Breast Cancer Tumor Board Cases 2024

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24th Multidisciplinary Management of Cancers: A Case-based Approach

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24th Multidisciplinary Management of Cancers: A Case-based Approach

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Disclosures

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Case 1:

- A 64-year-old woman presents after finding a lump in her left breast
- She reports no family history of cancer
- Diagnostic mammogram and ultrasound reveals 5.6 x 3.2 cm mass and 1.1 cm suspicious axillary lymph node
- Both undergo ultrasound-guided core biopsy:
  -Breast mass: grade 2 invasive ductal carcinoma, ER+ (3+, 90%), PR+ (2+, 50%), HER2 IHC 1+ (FISH negative)
  -LN: no malignant cells visualized

Case 1:

What additional breast imaging would you recommend?

A. None

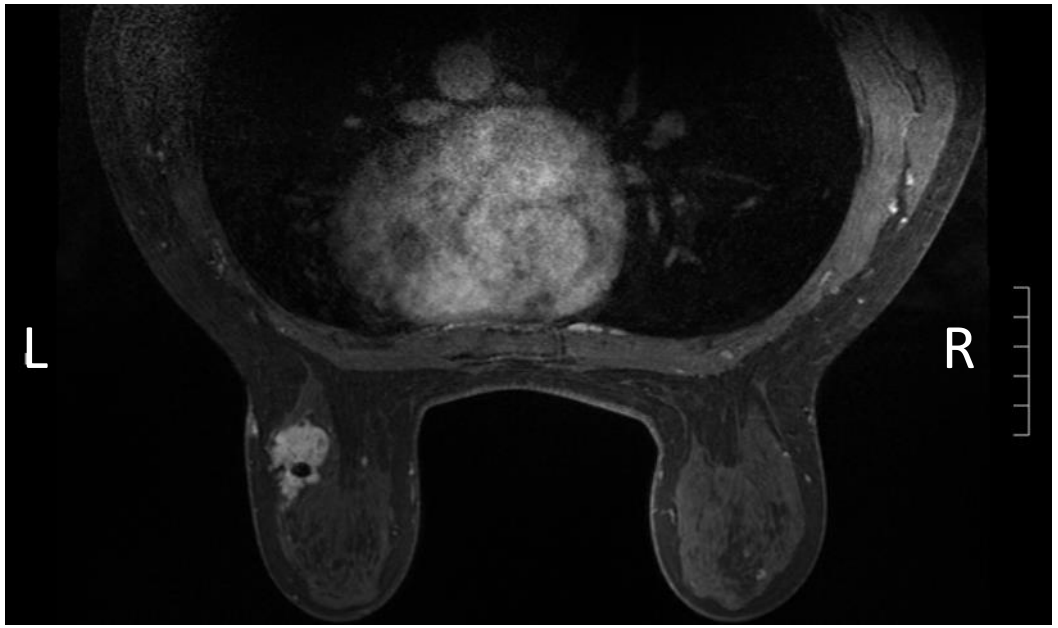
B. Breast MRI

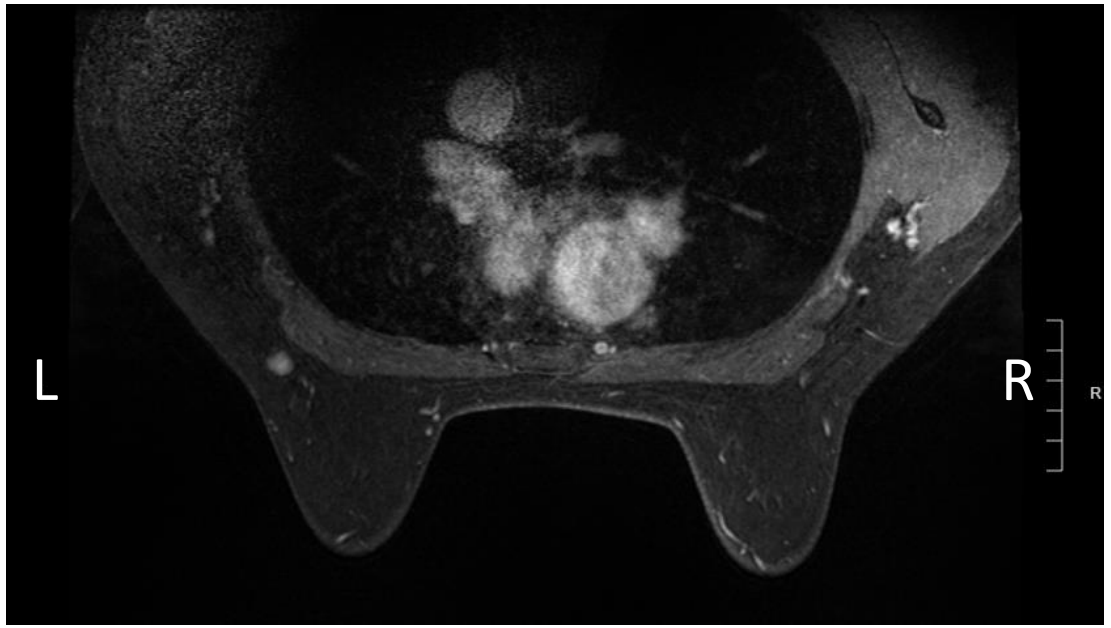
C. Axillary ultrasound

D. Breast MRI and axillary ultrasound

Case 1:

- Breast MRI is obtained showing no further suspicious areas
- A PET/CT is also obtained showing no areas of metastatic involvement





Case 1:

Would you refer this patient for genetic counseling?

A. Yes

B. No

Case 1:

ASCO Special Articles

Germline Testing in Patients With Breast Cancer: ASCO–Society of Surgical Oncology Guideline

Isabelle Bedrosian, MD[1]; Mark R. Somerfield, PhD[2]; Maria Isabel Achatz, MD, PhD[3]; Judy C. Boughey, MD[4]; Giuseppe Curigliano, MD, PhD[5,6]; Sue Friedman, DVM[7]; Wendy K. Kohlmann, MS[8]; Allison W. Kurian, MD, MSc[9]; Christine Laronga, MD[10]; Filipa Lynce, MD[11]; Barbara S. Norquist, MD[12]; Jennifer K. Plichta, MD, MS[13]; Patricia Rodriguez, MD[14]; Payal D. Shah, MD[15]; Marc Tischkowitz, MD, PhD[16]; Marie Wood, MD[17]; Siddhartha Yadav, MD[4]; Katherine Yao, MD[18]; and Mark E. Robson, MD[19]

Journal of Clinical Oncology (2024): JCO-23.

- All patients newly diagnosed with breast cancer with stage I-III or de novo stage IV/metastatic disease who are 65 years or younger at diagnosis should be offered BRCA1/2 testing

- Also to select patients >65 years based on personal history, family history, ancestry, or eligibility for poly(ADP-ribose) polymerase (PARP) inhibitor therapy

Case 1:

- Genetic testing reveals no pathologic mutations
- After being offered neoadjuvant therapy, the patient ultimately decides to proceed with surgery upfront
- She undergoes left breast simple mastectomy with SLNB
- Pathology:
  -7.4 cm of grade 3 IDC with lymphovascular space invasion.
  -0/7 LN, pT3pN0
  -ER-positive (3+, 91-100%), PR-positive (2+, 11-20%), HER2-negative by IHC 1+ (FISH ratio 1.05 with 2.68 HER2 copies/cell) with Ki67 30%.

Case 1:

What adjuvant chemotherapy would you recommend?

A. Taxotere and Cyclophosphamide (TC) x 4 cycles

B. Taxotere and Cyclophosphamide (TC) x 6 cycles

C. Doxorubicin, Cyclophosphamide and Paclitaxel (AC-T)

Long-Term Follow-Up of the Anthracyclines in Early Breast Cancer Trials (USOR 06-090, NSABP B-46-I/USOR 07132, and NSABP B-49 [NRG Oncology])

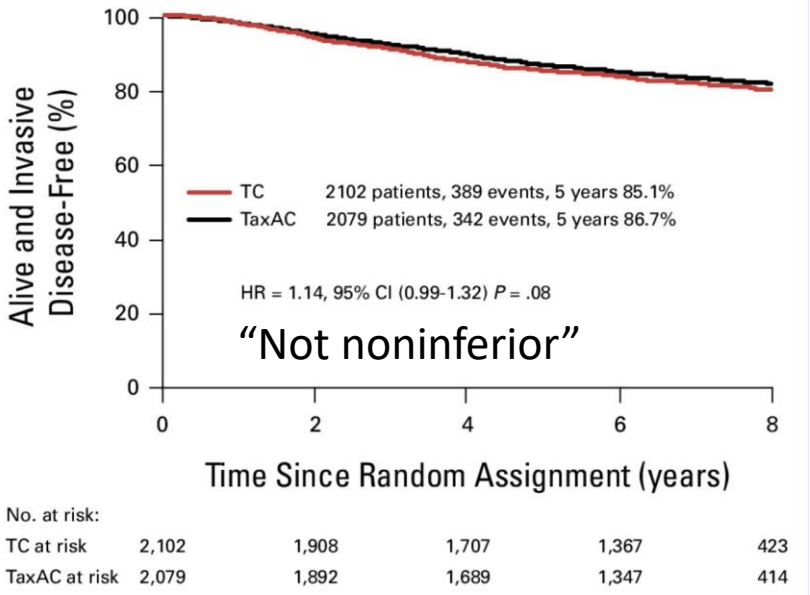
Charles E. Geyer Jr, MD[1,2]; Joanne L. Blum, MD, PhD[3]; Greg Yothers, PhD[4]; Lina Asmar, PhD[5]; Patrick J. Flynn, MD[6]; Nicholas J. Robert, MD[7]; Judith O. Hopkins, MD[8]; Joyce A. O'Shaughnessy, MD[9]; Priya Rastogi, MD[1,2,10]; Shannon L. Puhalla, MD[1,2]; Christie J. Hilton, DO[1,11]; Chau T. Dang, MD[12]; Henry Leonidas Gómez, MD, MSc, PhD[13]; Svetislava J. Vukelja, MD[14]; Alan P. Lyss, MD[15]; Devchand Paul, DO, PhD[5]; Adam M. Brufsky, MD, PhD[2,10]; Linda H. Colangelo, MS[4]; Sandra M. Swain, MD[1,16]; Eleftherios P. Mamounas, MD[1,17]; and Norman Wolmark, MD[1,2]

DOI https://doi.org/10.1200/JCO.23.01428

Median follow-up: 3.3 → 6.9 years

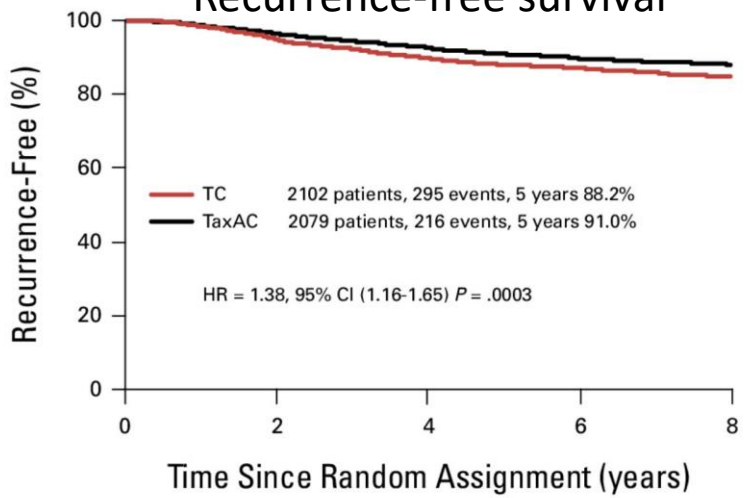
Original report(Blum et al 2017 *JCO*): IDFS HR 1.23, crossing threshold (1.18) for inferiority of TC compared to TaxAC

IDFS (primary)



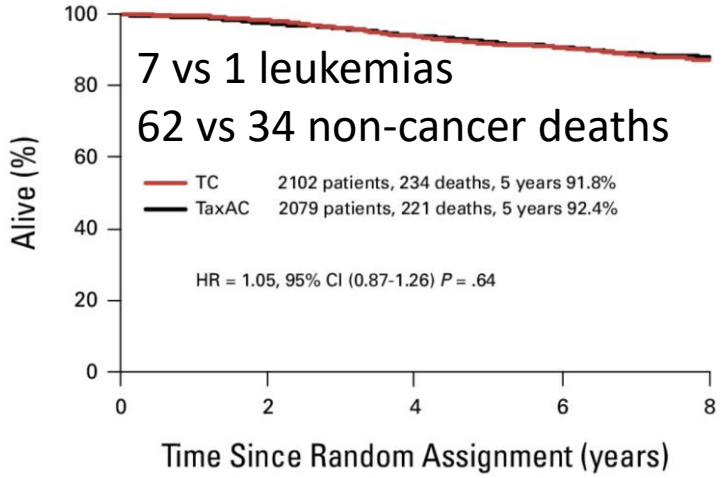
No. at risk:					
TC at risk	2,102	1,908	1,707	1,367	423
TaxAC at risk	2,079	1,892	1,689	1,347	414

Recurrence-free survival



No. at risk:					
TC at risk	2,102	1,919	1,729	1,398	430
TaxAC at risk	2,079	1,902	1,713	1,381	423

Overall survival



No. at risk:					
TC at risk	2,102	1,999	1,831	1,487	455
TaxAC at risk	2,079	1,945	1,770	1,444	436

Geyer et al 2024 *JCO*

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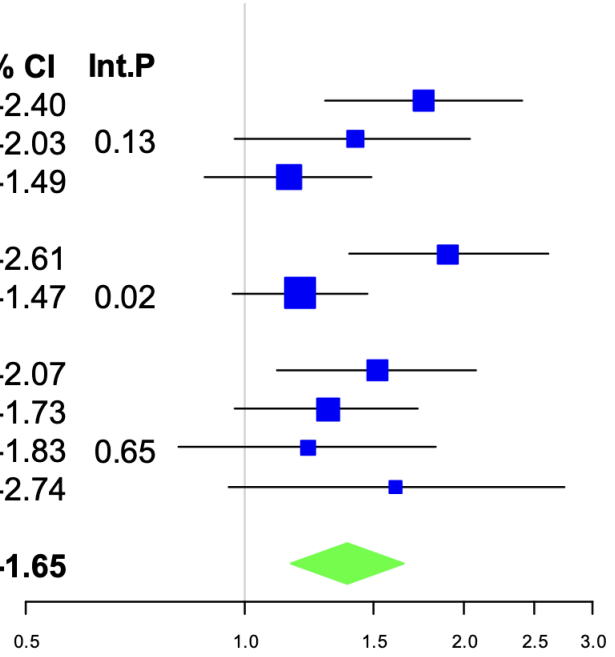
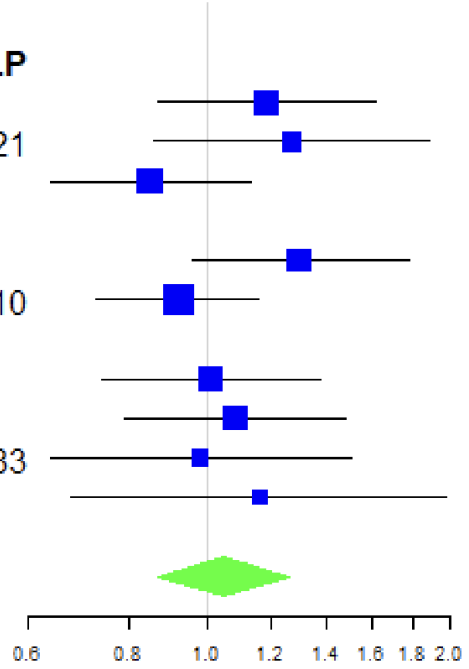
Recurrence-free survival

Protocol	Evnts (TaxAC)	Evnts (TC)	HR	95% CI	Int.P
USOR06090	61	111	1.76	1.29-2.40	
B-46/07132	50	68	1.40	0.97-2.03	0.13
B-49	105	116	1.15	0.88-1.49	
Hormone					
Neg	62	107	1.90	1.39-2.61	
Pos	154	188	1.19	0.96-1.47	0.02
Nodes+					
0	64	104	1.52	1.11-2.07	
1-3	84	105	1.30	0.97-1.73	
4-9	43	53	1.22	0.81-1.83	0.65
10+	25	33	1.61	0.95-2.74	
Overall	**216**	**295**	**1.38**	**1.16-1.65**	



Overall survival

Protocol	Evnts (TaxAC)	Evnts (TC)	HR	95% CI	Int.P
USOR06090	71	89	1.18	0.87-1.62	
B-46/07132	45	58	1.27	0.86-1.88	0.21
B-49	105	87	0.85	0.64-1.13	
Hormone					
Neg	75	94	1.30	0.96-1.77	
Pos	146	140	0.92	0.73-1.16	0.10
Nodes+					
0	76	84	1.01	0.74-1.38	
1-3	77	80	1.08	0.79-1.48	
4-9	41	42	0.98	0.64-1.51	0.83
10+	27	28	1.16	0.68-1.97	
Overall	**221**	**234**	**1.05**	**0.87-1.26**	



What proportion of these patients with ER+ tumors would we treat with chemotherapy at all today?

Postmenopausal node-positive regardless of OncotypeDX

T2N0 regardless of OncotypeDX

T1cN0 grade 3 regardless of OncotypeDX

Geyer et al 2024 *JCO*

Case 1:

- She subsequently decides to undergoes adjuvant AC-T chemotherapy

Case 1:

What do you recommend for post-mastectomy radiotherapy?

A. No adjuvant radiotherapy

B. Chest wall radiotherapy

C. Chest wall radiotherapy including axillary nodal fields but not internal mammary nodes

D. Chest wall radiotherapy with comprehensive (including internal mammary) lymph node coverage

Case 1:

- She undergoes Post Mastectomy Radiation Therapy (PMRT) and is started on anastrozole
- She returns to clinic to discuss further adjuvant therapies

Case 1:

Would you recommend an adjuvant CDK 4/6 inhibitor?
(Recall: node-negative; 7.4 cm of grade 3 disease with LVI and Ki67 30%)

A. No

B. Yes, abemaciclib

C. Yes, ribociclib

Case 1:

AJCC Anatomical Staging[1]	TN (M0)	NATALEE[2,3]	monarchE[4]
Stage IIA	T0N1	✓	Only if grade 3 or Ki-67 ≥20%
	T1N1	✓	Only if grade 3 or Ki-67 ≥20%
	T2N0	Only if G3 or G2 with Ki-67 ≥20% or high genomic risk[a]	✗
Stage IIB	T2N1	✓	Only if grade 3 or Ki-67 ≥20%
	T3N0	✓	✗
Stage IIIA	T0N2	✓	✓
	T1N2	✓	✓
	T2N2	✓	✓
	T3N1	✓	✓
	T3N2	✓	✓
Stage IIIB	T4N0	✓	✗
	T4N1	✓	Only if tumor size ≥5 cm or grade 3 or Ki-67 ≥20%
	T4N2	✓	✓
Stage IIIC	Any TN3	✓	✓

In monarchE, relatively few patients with stage II were allowed:
- N1 allowed only if grade 3 or Ki-67 ≥20%

In monarchE, within stage III,
- N0 not allowed (in IIIB)
- N1 (whether in IIIA or IIIB) allowed only if tumor size ≥5 cm, grade 3, or Ki-67 ≥20%

- NATALEE included N0 patients vs. monarchE

Slamon DJ et al. Ther Adv Med Oncol. 2023 May 29;15:17588359231178125.

Case 1: Take Home Points

- Guidelines for offering genetic testing to patients diagnosed with breast cancer vary widely, but there is a shift toward more testing.

- We should offer adjuvant CDK4/6 inhibitor to patients with high-risk ER-positive breast cancer. But how high risk?
  - Consensus re: patients meeting criteria for the monarchE study (N2 disease, or N1 with at least one of T3+, grade 3, or Ki67 at least 20%)
  - With NATALEE – maybe also the higher risk patients meeting that trial's eligibility?

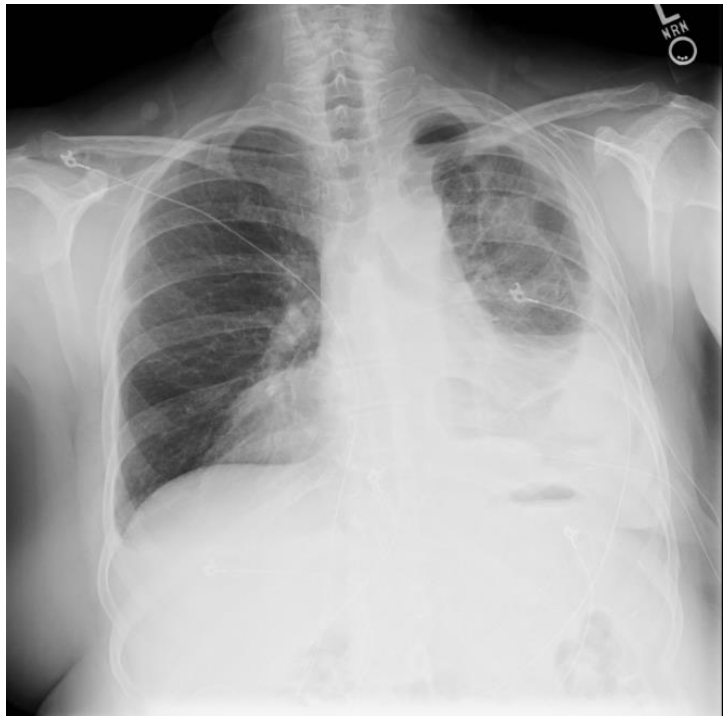
Case 2:

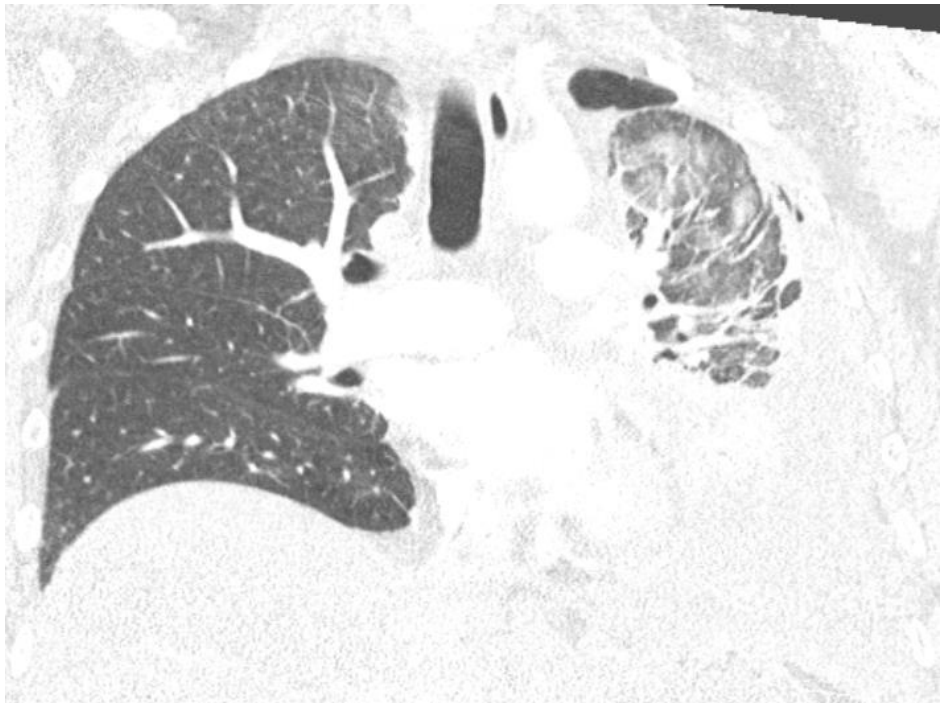
- 53-year-old postmenopausal woman with recurrent metastatic ER+/HER2- breast cancer. Her treatment course has been as follows:

  - **March 2011**: Initially presented with a mass on the left breast
  - **April 2011**: Biopsy showed ER-positive (> 95%, 3+), PR-positive (> 80%, 2+), HER2-negative (IHC 2+, FISH negative) grade 2 IDC
  - **December 2011**: Completed neoadjuvant chemotherapy with AC-T
  - **January 2012**: Bilateral mastectomy with left SLNB (1/3 micromet), pathology showing multifocal IDC, largest focus measuring 4.5 cm, grade 2, ypT2N1
  - **March 2012**: Completed PMRT
  - **April 2017**: Completed 5 years total of tamoxifen

Case 2:

July 2019: Presented to the emergency department with shortness of breath and found to have large left pleural effusion

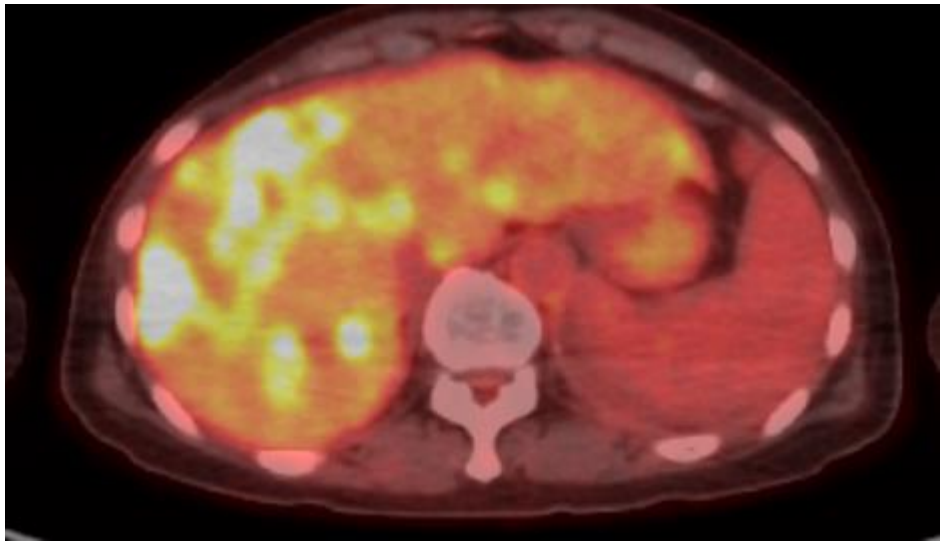




Case 2:

Hospital Work-Up:

- Thoracentesis cytology: Positive for malignant cells, consistent with metastatic breast carcinoma
- Biopsy with pathology of left parietal pleura: Metastatic adenocarcinoma – consistent with breast primary, ER-positive (> 95%, 3+), PR-positive (30%, 3+), HER2-negative (IHC 2+, 4.72 HER2 copies/cell and ratio 1.64)
- Labs: AST 271, ALT 237, AlkP 184 and total bilirubin of 1.2
- PET/CT CAP: Extensive liver involvement



Case 2:

What would you treat this patient with first?

A. Combination chemotherapy (e.g. docetaxel + cyclophosphamide; carboplatin + gemcitabine)

B. Single-agent chemotherapy (e.g. weekly paclitaxel; capecitabine)

C. Trastuzumab deruxtecan

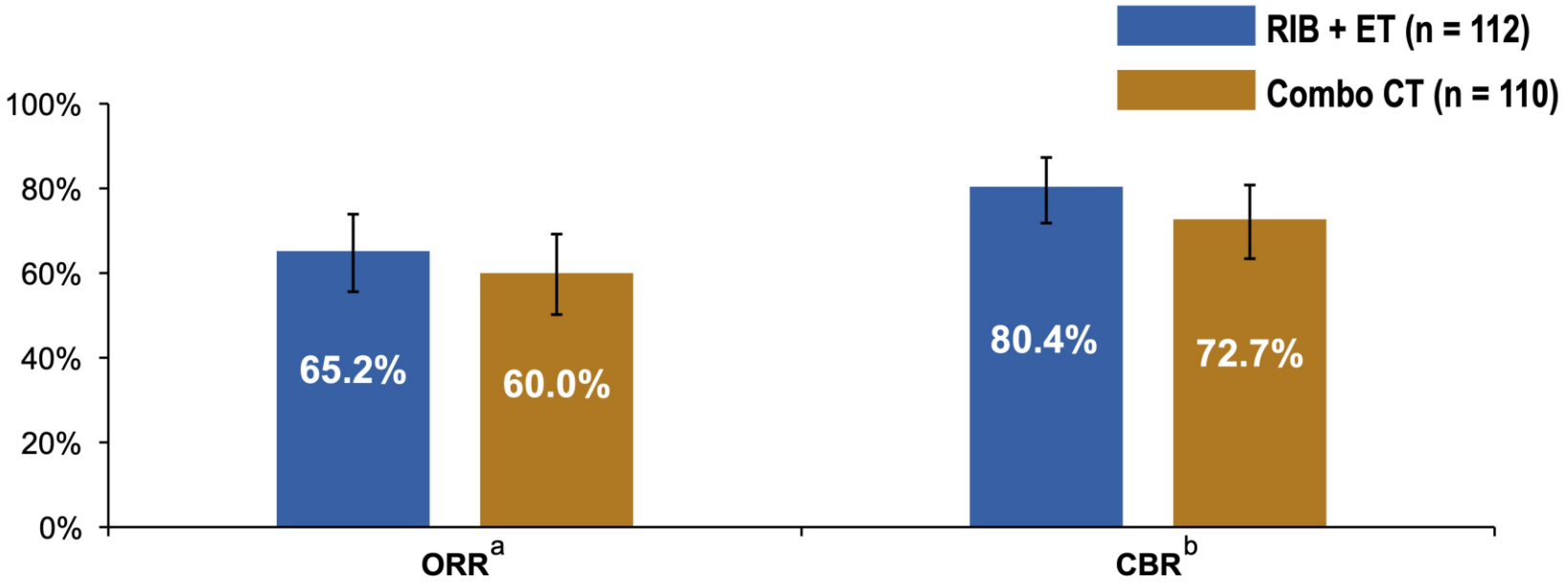
D. Aromatase inhibitor + CDK4/6 inhibitor

E. Other therapy not listed

Case 2:

San Antonio Breast Cancer Symposium®, December 6-10, 2022

ORR and CBR were similar between RIB + ET and combination CT



- A sensitivity analysis[c] confirmed the ORR and CBR findings in the safety set

CBR, clinical benefit rate; Combo CT, combination chemotherapy; CR, complete response; ET, endocrine therapy; ORR, overall response rate; PD, progressive disease; PR, partial response, RIB, ribociclib; SD, stable disease.
[a] Proportion of patients with CR or PR without confirmation (confirmation imaging was not mandatory according to study protocol); [b] Proportion of patients with CR or PR without confirmation or SD or non-CR/non-PD ≥24 weeks; [c] This analysis included all patients who received ≥1 dose of any component of the study treatment (safety set).

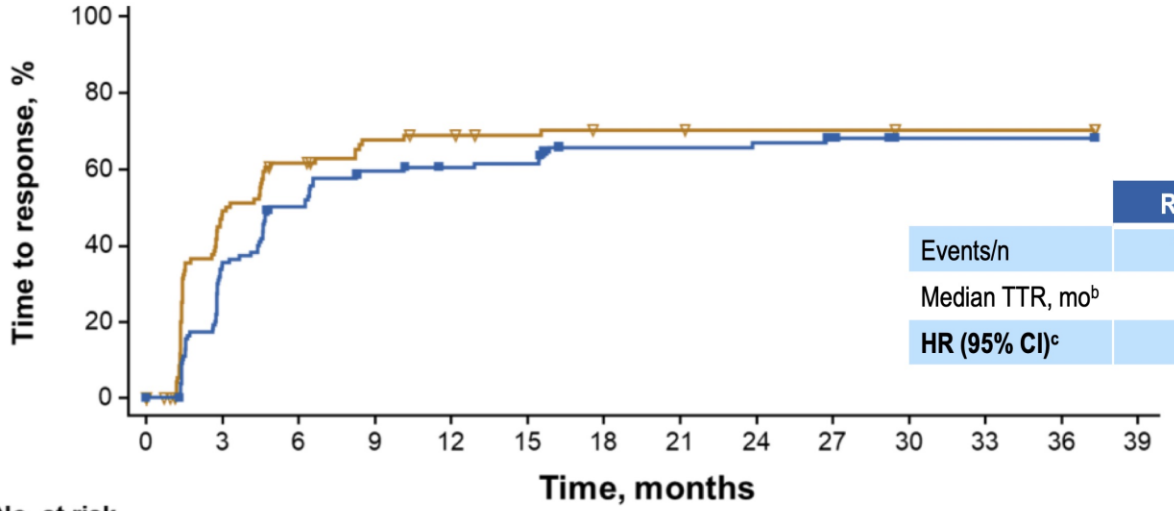
Ribociclib (RIB), Endocrine Therapy (ET), CT (chemotherapy)

Yen-Shen Lu. SABCS 2022 Abstract GS1-10.

Case 2:

San Antonio Breast Cancer Symposium®, December 6-10, 2022

Time to onset of response (TTR) for RIB + ET was similar to combination CT



	RIB + ET	Combo CT
Events/n	73/112	66/110[a]
Median TTR, mo[b]	4.9	3.2
HR (95% CI)[c]	**0.78 (0.56-1.09)**	

- A sensitivity analysis[d] confirmed the TTR findings in the safety set

Combo CT, combination chemotherapy; CR, complete response, ET, endocrine therapy; HR, hazard ratio; IRT, interactive response technology; PR, partial response; RIB, ribociclib.
[a] Ten patients in CT arm did not receive any treatment; [b] TTR is defined as the time from the date of randomization to the first documented response of either CR or PR without confirmation (confirmation imaging was not required according to study protocol); [c] HR is obtained from Cox Proportional-Hazards model stratified by liver metastasis and disease-free interval per IRT; [d] The sensitivity analysis excluded the 10 patients in the CT arm who did not receive any treatment and were removed from the denominator for the CT arm.

Yen-Shen Lu. SABCS 2022 Abstract GS1-10.

Case 2:

- She starts palbociclib + anastrozole
- PET/CT after 2.5 years shows progression in the liver (stable disease in the lung)

Case 2:

What type of tumor sequencing might you recommend for this patient?

A. Tumor sequencing of the pleural metastasis from her recurrence

B. Liquid biopsy now

C. Re-biopsy of a liver metastasis now with tumor sequencing

Case 2:

- She undergoes a liver biopsy and tumor sequencing:
  - TMB 11 Muts/Mb, ESR1 mutation (Y537C), CCND1/FGF3 amplification, FGFR1/ZNF703 amplification, MYC amplification, and PIK3CA (H1047R) mutation

Case 2: What would you treat this patient with next?

A. Fulvestrant + alpelisib

B. Fulvestrant + capivasertib

C. Fulvestrant + ribociclib

D. Fulvestrant + everolimus

E. Elacestrant

F. Capecitabine

G. Capecitabine + pembrolizumab

H. Trastuzumab deruxtecan

Case 2:

Once you suspect endocrine therapy-refractory disease, what would be your first recommended therapy (if no clinical trial available)?

A. Capecitabine

B. IV single-agent chemotherapy (taxane, eribulin, liposomal doxorubicin)?

C. Trastuzumab deruxtecan (assuming HER2 low)

D. Sacituzumab govitecan

Case 2: Take Home Points

- We have many options for targeted therapies in patients with metastatic ER+/HER2- breast cancer after progression on endocrine therapy in combination with CDK4/6 inhibitor therapy. How to optimally sequence these is not entirely clear.

Case 3:

- 49-year-old woman discovered to have a right-sided breast mass on screening mammogram
- Diagnostic mammogram with ultrasound and breast MRI confirm breast mass (size ranging from 1.6 cm on ultrasound to 1.9 cm on MRI) and no evidence of axillary involvement
- Ultrasound-guided biopsy demonstrates a pleomorphic invasive lobular carcinoma: grade 3, ER negative (<1%), PR negative (<1%), HER2 1+ (negative FISH), Ki67: 70%
- Genetic testing reveals no pathologic mutations

Case 3:

What do you recommend first?

A. Neoadjuvant chemotherapy

B. Upfront surgery

Case 3:

What neoadjuvant regimen would you recommend?

A. Carboplatin+paclitaxel and doxorubicin+cyclophosphamide with pembrolizumab (KEYNOTE-522)

B. Dose-dense AC (Doxorubicin/cyclophosphamide) followed by paclitaxel (AC-T), with pembrolizumab

C. AC-T

D. Docetaxel and carboplatin x 6 cycles with pembrolizumab

E. Docetaxel and carboplatin x 6 cycles

F. Something else

Case 3:

- She decides to undergo upfront right mastectomy with sentinel lymph node biopsy
- Pathology reveals a 4.3 cm area of involvement with 4/15 involved axillary lymph nodes
- Grade 3, ER negative (<1%), PR negative (<1%), HER2 1+ (negative FISH), Ki67: 60%
- Stage: pT2N2a

Case 3:

What adjuvant chemotherapy regimen do you recommend?

A. Doxorubicin/cyclophosphamide with paclitaxel (AC-T)

B. Carboplatin + paclitaxel and doxorubicin + cyclophosphamide with pembrolizumab (KEYNOTE-522)

C. AC-T + pembrolizumab

D. Something else

Case 3:

Alexandra/IMpassion030 phase 3 open-label study design

San Antonio Breast Cancer Symposium®
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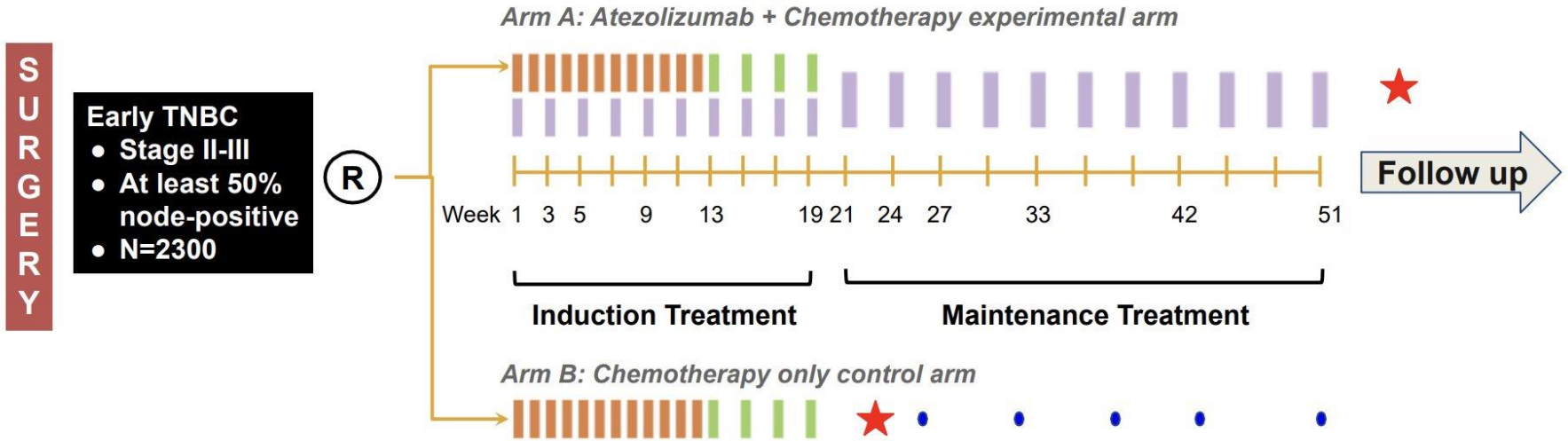

Stratification factors:

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)

Ignatiadis. SABCS 2023. Abstract GS01-03.

Case 3:

Primary efficacy endpoint: iDFS[a] (ITT population)

San Antonio Breast Cancer Symposium®
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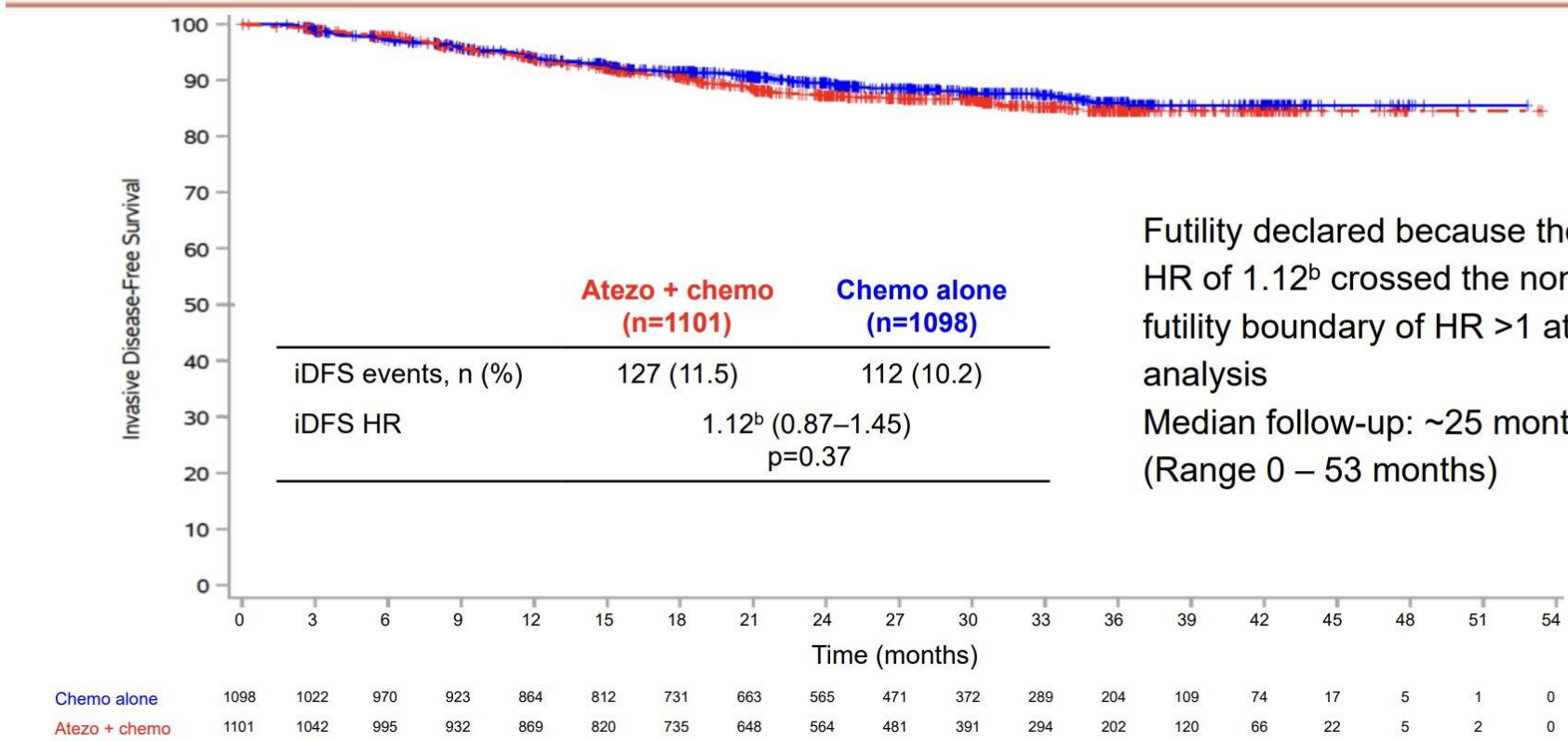


	Atezo + chemo (n=1101)	Chemo alone (n=1098)
iDFS events, n (%)	127 (11.5)	112 (10.2)
iDFS HR	1.12[b] (0.87–1.45) p=0.37	

Futility declared because the observed HR of 1.12[b] crossed the non-binding futility boundary of HR >1 at this interim analysis

Median follow-up: ~25 months (Range 0 – 53 months)

[a]Defined as the interval from randomization until date of first occurrence of an iDFS event, [b]stratified by PD-L1 status, Surgery, and Axillary Nodal Status

Ignatiadis. SABCS 2023. Abstract GS01-03.

Case 3:

- She completes adjuvant AC-T + pembrolizumab
- 8 months after completion she develops new cough with evidence of several new pulmonary nodules
- Biopsy of a lung nodule shows: ER negative (<1%), PR negative (<1%), HER2 IHC 1+ (negative FISH), CPS 15

Case 3:

What would you treat this patient with

A. Carboplatin+gemcitabine

B. Carboplatin+gemcitabine+pembrolizumab

C. Sacituzumab govitecan

D. Trastuzumab deruxtecan

Case 3:

She was subsequently started on Sacituzumab govitecan with a partial response, and which she currently remains on

Case 3:

Take home points:

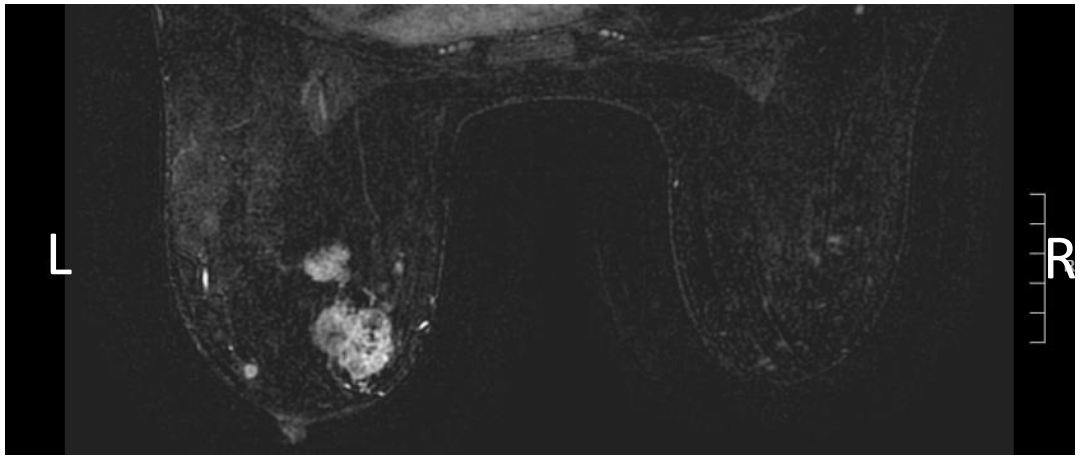
- It is not clear that immunotherapy is beneficial in the adjuvant setting; more data are coming (e.g. SWOG 1418)

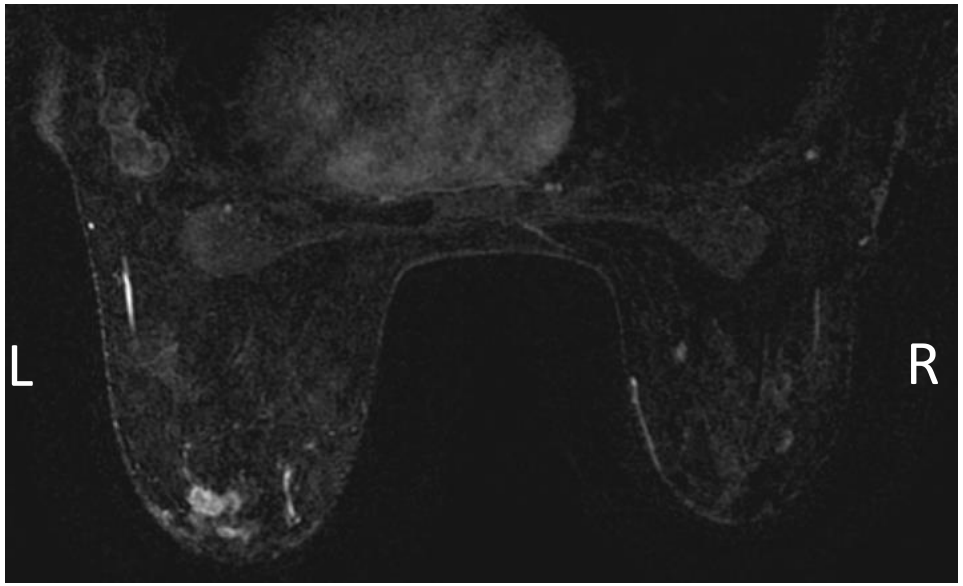
Case 4:

- 43-year-old premenopausal woman presented with palpable left breast mass

- MRI shows a large conglomerate of masses in the left inner breast measuring up to 3.1 cm; additional masses in the left upper breast measuring 1.8 and 1.7 cm, and multiple satellite lesions throughout the upper and central breast. There is also bulky axillary adenopathy, measuring 3.1 cm, and a suspicious 8 mm internal mammary node.

- PET/CT shows no evidence of distant metastasis





Case 4:

- She undergoes left breast and axillary ultrasound guided biopsy
- Pathology: ER+ (3+, 91-100%), PR (2+, 31-40%), HER2 3+, Ki67: 30-40%. Biopsied node is involved.
- She completes six cycles of neoadjuvant docetaxel, carboplatin, trastuzumab, and pertuzumab (TCHP)
- Follow-up MRI shows 1.5 cm area of enhancement in the lower inner breast and 1 cm mass in the upper inner breast, and resolved axillary lymphadenopathy

Case 4:

Would you offer lumpectomy?

A. Yes

B. No

Case 4:

What would you recommend for axillary surgery?

A. Sentinel lymph node biopsy

B. Axillary node dissection

C. Sentinel lymph node biopsy with plan to proceed with axillary lymph node dissection if at least 1 lymph node involved

D. Sentinel lymph node biopsy with plan to proceed with axillary lymph node dissection if a larger number of lymph nodes is involved

Case 4:

- She undergoes left breast mastectomy with ALND
- Residual disease present: 15mm x 14mm in the breast with 0/12 lymph nodes positive
- Stage: yp T1c N0
- IHC: ER+ (3+, 91-100%), PR- (<1%), HER2 3+

Case 4:

What do you recommend for post-mastectomy radiotherapy?

A. No adjuvant radiotherapy

B. Chest wall radiotherapy

C. Chest wall radiotherapy including nodal fields but not internal mammary nodes

D. Chest wall radiotherapy with comprehensive (including internal mammary) lymph node coverage

NRG Oncology/NSABP B-51/RTOG 1304: Study Design

- Randomized, open-label phase III trial

Stratified by type of surgery (mastectomy vs lumpectomy), HR status (+/-), HER2 status (+/-), adjuvant chemotherapy (Y/N), and breast pCR status (Y/N)

Patients with clinical T1-3, N1, M0 breast cancer; axillary LN+ by FNA or core needle biopsy; completed ≥8 wk of neoadjuvant chemotherapy (+ anti-HER2 therapy if HER2+); ypN0 by SLNB (≥2 nodes excised), ALND, or both after neoadjuvant chemotherapy; mastectomy or lumpectomy (N = 1641)

No regional nodal irradiation (n = 821)
Breast radiation if breast-conserving surgery
No chest wall radiation if mastectomy

Regional nodal irradiation (n = 820)
Breast radiation if breast-conserving surgery
Chest wall radiation if mastectomy

- Should patients who turn lymph node negative after NAT be treated with or without regional nodal irradiation?

Mamounas. SABCS 2023. Abstr GS02-07.

NRG Oncology/NSABP B-51/RTOG 1304: Efficacy

Parameter	No RNI (n = 784)	RNI (n = 772)	HR (95% CI)	*P* Value
IBCRFI events, n	59	50	0.88 (0.60-1.29)	.51
▪ 5-yr estimate of IBCRFI, %	91.8	92.7		
Isolated LRRFI events, %	11*	4†	0.37 (0.12-1.16)	.088
▪ 5-yr estimate of LRRFI, %	98.4	99.3		
DRFI events, n	48	46	1.00 (0.67-1.51)	.99
▪ 5-yr estimate of DRFI, %	93.4	93.4		
DFS events, n	83	85	1.06 (0.79-1.44)	.69
▪ 5-yr estimate of DFS, %	88.5	88.3		
	(n = 802)	(n = 800)	HR (95% CI)	*P* Value
OS events, n	45	49	1.12 (0.75-1.68)	.59
▪ 5-yr estimate of OS, %	94.0	93.6		

- No difference in outcome between groups suggests that downstaging cancer-positive regional lymph nodes with neoadjuvant chemotherapy can allow some patients to skip adjuvant regional nodal irradiation

Mamounas. SABCS 2023. Abstr GS02-07.

Case 4:

She is started on ovarian function supression + aromatase inhibitor and completes 14 cycles of adjuvant T-DM1.

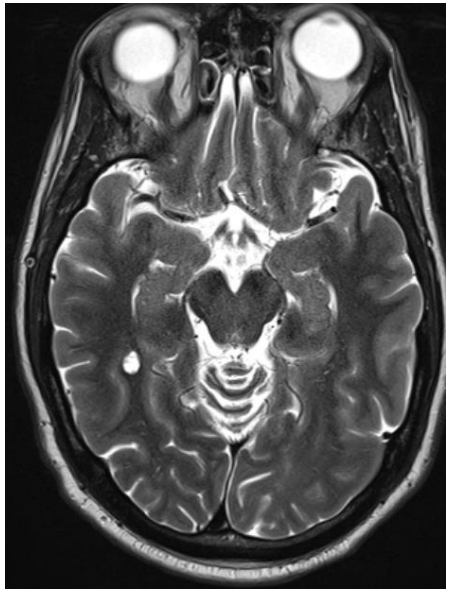
Would you recommend adjuvant neratinib?

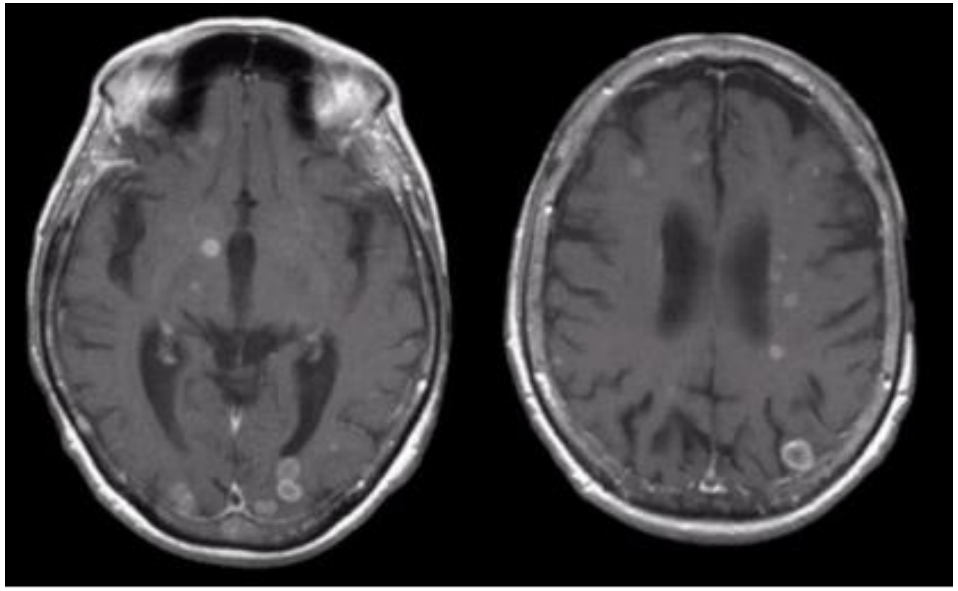
A. Yes

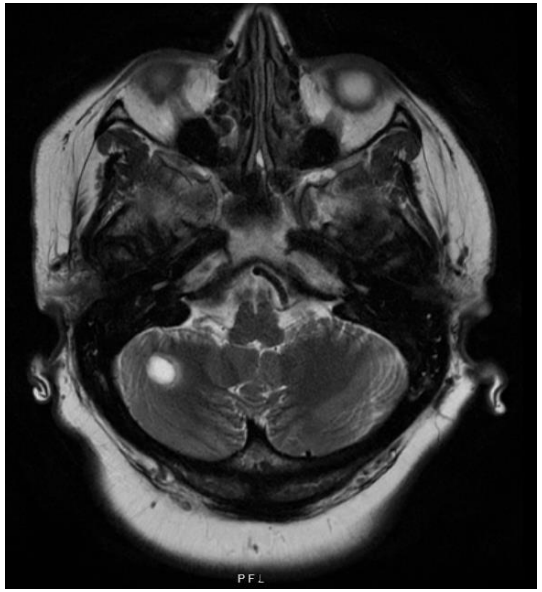
B. No

Case 4:

- She does not take neratinib
- After two years, while continuing on OFS + aromatase inhibitor, she reports new onset of headaches
- MRI is obtained below showing images below







Case 4:

- A PET/CT is obtained showing several areas of bone metastasis and multiple lung nodules
- A biopsy of a right lung nodule is performed showing metastatic breast cancer
  - ER+ (3+, 81-90%), PR+ (2+, 41-50%), HER2 3+, Ki67: 50%

Case 4:

What would you recommend for first-line therapy?

A. Cleopatra regimen (docetaxel, trastuzumab, pertuzumab)

B. HER2-CLIMB regimen (capecitabine, tucatinib, trastuzumab)

C. Trastuzumab deruxtecan

Case 4:

How would you treat her CNS metastatic disease assuming she has 15 lesions?

A. Systemic therapy alone (if medical oncologist selects something with known CNS penetration)

B. Whole brain radiotherapy

C. Serial stereotactic radiosurgery

Case 4:

- Her brain metastases are treated with Stereotactic Radiosurgery
- She is started on docetaxel + trastuzumab + pertuzumab, and continues on trastuzumab + pertuzumab after 8 cycles

Case 4:

Would you recommend the addition of endocrine therapy to HP maintenance?
Recall: disease recurred on OS/AI

A. No

B. Yes – an aromatase inhibitor

C. Yes – tamoxifen

D. Yes – would check for ESR1 mutation in liquid biopsy and add fulvestrant if positive

Case 4:

- After 8 months of therapy, she develops both lung and CNS progression
- CNS disease is again treated with Stereotactic Radiosurgery therapy

Case 4:

What would you recommend for next-line therapy?

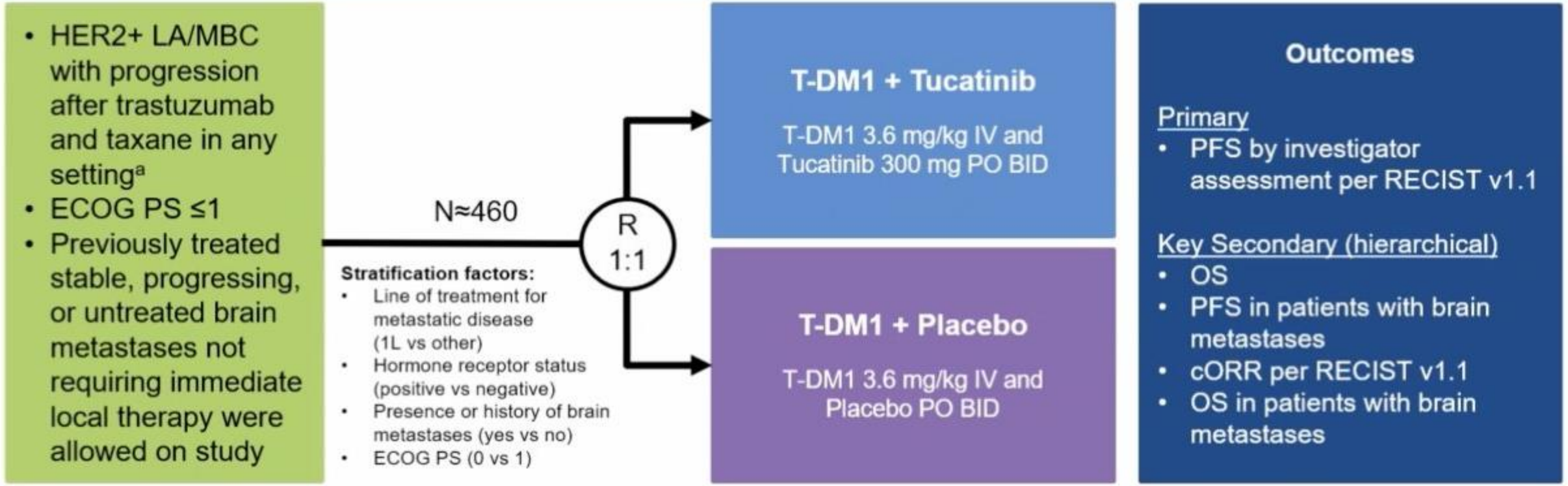
A. Trastuzumab deruxtecan

B. Tucatinib + trastuzumab + capecitabine (HER2CLIMB)

C. Trastuzumab emtansine (T-DM1) + tucatinib

San Antonio Breast Cancer Symposium®, December 5-9, 2023

HER2CLIMB-02 Study Design

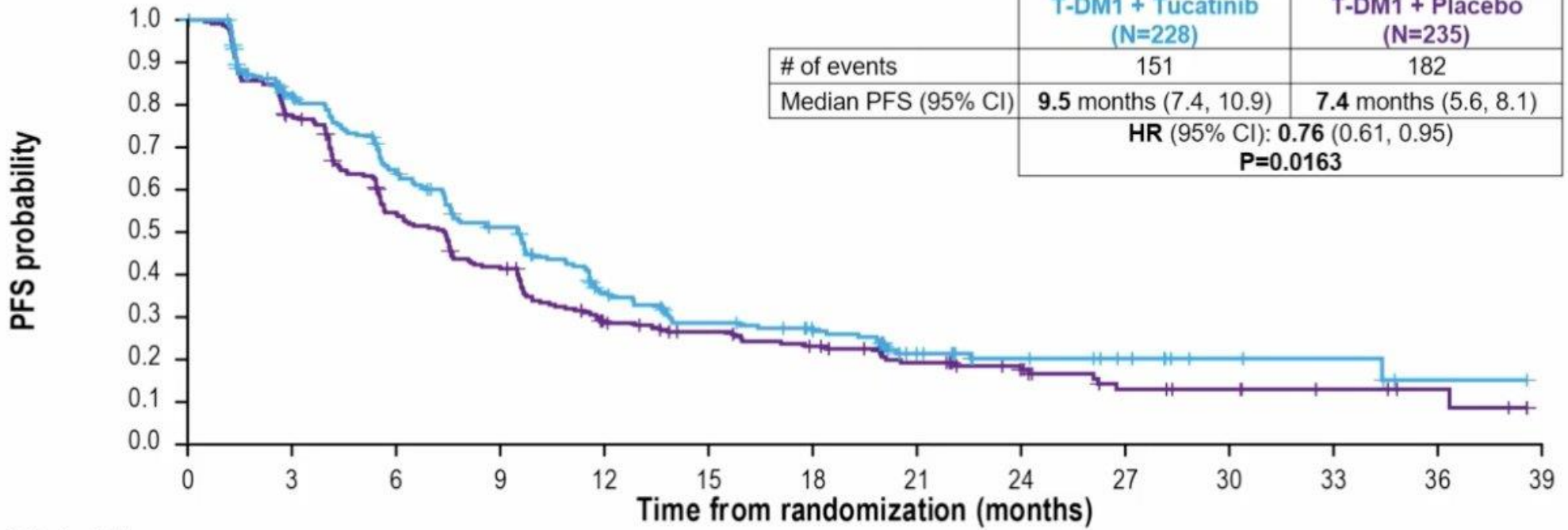


Survitz. SABCS 2023. Abstract GS01-10.

San Antonio Breast Cancer Symposium®, December 5-9, 2023

Progression-Free Survival

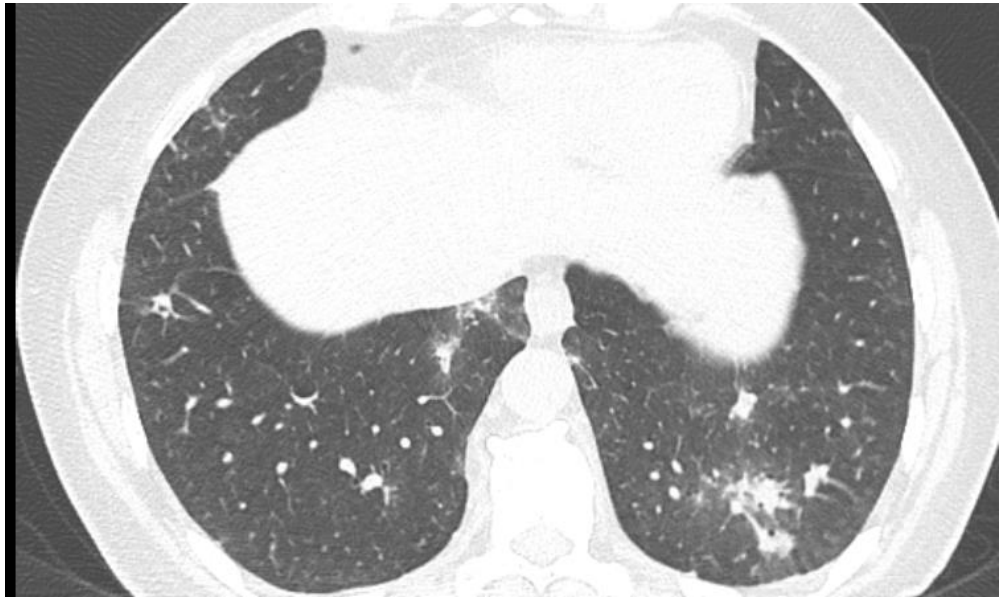
	T-DM1 + Tucatinib (N=228)	T-DM1 + Placebo (N=235)
# of events	151	182
Median PFS (95% CI)	**9.5** months (7.4, 10.9)	**7.4** months (5.6, 8.1)
	HR (95% CI): **0.76** (0.61, 0.95) **P=0.0163**	



Survitz. SABCS 2023. Abstract GS01-10.

Case 4:

- The patient is the placed on capecitabine + tucatinib + trastuzumab with progressive disease in the lung after approximately one year
- She starts trastuzumab deruxtecan with excellent response on follow-up CT at 9 weeks
- She gets COVID; symptoms are predominantly nasal congestion and fever and resolve quickly with paxlovid
- 3 weeks after her COVID symptoms resolve, she develops a slight cough. CT chest shows scattered new ground glass opacities.



Case 4:

You start her on prednisone. What do you do with the trastuzumab deruxtecan?

A. Permanently discontinue

B. Hold until cough resolves; re-start at a lower dose

C. Hold until cough and imaging findings (ground glass opacities) resolve; re-start at a lower dose

D. Dose reduce trastuzumab deruxtecan but continue with close monitoring

E. Something else

Case 4:

TABLE 1. T-DXd Prescribing Information and DESTINY-Breast03 and DESTINY-Breast04 Protocol-Recommended Dose Modifications for Pneumonitis/ILD[4,7,9]

Severity	Treatment	
Asymptomatic pneumonitis/ILD (grade 1)	Interrupt T-DXd until resolved to grade 0, then If resolved in 28 days or less from date of onset, maintain dose If resolved in >28 days from date of onset, reduce dose 1 level per the recommendations below However, if the grade 1 pneumonitis/ILD event occurs beyond cycle day 22 and has not resolved within 49 days from the last infusion, the drug should be discontinued Consider corticosteroid treatment (eg, ≥0.5 mg/kg/d prednisolone or equivalent) as soon as pneumonitis/ILD is suspected	
	Dose reduction schedule	Breast cancer
	Recommended starting dose	5.4 mg/kg
	First dose reduction	4.4 mg/kg
	Second dose reduction	3.2 mg/kg
	Requirement for further dose reduction	Discontinue treatment
Symptomatic pneumonitis/ILD (grade 2 or greater)	Permanently discontinue T-DXd Promptly initiate corticosteroid treatment (eg, ≥1 mg/kg/d prednisolone or equivalent and continue for ≥14 days, followed by gradual taper for ≥4 weeks) as soon as pneumonitis/ILD is suspected	

TABLE 2. Recommended Guidance for Toxicity Management of T-DXd–Induced Pneumonitis/ILD From the DESTINY-Breast03 and DESTINY-Breast04 Protocols[7,9]

Clinical Approach	Grade 1	Grade 2	Grades 3 and 4
Monitoring	Monitor and closely follow up in 2-7 days for onset of clinical symptoms and pulse oximetry	Monitor symptoms closely	Hospitalization required
Corticosteroid treatment	Consider starting systemic corticosteroids (eg, ≥0.5 mg/kg/d prednisone or equivalent) until improvement, followed by gradual taper over ≥4 weeks	Promptly start systemic corticosteroids (eg, ≥1 mg/kg/d prednisone or equivalent) for ≥14 days or until complete resolution of clinical and chest CT findings, followed by gradual taper over ≥4 weeks	Promptly initiate empiric high-dose methylprednisolone IV treatment (eg, 500-1,000 mg/d for 3 days), followed by ≥1 mg/kg/d of prednisone or equivalent for ≥14 days or until complete resolution of clinical and chest CT findings, followed by gradual taper over ≥4 weeks

JCO Oncol Pract 19:539-546

Case 4: Take Home Points

- Management of borderline or questionable grade 2 pneumonitis from trastuzumab deruxtecan is challenging and comes up a lot in clinical practice. Availability of other options and alternative explanations for symptoms and/or lung findings may factor into decision to attempt rechallenge. Pulmonology input is often crucial.

Case 5:

- 39-year-old premenopausal woman with 5.5 cm left breast mass discovered on screening mammogram and multiple involved axillary lymph nodes on ultrasound

- PET/CT: Hypermetabolic left axillary at levels I & II. Hypermetabolic internal mammary lymph nodes. No evidence of metastatic disease.

- Left breast and axillary core biopsy: Grade 3, IDC, ER-positive (3+, 90-100%), PR-positive (1+, 20-30%), HER2-negative (IHC 0, FISH not amplified), Ki67: 60%.

Case 5:

Neoadjuvant therapy is offered. What would you recommend?

A. Doxorubicin and cyclophosphamide followed by paclitaxel (ddAC-T)

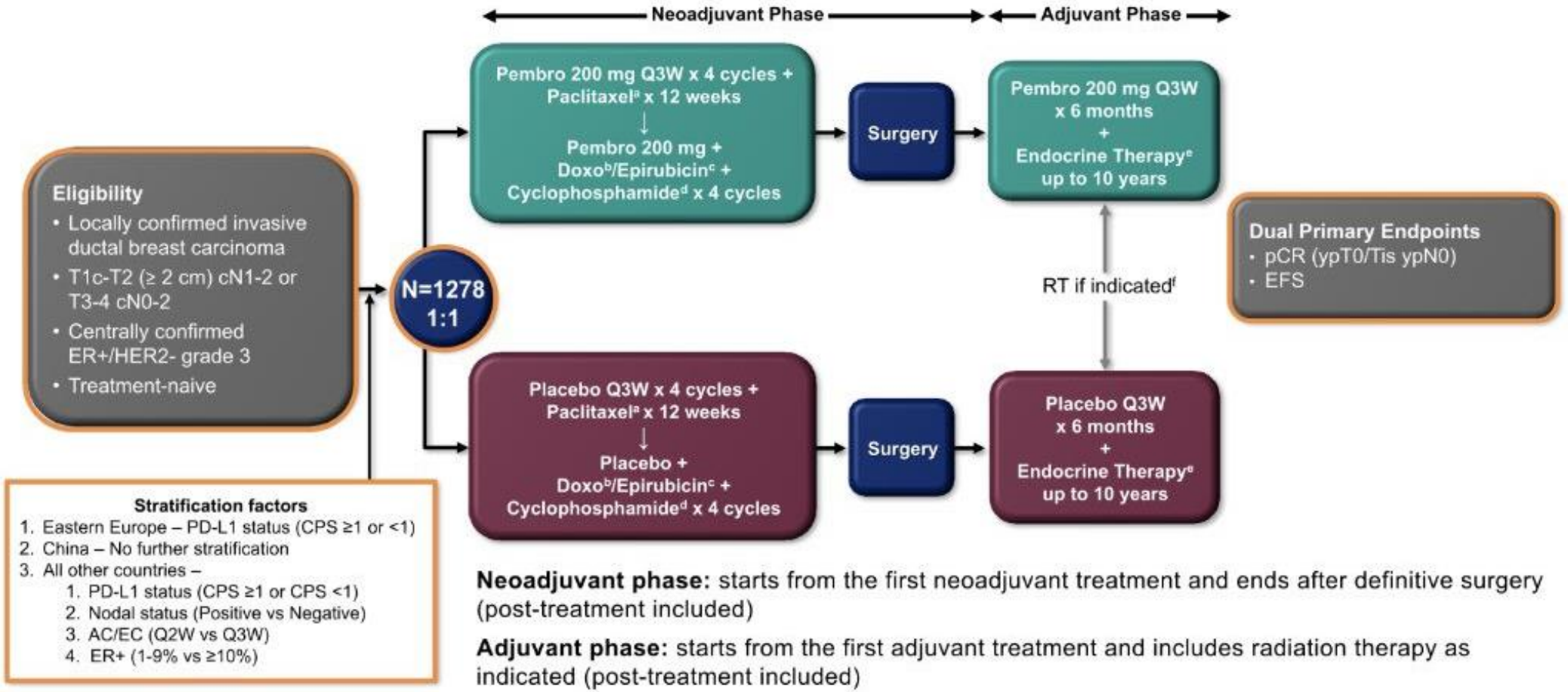
B. ddAC-T + pembrolizumab (Keynote-756)

C. TC x 6

D. Something else

Case 5:

KEYNOTE-756 Study Design (NCT03725059)



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

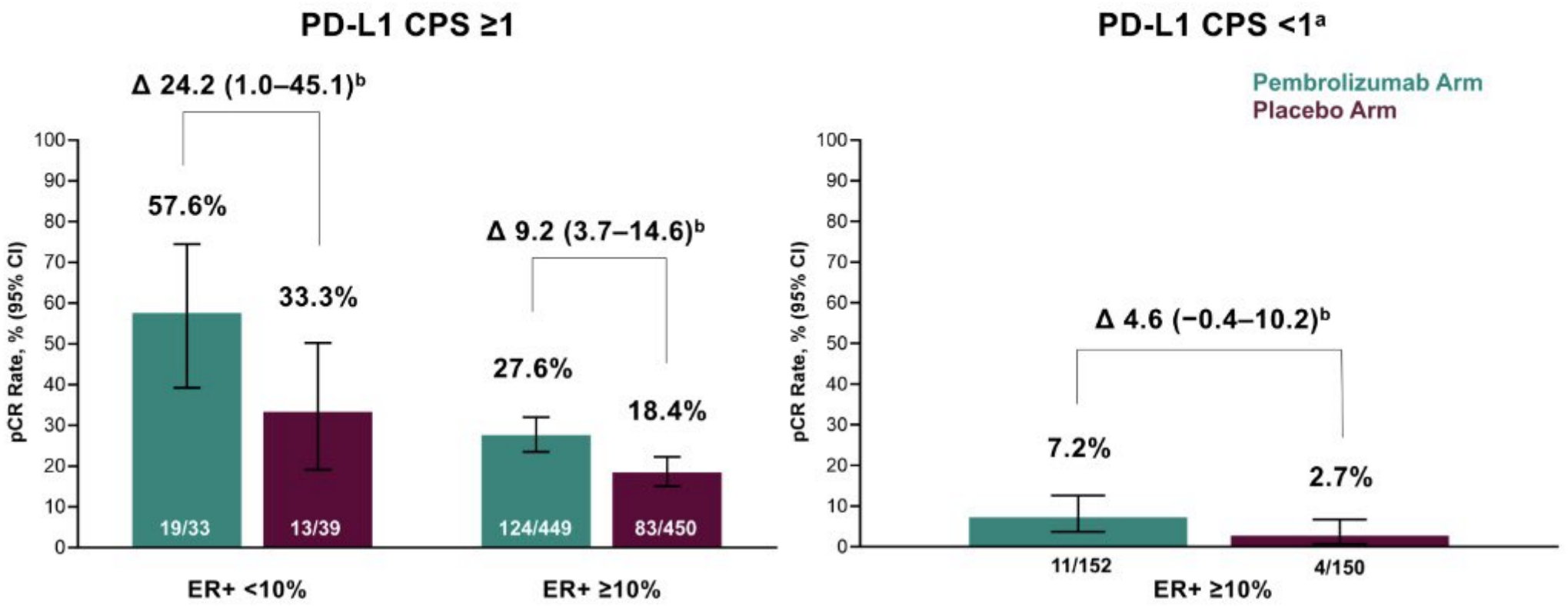
Adjuvant phase: starts from the first adjuvant treatment and includes radiation therapy as indicated (post-treatment included)

O'Shaughnessy. SABCS 2023. Abstract GS01-02.

Case 5:

San Antonio Breast Cancer Symposium®, December 5–9, 2023

Pathologic Complete Response at IA1 by ER Status and PD-L1 Expression



O'Shaughnessy. SABCS 2023. Abstract GS01-02.

Case 5:

- The patient completes neoadjuvant therapy with ddAC-T
- She undergoes bilateral mastectomy with left ALND with pathology demonstrating 2.2 cm of grade 3 residual disease and 4/12 positive LN, Grade 3, IDC, ER-positive (3+, >95%), PR-positive (3+, >95%), HER2-negative (IHC 0, FISH not amplified), Ki-67: 30%
- In consultation with cancer genetics it is discovered she harbors a pathologic germline mutation in *BRCA2*
- She starts ovarian suppression, aromatase inhibitor, and olaparib. After completion of 1 year of olaparib, she opts against ongoing targeted therapy with abemaciclib.

Case 5:

After completion of 5 years of ovarian suppression with aromatase inhibitor, what do you recommend?

A. Discontinue adjuvant endocrine therapy.

B. Stop OFS and, if she remains premenopausal, continue tamoxifen for an additional 5 years.

C. Continue OFS with aromatase inhibitor for an additional 2-5 years.

D. Check a Breast Cancer Index score and continue endocrine therapy past 5 years if H/I ratio is high.

E. Something else

Case 5: Take Home Points

- KEYNOTE-756 indicated pCR benefit for the addition of immunotherapy to neoadjuvant chemotherapy in grade 3 HR+/HER2- breast cancer. Many are awaiting EFS data before putting this into practice, but in the very high risk (especially if lower ER expression), some are considering.