



EPICS

Breast Cancer in 2023 and Beyond

Friday, May 19, 2023 Saturday, May 20, 2023

Report Contents



Content	Slide	e
Meeting Snapshot	3	
Faculty Panel	4	•
Meeting Agenda	5	
Strategic Recommendations	9	•
Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer	20	
The Changing Landscape of HER2+ Early Breast Cancer	28	•
Maximizing Potential Targeting of HER2 in HER2+ mBC	37	
Clinical Implications of HER2-Low Breast Cancer	45	•
Standard and Emerging Strategies for High-Risk, Early-Stage, Triple-Negative Breast Cancer	52	
Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer	61	•
Therapeutic Horizons in HR+ Early Breast Cancer	70	
Therapeutic Horizons in HR+ Advanced Breast Cancer	78	•
Old and New Targets in Breast Cancer	88	
General Discussion: Future Directions in Breast Cancer Treatment	93	•

APTITUDE HEALTH

Meeting Snapshot





DATE: May 19 and 20, 2023

DISEASE-STATE AND DATA PRESENTATIONS by key experts



INSIGHTS REPORT including postmeeting analyses and actionable recommendations

VIRTUAL CLOSED-DOOR ROUNDTABLE

EPICS



PANEL: Key experts inbreast cancer7 from US



BREAST CANCER-SPECIFIC DISCUSSIONS on

therapeutic advances and their application in clinical decision-making





Panel Consisting of 7 US Breast Cancer Experts



Peter A. Kaufman, MD University of Vermont **Cancer Center**



of Rhode Island

Hope S. Rugo, MD UCSF Helen Diller Family **Comprehensive Cancer Center**



Kelly McCann, MD, PhD UCLA Medicine

CHAIR:

Joyce A. O'Shaughnessy, MD Baylor Scott & White Charles A. Sammons Cancer Center



Banu Arun, MD UT MD Anderson Cancer Center

Peter Beitsch, MD **Dallas Surgical Group**



Meeting Agenda: Day 1 (1/2)



Time (CST)	Торіс	Speaker/Moderator
2.00 рм – 2.10 рм (10 min)	Welcome and Introductions	Joyce O'Shaughnessy, MD
2.10 рм – 2.25 рм (15 min)	Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer	William Sikov, MD
2.25 рм – 2.50 рм (25 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
2.50 РМ – 2.55 РМ (5 min)	Summary and 3 Key Takeaways	
2.55 рм – 3.10 рм (15 min)	The Changing Landscape of HER2+ Early Breast Cancer	Joyce O'Shaughnessy, MD
3.10 рм – 3.35 рм (25 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
3.35 рм – 3.40 рм (5 min)	Summary and 3 Key Takeaways	
3.40 рм – 3.55 рм (15 min)	BREAK	
3.55 РМ – 4.10 РМ (15 min)	Maximizing Potential Targeting of HER2 in HER2+ mBC	Kelly McCann, MD, PhD

APTITUDE HEALTH

Meeting Agenda: Day 1 (2/2)



Time (CST)	Торіс	Speaker/Moderator
4.10 рм – 4.35 рм (25 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
4.35 рм – 4.40 рм (5 min)	Summary and 3 Key Takeaways	
4.40 рм – 4.55 рм (15 min)	Clinical Implications of HER2-Low Breast Cancer	Banu Arun, MD
4.55 рм – 5.15 рм (20 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
5.15 рм – 5.20 рм (5 min)	Summary and 3 Key Takeaways	
5.20 рм – 5.35 рм (15 min)	Standard and Emerging Strategies for High-Risk, Early-Stage, Triple-Negative Breast Cancer	Joyce O'Shaughnessy, MD
5.35 рм – 5.55 рм (20 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
5.55 рм – 6.00 рм (5 min)	Summary and 3 Key Takeaways	
6.00 рм	Wrap-up and Overview of Day 2 Activities	Joyce O'Shaughnessy, MD

APTITUDE HEALTH

Meeting Agenda: Day 2 (1/2)



Time (CST)	Торіс	Speaker/Moderator
8.00 ам – 8.05 ам (5 min)	Introduction and Review Agenda for Day 2	Joyce O'Shaughnessy, MD
8.05 ам – 8.20 ам (15 min)	Current and Investigational Approaches in Metastatic Triple- Negative Breast Cancer	William Sikov, MD
8.20 ам – 8.50 ам (30 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
8.50 ам – 8.55 ам (5 min)	Summary and 3 Key Takeaways	
8.55 ам – 9.05 ам (10 min)	Therapeutic Horizons in HR+ Early Breast Cancer	Peter A. Kaufman, MD
9.05 ам – 9.25 ам (20 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
9.25 ам – 9.30 ам (5 min)	Summary and 3 Key Takeaways	
9.30 ам – 9.45 ам (15 min)	Break	





Meeting Agenda: Day 2 (2/2)



Time (CST)	Торіс	Speaker/Moderator
9.45 ам – 10.00 ам (15 min)	Therapeutic Horizons in HR+ Advanced Breast Cancer	Hope S. Rugo, MD
10.00 ам – 10.40 ам (40 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
10.40 ам – 10.45 ам (5 min)	Summary and 3 Key Takeaways	
10.45 ам – 10.55 ам (10 min)	Old and New Targets in Breast Cancer	Peter A. Kaufman, MD
10.55 ам – 11.20 ам (25 min)	Key Questions and Topics for Discussion	Joyce O'Shaughnessy, MD
11.20 ам – 11.25 ам (5 min)	Summary and 3 Key Takeaways	
11.25 ам – 11.55 ам (30 min)	General Discussion: Future Directions in Breast Cancer Treatment	Joyce O'Shaughnessy, MD
11.55 ам – 12.00 рм (5 min)	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 (1/2) Presented by William Sikov, MD

CURRENT STANDARD BIOMARKERS

> ER and PgR (IHC)

PROGNOSTIC AND PREDICTIVE GENOMIC ASSAYS

- > Oncotype DX
- Reserve and the second state of the second state and the second state is an angeing plane. We shall a second state and and provide the provide state of the second sta
- A This approach is seen as a post while to a prime proprieties is after programming to the destination of the destination of
- Part append 1.phase 5. approved to another second study 5. approved to another a second or advantage 4. append to another to an advantage 4. append to a second to an advantage 4. append to a second to a se
- A Top ANTIC Approximate to search as another to the specific particular and antiparticly dimension in and to be allocated as a static to the specific particular with antiparticly dimension. I uses which it is allocated, and with antianti-control to the segments and the segments and there, way its and





Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer (2/2) Presented by William Sikov, MD

GENETIC AND GENOMIC PROFILING INVESTIGATIONAL ASSAYS Germline genetic testing > ctDNA >



APTITUDE HEALTH

EPICS

Key Insights

Current and Emerging Biomarkers and Testing Methodologies in Breast Cancer

Experts Discussed Current Standard Biomarkers in Breast Cancer

MOLECULAR BIOMARKERS

Many molecular biomarkers for breast cancer are useful but need further optimization







EPICS

Experts Debated the Role of Ki67 Testing in Breast Cancer

EPICS

Ki67 AND ADJUVANT THERAPY DECISIONS

Most of the experts still consider Ki67 testing valuable, despite the change in







Experts Discussed Testing for Germline and Somatic Mutations

GERMLINE MUTATION TESTING AND NEXT-GEN SEQUENCING

Experts agreed that most patients with high-risk early-stage or metastatic









EPICS

Experts Considered the Potential Value of MRD Assessment in Breast Cancer

ctDNA TESTING FOR MINIMAL RESIDUAL DISEASE

ctDNA assessment is very promising for identifying patients who will likely







EPICS



EPICS

The Changing Landscape of HER2+ Early Breast Cancer



The Changing Landscape of HER2+ Early Breast Cancer (1/3) Presented by Joyce O'Shaughnessy, MD



ADJUVANT THERAPY FOR HER2+ BREAST CANCERS

> 10-year data from BCIRG 006, as well as from the TRAIN
ExteNET: Exploratory Analysis in HR+, HER2+









The Changing Landscape of HER2+ Early Breast Cancer (2/3) Presented by Joyce O'Shaughnessy, MD



DE-ESCALATED ADJUVANT APPROACHES FOR LOW-RISK HER2+ BREAST CANCERS

De-escalated HER2-targeted adjuvant regimens have











The Changing Landscape of HER2+ Early Breast Cancer (3/3) Presented by Joyce O'Shaughnessy, MD



INDIVIDUALIZING ADJUVANT THERAPY FOLLOWING PREOPERATIVE HER2-TARGETED THERAPY

For patients with residual disease following preoperative **Current Approach for (Neo)Adjuvant Treatment of** >





APTITUDE HEALTH

EPICS

Key Insights

The Changing Landscape of HER2+ Early Breast Cancer

Experts Debated Adjuvant and Neoadjuvant Therapy for Early-Stage HER2+ Breast Cancer

DIMINISHING ROLE FOR ANTHRACYCLINES

Most oncologists in the US have switched to a docetaxel-carboplatin backbone



APTITUDE HEALTH®



EPICS

Experts Discussed Individualizing Therapy for Early-Stage HER2+ Breast Cancer



HER2DX GENE EXPRESSION ASSAY

Experts do not currently use the HER2DX assay in their clinics







Experts Speculated on the Future of Treatment for Early-Stage HER2+ Breast Cancer (1/2)

POST-OP TREATMENT FOR RESIDUAL DISEASE

Experts predict that T-DXd will eventually replace T-DM1 as the treatment for







Experts Speculated on the Future of Treatment for Early-Stage HER2+ Breast Cancer (2/2)

MRD TESTING

Experts also envision a future in which some patients who achieve a pCR may









EPICS

Maximizing Potential Targeting of HER2 in HER2+ mBC



Maximizing Potential Targeting of HER2 in HER2+ mBC (1/3) Presented by Kelly McCann, MD, PhD



CURRENT TREATMENT ALGORITHM FOR HER2+ mBC

> A taxane plus trastuzumab plus pertuzumab remains the **DESTINY-Breast03: PFS**







Maximizing Potential Targeting of HER2 in HER2+ mBC (2/3) Presented by Kelly McCann, MD, PhD



ADVANCES FOR HER2+ BRAIN METASTASES

> Results from the HER2CLIMB trial showing a significant











Maximizing Potential Targeting of HER2 in HER2+ mBC (3/3) Presented by Kelly McCann, MD, PhD



INVESTIGATIONAL AGENTS IN CLINICAL TRIALS FOR HER2+ mBC







APTITUDE HEALTH

EPICS

Key Insights

Maximizing Potential Targeting of HER2 in HER2+ mBC

Experts Discussed Sequencing Strategies for HER2+ mBC

2L THERAPY

Most of the experts' choice of 2L therapy depends on the balance between



APTITUDE HEALTH®



EPICS

Experts Discussed Special Management Scenarios

CNS METASTASES

Most experts do not routinely screen asymptomatic patients with HER2+ mBC







EPICS

Experts Considered Areas of Need for Additional Investigation EPICS

ER+, HER2+ mBC

Experts see ER+, HER2+ mBC as a "mixed bag of cancers" and a different







EPICS

Clinical Implications of HER2-Low Breast Cancer



Clinical Implications of HER2-Low Breast Cancer (1/2) Presented by Banu Arun, MD



NEW TREATMENT PARADIGMS









Clinical Implications of HER2-Low Breast Cancer (2/2) Presented by Banu Arun, MD



UNANSWERED QUESTIONS AND AVENUES FOR FURTHER INVESTIGATION

> One key answer that needs to be determined is the








APTITUDE HEALTH®

EPICS

Key Insights

Clinical Implications of HER2-Low Breast Cancer

Experts Discussed the Use of T-DXd in HER2-Low and -Ultra-Low mBC

HER2-LOW mBC (IHC 1+ or 2+)

HER2 low (by IHC) is now a recognized subset of HR+, HER2– BC and TNBC,







Experts Discussed the Need for More Quantitative Assays to Assess HER2 Protein Expression

EPICS

SHORTCOMINGS OF IHC ASSAYS

One of the biggest needs in the field currently is an accurate quantitative assay





Experts Debated Unanswered Questions and Areas for Future Investigation

EPICS

DURATION OF THERAPY

One question that needs to be addressed in both the HER2+ and HER2-low









EPICS

Standard and Emerging Strategies for High-Risk, Early-Stage, Triple-Negative Breast Cancer



Standard and Emerging Strategies for High-Risk, Early-Stage, Triple-Negative Breast Cancer (1/3)



Presented by Joyce O'Shaughnessy, MD

KEYNOTE-522









Standard and Emerging Strategies for High-Risk, Early-Stage, Triple-Negative Breast Cancer (2/3)



Presented by Joyce O'Shaughnessy, MD

OTHER REPORTED (NEO)ADJUVANT TRIALS FOR TNBC









Standard and Emerging Strategies for High-Risk, Early-Stage, Triple-Negative Breast Cancer (3/3)



Presented by Joyce O'Shaughnessy, MD

ONGOING AND PLANNED (NEO)ADJUVANT TRIALS FOR TNBC











APTITUDE HEALTH

EPICS

Key Insights

Standard and Emerging Strategies for High-Risk, Early-Stage, Triple-Negative Breast Cancer

Experts Debated Current Standards and Practice Patterns for EPICS Early-Stage TNBC

KEYNOTE-522 IMPLICATIONS

KEYNOTE-522 is considered SOC for stage 2/3 TNBC, but the optimal treatment





Experts Discussed Practical Considerations in Patient Treatment

ALTERNATIVE ADJUVANT APPROACHES

For patients with BRCA-mutated TNBC who start with the KN-522 regimen,









Experts Discussed Immune-Related Adverse Events

TOXICITY MANAGEMENT

Experts perceive that patients experience more immune-related toxicities with







Experts Considered Unmet Needs and Areas for Future Investigation in Early-Stage TNBC

UNANSWERED RESEARCH QUESTIONS

There are many open questions that need to be addressed in future clinical











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 William Sikov, MD

PARP INHIBITION









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



Presented by William Sikov, MD

IMMUNE CHECKPOINT INHIBITION









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



Presented by William Sikov, MD

ADCs FOR mTNBC







APTITUDE HEALTH

EPICS

Key Insights

Current and Investigational Approaches in Metastatic Triple-Negative Breast Cancer

Experts Discussed the Use of PARP Inhibitors for mTNBC

EPICS

PARPI TIMING AND SEQUENCING

Monotherapy with a PARPi is considered a reasonable 1L treatment for an





Experts Considered Current and Future Biomarkers in TNBC



BIOMARKER TESTING

Experts support early testing for genetic and surface biomarkers so that a





Experts Debated the Sequence of ADCs in mTNBC



ADC SELECTION

Most experts currently prefer using SG first in their patients with mTNBC, and T-







Experts Discussed Emerging Agents and Assays in mTNBC

INVESTIGATIONAL STRATEGIES

Experts believe there is promise for targeted therapies for AR+ TNBC, and they









EPICS

Therapeutic Horizons in HR+ Early Breast Cancer



Therapeutic Horizons in HR+ Early Breast Cancer (1/2) Presented by Peter A. Kaufman, MD



ADJUVANT CDK4/6 INHIBITORS









Therapeutic Horizons in HR+ Early Breast Cancer (2/2) Presented by Peter A. Kaufman, MD



PARP INHIBITORS AND OTHER ADJUVANT STRATEGIES

> Adjuvant olaparib for 1 year is now standard of care for **OlvmpiA Overall Survival**





APTITUDE HEALTH

EPICS

Key Insights

Therapeutic Horizons in HR+ Early Breast Cancer

Experts Discussed the Use of Abemaciclib in the Adjuvant Setting

ADJUVANT ABEMACICLIB

Abemaciclib is considered "standard of care" in the adjuvant setting, in





Experts Speculated on the Implications of the NATALEE Results

ADJUVANT CDK4/6i SELECTION

Experts are enthusiastic about the prospect of having 2 CDK4/6 inhibitor







Experts Debated Treatment Strategies for HR+, HER2– gBRCA-Mutated Breast Cancer

PARPi, CDK4/6i, OR BOTH?

For patients with very-high-risk node-positive, gBRCA-mutated HR+, HER2-











Experts Speculated on the Potential Role for Oral SERDs in Early-Stage HR+ Breast Cancer

EPICS

ONGOING ADJUVANT SERD TRIALS









EPICS

Therapeutic Horizons in HR+ Advanced Breast Cancer



Therapeutic Horizons in HR+ Advanced Breast Cancer (1/3) Presented by Hope S. Rugo, MD



CDK4/6 INHIBITORS

All the CDK4/6i trials have demonstrated an improvement in >

OPTIONS FOLLOWING PROGRESSION ON CDK4/6i

> Endocrine combinations after progression on a CDK4/6i-







Therapeutic Horizons in HR+ Advanced Breast Cancer (2/3) Presented by Hope S. Rugo, MD



RECENT APPROVALS FOR HR+ mBC









Therapeutic Horizons in HR+ Advanced Breast Cancer (3/3) Presented by Hope S. Rugo, MD



INVESTIGATIONAL STRATEGIES FOR HR+ mBC







APTITUDE HEALTH

EPICS

Key Insights

Therapeutic Horizons in HR+ Advanced Breast Cancer

Experts Debated 1L Therapy Selection for HR+, HER2– mBC



1L ENDOCRINE THERAPY PLUS CDKi

The 1L therapy SOC is ET plus a CDK4/6i






Experts Debated Sequencing Endocrine Therapies After Progression on ET Plus CDKi

TARGETING THE PI3K/AKT/mTOR PATHWAY

Upon progression on a 1L CDKi plus ET, most experts change to an alternate ET







Experts Discussed Sequencing Considerations in HR+, HER2– mBC

MONITORING AND EVALUATING PATIENTS

More data are needed regarding how to best sequence available agents, and it







Experts Debated Sequencing ADCs and Cytotoxic Agents in HR+, HER2– mBC



T-DXd is preferred first over SG for patients with HER2-low HR+ mBC, while SG







Experts Considered Opportunities and Challenges in HR+, HER2– mBC

FUTURE DIRECTIONS WITH NEW ENDOCRINE AGENTS

Novel endocrine and biologics combinations are moving forward to maximize









EPICS

Old and New Targets in Breast Cancer



Old and New Targets in Breast Cancer (1/2) Presented by Peter A. Kaufman, MD



CONVENTIONAL CYTOTOXIC AGENTS

Conventional chemotherapy has not disappeared and will continue to be used for a time









Old and New Targets in Breast Cancer (2/2) Presented by Peter A. Kaufman, MD



NOVEL TARGETED AGENTS AND STRATEGIES

- > A number of novel ADCs and bispecific Abs are in various phases of development
 - 31.1.2. 2023. Annual of a segmenting splices and segmenting solutions. So patients for a segmention of a segment of the second second second second second for a second second second second second for a second second second second second second second for a second second second second second second second for a second second second second second second second for a second second second second second second second for a second second second second second second second for a second second second second second second second for a second second second second second second second for a second second second second second second second for a second second second second second second second for a second second second second second second second second for a second second second second second second second second for a second sec

Patritumab-DXd Phase I/II Study in HER3+ (IHC 2+/3+) BC







APTITUDE HEALTH

EPICS

Key Insights

Old and New Targets in Breast Cancer

Experts Discussed Investigational Agents for mBC

ORAL TAXANES

Experts are very interested in oral taxanes and would rapidly adopt one if it became available

> Multiple companies have performed trials on such agents, which demonstrated











APTITUDE HEALTH®

EPICS

Key Insights

General Discussion: Future Directions in Breast Cancer Treatment

Experts Discussed the Biggest Challenges in Breast Cancer Treatment Today (1/2)

TUMOR BIOLOGY

There is a need to better understand







Experts Discussed the Biggest Challenges in Breast Cancer Treatment Today (2/2)

ADHERENCE TO ORAL THERAPIES

Adherence historically has been low with endocrine therapy in the curative







Experts Considered Educational Gaps in the Community

EPICS

EDUCATIONAL NEEDS FOR COMMUNITY PRACTICES

Further education of community physicians is needed with regard to







Experts Speculated on the Future of Breast Cancer Management

PREDICTIONS FOR THE FUTURE

> The role of surgery will decrease as systemic treatments improve in the curative











- **US** 5901-C Peachtree Dunwoody Road NE Suite 200, Atlanta, GA 30328, US
- **EU** Wilhelmina van Pruisenweg 104 2595 AN The Hague, the Netherlands
- **UK** 6th Floor, 2 Kingdom Street London, W2 6BD, United Kingdom

aptitudehealth.com

