APTITUDE HEALTH®

EPICS

Conference Coverage: ASCO 2024 – Focus on Breast Cancer

Tuesday, June 11, 2024

Report Contents

EPICS

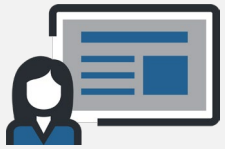
Meeting Snapshot

EPICS

EPICS

LIVE ROUNDTABLE

DATE:
June 11, 2024



DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in breast cancer
- > 4 from the US
- > 3 from Europe

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

Panel Consisting of 4 US and 3 European Breast Cancer Experts

EPICS

Mark Pegram, MD
Stanford University
School of Medicine

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

William Sikov, MD, FACP, FNCBC
Women & Infants Hospital

CHAIR:
Adam Brufsky, MD, PhD
University of Pittsburgh
School of Medicine

Peter Schmid, FRCP, MD, PhD
Barts Cancer Institute

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

Javier Cortés, MD, PhD
International Breast Cancer Center

APTITUDE HEALTH®

Meeting Agenda (1/2)

EPICS

Time (ET/CEST)	Topic	Speaker/Moderator
11.00 AM – 11.05 AM/ 17.00 – 17.05	Welcome and Introductions	Adam Brufsky, MD, PhD
11.05 AM – 11.20 AM/ 17.05 – 17.20	**New and Emerging Treatments in HER2+ Metastatic BC (mBC)**	Nadia Harbeck, MD, PhD
11.20 AM – 11.40 AM/ 17.20 – 17.40	Discussion: New and Emerging Treatments in HER2+ mBC	All
11.40 AM – 11.45 AM/ 17.40 – 17.45	Key Takeaways: HER2+ mBC	Nadia Harbeck, MD, PhD
11.45 AM – 12.00 PM/ 17.45 – 18.00	**New and Emerging Approaches in HR+, HER2– Early BC**	Mark Pegram, MD
12.00 PM – 12.20 PM/ 18.00 – 18.20	Discussion: New and Emerging Approaches in HR+, HER2– Early BC	All
12.20 PM – 12.25 PM/ 18.20 – 18.25	Key Takeaways: HR+, HER2– Early BC	Mark Pegram, MD
12.25 PM – 12.30 PM/ 18.25 – 18.30	Break	

Meeting Agenda (2/2)

EPICS

Time (ET/CEST)	Topic	Speaker/Moderator
12.30 PM – 12.40 PM/ 18.30 – 18.40	**New and Emerging Approaches in HR+, HER2– mBC**	Joyce A. O'Shaughnessy, MD
12.40 PM – 12.50 PM/ 18.40 – 18.50	**New and Emerging Approaches in HR+, HER2– mBC (cont.)**	Javier Cortés, MD, PhD
12.50 PM – 1.10 PM/ 18.50 – 19.10	Discussion: HR+, HER2– mBC	All
1.10 PM – 1.15 PM/ 19.10 – 19.15	Key Takeaways: HR+, HER2– mBC	Joyce A. O'Shaughnessy, MD, and Javier Cortés, MD, PhD
1.15 PM – 1.25 PM/ 19.15 – 19.25	**Advances in Early Triple-Negative Breast Cancer (TNBC)**	Peter Schmid, FRCP, MD, PhD
1.25 PM – 1.35 PM/ 19.25 – 19.35	Discussion: Advances in Early TNBC	All
1.35 PM – 1.45 PM/ 19.35 – 19.45	**Advances in Metastatic TNBC (mTNBC)**	William Sikov, MD, FACP, FNCBC
1.45 PM – 1.55 PM/ 19.45 – 19.55	Discussion: Advances in mTNBC	All
1.55 PM – 2.00 PM/ 19.55 – 20.00	Key Takeaways: Advances in Early and mTNBC	Peter Schmid, FRCP, MD, PhD, and William Sikov, MD, FACP, FNCBC
2.00 PM/ 20.00	Meeting Close	Adam Brufsky, MD, PhD

APTITUDE HEALTH®

EPICS

Congress Highlights

New and Emerging Treatments in HER2+ mBC

Trastuzumab and pertuzumab in combination with eribulin mesylate or a taxane as first-line chemotherapeutic treatment for HER2-positive, locally advanced or metastatic breast cancer: Results of a multicenter, randomized, non-inferiority phase 3 trial in Japan (JBCRG-M06/EMERALD)

Yamashita T, et al. Abstract 1007

EPICS

DESTINY-Breast07: Dose-expansion interim analysis of T-DXd monotherapy and T-DXd + pertuzumab in patients with previously untreated HER2+ mBC

Andre F, et al. Abstract 1009

EPICS

Trastuzumab deruxtecan in patients with breast cancer with brain metastases: The DE-REAL study

Botticelli A, et al. Abstract 1032

EPICS

STUDY POPULATION

- [illegible]

OUTCOME

- [illegible]

EXPERT CONCLUSIONS

[illegible]

ACE-Breast-02: A pivotal phase II/III trial of ARX788, a novel anti-HER2 antibody-drug conjugate (ADC), versus lapatinib plus capecitabine for HER2+ advanced breast cancer (ABC)

Xichun H, et al. Abstract 1020

EPICS

STUDY POPULATION

- [illegible]

OUTCOMES

- [illegible]

EXPERT CONCLUSIONS

[illegible]

Primary results from PATRICIA cohort C (SOLTI-1303), a randomized phase II study evaluating palbociclib with trastuzumab and endocrine therapy in pretreated HER2-positive and PAM50 luminal advanced breast cancer

Ciruelos EM, et al. Abstract 1008

EPICS

Tucatinib and trastuzumab for previously treated HER2−mutated metastatic breast cancer (SGNTUC−019): A phase 2 basket study

Pohlmann PR, et al. Abstract 1105

EPICS

Imlunestrant, an oral selective estrogen receptor degrader (SERD), in combination with human epidermal growth factor receptor 2 (HER2) directed therapy, with or without abemaciclib, in estrogen receptor (ER) positive, HER2 positive advanced breast cancer (aBC): EMBER phase 1a/1b study

Bhave MA, et al. Abstract 1027

EPICS

APTITUDE HEALTH®

EPICS

Key Insights

New and Emerging Treatments in HER2+ mBC

New and Emerging Treatments in HER2+ mBC

EPICS

No practice-changing data for HER2+ mBC were presented at ASCO 2024

New and Emerging Treatments in HER2+ mBC

EPICS

Maintenance with CDK4/6 inhibitors in HR+, HER2+ mBC

New and Emerging Treatments in HER2+ mBC

EPICS

Oral SERDs in HR+, HER2+ mBC

APTITUDE HEALTH®

EPICS

Congress Highlights

New and Emerging Approaches in HR+, HER2– Early BC

Prognostic utility of ctDNA detection in the monarchE trial of adjuvant abemaciclib plus endocrine therapy (ET) in HR+, HER2-, node-positive, high-risk early breast cancer (EBC)

Loi S, et al. Abstract LBA507

EPICS

BACKGROUND

Efficacy and genomic analysis of *HER2*-mutant, metastatic triple-negative breast cancer treated with neratinib alone or in combination with trastuzumab in the phase 2 SUMMIT basket trial

Jhaveri KL, et al. Abstract 1094

EPICS

BACKGROUND

Association of MammaPrint index and 3-year outcome of patients with HR+HER2- early-stage breast cancer treated with chemotherapy with or without anthracycline

O'Shaughnessy J, et al. Abstract 511

EPICS

BACKGROUND

Elucidating the immune active state of HR+HER2- MammaPrint High 2 early breast cancer

Coban EF, et al. Abstract 506

EPICS

BACKGROUND

- I-SPY 2 showed that patients with MammaPrint High 2 (H2), HR+, HER2- tumors

MammaPrint High 2 Tumors Have Increased Innate Immunity

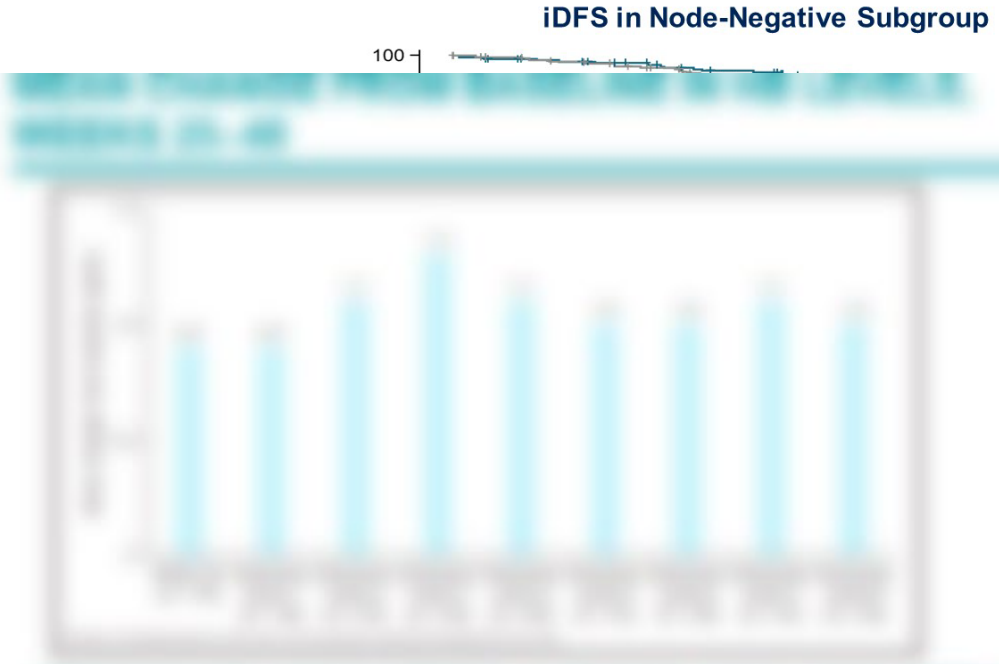
Macrophages | Dendritic Cells | Natural Killer

Baseline (BL) characteristics and efficacy endpoints for patients (pts) with node-negative (N0) HR+/HER2− early breast cancer (EBC): NATALEE trial

Yardley DA, et al. Abstract 512

EPICS

BACKGROUND

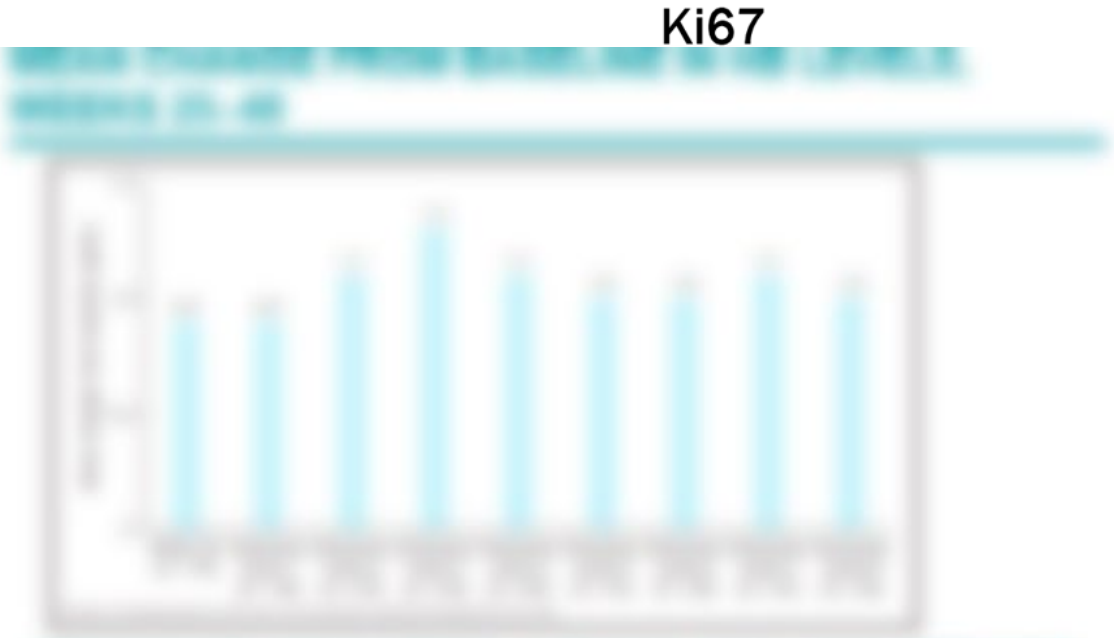


I-SPY2 Endocrine Optimization Pilot (EOP): Neoadjuvant amcenestrant +/- abemaciclib +/- letrozole in molecularly selected patients (pts) with HR+ HER2- stage 2/3 breast cancer (BC)

Chien AJ, et al. Abstract 601

EPICS

BACKGROUND



APTITUDE HEALTH®

EPICS

Key Insights

New and Emerging Approaches in HR+, HER2– Early BC

New and Emerging Approaches in HR+, HER2– Early BC

EPICS

Prognostic utility of ctDNA in HR+, HER2–, node-positive, high-risk early BC

New and Emerging Approaches in HR+, HER2– Early BC

EPICS

MammaPrint in HR+, HER2– high-risk early BC

APTITUDE HEALTH®

EPICS

Congress Highlights

New and Emerging Approaches in HR+, HER2– mBC

First-line inavolisib/placebo + palbociclib + fulvestrant (Inavo/Pbo+Palbo+Fulv) in patients (pts) with *PIK3CA*-mutated, hormone receptor-positive, HER2-negative locally advanced/metastatic breast cancer who relapsed during/within 12 months (mo) of adjuvant endocrine therapy completion: INAVO120 Phase III randomized trial additional analyses

Juric D, et al. Abstract 1003

EPICS

Time to discontinuation of next-line treatment, or

Palbociclib plus exemestane with GnRH agonist vs capecitabine in premenopausal patients with HR+/HER2- metastatic breast cancer: Updated survival results of the randomized phase 2 study Young-PEARL

Park YH, et al. Abstract LBA1002

EPICS

BACKGROUND

Primary PFS[a]

Abemaciclib plus fulvestrant vs fulvestrant alone for HR+, HER2- advanced breast cancer following progression on a prior CDK4/6 inhibitor plus endocrine therapy: Primary outcome of the phase 3 postMONARCH trial

Kalinsky K, et al. Abstract LBA1001

EPICS

BACKGROUND

Investigator-assessed PFS

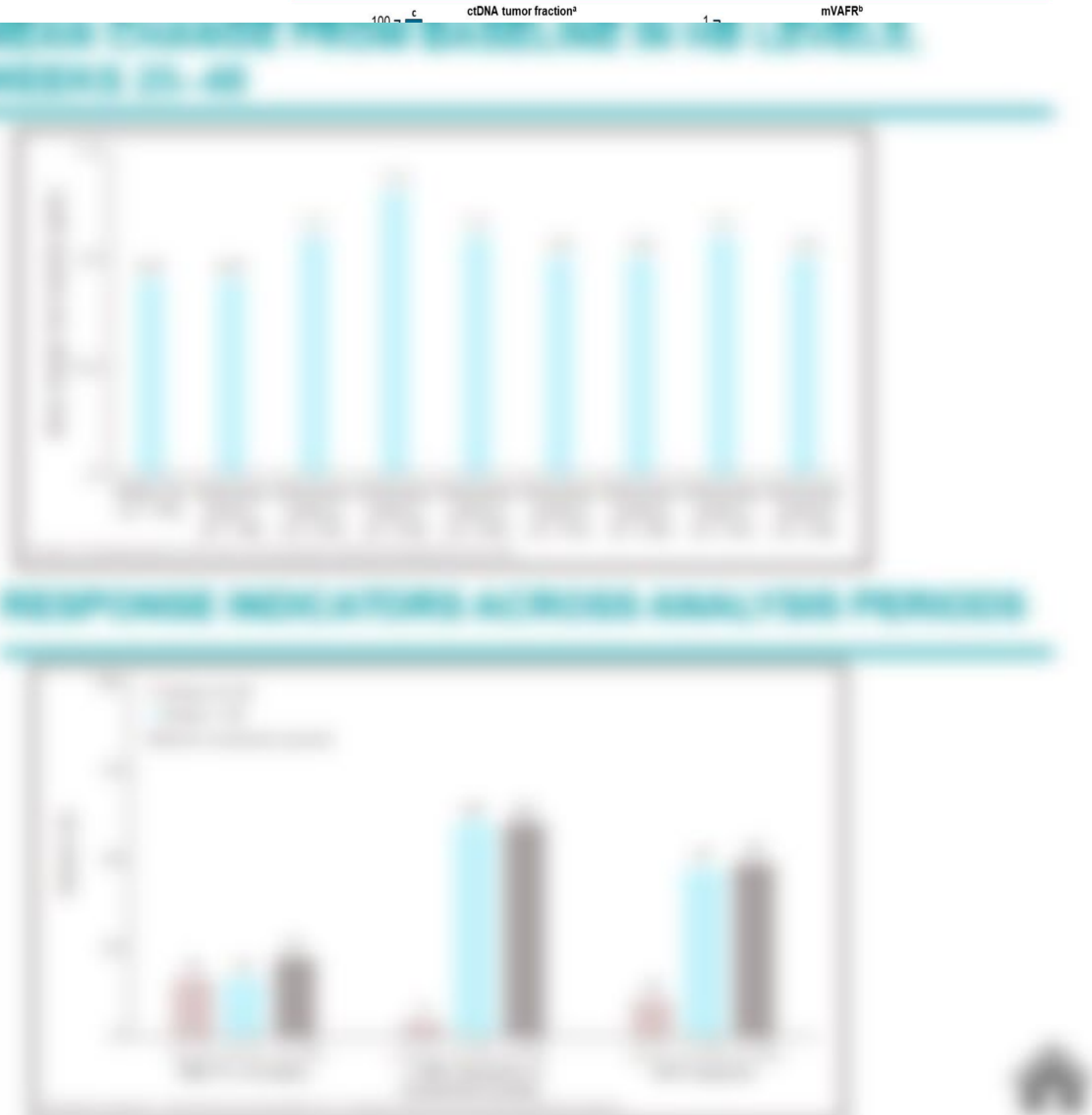
BLU-222, an investigational, oral, potent, and highly selective CDK2 inhibitor (CDK2i), as monotherapy in patients (pts) with advanced solid tumors and in combination with ribociclib (RIBO) and fulvestrant (FUL) in HR+/HER2− breast cancer (BC)

Juric D, et al. Abstract 1056

EPICS

BACKGROUND

Figure 5: Reduction in ctDNA was observed as measured by both tumor fraction and mVAFR methods in patients treated with BLU-222 + ribociclib + fulvestrant combination

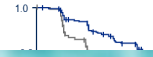


Trastuzumab deruxtecan (T-DXd) vs physician's choice of chemotherapy (TPC) in patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor receptor 2 (HER2)-low or HER2-ultralow metastatic breast cancer (mBC) with prior endocrine therapy (ET): Primary results from DESTINY-Breast06 (DB-06)

Curigliano G, et al. Abstract LBA1000

EPICS

PFS (BICR) in HER2-low: primary endpoint



Hazard ratio

Datopotamab deruxtecan (Dato-DXd) vs chemotherapy (CT) in previously treated inoperable or metastatic hormone receptor-positive, HER2-negative (HR+/HER2–) breast cancer (BC): Patient-reported outcomes (PROs) from the TROPION-Breast01 study

Pernas S, et al. Abstract 1006

EPICS

BACKGROUND

SACI-IO HR+: A randomized phase II trial of sacituzumab govitecan with or without pembrolizumab in patients with metastatic hormone receptor-positive/HER2-negative breast cancer

Garrido-Castro AC, et al. Abstract LBA1004

EPICS

BACKGROUND

STUDY POPULATION

- [illegible]

OUTCOMES

- [illegible]

EXPERT CONCLUSIONS

[illegible]

Progression-Free Survival

Treatment Arm	SG + Pembrolizumab (N=52)	SG (N=52)
N PFS events	[illegible]	[illegible]

Interim analysis (IA) of the giredestrant (G) + everolimus (EVERO) arm in MORPHEUS Breast Cancer (BC): A phase I/II study of G treatment (tx) combinations in patients (pts) with estrogen receptor-positive (ER+), HER2-negative, locally advanced/metastatic BC (LA/mBC)

Wander SA, et al. Abstract 1059

EPICS

BACKGROUND

- ET plus CDK4/6i is the first-line therapy of ER+ mBC. Finding effective ET combinations after progression remains a challenge; however, targeting the Akt/mTOR pathway is a promising approach
- Giredestrant (G) is a highly potent, nonsteroidal, oral (PO), selective ER antagonist and degrader that is well tolerated and achieves robust ER occupancy
- A 16-week IA of the G plus EVERO (an approved mTOR inhibitor) vs EVERO arm in MORPHEUS BC (NCT04802759) was presented

OUTCOME

- Confirmed ORR in the G plus EVERO arm was 40% (n=15)
- Partial responses were reported in 40% of patients (n=6)
- 40% of patients (n=6) had SD
- DCR was 53.3% (n=8)
- Median PFS was 7.62 mo with everolimus and 4.67 mo without

EXPERT CONCLUSIONS

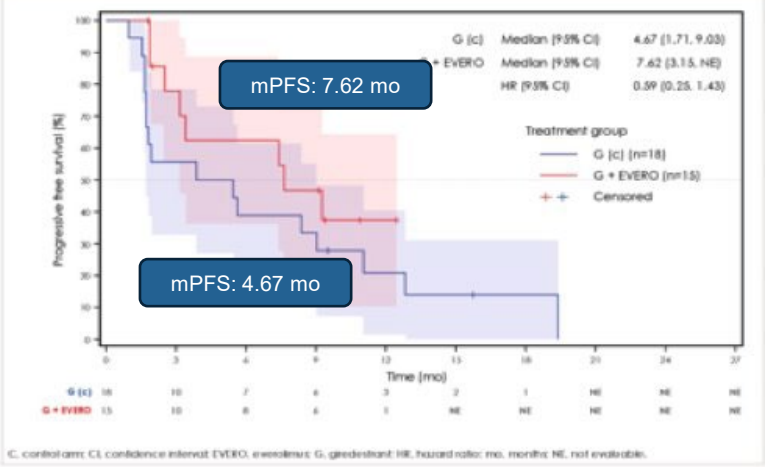
- *"This is an important study because this is the basis for the evERA trial"*
- *"Small numbers; the signal is clear"*

Table 2: Best confirmed overall response rates

Pts, n (%)	Giredestrant (n = 18)	Giredestrant + everolimus (n = 15)
Responders	5.6%	40%
95% CI		
CR	0	0
95% CI	(0.00, 18.53)	(0.00, 21.80)
PR	1 (5.6)	6 (40.0)
95% CI	(0.14, 27.29)	(16.34, 67.71)
SD	9 (50.0)	6 (40.0)
95% CI	(26.02, 73.98)	(16.34, 67.71)
PD	7 (38.9)	3 (20.0)
95% CI	(17.30, 64.25)	(4.33, 48.09)
NE/missing	1 (5.6)	0
DCR	9 (50.0)	8 (53.3)*
95% CI	(26.02, 73.98)	(26.59, 78.73)
CBR	7 (38.9)	7 (46.7)*
95% CI	(17.30, 64.25)	(21.27, 73.41)

* Data missing from two subjects who discontinued study therapy without PD.
CBR, clinical benefit rate; CI, confidence interval; CR, complete response; DCR, disease control rate; NE, not evaluable; PD, disease progression; PR, partial response; pts, patients; SD, stable disease.

Figure 3: Progression-free survival



C, control arm; CI, confidence interval; EVERO, everolimus; G, giredestrant; HR, hazard ratio; mo, months; NE, not evaluable.

APTITUDE HEALTH®

Elacestrant in combination with abemaciclib in patients (pts) with brain metastasis from estrogen receptor-positive (ER+), HER2-negative (HER2-) breast cancer: Preliminary data from ELECTRA, an open-label, multicenter, phase 1b/2 study

Ibrahim NK, et al. Abstract 1064

EPICS

Best Tumor Response

Elacestrant in various combinations in patients (pts) with estrogen receptor-positive (ER+), HER2-negative (HER2-) locally advanced or metastatic breast cancer (adv/mBC): Preliminary data from ELEVATE, a phase 1b/2, open-label, umbrella study

Rugo HS, et al. Abstract 1069

EPICS

APTITUDE HEALTH®

EPICS

Key Insights

New and Emerging Approaches in HR+, HER2– mBC

New and Emerging Approaches in HR+, HER2– Metastatic BC

EPICS

First-line treatment for *PIK3CA*-mutated HR+, HER2– mBC

New and Emerging Approaches in HR+, HER2– Metastatic BC

EPICS

Premenopausal patients with HR+, HER2– mBC

New and Emerging Approaches in HR+, HER2– Metastatic BC

EPICS

T-DXd in HER2-low and -ultralow HR+, HER2– mBC

APTITUDE HEALTH®

EPICS

Congress Highlights

Advances in Early TNBC

A-BRAVE trial: A phase III randomized trial with avelumab in early triple-negative breast cancer with residual disease after neoadjuvant chemotherapy or at high risk after primary surgery and adjuvant chemotherapy

Conte PF, et al. Abstract LBA500

EPICS

Disease-Free Survival, ITT

Rates of pathologic complete response (pCR) after datopotamab deruxtecan (Dato) plus durvalumab (Durva) in the neoadjuvant setting: Results from the I-SPY2.2 trial

Shatsky RA, et al. Abstract LBA501

EPICS

BACKGROUND

A randomized, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo) adjuvant therapy in patients with early triple-negative breast cancer: Korean Cancer Study Group BR 15-1 PEARLY trial

Sohn J, et al. Abstract LBA502

EPICS

Phase II study of neoadjuvant ipilimumab and nivolumab in combination with paclitaxel following anthracycline-based chemotherapy in patients with treatment resistant stage III triple negative breast cancer (TNBC): BCT1702—Survival results

Loi S, et al. Abstract 608

EPICS

APTITUDE HEALTH®

EPICS

Key Insights

Advances in Early TNBC

Advances in Early TNBC

EPICS

No practice-changing data for early TNBC were presented at ASCO 2024

APTITUDE HEALTH®

EPICS

Congress Highlights

Advances in mTNBC

Enfortumab vedotin (EV) in triple-negative breast cancer (TNBC) and HR+/HER2- breast cancer (BC) cohorts of EV-202

Giordano A, et al. Abstract 1005

EPICS

BACKGROUND

Triple-Negative Breast Cancer

Sacituzumab tirumotecan (SKB264/MK-2870) in patients (pts) with previously treated locally recurrent or metastatic triple-negative breast cancer (TNBC): Results from the phase III OptiTROP-Breast01 study

Xu B, et al. Abstract 104

EPICS

Sequential combination of sacituzumab govitecan and talazoparib in metastatic triple negative breast cancer (mTNBC): Results from a phase II study

Occhiogrosso Abelman R, et al. Abstract 1102

EPICS

BACKGROUND

Ipatasertib (IPA) combined with non-taxane chemotherapy (CT) for patients (pts) with previously treated advanced triple-negative breast cancer (aTNBC): The PATHFINDER phase IIa trial

Gion M, et al. Abstract 1098

EPICS

BACKGROUND

APTITUDE HEALTH®

EPICS

Key Insights

Advances in mTNBC

Advances in mTNBC

EPICS

No practice-changing data for mTNBC were presented at ASCO 2024

APTITUDE HEALTH®

US 5901-B Peachtree Dunwoody Road
Suite 415, Atlanta, GA 30328, US

EU Laan van Nieuw Oost-Indië 133 F
2593 BM The Hague, the Netherlands

UK 6th Floor, 2 Kingdom Street
London, W2 6BD, United Kingdom

aptitudehealth.com