



EPICS

Global Perspectives in Current and Future Management of Breast Cancer

November 7 and 8, 2023
Full Report

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VIRTUAL CLOSED-DOOR ROUNDTABLE



DATES:
November 7 and 8,
2023



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



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts in
breast cancer

- > 5 from the US
- > 5 from the EU



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

Panel Consisting of 5 US and 5 EU Breast Cancer Experts

EPICS



Mark Pegram, MD
Stanford University
School of Medicine



Melinda L. Telli, MD
Stanford University
School of Medicine



Co-Chair
Joyce A. O'Shaughnessy, MD
Baylor-Sammons Cancer Center



Komal Jhaveri, MD, FACP
Memorial Sloan Kettering
Cancer Center



Reshma L. Mahtani, DO
Miami Cancer Institute, Baptist
Health South Florida

Peter Schmid, MD, PhD
St Bartholomew's Hospital



Joseph Gligorov, MD, PhD
Tenon Hospital (AP-HP)



Valentina Guarneri, MD, PhD
University of Padua



Javier Cortés, MD, PhD
International Breast Cancer
Center



Co-Chair
Nadia Harbeck, MD, PhD
Ludwig-Maximilian
University of Munich



Meeting Agenda: Day 1 – November 7, 2023

EPICS

Time (CST/CET)	Topic	Speaker/Moderator
9.00 AM – 9.05 AM/16.00 – 16.05 (5 min)	Welcome and Introductions	Joyce O’Shaughnessy, MD
9.05 AM – 9.15 AM/16.05 – 16.15 (10 min)	Current and Emerging Biomarkers and Testing Methodologies in BC	Mark Pegram, MD
9.15 AM – 9.40 AM/16.15 – 16.40 (25 min)	Key Questions and Topics for Discussion	Joyce O’Shaughnessy, MD
9.40 AM – 9.45 AM/16.40 – 16.45 (5 min)	Summary and 3 Key Takeaways	Mark Pegram, MD
9.45 AM – 9.55 AM/16.45 – 16.55 (10 min)	Therapeutic Horizons in HR+ Advanced BC	Komal Jhaveri, MD, FACP
9.55 AM – 10.20 AM/16.55 – 17.20 (25 min)	Key Questions and Topics for Discussion	Nadia Harbeck, MD, PhD
10.20 AM – 10.25 AM/17.20 – 17.25 (5 min)	Summary and 3 Key Takeaways	Komal Jhaveri, MD, FACP
10.25 AM – 10.35 AM/17.25 – 17.35 (10 min)	Break	
10.35 AM – 10.45 AM/17.35 – 17.45 (10 min)	Clinical Implications of HER2-Low BC	Reshma L. Mahtani, DO
10.45 AM – 11.10 AM/17.45 – 18.10 (25 min)	Key Questions and Topics for Discussion	Nadia Harbeck, MD, PhD
11.10 AM – 11.15 AM/18.10 – 18.15 (5 min)	Summary and 3 Key Takeaways	Reshma L. Mahtani, DO
11.15 AM – 11.25 AM/18.15 – 18.25 (10 min)	Maximizing Potential Targeting of HER2 in HER2+ mBC	Joseph Gligorov, MD, PhD
11.25 AM – 11.50 AM/18.25 – 18.50 (25 min)	Key Questions and Topics for Discussion	Joyce O’Shaughnessy, MD
11.50 AM – 11.55 AM/18.50 – 18.55 (5 min)	Summary and 3 Key Takeaways	Joseph Gligorov, MD, PhD
11.55 AM – 12.00 PM/18.55 – 19.00 (5 min)	Conclusions and Closing	Joyce O’Shaughnessy, MD



Meeting Agenda: Day 2 – November 8, 2023

EPICS

Time (CST/CET)	Topic	Speaker/Moderator
11.00 AM – 11.05 AM/18.00 – 18.05 (5 min)	Introduction and Review Agenda for Day 2	Nadia Harbeck, MD, PhD
11.05 AM – 11.15 AM/18.05 – 18.15 (10 min)	Therapeutic Horizons in HR+ Early BC	Peter Schmid, MD, PhD
11.15 AM – 11.40 AM/18.15 – 18.40 (25 min)	Key Questions and Topics for Discussion	Joyce O’Shaughnessy, MD
11.40 AM – 11.45 AM/18.40 – 18.45 (5 min)	Summary and 3 Key Takeaways	Peter Schmid, MD, PhD
11.45 AM – 11.55 AM/18.45 – 18.55 (10 min)	The Changing Landscape of HER2+ Early BC	Valentina Guarneri, MD, PhD
11.55 AM – 12.20 PM/18.55 – 19.20 (25 min)	Key Questions and Topics for Discussion	Nadia Harbeck, MD, PhD
12.20 PM – 12.25 PM/19.20 – 19.25 (5 min)	Summary and 3 Key Takeaways	Valentina Guarneri, MD, PhD
12.25 PM – 12.35 PM/19.25 – 19.35 (10 min)	Break	
12.35 PM – 12.45 PM/19.35 – 19.45 (10 min)	Standard and Emerging Strategies for High-Risk, Early-Stage TNBC	Melinda Telli, MD
12.45 PM – 1.10 PM/19.45 – 20.10 (25 min)	Key Questions and Topics for Discussion	Joyce O’Shaughnessy, MD
1.10 PM – 1.15 PM/20.10 – 20.15 (5 min)	Summary and 3 Key Takeaways	Melinda Telli, MD
1.15 PM – 1.25 PM/20.15 – 20.25 (10 min)	Current and Investigational Approaches in Metastatic TNBC	Javier Cortés, MD, PhD
1.25 PM – 1.50 PM/20.25 – 20.50 (25 min)	Key Questions and Topics for Discussion	Nadia Harbeck, MD, PhD
1.50 PM – 1.55 PM/20.50 – 20.55 (5 min)	Summary and 3 Key Takeaways	Javier Cortés, MD, PhD
1.55 PM – 2.00 PM/20.55 – 21.00 (5 min)	Conclusions and Wrap-Up	Nadia Harbeck, MD, PhD



EPICS

Current and Emerging Biomarkers and Testing Methodologies in BC



Current and Emerging Biomarkers and Testing Methodologies in BC (1/2)

Presented by Mark Pegram, MD

CONVENTIONAL AND NOVEL METHODS FOR BIOMARKER DETECTION

> Biomarkers play a pivotal role in precision medicine, as they guide patient

STUDY POPULATION

1000 patients with metastatic breast cancer... (text is blurred)

RESULTS

Median overall survival was 12.1 months... (text is blurred)

CONCLUSIONS

Combining conventional and novel biomarkers... (text is blurred)

BIOMARKER TESTING METHODOLOGIES IN THE CLINICAL SETTING



RESPONSE MODIFICATION BY BIOMARKER ANALYSIS





Current and Emerging Biomarkers and Testing Methodologies in BC (2/2)

Presented by Mark Pegram, MD

PHASES OF BIOMARKER DEVELOPMENT

> Biomarker development can be separated roughly into 3 phases: (1) preclinical biomarker identification and analytical validation, (2) clinical



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Key Insights

CURRENT AND EMERGING BIOMARKERS AND TESTING METHODOLOGIES IN BREAST CANCER

Evolution of biomarkers

- > Breast cancer biomarkers are evolving from conventional markers in IHC such as ER, PR, and HER2+ to genetic markers with therapeutic

CURRENT AND EMERGING BIOMARKERS AND TESTING METHODOLOGIES IN BREAST CANCER (cont.)

Biomarker and assay platform development and validation

- **Preclinical studies** - **Phase I** - **Phase II**
 - Focuses on the validation of biomarker platform in patients in real time, and these biomarkers can potentially be targeted
- **Phase III** - **Phase IV** - **Phase V**
 - The approach is used as effective, working with, and usually applicable to many patients
- **Phase I** - **Phase II** - **Phase III** - **Phase IV** - **Phase V**
 - This approach is used as a good solution for a patient population in which going to phase III is difficult. It is used as effective and safe
- **Phase I** - **Phase II** - **Phase III** - **Phase IV** - **Phase V**
 - Focuses on the validation of biomarker platform in patients with advanced disease. They would like to see phase II data to confirm the activity in this setting
- **Phase I** - **Phase II** - **Phase III** - **Phase IV** - **Phase V**
 - The approach is used as a good solution for a patient population with advanced disease. It can be used as effective, safe and well-tolerated. Some of the responses seen were clearly very durable

EPICS

Therapeutic Horizons in HR+ Advanced BC



Therapeutic Horizons in HR+ Advanced BC (1/4)

Presented by Komal Jhaveri, MD, FACP

FIRST-LINE: UPDATES FROM ESMO 2023

POST-CDK4/6 INHIBITION: MOVE TO PERSONALIZATION

> The final data from the FALCON trial

STUDY POPULATION

Final data from the FALCON trial showing overall survival and progression-free survival in HR+ advanced BC patients. The study compared a CDK4/6 inhibitor with an endocrine therapy versus endocrine therapy alone. The CDK4/6 inhibitor group showed significantly better overall survival and progression-free survival compared to the endocrine therapy alone group.

RESULTS

Overall survival (OS) was significantly better in the CDK4/6 inhibitor group compared to the endocrine therapy alone group. Progression-free survival (PFS) was also significantly better in the CDK4/6 inhibitor group.

KEY TAKEAWAYS

CDK4/6 inhibition significantly improves overall survival and progression-free survival in HR+ advanced BC patients. This finding supports the use of CDK4/6 inhibitors in combination with endocrine therapy as first-line treatment for HR+ advanced BC.

POST-CDK4/6 INHIBITION: MOVE TO PERSONALIZATION



RESPONSE: MOVING TOWARD PERSONALIZATION





Therapeutic Horizons in HR+ Advanced BC (2/4)

Presented by Komal Jhaveri, MD, FACP



POST-CDK4/6 INHIBITION: MOVE TO PERSONALIZATION (cont.)

Oral SERDs

> Elacestrant was the first oral SERD approved for the use in patients with HR+, HER2-, *ESR1*-mutated advanced or metastatic BC with





Therapeutic Horizons in HR+ Advanced BC (3/4)

Presented by Komal Jhaveri, MD, FACP



POST-CDK4/6 INHIBITION: MOVE TO PERSONALIZATION (cont.)

PI3K inhibitors

> The BYLieve study (NCT03056755) demonstrated activity of alpelisib plus fulvestrant in patients with *PIK3CA*-mutated, HR+, HER2-





Therapeutic Horizons in HR+ Advanced BC (4/4)

Presented by Komal Jhaveri, MD, FACP



POST-CDK4/6 INHIBITION: MOVE TO PERSONALIZATION (cont.)

ADCs

> Latest findings from the DESTINY-Breast04 trial (NCT03734029) demonstrate a sustained improvement in OS. Trastuzumab deruxtecan



EPICS

Key Insights

HR+ Advanced Breast Cancer (1/2)

THERAPEUTIC HORIZONS IN HR+ ADVANCED BREAST CANCER

APPROVED APPROVAL 1/2024 - (NDA) - (IND) - (IND) - (IND)

- The agency believes the combination of endocrine therapy and capivasertib is a promising approach for patients with HR+ advanced breast cancer, and these combinations are potentially to be tested

PROMISING PRELIMINARY AND EFFICACY RESULTS FROM AN ONGOING PHASE III STUDY OF ENDOCRINE THERAPY WITH PROMISING RESULTS IN COMBINATION WITH CAPIVASERTIB IN HR+ ADVANCED BREAST CANCER

- The agency is aware of efficacy results with endocrine therapy in HR+ advanced breast cancer

ENDOCRINE THERAPY COMBINATION APPROVED FOR PATIENTS WITH HR+ ADVANCED BREAST CANCER TO BE TESTED IN AN ONGOING PHASE III STUDY OF ENDOCRINE THERAPY WITH PROMISING RESULTS IN COMBINATION WITH CAPIVASERTIB IN HR+ ADVANCED BREAST CANCER

- The agency is aware of a great number of patients who are currently receiving endocrine therapy in HR+ advanced breast cancer

APPROVED APPROVAL 1/2024 - (NDA) - (IND) - (IND) - (IND)

- The agency believes the combination of endocrine therapy and fulvestrant is a promising approach for patients with HR+ advanced breast cancer, and these combinations are potentially to be tested

APPROVED APPROVAL 1/2024 - (NDA) - (IND) - (IND) - (IND)

- The agency believes the combination of endocrine therapy and fulvestrant is a promising approach for patients with HR+ advanced breast cancer, and these combinations are potentially to be tested



THERAPEUTIC HORIZONS IN HR+ ADVANCED BREAST CANCER (cont.)

Post-CDK4/6 inhibitor progression (cont.)

- > Fulvestrant plus everolimus remains another option in this setting, albeit with limited post-CDK4/6 inhibitor progression data and notable toxicities

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Clinical Implications of HER2-Low BC



Clinical Implications of HER2-Low BC (1/2)

Presented by Reshma L. Mahtani, DO

ADCs FOR THE TREATMENT OF HER2-LOW DISEASE

Trastuzumab deruxtecan

> The phase III DESTINY-Breast04 trial (NCT03734029) observed significantly longer PFS and OS with trastuzumab deruxtecan than with

[The following content is intentionally blurred for privacy and security.]



Clinical Implications of HER2-Low BC (2/2)

Presented by Reshma L. Mahtani, DO

ADCs FOR THE TREATMENT OF HER2-LOW DISEASE (cont.)

Novel ADCs in development

- > SKB264 consists of an antibody targeting TROP2 coupled to topoisomerase I inhibitor payload similar to ADCs currently used in clinic.

STUDY POPULATION

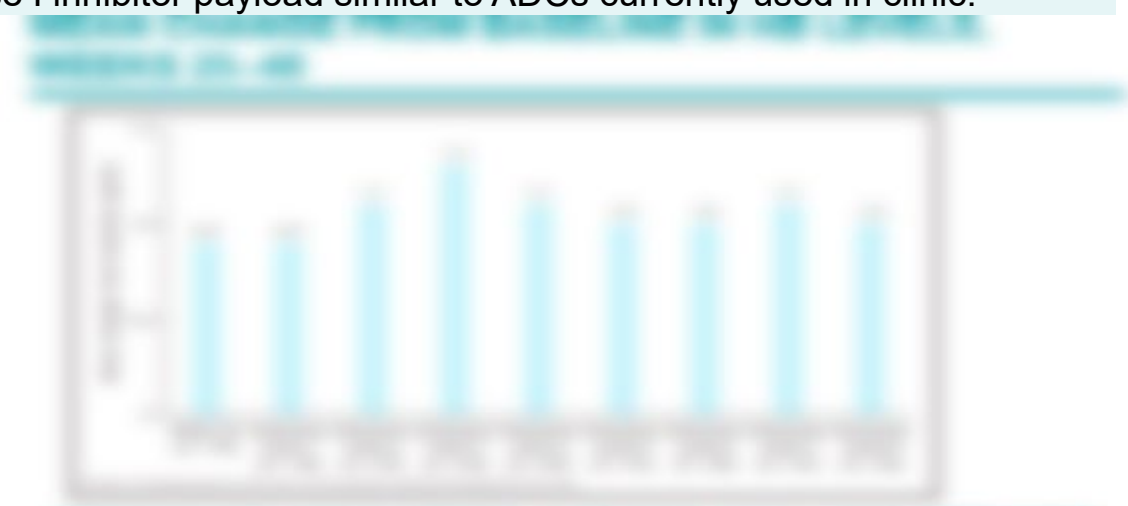
HER2-low (IHC 1+ or 2+) breast cancer patients with a history of prior adjuvant systemic therapy. The study population included patients with a history of prior adjuvant systemic therapy, including chemotherapy, endocrine therapy, and targeted therapy. The study population was stratified by prior adjuvant systemic therapy, including chemotherapy, endocrine therapy, and targeted therapy. The study population was stratified by prior adjuvant systemic therapy, including chemotherapy, endocrine therapy, and targeted therapy.

RESULTS

SKB264 demonstrated a statistically significant improvement in overall survival compared to the control group. The median overall survival was significantly longer in the SKB264 group compared to the control group. The study results demonstrated a statistically significant improvement in overall survival compared to the control group.

CONCLUSIONS

SKB264 demonstrated a statistically significant improvement in overall survival compared to the control group. The study results demonstrated a statistically significant improvement in overall survival compared to the control group.



EPICS

Key Insights

HER2-Low Breast Cancer (1/2)

CLINICAL IMPLICATIONS OF HER2-LOW BREAST CANCER

HER2-LOW BREAST CANCER: DEFINITION AND CLINICAL IMPLICATIONS

HER2-low breast cancer is defined as breast cancer with a HER2 expression level of 1+ or 2+ on immunohistochemistry (IHC) or a HER2/neu gene amplification level of less than 2.0 on fluorescence in situ hybridization (FISH). This category includes approximately 42% of breast cancer cases.

HER2-low breast cancer is associated with a higher risk of relapse and death compared to HER2-negative breast cancer. However, the use of HER2-targeted therapies, such as trastuzumab, can improve outcomes for HER2-low breast cancer patients.

CLINICAL IMPLICATIONS OF HER2-LOW BREAST CANCER

HER2-low breast cancer is associated with a higher risk of relapse and death compared to HER2-negative breast cancer. However, the use of HER2-targeted therapies, such as trastuzumab, can improve outcomes for HER2-low breast cancer patients.

CLINICAL IMPLICATIONS OF HER2-LOW BREAST CANCER

HER2-low breast cancer is associated with a higher risk of relapse and death compared to HER2-negative breast cancer. However, the use of HER2-targeted therapies, such as trastuzumab, can improve outcomes for HER2-low breast cancer patients.



HER2-Low Breast Cancer (2/2)

CLINICAL IMPLICATIONS OF HER2-LOW BREAST CANCER (cont.)

KEY POINTS: HER2-low breast cancer is a distinct subtype of breast cancer, characterized by low levels of HER2 expression. It is associated with a better prognosis compared to HER2-positive breast cancer, but a worse prognosis compared to HER2-negative breast cancer. Treatment options for HER2-low breast cancer include endocrine therapy, chemotherapy, and targeted therapy. Clinical trials are ongoing to evaluate the efficacy of HER2-targeted therapies in this population.

PROGNOSIS: HER2-low breast cancer is associated with a better prognosis compared to HER2-positive breast cancer, but a worse prognosis compared to HER2-negative breast cancer. The prognosis is influenced by factors such as tumor size, lymph node involvement, and the presence of other biomarkers.

TREATMENT: Treatment options for HER2-low breast cancer include endocrine therapy, chemotherapy, and targeted therapy. Clinical trials are ongoing to evaluate the efficacy of HER2-targeted therapies in this population.



EPICS

Maximizing Potential Targeting of HER2 in HER2+ mBC



Maximizing Potential Targeting of HER2 in HER2+ mBC (1/3)

Presented by Joseph Gligorov, MD, PhD



RECENT DATA IN HER2+ BC WITH BRAIN METASTASES

> Results from the HER2CLIMB trial (NCT02614794) still represent the most extensive dataset for patients with intracranial involvement,

Blurred content area containing additional text and bullet points related to the HER2CLIMB trial and brain metastases.



Maximizing Potential Targeting of HER2 in HER2+ mBC (2/3)

Presented by Joseph Gligorov, MD, PhD

REAL-WORLD DATA FOR TUCATINIB

> Real-world data indicate the HER2CLIMB regimen's sustained effectiveness in patients with HER2+ mBC, regardless of the number of prior

STUDY POPULATION

HER2+ mBC patients with a history of prior systemic therapy for mBC. The study population included patients who had received 1-4 prior systemic therapies for mBC. The median number of prior systemic therapies was 2. The study population was heterogeneous in terms of prior therapy, including taxanes, anthracyclines, and aromatase inhibitors. The study population was also heterogeneous in terms of disease characteristics, including stage, performance status, and comorbidities. The study population was representative of the real-world population of HER2+ mBC patients.

RESULTS

The study population was heterogeneous in terms of prior therapy, including taxanes, anthracyclines, and aromatase inhibitors. The study population was also heterogeneous in terms of disease characteristics, including stage, performance status, and comorbidities. The study population was representative of the real-world population of HER2+ mBC patients.

KEY CONCLUSIONS

The study population was heterogeneous in terms of prior therapy, including taxanes, anthracyclines, and aromatase inhibitors. The study population was also heterogeneous in terms of disease characteristics, including stage, performance status, and comorbidities. The study population was representative of the real-world population of HER2+ mBC patients.

REAL-WORLD DATA ON TUCATINIB EFFECTIVENESS



RESPONSE RATES BY PRIOR THERAPY AND HER2 STATUS





Maximizing Potential Targeting of HER2 in HER2+ mBC (3/3)

Presented by Joseph Gligorov, MD, PhD

EVOLUTION OF TREATMENT SEQUENCE

> Sequencing decisions continue to evolve, as more data on

STUDY POPULATION

HER2+ mBC patients with a history of prior adjuvant therapy...
Median OS was 20.1 months in the trastuzumab group vs 17.1 months in the control group.
Median OS was 20.1 months in the trastuzumab group vs 17.1 months in the control group.

RESULTS

Median OS was 20.1 months in the trastuzumab group vs 17.1 months in the control group.
Median OS was 20.1 months in the trastuzumab group vs 17.1 months in the control group.

KEY CONCLUSIONS

Continuing trastuzumab treatment beyond week 23 provides clinical benefit in HER2+ mBC patients and decreases the proportion of patients with...

HER2+ mBC PATIENTS ENROLLING IN THE CLINICAL TRIALS



RESPONSE RATES AND TOXICITY ACROSS ANALYSED PERIODS



EPICS

Key Insights

HER2+ Advanced Breast Cancer (1/2)

MAXIMIZING POTENTIAL TARGETING OF HER2 IN HER2+ METASTATIC BREAST CANCER

KEY TAKEAWAYS

- HER2+ metastatic breast cancer (MBC) is a heterogeneous disease with diverse clinical presentations and outcomes.
- Systemic therapy is the mainstay of treatment, with HER2-targeted therapy playing a central role in the treatment paradigm.
- Combining HER2-targeted therapy with other systemic agents, such as chemotherapy and endocrine therapy, can improve outcomes.
- Local therapy, including surgery and radiation, may be used to manage local disease and improve quality of life.
- Close collaboration between medical oncology, surgical oncology, and radiation oncology is essential for optimal patient care.

HER2-TARGETED THERAPY

HER2-targeted therapy, including trastuzumab, pertuzumab, and trastuzumab deruxtecan, has significantly improved outcomes in HER2+ MBC. The combination of trastuzumab and pertuzumab with chemotherapy is the standard of care for first-line treatment. Trastuzumab deruxtecan is a novel antibody-drug conjugate that has shown promising results in clinical trials, including in patients who have received prior HER2-targeted therapy.

COMBINATION THERAPY

Combining HER2-targeted therapy with other systemic agents, such as chemotherapy and endocrine therapy, can improve outcomes. For example, the combination of trastuzumab and pertuzumab with chemotherapy is the standard of care for first-line treatment. In addition, the combination of trastuzumab deruxtecan with endocrine therapy is being evaluated in clinical trials.

LOCAL THERAPY

Local therapy, including surgery and radiation, may be used to manage local disease and improve quality of life. For example, surgery may be used to remove a primary tumor or a metastatic lesion. Radiation therapy may be used to treat local disease or to palliate symptoms.



MAXIMIZING POTENTIAL TARGETING OF HER2 IN HER2+ METASTATIC BREAST CANCER (cont.)

Current treatment landscape (cont.)

- > Sequencing strategies in subsequent treatment lines lack clear definitions, emphasizing an important area of clinical investigation, especially

EPICS

Therapeutic Horizons in HR+ Early BC



Therapeutic Horizons in HR+ Early BC (1/3)

Presented by Peter Schmid, MD, PhD

ADJUVANT CDK4/6 INHIBITORS

> The 5-year update of the monarchE trial (NCT03155997)

STUDY POPULATION

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

RESULTS

5-year overall survival... (text is blurred)

KEY CONCLUSIONS

Adding CDK4/6 inhibitor... (text is blurred)

5-YEAR OVERALL SURVIVAL IN THE LATEST MONARCH E-5



RESPONSE, TOXICITY, AND OTHER ANALYSIS PARAMETERS





Therapeutic Horizons in HR+ Early BC (2/3)

Presented by Peter Schmid, MD, PhD

ADJUVANT ORAL SERDs

CHEMOTHERAPY

> The phase III lidERA trial

> Latest findings from the TAILORx study (NCT00310180) confirm that women with an Oncotype

STUDY POPULATION

10,000 women with HR+ BC, median age 55, 10% with lymph node metastases, 20% with distant metastases, 70% with no metastases, median follow-up 5.5 years. All patients received tamoxifen. The lidERA group received 1500 mg of endocrine therapy (ET) daily, while the control group received 1000 mg daily. The primary endpoint was overall survival (OS). The secondary endpoint was progression-free survival (PFS). The study was powered to detect a 10% improvement in OS.

RESULTS

OS: 1000 mg ET group (n=5000) vs 1500 mg ET group (n=5000). Median OS: 10.5 years vs 11.5 years (p=0.001). PFS: 1000 mg ET group vs 1500 mg ET group. Median PFS: 4.5 years vs 5.5 years (p=0.001).

KEY TAKEAWAYS

Increasing endocrine therapy to 1500 mg daily significantly improved OS and PFS in women with HR+ BC. This finding supports the use of higher doses of ET in this population.





Therapeutic Horizons in HR+ Early BC (3/3)

Presented by Peter Schmid, MD, PhD

IMMUNOTHERAPY

> Results from both the KEYNOTE-756 trial (NCT03725059) and the CheckMate 7FL trial (NCT04109066) suggest that adding a PD-1

[The following content is intentionally blurred to represent a large block of text on a slide.]

KEYNOTE-756: A phase III, open-label, randomized study to assess safety and efficacy of pembrolizumab + trastuzumab vs pembrolizumab + placebo in patients with early-stage HR+ BC. (NCT03725059)

- Results suggest the combination of pembrolizumab + trastuzumab is preferred to pembrolizumab + placebo in early-stage HR+ BC.

CheckMate 7FL: A phase III, open-label, randomized study to assess safety and efficacy of nivolumab + trastuzumab vs nivolumab + placebo in patients with early-stage HR+ BC. (NCT04109066)

- Results suggest the combination of nivolumab + trastuzumab is preferred to nivolumab + placebo in early-stage HR+ BC.

Overall, these results suggest that adding a PD-1 inhibitor to trastuzumab in early-stage HR+ BC is preferred to adding a PD-1 inhibitor to placebo.

EPICS

Key Insights

HR+ Early Breast Cancer (1/3)

THERAPEUTIC HORIZONS IN HR+ EARLY BREAST CANCER

INTRODUCTION

Therapeutic horizons in HR+ early breast cancer are defined by the time point at which the benefit of a treatment is no longer statistically significant compared to the control group. This is often determined by the time to event (TTE) analysis, which compares the time from randomization to the occurrence of a specific event (e.g., death, relapse, or progression).

KEY POINTS

- 1. The therapeutic horizon is the duration of time during which a treatment is shown to be superior to the control group.
- 2. The therapeutic horizon is often determined by the time to event (TTE) analysis, which compares the time from randomization to the occurrence of a specific event (e.g., death, relapse, or progression).
- 3. The therapeutic horizon is often determined by the time to event (TTE) analysis, which compares the time from randomization to the occurrence of a specific event (e.g., death, relapse, or progression).

CONCLUSION

The therapeutic horizon in HR+ early breast cancer is a critical concept for clinicians and patients alike. It represents the duration of time during which a treatment is shown to be superior to the control group. This is often determined by the time to event (TTE) analysis, which compares the time from randomization to the occurrence of a specific event (e.g., death, relapse, or progression).



THERAPEUTIC HORIZONS IN HR+ EARLY BREAST CANCER (cont.)

Adjuvant chemotherapy

- > Adjuvant therapy for HR+, HER2- disease is shifting toward a risk-tailored and individualized approach that minimizes the use of chemotherapy.

HR+ Early Breast Cancer (3/3)

THERAPEUTIC HORIZONS IN HR+ EARLY BREAST CANCER (cont.)

(This section contains blurred text, likely representing a table or detailed text content related to therapeutic horizons in HR+ early breast cancer.)



EPICS

The Changing Landscape of HER2+ Early BC



The Changing Landscape of HER2+ Early BC (1/2)

Presented by Valentina Guarneri, MD, PhD

INDIVIDUALIZING TREATMENT

> The neoadjuvant setting may serve as a tool for treatment personalization

STUDY POPULATION

HER2+ (IHC 3+) early-stage BC patients with a 1-3cm tumor, no lymph node involvement, and a 1-3cm tumor. Patients were randomized to receive either standard of care (SOC) or SOC + neoadjuvant treatment. The SOC group received SOC, and the SOC + neoadjuvant group received SOC + neoadjuvant treatment. The SOC + neoadjuvant group had a higher rate of pathologic complete response (pCR) compared to the SOC group. The SOC + neoadjuvant group also had a higher rate of breast-conserving surgery (BCS) compared to the SOC group. The SOC + neoadjuvant group had a higher rate of mastectomy compared to the SOC group. The SOC + neoadjuvant group had a higher rate of distant recurrence compared to the SOC group. The SOC + neoadjuvant group had a higher rate of local recurrence compared to the SOC group. The SOC + neoadjuvant group had a higher rate of overall survival compared to the SOC group.

RESULTS

80% of patients achieved pCR. 15% of patients achieved BCS. 85% of patients underwent mastectomy. 10% of patients had distant recurrence. 15% of patients had local recurrence. 85% of patients had overall survival.

KEY TAKEAWAYS

Neoadjuvant treatment may serve as a tool for treatment personalization in HER2+ early-stage BC patients. The SOC + neoadjuvant group had a higher rate of pCR, BCS, and overall survival compared to the SOC group.

HER2+ EARLY-STAGE BC PATIENTS: RESPONSE TO SOC VS SOC + NEOADJUVANT TREATMENT



RESPONSE RATES BY RECURRENCE ANALYSIS PERIOD





The Changing Landscape of HER2+ Early BC (2/2)

Presented by Valentina Guarneri, MD, PhD



DE-ESCALATION AND ESCALATION STRATEGIES

ONGOING TRIALS

> The 10-year update of the phase III Short-HER trial (NCT00629278)

> DESTINY-Breast11 (NCT05113251) is evaluating

[Faded content area containing detailed text and bullet points related to clinical trials and treatment strategies.]

EPICS

Key Insights

HER2+ Early Breast Cancer (1/2)

THE CHANGING LANDSCAPE OF HER2+ EARLY BREAST CANCER

Neoadjuvant setting

> Neoadjuvant therapy in HER2+ early breast cancer offers the unique possibility of selecting adjuvant therapies according to pathologic

HER2+ Early Breast Cancer (2/2)

THE CHANGING LANDSCAPE OF HER2+ EARLY BREAST CANCER (cont.)

KEY TAKEAWAYS

- HER2+ early breast cancer is a heterogeneous disease with varying clinical outcomes.
- Standard of care includes trastuzumab-based therapy, with newer agents like trastuzumab deruxtecan showing improved outcomes.
- Genomic subtyping (e.g., T-SPICE) is increasingly used to guide treatment decisions.
- Adjuvant endocrine therapy remains a key component of treatment for hormone receptor-positive disease.

ADJUVANT THERAPY

- Trastuzumab-based therapy is the standard of care for HER2+ early breast cancer.
- Trastuzumab deruxtecan (T-DXd) is a newer agent showing improved outcomes compared to trastuzumab.
- Adjuvant endocrine therapy is a key component of treatment for hormone receptor-positive disease.
- Genomic subtyping (e.g., T-SPICE) is increasingly used to guide treatment decisions.

SYSTEMIC THERAPY

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EPICS

**Standard and Emerging
Strategies for High-Risk,
Early-Stage TNBC**



Standard and Emerging Strategies for High-Risk, Early-Stage TNBC (2/2)

Presented by Melinda Telli, MD

UTILITY OF ctDNA IN GUIDING THERAPY

> c-TRAK-TN (NCT03145961) was the first prospective study to assess ctDNA for MRD detection in patients with moderate- and high-risk

[The following content is intentionally blurred for privacy and readability.]

Study 1: c-TRAK-TN (NCT03145961)

- Prospective study to assess ctDNA for MRD detection in patients with moderate- and high-risk TNBC.
- Primary endpoint: Overall survival (OS).
- Secondary endpoints: Disease-free survival (DFS), progression-free survival (PFS), and quality of life.
- Results: ctDNA detection was associated with improved OS and DFS.

Study 2: [Study Name]

- Prospective study to assess ctDNA for MRD detection in patients with moderate- and high-risk TNBC.
- Primary endpoint: Overall survival (OS).
- Secondary endpoints: Disease-free survival (DFS), progression-free survival (PFS), and quality of life.
- Results: ctDNA detection was associated with improved OS and DFS.

Study 3: [Study Name]

- Prospective study to assess ctDNA for MRD detection in patients with moderate- and high-risk TNBC.
- Primary endpoint: Overall survival (OS).
- Secondary endpoints: Disease-free survival (DFS), progression-free survival (PFS), and quality of life.
- Results: ctDNA detection was associated with improved OS and DFS.

EPICS

Key Insights

Early Triple-Negative Breast Cancer (1/2)

STANDARD AND EMERGING STRATEGIES FOR HIGH-RISK, EARLY-STAGE, TRIPLE-NEGATIVE BREAST CANCER

STANDARD OF CARE

EMERGING STRATEGIES

CLINICAL TRIALS

CONCLUSIONS



Early Triple-Negative Breast Cancer (2/2)

STANDARD AND EMERGING STRATEGIES FOR HIGH-RISK, EARLY-STAGE, TRIPLE-NEGATIVE BREAST CANCER (cont.)

Standard of Care: For high-risk, early-stage TNBC, the standard of care is a combination of chemotherapy and endocrine therapy. The chemotherapy regimen typically includes cyclophosphamide, epirubicin, and fluorouracil (CEF), or cyclophosphamide, epirubicin, and fluorouracil (CEF) with paclitaxel. Endocrine therapy includes tamoxifen or toremifene. The combination of chemotherapy and endocrine therapy is the standard of care for high-risk, early-stage TNBC.

Emerging Strategies: Emerging strategies for high-risk, early-stage TNBC include the use of immunotherapy, targeted therapy, and novel chemotherapy regimens. Immunotherapy, such as pembrolizumab, is being evaluated in clinical trials for high-risk, early-stage TNBC. Targeted therapy, such as trastuzumab, is also being evaluated in clinical trials for high-risk, early-stage TNBC. Novel chemotherapy regimens, such as the combination of cyclophosphamide, epirubicin, and fluorouracil (CEF) with paclitaxel and carboplatin, are also being evaluated in clinical trials for high-risk, early-stage TNBC.

Key Considerations: Key considerations for high-risk, early-stage TNBC include the use of immunotherapy, targeted therapy, and novel chemotherapy regimens. Immunotherapy, such as pembrolizumab, is being evaluated in clinical trials for high-risk, early-stage TNBC. Targeted therapy, such as trastuzumab, is also being evaluated in clinical trials for high-risk, early-stage TNBC. Novel chemotherapy regimens, such as the combination of cyclophosphamide, epirubicin, and fluorouracil (CEF) with paclitaxel and carboplatin, are also being evaluated in clinical trials for high-risk, early-stage TNBC.



EPICS

Current and Investigational Approaches in Metastatic TNBC



Current and Investigational Approaches in Metastatic TNBC (1/3)

Presented by Javier Cortés, MD, PhD

ROLE OF IMMUNOTHERAPY

TREATMENT OPTIONS FOR BRCA MUTATION CARRIERS

> Three phase III trials investigated the

> The TNT trial (NCT00532727) demonstrated platinum chemotherapy is an



Current and Investigational Approaches in Metastatic TNBC (2/3)

Presented by Javier Cortés, MD, PhD

ROLE OF ADCs

> Sacituzumab govitecan showed survival benefit in the ASCENT trial (NCT02574455), with a median OS increase from 6.7 months to 12.1

[The following content is intentionally blurred for privacy and readability.]



Current and Investigational Approaches in Metastatic TNBC (3/3)

Presented by Javier Cortés, MD, PhD

CURRENT TREATMENT LANDSCAPE

> Initial considerations for treatment usually involve the

STANDARD OF CARE

Standard of care for metastatic TNBC involves a combination of chemotherapy and endocrine therapy. The most commonly used chemotherapy regimens include docetaxel, epirubicin, and cyclophosphamide (DEC), or docetaxel, epirubicin, and cyclophosphamide (DEC) plus trastuzumab. Endocrine therapy is also used, particularly in hormone receptor-positive (HR+) TNBC. The overall goal is to improve survival and quality of life.

NEW APPROACHES

New approaches include targeted therapies, immunotherapy, and novel combinations. Targeted therapies like trastuzumab and pertuzumab are used in HR+ TNBC. Immunotherapy, such as pembrolizumab, is used in HR- TNBC. Novel combinations of chemotherapy and targeted therapies are being investigated.

KEY CONCLUSIONS

Key conclusions include the importance of personalized medicine and the need for further research in metastatic TNBC. The combination of chemotherapy and endocrine therapy remains the standard of care, but new approaches are showing promise.

RESPONSE RATE BY TREATMENT APPROACH



RESPONSE RATE BY TREATMENT APPROACH (Continued)



EPICS

Key Insights

Advanced Triple-Negative Breast Cancer (1/2)

CURRENT AND INVESTIGATIONAL APPROACHES IN METASTATIC TRIPLE-NEGATIVE BREAST CANCER

Systemic Therapy

Standard of care for metastatic TNBC includes a combination of chemotherapy and endocrine therapy. The most commonly used chemotherapy regimens are taxane-based (paclitaxel, docetaxel) and platinum-based (cisplatin, carboplatin). Endocrine therapy, such as tamoxifen or toremifene, is used for hormone receptor-positive metastatic TNBC. Immunotherapy, specifically pembrolizumab, is approved for first-line treatment of metastatic TNBC. Investigational approaches include novel immunotherapies, targeted therapies, and combination regimens.

Local Therapy

Local therapy, including surgery and radiation, is used to manage local disease and improve quality of life. Surgery is typically performed for palliative purposes in metastatic TNBC. Radiation therapy is used for pain relief and to control local disease progression.

Supportive Care

Supportive care is essential for managing symptoms and improving quality of life. This includes pain management, anti-nausea medications, and psychosocial support. Clinical trials are ongoing to evaluate novel supportive care interventions.

Advanced Triple-Negative Breast Cancer (2/2)


CURRENT AND INVESTIGATIONAL APPROACHES IN METASTATIC TRIPLE-NEGATIVE BREAST CANCER (cont.)

Current Standard of Care: The standard of care for metastatic TNBC is a combination of chemotherapy and immunotherapy. The most commonly used chemotherapy regimens include docetaxel, epirubicin, and cyclophosphamide (DEC). Immunotherapy, specifically atezolizumab, is used in combination with docetaxel and cyclophosphamide (DCC). The combination of atezolizumab, docetaxel, and cyclophosphamide (DCC) is the current standard of care for metastatic TNBC.

Investigational Approaches: Several investigational approaches are being evaluated in clinical trials for metastatic TNBC. These include the use of novel immunotherapies, such as checkpoint inhibitors, and the combination of immunotherapy with chemotherapy. Other approaches include the use of targeted therapies, such as PARP inhibitors, and the use of novel drug delivery systems, such as liposomes and nanoparticles.

Future Directions: The future of metastatic TNBC treatment lies in the development of novel immunotherapies and the combination of immunotherapy with chemotherapy. The use of novel drug delivery systems, such as liposomes and nanoparticles, may also improve the efficacy of chemotherapy. The combination of immunotherapy with chemotherapy is expected to be the standard of care for metastatic TNBC in the near future.





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