



EPICS

Breast Cancer in 2024 and Beyond

April 12–13, 2024

Dallas, TX

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EPICS

VIRTUAL CLOSED-DOOR ROUNDTABLE



DATE:
April 12–13, 2024



**DISEASE-STATE AND
DATA PRESENTATIONS**
by key experts



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
breast cancer
> 9 from US



**BREAST CANCER-
SPECIFIC DISCUSSIONS** on
therapeutic advances and
their application in clinical
decision-making

Panel Consisting of 9 Breast Cancer Experts From the US



Mark Pegram, MD
Stanford University School of Medicine

Kelly McCann, MD, PhD
UCLA Medicine

Peter Beitsch, MD
Dallas Surgical Group

Adam Brufsky, MD, PhD
UPMC Hillman Cancer Center

Monica Fornier, MD
Memorial Sloan Kettering Cancer Center
(Day 2 only)

CHAIR
Joyce O'Shaughnessy, MD
Texas Oncology

William Sikov, MD
Women & Infants Hospital of Rhode Island

Peter A. Kaufman, MD
University of Vermont Cancer Center

Reshma Mahtani, DO
University of Miami Health System



Meeting Agenda Day 1

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Time (EST)	Topic	Presenter
2.00 PM – 2.10 PM	Welcome and Introductions	Joyce O'Shaughnessy, MD
2.10 PM – 2.25 PM	Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer	Peter Beitsch, MD
2.25 PM – 2.55 PM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
2.55 PM – 3.10 PM	Evolving Standards for Early-Stage HER2+ Breast Cancer	Mark Pegram, MD
3.10 PM – 3.40 PM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
3.40 PM – 3.55 PM	BREAK	
3.55 PM – 4.10 PM	Optimizing the Management of HER2+ mBC With Current and Emerging Agents	Adam Brufsky, MD, PhD
4.10 PM – 4.40 PM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
4.40 PM – 4.55 PM	HER2-Low Breast Cancer – Expanding the Spectrum of Targetability	Reshma Mahtani, DO
4.55 PM – 5.20 PM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
5.20 PM – 5.35 PM	Current and Future Prospects for High-Risk, Early-Stage, Triple-Negative Breast Cancer	William Sikov, MD
5.35 PM – 6.00 PM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
6.00 PM	Wrap-Up and Overview of Day 2 Activities	Joyce O'Shaughnessy, MD



Meeting Agenda Day 2

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Time (EST)	Topic	Presenter
8.00 AM – 8.05 AM	Introduction and Review Agenda for Day 2	Joyce O'Shaughnessy, MD
8.05 AM – 8.20 AM	Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer	Kelly McCann, MD, PhD
8.20 AM – 8.55 AM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
8.55 AM – 9.10 AM	Expanding Options for High-Risk HR+, HER2– Early Breast Cancer	Joyce O'Shaughnessy, MD
9.10 AM – 9.40 AM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
9.40 AM – 9.55 AM	BREAK	
9.55 AM – 10.10 AM	Evolving Paradigms in HR+, HER2– Metastatic Breast Cancer	Peter A. Kaufman, MD
10.10 AM – 10.55 AM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
10.55 AM – 11.05 AM	New Targets in Breast Cancer	Mark Pegram, MD
11.05 AM – 11.25 AM	Discussion and Key Takeaways	Moderator: Joyce O'Shaughnessy, MD
11.25 AM – 11.55 AM	General Discussion: Future Directions in Breast Cancer Treatment	Moderator: Joyce O'Shaughnessy, MD
11.55 AM – 12.00 PM	Conclusions and Wrap-Up	Joyce O'Shaughnessy, MD



EPICS

Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer



Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (1/3)

Presented by Peter Beitsch, MD

RISK ASSESSMENT IN HR+, HER2- EARLY BREAST CANCER

> For decision-making about adjuvant therapy for patients with

ASCO Adjuvant Biomarker Guidelines (2022)

STUDY POPULATION

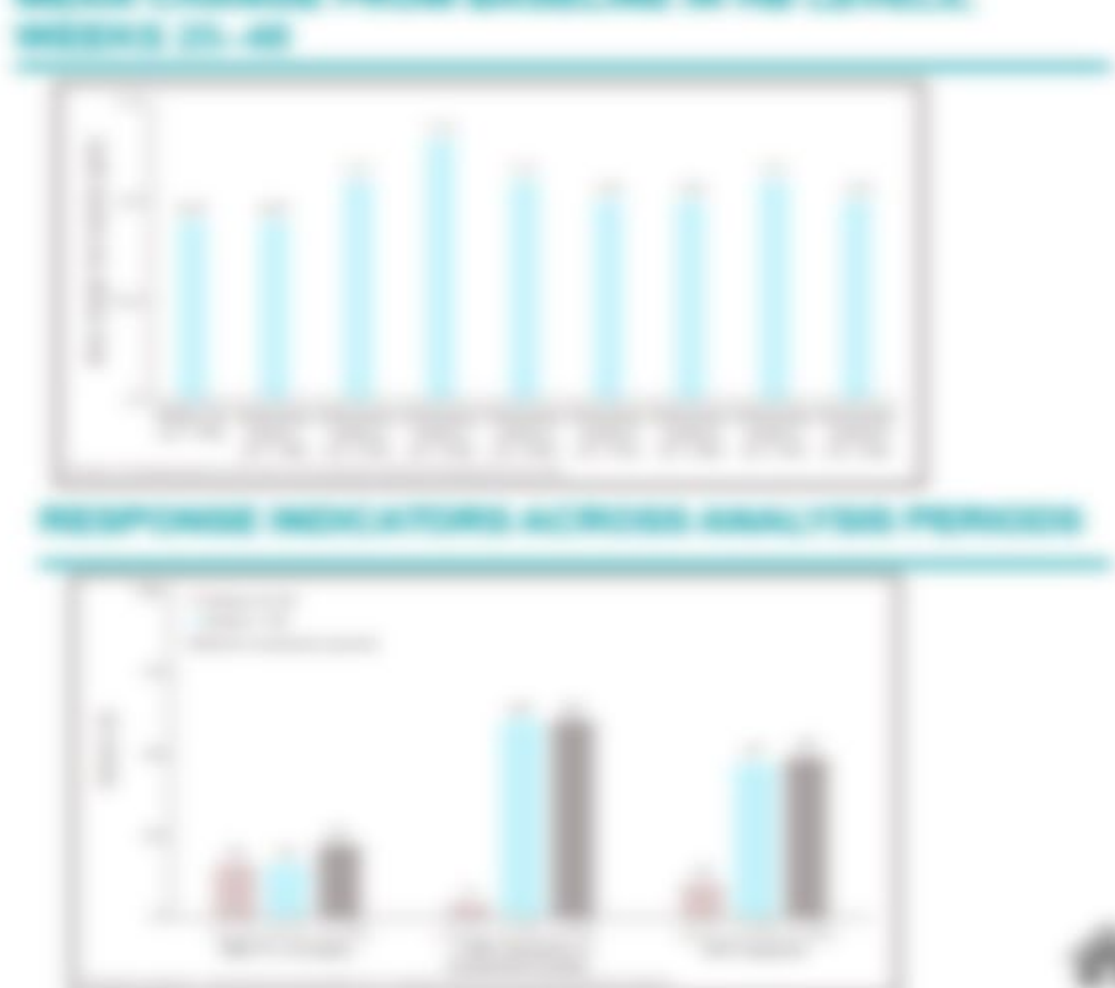
1. 10,000 patients with early-stage breast cancer, HR+, HER2-, node-negative, T1-T2, pN0-1, stage I-II, with a median age of 55 years. The population was divided into two groups: 5,000 patients with a median age of 55 years and 5,000 patients with a median age of 65 years. The population was further divided into two groups: 2,500 patients with a median age of 55 years and 2,500 patients with a median age of 65 years.

INTERVENTIONS

1. 5,000 patients with a median age of 55 years received tamoxifen. 5,000 patients with a median age of 65 years received tamoxifen.

KEY RESULTS

1. Tamoxifen significantly reduced the risk of breast cancer recurrence in both age groups.





Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (2/3)

Presented by Peter Beitsch, MD

ACTIONABLE BIOMARKERS IN BREAST CANCER

> The full spectrum of HER2 expression is now recognized as

PI3K Pathway and Selection Biomarkers





Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (3/3)

Presented by Peter Beitsch, MD

MRD TESTING IN BREAST CANCER

> Minimal/measurable residual disease (MRD)

Potential Uses for MRD Testing



EPICS

Key Insights

**Current and Emerging Biomarkers and
Testing Methodologies in Breast Cancer**

Experts Discussed Tools for Guiding Treatment in Early-Stage Breast Cancer

Supporting tools will help identify the optimal sequencing of agents.

- 1. Experts are still using a combination of the sequenced agent combination and traditional therapy, followed by TDMT, according to most patients.
- 2. Most experts are using traditional chemotherapy therapies, but will provide the sequenced agent to patients with evidence of drug resistance.
- 3. The sequenced agent may also be used in the neoadjuvant setting, before TDMT, in patients with documented drug resistance.
 - Provided a good assessment, experts are divided on whether they would normally use TDMT or traditional chemotherapy.
 - Results of the ongoing NCT01824501 trial comparing traditional chemotherapy to TDMT will help to clarify the optimal sequencing of these drugs.
- 4. Traditional chemotherapy and the sequenced agent may also be used earlier than starting in patients who were following treatment with traditional chemotherapy and TDMT in the neoadjuvant setting, but this represents a small fraction of patients.
- 5. Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 2 drug, versus what has been in the past).
- 6. The sequencing efficacy of traditional chemotherapy and the sequenced agent have varied after options, such as traditional chemotherapy combinations, venetoclax, and metformin, in the form of therapy.



Dr. [Name]
The goal is to use all of your [options] and use what you [know] in the case of [resistance] and [sequencing] in the adjuvant setting, but you [do not] want to [start] with [sequencing] if you [do not] have [evidence] of [drug resistance] to [start] with [sequencing] in [neoadjuvant] setting to [achieve] the [best] [possible] [outcome].

GERMLINE MUTATION TESTING

Testing for germline mutations will help identify the optimal sequencing of agents

- Experts are still using a combination of the sequenced agent combinations and pharmacokinetic testing, followed by TDM, according to most patients
- Most experts are using pharmacokinetic biomarker testing, but will provide the needed data for patients with evidence of drug resistance
- The needed data may also be used in the retrospective setting, before TDM, for patients with documented drug resistance
 - Providers in some scenarios, experts are divided on whether they would routinely use TDM or pharmacokinetic biomarker testing
 - Results of the ongoing 2017 HIV Research for Improving Treatment Biomarkers or TDM will help to clarify the optimal sequencing of these tests
- Pharmacokinetic biomarkers and the needed data may also be used earlier than testing in patients who were following treatment with combination, antiretroviral, and TDM in the retrospective setting, but this represents a small fraction of patients
- Patient preferences can also factor into the sequencing of these tests (slide 10, 11 slide 12, 13 slide 14, 15 slide 16)
- The improved efficacy of combination, antiretroviral, and the needed sequenced agent combinations, such as combination chemotherapy combinations, results, and sequencing, is one form of therapy



Dr. [Name]
[Blurred text describing the expert's role and findings related to germline mutation testing and treatment optimization.]

Experts Debated the Potential Role of MRD Testing in Breast Cancer

Experts will debate the optimal sequencing of agents

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Experts Speculated on Other Investigational Biomarker Assays

EPICS

HER2DX

Experts are still using a combination of the original immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) assays to test patients.

Most experts are using immunohistochemistry (IHC) assays, but will probably be testing IHC for patients with evidence of high expression.

The IHC assay may also be used in the metastatic setting, before FISH, for patients with documented high expression.

- 1. Provided a good assessment, experts are divided on whether they would currently use FISH or immunohistochemistry (IHC).
- 2. Results of the ongoing HER2DX (NCT01825001) trial comparing immunohistochemistry or FISH will help to clarify the optimal use of these assays.

Immunohistochemistry and the IHC assay may also be used earlier than testing in patients who were following treatment with immunohistochemistry and FISH in the metastatic setting, but this represents a small fraction of patients.

FISH assessment can also factor into the assessment of these two assays (eg, 2 drug vs 1 drug, versus dual vs one vs neither).

The improved efficacy of immunohistochemistry and the IHC assay have opened other options, such as immunohistochemistry combinations, serial, and sequential, in the use of therapy.



Dr. [Name]
The use of a combination of
IHC and FISH assays is the most
commonly used method of
assessing HER2 expression in
the metastatic setting. For use
in early-stage trials, IHC is
the preferred method, but FISH
may be used to confirm high
expression in patients with
IHC-positive results.
Immunohistochemistry



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Evolving Standards for Early-Stage HER2+ Breast Cancer



Evolving Standards for Early-Stage HER2+ Breast Cancer (1/2)

Presented by Mark Pegram, MD



CURRENT STANDARDS OF CARE

> Neoadjuvant chemotherapy with trastuzumab and pertuzumab is the

KATHERINE Second Interim OS Analysis

Timeline of FDA Approvals for HER2+ Breast Cancer

Year	2005	2006	2007	2008	2009	2010	2011
2005							
2006		2006					
2007			2007				
2008				2008			
2009					2009		
2010						2010	
2011							2011





Evolving Standards for Early-Stage HER2+ Breast Cancer (2/2)

Presented by Mark Pegram, MD



AREAS OF INVESTIGATION

> Key ongoing trials in the early-stage setting

CompassHER2 Trial Design

Timeline of FDA Approvals for HER2+ Breast Cancer

Year	2010	2011	2012	2013	2014	2015	2016
2010							
2011		2011					
2012			2012				
2013				2013			
2014					2014		
2015						2015	
2016							2016



EPICS

Key Insights

**Evolving Standards for Early-Stage HER2+
Breast Cancer**

Experts Discussed Current Practice Patterns in the Treatment of Early-Stage HER2+ Breast Cancer

Key Takeaways:

- 1. Trastuzumab is used in combination with epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) for early-stage HER2+ breast cancer.
- 2. Most experts use trastuzumab deuterium derivative (TDM) for patients with evidence of HER2 overexpression.
- 3. The trastuzumab deuterium derivative may also be used in the adjuvant setting, before TDM, for patients with overexpression of HER2.
- 4. Trastuzumab is used as a first-line treatment, and experts are divided on whether they would routinely use TDM in combination with trastuzumab.
- 5. Results of the ongoing HER2+ Breast Cancer Comparison Trastuzumab Deuterium vs TDM will help to clarify the optimal sequencing of these drugs.
- 6. Trastuzumab deuterium and the trastuzumab deuterium may also be used earlier than trastuzumab in patients who were following treatment with trastuzumab, pertuzumab, and TDM in the neoadjuvant setting, for the treatment of a small fraction of patients.
- 7. Trastuzumab deuterium can also be used in the sequencing of these two agents (eg, TDM first or TDM second) about half the time in practice.
- 8. The comparative efficacy of trastuzumab deuterium and the trastuzumab deuterium have not been fully evaluated, such as trastuzumab deuterium combination, overall, and sequencing, in the use of therapy.



Dr. [Name]
The use of trastuzumab deuterium and the trastuzumab deuterium in the adjuvant setting, for patients with evidence of HER2 overexpression, is a key topic in the current practice patterns in the treatment of early-stage HER2+ breast cancer. The use of trastuzumab deuterium and the trastuzumab deuterium in the adjuvant setting, for patients with evidence of HER2 overexpression, is a key topic in the current practice patterns in the treatment of early-stage HER2+ breast cancer.

Experts Considered the Challenge of Selecting Patients for De-escalated Adjuvant Therapy

Experts will also consider the optimal sequencing of agents.

- Experts are still using a combination of the regimen of breast-conserving surgery and endocrine therapy, followed by TDMT, primarily for most patients.
- Most experts are using endocrine-based adjuvant therapy, but will consider the limited data for patients with evidence of local recurrence.
- The limited data may also be used in the adjuvant setting, before TDMT, for patients with documented local recurrence.
 - Provided a good assessment, experts are divided on whether they would consider use of TDMT in endocrine-based therapy.
 - Results of the ongoing BC19 (NCT01800001) comparing endocrine-based therapy to TDMT will help to clarify the optimal sequencing of these agents.
- Endocrine-based therapy and the limited data may also be used earlier than intended in patients who were following treatment with endocrine-based therapy and TDMT in the neoadjuvant setting, but this represents a small fraction of patients.
- Future endocrine use also looks into the sequencing of these two agents (eg, 1 drug or 2 drug, versus what has been in practice).
- The sequencing efficacy of endocrine-based therapy and the limited regimen have varied after surgery, such as endocrine-based chemotherapy combinations, surgery, and sequencing, in the form of therapy.



Dr. [Name]
[Faded text describing the expert's role and the content of their presentation, including mentions of 'adjuvant therapy' and 'sequencing'.]



Experts Discussed Current Challenges and Unmet Needs in Managing Early-Stage HER2+ Breast Cancer

Key takeaways from the discussion include:

- The current standard of care for early-stage HER2+ breast cancer is a combination of trastuzumab, pertuzumab, and docetaxel, followed by TDM1. However, the need for better outcomes is driving the search for new therapies.
- The combination of trastuzumab, pertuzumab, and docetaxel is the current standard of care, but it is not clear if this combination is the best for all patients.
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Dr. [Name]
[Title]
[Affiliation]
[Institution]

Dr. [Name] discussed the current challenges and unmet needs in managing early-stage HER2+ breast cancer. He highlighted the importance of patient-centered care and the need for more personalized treatment options. He also discussed the role of clinical trials in advancing the field and the need for better outcomes for patients.

Experts Speculated About Future Changes to Treatment Patterns for Early-Stage HER2+ Breast Cancer

Experts are still using a combination of the regimen of trastuzumab plus endocrine and chemotherapy therapy, followed by TDM1, according to most patients.

Most experts are using trastuzumab dectabine therapy, but will probably be looking again for patients with evidence of local recurrence.

The standard of care may also be used in the adjuvant setting, before TDM1, for patients with recurrent local recurrence.

- 1. Trastuzumab is used intravenously, experts are divided on whether they would normally use TDM1 or trastuzumab dectabine therapy.
- 2. Results of the ongoing HER2+ Breast Cancer Comparing Trastuzumab Dectabine vs TDM1 will help to clarify the optimal sequencing of these drugs.

Trastuzumab dectabine and the standard of care may also be used earlier than standard in patients who were following treatment with trastuzumab, endocrine, and TDM1 in the neoadjuvant setting, but this represents a small fraction of patients.

Trastuzumab dectabine can also be used in the neoadjuvant setting, but this represents a small fraction of patients.

The neoadjuvant efficacy of trastuzumab dectabine and the standard regimen have proven other options, such as trastuzumab chemotherapy combinations, endocrine, and immunotherapy, is also being explored.



Dr. [Name]
The standard of care of trastuzumab plus endocrine and chemotherapy therapy is the mainstay of treatment for early-stage HER2+ breast cancer. In the adjuvant setting, trastuzumab plus endocrine and chemotherapy therapy is the standard of care. In the neoadjuvant setting, trastuzumab plus endocrine and chemotherapy therapy is also used. The results of the ongoing HER2+ Breast Cancer Comparing Trastuzumab Dectabine vs TDM1 will help to clarify the optimal sequencing of these drugs.



EPICS

Optimizing the Management of HER2+ mBC With Current and Emerging Agents



Optimizing the Management of HER2+ mBC With Current and Emerging Agents (1/3)

Presented by Adam Brufsky, MD, PhD

CURRENT ALGORITHM

> A CI FOPATRA-like regimen (taxane +

NCCN Guidelines V4.2023





Optimizing the Management of HER2+ mBC With Current and Emerging Agents (2/3)

Presented by Adam Brufsky, MD, PhD

EMERGING DATA

> The HER2CLIMB02 trial compared T-DM1 + tucatinib in

HER2CLIMB-02: PFS





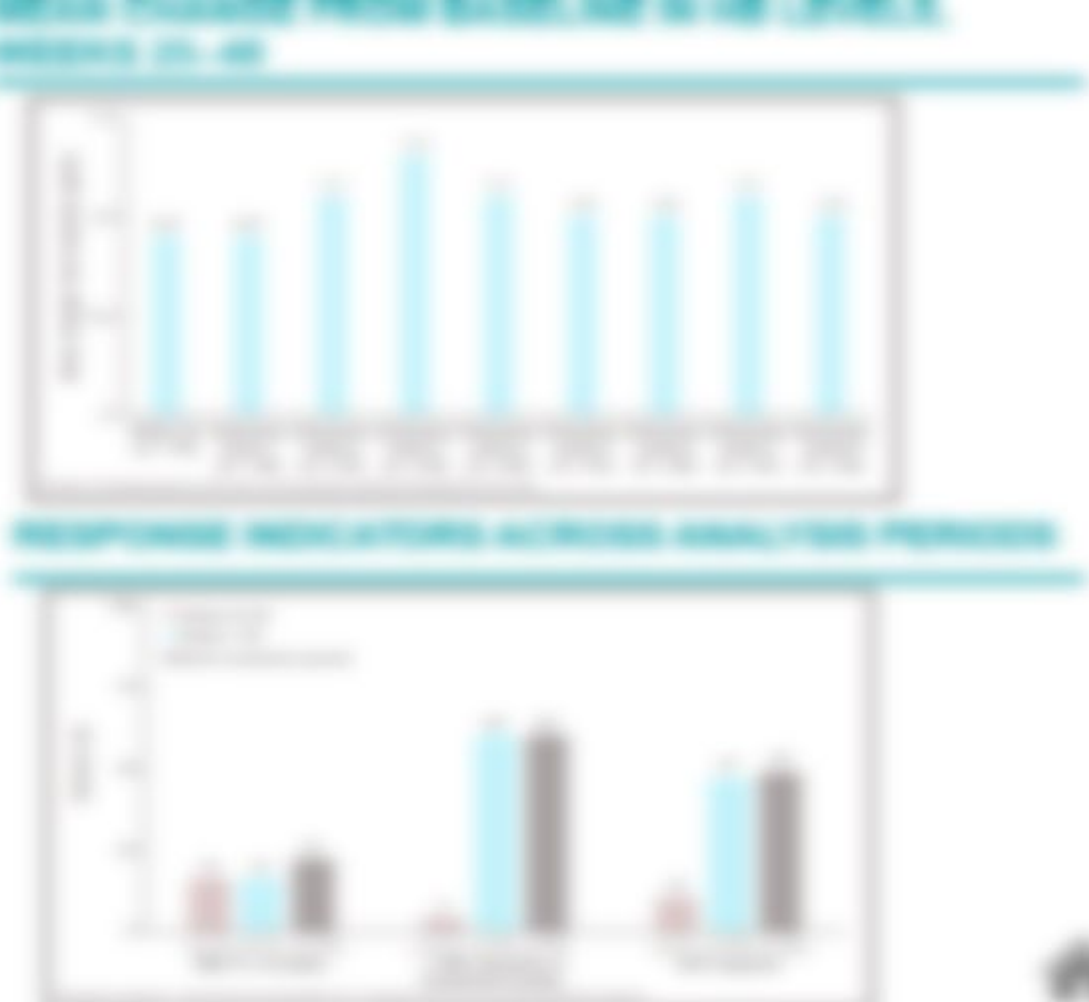
Optimizing the Management of HER2+ mBC With Current and Emerging Agents (3/3)

Presented by Adam Brufsky, MD, PhD

ONGOING TRIALS

> DESTINY-Breast09 is comparing first-line treatment with

DESTINY-Breast09 Trial Design



EPICS

Key Insights

**Optimizing the Management of HER2+ mBC
With Current and Emerging Agents**

Experts Speculated on a Potential Role for T-DXd in the First-Line Setting

Experts are still using a combination of the regimen of trastuzumab plus pertuzumab and docetaxel, followed by T-DXd, according to most patients.

Other experts are using trastuzumab deruxtecan, but will probably be looking back to patients with evidence of brain metastases.

The trastuzumab regimen may also be used in the second-line setting, before T-DXd, in patients with documented brain metastases.

- Provided a good response, experts are divided on whether they would normally use T-DXd in trastuzumab deruxtecan therapy.
- Results of the ongoing HER2CLM3 breast cancer comparing trastuzumab deruxtecan to T-DXd will help to clarify the optimal sequencing of these drugs.

Trastuzumab deruxtecan and the trastuzumab regimen may also be used earlier than described in patients who were following treatment with trastuzumab, pertuzumab, and T-DXd in the second-line setting, but this represents a small fraction of patients.

Trastuzumab can also factor into the sequencing of these two agents (eg, 2 drugs or 1 drug, versus what has been in practice).

The sequencing efficacy of trastuzumab deruxtecan and the trastuzumab regimen have proven other options, such as trastuzumab chemotherapy combinations, capecitabine, and lapatinib, in late lines of therapy.



Dr. [Name]
The expert is an expert in breast cancer and is currently a professor at the University of [Name]. He has been a member of the American Society of Clinical Oncology (ASCO) and the European Society of Medical Oncology (ESMO) for many years. He has also been a member of the National Cancer Institute (NCI) and the National Institutes of Health (NIH). He has published numerous articles in the field of breast cancer and has been involved in several clinical trials. He is currently a member of the Breast International Group (BIG) and the International Breast Cancer Trialists' Collaborative Group (IBCTC).



Experts Debated Management and Potential Prevention of HER2+ Brain Metastases

Experts will discuss the optimal sequencing of agents

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Experts Discussed Unmet Needs and Future Directions in the Treatment of HER2+ mBC (1/2)

Experts will discuss the unmet needs of patients with HER2+ mBC and the current standard of care. The discussion will focus on the need for more effective treatments, particularly in the setting of resistance to trastuzumab and pertuzumab. The discussion will also address the need for more effective treatments in the setting of resistance to trastuzumab and pertuzumab. The discussion will also address the need for more effective treatments in the setting of resistance to trastuzumab and pertuzumab. The discussion will also address the need for more effective treatments in the setting of resistance to trastuzumab and pertuzumab.



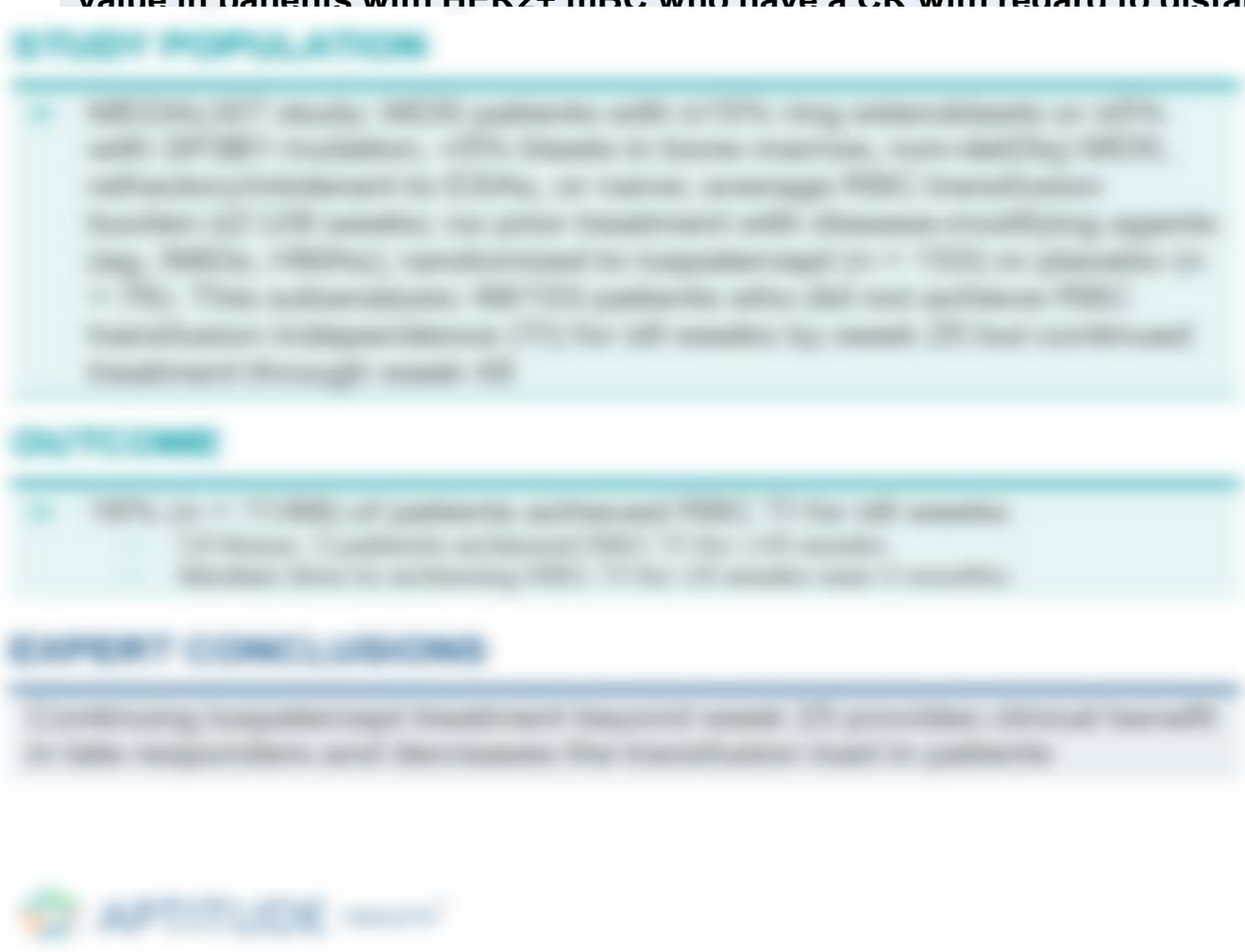
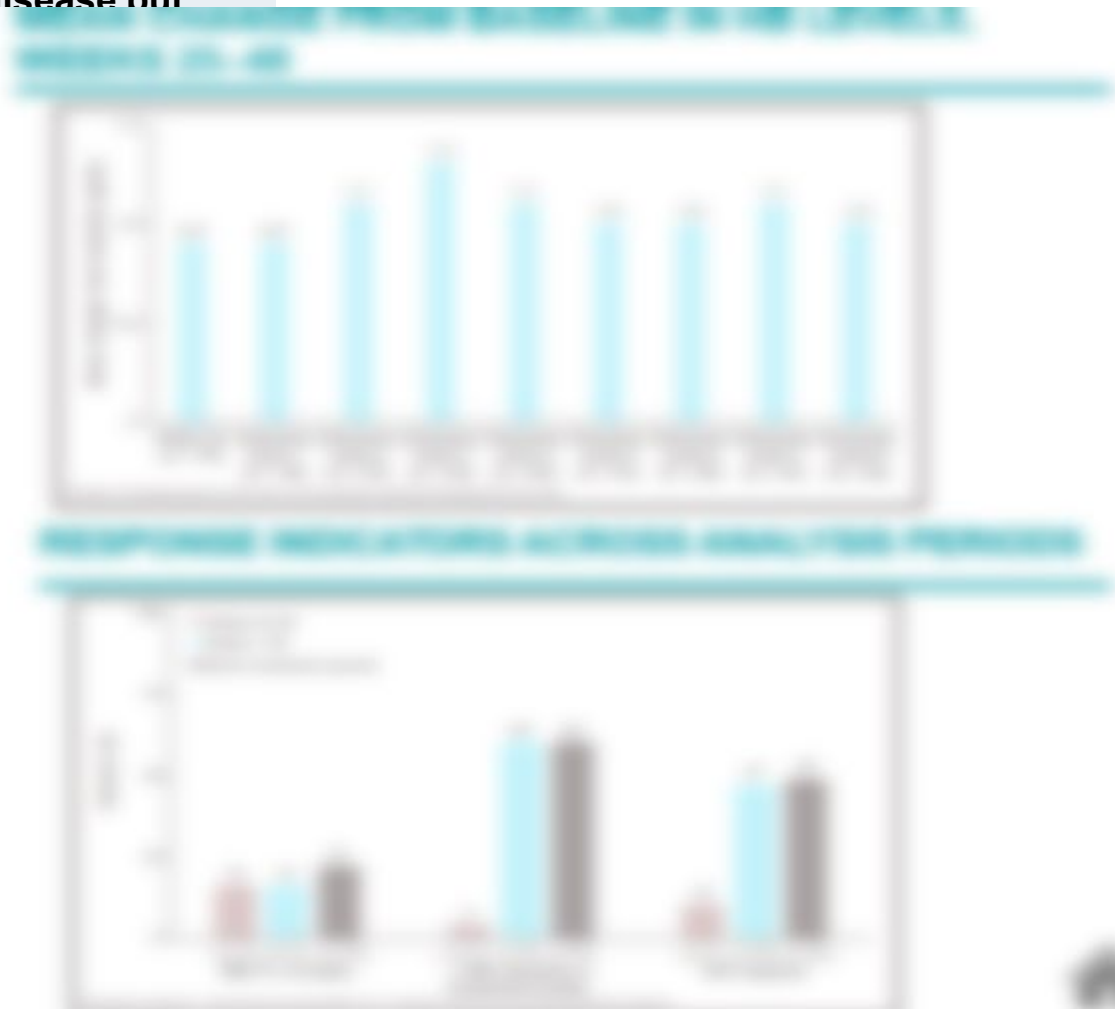
Dr. [Name]
[Title]
[Affiliation]
[Institution]

Experts Discussed Unmet Needs and Future Directions in the Treatment of HER2+ mBC (2/2)

LOCALIZED THERAPIES

Experts suggested it would be worthwhile to investigate whether mastectomy is of value in patients with HER2+ mBC who have a CR with regard to distant disease but

ZW49: Bispecific HER2 ADC



EPICS

HER2-Low Breast Cancer – Expanding the Spectrum of Targetability



HER2-Low Breast Cancer – Expanding the Spectrum of Targetability (1/3)

Presented by Reshma Mahtani, DO

HER2 CLASSIFICATION PARADIGMS

> The development of more-potent HER2-targeted ADCs

HER2 TESTING AND CLASSIFICATION

STUDY POPULATION

HER2-low breast cancer patients with a HER2 expression level of 1+ or 2+ on immunohistochemistry (IHC) or a HER2 gene amplification level of 1.0 or less on fluorescence in situ hybridization (FISH). The study population included patients who had not received prior systemic anticancer therapy for breast cancer.

DESIGN

A phase II, randomized, controlled trial comparing the efficacy and safety of trastuzumab emtansine (T-DM1) versus trastuzumab in patients with HER2-low breast cancer.

KEY CONCLUSIONS

T-DM1 demonstrated superior efficacy compared to trastuzumab in patients with HER2-low breast cancer, including overall survival and progression-free survival.





HER2-Low Breast Cancer – Expanding the Spectrum of Targetability (2/3)

Presented by Reshma Mahtani, DO

ADCs IN HER2-LOW mBC

> DESTINY-Breast04 results showed a significant

DESTINY-Breast04: Updated OS Analysis





HER2-Low Breast Cancer – Expanding the Spectrum of Targetability (3/3)

Presented by Reshma Mahtani, DO

ONGOING TRIALS AND AREAS OF INVESTIGATION

> DESTINY-Breast06 is comparing T-DXd vs TPC

DESTINY-Breast06 Trial Design



RESPONSE RATES AND CLINICAL BENEFIT



EPICS

Key Insights

HER2-Low Breast Cancer – Expanding the Spectrum of Targetability

Experts Discussed Sequencing ADCs in HER2-Low mBC

SEQUENCING CONSIDERATIONS

Sequencing considerations will vary greatly by patient population of agents

- 1. Trastuzumab and lapatinib are used in the adjuvant setting in breast cancer patients and metastatic disease, followed by TDM1 maintenance in most patients
- 2. Most experts are using trastuzumab deruxtecan (TDXD) but will provide the second-line option for patients with evidence of prior resistance
- 3. The second-line option may also be used in the metastatic setting before TDM1 in patients with documented prior resistance
 - Provided a good performance, experts are divided on whether they would typically use TDM1 or trastuzumab deruxtecan
 - Results of the ongoing HER2-Low Breast Cancer Sequencing Trastuzumab Deruxtecan vs TDM1 will help to clarify the optimal sequencing of these ADCs
- 4. Trastuzumab deruxtecan and the second-line option may also be used earlier than intended in patients who were following treatment with trastuzumab, pertuzumab, and TDM1 in the metastatic setting, but this represents a small fraction of patients
- 5. Patient performance can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in practice)
- 6. The sequencing efficacy of trastuzumab deruxtecan and the second-line option have varied after options, such as trastuzumab chemotherapy combinations, capecitabine, and metformin, in late lines of therapy



Dr. [Name]
The second-line option of trastuzumab deruxtecan is a great option in the metastatic setting, but we have to make sure that we have good data that the drug works with a standard of care. We need to have multiple options to address the TDM1 - agent, versus drug, combination.



Experts Considered Ongoing Trials and Investigational Strategies for HER2-Low Breast Cancers

Experts will discuss the optimal sequencing of agents...

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Experts will discuss the optimal sequencing of agents...

Experts Discussed Biomarkers and Patient Selection

HER2 ASSESSMENT BY IHC

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Experts will discuss the optimal sequencing of agents

Experts will discuss the optimal sequencing of agents

Experts Speculated on Mechanisms of Resistance to ADCs

RESISTANCE TO T-DXd

Experts are still using a combination of the regimen of trastuzumab and pertuzumab, followed by T-DXd, according to most patients.

Most experts are using trastuzumab deruxtecan therapy, but will probably be looking for patients with evidence of trastuzumab resistance.

The trastuzumab regimen may also be used in the maintenance setting, before T-DXd, in patients with trastuzumab trastuzumab resistance.

- Proposed to use trastuzumab, experts are divided on whether they would normally use T-DXd in trastuzumab deruxtecan therapy.
- Results of the ongoing HER2-DM1-DM2 trial comparing trastuzumab deruxtecan to T-DXd will help to clarify the optimal sequencing of these drugs.

Trastuzumab deruxtecan and the trastuzumab regimen may also be used earlier than trastuzumab in patients who were following treatment with trastuzumab, pertuzumab, and T-DXd in the maintenance setting, but this represents a small fraction of patients.

Trastuzumab deruxtecan may also factor into the sequencing of these two agents by 2 drugs in 1 drug, versus about half use in trastuzumab.

The sequential efficacy of trastuzumab deruxtecan and the trastuzumab regimen have varied after patients, such as trastuzumab chemotherapy combinations, trastuzumab, and trastuzumab, in the form of therapy.



Dr. [Name]
[Title]
[Affiliation]
[Contact Info]

EPICS

**Current and Future Prospects
for High-Risk, Early-Stage,
Triple-Negative Breast Cancer**



Current and Future Prospects for High-Risk, Early-Stage, Triple-Negative Breast Cancer (1/3)

Presented by William Sikov, MD

IMMUNOTHERAPY FOR EARLY-STAGE DISEASE

> Updated analysis of KEYNOTE-522 with 63-month follow-up

KEYNOTE-522: EFS

KEYNOTE-522: EFS



KEYNOTE-522: OS





Current and Future Prospects for High-Risk, Early-Stage, Triple-Negative Breast Cancer (2/3)

Presented by William Sikov, MD

CHEMOTHERAPY AND TARGETED THERAPY

> Trials have investigated escalating and de-escalating

Brightness: EFS





Current and Future Prospects for High-Risk, Early-Stage, Triple-Negative Breast Cancer (3/3)

Presented by William Sikov, MD

ONGOING TRIALS FOR EARLY-STAGE TNBC

> The GeparDouze/NSABP B-59 trial is evaluating neoadjuvant

OptimICE-pCR: Trial Design



EPICS

Key Insights

**Current and Future Prospects for High-Risk,
Early-Stage, Triple-Negative Breast Cancer**

Experts Discussed Considerations Regarding Use of the KEYNOTE-522 Regimen

Keynote-522 will help clarify the optimal sequencing of agents

- 1. Experts are still using a combination of the regimen of pembrolizumab and ipilimumab followed by TDM1, however, for most patients
- 2. Most experts are using pembrolizumab monotherapy, but will provide the second cycle to patients with evidence of tumor regression
- 3. The second cycle may also be used in the maintenance setting, before TDM1, for patients with documented tumor regression
 - Provided a good performance, experts are divided on whether they would consider use TDM1 or pembrolizumab monotherapy
 - Results of the ongoing IMpower133 trial comparing pembrolizumab monotherapy or TDM1 will help to clarify the optimal sequencing of these agents
- 4. Pembrolizumab monotherapy and the second cycle may also be used earlier than starting a patient who were following treatment with pembrolizumab, ipilimumab, and TDM1 in the maintenance setting, but this represents a small fraction of patients
- 5. Patient performance can also factor into the sequencing of these two agents (eg. 1 drug vs 2 drug, overall health, etc.)
- 6. The sequential efficacy of pembrolizumab monotherapy and the second regimen have proven other options, such as pembrolizumab chemotherapy combination, nivolumab, and ipilimumab, in this line of therapy



Keynote-522 will help clarify the optimal sequencing of agents

Experts are still using a combination of the regimen of pembrolizumab and ipilimumab followed by TDM1, however, for most patients

Most experts are using pembrolizumab monotherapy, but will provide the second cycle to patients with evidence of tumor regression

The second cycle may also be used in the maintenance setting, before TDM1, for patients with documented tumor regression

Provided a good performance, experts are divided on whether they would consider use TDM1 or pembrolizumab monotherapy

Results of the ongoing IMpower133 trial comparing pembrolizumab monotherapy or TDM1 will help to clarify the optimal sequencing of these agents

Pembrolizumab monotherapy and the second cycle may also be used earlier than starting a patient who were following treatment with pembrolizumab, ipilimumab, and TDM1 in the maintenance setting, but this represents a small fraction of patients

Patient performance can also factor into the sequencing of these two agents (eg. 1 drug vs 2 drug, overall health, etc.)

The sequential efficacy of pembrolizumab monotherapy and the second regimen have proven other options, such as pembrolizumab chemotherapy combination, nivolumab, and ipilimumab, in this line of therapy



Experts Discussed Options for Further Escalation in Patients With Very-High-Risk TNBC or Residual Disease After Surgery

Experts discussed options for further escalation in patients with very-high-risk TNBC or residual disease after surgery.

- The experts discussed the use of immunotherapy, including pembrolizumab, in combination with chemotherapy, as a potential option for further escalation in patients with very-high-risk TNBC or residual disease after surgery.
- The experts also discussed the use of targeted therapy, such as trastuzumab, in combination with chemotherapy, as a potential option for further escalation in patients with very-high-risk TNBC or residual disease after surgery.
- The experts also discussed the use of radiation therapy, such as stereotactic body radiotherapy (SBRT), as a potential option for further escalation in patients with very-high-risk TNBC or residual disease after surgery.
- The experts also discussed the use of surgery, such as mastectomy, as a potential option for further escalation in patients with very-high-risk TNBC or residual disease after surgery.



Dr. [Name]
[Title]
[Affiliation]

Dr. [Name] discussed the use of immunotherapy, including pembrolizumab, in combination with chemotherapy, as a potential option for further escalation in patients with very-high-risk TNBC or residual disease after surgery.

Experts Discussed the Need for Better Biomarkers to Individualize Treatment for Early-Stage TNBC

Experts discussed the need for better biomarkers to individualize treatment for early-stage TNBC. The discussion focused on the importance of identifying biomarkers that can predict response to treatment and guide the selection of the most appropriate therapy for each patient. Key points discussed include:

- The need for biomarkers that can identify patients who will benefit from specific treatments, such as immunotherapy, targeted therapy, and chemotherapy.
- The importance of understanding the underlying biology of TNBC and how it varies among different subtypes of the disease.
- The need for more comprehensive biomarker testing, including genomic, proteomic, and transcriptomic analysis.
- The importance of validating biomarkers in large, prospective clinical trials to ensure their reliability and clinical utility.
- The need for better communication and collaboration between clinicians, researchers, and patients to advance the field of precision oncology for TNBC.



Panelists discussed the need for better biomarkers to individualize treatment for early-stage TNBC. The discussion focused on the importance of identifying biomarkers that can predict response to treatment and guide the selection of the most appropriate therapy for each patient. Key points discussed include:

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- The importance of validating biomarkers in large, prospective clinical trials to ensure their reliability and clinical utility.
- The need for better communication and collaboration between clinicians, researchers, and patients to advance the field of precision oncology for TNBC.

EPICS

Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer



Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (1/3)

Presented by Kelly McCann, MD, PhD

TNBC SUBTYPES

> TNBC is composed of a heterogeneous variety of subtypes

Lehmann Model





Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (2/3)

Presented by Kelly McCann, MD, PhD

CURRENT TREATMENT OPTIONS

> Chemotherapy + pembrolizumab is recommended first line for

ASCENT: Overall Survival





Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer (3/3)

Presented by Kelly McCann, MD, PhD

INVESTIGATIONAL STRATEGIES

> Ongoing studies are evaluating PARPi in combination with

ROR1 and Drug Efflux Pump Modulation



EPICS

Key Insights

**Current and Investigational Approaches in
Metastatic Triple-Negative Breast Cancer**

Experts Discussed the Use of Immune Checkpoint Inhibitors and PARP Inhibitors in mTNBC

Experts will discuss the optimal sequencing of agents

- 1. Experts will discuss the optimal sequencing of agents
- 2. Experts will discuss the use of immune checkpoint inhibitors and PARP inhibitors, followed by TDM1, in early-stage trials
- 3. Experts will discuss the use of immune checkpoint inhibitors, but will provide the limited data for patients with evidence of prior metastases
- 4. The limited data may also be used in the metastatic setting, before TDM1, in patients with recurrent prior metastases
 - 1. Provided a good response, experts are divided on whether they would consider use of TDM1 in metastatic disease
 - 2. Results of the ongoing IMBR150 trial comparing trastuzumab monotherapy to TDM1 will help to clarify the optimal sequencing of these drugs
- 5. Trastuzumab monotherapy and the limited data may also be used earlier than starting in patients who were following treatment with trastuzumab, pertuzumab, and TDM1 in the metastatic setting, but this represents a small fraction of patients
- 6. Future studies will also focus on the sequencing of these two agents (eg, 1 drug or 2 drug, versus what has been in practice)
- 7. The sequencing efficacy of trastuzumab monotherapy and the limited data have opened other options, such as trastuzumab chemotherapy combinations, venetoclax, and metformin, in late-line therapy



Dr. [Name]
[Blurred text]



Experts Discussed the Use of ADCs in mTNBC

ADC SELECTION

Experts will discuss the optimal sequencing of agents

- 1. Experts will discuss the optimal sequencing of agents in the treatment of mTNBC, including the use of ADCs, chemotherapy, and immunotherapy, followed by TDMT, as well as the use of ADCs in the treatment of mTNBC.
- 2. Experts will discuss the use of ADCs in the treatment of mTNBC, including the use of ADCs in the treatment of mTNBC.
- 3. The use of ADCs in the treatment of mTNBC will be discussed, including the use of ADCs in the treatment of mTNBC.
- 4. The use of ADCs in the treatment of mTNBC will be discussed, including the use of ADCs in the treatment of mTNBC.
- 5. The use of ADCs in the treatment of mTNBC will be discussed, including the use of ADCs in the treatment of mTNBC.
- 6. The use of ADCs in the treatment of mTNBC will be discussed, including the use of ADCs in the treatment of mTNBC.
- 7. The use of ADCs in the treatment of mTNBC will be discussed, including the use of ADCs in the treatment of mTNBC.
- 8. The use of ADCs in the treatment of mTNBC will be discussed, including the use of ADCs in the treatment of mTNBC.
- 9. The use of ADCs in the treatment of mTNBC will be discussed, including the use of ADCs in the treatment of mTNBC.
- 10. The use of ADCs in the treatment of mTNBC will be discussed, including the use of ADCs in the treatment of mTNBC.



Dr. [Name]
[Title]
[Institution]

[Blurred text]

Experts Speculated on the Outcomes and Implications of Ongoing Trials for mTNBC

Experts are still using a combination of the regimen of docetaxel plus trastuzumab and epirubicin, followed by TDM1, according to most patients.

Other experts are using trastuzumab deruxtecan, but will probably be looking again for patients with evidence of brain metastases.

The standard regimen may also be used in the neoadjuvant setting, before TDM1, for patients with documented brain metastases.

- Provided a good experience, experts are divided on whether they would currently use TDM1 in trastuzumab deruxtecan therapy.
- Results of the ongoing IMBR15 (trastuzumab deruxtecan vs trastuzumab deruxtecan + TDM1) will help to clarify the optimal sequencing of these drugs.

Trastuzumab deruxtecan and the standard regimen may also be used earlier than starting in patients who were following treatment with trastuzumab, epirubicin, and TDM1 in the neoadjuvant setting, but this represents a small fraction of patients.

Future publications can also focus on the sequencing of these two agents (eg, 1 drug or 1 drug, versus about how long to continue).

The comparative efficacy of trastuzumab deruxtecan and the standard regimen have opened other options, such as trastuzumab chemotherapy combinations, venetoclax, and metformin, in late lines of therapy.



Dr. [Name]
The expert is an expert in breast cancer and is currently a professor at the University of [Name]. He has been involved in the design and implementation of clinical trials in the area of breast cancer, including the IMBR15 trial. He is currently a member of the Breast Cancer Clinical Trials Network and is involved in the design and implementation of clinical trials in the area of breast cancer.

Experts Discussed Unmet Needs and Future Directions in mTNBC

...will help identify the optimal sequencing of agents

- Experts are still using a combination of the regimen of docetaxel plus trastuzumab and epirubicin/trastuzumab, followed by TDM1, according to most patients
- Most experts are using trastuzumab dectabazine therapy, but will probably be treating more patients with evidence of liver metastases
- The trastuzumab dectabazine may also be used in the maintenance setting, before TDM1, in patients with asymptomatic liver metastases
 - Preferred to used maintenance, experts are divided on whether they would normally use TDM1 or trastuzumab dectabazine therapy
 - Results of the ongoing TDM1-TDM1 dectabazine comparing trastuzumab dectabazine as TDM1 will help to clarify the optimal sequencing of these drugs
- Trastuzumab dectabazine and the trastuzumab dectabazine may also be used earlier than trastuzumab in patients who were following treatment with trastuzumab, pertuzumab, and TDM1 in the maintenance setting, but this represents a small fraction of patients
- Patient preferences can also factor into the sequencing of these two agents (eg, 1 drug vs 1 drug versus about how long to continue)
- The sequencing efficacy of trastuzumab dectabazine and the trastuzumab regimen have covered other options, such as trastuzumab chemotherapy combinations, oral and intravenous, in late lines of therapy



Dr. [Name]
...is an expert in the field of breast cancer and is currently at [Institution]. He has been involved in the development of several clinical trials and has published numerous articles in the field of breast cancer treatment. He is currently serving as a consultant to [Company] and is also a member of the [Committee].

EPICS

**Expanding Options for
High-Risk HR+, HER2– Early
Breast Cancer**



Expanding Options for High-Risk HR+, HER2- Early Breast Cancer (1/3)

Presented by Joyce O'Shaughnessy, MD

PREMENOPAUSAL HR+, HER2- BREAST CANCER

> Results from the TAILORx and RxPONDER trials suggest that

OFFSET Trial Design

TAILORx Trial Design: Randomized, Prospective, Multicenter, Phase III, Adjuvant Breast Cancer Trial



RxPONDER Trial Design: Randomized, Prospective, Multicenter, Phase III, Adjuvant Breast Cancer Trial





Expanding Options for High-Risk HR+, HER2- Early Breast Cancer (2/3)

Presented by Joyce O'Shaughnessy, MD

ADJUVANT CDK4/6 INHIBITORS

> Updated data from the monarchE trial showed a 7.6%

STUDY POPULATION

1. 10,000 patients with HR+, HER2- early breast cancer... (text is blurred)

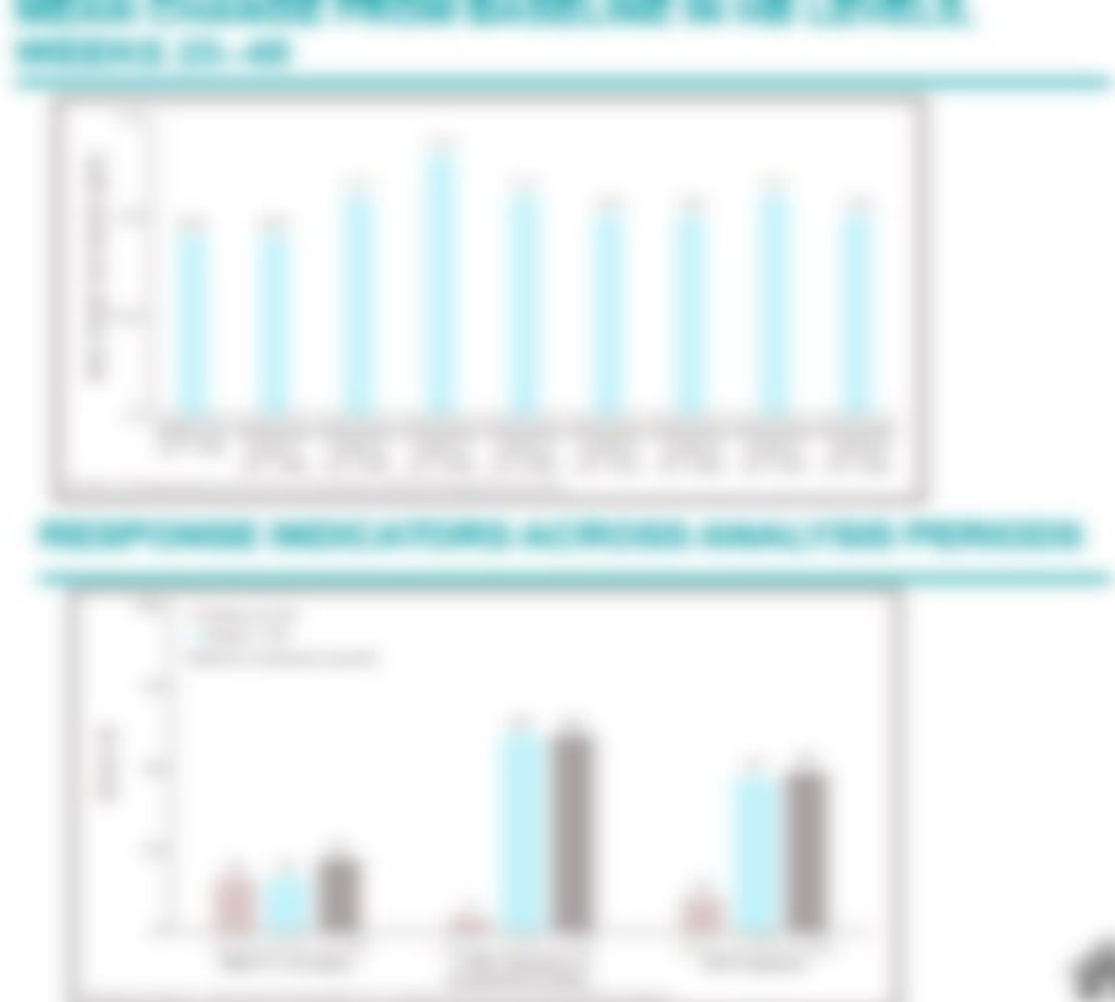
RESULTS

1. 10% of patients... (text is blurred)

KEY CONCLUSIONS

1. Adjuvant CDK4/6 inhibition... (text is blurred)

NATALEE: iDFS





Expanding Options for High-Risk HR+, HER2- Early Breast Cancer (3/3)

Presented by Joyce O'Shaughnessy, MD

PERIOPERATIVE IMMUNE CHECKPOINT INHIBITION

> KEYNOTE-756 randomized patients with grade 3 ER+, HER2- breast

pCR Rates by PD-L1 and ER Status



EPICS

Key Insights

**Expanding Options for High-Risk HR+, HER2–
Early Breast Cancer**

Experts Debated the Necessity of Chemotherapy for Premenopausal Patients

Experts will debate the optimal sequencing of agents...

- 1. Experts will debate the optimal sequencing of agents...
- 2. Experts will debate the optimal sequencing of agents...
- 3. Experts will debate the optimal sequencing of agents...
- 4. Experts will debate the optimal sequencing of agents...
- 5. Experts will debate the optimal sequencing of agents...
- 6. Experts will debate the optimal sequencing of agents...
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Experts will debate the optimal sequencing of agents...

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Experts will debate the optimal sequencing of agents...

Experts will debate the optimal sequencing of agents...



Experts Discussed Current Use of Adjuvant Abemaciclib for High-Risk, Early-Stage HR+, HER2- Breast Cancer

Experts discussed the current use of adjuvant abemaciclib for high-risk, early-stage HR+, HER2- breast cancer. The discussion focused on the use of abemaciclib in combination with endocrine therapy and chemotherapy, and the role of abemaciclib in the management of these patients. The experts discussed the use of abemaciclib in combination with endocrine therapy and chemotherapy, and the role of abemaciclib in the management of these patients. The experts discussed the use of abemaciclib in combination with endocrine therapy and chemotherapy, and the role of abemaciclib in the management of these patients.



Dr. [Name]
The use of abemaciclib in combination with endocrine therapy and chemotherapy is a key component of the management of high-risk, early-stage HR+, HER2- breast cancer. The experts discussed the use of abemaciclib in combination with endocrine therapy and chemotherapy, and the role of abemaciclib in the management of these patients.



Experts Speculated on the Use of Adjuvant Ribociclib If Approved

Experts are still using a combination of the regimen of docetaxel plus trastuzumab and epirubicin therapy, followed by TDM1, according to most patients.

Other experts are using trastuzumab deruxtecan therapy, but will probably be looking again for patients with evidence of brain metastases.

The trastuzumab regimen may also be used in the neoadjuvant setting, before TDM1, for patients with documented brain metastases.

- Provided a good assessment, experts are divided on whether they would normally use TDM1 or trastuzumab deruxtecan therapy.
- Results of the ongoing HER2-DM1-Breast011 trial comparing trastuzumab deruxtecan to TDM1 will help to clarify the optimal sequence of these drugs.

Trastuzumab deruxtecan and the trastuzumab regimen may also be used earlier than starting in patients who were following treatment with trastuzumab, epirubicin, and TDM1 in the neoadjuvant setting, but this represents a small fraction of patients.

Other professionals can also factor into the sequencing of these two agents (eg, 2 drugs or 1 drug, versus about how long to last).

The sequencing efficacy of trastuzumab deruxtecan and the trastuzumab regimen have proven other options, such as trastuzumab chemotherapy combinations, venetoclax, and metformin, in late lines of therapy.



Dr. [Name]
The expert is an expert in breast cancer and is currently a professor at the University of [Name]. He has been involved in the design and implementation of clinical trials in the area of breast cancer, including the use of trastuzumab deruxtecan in the adjuvant setting. He has also been involved in the use of trastuzumab deruxtecan in the neoadjuvant setting. He has also been involved in the use of trastuzumab deruxtecan in the metastatic setting. He has also been involved in the use of trastuzumab deruxtecan in the adjuvant setting. He has also been involved in the use of trastuzumab deruxtecan in the neoadjuvant setting. He has also been involved in the use of trastuzumab deruxtecan in the metastatic setting.

Experts Discussed Results From Perioperative Immune Checkpoint Inhibitor Trials for ER+, HER2- Breast Cancer

Experts discussed the optimal sequencing of agents in perioperative immune checkpoint inhibitor trials for ER+, HER2- breast cancer. The discussion focused on the use of immune checkpoint inhibitors (ICIs) in the perioperative setting, including the use of ICIs in combination with endocrine therapy and chemotherapy. The experts discussed the results of several clinical trials, including the results of the IMB1 trial, which compared the use of pembrolizumab with endocrine therapy and chemotherapy in the perioperative setting. The experts also discussed the results of the IMB2 trial, which compared the use of pembrolizumab with endocrine therapy and chemotherapy in the perioperative setting. The experts discussed the importance of patient selection and the need for further research in this area.



Dr. [Name] discussed the results of the IMB1 trial, which compared the use of pembrolizumab with endocrine therapy and chemotherapy in the perioperative setting. The trial showed that the combination of pembrolizumab with endocrine therapy and chemotherapy resulted in improved overall survival compared to endocrine therapy and chemotherapy alone. The experts discussed the importance of patient selection and the need for further research in this area.



EPICS

Evolving Paradigms in HR+, HER2– Metastatic Breast Cancer



Evolving Paradigms in HR+, HER2- Metastatic Breast Cancer (1/4)

Presented by Peter A. Kaufman, MD

CDK4/6 INHIBITORS

> To date, ribociclib and abemaciclib have demonstrated OS

RIGHT Choice: PFS





Evolving Paradigms in HR+, HER2- Metastatic Breast Cancer (2/4)

Presented by Peter A. Kaufman, MD

PI3K/AKT INHIBITORS

> Alpelisib (PI3Ki) + fulvestrant is approved for patients with previously treated

INAVO120: PFS

INAVO120: PFS



RESPONSE: METASTASIS IN OTHER ANATOMICAL SITES





Evolving Paradigms in HR+, HER2- Metastatic Breast Cancer (3/4)

Presented by Peter A. Kaufman, MD

NOVEL ER-TARGETING AGENTS

Numerous novel ER-targeting endocrine agents are in

MOAs of Novel Endocrine Agents

STUDY POPULATION

1. 1000 patients with HR+, HER2- metastatic breast cancer... (text is blurred)

RESULTS

1. 1000 patients with HR+, HER2- metastatic breast cancer... (text is blurred)

KEY CONCLUSIONS

1. 1000 patients with HR+, HER2- metastatic breast cancer... (text is blurred)





Evolving Paradigms in HR+, HER2- Metastatic Breast Cancer (4/4)

Presented by Peter A. Kaufman, MD

TROP-2 ANTIBODY-DRUG CONJUGATES

> TROPiCS-02 compared SG vs TPC in patients with

TROPiCS-02 Overall Survival



EPICS

Key Insights

Evolving Paradigms in HR+, HER2– Metastatic Breast Cancer

Experts Discussed the Use of CDK4/6 Inhibitors for HR+, HER2- mBC

Experts will discuss the optimal sequencing of agents

- 1. Experts will discuss the optimal sequencing of agents
- 2. Experts will discuss the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.
- 3. The use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.
- 4. The use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.
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- 6. The use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.
- 7. The use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.
- 8. The use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.
- 9. The use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.
- 10. The use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.



Experts will discuss the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1, and the use of CDK4/6 inhibitors in the setting of endocrine therapy and chemotherapy, followed by TDM1.



Experts Considered Evolving Algorithms with PI3K/AKT Inhibitors

Experts will now study the optimal sequencing of agents

- 1. Experts are now using a combination of the regimen of docetaxel plus metformin and pipecolinic bromide, followed by TDM1, sequentially, in most patients.
- 2. Most experts are using metformin plus docetaxel, but will probably be adding docetaxel to patients with evidence of liver metastases.
- 3. The docetaxel regimen may also be used in the sequential setting, before TDM1, in patients with documented liver metastases.
 - Preferred to use sequential regimens are divided on whether they would normally use TDM1 or metformin plus docetaxel.
 - Results of the ongoing 003 trial (NCT01890001) are comparing metformin plus docetaxel to TDM1, and may in turn, be used to study the optimal sequencing of these agents.
- 4. Metformin plus docetaxel and the docetaxel regimen may also be used before the addition of a patient who was receiving treatment with metformin, pipecolinic bromide, and TDM1 in the sequential setting, but this represents a small fraction of patients.
- 5. Future studies will also focus on the sequencing of these two agents (eg, 1 drug at a time, versus about the same time).
- 6. The sequential efficacy of metformin plus docetaxel and the docetaxel regimen have yielded other options, such as metformin plus chemotherapy combinations, metformin, and metformin, in the form of therapy.



In the future, we will be using a combination of the regimen of docetaxel plus metformin and pipecolinic bromide, followed by TDM1, sequentially, in most patients.

Most experts are using metformin plus docetaxel, but will probably be adding docetaxel to patients with evidence of liver metastases.

The docetaxel regimen may also be used in the sequential setting, before TDM1, in patients with documented liver metastases.

Preferred to use sequential regimens are divided on whether they would normally use TDM1 or metformin plus docetaxel.

Results of the ongoing 003 trial (NCT01890001) are comparing metformin plus docetaxel to TDM1, and may in turn, be used to study the optimal sequencing of these agents.

Metformin plus docetaxel and the docetaxel regimen may also be used before the addition of a patient who was receiving treatment with metformin, pipecolinic bromide, and TDM1 in the sequential setting, but this represents a small fraction of patients.

Future studies will also focus on the sequencing of these two agents (eg, 1 drug at a time, versus about the same time).

The sequential efficacy of metformin plus docetaxel and the docetaxel regimen have yielded other options, such as metformin plus chemotherapy combinations, metformin, and metformin, in the form of therapy.

benefited by 2L mavelon, or even the addition of mavelon at progression.



Experts Discussed Oral SERDs and Other Novel Endocrine Therapies

Experts will discuss the optimal sequencing of agents

- Experts are still using a combination of the regimen of aromatase plus endocrine and endocrine therapy, followed by TDM1, according to most patients
- Most experts are using endocrine monotherapy, but will provide the second agent to patients with evidence of local recurrence
- The second agent may also be used in the adjuvant setting, before TDM1, in patients with recurrent local recurrence
 - Provided a good assessment, experts are divided on whether they would consider use TDM1 or endocrine monotherapy
 - Results of the ongoing SERENA2 trial will help to clarify the optimal sequencing of these agents
- Endocrine monotherapy and the second agent may also be used earlier than starting in patients who were following treatment with endocrine, aromatase, and TDM1 in the metastatic setting, but this represents a small fraction of patients
- Patient preferences can also factor into the sequencing of these two agents (eg, 2 drugs vs 1 drug, versus what has been in the past)
- The sequencing efficacy of endocrine monotherapy and the second agent have varied after options, such as endocrine chemotherapy combinations, steroids, and immunotherapy, in late lines of therapy



Dr. [Name]
[Blurred text describing the speaker's role and the content of their presentation]

Experts Discussed Current Practice Patterns With ADCs in HR+, HER2- mBC

Experts will discuss the optimal sequencing of agents

- Experts are not using a combination of the regimen of trastuzumab and pertuzumab, followed by TDM1, sequentially, in most patients
- Most experts are using trastuzumab dectabine therapy, but will prescribe the trastuzumab agent for patients with evidence of local recurrence
- The trastuzumab agent may also be used in the adjuvant setting, before TDM1, for patients with documented local recurrence
 - Preferred in most circumstances, experts are divided on whether they would normally use TDM1 or trastuzumab dectabine therapy
 - Results of the ongoing TDM1/HER2 dectabine vs trastuzumab dectabine as TDM1 will help to clarify the optimal sequencing of these agents
- Trastuzumab dectabine and the trastuzumab agent may also be used earlier than starting a patient who was following treatment with trastuzumab, pertuzumab, and TDM1 in the neoadjuvant setting, but this represents a small fraction of patients
- Trastuzumab dectabine can also factor into the sequencing of these two agents (eg, 1 drug or 2 drug, versus about how long to continue)
- The sequencing efficacy of trastuzumab dectabine and the trastuzumab agent have varied after patients, such as trastuzumab chemotherapy combinations, venetoclax, and metformin, in late lines of therapy



Dr. [Name]
The speaker is an expert in breast cancer treatment and will discuss the optimal sequencing of agents in the setting of local recurrence in the adjuvant setting, for use in patients with documented local recurrence. The speaker will discuss the optimal sequencing of these agents (eg, 1 drug or 2 drug, versus about how long to continue) and the sequencing efficacy of trastuzumab dectabine and the trastuzumab agent have varied after patients, such as trastuzumab chemotherapy combinations, venetoclax, and metformin, in late lines of therapy.



EPICS

New Targets in Breast Cancer



New Targets in Breast Cancer (1/2)

Presented by Mark Pegram, MD

HER2-MUTATED mBC

> Approximately 1%–2% of breast cancers harbor a

SUMMIT Trial: Response





New Targets in Breast Cancer (2/2)

Presented by Mark Pegram, MD

TARGETING HER3

> HER3 is overexpressed in ~30%–70% of breast cancers,

Patritumab Deruxtecan: Response



EPICS

Key Insights

New Targets in Breast Cancer

Experts Discussed *HER2* Mutations and HER3 as Therapeutic Targets in mBC

Experts will discuss the optimal sequencing of agents

- Experts will discuss a combination of the regimen of trastuzumab and pertuzumab, followed by TDM1, as optimal for most patients
- Most experts are using trastuzumab deruxtecan, but will provide the limited data for patients with evidence of HER2 resistance
- The limited data may also be used in the metastatic setting, before TDM1, for patients with trastuzumab HER2 resistance
 - Provided a good performance, experts are divided on whether they would consider use of TDM1 in trastuzumab deruxtecan therapy
 - Results of the ongoing HER2-DM1-Breast019 comparing trastuzumab deruxtecan to TDM1 will help to clarify the optimal sequencing of these agents
- Trastuzumab deruxtecan and the limited data may also be used earlier than starting in patients who were following treatment with trastuzumab, pertuzumab, and TDM1 in the metastatic setting, but this represents a small fraction of patients
- Trastuzumab can also factor into the sequencing of these two agents (eg, 1 drug or 2 drug, versus what has been in practice)
- The sequencing efficacy of trastuzumab deruxtecan and the limited regimen have opened other options, such as trastuzumab chemotherapy combinations, venetoclax, and regorafenib, in late lines of therapy



Dr. [Name]
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Experts Considered Novel Immune-Based Therapies for Breast Cancer

Experts will consider the optimal sequencing of agents

- 1. Experts will consider a combination of the immune checkpoint inhibitors and anti-HER2 therapy, followed by TDM1, as optimal for most patients.
- 2. Most experts are using immunotherapy, endocrine therapy, but will prioritize the immune checkpoint for patients with evidence of tumor metastases.
- 3. The immune checkpoint may also be used in the neoadjuvant setting, before TDM1, for patients with documented tumor metastases.
 - Preferred in most neoadjuvant settings are divided on whether they would consider use TDM1 or immunotherapy, endocrine therapy.
 - Results of the ongoing IMBR150 breast cancer comparing immunotherapy, endocrine or TDM1 will help to clarify the optimal sequencing of these agents.
- 4. Immunotherapy, endocrine and the immune checkpoint may also be used earlier than starting in patients who were following treatment with immunotherapy, anti-HER2, and TDM1 in the neoadjuvant setting, but this represents a small fraction of patients.
- 5. Future endocrine use also factor into the sequencing of these new agents (eg. 2 drugs or 3 drug, consider about how best to sequence).
- 6. The sequencing efficacy of immunotherapy, endocrine and the immune checkpoint have varied other options, such as immunotherapy chemotherapy combinations, endocrine and immunotherapy, or other form of therapy.



Dr. [Name]
The expert is an expert in breast cancer and is currently a professor at the University of [Name]. He is currently a member of the [Name] and is currently a member of the [Name]. He is currently a member of the [Name] and is currently a member of the [Name]. He is currently a member of the [Name] and is currently a member of the [Name].

EPICS

Key Insights

**General Discussion: Future Directions in
Breast Cancer Treatment**

Experts Debated the Potential Utility of MRD Testing in Breast Cancer

Experts will debate the optimal sequencing of agents in the adjuvant setting for breast cancer patients, including the use of MRD testing, in a panel discussion.

Panelists will discuss the use of MRD testing in the adjuvant setting, including the use of MRD testing in the adjuvant setting, including the use of MRD testing in the adjuvant setting.

Panelists will discuss the use of MRD testing in the adjuvant setting, including the use of MRD testing in the adjuvant setting.

Panelists will discuss the use of MRD testing in the adjuvant setting, including the use of MRD testing in the adjuvant setting.



Panelists will discuss the use of MRD testing in the adjuvant setting, including the use of MRD testing in the adjuvant setting.

Experts Discussed Challenges Facing Community Oncologists



GAPS IN THE COMMUNITY SETTING

Experts will discuss the optimal sequencing of agents

- 1. Experts will discuss the optimal sequencing of agents in the community setting, including the use of immunotherapy and targeted therapy, followed by TDMT, and the use of immunotherapy in the community setting.
- 2. The use of immunotherapy and targeted therapy in the community setting will be discussed, including the use of immunotherapy in the community setting.
- 3. The use of immunotherapy and targeted therapy in the community setting will be discussed, including the use of immunotherapy in the community setting.
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- 8. The use of immunotherapy and targeted therapy in the community setting will be discussed, including the use of immunotherapy in the community setting.
- 9. The use of immunotherapy and targeted therapy in the community setting will be discussed, including the use of immunotherapy in the community setting.
- 10. The use of immunotherapy and targeted therapy in the community setting will be discussed, including the use of immunotherapy in the community setting.



Dr. [Name]
The use of immunotherapy and targeted therapy in the community setting will be discussed, including the use of immunotherapy in the community setting.




Experts Speculated on Future Developments and Practices in Breast Cancer

Experts will likely study the optimal sequencing of agents

- 1. Experts are still using a combination of the regimen of breast-conserving and adjuvant therapy, followed by TDMT, according to most patients.
- 2. Most experts are using breast-conserving approaches, but will probably be looking for patients with evidence of local recurrence.
- 3. The breast-conserving approach may also be used in the neoadjuvant setting, before TDMT, for patients with recurrent local recurrences.
 - Provided a good assessment, experts are divided on whether they would normally use TDMT in breast-conserving therapy.
 - Results of the ongoing BC17 (TRIO-Breast01) trial comparing breast-conserving therapy to TDMT will help to clarify the optimal sequencing of these agents.
- 4. Breast-conserving therapy and the breast-conserving approach may also be used earlier than starting in patients who were following treatment with breast-conserving approaches and TDMT in the neoadjuvant setting, but this represents a small fraction of patients.
- 5. Future approaches may also focus on the sequencing of these two agents (eg, 1 drug or 2 drug, versus about how long to do them).
- 6. The improved efficacy of breast-conserving approaches and the breast-conserving have opened other options, such as breast-conserving chemotherapy combinations, targeted and immunotherapy, in some form of therapy.



Dr. [Name]
The [Name] is a [Name] of [Name]
[Name] and [Name] [Name]
[Name] in the [Name] of [Name]
[Name] and [Name] [Name]
[Name] in the [Name] setting, but [Name]
[Name] in [Name] [Name] [Name]
[Name] [Name] [Name] [Name]
[Name] [Name] [Name] [Name]
[Name] [Name] [Name] [Name]
[Name] [Name] [Name] [Name]
[Name] [Name] [Name] [Name]



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