Cancer Conference Update: What Happened at the 2020 San Antonio Breast Cancer Symposium®

Session 1: Management of HER2-Positive Breast Cancer

Monday, January 25, 2021 5:00 PM - 6:00 PM ET

Faculty
Erika Hamilton, MD



Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Eisai Inc, Genentech, a member of the Roche Group, and Merck.



Dr Love — Disclosures

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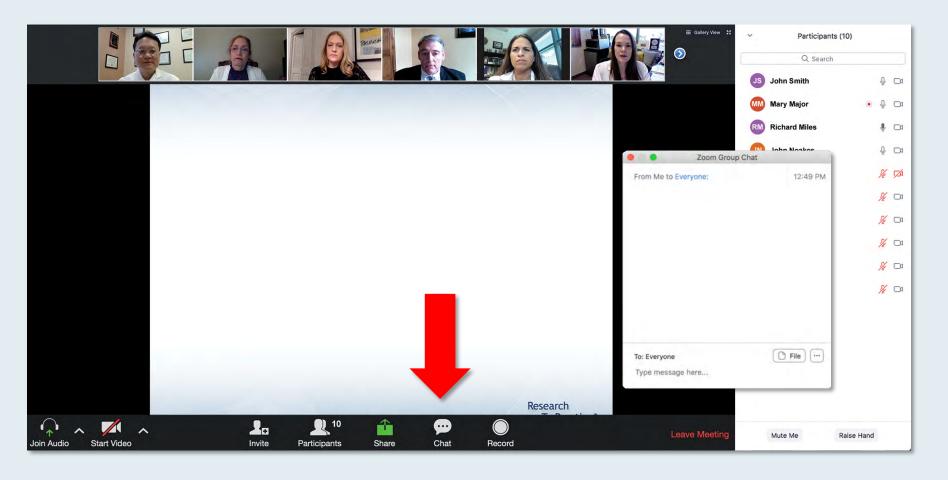


Dr Hamilton — Disclosures

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We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.



Familiarizing Yourself with the Zoom Interface How to answer poll questions

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ONCOLOGY TODAY

WITH DR NEIL LOVE

The Role of PARP Inhibition in the Management of Breast Cancer



HOPE S RUGO, MD
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Year in Review — Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology: Targeted Therapy for Lung Cancer

Tuesday, January 26, 2021 5:00 PM - 6:00 PM ET

Faculty
Joel W Neal, MD, PhD
Paul K Paik, MD



Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Hepatocellular Carcinoma (Part 1 of a 3-Part Series)

Wednesday, January 27, 2021 5:00 PM - 6:30 PM ET

Faculty

Richard S Finn, MD
Tim Greten, MD
James J Harding, MD
Ahmed Omar Kaseb, MD, CMQ



Year in Review — Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology: Multiple Myeloma

Thursday, January 28, 2021 5:00 PM - 6:00 PM ET

Faculty

Rafael Fonseca, MD Jonathan L Kaufman, MD



Year in Review — Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology: Bladder Cancer and Renal Cell Carcinoma

Tuesday, February 2, 2021 5:00 PM - 6:00 PM ET

Faculty

Sumanta K Pal, MD David I Quinn, MBBS, PhD



Recent Advances in Hematologic Oncology: A 4-Part Live Webinar Series Reviewing Key Data and Presentations from the 62nd ASH Annual Meeting

Part 2 — Hodgkin and Non-Hodgkin Lymphoma

Wednesday, February 3, 2021 5:00 PM - 6:00 PM ET

Faculty

John Kuruvilla, MD John P Leonard, MD Michael E Williams, MD, ScM



Cases from the Community: Investigators Discuss Emerging Research and Actual Patients with Gastroesophageal Cancers (Part 2 of a 3-Part Series)

Thursday, February 4, 2021 5:00 PM - 6:30 PM ET

Faculty

Daniel Catenacci, MD Yelena Y Janjigian, MD Rutika Mehta, MD, MPH Zev Wainberg, MD, MSc



Meet The ProfessorManagement of Lung Cancer

Friday, February 5, 2021 12:00 PM - 1:00 PM ET

Faculty
Joshua Bauml, MD



Cancer Conference Update: What Happened at the 2020 San Antonio Breast Cancer Symposium®

Session 1: Triple-Negative Breast Cancer Monday, January 11, 2021

5:00 – 6:00 PM ET **Faculty**

P Kelly Marcom, MD

Session 2: Triple-Negative Breast Cancer Monday, February 22, 2021

5:00 - 6:00 PM ET

FacultyJoyce O'Shaughnessy, MD

Session 1: HER2-Positive Breast Cancer

Monday, January 25, 2021

5:00 – 6:00 PM ET

Faculty

Erika Hamilton, MD

Session 2: HER2-Positive Breast Cancer

Monday, March 8, 2021

5:00 – 6:00 PM ET

Faculty

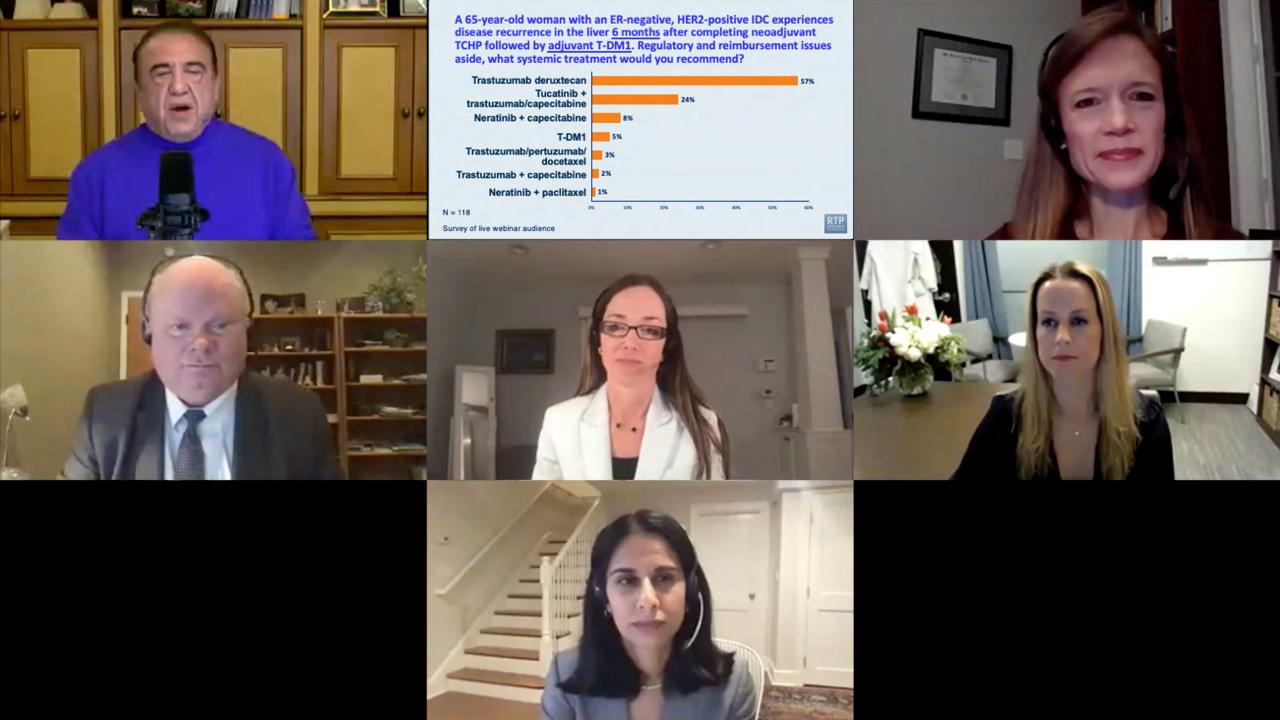
Mark D Pegram, MD



Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.







Atif Hussein, MD, MMM Program Director, Hematology/Oncology Fellowship Medical Director, Oncology Clinical Research Chairman, Cancer Committee Memorial Healthcare System Clinical Associate Professor Florida International University Herbert Wertheim College of Medicine Hollywood, Florida























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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of HER2-Positive Breast Cancer

Thursday, December 10, 2020 8:30 PM - 10:00 PM ET

Faculty

Carey K Anders, MD Mark D Pegram, MD Erika Hamilton, MD Sara M Tolaney, MD, MPH

Sara Hurvitz, MD

Moderator

Neil Love, MD



Presentation Library

HER2-Positive Breast Cancer, Thursday, December 10, 2020

Considerations in the Care of Patients with Localized HER2-Positive Breast Cancer (BC) Receiving Neoadjuvant Systemic Therapy Mark D Pegram, MD

Download Slides

Adjuvant and Extended-Adjuvant Therapy for Patients with Localized HER2-Positive BC Sara M Tolaney, MD, MPH

Download Slides

Optimizing the Management of HER2-Positive Metastatic BC (mBC) Sara Hurvitz, MD

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Treatment of HER2-Positive Brain Metastases
Carey K Anders, MD

Download Slides

Incidence and Management of Adverse Events Associated with HER2-Targeted Therapies Erika Hamilton, MD

Download Slides



HER2-Positive Breast Cancer Survey Participants

- 1. Carey K Anders, MD
- 2. Aditya Bardia, MD, MPH
- 3. Joanne L Blum, MD, PhD
- 4. Adam M Brufsky, MD, PhD
- 5. Howard A Burris III, MD
- 6. Harold J Burstein, MD, PhD
- 7. Lisa A Carey, MD
- 8. Charles E Geyer Jr, MD
- 9. Matthew Goetz, MD
- 10. Erika Hamilton, MD
- 11. Sara Hurvitz, MD
- 12. Virginia Kaklamani, MD, DSc
- 13. Hannah M Linden, MD

- 14. Eleftherios P Mamounas, MD, MPH
- 15. P Kelly Marcom, MD
- 16. Jennifer M Matro, MD
- 17. Kathy D Miller, MD
- 18. Rita Nanda, MD
- 19. Ruth O'Regan, MD
- 20. Joyce O'Shaughnessy, MD
- 21. Mark D Pegram, MD
- 22. Lajos Pusztai, MD, DPhil
- 23. Joseph A Sparano, MD
- 24. Sandra M Swain, MD
- 25. Sara M Tolaney, MD, MPH



Faculty



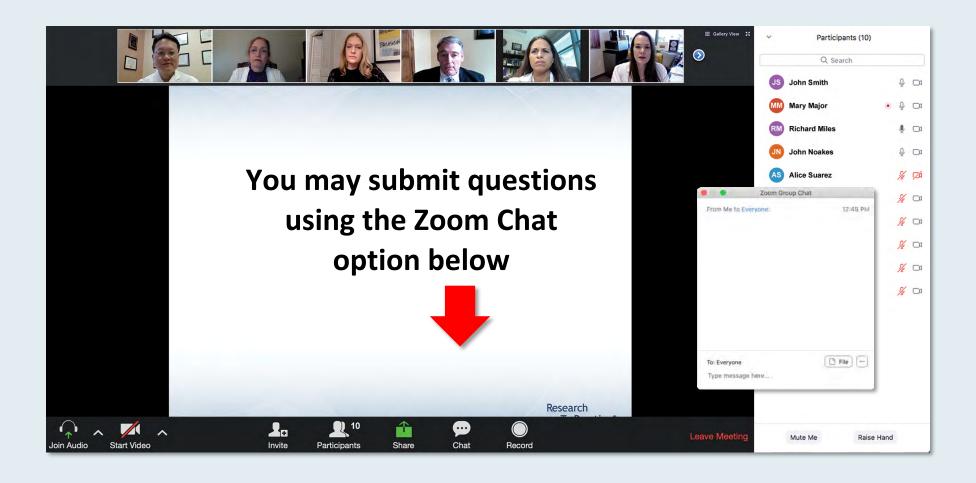
Erika Hamilton, MD
Director, Breast and Gynecologic
Research Program
Sarah Cannon Research Institute
Nashville, Tennessee



Moderator
Neil Love, MD
Research To Practice
Miami, Florida



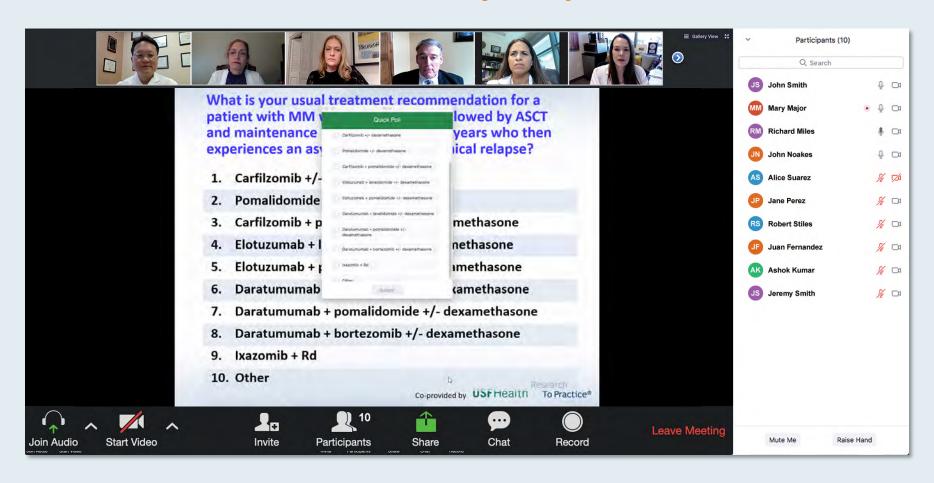
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The Role of PARP Inhibition in the Management of Breast Cancer

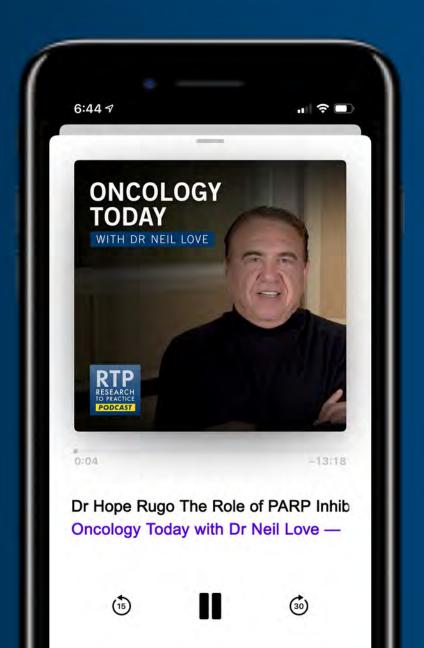


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Atif Hussein, MD, MMM

Program Director, Hematology/Oncology Fellowship
Medical Director, Oncology Clinical Research
Chairman, Cancer Committee, Memorial Healthcare System
Clinical Associate Professor, Florida International University Herbert
Wertheim College of Medicine
Hollywood, Florida



Laurie Matt-Amaral, MD, MPH
Attending Physician
Cleveland Clinic Akron General Medical Center
Medina, Ohio



Agenda

Module 1: Dr Matt-Amaral — A 42-year-old premenopausal woman with ER-positive, HER2-positive, node-negative breast cancer

Module 2: SABCS 2020 Review — Part 1

Module 3: Dr Hussein — A 43-year-old woman with ER/PR-negative, HER2-positive breast cancer with brain metastasis

Module 4: SABCS 2020 Review — Part 2

Module 5: Dr Matt-Amaral — A 73-year-old woman with clinical T4 ER/PR-negative, HER2-positive breast cancer

Module 6: Dr Hussein — A 36-year-old physician with ER/PR-negative, HER2-positive, node-positive breast cancer during pregnancy





Do you remember 2005?



DEPOSITION OF LACE

OCTOBER 6, 2011

FOR MY NO. 14

Adjuvant Trastuzumab in HER2-Positive Breast Cancer

ORIGINAL ARTICLE

Trastuzumab plus Adjuvant Chemotherapy for Operable HER2-Positive Breast Cancer

The NEW ENGLAND
JOURNAL of MEDICINE

MERCHANISM AND OF THEIR

OCTOBER 20, 2005

THE ARE NO 16

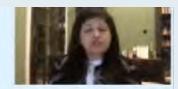
Trastuzumab after Adjuvant Chemotherapy in HER2-Positive Breast Cancer "The results are simply stunning. They're not evolutionary, they're revolutionary." NEJM 2005





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Ongoing questions in therapy for HER2+ breast cancer

Optimal sequence of therapy in metastatic disease as novel agents are introduced?

Chemotherapy-free approach in 1st line ER+, HER2+ disease?

Increase patient engagement and participation in de-escalation trials? De-escalate therapy while maintaining benefits and lessening toxicity?

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Agenda

Module 1: Dr Matt-Amaral — A 42-year-old premenopausal woman with ER-positive, HER2-positive, node-negative breast cancer

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Case Presentation: A 42-year-old premenopausal woman with ER-positive, HER2-positive, nodenegative breast cancer



Laurie Matt-Amaral, MD, MPH

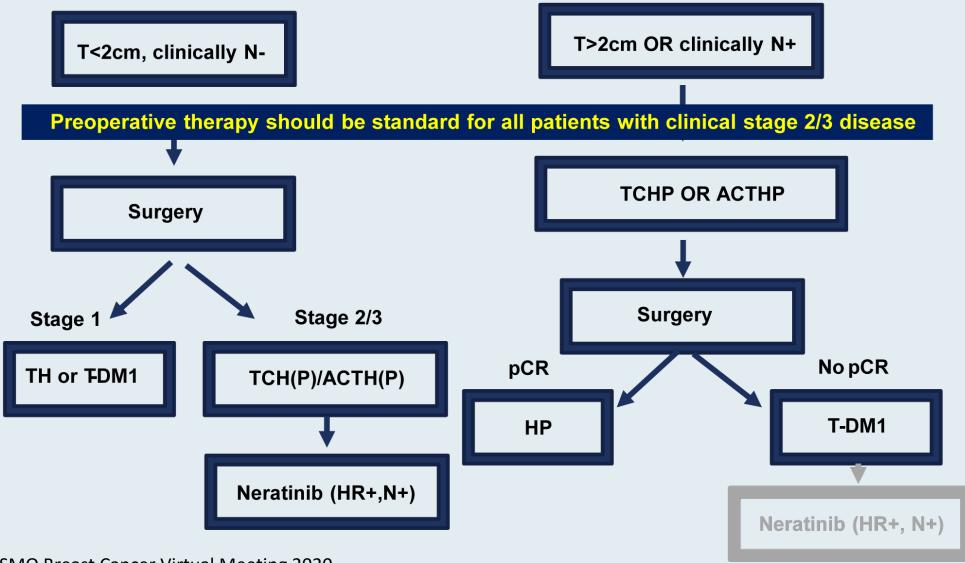
- Mastectomy for ER-positive DCIS revealed a 1.3-cm, ER-positive,
 PR-negative, HER2-positive, node-negative IDC
- PMH: Depression
- Genetic testing: PMS2 VUS
- Patient is not interested in receiving adjuvant chemotherapy
- Plan: Trastuzumab plus either tamoxifen or Al/ovarian suppression

Questions

- For which patients do you decide to use post-adjuvant neratinib?
- Any tips about how to manage the diarrhea?



Current Approach for Treatment of HER2+ Breast Cancer: 2020





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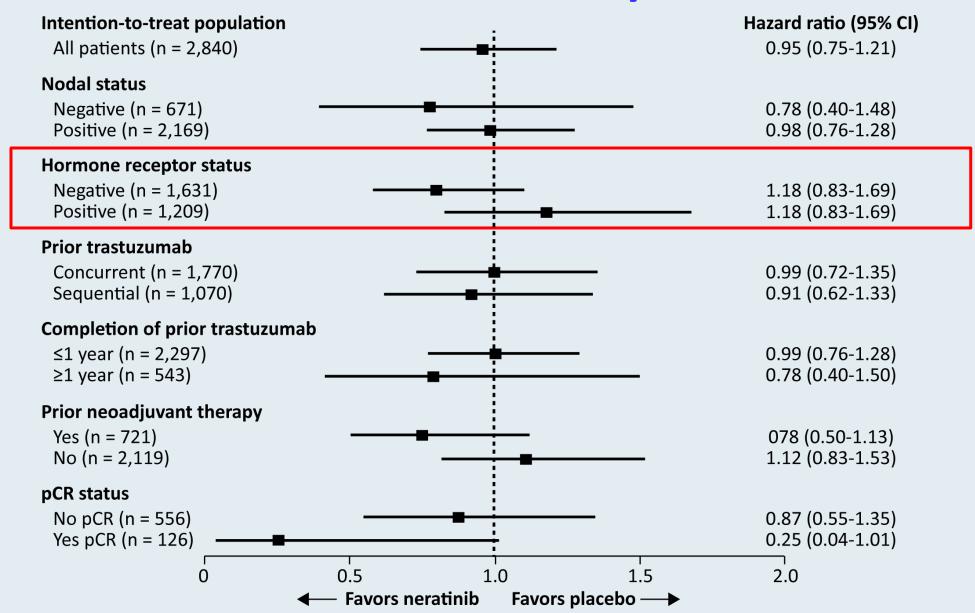
Continued efficacy of neratinib in patients with HER2positive early-stage breast cancer: Final overall survival analysis from the randomized phase 3 ExteNET trial

Holmes FA et al.

SABCS 2020; Abstract PD3-03



ExteNET: Final Overall Survival Analysis





Final analysis of PERTAIN: A randomized, two-arm, openlabel, multicenter phase II trial assessing the efficacy and safety of first-line pertuzumab given in combination with trastuzumab plus an aromatase inhibitor in patients with HER2-positive and hormone receptor-positive metastatic or locally advanced breast cancer

Arpino G et al.

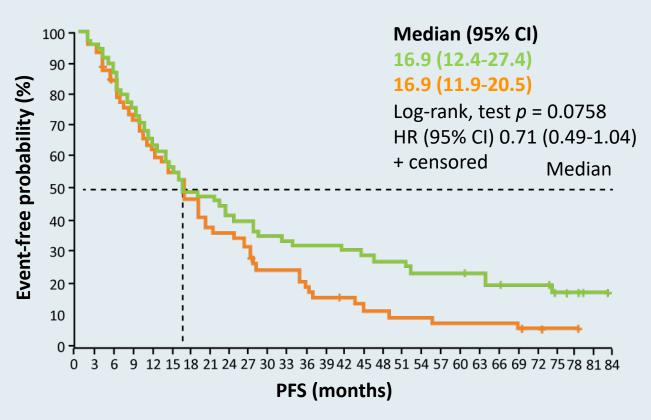
SABCS 2020; Abstract PD3-02

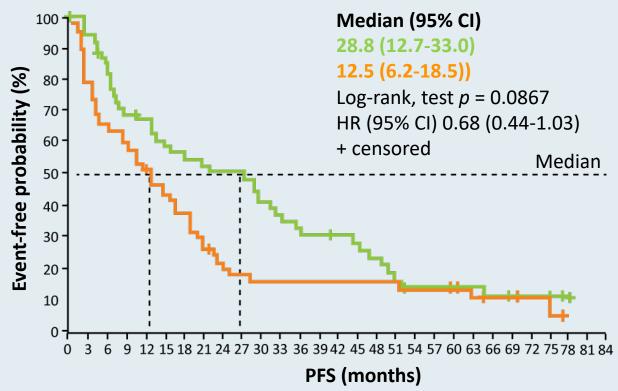


PERTAIN: Progression-Free Survival

Received Induction Therapy

No Induction Therapy







The DAPHNE trial: A feasibility study of chemotherapy deescalation based on response to neoadjuvant paclitaxel-HP (THP) in HER2-positive breast cancer

Waks AG et al.

SABCS 2020; Abstract PD3-05



DAPHNe: Trial of Chemotherapy De-escalation

TRIAL SCHEMA

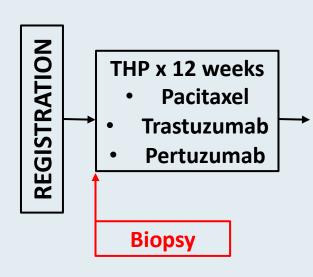
Open at Dana-Farber/Harvard Cancer Center (+ satellites) Enrollment 11/2018 - 1/2020

Assessment of adjuvant therapy decision-making:

- **Patient questionnaires administered**
- Standardized medical record review

Eligibility:

- Anatomic stage II-III HER2+ breast cancer
- Breast tumor ≥1.5 cm
- ER/PR pos or negative



surgery Or, if clinical residual disease post-THP:

biopsy → additional pre-op chemo

Definitive

Surgical tissue

collection

If pCR* (breast and nodes), complete 52 wks HP**

If no pCR, standard therapy per investigator discretion, and complete 52 wks T-DM1

Follow-up for recurrence/survival



* pCR defined as: ypT0/is ypN0

**concurrent endocrine tx allowed if HR+

Patient perspectives on chemotherapy de-escalation: "Don't de-escalate! I don't want to die!"

Rocque G et al.

SABCS 2020; Abstract PD3-10



San Antonio Breast Cancer Symposium®, December 8-11, 2020

43% of patients were not interested in de-escalatic clinical trials



FEAR OF RECURRENCE

"We need to do everything we can so it doesn't come back."

TRUST

"You assemble your treatment team of people and you trust and you kind of take their recommendation...I truly put my faith in my doctor."

Fear of recurrence and regret were common <u>barriers</u>

Trust in the physician and avoiding toxicity were common facilitators

Patients disliked "de-escalation," preferring patient-centric language (e.g. customized or personalized).

The COVID-19 pandemic increased patient interest in de-escalation.

FEAR OF REGRET

"I think people are afraid that they will regret their decision."

AVOIDING TOXICITY

"I know how harsh it is and as the saying goes: it's not the cancer, it's the chemo. So I think that [de-escalation] would be great."

PANDEMIC

"I wouldn't worry about getting the chemo as much as I would worry about getting the virus."

Rocque G, et al. SABCS 2020 (PD3-10; abstract 272)

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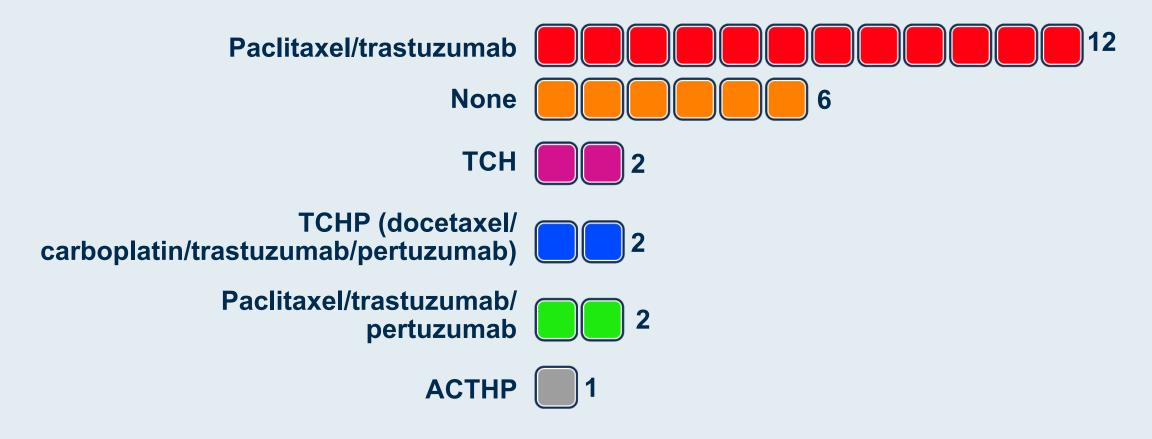
Which neoadjuvant systemic therapy, if any, would you generally recommend for a 65-year-old patient with a 1.5-cm, ER-negative, HER2-positive, node-negative infiltrating ductal carcinoma (IDC)?

- 1. None
- 2. Paclitaxel/trastuzumab
- 3. Paclitaxel/trastuzumab/pertuzumab
- 4. ACTH (doxorubicin/cyclophosphamide/paclitaxel/trastuzumab)
- 5. ACTHP (ACTH/pertuzumab)
- 6. TCH (docetaxel/carboplatin/trastuzumab)
- 7. TCHP (TCH/pertuzumab)
- 8. Other



Which neoadjuvant systemic therapy, if any, would you generally recommend for a patient with an ER-negative, HER2-positive IDC with the following characteristics?

Age: 65, Tumor size: 1.5 cm, Nodal status: Node-negative

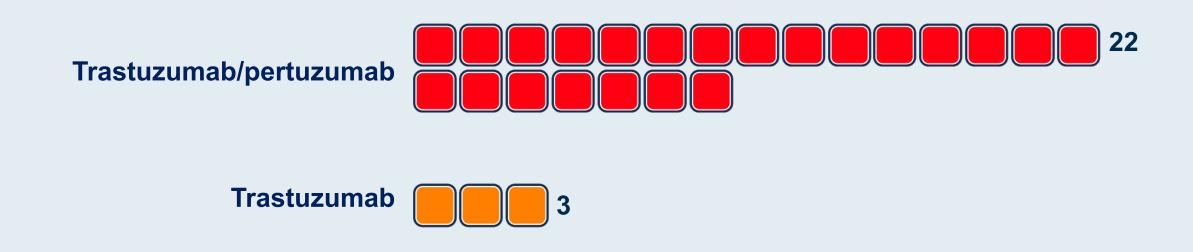


A 65-year-old woman presents with a 3.4-cm, ER-negative, HER2-positive IDC with biopsy-proven axillary nodes and receives neoadjuvant TCHP. Regulatory and reimbursement issues aside, what adjuvant anti-HER2 therapy would you recommend if at surgery the patient were found to have a pathologic complete response?

- 1. Trastuzumab
- 2. Trastuzumab/pertuzumab
- 3. T-DM1
- 4. Trastuzumab → neratinib
- 5. Trastuzumab/pertuzumab → neratinib
- 6. T-DM1 \rightarrow neratinib
- 7. Other



A 65-year-old woman presents with a 3.4-cm, ER-negative, HER2-positive IDC with biopsy-proven axillary nodes and receives neoadjuvant TCHP. Regulatory and reimbursement issues aside, what adjuvant anti-HER2 therapy would you recommend if at surgery the patient were found to have a pathologic complete response?



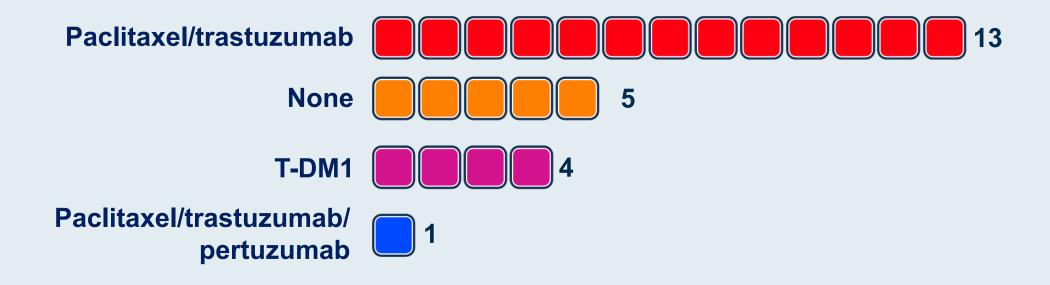
An <u>80-year-old</u> woman presents with a <u>0.6-cm</u>, ER-negative, HER2-positive, node-negative IDC. Regulatory and reimbursement issues aside, what adjuvant systemic therapy would you recommend?

- 1. None
- 2. Paclitaxel/trastuzumab
- 3. Paclitaxel/trastuzumab/pertuzumab
- 4. TCH
- 5. TCHP
- 6. T-DM1
- 7. Other



Regulatory and reimbursement issues aside, what adjuvant systemic therapy would you recommend for a patient with an ER-negative, HER2-positive, node-negative IDC with the following characteristics?

Age: 80, Tumor size: 0.6 cm



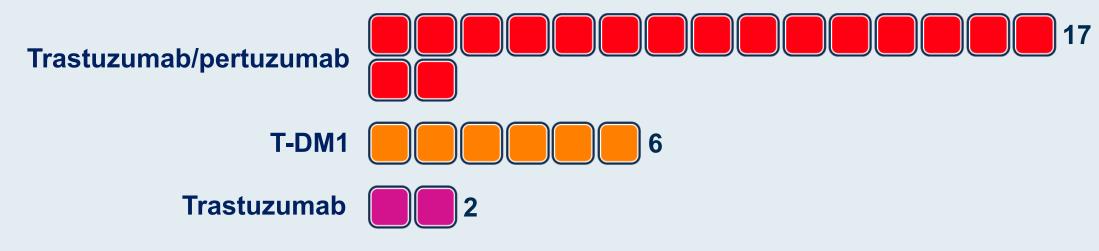
A 65-year-old woman presents with a 1.3-cm, <u>ER-positive</u>, HER2-positive IDC with <u>2 positive sentinel nodes</u>. Regulatory and reimbursement issues aside, what adjuvant anti-HER2 therapy would you recommend?

- 1. Trastuzumab
- 2. Trastuzumab/pertuzumab
- 3. T-DM1
- 4. Trastuzumab → neratinib
- 5. Trastuzumab/pertuzumab → neratinib
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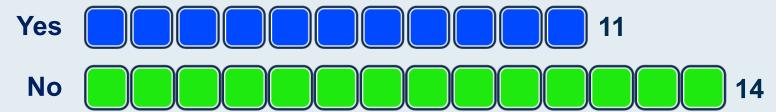


Regulatory and reimbursement issues aside, what adjuvant anti-HER2 therapy would you recommend for a 65-year-old patient with a 1.3-cm, HER2-positive IDC with the following characteristics?

ER-positive, 2 positive sentinel nodes



Postadjuvant neratinib?



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Case Presentation: A 43-year-old woman with ER/PR-negative, HER2-positive breast cancer with brain metastasis



Atif Hussein, MD, MMM

- 1/2016: Stage IIIC Grade 3 left, ER/PR-negative, HER2-positive IDC
 - S/p neoadjuvant TCH-P x 6 \rightarrow left MRM and ALND, adjuvant RT and trastuzumab (completed 2/2017)
 - 3/2018: Completed adjuvant neratinib study (ExteNET)
- 3/2019: Resection of 4-cm ER/PR-negative, HER2-positive left parietal mass → SBRT
 - CT chest/abdomen/pelvis and bone scan: Negative
- 4/2019: Capecitabine/lapatinib
- 7/2019 brain MRI: New left parietal lesion at previous site → second subtotal resection
- 10/2019: T-DM1
- 1/2020 brain MRI: Complete resolution of left parietal mass
- 12/2020: T-DM1 cycle 22. Brain MRIs, CT and bone scans No evidence of disease

Question

If this patient presented today post-neratinib, lapatinib and capecitabine, what treatment would you recommend – T-DM1, tucatinib, capecitabine/trastuzumab, other?

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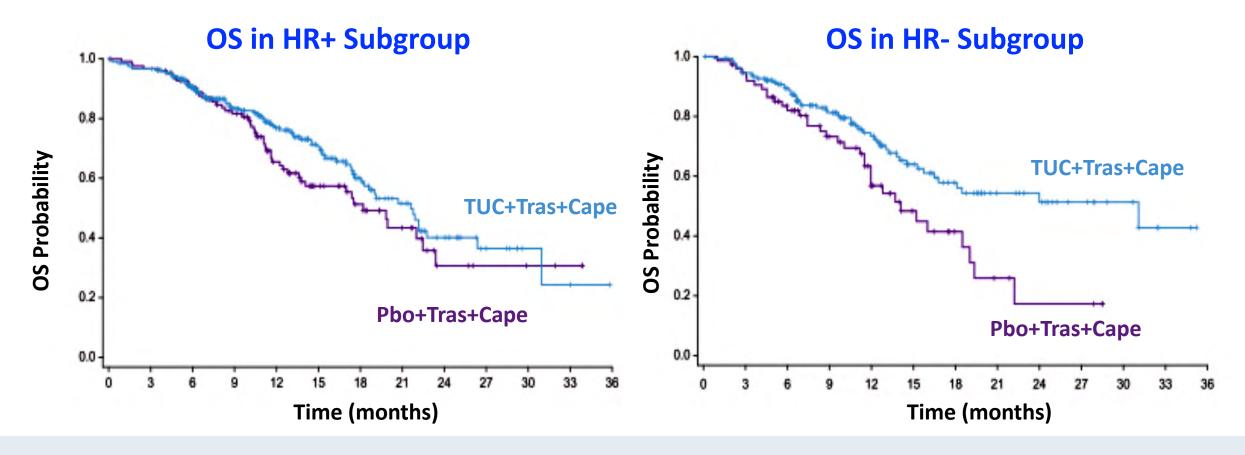
Tucatinib vs placebo in combination with trastuzumab and capecitabine for patients with locally advanced unresectable or HER2-positive metastatic breast cancer (HER2CLIMB): Outcomes by hormone receptor status

Hamilton E et al.



OS by HR Status in the Total Study Population

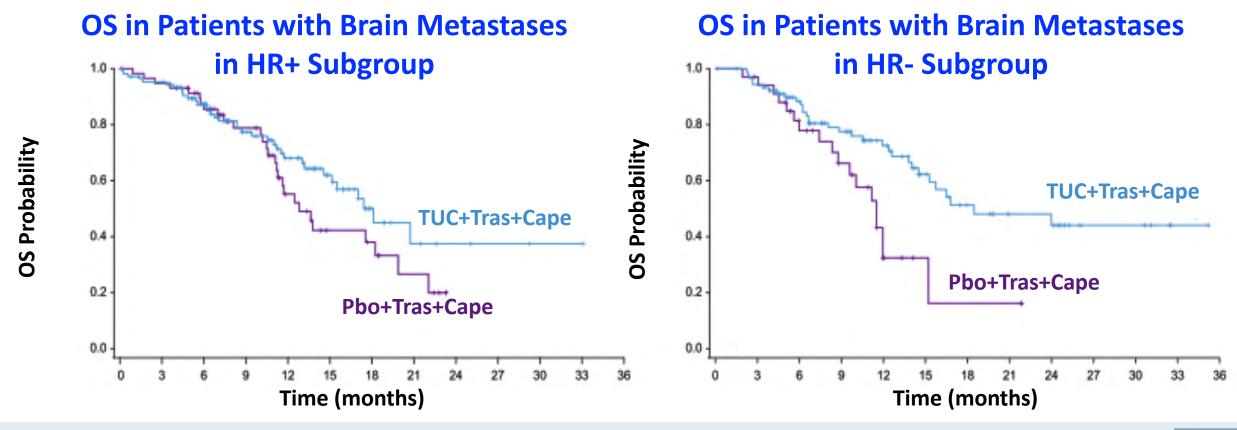
 Clinically meaningful improvement of OS was observed in patients on the tucatinib arm regardless of hormone receptor status.





OS by HR Status in Patients with Baseline Brain Metastases

 OS was numerically improved in patients with brain metastases in the tucatinib arm in both hormone receptor subgroups.



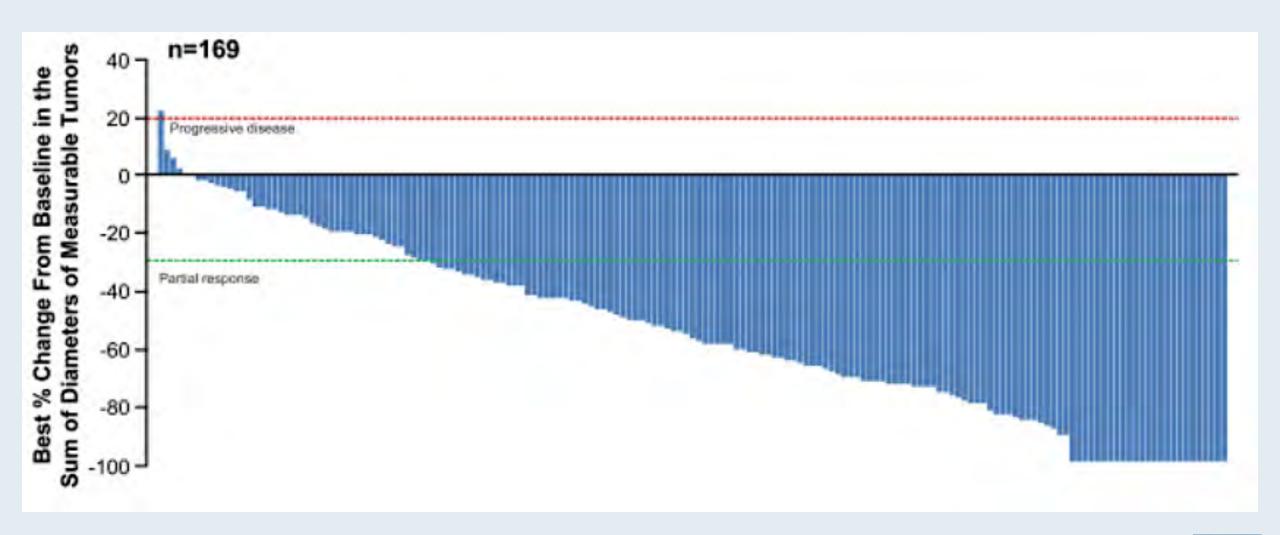


Updated results from DESTINY-Breast01, a phase 2 trial of trastuzumab deruxtecan (T-DXd) in HER2 positive metastatic breast cancer

Modi S et al.

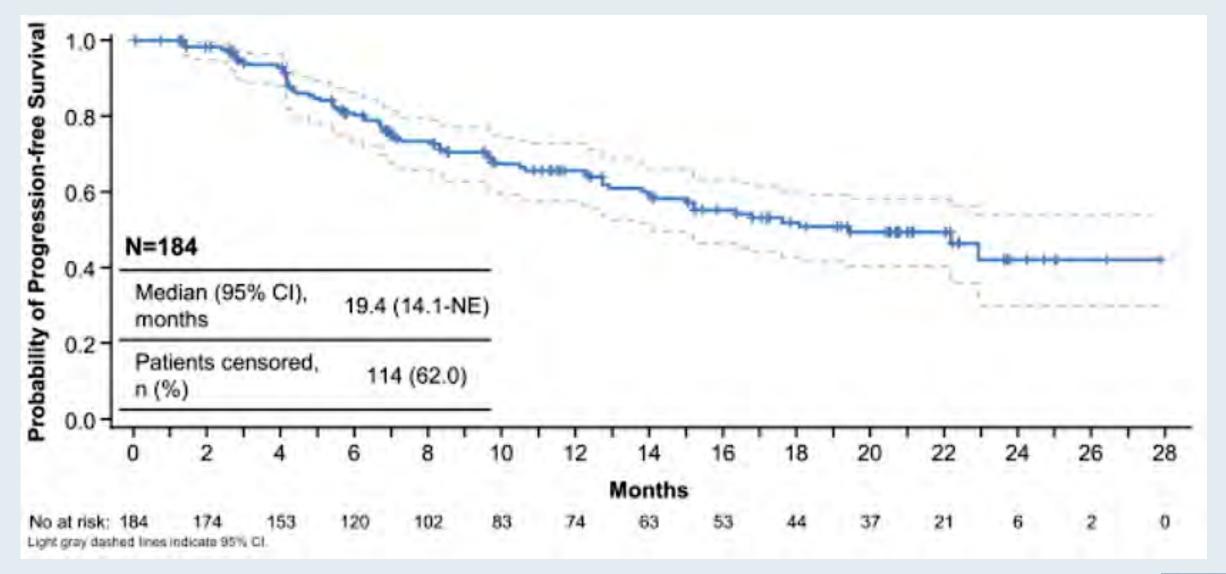


DESTINY-Breast01: Best Percentage Change in Tumor Size from Baseline



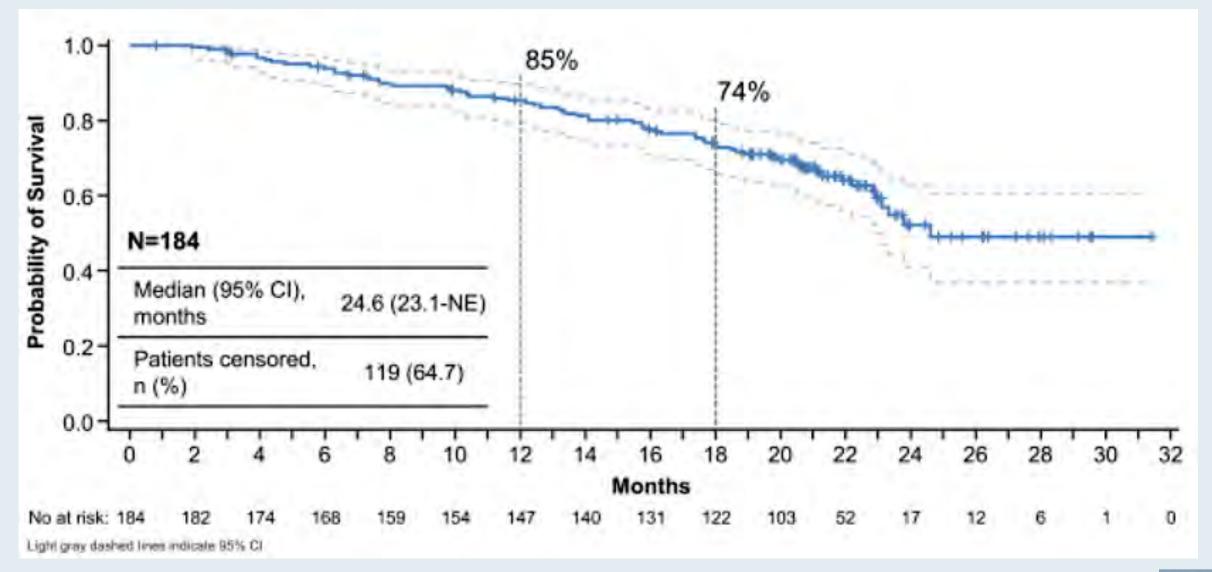


DESTINY-Breast01: Progression-Free Survival





DESTINY-Breast01: Overall Survival





Trastuzumab deruxtecan (T-DXd; DS-8201) with nivolumab in patients with HER2-expressing, advanced breast cancer: A 2-part, phase 1b, multicenter, open-label study

Hamilton E et al.



T-DXd with Nivolumab: Trial Schema

Part 1: Dose escalation Key eligibility criteria Part 2: Dose expansion 3+3+3 design HER2-expressing T-DXd 3.2 mg/kg q3w Cohort 1: HER2-positive (IHC 3+ or advanced/metastatic IHC 2+/ISH+) BC after T-DM1 breast or urothelial cancer n=29 Nivo 360 mg q3w $(n=4)^a$ ECOG PS 0-1 Cohort 2: HER2-low (IHC 1+ or IHC 2+/ISH-) BC after standard treatment ≥1 measurable lesion per n=16 RECIST 1.1 RDE T-DXd 5.4 mg/kg q3w Cohort 3: HER2-high expressing (IHC 2+/3+) UC after Ctx and IO naive No prior T-DXd or Nivo Nivo 360 mg q3w n≈30 (planned) (n=3)b Meets criteria for 1 of the Cohort 4: HER2-low (IHC 1+) UC 4 cohorts in part 2 after Ctx and IO naive n≈15 (planned)



A randomized, open-label, phase III trial of pertuzumab retreatment in HER2-positive, locally advanced/metastatic breast cancer patients previously treated with pertuzumab, trastuzumab, and chemotherapy: The Japan Breast Cancer Research Group-M05 (PRECIOUS) study

Yamamoto Y et al.

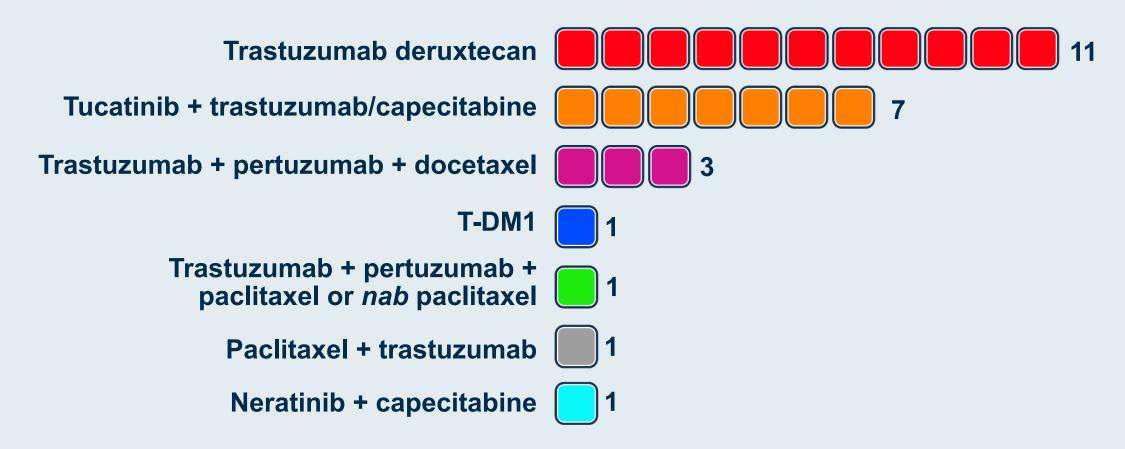


A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the liver <u>6 months</u> after completing neoadjuvant TCHP followed by <u>adjuvant T-DM1</u>. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

- 1. Trastuzumab/pertuzumab/docetaxel
- 2. T-DM1
- 3. Neratinib + paclitaxel
- 4. Neratinib + capecitabine
- 5. Tucatinib + trastuzumab/capecitabine
- 6. Trastuzumab deruxtecan
- 7. Trastuzumab + capecitabine
- 8. Other



A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the liver <u>6 months</u> after completing neoadjuvant TCHP followed by <u>adjuvant T-DM1</u>. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

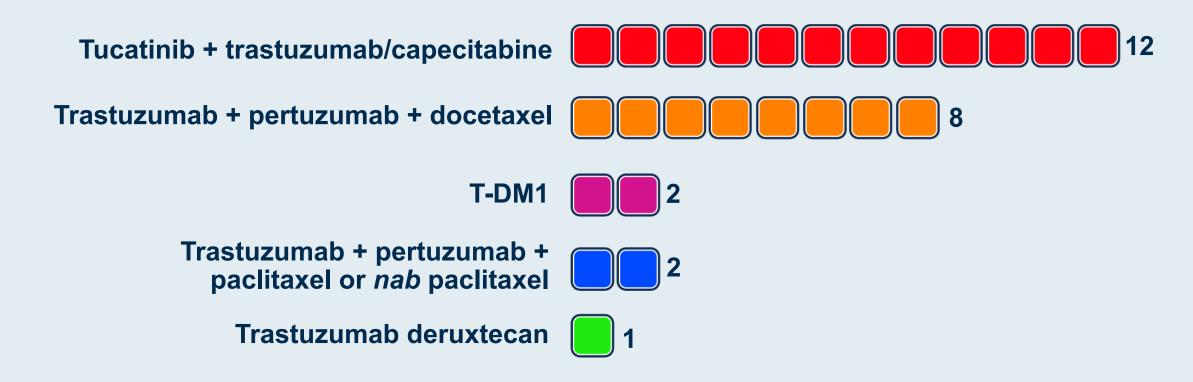


A 65-year-old woman with an ER-negative, HER2-positive IDC experiences disease recurrence in the <u>liver and brain</u> 18 months after completing neoadjuvant TCHP followed by <u>adjuvant</u> <u>trastuzumab/pertuzumab</u>. Regulatory and reimbursement issues aside, what systemic treatment would you recommend?

- 1. Trastuzumab/pertuzumab/docetaxel
- 2. T-DM1
- 3. Neratinib + paclitaxel
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Case Presentation: A 73-year-old woman with clinical T4 ER/PR-negative, HER2-positive breast cancer



Laurie Matt-Amaral, MD, MPH

- Presents with clinical T4 breast cancer whole breast involved with peau d'orange and lymphadenopathy
 - Patient suffered a fall, experienced soreness afterwards, delayed seeking medical attention
- Neoadjuvant taxane/platinum plus dual anti-HER2 therapy

Question

Which patients should be considered for post-neoadjuvant T-DM1 therapy?



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Case Presentation: A 36-year-old physician with ER/PR-negative, HER2-positive, node-positive breast cancer during pregnancy

- 5/2019: Diagnosed with right, ER/PR-negative, HER2-positive, node-positive IDC at 19 weeks pregnant with her second child
- 6/2019 9/2019: AC x 6
- 10/2019: Delivery of a healthy baby girl
- 10/2019 PET/CT: Disease in right breast and axilla but no distant metastases
- 10/2019 02/2020: Trastuzumab/pertuzumab/docetaxel/carboplatin x 6
- 3/2020: Right modified radical mastectomy, left prophylactic mastectomy
 - Residual disease: 7-mm IDC in right breast, 7/12 positive axillary nodes
 - Residual Cancer Burden: 3.753, Residual Cancer Burden Class: RCB-III
- 3/2020 3/2021: T-DM1

Question

- What is the safest treatment regimen to administer during pregnancy?
- Would you consider neratinib after completion of T-DM1?



Atif Hussein, MD, MMM



Year in Review — Clinical Investigators Provide Perspectives on the Most Relevant New Publications, Data Sets and Advances in Oncology: Targeted Therapy for Lung Cancer

Tuesday, January 26, 2021 5:00 PM - 6:00 PM ET

Faculty
Joel W Neal, MD, PhD
Paul K Paik, MD

Moderator Neil Love, MD



Thank you for joining us!

CME credit information will be emailed to each participant within 3 business days.

