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EPICS

Global Perspectives in Current and Future Management of Breast Cancer

November 7 and 8, 2023
Full Report

Report Contents

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Meeting Snapshot

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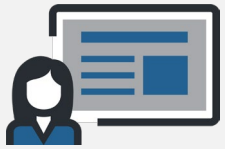
VIRTUAL CLOSED-DOOR ROUNDTABLE

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

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Mark Pegram, MD
Stanford University
School of Medicine

Melinda L. Telli, MD
Stanford University
School of Medicine

Komal Jhaveri, MD, FACP
Memorial Sloan Kettering
Cancer Center

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

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

Peter Schmid, MD, PhD
St Bartholomew's Hospital

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

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

Valentina Guarneri, MD, PhD
University of Padua

Javier Cortés, MD, PhD
International Breast Cancer
Center

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Meeting Agenda: Day 1 – November 7, 2023

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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

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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

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CONVENTIONAL AND NOVEL METHODS FOR BIOMARKER DETECTION

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

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

Presented by Mark Pegram, MD

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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

Biomarkers (1/2)

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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

[redacted]

Biomarkers (2/2)

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

Biomarker and assay platform development and validation

[redacted]

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Therapeutic Horizons in HR+ Advanced BC

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

Presented by Komal Jhaveri, MD, FACP

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FIRST-LINE: UPDATES FROM ESMO 2023

> The final data from the FALCON trial

POST-CDK4/6 INHIBITION: MOVE TO PERSONALIZATION

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

Presented by Komal Jhaveri, MD, FACP

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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

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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

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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

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Key Insights

HR+ Advanced Breast Cancer (1/2)

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THERAPEUTIC HORIZONS IN HR+ ADVANCED BREAST CANCER

was based on the exploratory PFS analysis in the 313 patients whose tumors did not have an *AKT* pathway alteration.
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-capivasertib-fulvestrant-breast-cancer

HR+ Advanced Breast Cancer (2/2)

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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

[redacted]

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Clinical Implications of HER2-Low BC

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

Presented by Reshma L. Mahtani, DO

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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

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

Presented by Reshma L. Mahtani, DO

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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.

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Key Insights

HER2-Low Breast Cancer (1/2)

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CLINICAL IMPLICATIONS OF HER2-LOW BREAST CANCER

HER2-Low Breast Cancer (2/2)

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

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Maximizing Potential Targeting of HER2 in HER2+ mBC

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

Presented by Joseph Gligorov, MD, PhD

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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,

[redacted]

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

Presented by Joseph Gligorov, MD, PhD

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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

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

Presented by Joseph Gligorov, MD, PhD

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EVOLUTION OF TREATMENT SEQUENCE

> Sequencing decisions continue to evolve, as more data on

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Key Insights

HER2+ Advanced Breast Cancer (1/2)

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MAXIMIZING POTENTIAL TARGETING OF HER2 IN HER2+ METASTIC BREAST CANCER

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*https://www.clinicaltrialsarena.com/news/seagen-reports-positive-data-on-tukysa-from-phase-iii-breast-cancer-trial/?cf-view

HER2+ Advanced Breast Cancer (2/2)

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

Current treatment landscape (cont.)

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

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Therapeutic Horizons in HR+ Early BC

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

Presented by Peter Schmid, MD, PhD

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ADJUVANT CDK4/6 INHIBITORS

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

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

Presented by Peter Schmid, MD, PhD

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ADJUVANT ORAL SERDs

> The phase III lidERA trial

CHEMOTHERAPY

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

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

Presented by Peter Schmid, MD, PhD

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IMMUNOTHERAPY

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

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Key Insights

HR+ Early Breast Cancer (1/3)

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THERAPEUTIC HORIZONS IN HR+ EARLY BREAST CANCER

HR+ Early Breast Cancer (2/3)

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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.

[illegible]

HR+ Early Breast Cancer (3/3)

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

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The Changing Landscape of HER2+ Early BC

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

Presented by Valentina Guarneri, MD, PhD

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INDIVIDUALIZING TREATMENT

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

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

Presented by Valentina Guarneri, MD, PhD

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DE-ESCALATION AND ESCALATION STRATEGIES

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

ONGOING TRIALS

> DESTINY-Breast11 (NCT05113251) is evaluating

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Key Insights

HER2+ Early Breast Cancer (1/2)

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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)

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

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

Standard and Emerging Strategies for High-Risk, Early-Stage TNBC (1/2)

Presented by Melinda Telli, MD

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CURRENT STATE AND ONGOING RESEARCH WITH IMMUNOTHERAPY IN EARLY-STAGE TNBC

- Addition of pembrolizumab to neoadjuvant chemotherapy followed by adjuvant pembrolizumab resulted in a significantly increased pCR rate

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

Presented by Melinda Telli, MD

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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

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Key Insights

Early Triple-Negative Breast Cancer (1/2)

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

Early Triple-Negative Breast Cancer (2/2)

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

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Current and Investigational Approaches in Metastatic TNBC

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

Presented by Javier Cortés, MD, PhD

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ROLE OF IMMUNOTHERAPY

> Three phase III trials investigated the

TREATMENT OPTIONS FOR *BRCA* MUTATION CARRIERS

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

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

Presented by Javier Cortés, MD, PhD

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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

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

Presented by Javier Cortés, MD, PhD

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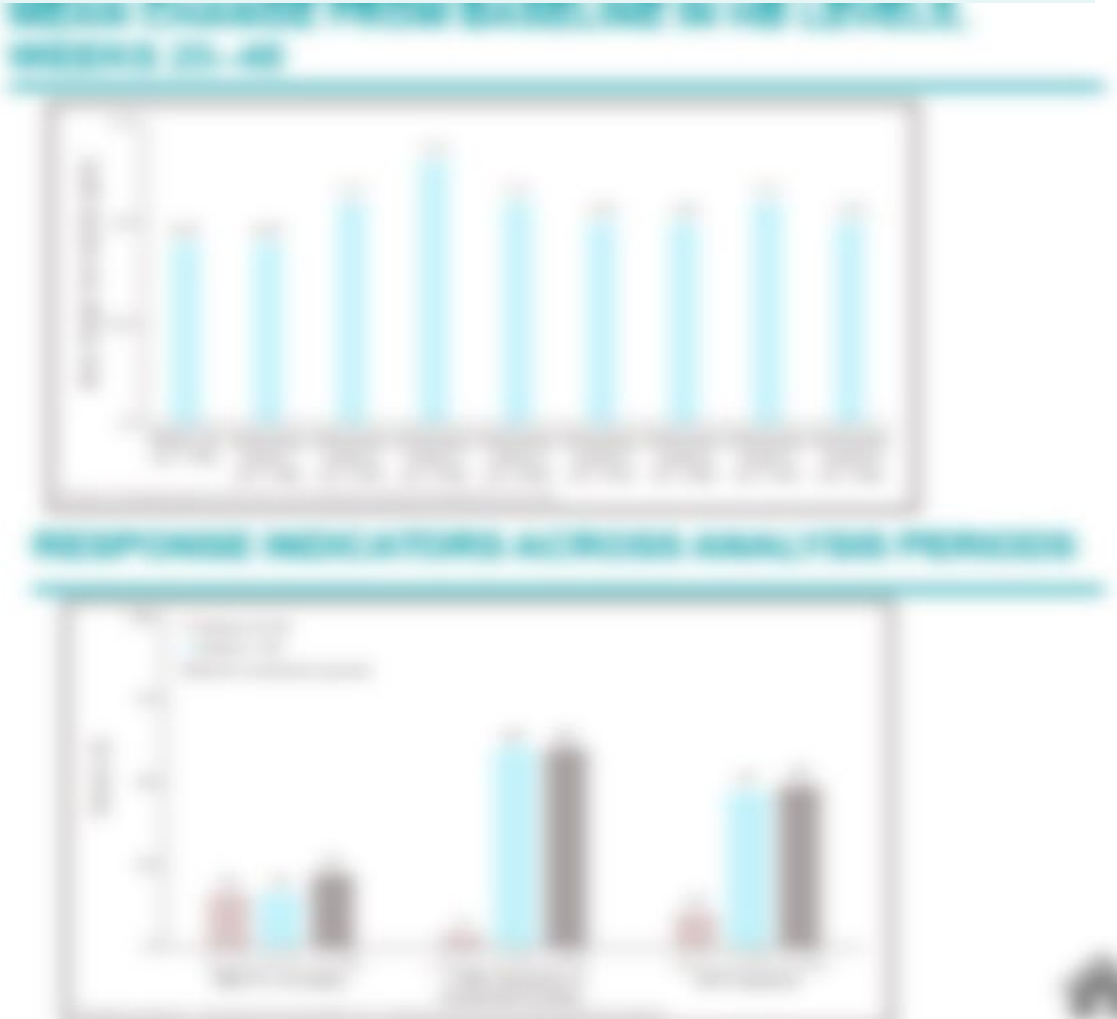
CURRENT TREATMENT LANDSCAPE

> Initial considerations for treatment usually involve the



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Advanced Triple-Negative Breast Cancer (1/2)

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CURRENT AND INVESTIGATIONAL APPROACHES IN METASTATIC TRIPLE-NEGATIVE BREAST CANCER

Advanced Triple-Negative Breast Cancer (2/2)

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

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*Robson ME, et al. *Eur J Cancer*. 2023;184:39-47.

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