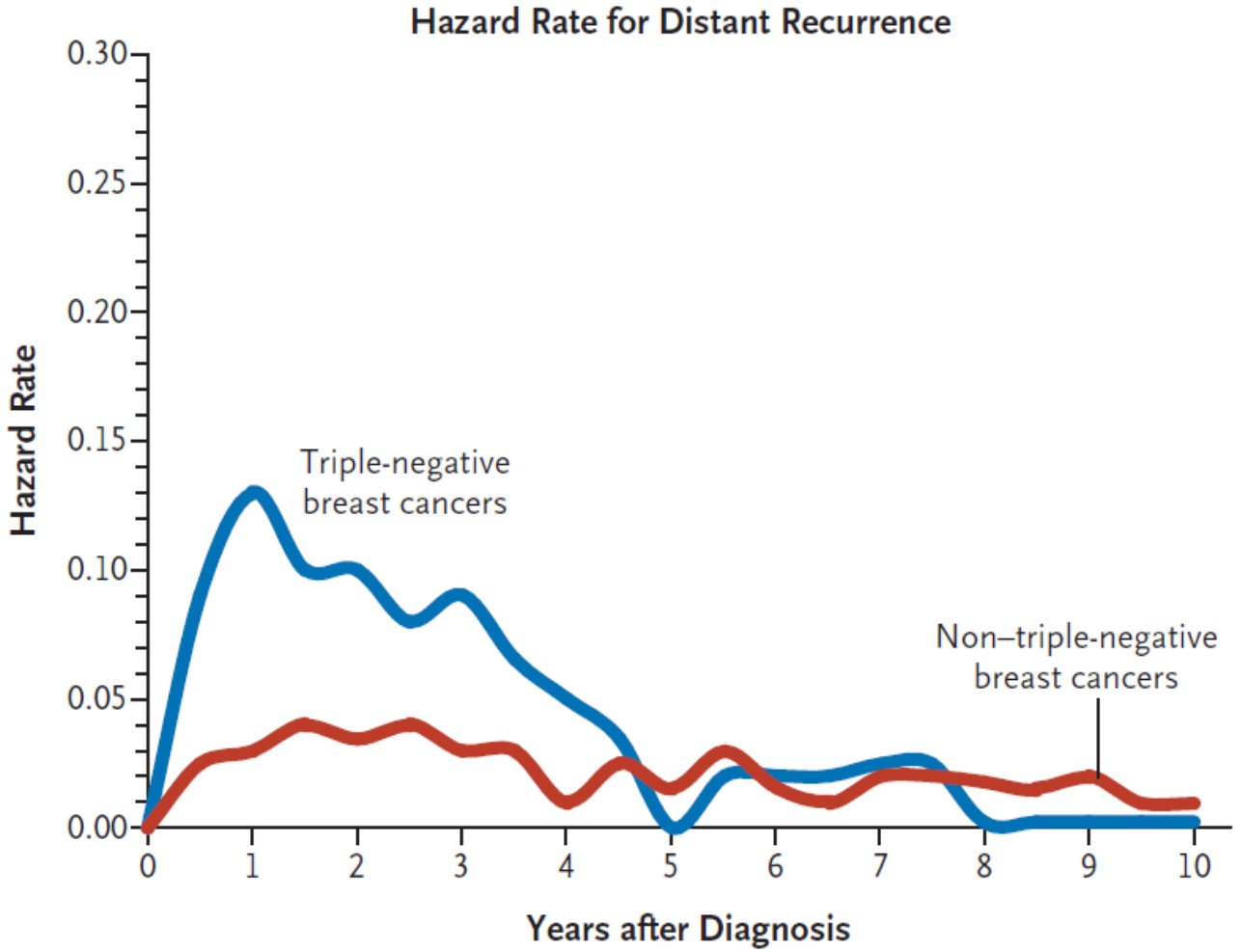


Figure from Foulkes WD, et al. *N Engl J Med*. 2010.

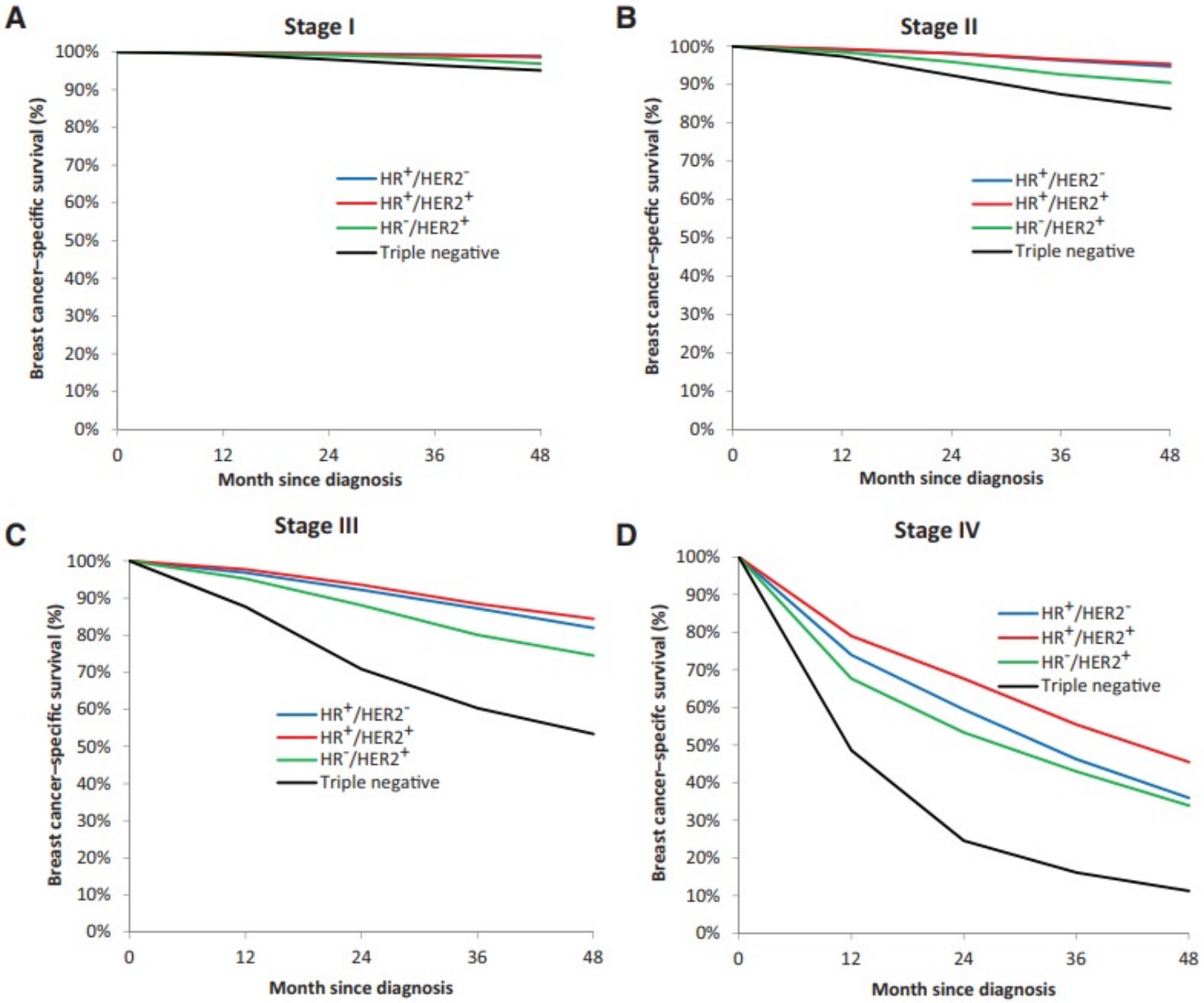
Slide courtesy of Sara Tolaney

ER+, estrogen receptor-positive; TNBC, triple-negative breast cancer.

1. Dent R, et al. *Clin Cancer Res*. 2007; 2. Gaedcke J, et al. *Mod Pathol*. 2007; 3. Foulkes WD, et al. *N Engl J Med*. 2010; 4. Nofech-Mozes, et al. *Breast Cancer Res Treat*. 2009.

TNBC: shorter survival despite anthracycline and taxane chemotherapy

- Four-year breast cancer-specific survival by stage and molecular subtypes using SEER registry data
- Women diagnosed 2010-2013

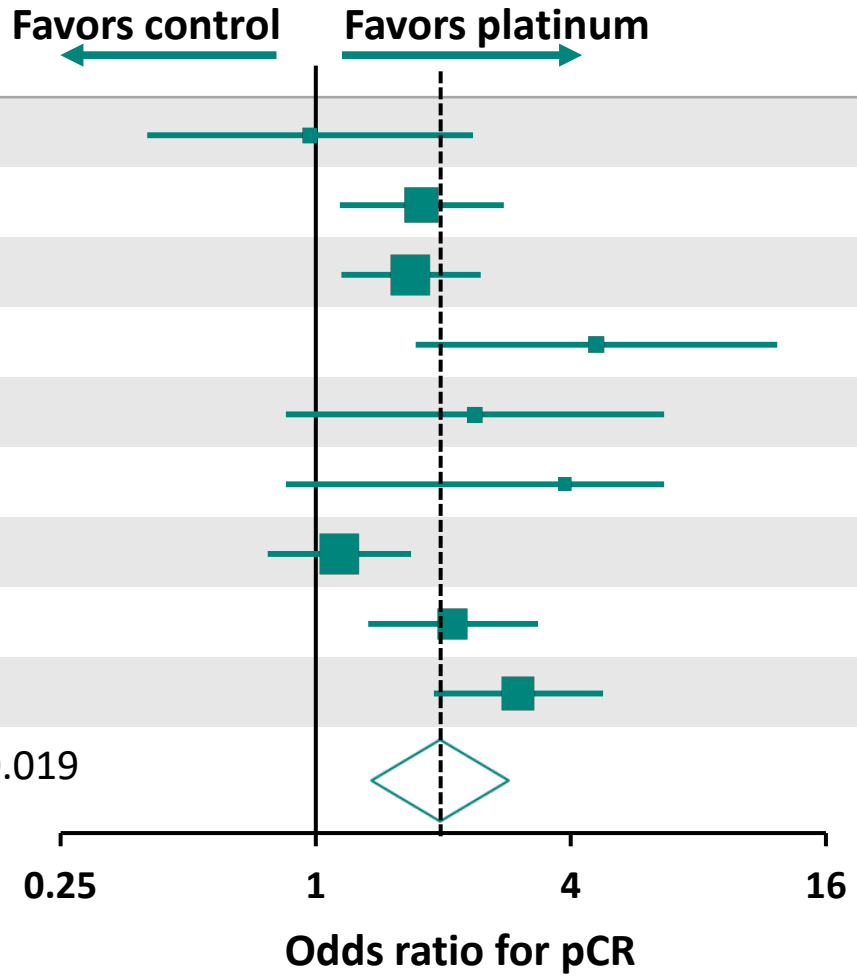


SEER: Surveillance, Epidemiology and End Results
Howlander N et al. *Cancer Epidemiol Biomarkers Prev*. 2018.

Neoadjuvant/Adjuvant Treatment of TNBC: adding other therapies to anthracycline and taxane chemotherapy

- Carboplatin
- Immunotherapy
- Capecitabine
- PARP inhibitor

Neoadjuvant therapy: increased pCR with addition of carboplatin



		HR (95% CI)	n/N	n/N
GEICAM/2006-03	2012	0.97 (0.40, 2.35)	14/47	14/46
GeparSixto GBG66	2014	1.78 (1.14, 2.78)	90/158	67/157
CALGB 40603 Alliance	2014	1.68 (1.15, 2.45)	119/221	87/212
UMIN000003355	2014	4.60 (1.72, 12.27)	23/37	10/38
Aguilar Martinez et al.	2015	2.38 (0.85, 6.64)	18/30	12/31
NCT01276769	2016	3.88 (0.85, 6.64)	17/44	6/43
GeparOcto GBG84	2017	1.14 (0.77, 1.68)	105/203	97/200
WSG-ADAPT	2018	2.11 (1.33, 3.35)	67/146	51/178
BrighTNess	2018	3.01 (1.90, 4.77)	92/160	49/158
Random effect (I-squared = 56.3%, *P*=0.019		1.96 (1.46, 2.62)	545/1046	393/1063

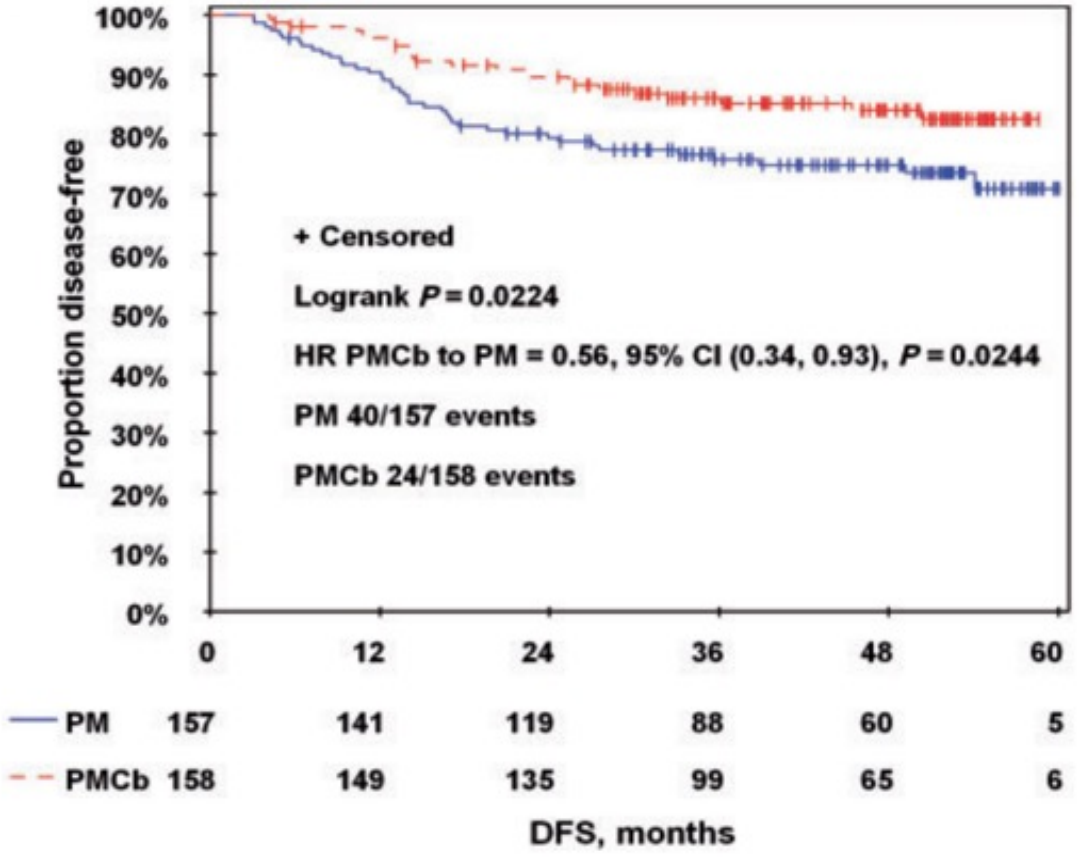
Platinum-based NACT increased pCR rate from 37.0% to 52.1% (OR 1.96, 95% CI 1.46–2.62, P < 0.001)

pCR: pathologic complete response

Poggio F, et al. *Annals of Oncology*. 2018;29:1497-1508.

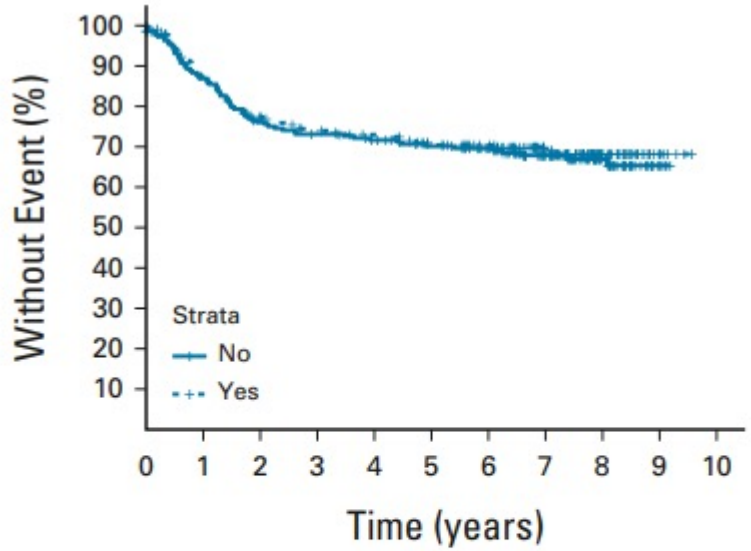
Neoadjuvant therapy: differing EFS data with addition of carboplatin

GeparSixto



PM: paclitaxel and liposomal doxorubicin
Loibl et al. *Ann Oncol* 2018

CALGB 40603



No. at risk:

No	218	184	158	151	145	137	126	93	44	5	0
Yes	225	187	163	151	144	132	122	84	39	6	0

Carbo	Event/ Total	5-Y Survival Estimates % (95% CI)[a]	HR (95% CI)[b]	*P*
No	69/218	70.1 (64.2 to 76.6)	Reference	.7210[c]
Yes	66/225	70.4 (64.5 to 76.8)	0.94 (0.67 to 1.32)	

[a]Kaplan-Meier method; [b]Cox model; [c]Log-rank test

Shepherd et al. *J Clin Oncol* 2022.

Neoadjuvant therapy: BrighTNess EFS data with addition of carboplatin

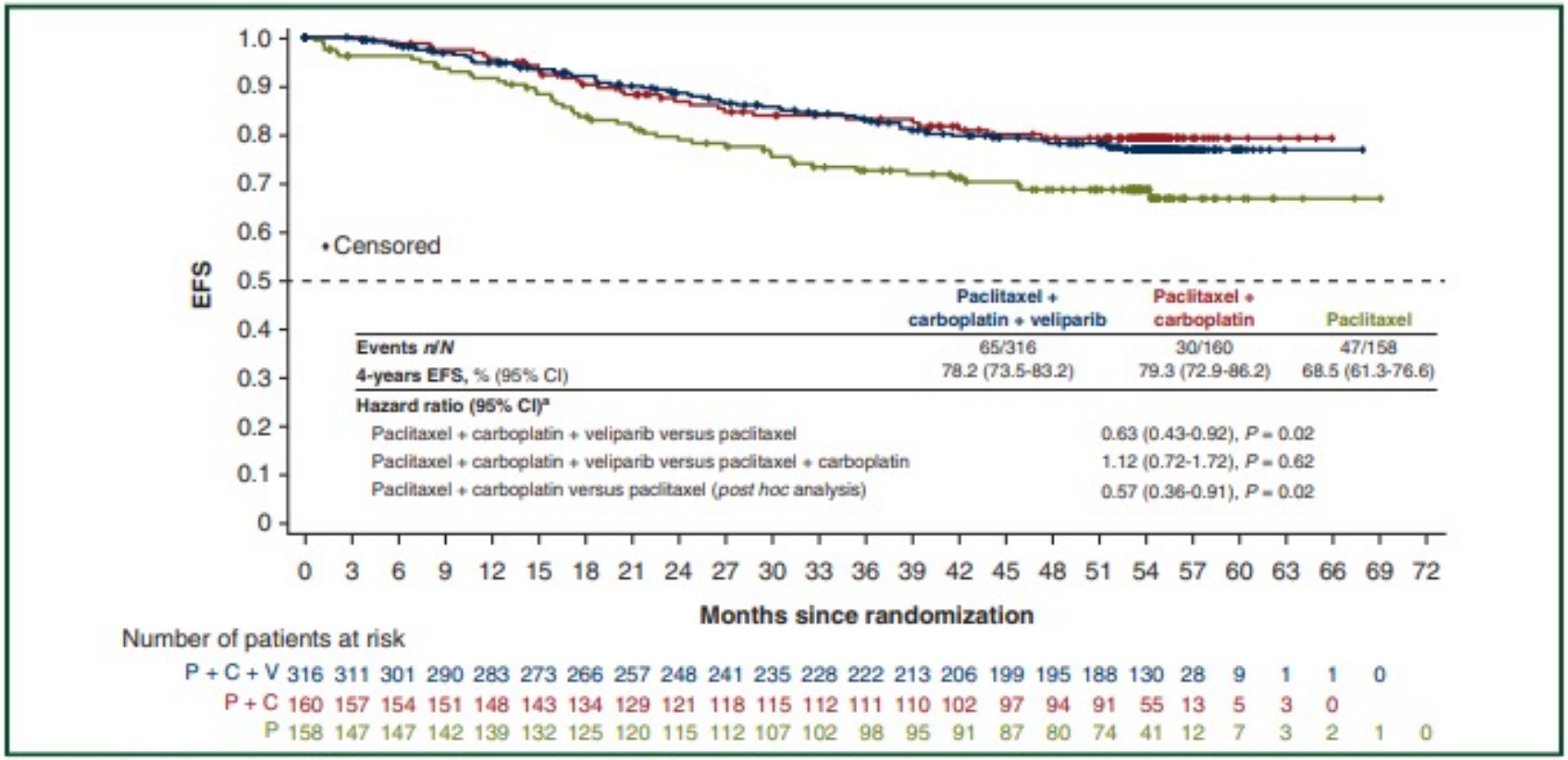
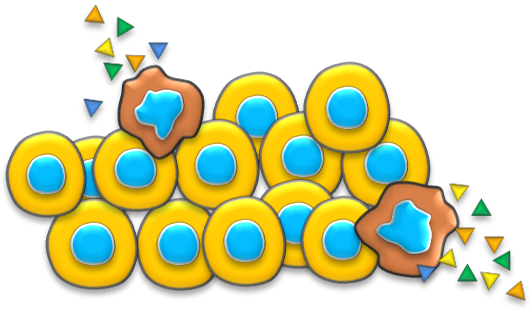


Figure 2. EFS with a median of ≥4.5 years of follow-up.
Final analysis of EFS carried out ≥4 years after surgery.
C, carboplatin; CI, confidence interval; EFS, event-free survival; *gBRCA*, germline *BRCA*; P, paclitaxel; V, veliparib.
[a]Stratified by *gBRCA* status, lymph node status, and planned doxorubicin/cyclophosphamide dose intensity.

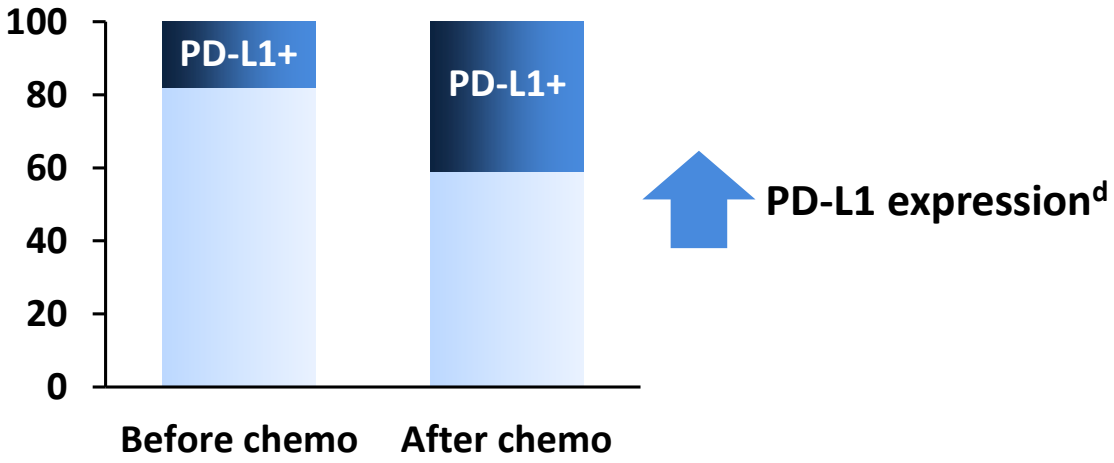
Median follow-up: 4.5y

Neoadjuvant therapy: rationale for combining checkpoint inhibitor and chemotherapy

- Chemotherapy results in:

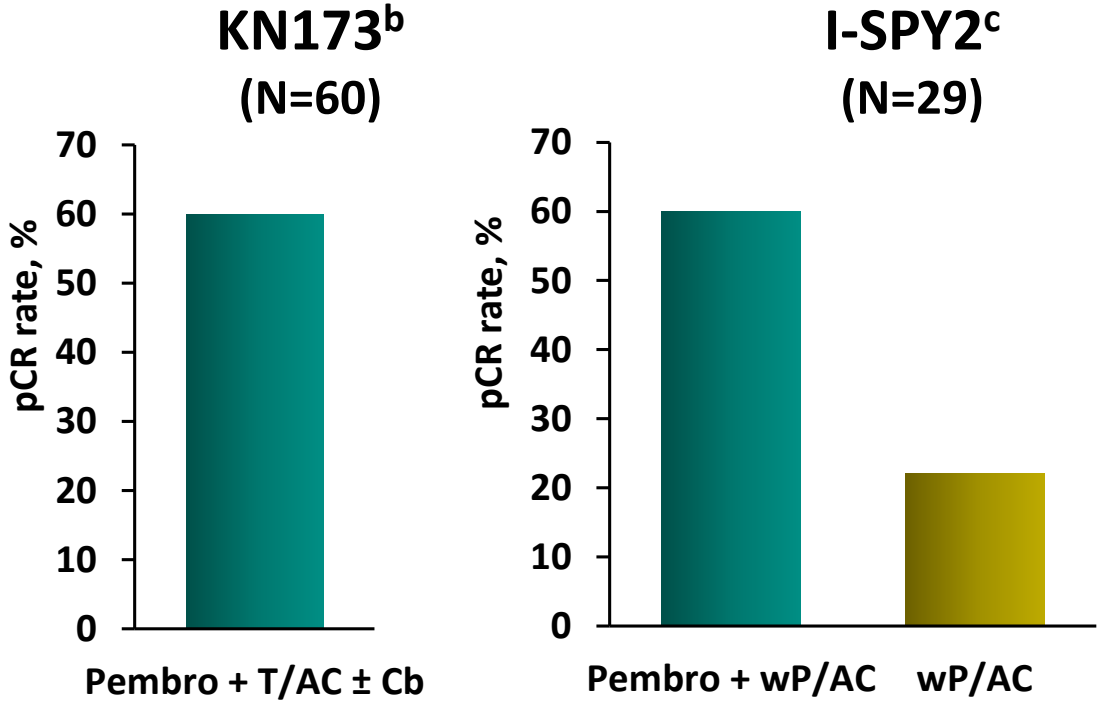


Tumor lysis and antigen shedding[a]



PD-L1 expression[d]

- Pembrolizumab plus standard neoadjuvant chemotherapy in TNBC



pCR=pathologic complete response as defined as ypT0/Tis ypN0; TNBC=triple-negative breast cancer; PAC=paclitaxel, doxorubicin, cyclophosphamide.

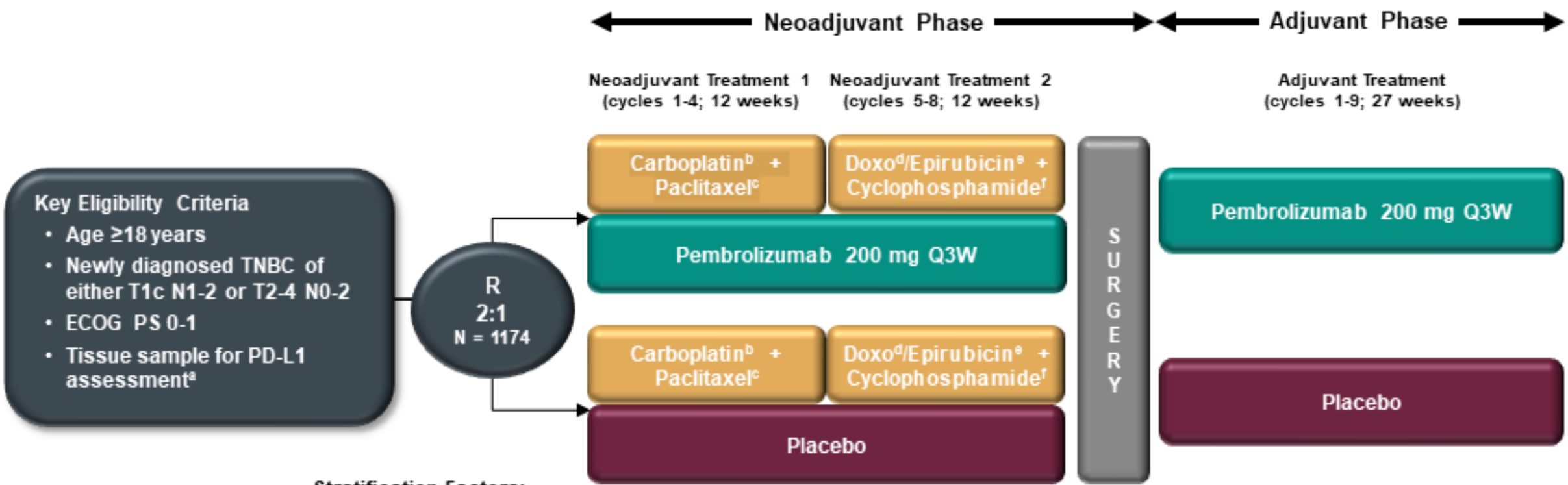
[a] Economopoulou P, et al. *Ann Oncol*. 2016;27:1675-1685; [b] Schmid P, et al. *Ann Oncol*. 2020;31:569-581; [c] Nanda R, et al. *JAMA Oncol*. 2020;6(5):1-9. Epub ahead of print;
[d] Bailly C, et al. *NAR Cancer*. March 2020;2(1).

Immunotherapy in early-stage TNBC

	I-SPY2[a] Pembrolizumab	KEYNOTE-522[b] Pembrolizumab	NEOTRIP[c] Atezolizumab	IMpassion 031[d] Atezolizumab	GEPARNUEVO[e] Durvalumab
Total patients	69/181	602/1174	280	333	174
Target	PD-1	PD-1	PD-L1	PD-L1	PD-L1
Stage	II/III	II/III	Included N3	II/III	35% stage I
Anthracyclines	Yes	Yes	No	Yes	Yes
Carboplatin	No	Yes	Yes	No	No
pCR rate	60% vs 22% (graduated)	65% vs 51% (p=0.00055)	44% vs 41% (p=0.66)	58% vs 41% (p=0.0044)	53% vs 44% (p=0.287)

- Anthracyclines and stage are key factors determining benefit from neoadjuvant immunotherapy
- PD-L1 status does not matter when immune system is intact
- Other variables may play role, such as tumor-infiltrating lymphocytes

KEYNOTE-522 Study Design (NCT03036488)



Stratification Factors:
- Nodal status (+ vs -)
- Tumor size (T1/T2 vs T3/T4)
- Carboplatin schedule (QW vs Q3W)

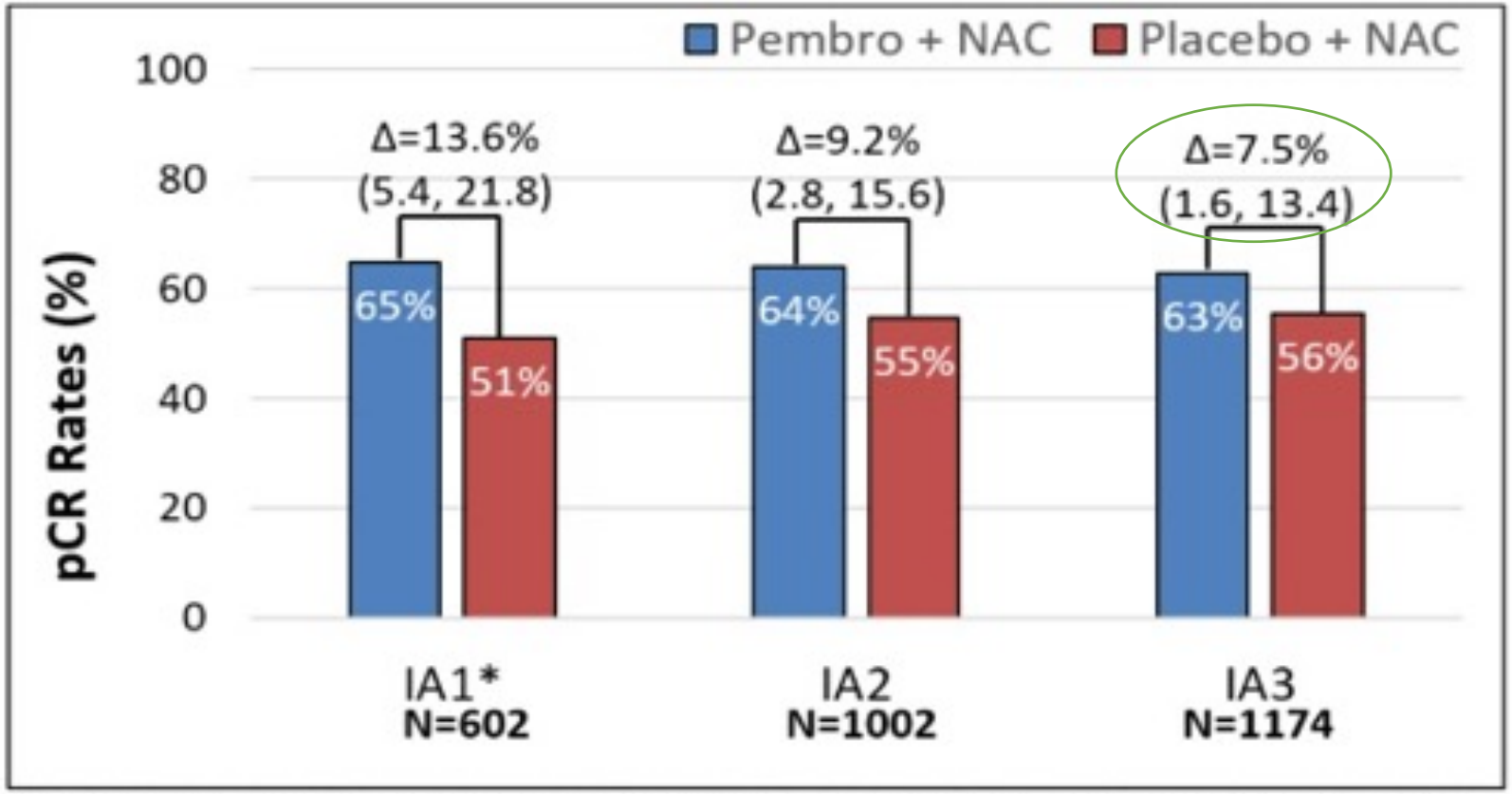
Neoadjuvant phase: starts from the first neoadjuvant treatment and ends after definitive surgery (post treatment included)

Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post treatment included)

[a]Must consist of at least 2 separate tumor cores from the primary tumor.
[b]Carboplatin dose was AUC 5 Q3W or AUC 1.5 QW.
[c]Paclitaxel dose was 80 mg/m² QW.
[d]Doxorubicin dose was 60 mg/m² Q3W.
[e]Epirubicin dose was 90 mg/m² Q3W.
[f]Cyclophosphamide dose was 600 mg/m² Q3W.

Neoadjuvant therapy: Keynote-522 pCR

pCR across interim analyses*



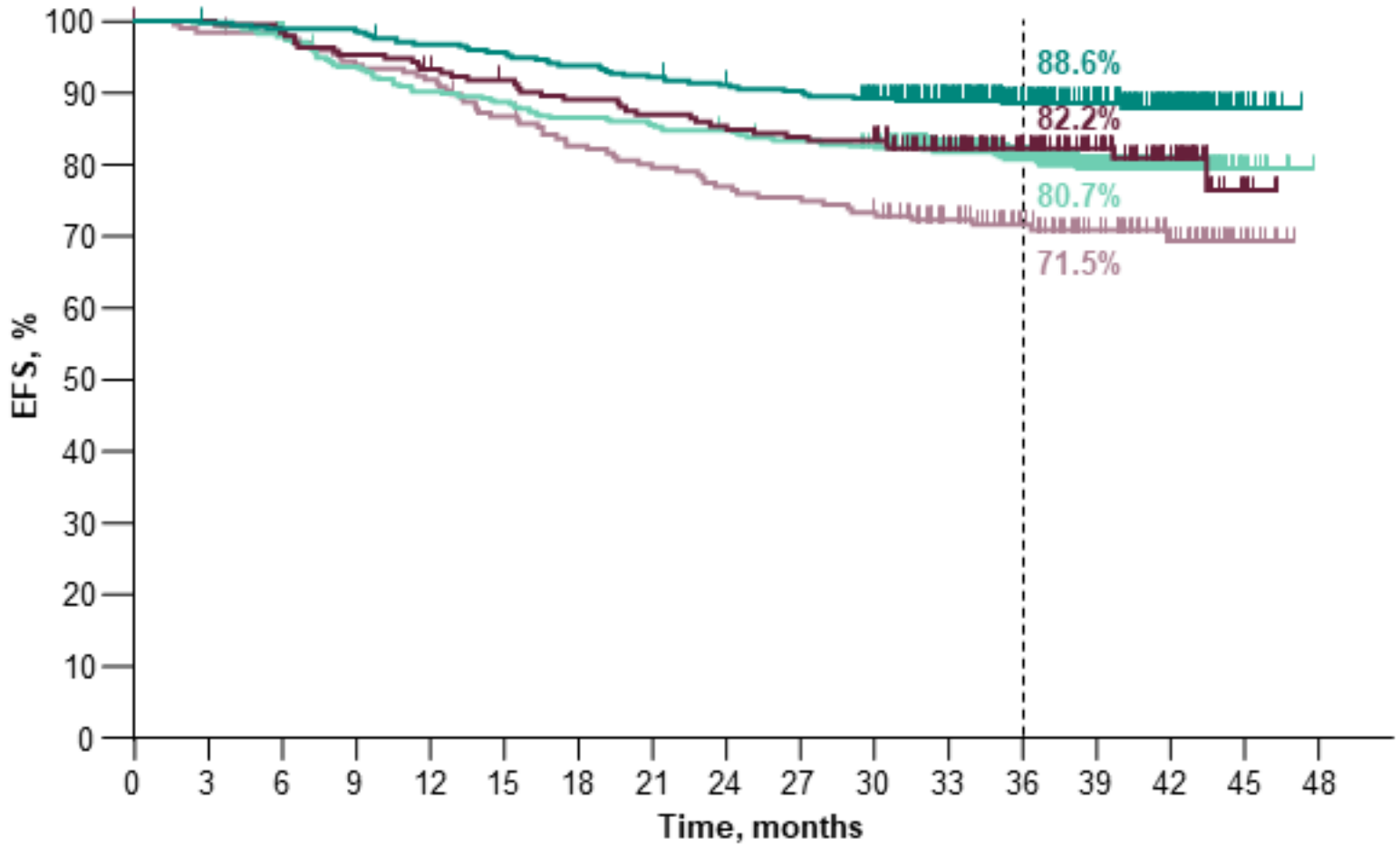
* Statistical boundary was crossed with p-value 0.00055; compare with allocated α of 0.003

*FDA ODAC meeting, 02/09/21

EFS by Nodal Status

Node Negative	Events	HR (95% CI)
Pembro+Chemo/Pembro	11.4%	0.58 (0.37-0.91)
Pbo+Chemo/Pbo	18.6%	

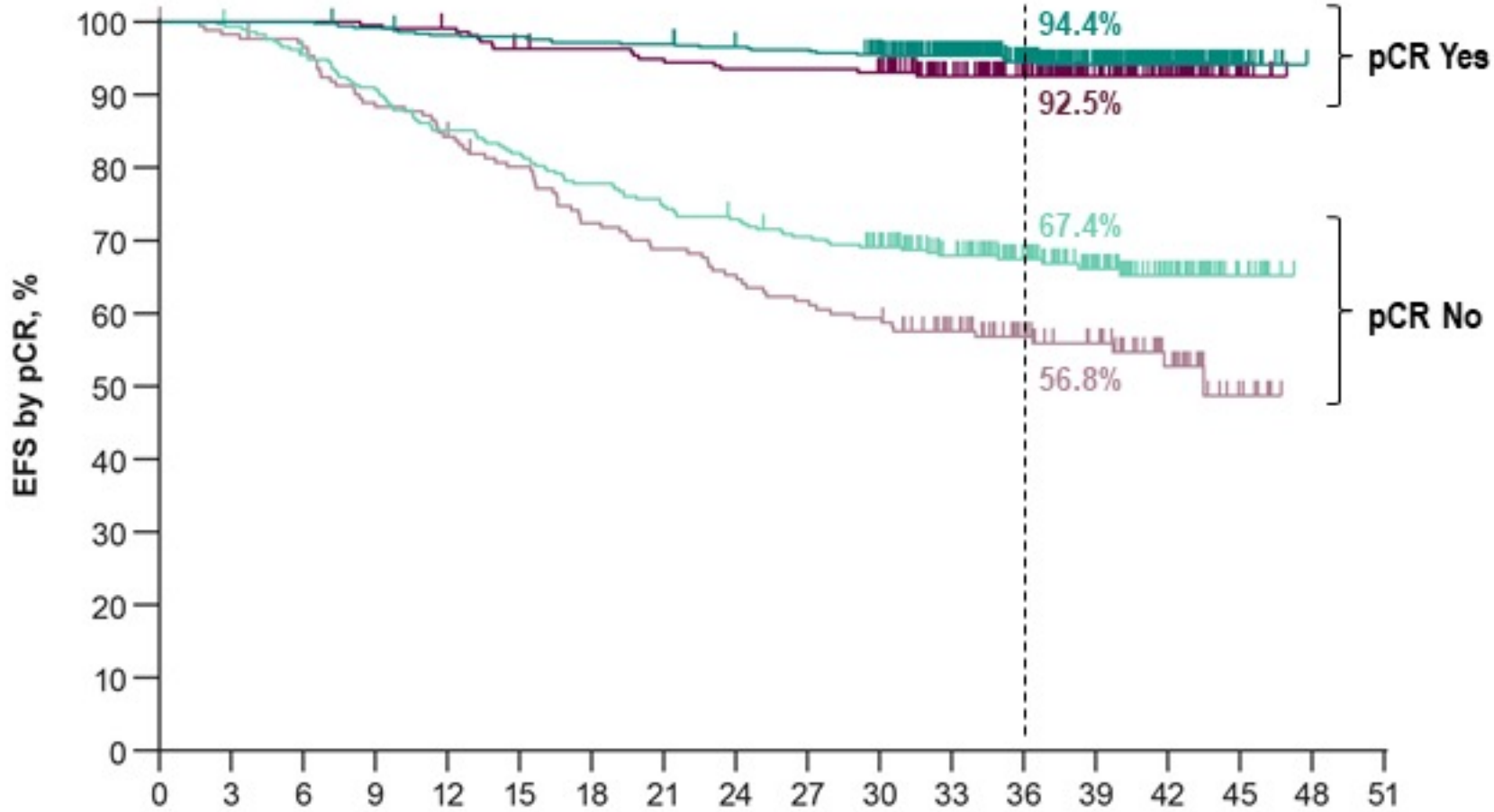
Node Positive	Events	HR (95% CI)
Pembro+Chemo/Pembro	19.6%	0.65 (0.46-0.91)
Pbo+Chemo/Pbo	29.1%	



No. at risk																	
Pembro+Chemo/Pembro, Node Negative	376	374	371	371	362	358	351	345	338	335	322	272	212	151	81	16	0
Pbo+Chemo/Pbo, Node Negative	194	193	190	184	179	174	169	165	162	159	157	131	101	71	39	7	0
Pembro+Chemo/Pembro, Node Positive	408	407	398	380	366	360	351	347	343	336	330	279	221	152	84	12	0
Pbo+Chemo/Pbo, Node Positive	196	193	192	184	179	168	159	154	148	145	140	119	94	69	44	10	0

Data cutoff date: March 23, 2021.

EFS by pCR (ypT0/Tis ypN0)

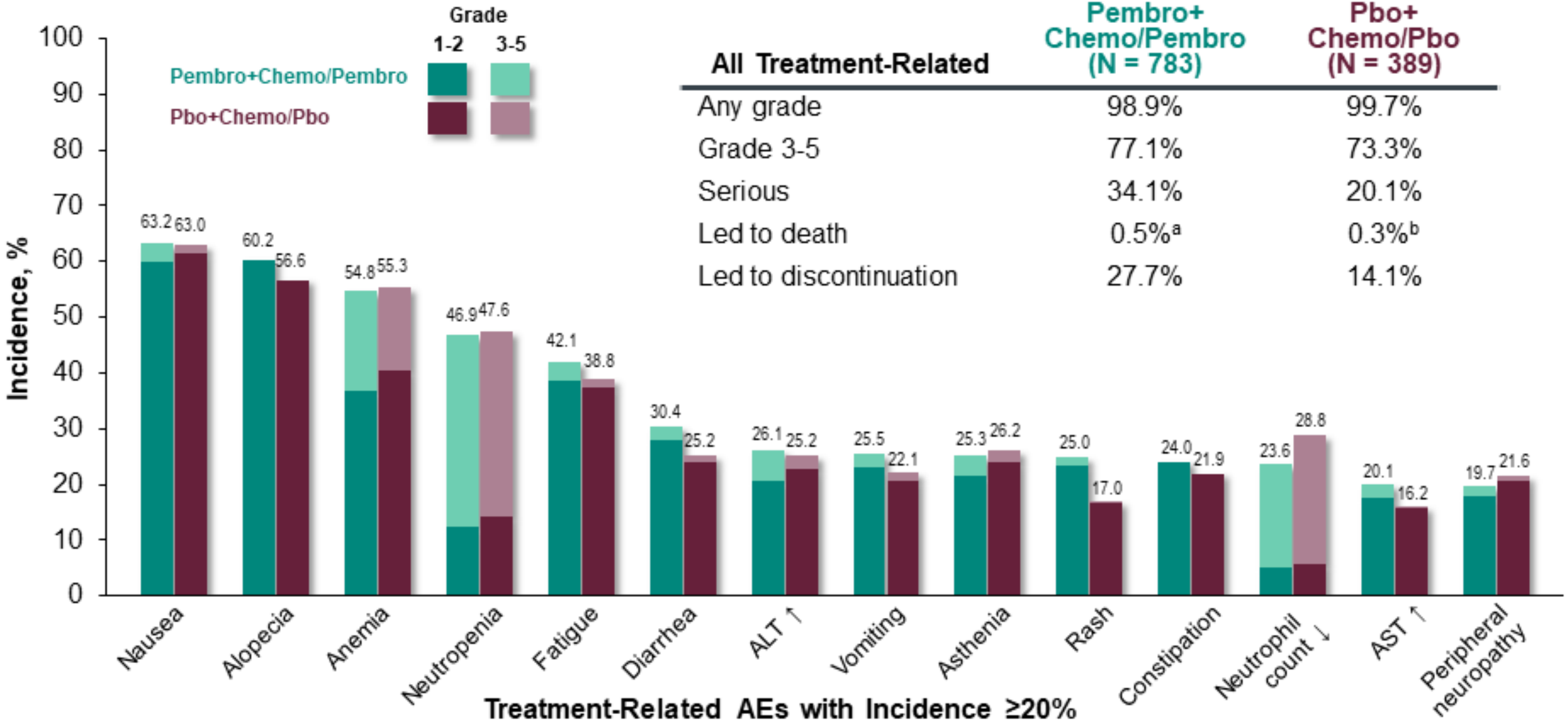


No. at Risk																		
Pembro + Chemo/Pembro Responder	494	494	494	489	483	482	478	477	472	470	460	387	307	220	122	18	0	0
Pbo + Chemo/Pbo Responder	217	217	217	216	214	207	206	203	200	200	197	165	130	87	56	9	0	0
Pembro + Chemo/Pembro Non-Responder	290	287	275	262	245	236	224	215	209	201	192	164	126	83	43	10	0	0
Pbo + Chemo/Pbo Non-Responder	173	169	165	152	144	135	122	116	110	104	100	85	65	53	27	8	0	0

Data cutoff date: March 23, 2021.

Treatment-Related AEs in Combined Phases

All Treatment-Related	Pembro+ Chemo/Pembro (N = 783)	Pbo+ Chemo/Pbo (N = 389)
Any grade	98.9%	99.7%
Grade 3-5	77.1%	73.3%
Serious	34.1%	20.1%
Led to death	0.5%[a]	0.3%[b]
Led to discontinuation	27.7%	14.1%



Treatment-Related AEs with Incidence ≥20%

[a]1 patient from sepsis and multiple organ dysfunction syndrome; 1 patient from pneumonitis; 1 patient from pulmonary embolism; 1 patient from autoimmune encephalitis. [b]1 patient from septic shock. Data cutoff date: March 23, 2021.

Residual disease after neoadjuvant therapy: capecitabine

Pts 20-74 yrs of age

stage I-IIIB HER2- BC and residual disease

(non-pCR or pN+) after neoadjuvant chemotherapy* and surgery;

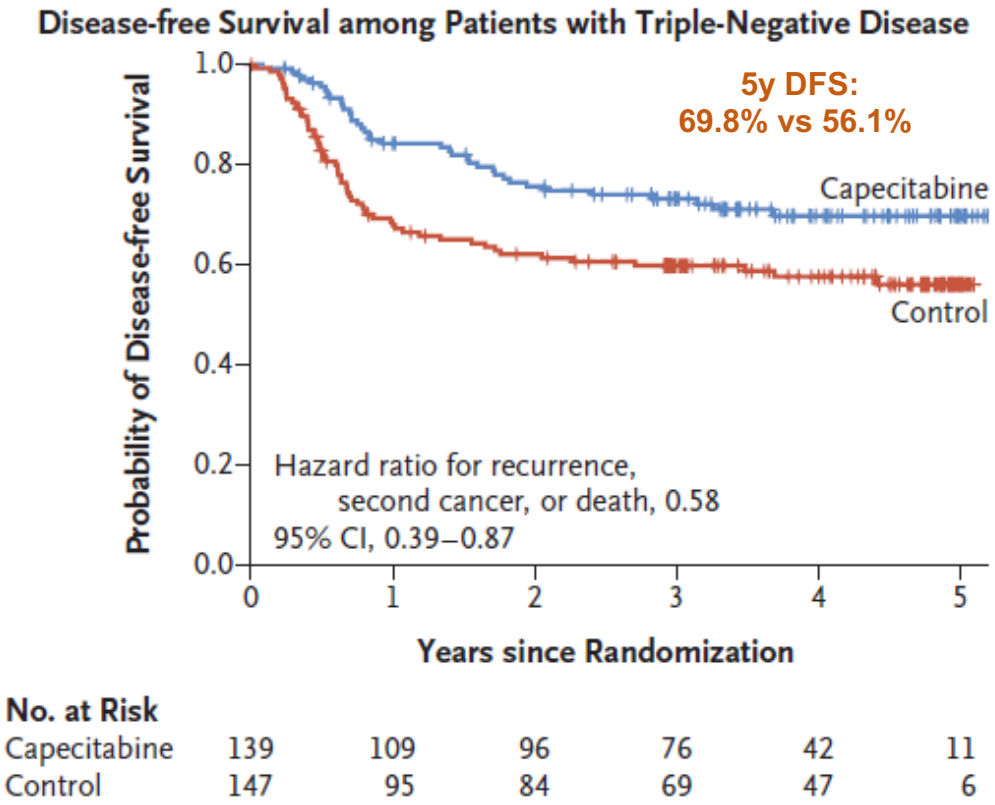
ECOG PS 0 or 1;

no previous oral fluoropyrimidines

(N = 910)†

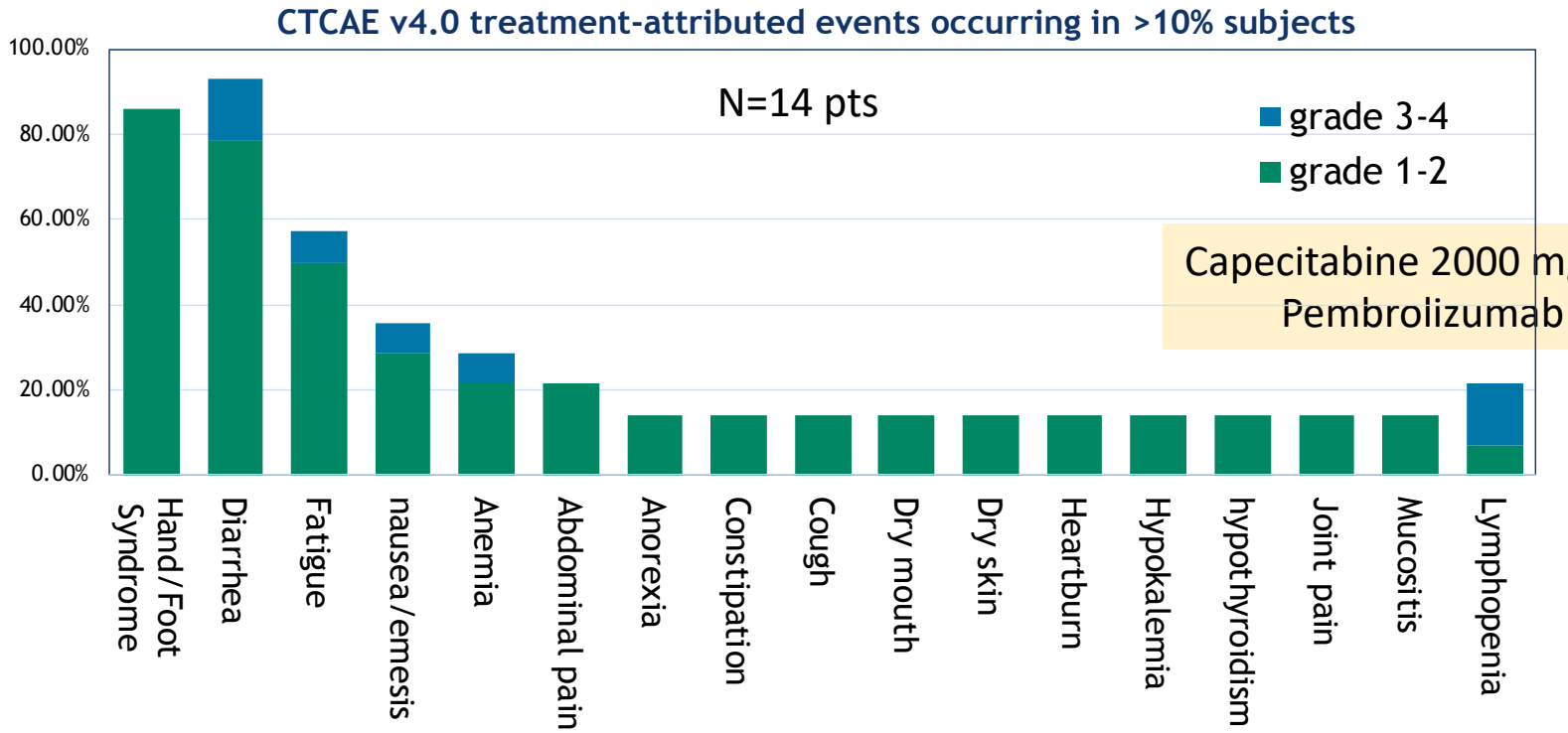
→ Capecitabine
2500 mg/m²/day PO Days 1-14
Q3W for 8 cycles‡
Hormonal therapy if ER/PgR+
(n = 455)†

→ Hormonal therapy if ER/PgR+
No further therapy if ER/PgR-
(n = 455)†



Masuda N et al. *N Engl J Med* 2017

Capecitabine + Pembrolizumab in metastatic disease



Capecitabine 2000 mg BID, 7d on/7d off
Pembrolizumab 200 mg Q3W

Dose level	0	-1	-2	-3
Cape	2000mg BID	1500mg BID	1300mg BID	1150mg BID
% at wk6	79% (11/14)	7% (1/14)	7% (1/14)	7% (1/14)
% at wk12	22% (2/9)	56% (5/9)	11% (1/9)	11% (1/9)

Page D et al. ASCO 2019.

OlympiA: Trial schema

- Local genetic testing or on-study central screening (Myriad Genetics Inc.)
- Germline pathogenic or likely pathogenic *BRCA1/2* mutation
- HER2–negative (hormone receptor–positive or TNBC)
- Stage II-III Breast Cancer or lack of PathCR to NACT

Neoadjuvant Group
- *TNBC:* non-pCR
- *Hormone receptor–positive:* non-pCR and CPS+EG score ≥ 3

≥ 6 cycles Neoadjuvant Chemotherapy → **Surgery** → **+/- Radiotherapy**

Adjuvant Group
- *TNBC:* ≥ pT2 or ≥ pN1
- *Hormone receptor–positive:* ≥ 4 positive lymph nodes

Surgery → **≥ 6 cycles Adjuvant Chemotherapy** → **+/- Radiotherapy**

1:1 Randomization N=1836

Olaparib 300 mg twice daily for 1 year

Placebo twice daily for 1 year

Primary End Point
- Invasive disease-free survival (IDFS) by STEEP system[1]

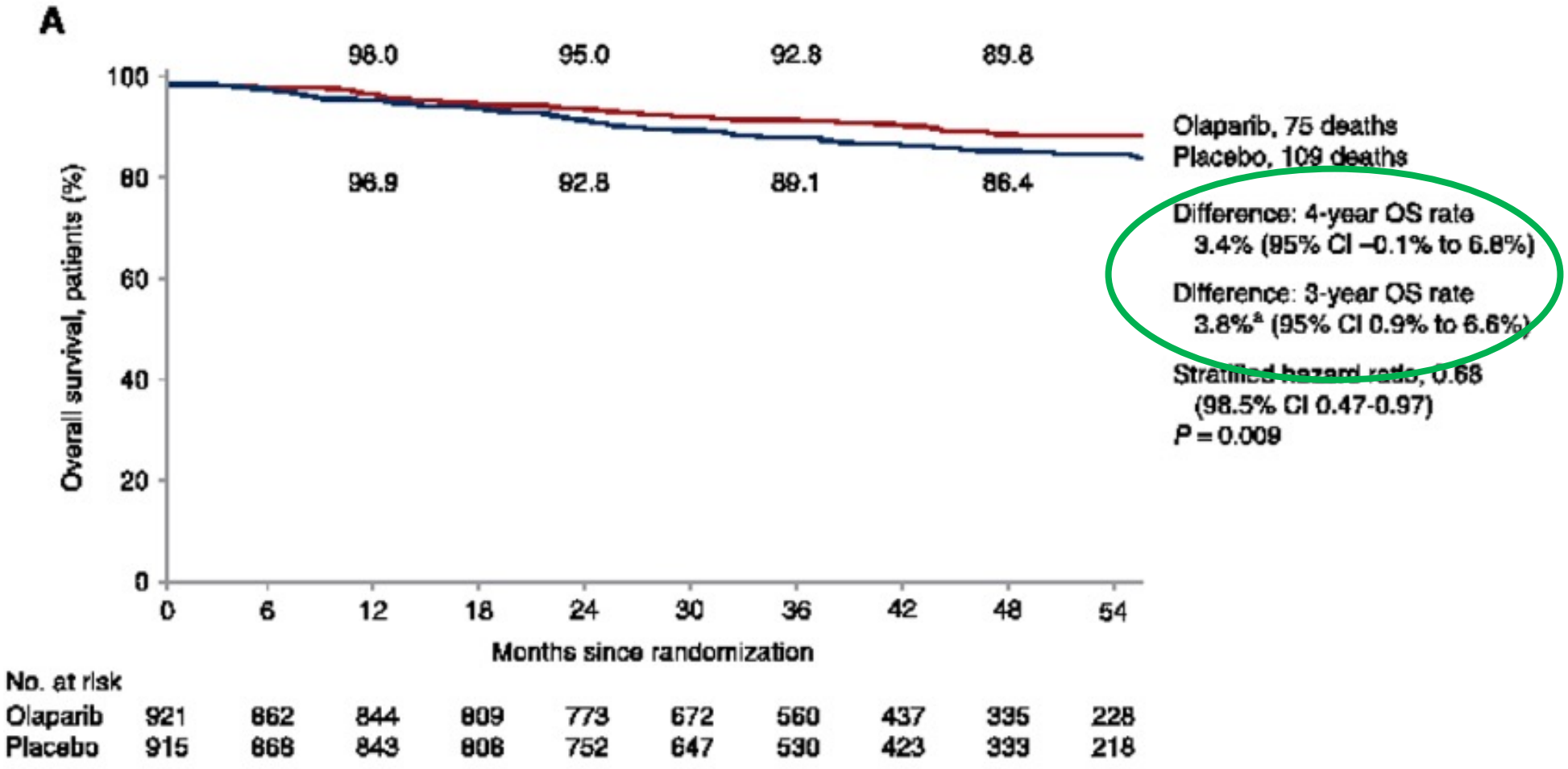
Secondary End Points
- Distant disease-free survival[1] (DDFS)
- Overall survival[1] (OS)
- BRCA1/2 associated cancers
- Symptom / Health related QoL
- Safety

Stratification Factors
- Hormone receptor–positive vs. TNBC
- Neoadjuvant vs. adjuvant
- Prior platinum-based chemotherapy (yes vs. no)

Concurrent Adjuvant Therapy
- Endocrine therapy
- Bisphosphonates
- No 2nd Adjuvant Chemotherapy

Hormone receptor +ve defined as ER and/or PgR positive (IHC staining ≥ 1%)
Triple Negative defined as ER and PgR negative (IHC staining < 1%)
[1]Hudis CA, J Clin Oncol 2007

OlympiA: overall survival



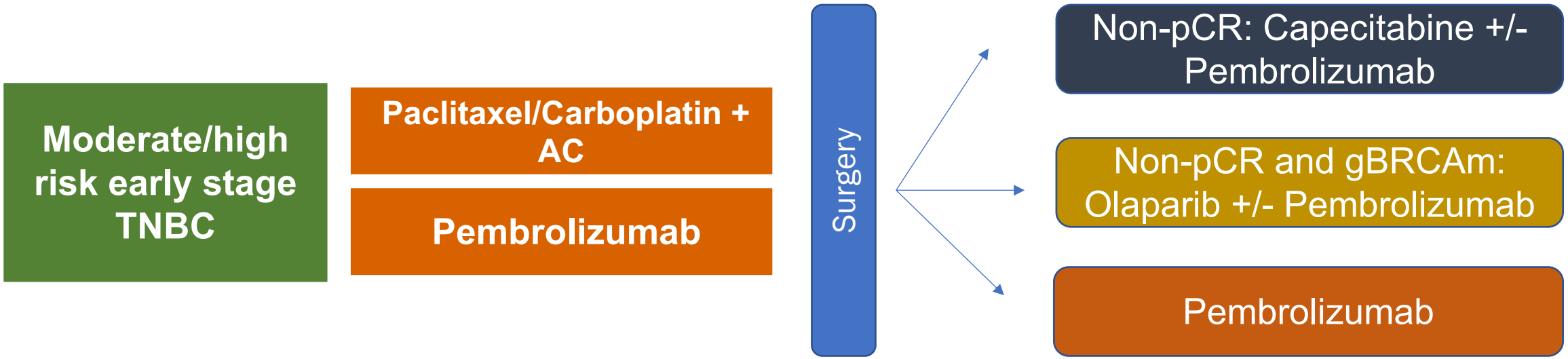
Geyer CE et al. *Ann Oncol*. 2022

Olaparib + pembrolizumab for residual disease

- No randomized data showing that immunotherapy adds benefit to adjuvant olaparib for residual disease
- Possible synergistic activity
- Safety data from the phase II MEDIOLA study[1] (olaparib + durvalumab) and TOPACIO/KEYNOTE-162 study[2] (niraparib + pembrolizumab) in metastatic disease
- Consider olaparib + pembrolizumab in patients with BRCA mutation and TNBC with residual disease

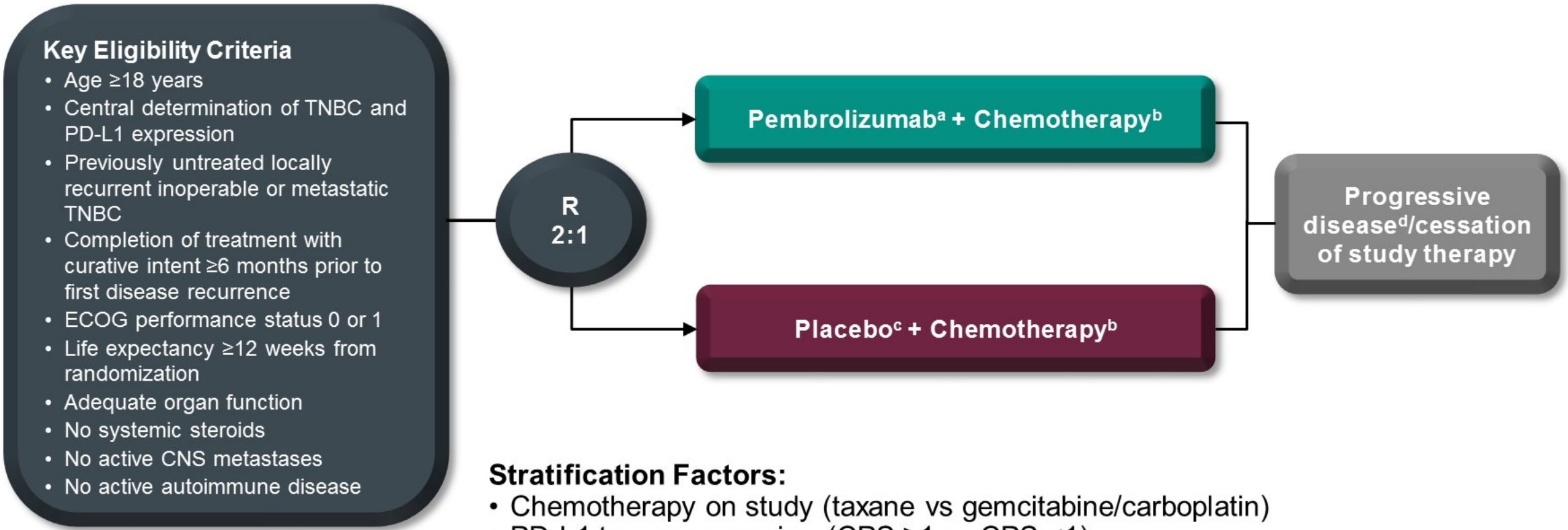
1. Domchek SM et al. *Lancet Oncol*. 2020
2. Konstantinopoulos PA et al. *JAMA Oncol* 2019

Approach to early stage TNBC



TNBC: triple-negative breast cancer; gBRCAm: germline BRCA mutation; pCR: pathologic complete response

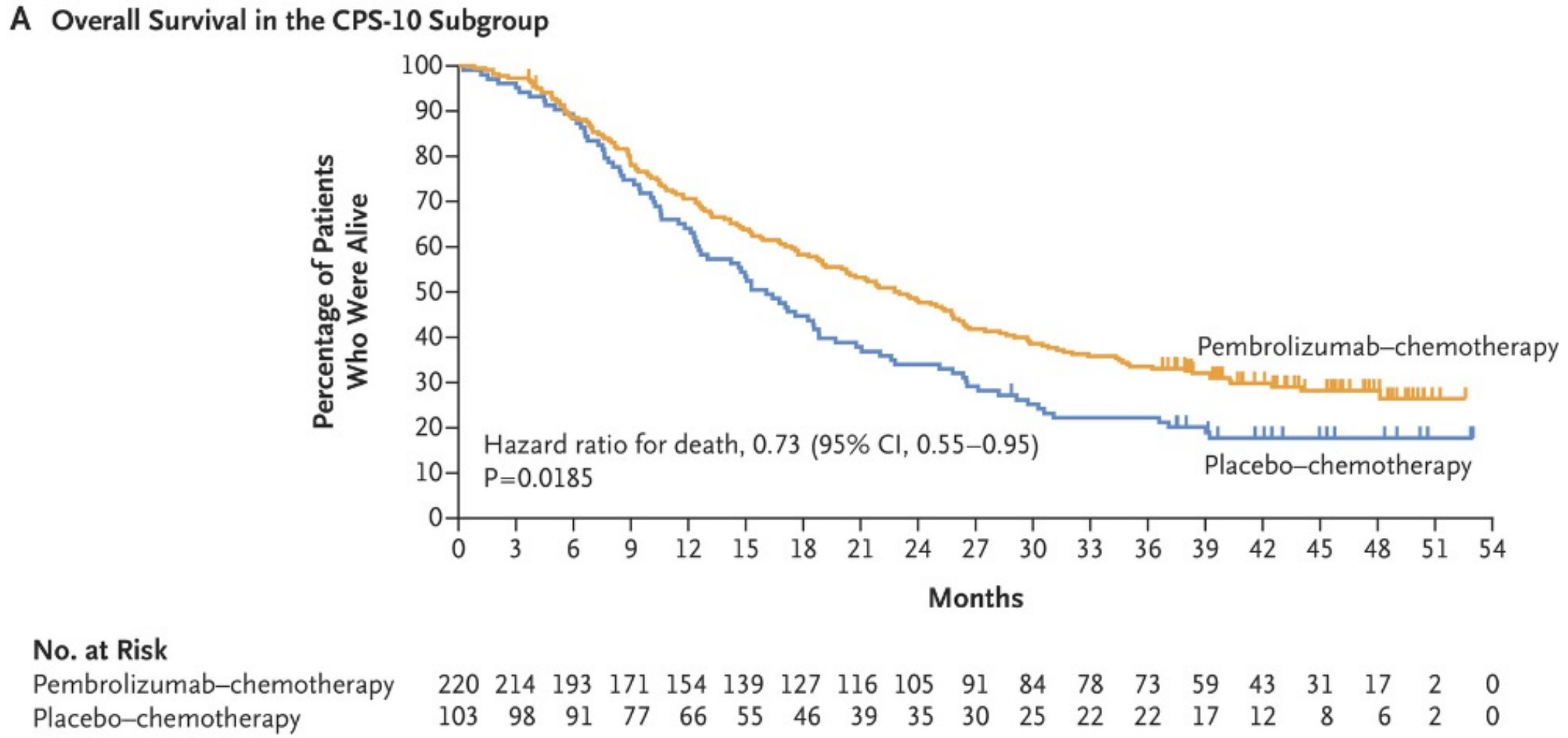
KEYNOTE-355 Study Design (NCT02819518)



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)

[a]Pembrolizumab 200 mg intravenous (IV) every 3 weeks (Q3W)
[b]Chemotherapy dosing regimens are as follows:
Nab-paclitaxel 100 mg/m^2 IV on days 1, 8, and 15 every 28 days
Paclitaxel 90 mg/m^2 IV on days 1, 8, and 15 every 28 days
Gemcitabine 1000 mg/m^2/carboplatin AUC 2 on days 1 and 8 every 21 days
[c]Normal saline
[d]Treatment 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: Overall Survival at PD-L1 CPS ≥10



Cortes J et al. *N Engl J Med*. 2022

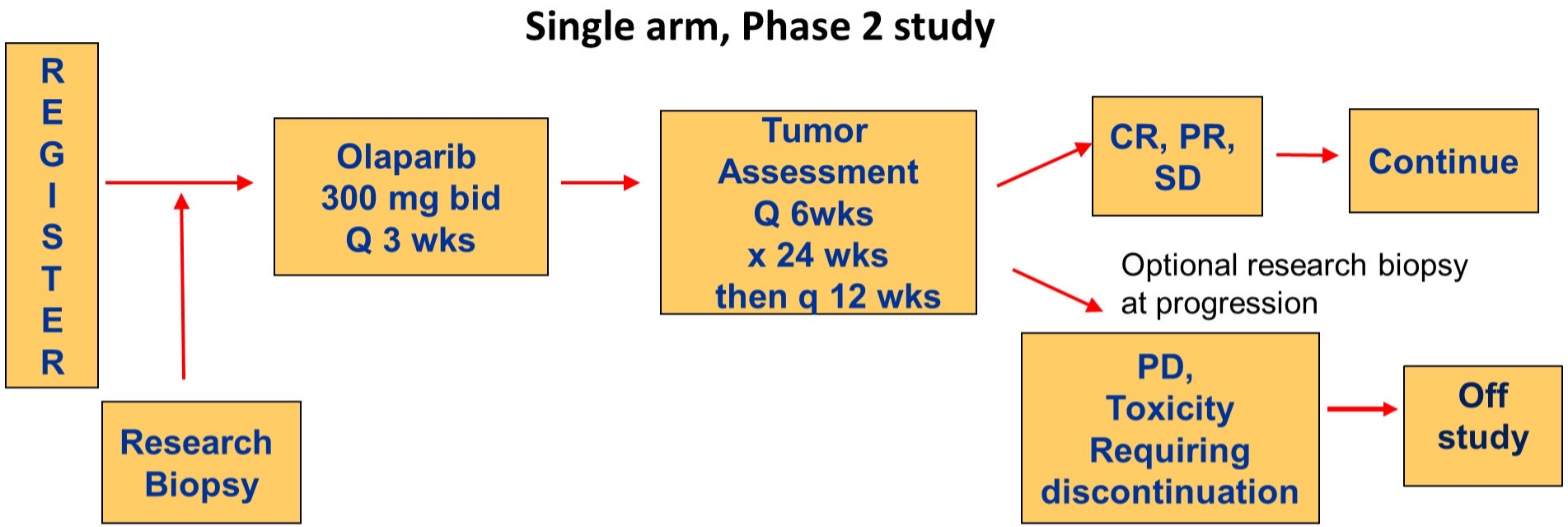
Efficacy of PARP inhibitors in patients with BRCA mutation and metastatic breast cancer

	OlympiAD[1] Olaparib vs. TPC	**EMBRACA**[2] Talazoparib vs. TPC	**BROCADE3**[3] Carbo/paclitaxel + veliparib or placebo
PFS	**5.6 mos** vs. 2.9 mos **HR = 0.43** 95% CI (0.29-0.63)	**5.8 mos** vs. 2.9 mos **HR= 0.60** 95% CI (0.41-0.87)	**14.5 mos** vs. 12.6 mos **HR=0.71** 95% CI (0.57-0.88)
ORR	**51.8%** vs. 5.4% (n=83) (n=37)	**61.8%** vs. 12.5% (n=102) (n=48)	

1. Robson M et al. *N Engl J Med* 2017
2. Litton JK et al. *N Engl J Med* 2018
3. Dieras V et al. *Lancet Oncol* 2020

TBCRC-048

Schema: Olaparib Expanded



Cohort 1: Germline Mutation
Cohort 2: Somatic Mutation

s*BRCA1/2* allowed if g*BRCA* negative

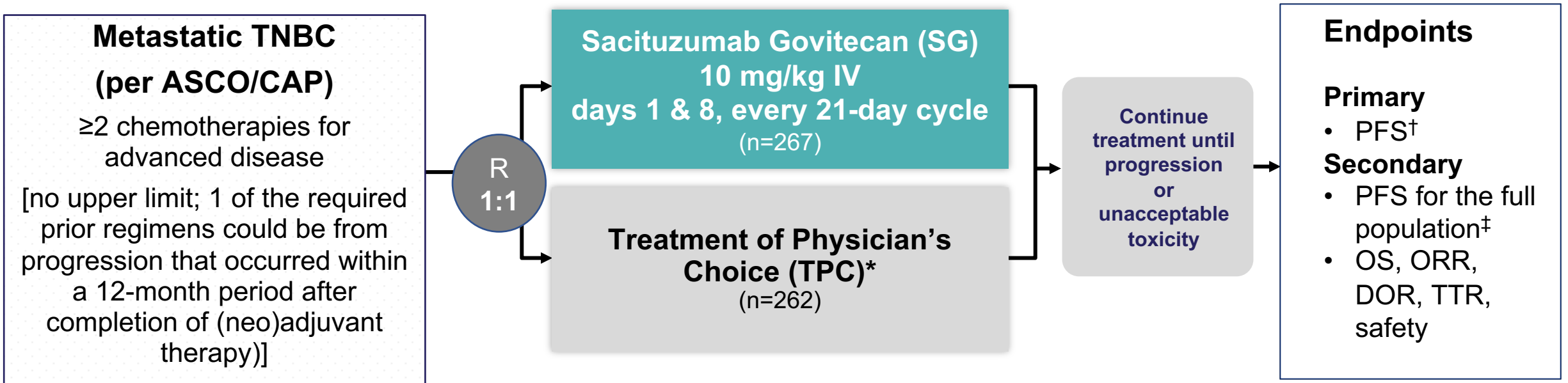
ATM, ATR, BAP1, BARD1, BLM, BRIP1 (FANCJ), CHK1 (CHEK1), CHEK2 , CDK12, FANCA, FANCC, FANCD2, FANCF, MRE11A, NBN (NBS1), PALB2, RAD50, RAD51C, RAD51D, WRN

TBCRC 048: Olaparib Expanded benefit in germline PALB2 and somatic BRCA mutation

PALB2 N=13	s*BRCA1/2* N=17	*ATM & CHEK2* N=17
Germline: 9/11 PR (82%) 10/11 had tumor regression; 1 SD > 1 yr **Somatic: 0/2 – both SD (limited assessments)**	**8/16 PR (50%)**	**0/13 germline** **0/4 somatic**

Tung N et al, *J Clin Oncol* 2020

ASCENT: A Phase 3 Confirmatory Study of Sacituzumab Govitecan in Refractory/Relapsed mTNBC



NCT02574455

Stratification factors

- Number of prior chemotherapies (2-3 vs >3)
- Geographic region (North America vs Europe)
- Presence/absence of known brain metastases (yes/no)

Data cutoff: March 11, 2020

ASCENT was halted early due to compelling evidence of efficacy per unanimous DSMC recommendation. Here, we report the primary results from ASCENT, including PFS and OS.

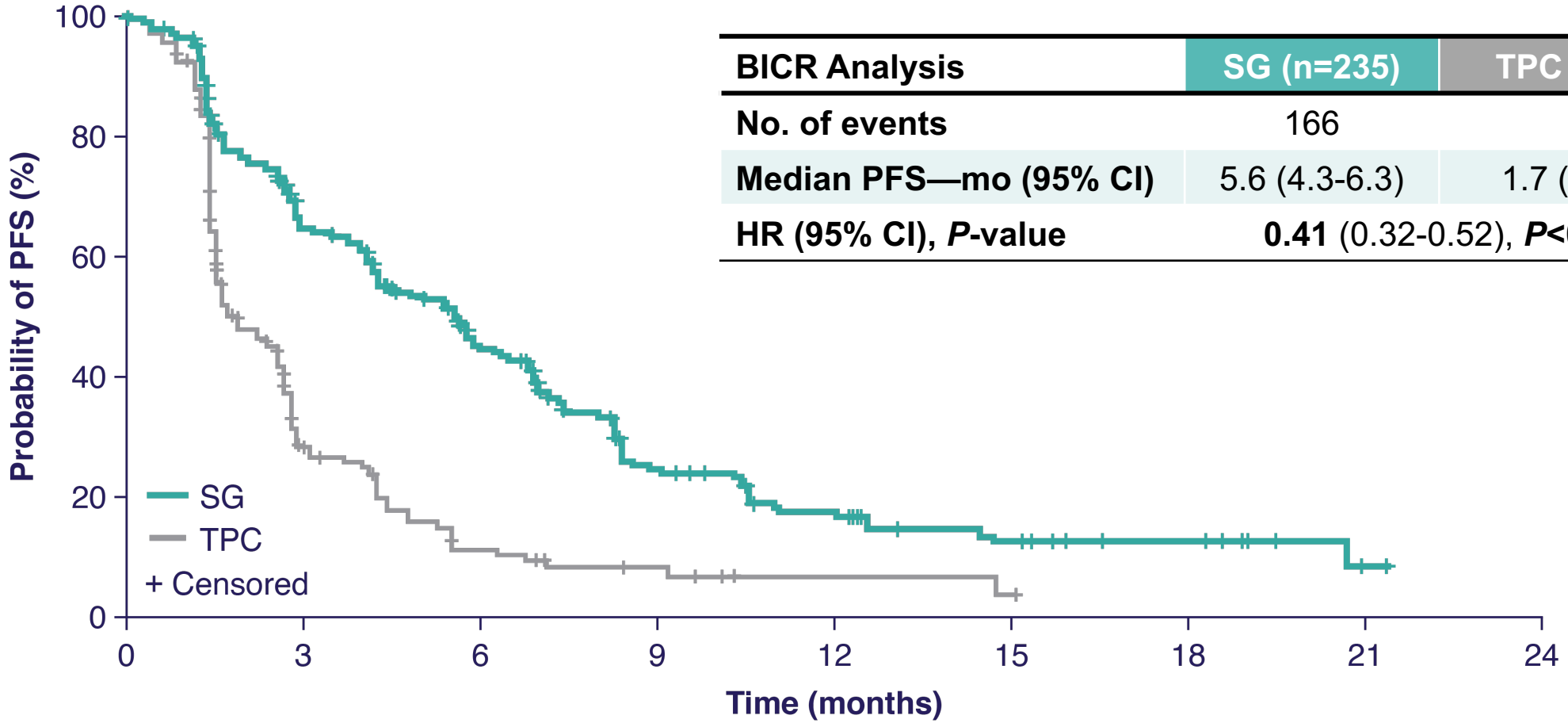
*TPC: eribulin, vinorelbine, gemcitabine, or capecitabine. †PFS measured by an independent, centralized, and blinded group of radiology experts who assessed tumor response using RECIST 1.1 criteria in patients without brain metastasis. ‡The full population includes all randomized patients (with and without brain metastases). Baseline brain MRI only required for patients with known brain metastasis.

ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; DOR, duration of response; DSMC, Data Safety Monitoring Committee; IV, intravenous; mTNBC, metastatic triple-negative breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

National Institutes of Health. https://clinicaltrials.gov/ct2/show/NCT02574455.

Bardia A et al, ESMO 2020

Progression-Free Survival (BICR Analysis)



BICR Analysis	SG (n=235)	TPC (n=233)
No. of events	166	150
Median PFS—mo (95% CI)	5.6 (4.3-6.3)	1.7 (1.5-2.6)
HR (95% CI), *P*-value	**0.41** (0.32-0.52), ***P*<0.0001**	

Number of patients at risk

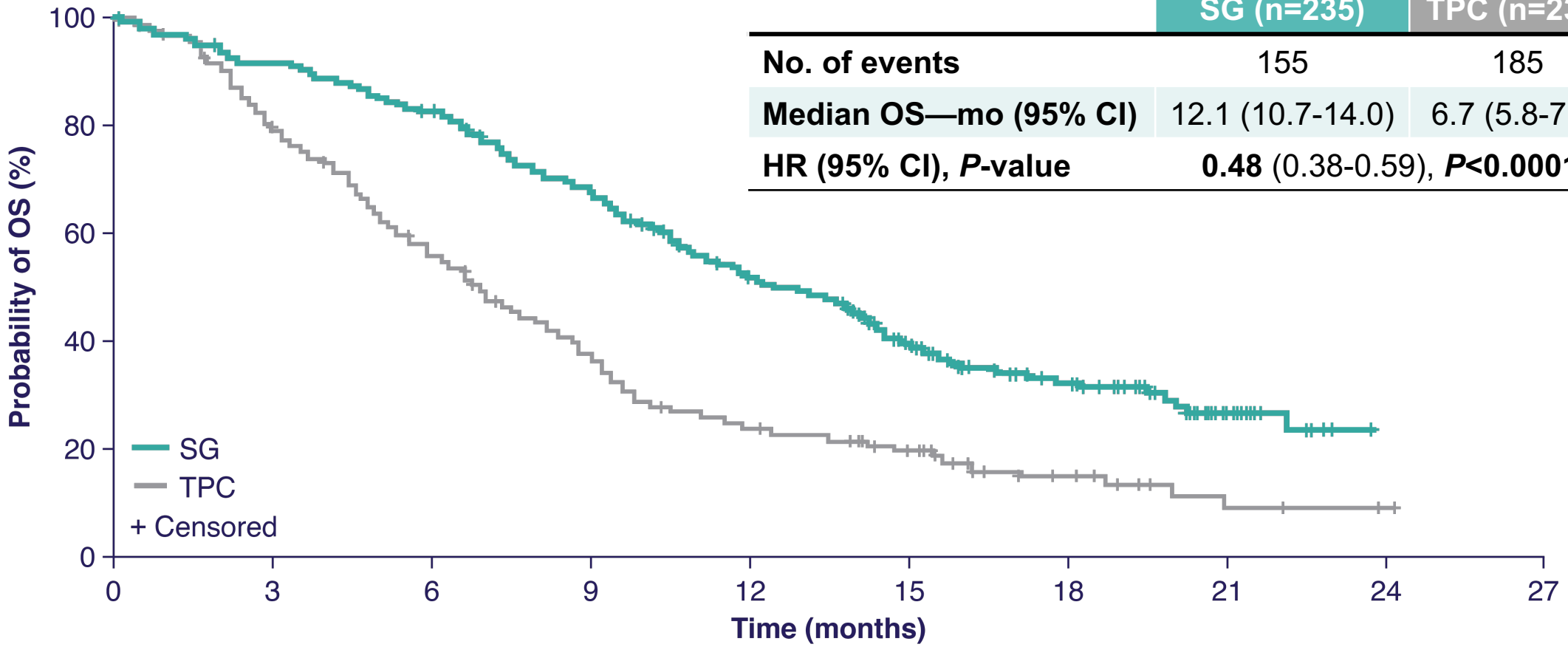
SG	235	222	166	134	127	104	81	63	54	37	33	24	22	16	15	13	9	8	8	5	3	1	0
TPC	233	179	78	35	32	19	12	9	7	6	4	2	2	2	2	1	0	0	0	0	0	0	0

Primary endpoint (PFS) assessed by independent central review in the brain metastases-negative population, as pre-defined in the study protocol.
Secondary endpoint (PFS) assessed in the full population (brain metastases-positive and -negative) and PFS benefit was consistent (HR=0.43 [0.35-0.54], *P*<0.0001).
BICR, blind independent central review; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Bardia A et al, ESMO 2020

Overall Survival

	SG (n=235)	TPC (n=233)
No. of events	155	185
Median OS—mo (95% CI)	12.1 (10.7-14.0)	6.7 (5.8-7.7)
HR (95% CI), *P*-value	**0.48** (0.38-0.59), ***P*<0.0001**	



Number of patients at risk

SG	235	228	220	214	206	197	190	174	161	153	135	118	107	101	90	70	52	43	37	30	21	13	8	1	0	0
TPC	233	214	200	173	156	134	117	99	87	74	56	50	45	41	37	30	20	14	11	7	4	3	3	2	1	0

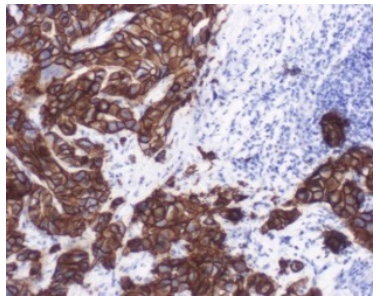
Assessed by independent central review in the brain metastases-negative population.
OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Bardia A et al, ESMO 2020

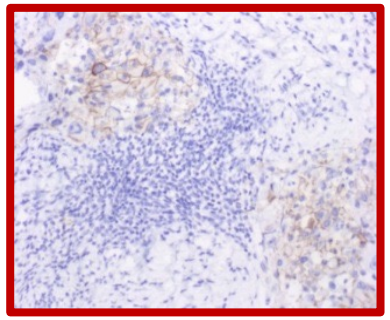
Prevalence of HER2-low by HR-status

HER2 IHC examples

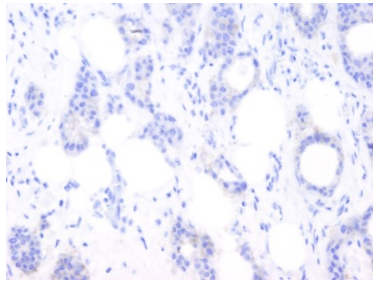
HER2+



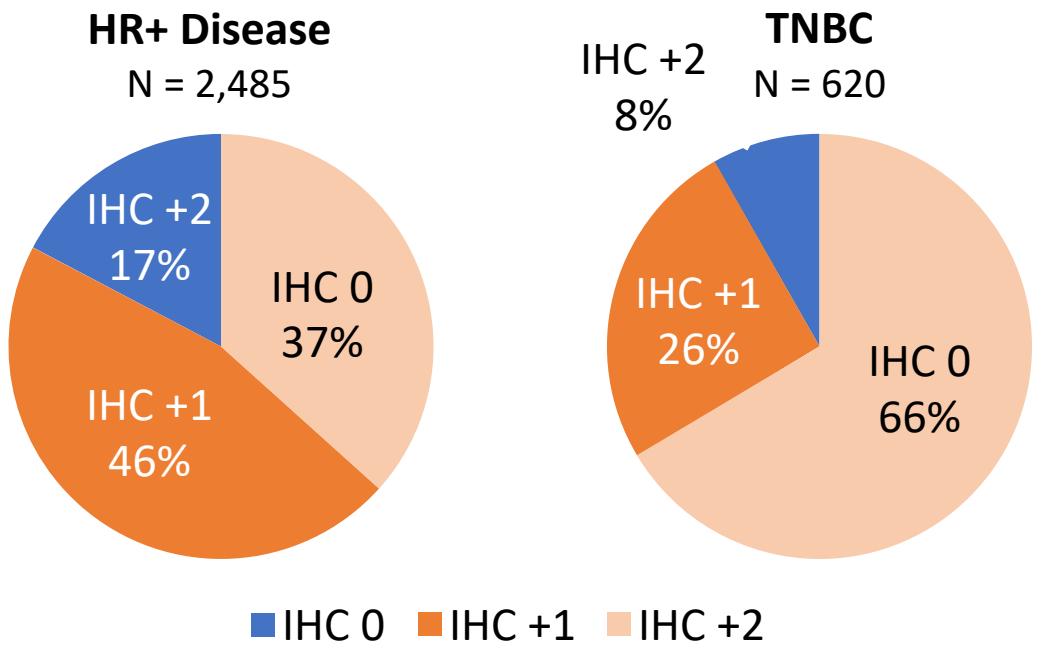
HER2-low



HER2-



HER2-negative



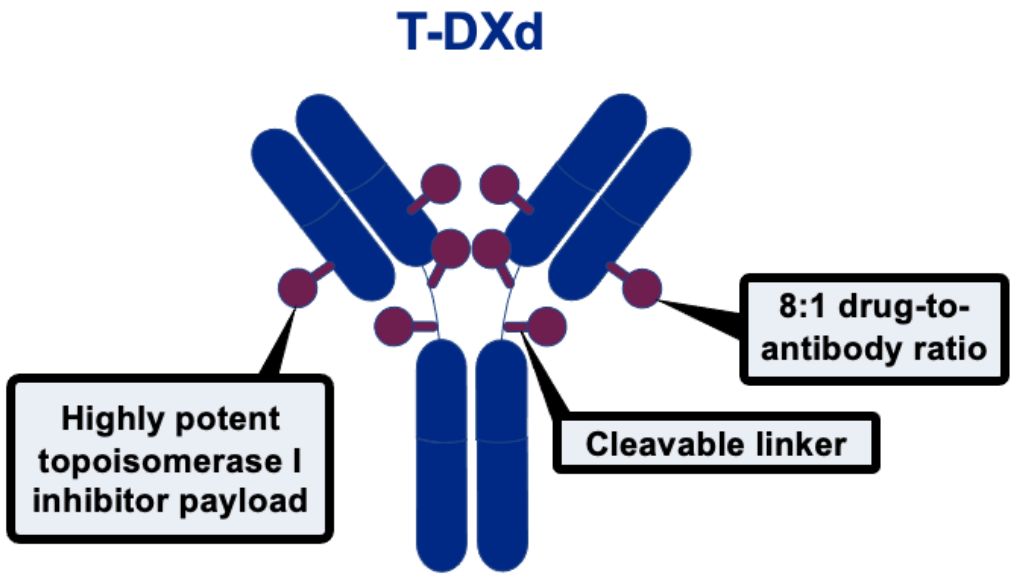
- 34% to 63% of breast cancer patients considered HER2-negative under current guidelines express low levels of HER2

HER2: human epidermal growth factor receptor 2; HR: hormone receptor; IHC: immunohistochemical staining; TNBC: triple negative breast cancer

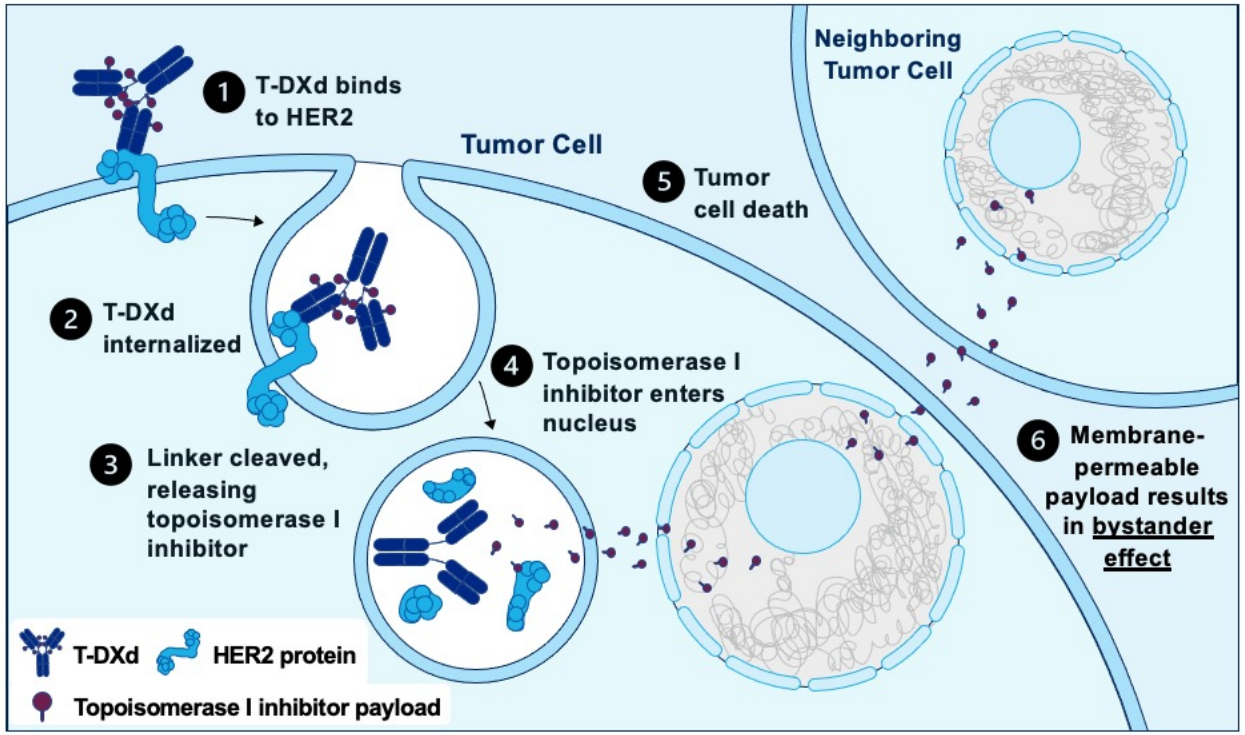
Schettini. ESMO Breast Cancer Virtual Meeting 2020. Abstr 23P. Slide courtesy of Aleix Prat.

Trastuzumab Deruxtecan (T-DXd)

STRUCTURE AND MECHANISM OF ACTION



Internalization of T-DXd leads to release of the DXd payload and subsequent cell death in the target tumor cell and neighboring tumor cells through the bystander effect



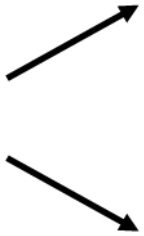
Modi S, et al. ASCO Annual Meeting 2022

DESTINY-Breast04: Trastuzumab Deruxtecan vs Chemotherapy in Previously Treated HER2-low BC

- International, randomized, open-label phase III study

21-d cycles

Women and men with unresectable and/or metastatic HER2-low breast cancer; progression on endocrine therapy, 1-2 prior lines chemotherapy; no prior HER2 positivity (IHC3+ or ISH+) (planned N = 540)



Trastuzumab deruxtecan
10 mg/kg on Day 1 and 8

Chemotherapy*

*Investigator's choice of **capecitabine**, **eribulin**, **gemcitabine**, **paclitaxel**, or **nab-paclitaxel**.

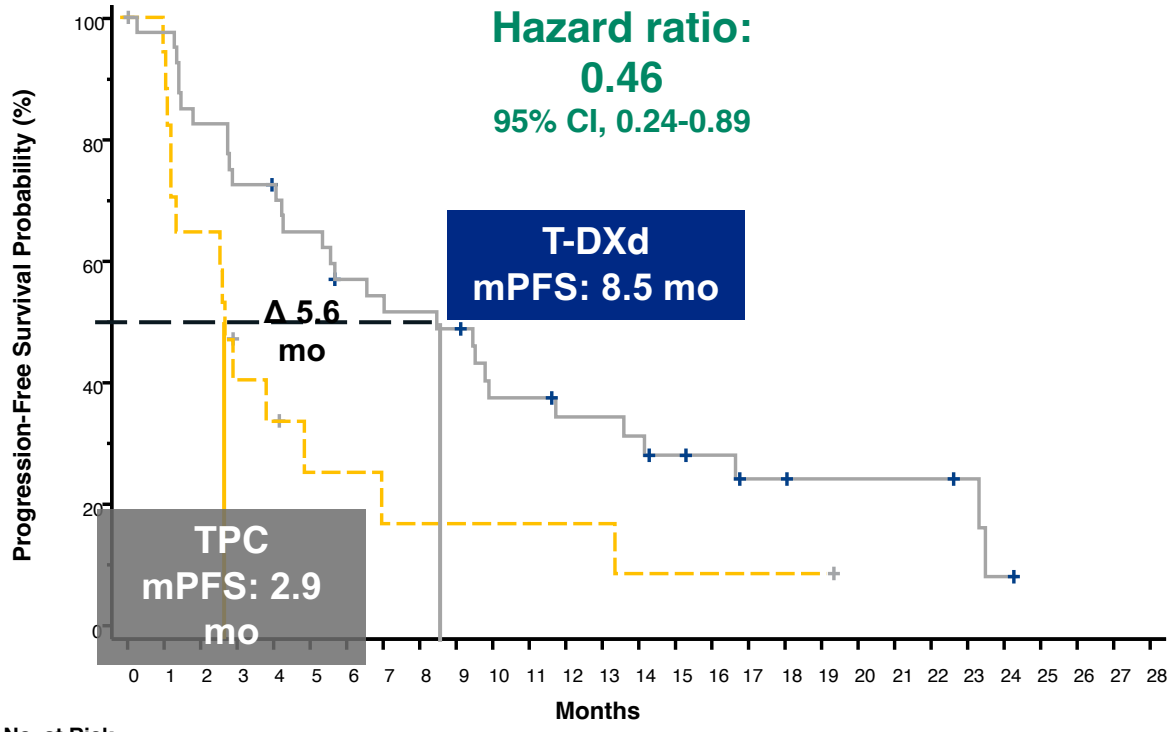
- Primary endpoints: PFS per BICR
- Secondary endpoints: OS, DoR, ORR, PFS per investigator

BOR: best overall response; ECOG PS: Eastern Cooperative Oncology Group performance status; LHRH: luteinizing hormone-releasing hormone; TTD: time to deterioration.

Modi S et al. *N Engl J Med* 2022.

PFS and OS in HR− (Exploratory Endpoints)

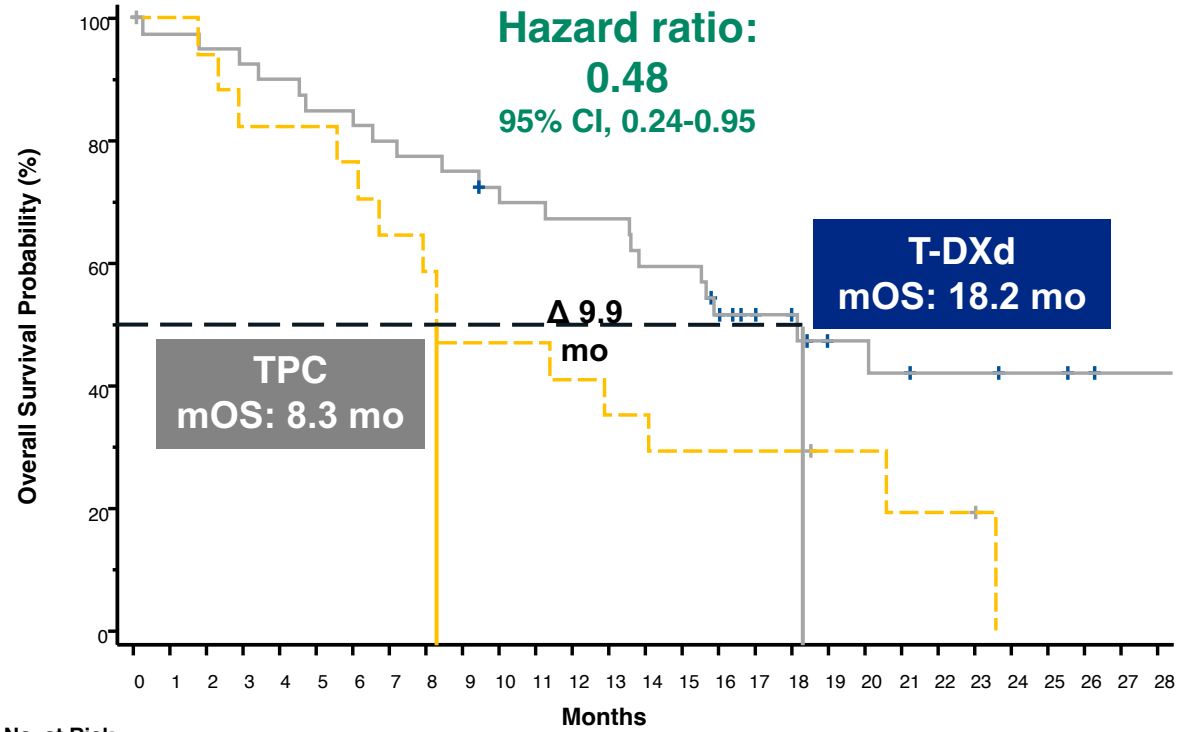
PFS



No. at Risk

T-DXd (n = 40):	40	39	33	29	28	25	21	20	19	18	13	13	11	11	10	8	7	5	5	4	4	4	4	3	1	0
TPC (n = 18):	18	17	11	7	6	4	3	3	2	2	2	2	2	2	1	1	1	1	1	1	0					

OS



No. at Risk

T-DXd (n = 40):	40	39	38	37	36	34	34	32	31	30	28	27	26	26	23	23	19	14	13	9	9	8	7	7	6	6	5	4	4
TPC (n = 18):	18	17	16	14	14	14	3	11	10	8	8	8	7	6	6	5	5	5	5	3	3	2	2	2	0				

HR: hormone receptor; mOS: median overall survival; mPFS: median progression-free survival; OS: overall survival; PFS: progression-free survival; T-DXd: trastuzumab deruxtecan; TPC: treatment of physician's choice.
For efficacy in the hormone receptor–negative cohort, hormone receptor status is based on data from the electronic data capture corrected for misstratification.

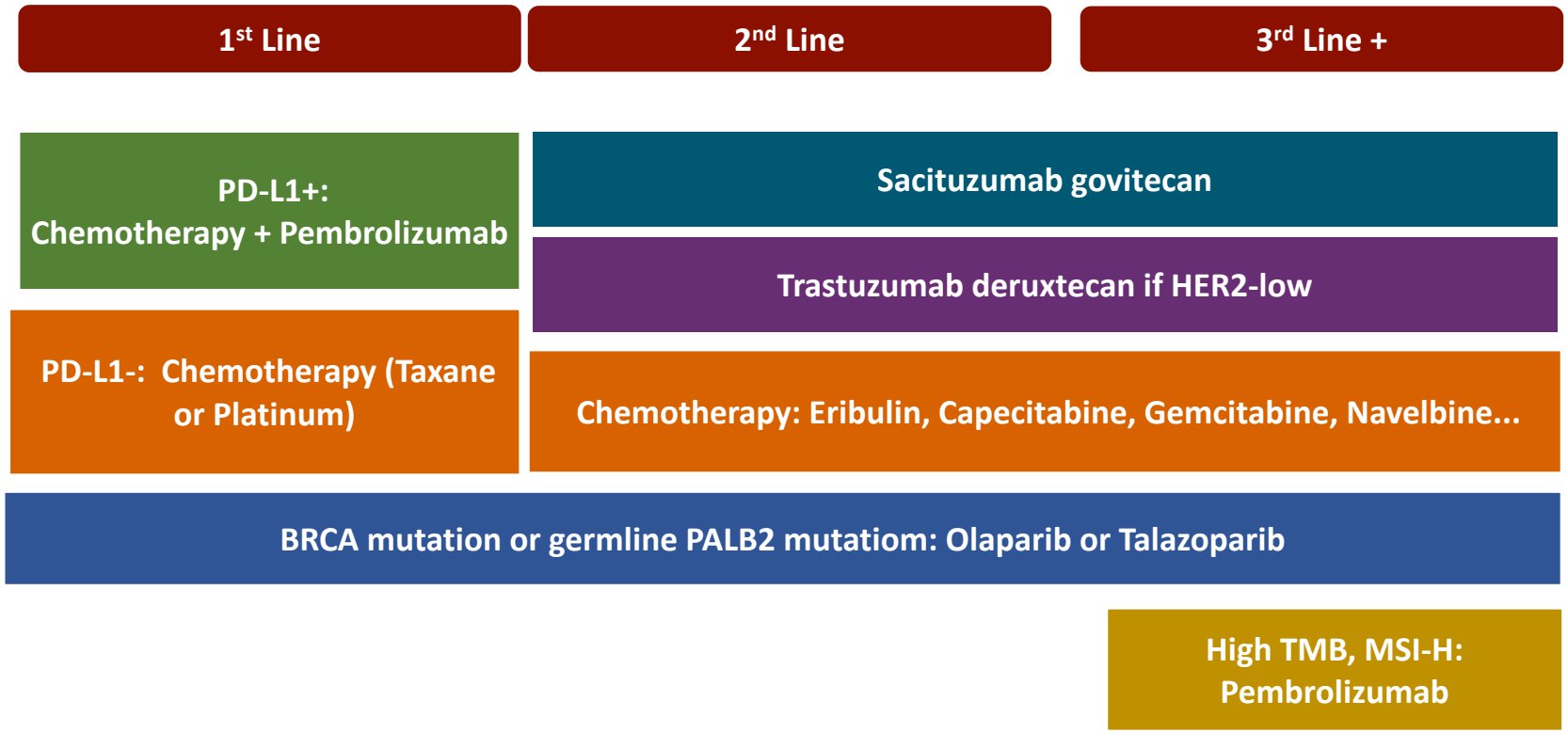
ASCENT vs DESTINY-Breast04 mTNBC Subset: efficacy overview

- Sacituzumab has demonstrated efficacy in the ITT population of patients with mTNBC in a dedicated phase 3 study regardless of HER2- status[1,3]
- T-DXd has shown preliminary efficacy data in a small subset of patients with mTNBC in an exploratory analysis of 58 patients[2]
- Due of differences in patient populations, direct comparisons between any of the study endpoints cannot be made

	ASCENT	DESTINY-Breast04
Population size	Patients with mTNBC: N=529[1] Of patients with centrally assessed HER2 status[3] HER2-IHC 0 = 70% (293/416), 149 treated with SG HER2-low = 30% (123/416), 63 treated with SG	Patients with mTNBC (n=58; 40 treated with T-DXd); subset of study population of patients with HER2-low disease (N=557)[2]
Statistical considerations	Efficacy in patients with mTNBC is the primary endpoint of the study[1]	Efficacy in patients with mTNBC is an exploratory endpoint[4]
Efficacy	Statistically significant and clinically meaningful improvements in PFS, OS, and ORR with SG versus TPC regardless of HER2-negative subtype[3]	Numerical improvements in PFS,[2] OS,[2] and ORR[2] with T-DXd versus TPC
Implications for mTNBC treatment	SG has demonstrated efficacy in all mTNBC patients including those with HER2-low and those with HER2-IHC 0 disease[3]	T-DXd has demonstrated efficacy only in patients with HER2-low[2]

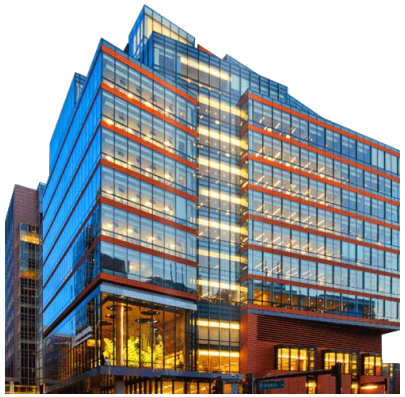
1. Bardia A, et al. *N Engl J Med* 2021
2. Modi S, et al. 2022;
3. Hurvitz SA, et al. ES*N Engl J Med* MO Breast 2022
4. Modi S, et al. ASCO 2022

Approach to metastatic TNBC



Conclusions: early stage TNBC

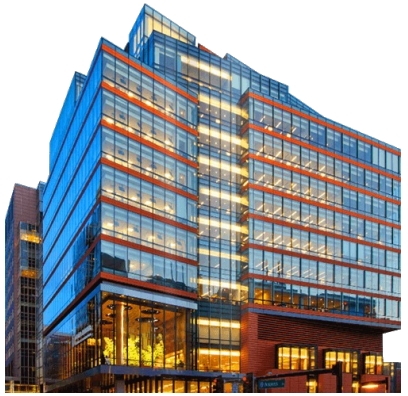
- TNBC has a higher risk of recurrence and poorer prognosis than other breast cancer subtypes
- Neoadjuvant checkpoint inhibition with chemotherapy is standard of care for stage 2 and 3 TNBC
- Given potential long-term toxicities, need to develop biomarker predictors of benefit to help to identify patients who can avoid checkpoint inhibitors and be treated with chemotherapy alone
- For residual disease, adding capecitabine or olaparib improves outcomes



Dana-Farber
Cancer Institute

Conclusions: metastatic TNBC

- Biomarker information is needed to determine therapy recommendations in TNBC: PDL1, BRCA and PALB2 mutations, HER2-low, Tumor Mutation Burden/MSI
- First-line therapy with chemotherapy + pembrolizumab is standard of care for PDL1+ mTNBC
- ADCs currently are the standard of care for second-line therapy
  - TNBC with HER2-low: slight preference for sacituzumab govitecan over trastuzumab deruxtecan given robust phase 3 data



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ADC: Antibody Drug Conjugate