APTITUDE HEALTH®

EPICS

EPICS ASCO CONFERENCE COVERAGE: BREAST CANCER

Virtual meeting, June, 2020

EXECUTIVE SUMMARY

BACKGROUND

EPICS

- On June 3, 2020, Aptitude Health brought together a group of scientists and clinical investigators with expertise in breast cancer to attend an expert panel
- The goal of the expert panel was to discuss the latest therapeutic developments and translational research in breast cancer treatment, apply these advances to dynamic and oftentimes individualized clinical decision-making, and explore how emerging data will affect ongoing research, development of new compounds, and future treatment paradigms

FACULTY

EPICS

- Adam Brufsky, MD, PhD (chair)
  - UPMC Hillman Cancer Center-University of Pittsburgh MC
  - Pittsburgh, PA
- Pierfranco Conte, MD
  - University of Padova, Veneto Oncological Institute
  - Padova, Italy
- William Gradishar, MD
  - Northwestern University Feinberg School of Medicine
  - Chicago, IL
- Nadia Harbeck, MD, PhD
  - University of Munich
  - Munich, Germany
- Christian Jackisch, MD, PhD
  - Sana Klinikum Offenbach
  - Offenbach, Germany
- Joyce O'Shaughnessy, MD
  - Baylor-Sammons Cancer Center
  - Dallas, TX
- Mark Pegram, MD
  - Stanford University
  - Stanford, CA

AGENDA

EPICS

Time (EST)	Topic	Speaker/Moderator
1.00 PM (10 min)	Welcome and Introductions	Adam Brufsky, MD, PhD
1.10 PM (10 min)	**Advances in Triple-Negative Breast Cancer**	Pierfranco Conte, MD
1.20 PM (15 min)	Discussion	All
1.35 PM (5 min)	Key Takeaways	Adam Brufsky, MD, PhD/ Pierfranco Conte, MD
1.40 PM (20 min)	**Evolving Therapies for Hormone Receptor-Positive Breast Cancer**	Nadia Harbeck, MD, PhD
2.00 PM (30 min)	Discussion	All
2.30 PM (5 min)	Key Takeaways	Adam Brufsky, MD, PhD/ Nadia Harbeck, MD, PhD
2.35 PM (10 min)	**New Therapeutic Approaches for Early Stage and Metastatic HER2+ Breast Cancer**	Mark Pegram, MD
2.45 PM (20 min)	Discussion	All
3.05 PM (5 min)	Key Takeaways	Adam Brufsky, MD, PhD/ Mark Pegram, MD
3.10 PM (10 min)	**Insights Into Immune-Based and Chemotherapy for Breast Cancer**	Joyce O'Shaughnessy, MD
3.20 PM (10 min)	Discussion	All
3.30 PM (5 min)	Key Takeaways	Adam Brufsky, MD, PhD/ Joyce O'Shaughnessy, MD
3.35 PM (5 min)	Closing Remarks	Adam Brufsky, MD, PhD

QUOTES (1/2)

EPICS

"TNBC is becoming a really heterogeneous group of breast cancer patients; we will have very soon multiple therapeutic options."

QUOTES (2/2)

EPICS

APTITUDE HEALTH®

EPICS

Advances in Triple-Negative Breast Cancer

PIERFRANCO CONTE, MD

TNBC ABSTRACTS

EPICS

1000: KEYNOTE-355: RANDOMIZED, DOUBLE-BLIND, PHASE III STUDY OF PEMBROLIZUMAB + CHEMOTHERAPY VERSUS PLACEBO + CHEMOTHERAPY FOR PREVIOUSLY UNTREATED LOCALLY RECURRENT INOPERABLE OR METASTATIC TRIPLE-NEGATIVE BREAST CANCER. FIRST AUTHOR: JAVIER CORTES

Background

> KEYNOTE-355 is a phase III trial of pembrolizumab plus chemotherapy vs placebo plus chemotherapy for previously

Results

> There was a numeric, nonsignificant difference in PFS for the intent-to-treat population favoring pembrolizumab (7.5

TNBC ABSTRACTS

EPICS

1013: ASSOCIATION OF TUMOR MUTATIONAL BURDEN (TMB) AND CLINICAL OUTCOMES WITH PEMBROLIZUMAB (PEMBRO) VERSUS CHEMOTHERAPY (CHEMO) IN PATIENTS WITH METASTATIC TRIPLE-NEGATIVE BREAST CANCER (MTNBC) FROM KEYNOTE-119. FIRST AUTHOR: ERIC P. WINER

Background

> A subgroup analysis of the KEYNOTE-119 trial was presented. This phase III randomized study compared

TNBC ABSTRACTS

EPICS

1001: RESULTS OF A PHASE II RANDOMIZED TRIAL OF CISPLATIN +/- VELIPARIB IN METASTATIC TRIPLE-NEGATIVE BREAST CANCER (TNBC) AND/OR GERMLINE BRCA-ASSOCIATED BREAST CANCER (SWOG S1416). FIRST AUTHOR: PRIYANKA SHARMA

Background

- SWOG S1416 is a phase II randomized trial of cisplatin plus veliparib vs cisplatin plus placebo in patients with

TNBC ABSTRACTS

EPICS

1002: TBCRC 048: A PHASE II STUDY OF OLAPARIB MONOTHERAPY IN METASTATIC BREAST CANCER PATIENTS WITH GERMLINE OR SOMATIC MUTATIONS IN DNA DAMAGE RESPONSE (DDR) PATHWAY GENES (OLAPARIB EXPANDED). FIRST AUTHOR: NADINE M. TUNG

Background

- This was a phase II trial in mBC pts with germline or somatic mutations in DDR genes. Most of the patients

TNBC ABSTRACTS

TPS1109: A PHASE III TRIAL OF CAPIVASERTIB AND PACLITAXEL IN FIRST-LINE TREATMENT OF PATIENTS WITH METASTATIC TRIPLE-NEGATIVE BREAST CANCER (CAPitello290). FIRST AUTHOR: PETER SCHMID

DISCUSSION – PD-1/PD-L1 INHIBITORS IN TNBC (1/2)

EPICS

- The KEYNOTE-355 trial, a phase III study of pembrolizumab plus chemotherapy vs placebo plus

DISCUSSION – PD-1/PD-L1 INHIBITORS IN TNBC (2/2)

- PD-L1 expression is not a predictor of immunotherapy efficacy, but it is more prognostic in 3 TNBC

DISCUSSION – PARP INHIBITORS IN TNBC

EPICS

- Trials with PARP inhibitors (PARPi's) showed clear benefit in TNBC patients with g*BRCA* mutations

DISCUSSION – TREATMENT SEQUENCING IN TNBC

EPICS

At present, there is no optimal treatment sequence for patients with co-expression of multiple biomarkers

DISCUSSION – NOVEL THERAPIES IN TNBC (1/2)

- TNBC is becoming a heterogeneous group of BC patients

DISCUSSION – NOVEL THERAPIES IN TNBC (2/2)

- Sacituzumab govitecan is a promising new agent in the TNBC treatment landscape. It has recently

APTITUDE HEALTH®

EPICS

Evolving Therapies for Hormone Receptor-Positive Breast Cancer

NADIA HARBECK, MD, PHD

HR+ BC ABSTRACTS

EPICS

505: LETROZOLE + RIBOCICLIB VERSUS LETROZOLE + PLACEBO AS NEOADJUVANT THERAPY FOR ER+ BREAST CANCER (FELINE TRIAL). FIRST AUTHOR: QAMAR J. KHAN

Background

- The FELINE trial is a randomized, 3-arm adjuvant trial with 6 cycles of letrozole plus intermittent-dose ribociclib

HR+ BC ABSTRACTS

EPICS

601: ADAPTCYCLE: ADJUVANT DYNAMIC MARKER-ADJUSTED PERSONALIZED THERAPY (ADAPT) COMPARING ENDOCRINE THERAPY PLUS RIBOCICLIB VERSUS CHEMOTHERAPY IN INTERMEDIATE-RISK HR+/HER2- EARLY BREAST CANCER (EBC). FIRST AUTHOR: NADIA HARBECK

Background

- The ADAPTcycle trial, a phase III prospective study, is ongoing with adjuvant cyclin-dependent kinase 4/6

HR+ BC ABSTRACTS

EPICS

531: PHASE II STUDY OF ADJUVANT ENDOCRINE THERAPY WITH CDK 4/6 INHIBITOR, RIBOCICLIB, FOR LOCALIZED ER+/HER2- BREAST CANCER (LEADER). FIRST AUTHOR: LAURA SPRING

Background

- The LEADER trial is an adjuvant study using endocrine therapy with ribociclib for localized BC with 2 different

HR+ BC ABSTRACTS

EPICS

1007: PARSIFAL: A RANDOMIZED, MULTICENTER, OPEN-LABEL, PHASE II TRIAL TO EVALUATE PALBOCICLIB IN COMBINATION WITH FULVESTRANT OR LETROZOLE IN ENDOCRINE-SENSITIVE PATIENTS WITH ESTROGEN RECEPTOR (ER)[+]/HER2[-] METASTATIC BREAST CANCER. FIRST AUTHOR: ANTONIO LLOMBART-CUSSAC

Background

- The phase II PARSIFAL trial is investigating palbociclib plus letrozole or palbociclib plus fulvestrant in the first-

HR+ BC ABSTRACTS

EPICS

1006: ALPELISIB (ALP) + FULVESTRANT (FUL) IN PATIENTS (PTS) WITH PIK3CA-MUTATED (MUT) HORMONE RECEPTOR-POSITIVE (HR+), HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2-NEGATIVE (HER2–) ADVANCED BREAST CANCER (ABC) PREVIOUSLY TREATED WITH CYCLIN-DEPENDENT KINASE 4/6 INHIBITOR (CDKI) + AROMATASE INHIBITOR (AI): BYLIEVE STUDY RESULTS. FIRST AUTHOR: HOPE S. RUGO

Background

- BYLieve is a noncomparative cohort study with alpelisib plus fulvestrant in patients who previously received

EPICS

SELECTIVE ESTROGEN RECEPTOR DEGRADERS/DOWNREGULATORS (SERDS) IN BC

The following abstracts were summarized and discussed

HR+ BC ABSTRACTS

SERDS IN BC

Background

- Efficacy of fulvestrant, the only approved SERD, may be limited by poor bioavailability. Oral SERDs may

HR+ BC ABSTRACTS

EPICS

1038: ADDITION OF ENDOCRINE THERAPY TO DUAL ANTI-HER2 TARGETED THERAPY IN INITIAL TREATMENT OF HER2+/HR+ METASTATIC BREAST CANCER. FIRST AUTHOR: MATTHEW LOFT

Background

> A nonrandomized meta-analysis from an Australian database that examined dual targeted therapy plus

DISCUSSION – HR+ EARLY BC (1/2)

EPICS

- Several presented trials evaluated the role of CDK4/6i in early stages of HR+ BC (FELINE: neoadjuvant

DISCUSSION – HR+ EARLY BC (2/2)

EPICS

- PALLAS, a phase III study of early stage HR+, HER2– BC with palbociclib in the adjuvant setting, is unlikely to

DISCUSSION – FIRST-LINE TREATMENT OF HR+ ADVANCED BC

EPICS

- CDKi's are established first-line treatment of HR+, HER2– advanced BC

DISCUSSION – SECOND-LINE TREATMENT OF HR+ ADVANCED BC

EPICS

Second-line treatment

> The advisors would not rechallenge with CDKi in case of true progression due to class effect. In case of treatment failure due to safety, they would switch to another, better CDKi with a different toxicity profile

DISCUSSION – NOVEL AGENTS IN HR+ ADVANCED BC

EPICS

- Oral SERDs are promising new agents
  - Some oral SERDs are active in patients who received multiple prior therapies. Advisors are interested in

DISCUSSION – TRIPLE-POSITIVE BC

Dual anti-HER2–targeted therapy with chemotherapy for triple-positive BC patients is in clinical

APTITUDE HEALTH®

EPICS

New Therapeutic Approaches for Early Stage and Metastatic HER2+ Breast Cancer

MARK PEGRAM, MD

HER2+ BC ABSTRACTS

EPICS

501: THREE-YEAR FOLLOW-UP OF NEOADJUVANT CHEMOTHERAPY WITH OR WITHOUT ANTHRACYCLINES IN THE PRESENCE OF DUAL HER2-BLOCKADE FOR HER2-POSITIVE BREAST CANCER (TRAIN-2): A RANDOMIZED PHASE III TRIAL. FIRST AUTHOR: ANNA VAN DER VOORT

Background

- The TRAIN-2 study was designed to obstruct the use of anthracyclines in the neoadjuvant setting of HER2+

HER2+ BC ABSTRACTS

EPICS

500: PRIMARY ANALYSIS OF KAITLIN: A PHASE III STUDY OF TRASTUZUMAB EMTANSINE (T-DM1) + PERTUZUMAB VERSUS TRASTUZUMAB + PERTUZUMAB + TAXANE, AFTER ANTHRACYCLINES AS ADJUVANT THERAPY FOR HIGH-RISK HER2-POSITIVE EARLY BREAST CANCER (EBC). FIRST AUTHOR: NADIA HARBECK

Background

- The KAITLIN trial was a large (n = 1846) phase III adjuvant trial in high-risk HER2+ early BC patients using T-

HER2+ BC ABSTRACTS

EPICS

508: PRIMARY RESULTS OF NRG ONCOLOGY / NSABP B-43: PHASE III TRIAL COMPARING CONCURRENT TRASTUZUMAB (T) AND RADIATION THERAPY (RT) WITH RT ALONE FOR WOMEN WITH HER2-POSITIVE DUCTAL CARCINOMA IN SITU (DCIS) AFTER LUMPECTOMY. FIRST AUTHOR: MELODY A. COBLEIGH

Background

- A prospective phase III adjuvant trial (n = 2014) with the addition of trastuzumab to radiation therapy vs

HER2+ BC ABSTRACTS

EPICS

1005: TUCATINIB VERSUS PLACEBO ADDED TO TRASTUZUMAB AND CAPECITABINE FOR PATIENTS WITH PREVIOUSLY TREATED HER2+ METASTATIC BREAST CANCER WITH BRAIN METASTASES (HER2CLIMB). FIRST AUTHOR: NANCY U. LIN

Background

- In the phase III HER2CLIMB trial, tucatinib in combination with trastuzumab and capecitabine resulted in better

HER2+ BC ABSTRACTS

EPICS

1040: SOPHIA ANALYSIS BY CHEMOTHERAPY (CTX) CHOICE: A PHASE III (P3) STUDY OF MARGETUXIMAB (M) + CTX VERSUS TRASTUZUMAB (T) + CTX IN PATIENTS (PTS) WITH PRETREATED HER2+ METASTATIC (MET) BREAST CANCER (MBC). FIRST AUTHOR: SANTIAGO ESCRIVÁ

Background

- In the phase III SOPHIA trial, margetuximab plus chemotherapy led to significant improvements in PFS and

HER2+ BC ABSTRACTS – CT DE-ESCALATION

515: DE-ESCALATED CHEMOTHERAPY VERSUS ENDOCRINE THERAPY PLUS PERTUZUMAB+ TRASTUZUMAB FOR HR+/HER2+ EARLY BREAST CANCER (BC): FIRST EFFICACY RESULTS FROM THE NEOADJUVANT WSG-TP-II STUDY. FIRST AUTHOR: OLEG GLUZ

Background

- The WSG-TP-II study compared a de-escalated chemotherapy plus pertuzumab plus trastuzumab vs

HER2+ BC ABSTRACTS – CT DE-ESCALATION

503: CHEMOTHERAPY (CT) DE-ESCALATION USING AN FDG-PET/CT (F-PET) AND PATHOLOGICAL RESPONSE-ADAPTED STRATEGY IN HER2[+] EARLY BREAST CANCER (EBC): PHERGAIN TRIAL. FIRST AUTHOR: JAVIER CORTES

Background

- The PHERGAIN study is a chemotherapy de-escalation trial with TCHP in Arm A and endocrine therapy plus

HER2+ BC ABSTRACTS – DESTINY-BREAST01 SUBGROUP ANALYSIS

EPICS

1036: TRASTUZUMAB DERUXTECAN FOR HER2-POSITIVE METASTATIC BREAST CANCER: DESTINY-BREAST01 SUBGROUP ANALYSIS. FIRST AUTHOR: SHANU MODI

138O ESMO BREAST CANCER: CNS METASTASES IN HER2-POSITIVE METASTATIC BREAST CANCER TREATED WITH TRASTUZUMAB DERUXTECAN: DESTINY-BREAST01 SUBGROUP ANALYSES. FIRST AUTHOR: GUY JERUSALEM

Background

- In the phase II DESTINY-Breast01 trial, trastuzumab deruxtecan showed durable antitumor activity (ORR was 60.9% and

DISCUSSION – HER2+ EARLY BC (1/2)

EPICS

- Neoadjuvant therapy of BC in TRAIN-2 clearly shows that anthracyclines do not improve efficacy, and are

DISCUSSION – HER2+ EARLY BC (2/2)

- KAITLIN did not meet its co-primary endpoints. Replacing adjuvant taxane and trastuzumab with ado-

DISCUSSION – HER2+ DCIS BC

- The idea that trastuzumab can increase radiotherapy effectiveness was only partially supported by

DISCUSSION – CT DE-ESCALATION IN HER2+, HR+ BC

EPICS

- In the WSG-TP-II de-escalation study dual HER2+ blockade plus paclitaxel showed promising

DISCUSSION – R/R HER2+, HR+ MBC (1/2)

- The advisors found the CNS data very impressive from the HER2CLIMB trial with tucatinib in HER2+

DISCUSSION – R/R HER2+, HR+ MBC (2/2)

- The multivariate analysis of the SOPHIA trial showed favorable interactions between margetuximab and

APTITUDE HEALTH®

EPICS

Insights Into Immune-Based and Chemotherapy for Breast Cancer

JOYCE O'SHAUGHNESSY, MD

IMMUNE-BASED AND CHEMOTHERAPY FOR BC ABSTRACTS

EPICS

1014: RESULTS OF ENCORE 602 (TRIO025), A PHASE II, RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLINDED, MULTICENTER STUDY OF ATEZOLIZUMAB WITH OR WITHOUT ENTINOSTAT IN PATIENTS WITH ADVANCED TRIPLE-NEGATIVE BREAST CANCER (ATNBC). FIRST AUTHOR: JOYCE O'SHAUGHNESSY

Background

- The ENCORE trial is a randomized phase II trial of atezolizumab with or without the HDAC inhibitor entinostat

IMMUNE-BASED AND CHEMOTHERAPY FOR BC ABSTRACTS

EPICS

TPS598: PHASE III RANDOMIZED STUDY OF ADJUVANT TREATMENT WITH THE ANTI-PD-L1 ANTIBODY AVELUMAB FOR HIGH-RISK TRIPLE NEGATIVE BREAST CANCER PATIENTS: THE A-BRAVE TRIAL. FIRST AUTHOR: PIER F. CONTE

Background

- The A-BRAVE trial is an ongoing adjuvant avelumab trial in high-risk, primary TNBC patients, who have

IMMUNE-BASED AND CHEMOTHERAPY FOR BC ABSTRACTS

EPICS

TPS596: KEYLYNK-009: A PHASE II/III, OPEN-LABEL, RANDOMIZED STUDY OF PEMBROLIZUMAB (PEMBRO) PLUS OLAPARIB VS PEMBRO PLUS CHEMOTHERAPY AFTER INDUCTION WITH FIRST-LINE PEMBRO PLUS CHEMOTHERAPY IN PATIENTS WITH LOCALLY RECURRENT INOPERABLE OR METASTATIC TRIPLE-NEGATIVE BREAST CANCER (TNBC). FIRST AUTHOR: HOPE S. RUGO

Background

IMMUNE-BASED AND CHEMOTHERAPY FOR BC ABSTRACTS

EPICS

TPS599: PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF ADAGLOXAD SIMOLENIN (OBI-822) AND OBI-821 TREATMENT IN PATIENTS WITH EARLY-STAGE TRIPLE-NEGATIVE BREAST CANCER (TNBC) AT HIGH RISK FOR RECURRENCE. FIRST AUTHOR: HOPE S. RUGO

Background

- The GLORIA trial is ongoing with adagloxad simolenin, an anti-Globo H vaccine, as maintenance therapy in

IMMUNE-BASED AND CHEMOTHERAPY FOR BC ABSTRACTS

EPICS

TPS1105: A PHASE II TRIAL OF NIVOLUMAB (NIVO) + ABEMACICLIB (ABE) OR PALBOCICLIB (PAL) + ANASTROZOLE (ANA) IN POSTMENOPAUSAL WOMEN AND MEN WITH ESTROGEN RECEPTOR (ER)+/HUMAN EPIDERMAL GROWTH FACTOR 2 (HER2)- PRIMARY BREAST CANCER (BC): CHECKMATE 7A8. FIRST AUTHOR: SARA M. TOLANEY

Background

- CheckMate 7A8 is a phase II presurgery trial of nivolumab plus palbociclib plus anastrozole in postmenopausal

DISCUSSION – IMMUNOTHERAPIES IN BC (1/2)

- ENCORE 602 (TRIO025) failed to show a statistically significant increase in PFS with the addition

DISCUSSION – IMMUNOTHERAPIES IN BC (2/2)

- Immunotherapy has not arrived in breast cancer yet, and there are many open questions to be

DISCUSSION – NOVEL THERAPIES IN BC

- There is increasing interest in ADCs; T-DM1 and trastuzumab deruxtecan are available in BC

APTITUDE HEALTH®

US Headquarters
5901-C Peachtree Dunwoody Road NE
Suite 200, Atlanta, GA 30328, US

EU Headquarters
Wilhelmina van Pruisenweg 104
2595 AN The Hague, the Netherlands

aptitude-health.com