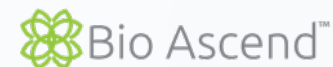


— 2nd Annual —

Atlanta Breast Cancer

CONFERENCE

September 19, 2026



Case Presentation: L.P.

Caroline Breit, Breast Surgical Oncology Fellow

Atlanta Breast Cancer Conference: Fellows Case Discussion

September 19, 2026

HPI

- **67F underwent screening mammogram 5/01/25, subsequent diagnostic mammogram and US 5/15/25 demonstrating 1.8cm heterogenous mass with indistinct margins in the right breast**
- **US-guided biopsy: Right invasive mammary carcinoma with lobular features, Grade 2, ER-/PR-/Her2- (TNBC), Ki-67 10-20%**
- **MRI 6/16/25: Enhancing mass with clip artifact at biopsy-proven site of malignancy, 2.7 x 1.8 x 2cm with additional clumped enhancement contiguous with index carcinoma, overall span 4.7cm**
- **cT1cN0M0 (Mammo) vs cT2N0M0 (MRI)**

Treatment

- **Treatment team favored upfront surgery over neoadjuvant treatment given Grade 1 tumor with lobular features with low Ki-67**
- **7/11/2025 Right Total Mastectomy, R SLNB, Left Prophylactic Total Mastectomy**
 - *Right Mastectomy:*
 - *Invasive mammary carcinoma, Grade 2*
 - *Tumor measures at least 25mm*
 - *LVI present*
 - *Margins free of tumor*
 - *Right Sentinel Lymph Node: Positive for carcinoma (2/2)*
 - *1 lymph node with largest tumor deposit measures 2mm*
 - *1 lymph node with micrometastasis*
 - *No evidence of extranodal invasion*

**Pathologic Stage
IIB (pT2N1aMx)**

- **Adjuvant Chemotherapy: Completed four cycles of TC (9/5/25-11/7/25)**
- **Adjuvant XRT: PMRT + RNI 42.56Gy in 16 fractions to chest wall and regional lymph nodes including IMN (completed 12/22/2025)**
- **CT A/P performed 5/13/2026 as routine follow up for adrenal adenoma**
 - **Multiple new lytic and sclerotic lesions throughout the osseus structures, concerning for osseus metastatic disease**
 - **Stable left adrenal adenoma (1.2cm)**
- **6/11/2026 Right Iliac Bone Biopsy**
 - **Metastatic carcinoma consistent with breast primary (ER-/PR-/HER2-)**
 - **PDL1 negative**
- **Datopotamab deruxtecan started 6/09/26**
- **Last follow up 9/01/26**

Discussion

- Neoadjuvant chemotherapy vs upfront surgery in early stage, clinically node negative, triple negative breast cancer
 - Candidate for KEYNOTE-522 regimen based on pre-operative MRI (T2N0)¹
 - Would response to NAC have impacted her adjuvant treatment regimen?
- Management of her axilla would have differed with NAC
 - ASCO/ASTRO guidelines support PMRT with RNI and omission of ALND in patients with cT1-3N0 invasive breast cancer undergoing mastectomy with 1-2 positive SLN²
 - In setting of NAC, cN0 patients with +SLN require ALND

— 2nd Annual —

Atlanta Breast Cancer

CONFERENCE

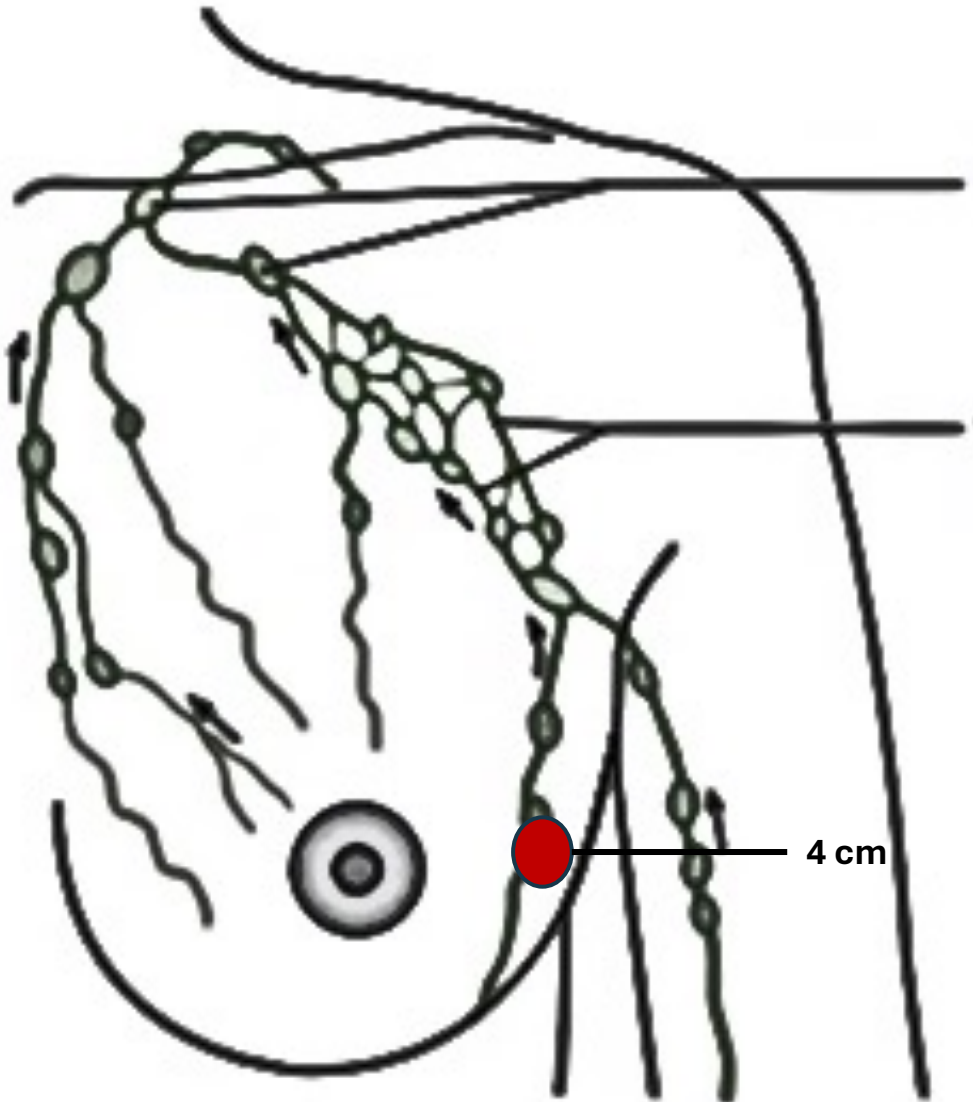
September 19, 2026

Node-Positive ER+/HER2- Breast Cancer in a Premenopausal Female

Hasiya Okorozo, MD, MPH

Oncology Clinical Fellow

Winship Cancer Institute of Emory



History

42-year-old premenopausal female who presented with a **6-week history of a self-palpated mass along the lateral aspect of her left breast.**

Significant family history of breast cancer;
prior genetic testing negative

Physical Exam

Palpable **left breast mass at 3 o'clock position, 4 cm from the NAC**, no palpable axillary lymphadenopathy

Imaging

- Diagnostic mammogram – ***focal asymmetry*** in the L breast at 3'0 clock position, dense breast tissue, BI-RADS 4 (suspicious for malignancy)
- Left Breast US: Ill-defined ***16 mm mass at the 3'0 clock position, 4 cm from NAC***, with benign-appearing axillary lymph nodes
- Bilateral breast MRI: ***18mm enhancing mass*** in the left lower quadrant, 4 cm from NAC, with indistinct margins. No other enhancing masses. In the left axilla, largest lymph node measures approximately 15 mm in maximal diameter and has a ***benign*** appearance. No other abnormalities in either breast or adenopathy.

Q1.

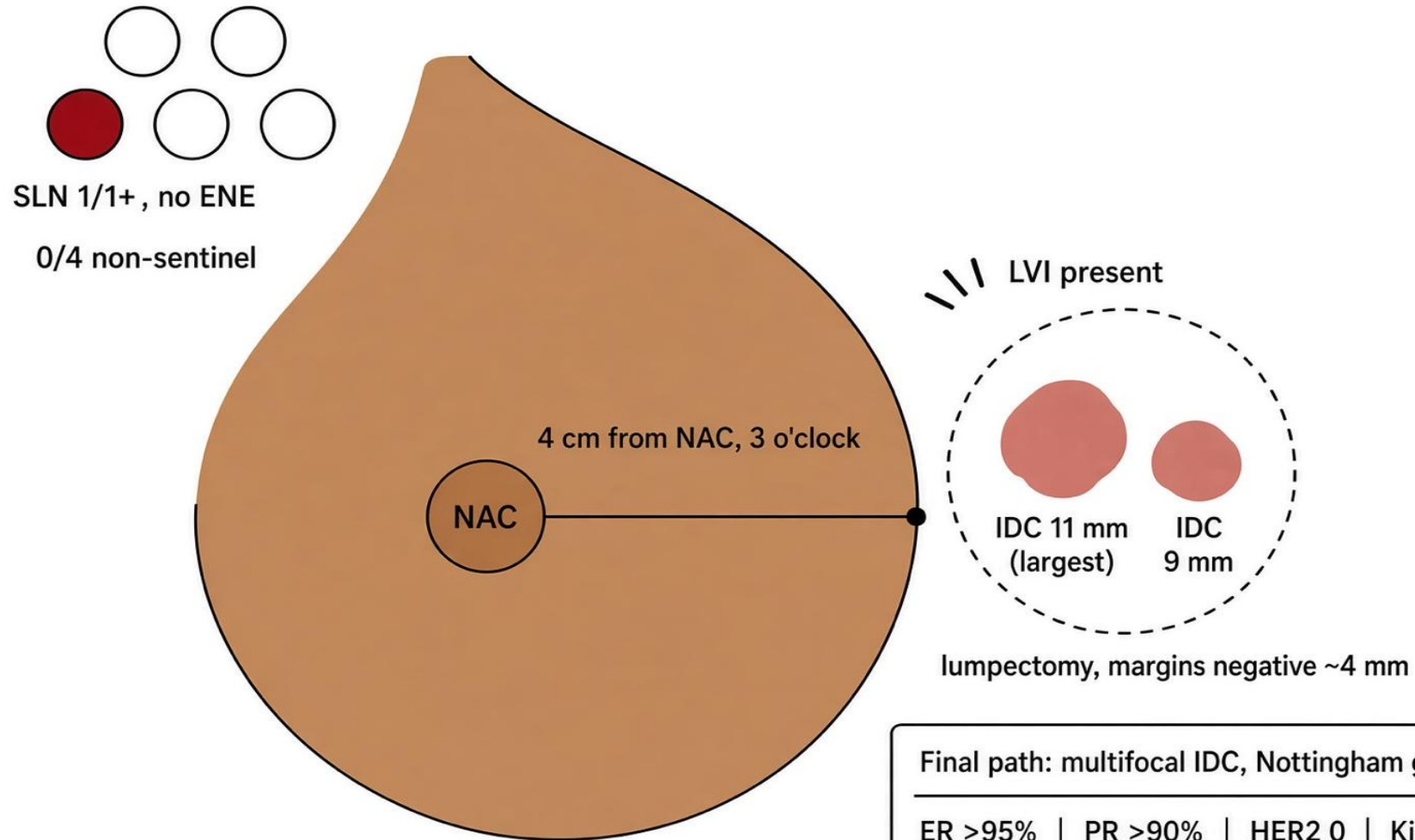
When would you consider/order a breast MRI, particularly in younger women?

Core Needle Biopsy

Path: Moderately diff.
Invasive ductal
adenocarcinoma (IDC),
Nottingham grade 2, ER
95%, PR 90%, HER2 0
(negative), Ki-67 18%.

Intermediate-grade DCIS

Lumpectomy + SLNB



Final path: multifocal IDC, Nottingham grade 2

ER >95% | PR >90% | HER2 0 | Ki-67 16%

Stage: pT1 N1 (IIA)

Clinical trials on Multigene assays in localized ER+/HER2- Breast cancer

The Genomic Trial Landscape

Trial	 Assay	 Nodal Status Allowed	 Menopausal Population	 Key Finding on Chemo Benefit
TAILORx	Oncotype DX (21-gene)	N0	Pre + Post	Endocrine therapy non-inferior overall; age ≤ 50 benefit from chemo at RS 16-25.
RxPONDER	Oncotype DX (21-gene)	1-3 nodes	Pre + Post	Postmenopausal: no chemo benefit. Premenopausal: chemo benefit likely OFS-mediated.
MINDACT	MammaPrint (70-gene)	Up to 3 nodes	Pre + Post	High clinical / low genomic risk: chemo omission safe.
OPTIMA	Prosigna (PAM50)	Up to 9 nodes (N1-N2)	Pre + Post (Ages ≥ 40)	Investigating if chemo omission is safe in higher-risk nodal involvement for low ROR (≤ 60).

Q2.

How are you implementing the Prosigna assay testing into your workflow in your institution? Who sends the test (oncology vs. surgery)?

Q3.

Have you had instances where you performed two different genomic assays? What was the rationale, and how did it influence your treatment decision?

Q4.

Are there any other assays your institution uses?
What is the discussion between surgery and
oncology? How do you decide who will send the
assay?

Patient Report

PATIENT

SPECIMEN INFORMATION

ORDERING CLINICIAN

CLINICAL AND PATHOLOGY INFORMATION

SPECIMEN

Surgical Resection

TUMOR SIZE

≤2 cm

LYMPH NODE STATUS

Node-positive

HORMONE RECEPTOR STATUS

ER+ / PR+

MENOPAUSAL STATUS

Pre-menopausal

PROSIGNA TEST RESULT

Risk of Recurrence
(ROR) Score^{1,2}

36

(Score ranges 0-100)

10-Year Probability of Distant
Recurrence (DR)^{1,2}

8%

With standard locoregional therapy
and 5 years of endocrine therapy

Predicted
Chemotherapy Benefit^{2,3}

No

Intrinsic Subtype

Luminal A

Prosigna Test Result Summary

A Risk of Recurrence (ROR) Score of 36 results in a 10-year Probability of Distant Recurrence of 8% and no Predicted Chemotherapy Benefit.

Prosigna Breast Risk of Recurrence Test Patient Report

REPORT STATUS: FINAL
PAGE: 2 of 3

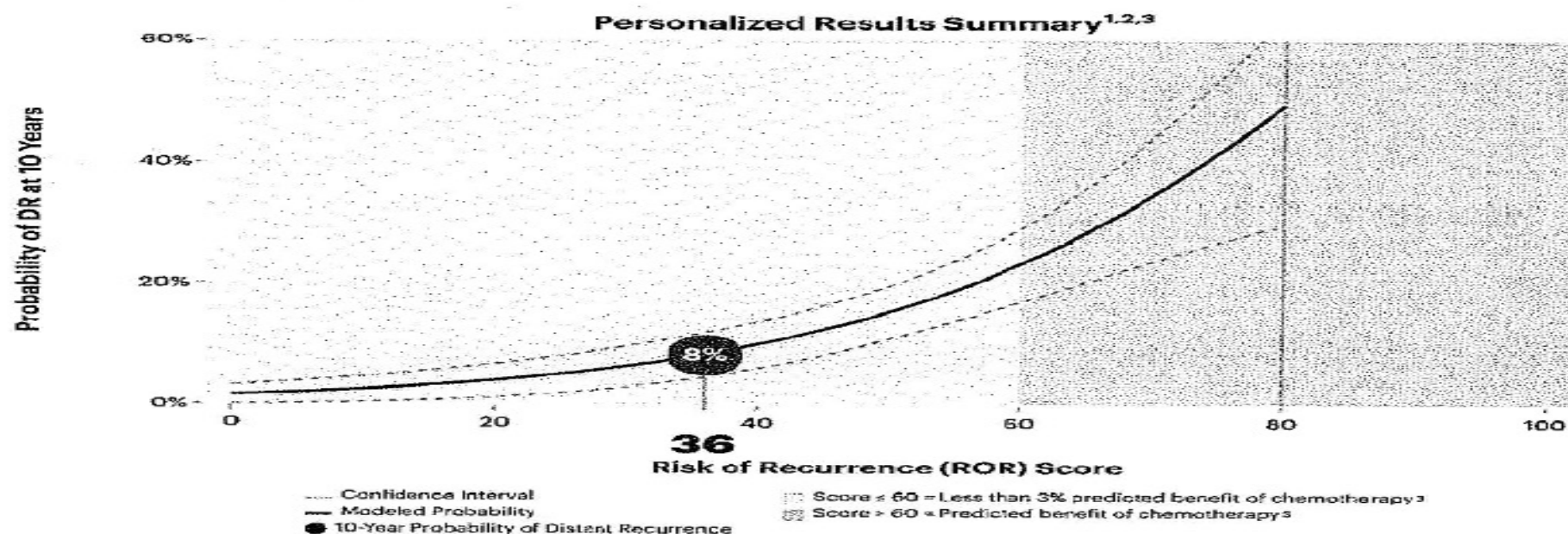
PATIENT

SPECIMEN INFORMATION

ORDERING CLINICIAN

ADDITIONAL CLINICAL EVIDENCE

Prognosis for node-positive breast cancer patients was determined based on the probability of distant recurrence (DR) for this patient population in the validation study ABCSG-8. This study analyzed 382 node-positive samples using a prospectively defined analysis plan. The data shown are for post-menopausal women with hormone receptor-positive, node-positive, stage II breast cancer that received 5 years of endocrine therapy.⁴



Prognostic Estimate

	ROR Score	Risk Estimate
Low	0-40	6% (3-12%)
High	41-100	24% (18-31%)

Risk category is provided to guide the interpretation of the ROR score using cutoffs related to clinical outcome for the provided lymph node status.

Proliferation Score: 40

Proliferation scores range from 0 (low proliferation) to 100 (high proliferation) and are calculated from a subset of 18 genes associated with proliferation.¹ Correspondence of Prosigna test proliferation score with histopathological proliferation score is not established. The proliferation score is only reported as a constituent component of the Prosigna[®] test.

Q5.

If this was N2 disease, does a low ROR in a patient with 4-9 positive nodes give you enough confidence to omit chemotherapy, or do clinical factors still override the assay in higher nodal burden?

Q6.

How should we translate the OPTIMA ≤ 60 de-escalation cutoff into practice given that commercial reports place N+ patients with ROR > 40 as high risk? Are we comfortable sparing chemotherapy in the 41-60 intermediate group?

Treatment Plan

Post-lumpectomy RT 5,000 cGy in 25 fractions (currently undergoing)

OFS initiated with plan for Letrozole post- RT completion

Targeted therapy – Planned integration of CDK4/6 inhibitors

Chemotherapy omitted

Q7.

As adjuvant CDK4/6i become standard for high-risk HR+ disease, how does a patient's genomic assay result influence your decision to add chemotherapy versus proceed to endocrine therapy plus a CDK4/6i as was done in this case?

Q8.

If this patient had a known N1 disease at presentation, how would that impact your decision on giving neoadjuvant versus adjuvant systemic therapy?

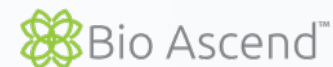
Thank you!

— 2nd Annual —

Atlanta Breast Cancer

CONFERENCE

September 19, 2026



Fellows Case Presentation

Atlanta Breast Conference

September 19, 2026

Sarah Keshwani

K.M.

51 year old female (post-menopausal) who presented for screening mammogram in April 2026.

Screening mammogram: calcifications medial right breast and architectural distortion

Diagnostic mammogram and US: mass at 10:00 and calcifications medial to this mass

Biopsy: LCIS in both mass and calcifications

Concordance: Mass-forming LCIS is discordant

K.M.

Surgery: Right breast seed guided partial mastectomy

Surgical pathology: Invasive lobular carcinoma (1.3cm), grade 1, ER+/PR-HER2-

Stage: pT1cNxM0

Treatment

- **Surg onc: SLNB omitted**
- **Med onc: Oncotype 12, no adjuvant chemotherapy, will receive adjuvant endocrine therapy (anastrozole)**
- **Rad onc: Adjuvant radiation treatment**

Discussion Points

Criteria for omission of SNLB

- **Emory criteria: age >60, no LVI, grade 1 or 2, cT1, ER+/HER2-**
- **ASCO guidelines: SLNB omission for age >50 and postmenopausal with negative findings on preop US, grade 1-2, <2cm HR+/HER2- invasive ductal cancer**
- **NCCN guidelines: same criteria as above can be considered for omission of SLNB, caution should be used in those with lobular histology**

Changes in practice with lobular histology

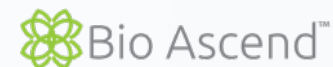
- **Scardina et al., 2026: Axillary Nodal Positivity in Early-Stage Invasive Lobular Carcinoma: Implications for Sentinel Lymph Node Biopsy Omission**
 - **20.2% of patients with early-stage clinically node negative ILC harbor occult axillary metastasis**
 - **Pathologic tumor size was the primary determinant of nodal involvement**
 - **Omission of SLNB in ILC may carry a risk of axillary understaging with potential therapeutic implications**

— 2nd Annual —

Atlanta Breast Cancer

CONFERENCE

September 19, 2026





Neoadjuvant/Adjuvant Systemic Therapy for HER2+ Operable Breast Cancer

Shalini Vemuru, MD

Emory Hematology/Oncology Fellow

PGY-5



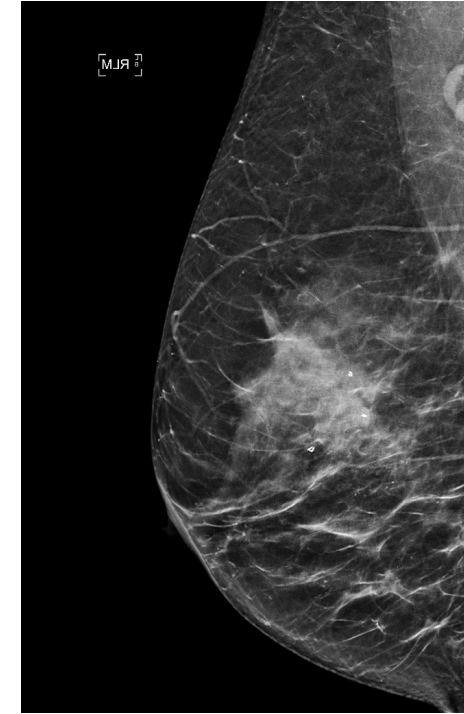
I have no financial disclosures.

Patient Case

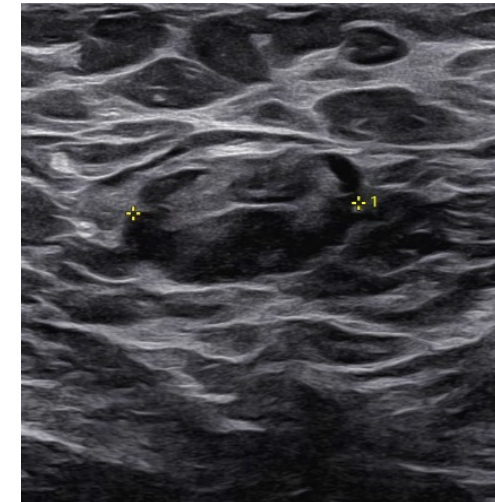
A 50 F presents to your clinic with the following history:

- Screening MMG: R **breast mass** in UOQ
- Diagnostic ultrasound: **2.1 x 1.6 x 1.2 cm** irregular hypoechoic mass in the right breast @ 9:00 and **suspicious 1.7 x 1.0 x 1.0 cm R axillary lymph node**.
- R breast and R axillary ultrasound-guided biopsies
 - R breast core biopsy: invasive ductal carcinoma, grade 1-2
 - ER 0.8%, PR 0.1%, **HER2 3+**
 - R axillary lymph node: metastatic carcinoma
- Diagnostic MMG: Calcifications spanning up to 8.4 cm AP x 9.5 cm craniocaudal
- Bilateral Breast MRI: Irregular mass in the right breast measuring 20 x 15 x 25 mm with non-mass enhancement of 40 x 30 x 20 mm; abnormal right axillary lymph node

Clinical Staging: T(2-3)N1
HER2+ IDC
ER- and PR-



Diagnostic
Mammogram:
RLM



Diagnostic
Axillary
Ultrasound

Panel: What Would You Do for This Patient?

Clinical Stage T(2-3)N1 R Breast IDC

HER2 3+ (strongly HER2+)

ER- and PR-

- What would make you consider DESTINY-Breast11 (4 cycles of T-DXd followed by 4 cycles of THP) over neoadjuvant TCHP or THP?
- What if she were node-negative? Would you consider THP prior to T-DXd?
- What if she were triple-positive?

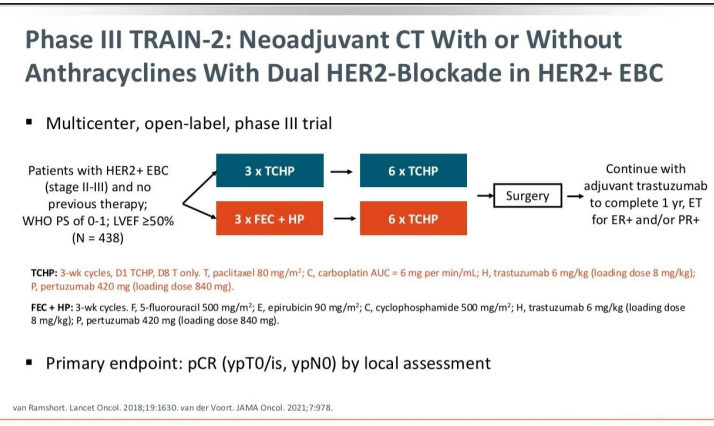
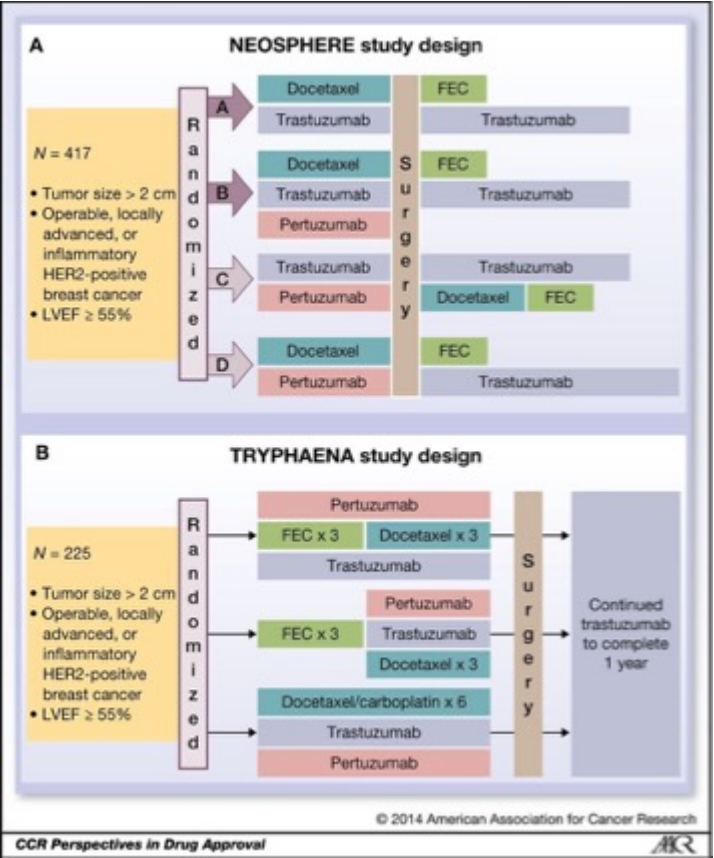
Historical Neoadjuvant Therapy for High-Risk Operable HER2+ Breast Cancer

NEOSPHERE: pCR % was highest in the **neoadjuvant THP arm** (given for **4 cycles**) at 45.8% (p=0.014).

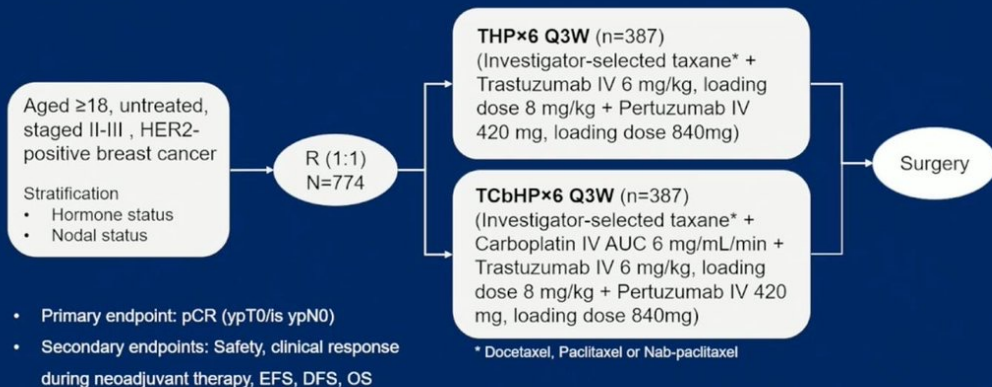
TRYPHAENA: TCHP arm (given for **6 cycles w/o** anthracycline-based therapy) showed comparable pCR % to anthracycline-based regimens with THP (66% v 57%). pCR was an exploratory endpoint.

TRAIN-2: Nearly identical pCR rates (68 v 67%) in patients that received neoadjuvant TCHP with and without anthracycline.

Therefore, standard of care neoadjuvant chemotherapy for HER2+ breast cancer became **TCHP (without anthracyclines)**.



neoCARHP Study Design (NCT04858529)

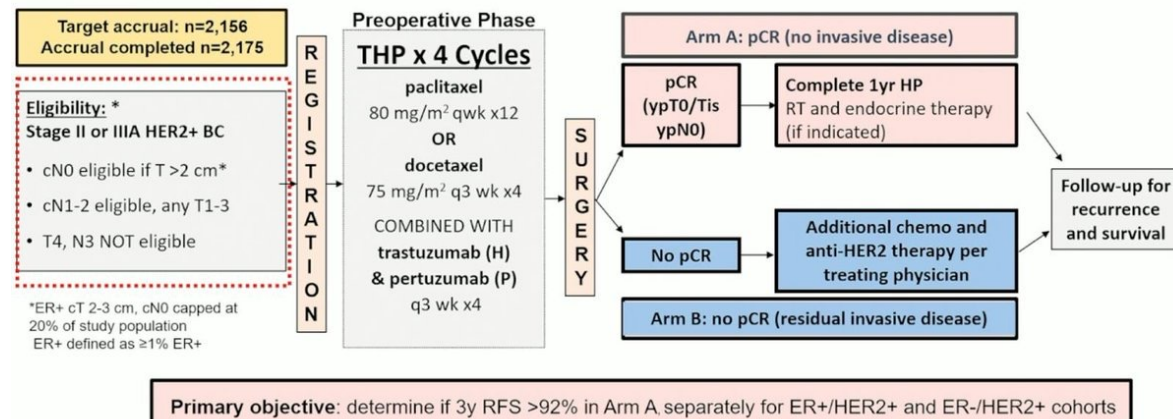


Phase III Randomized-Control, Noninferiority Trial

- pCR rates 65.9% v 64.1%
- Noninferiority endpoint met
 - 1.8; 95% CI -8.5 to 5.0; $P = 0.0089$
- Stratification by HR status:
 - ER-/PR- tumors had higher pCR rates in both arms compared with ER+/PR+ tumors

EA1181 CompassHER2 pCR: Study design

Activation Feb 2020
Accrued thru Oct 2023



Phase II Single-Arm Study

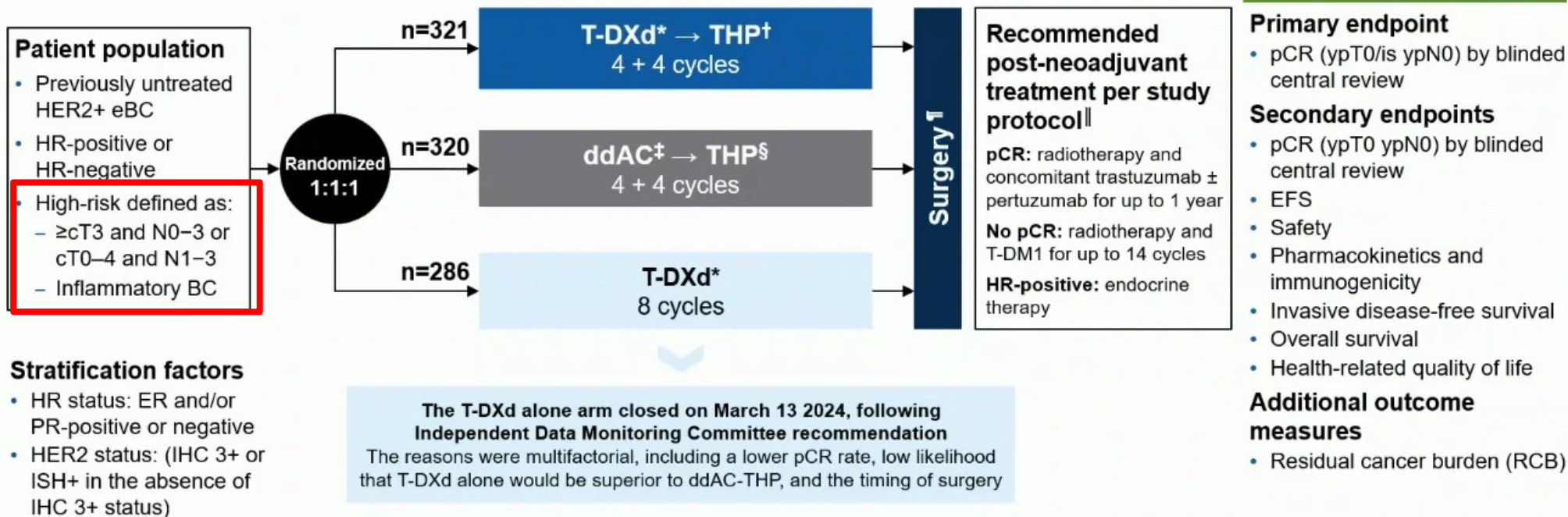
- Overall pCR Rate: 43.8%
- HER2+/HR- pCR rate: 63.7%**
- HER2+/HR+ pCR rate: 32.4%**
- Factors that predicted better pCR: ER/PR negativity, HER 2 3+ (strongly +), weekly paclitaxel

De-Escalation Trials

In higher-risk operable HER2 + breast cancer,
can we do better?

DESTINY-Breast11 study design

A randomized, global, multicenter, open-label, Phase 3 study
(NCT05113251)



High-resolution computed tomography chest scans were performed every 6 weeks during treatment; if ILD/pneumonitis was suspected while receiving T-DXd, treatment was interrupted and a full investigation completed. Echocardiograms or multigated acquisition scans were performed during screening (<28 days prior to randomization), during treatment (<3 days before Cycle 5), and at end of treatment to assess left ventricular ejection fraction. *5.4 mg/kg Q3W; †paclitaxel (80 mg/m² QW) + trastuzumab (6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W); ‡doxorubicin (60 mg/m² Q2W) + cyclophosphamide (600 mg/m² Q2W); §paclitaxel (80 mg/m² QW) + trastuzumab (8 mg/kg loading dose followed by 6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W); ||the recommended window for surgery was 3–6 weeks following administration of the last dose of neoadjuvant study treatment; †administered as part of the patient's SOC at the investigator's discretion. cT, clinical tumor stage; ER, estrogen receptor; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH+, in situ hybridization-positive; N, nodal stage; PR, progesterone receptor; QXW, every X weeks; T-DM1, trastuzumab emtansine; ypT0/is ypN0, absence of invasive cancer in the breast and axillary nodes; ypT0 ypN0, absence of invasive and in-situ cancer in the breast and axillary nodes

Nadia Harbeck, MD

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

Patient Characteristics

DESTINY-Breast11

Patient demographics and key baseline characteristics

		T-DXd-THP (n=321)	ddAC-THP (n=320)	T-DXd (n=286)
Median (range) age, years		50 (25–82)	50 (23–79)	50 (23–79)
Female, n (%)		321 (100)	320 (100)	286 (100)
Geographical region, n (%)	Asia	152 (47.4)	152 (47.5)	124 (43.4)
	Western Europe	69 (21.5)	77 (24.1)	66 (23.1)
	North America	43 (13.4)	41 (12.8)	52 (18.2)
	Rest of world*	57 (17.8)	50 (15.6)	44 (15.4)
Race, n (%)†	Asian	160 (49.8)	157 (49.1)	127 (44.4)
	White	140 (43.6)	137 (42.8)	139 (48.6)
	Black or African American	5 (1.6)	7 (2.2)	7 (2.4)
	Other	12 (3.7)	10 (3.1)	8 (2.8)
Eastern Cooperative Oncology Group performance status score, n (%)	0	278 (86.6)	280 (87.5)	252 (88.1)
	1	43 (13.4)	40 (12.5)	34 (11.9)
HER2 status, n (%)‡	IHC 3+	280 (87.2)	283 (88.4)	254 (88.8)
	Other	40 (12.5)	36 (11.3)	32 (11.2)
HR status, n (%)§	Positive¶	236 (73.5)	235 (73.4)	205 (71.7)
Clinical tumor stage, n (%)	cT0–2	176 (54.8)	188 (58.8)	157 (54.9)
	cT3–4	145 (45.2)	132 (41.3)	129 (45.1)
Nodal status, n (%)	N0	26 (8.1)	35 (10.9)	20 (7.0)
	N+	287 (89.4)	281 (87.8)	254 (88.8)

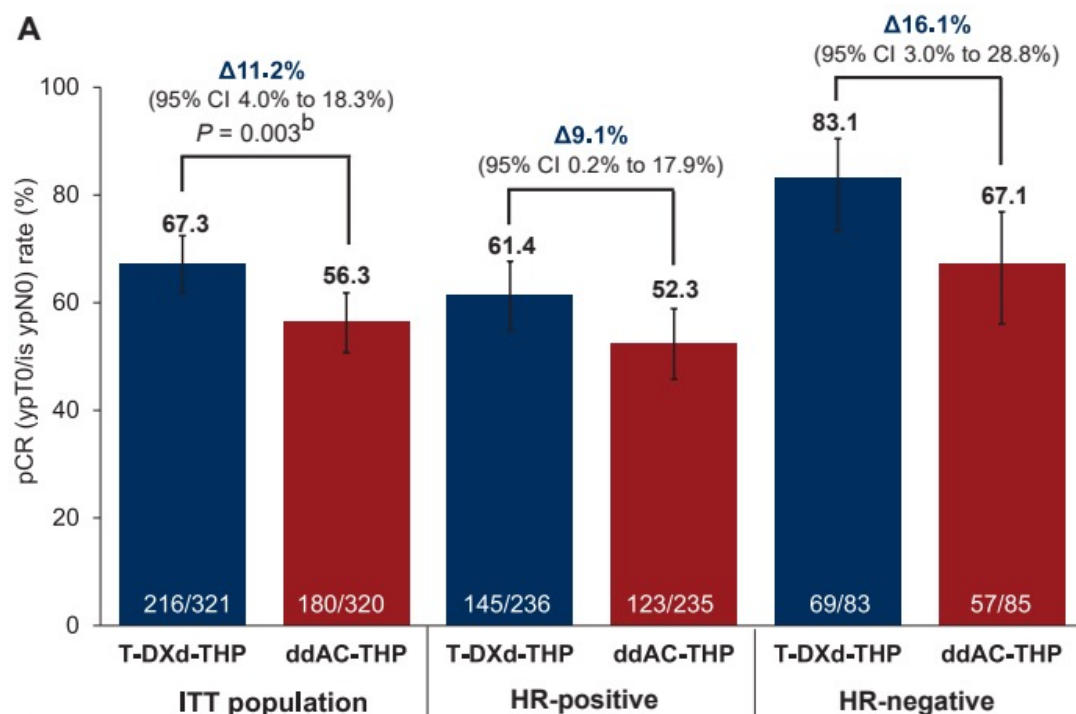
*Asia, Oceania, T-DXd, Positive, Rest of world, and Eastern Cooperative Oncology Group performance status score, not reported for four patients (1.2%), three patients (0.9%), and two patients (0.6%) in the T-DXd-THP, ddAC-THP, and T-DXd alone arms, respectively. †Genitally assigned sex. ‡Not categorized for one patient (0.3%) in the T-DXd-THP arm and missing for one patient (0.3%) in the ddAC-THP arm; §the proportion of patients with HR-negative disease was capped at 30% to reflect natural prevalence. Missing for two patients (0.6%) and one patient (0.3%) in the T-DXd-THP and T-DXd alone arms, respectively; ¶ER and/or PR-positive per electronic case report form data; ||unknown in eight patients (2.5%), four patients (1.3%), and 12 patients (4.2%) in the T-DXd-THP, ddAC-THP, and T-DXd alone arms, respectively

Nadia Harbeck, MD

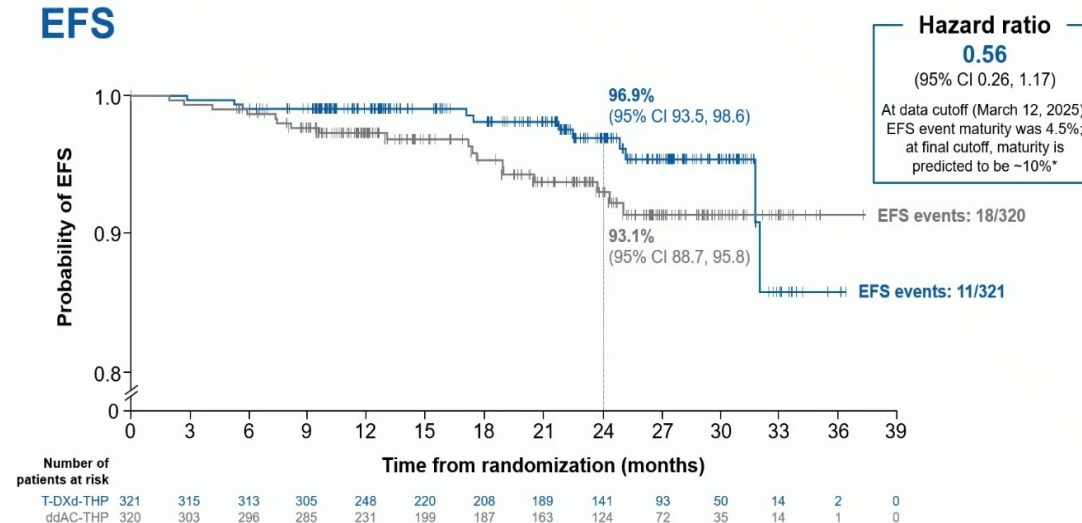
Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

ESMO
EUROPEAN SOCIETY
OF MEDICAL ONCOLOGY

DESTINY-Breast1 pCR and EFS



EFS



An early positive trend in EFS was observed, favoring T-DXd-THP vs ddAC-THP

The median duration of follow-up was 24.3 months with T-DXd-THP and 23.6 months with ddAC-THP. *Predicted maturity assumes that the observed EFS hazard ratio continues after data cutoff (March 12, 2025)

Nadia Harbeck, MD

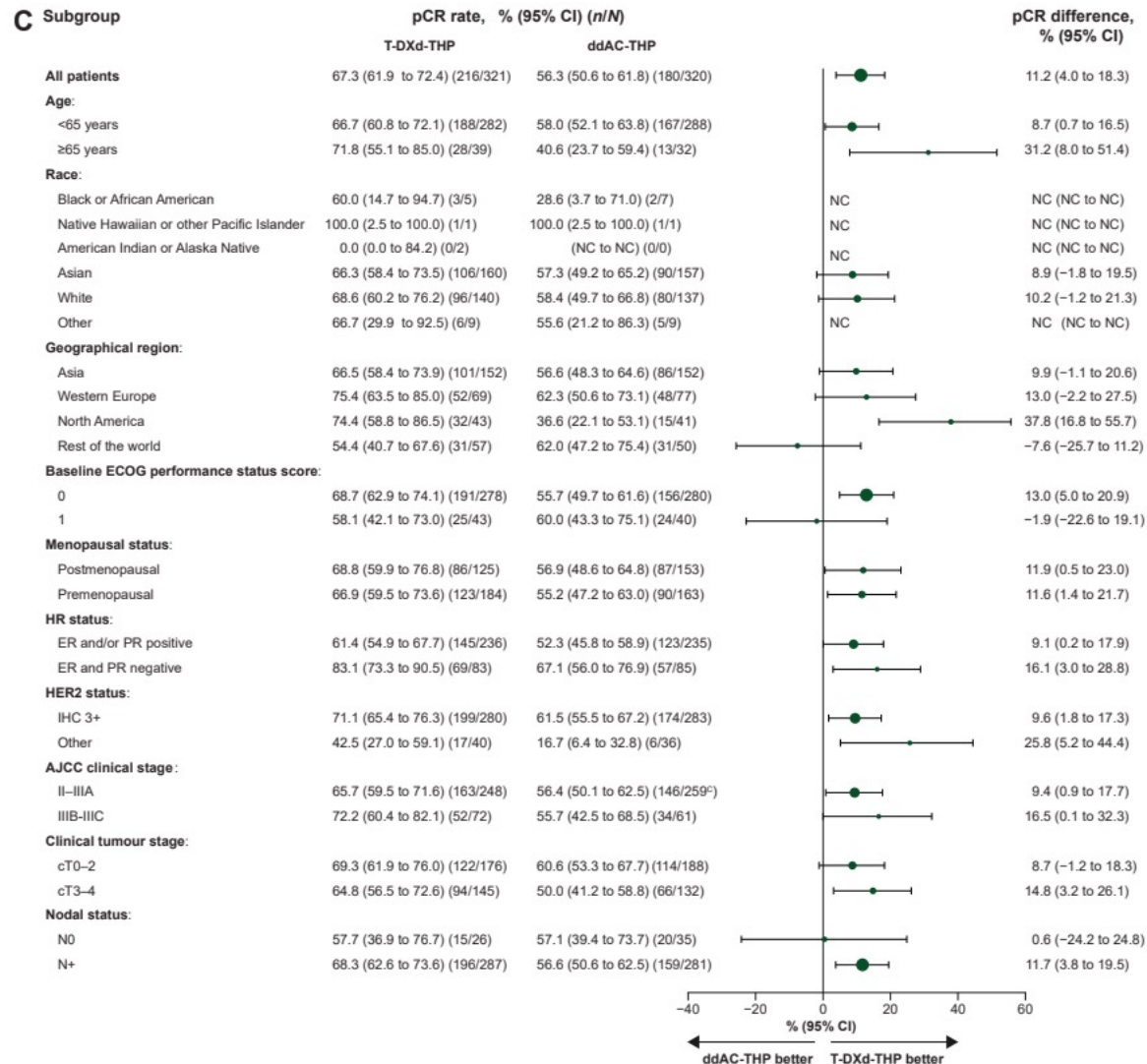
Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.



T-DXd-THP is favored across these populations

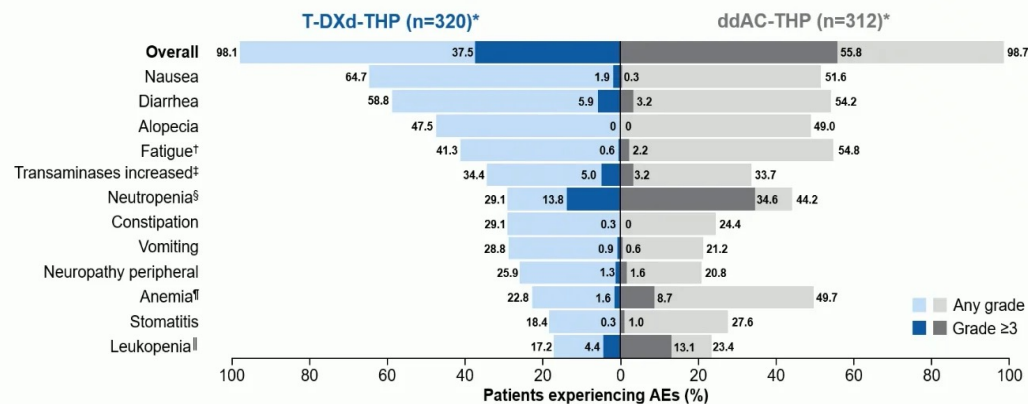
Immature EFS data

DESTINY-Breast1 1: Subgroup Analyses



DESTINY-Breast11: Safety and Tolerability

TEAEs in at least 20% of patients in either arm



T-DXd-THP had fewer any-grade and Grade ≥3 hematological and fatigue events than ddAC-THP
Aside from nausea, gastrointestinal toxicity was comparable between arms

*Safety analyses included all patients who received at least one dose of any study treatment. †Grouped term: fatigue, asthenia, malaise, and lethargy. ‡Grouped term: transaminases increased, aspartate transaminase increased, alanine transaminase increased, gamma-glutamyl transferase increased, liver function test abnormal, hypertransaminasemia, hepatic function abnormal, and liver function test increased. §Grouped term: neutrophil count decreased and neutropenia. ¶Grouped term: hemoglobin decreased, red blood cell count decreased, and anemia and hematocrit decreased. ||Grouped term: white blood cell count decreased and leukopenia. TEAE, treatment-emergent adverse event

Nadia Harbeck, MD

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.



T-DXd alone arm: safety summary

n (%)	T-DXd (n=283)*	ddAC-THP (n=312)*
Any AE	276 (97.5)	308 (98.7)
Grade ≥3	64 (22.6)	174 (55.8)
Any serious AE	29 (10.2)	63 (20.2)
AE leading to any dose reduction	19 (6.7)	60 (19.2)
AE leading to any drug interruption	51 (18.0)	170 (54.5)
AE leading to any treatment discontinuation	22 (7.8)	31 (9.9)
Any AE with outcome of death†	1 (0.4)	2 (0.6)
AE of special interest		
Drug-related adjudicated ILD/pneumonitis	14 (4.9)	16 (5.1)
Grade ≥3	0	6 (1.9)
Grade 5	0	1 (0.3)
Left ventricular dysfunction	2 (0.7)	19 (6.1)
Grade ≥3	0	6 (1.9)
Grade 5	0	0
AE leading to surgical delay‡	18 (6.4)	8 (2.6)

The overall safety profile of T-DXd alone was favorable vs ddAC-THP, with reduced rates of Grade ≥3 AEs, serious AEs, treatment reductions/interruptions, and left ventricular dysfunction
ILD incidence was low and similar in both arms

High-resolution computed tomography chest scans were performed every 6 weeks during treatment; if ILD/pneumonitis was suspected while receiving T-DXd, treatment was interrupted and a full investigation completed. Echocardiograms or multigated acquisition scans were performed during screening (<28 days prior to randomization), during treatment (<3 days before Cycle 5), and at end of treatment to assess left ventricular ejection fraction. Median total treatment duration of whole regimen was 24.0 months (T-DXd) and 21.0 months (ddAC-THP). *Safety analyses included all patients who received at least one dose of any study treatment. †T-DXd alone arm: pulmonary embolism considered by investigator to be unrelated to study treatment (n=1); ddAC-THP arm: investigator-determined drug-related bacterial encephalitis (n=1), drug-related pneumonitis adjudicated by the ILD Adjudication Committee (n=1). ‡Defined as surgery not occurring within 3-6 weeks after the last cycle of neoadjuvant treatment

Nadia Harbeck, MD

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.



Panel: What Would You Do For This Patient?

Clinical Stage T(2-3)N1 R Breast IDC

HER2 3+ (strongly HER2+)

ER- and PR-

- If using the DB-11 regimen, are you getting repeat breast imaging between T-DXd and THP to assess response?
- What if she were a heavy smoker? Or had underlying lung disease?
- If choosing DB-11, how often are you getting a CT Chest to assess for ILD?
- What if she develops ILD during the T-DXd portion of regimen?

Back to the Case

- She underwent systemic imaging to confirm M0 disease
- She was started on the DESTINY-Breast11 regimen given that her tumor is node-positive and strongly HER2 positive
- After cycle 4, her response to treatment will be assessed with breast imaging
- CT Chest every 6 weeks to surveil for ILD
- At time of surgery if her tumor achieves pCR, she will complete one year of HER2-directed therapy (trastuzumab + pertuzumab)
- If she does not achieve pCR, what next?

After neoadjuvant therapy, what if pCR is not achieved?

San Antonio Breast Cancer Symposium December 4–8, 2018

KATHERINE Study Design

- cT1-4/N0-3/M0 at presentation (cT1a-b/N0 excluded)
- Centrally confirmed HER2-positive breast cancer
- Neoadjuvant therapy must have consisted of
 - Minimum of 6 cycles of chemotherapy
 - Minimum of 9 weeks of taxane
 - Anthracyclines and alkylating agents allowed
 - All chemotherapy prior to surgery
 - Minimum of 9 weeks of trastuzumab
 - Second HER2-targeted agent allowed
- Residual invasive tumor in breast or axillary nodes
- Randomization within 12 weeks of surgery

R
1:1
N=1486

T-DM1
3.6 mg/kg IV Q3W
14 cycles

Trastuzumab
6 mg/kg IV Q3W
14 cycles

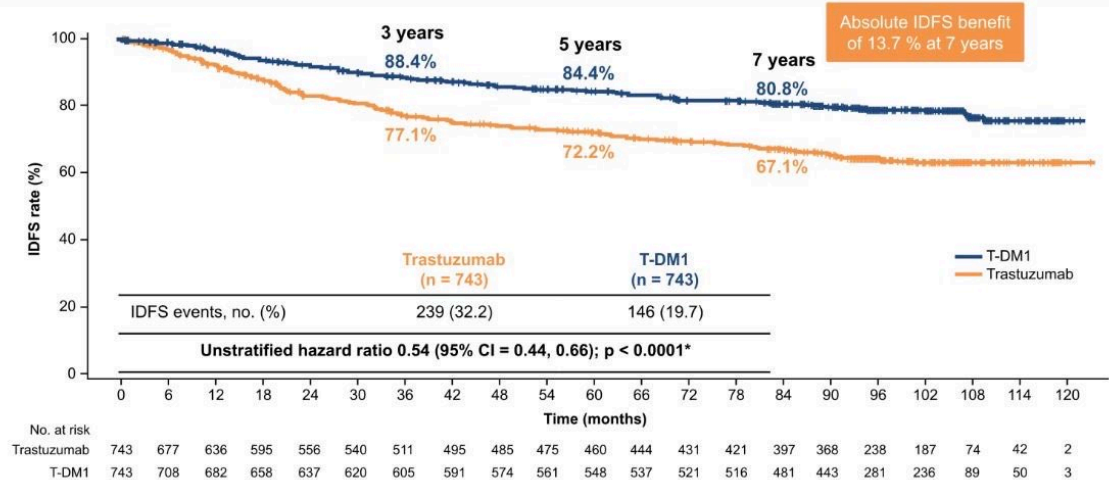
Radiation and endocrine therapy
per protocol and local guidelines

Stratification factors:

- Clinical presentation: Inoperable (stage cT4 or cN2–3) vs operable (stages cT1-3N0-1)
- Hormone receptor: ER or PR positive vs ER negative and PR negative/unknown
- Preoperative therapy: Trastuzumab vs trastuzumab plus other HER2-targeted therapy
- Pathological nodal status after neoadjuvant therapy: Positive vs negative/not done

This presentation is the intellectual property of Charles E. Geyer Jr. Contact him at cgeyer@vcu.edu for permission to reprint and/or distribute.

KATHERINE IDFS final analysis; median follow-up 8.4 years (101 months)



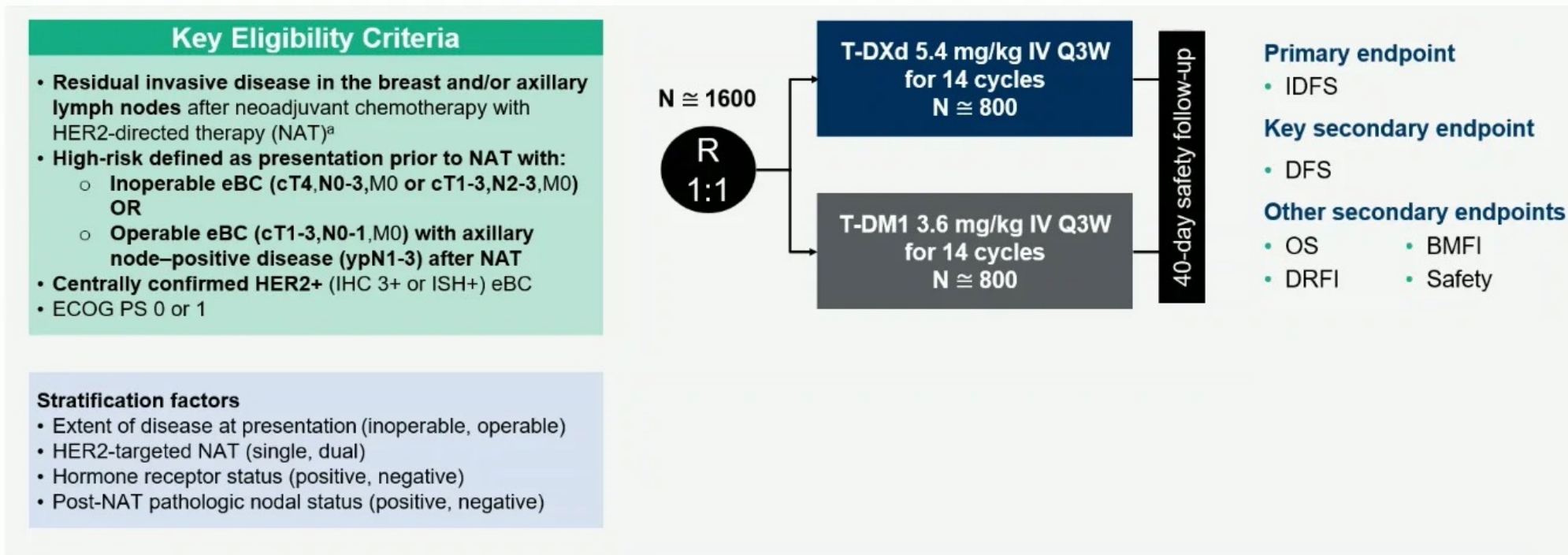
* p-value for IDFS is now exploratory given the statistical significance was established at the primary analysis.
CI, confidence interval; IDFS, invasive disease-free survival; T-DM1, ado-trastuzumab emtansine.

This presentation is the intellectual property of the authors. Contact Sibylle Loibl@sbg.de for permission to reprint and/or distribute.

For residual disease, T-DM1 became the adjuvant standard of care

DESTINY-Breast05 study design

A global, multicenter, randomized, open-label, phase 3 trial (NCT04622319)



BMFI, brain metastasis-free interval; CT, computed tomography; eBC, early breast cancer; DCO, data cutoff; DFS, disease-free survival; DRFI, distant recurrence-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; IDFS, invasive disease-free survival; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; NAT, neoadjuvant therapy; OS, overall survival; Q3W, every 3 weeks; R, randomization; RT, radiotherapy; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aNAT is defined as ≥16 weeks' NAT with ≥9 weeks trastuzumab ± pertuzumab and ≥9 weeks taxane-based chemotherapy.

Dr Charles E Geyer Jr

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

DESTINY-Breast05 Outcomes	
3-year invasive disease-free survival	92.4% (T-DXd) v 83.7% (T-DM1) HR 0.47; p < 0.0001
3-year disease-free survival	92.3% (T-DXd) v 83.5% (T-DM1) HR 0.47, p < 0.0001
3-year brain metastasis-free interval	97.6% (T-DXd) v 95.8% (T-DM1) HR 0.64, 95 CI: 0.35 -1.17
3-year distant-recurrence interval	93.9 (T-DXd) v 86.1% (T-DM1) HR 0.49, 95 CI: 0.34-0.71
Overall survival	Not yet mature

Adverse events of special interest: ILD/pneumonitis and LV dysfunction

n (%)	Adjudicated Drug-related ILD					
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
T-DXd (n = 806)^a	77 (9.6)	16 (2.0)	52 (6.5)	7 (0.9)	0	2 (0.2)
T-DM1 (n = 801)^a	13 (1.6)	8 (1.0)	5 (0.6)	0	0	0

Adjuvant radiotherapy timing (sequential or concurrent) showed no differences in adjudicated drug-related ILD
 Similar distributions of any grade adjudicated drug-related ILD events were observed with sequential and concurrent radiotherapy in both treatment arms (T-DXd: 10.7% and 9.6.% vs T-DM1: 2.6% and 1.0%, respectively)

n (%)	LV dysfunction					
	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
T-DXd (n = 806)^a	23 (2.9)	1 (0.1)	20 (2.5)	2 (0.2)	0	0
T-DM1 (n = 801)^a	14 (1.7)	0	11 (1.4)	3 (0.4)	0	0

CT, computed tomography; ILD, interstitial lung disease; LV, left ventricular; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan.

^aAll patients who received at least 1 dose of study treatment.

Dr Charles E Geyer Jr

Content of this presentation is copyright and responsibility of the author. Permission is required for re-use.

Panel: What Would You Do For This Patient?

- For whom would you consider the DB-05 regimen?
- What if they received DB-11 in the neoadjuvant setting?
- How often are you getting chest CT scans during adjuvant T-DXd?
- If the patient is getting adjuvant radiation, are you starting concomitant T-DXd or waiting until after radiation?
- What if they develop Grade 2 or higher ILD in the adjuvant setting? Do you pivot to HP or T-DM1 (Kadcyla)?

Conclusions

- In patients with higher risk HER2+ (Stage II-III) eBC, the DESTINY-Breast11 regimen is an FDA-approved neoadjuvant therapy
- If pCR is not achieved and residual disease remains, the DESTINY-Breast05 regimen is now an FDA-approved therapy
 - Consider DB05 if significant residual disease remains, particularly nodal disease
 - If residual disease remains in the breast only, I would strongly consider T-DM1 given the safety and tolerability challenges with 14 cycles of T-DXd
- It is important to monitor for ILD while on this regimen

Acknowledgments

- Thank you to Dr. Jane Meisel, my mentor, who helped me develop and review these slides!
- Thank you also to Dr. Kevin Kalinsky for giving me this opportunity to present at The Atlanta Breast Conference

References

- Gianni L, Pienkowski T, Im YH, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. *Lancet Oncol*. 2012;13(1):25-32. doi:10.1016/S1470-2045(11)70336-9
- Schneeweiss A, Chia S, Hickish T, et al. Pertuzumab plus trastuzumab in combination with standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer: a randomized phase II cardiac safety study (TRYPHAENA). *Ann Oncol*. 2013;24(9):2278-2284. doi:10.1093/annonc/mdt182
- van Ramshorst MS, van der Voort A, van Werkhoven ED, et al. Neoadjuvant chemotherapy with or without anthracyclines in the presence of dual HER2 blockade for HER2-positive breast cancer (TRAIN-2): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol*. 2018;19(12):1630-1640. doi:10.1016/S1470-2045(18)30570-9
- Gao HF, Ye GL, Lin Y, et al. Neoadjuvant Taxane Plus Trastuzumab and Pertuzumab With or Without Carboplatin in Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer: The Randomized Noninferiority Phase III neoCARHP Trial. *J Clin Oncol*. 2026;44(17):1587-1596. doi:10.1200/JCO-25-02176
- Tung N, Zhao F, DeMichele A, et al. Pathologic Complete Response (pCR) Rate and Predictors of Response to Taxane, Trastuzumab, and Pertuzumab in HER2-Positive Breast Cancer: Secondary Analyses of EA1181/CompassHER2 pCR. *J Clin Oncol*. Published online August 20, 2026. doi:10.1200/JCO-25-02255
- Harbeck N, Modi S, Pusztai L, et al. Neoadjuvant trastuzumab deruxtecan alone or followed by paclitaxel, trastuzumab, and pertuzumab for high-risk HER2-positive early breast cancer (DESTINY-Breast11): a randomised, open-label, multicentre, phase III trial. *Ann Oncol*. 2026;37(2):166-179. doi:10.1016/j.annonc.2025.10.019
- Loibl S, Park YH, Shao Z, et al. Trastuzumab Deruxtecan in Residual HER2-Positive Early Breast Cancer. *N Engl J Med*. 2026;394(9):845-857. doi:10.1056/NEJMoa2514661

— 2nd Annual —

Atlanta Breast Cancer

CONFERENCE

September 19, 2026



12:50 – 2:20 PM

Fellows Case Discussion



MODERATOR

Kevin Kalinsky, MD, MS,
FASCO



FELLOW

Caroline Breit, MD



FELLOW

Hasiya Okoroza, MD, MPH



FELLOW

Sarah Keshwani, MD



FELLOW

Shalini Vemuru, MD