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Conference Coverage: ASCO 2023 – Focus on Breast Cancer

Full Report

June 13, 2023

Report Contents

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Meeting Snapshot

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LIVE ROUNDTABLE

DATE:
June 13, 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
- 4 from Europe

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

Panel Consisting of 5 US and 4 European Breast Cancer Experts

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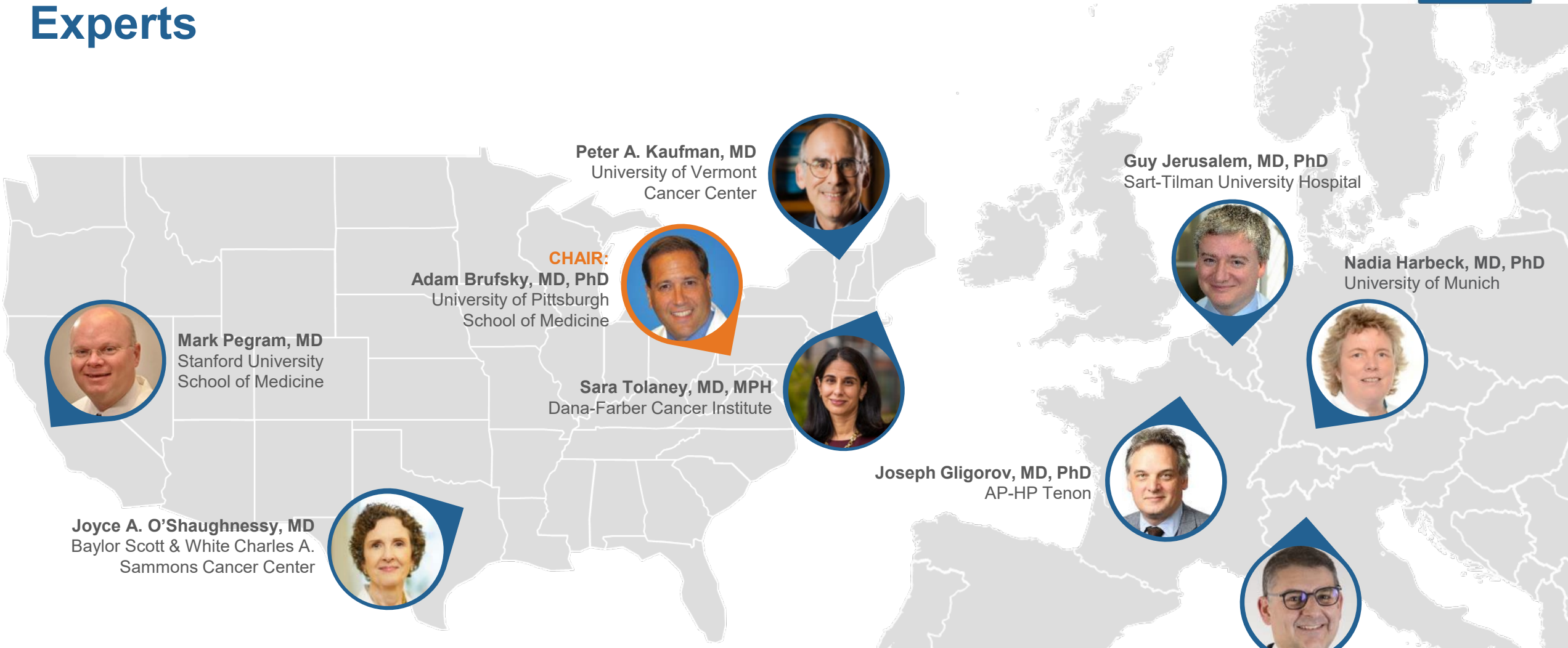

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University of Vermont Cancer Center

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Giuseppe Curigliano, MD, PhD
University of Milano/European Institute of Oncology

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Meeting Agenda (1/2)

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Time (ET/CEST)	Topic	Speaker/Moderator
10.00 AM – 10.05 AM 16.00 – 16.05	Welcome and Introductions	Adam Brufsky, MD, PhD
10.05 AM – 10.15 AM 16.05 – 16.15	**New and Emerging Treatments in HER2+ Early BC**	Joyce O'Shaughnessy, MD
10.15 AM – 10.25 AM 16.15 – 16.25	**New and Emerging Treatments in HER2+ Metastatic BC**	Giuseppe Curigliano, MD, PhD
10.25 AM – 11.00 AM 16.25 – 17.00	Discussion: New and Emerging Treatments in HER2+ BC	All
11.00 AM – 11.05 AM 17.00 – 17.05	Key Takeaways: HER2+ BC	Joyce O'Shaughnessy, MD, and Giuseppe Curigliano, MD, PhD
11.05 AM – 11.20 AM 17.05 – 17.20	**New and Emerging Approaches in HR+, HER2– Early BC**	Peter A. Kaufman, MD
11.20 AM – 11.40 AM 17.20 – 17.40	Discussion: New and Emerging Approaches in HR+, HER2– Early BC	All
11.40 AM – 11.45 AM 17.40 – 17.45	Break	

Meeting Agenda (2/2)

EPICS

Time (ET/CEST)	Topic	Speaker/Moderator
11.45 AM – 12.00 PM 17.45 – 18.00	**New and Emerging Approaches in HR+, HER2– Metastatic BC**	Nadia Harbeck, MD, PhD
12.00 PM – 12.15 PM 18.00 – 18.15	Discussion: New and Emerging Approaches in HR+, HER2– Metastatic BC	All
12.15 PM – 12.20 PM 18.15 – 18.20	Key Takeaways: HR+, HER2– BC	Peter A. Kaufman, MD, and Nadia Harbeck, MD, PhD
12.20 PM – 12.30 PM 18.20 – 18.30	**Advances in Early and Metastatic Triple-Negative Breast Cancer (TNBC)**	Joseph Gligorov, MD, PhD
12.30 PM – 12.50 PM 18.30 – 18.50	Discussion: Advances in TNBC	All
12.50 PM – 12.55 PM 18.50 – 18.55	Key Takeaways: TNBC	Joseph Gligorov, MD, PhD
12.55 PM – 1.00 PM 18.55 – 19.00	Meeting Close	Adam Brufsky, MD, PhD

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Congress Highlights

New and Emerging Treatments in HER2+ Early and Metastatic BC

3-year invasive disease-free survival (iDFS) of the strategy-based, randomized phase II PHERGain trial evaluating chemotherapy (CT) de-escalation in human epidermal growth factor receptor 2-positive (HER2[+]) early breast cancer (EBC)

Cortes J, et al, et al. LBA506

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Primary Endpoint: pCR in ^{18}F-FDG-PET responders in group B

Nine-weeks versus one-year trastuzumab for early-stage HER2+ breast cancer: 10-year update of the Short-HER phase III randomized trial

Conte PF, et al. LBA637

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BACKGROUND

> ShortHER is a phase III noninferiority, randomized trial comparing 9 weeks

ShortHER Trial

10-year DFS & OS by treatment arm (Kaplan-Meier curves)

Oral paclitaxel and dostarlimab with or without trastuzumab in early-stage, high-risk breast cancer: Results from the neoadjuvant ISPY 2 TRIAL

Shatsky RA, et al. LBA612

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BACKGROUND

> I-SPY2 is a multicenter, phase II trial using response-adaptive randomization

Primary Efficacy Results

➢ OPE + D +/- T did not graduate in any of the predefined subtypes.

Do tumor infiltrating lymphocytes (TILs) predict benefits from trastuzumab therapy for HER2 positive breast cancer? Meta-analysis of individual patient data from 4097 women in 5 trials

Hills RK, et al. 508

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BACKGROUND

> High TIL counts are associated with a lower risk of BC recurrence, especially

Investigating prognostic effect of TILs on recurrence

Impact of race on BluePrint genomic subtyping in HER2+ breast cancer

Reid SA, et al. 564

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BACKGROUND

> BC is the leading cause of cancer-related deaths in Black women, who are

Figure 1. Frequency of (A,B) MammaPrint risk category and (C,D) BluePrint molecular subtype among Black and White women with HR+HER2+ and HR-HER2+ tumors.

A phase 2 study of HER3-DXd in patients (pts) with metastatic breast cancer (MBC)

Hamilton E, et al. 1004

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BACKGROUND

> HER3-DXd is an antibody-drug conjugate (ADC) comprising a fully human anti-

Treatment Received and Dose Modifications

An age-specific pooled analysis of trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-positive (HER2+) metastatic breast cancer (mBC) from DESTINY-Breast01, -02, and -03

Krop I, et al. 1006

EPICS

BACKGROUND

> T-DXd is approved for use in patients with HER2+ unresectable or mBC after a

Efficacy of tucatinib+trastuzumab+capecitabine (TTC) after trastuzumab-deruxtecan (T-DXd) exposure in Her2-positive metastatic breast cancer: A French multicentre retrospective study

Frenel JS, et al. 1014

EPICS

BACKGROUND

> Recent guidelines have positioned T-DXd as a preferred treatment in the second-

Characteristics, n (%)		n=101
Female		101 (100%)
Age (years), median (range)		56 (30-84)
Age	<65 years	79 (78.2%)
	≥65 years	22 (21.8%)

Real-world patient characteristics and treatment patterns associated with tucatinib therapy in patients with HER2+ metastatic breast cancer

Anders CK, et al. 1051

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BACKGROUND

> This retrospective study was conducted to assess the impact of tucatinib-based

Effectiveness outcome	Overall (N=528)	2L + 3L (n=318)	Following T-DXd (n=61)

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Key Insights

New and Emerging Treatments in HER2+ Early and Metastatic BC

New and Emerging Treatments in HER2+ Early BC

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HER2+ Early BC

De-escalation treatment strategies

> Data from the PHERGain trial are regarded as very interesting; they demonstrate that PET and PET tracers can now be used in de-escalation

New and Emerging Treatments in HER2+ Early BC

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HER2+ Early BC

De-escalation treatment strategies (continued)

- The data from 9-week vs 1-year trastuzumab in the ShortHER trial are not deemed practice changing. They are considered interesting for a

New and Emerging Treatments in HER2+ Early BC

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HER2+ Early BC

Biomarkers

> Studying TILs as a predictive biomarker of trastuzumab therapy is considered irrelevant in the modern era of gene expression assays.

New and Emerging Treatments in HER2+ Metastatic BC

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HER2+ Metastatic BC

- No practice-changing data were presented at ASCO
- The age-specific pooled analysis of the DESTINY-Breast01, -02, and -03 trials showed that the elderly population can tolerate well the full

*Kaufman PA, et al. SABCS 2022. Abstract P4-03-30.

New and Emerging Treatments in HER2+ Metastatic BC

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HER2+ Metastatic BC

- The results of the phase II study with HER3-DXd (patritumab deruxtecan) are considered interesting, but more data are needed
  - It is important to understand the biology of why the agent is active regardless of HER3 membrane expression. ". . . *It's difficult where to*

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Congress Highlights

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

Effects of ovarian ablation or suppression on breast cancer recurrence and survival: Patient-level meta-analysis of 14,993 pre-menopausal women in 25 randomized trials

Gray R, et al. 503

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BACKGROUND

> This analysis reports on a collaborative meta-analysis of individual participant data from

Trials split by use of chemotherapy

(A_1) No chemotherapy (12 trials: 3,934 women)

Phase III NATALEE trial of ribociclib + endocrine therapy as adjuvant treatment in patients with HR+/HER2− early breast cancer

Slamon D, et al. LBA500

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BACKGROUND

- The phase III NATALEE trial evaluated adjuvant ribociclib + endocrine therapy in a

Efficacy and safety results by age in monarchE: Adjuvant abemaciclib combined with endocrine therapy (ET) in patients with HR+, HER2-, node-positive, high-risk early breast cancer (EBC)

Hamilton E, et al. 501

EPICS

BACKGROUND

> The efficacy and safety by age subgroups in monarchE were reported, to help

Older Patients Derived Similar Abemaciclib Benefit to ITT Population

Biomarkers predicting response to 5 immunotherapy arms in the neoadjuvant I-SPY2 trial for early-stage breast cancer (BC): Evaluation of immune subtyping in the response predictive subtypes (RPS)

Wolf DM, et al. 102

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BACKGROUND

> It was previously shown that in the first PD-1 inhibitor (PD1-inh) arm of I-SPY2,

Continuous qualifying biomarker results in 5 IO arms

MammaPrint Index as a predictive biomarker for neoadjuvant chemotherapy response and outcome in patients with HR+ HER2- breast cancer in NBRST

Beitsch PD, et al. 521

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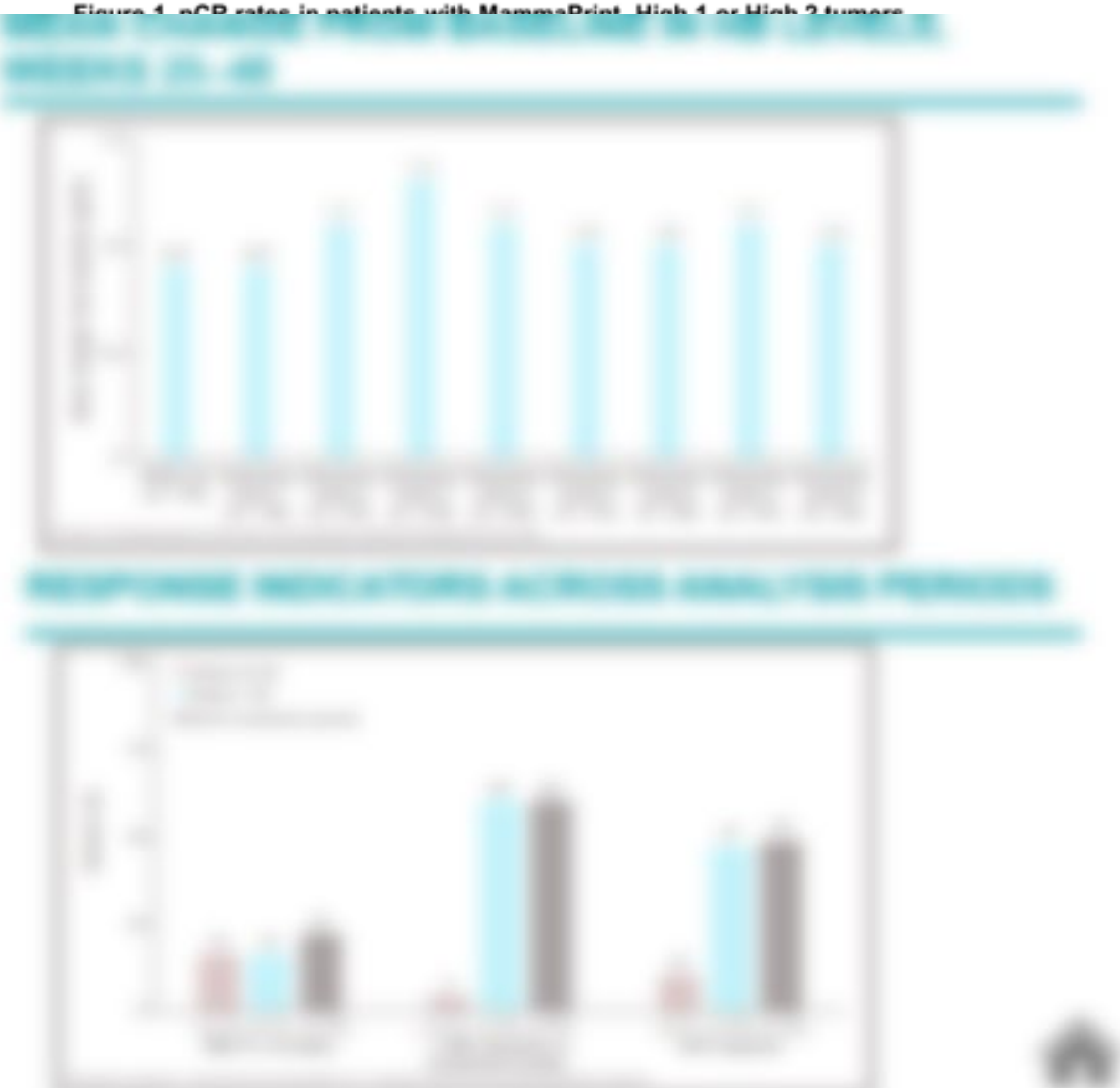
BACKGROUND

> The 70-gene MammaPrint (MP) test classifies HR+, HER2– early-stage BC



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Key Insights

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

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

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NATALEE Trial

- The phase III NATALEE trial met its primary endpoint, and the data are exciting; if it remains positive, it will enlarge the population of patients

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

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NATALEE Trial

Safety

- There was a high rate of AE-related discontinuation (19%), and the experts questioned this: *"I'm not so sure whether it's all protocol*

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

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Genomic Assays

> MammaPrint is used by one expert for neoadjuvant and, sometimes, adjuvant decisions

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Congress Highlights

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

Primary outcome analysis of the phase 3 SONIA trial (BOOG 2017-03) on selecting the optimal position of cyclin-dependent kinases 4 and 6 (CDK4/6) inhibitors for patients with hormone receptor-positive (HR+), HER2-negative (HER2-) advanced breast cancer (ABC)

Sonke G, et al. LBA1000

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BACKGROUND

> Most international guidelines advise first-line use of CDK4/6i in patients with

Second-line endocrine therapy (ET) with or without palbociclib (P) maintenance in patients (pts) with hormone receptor-positive (HR[+])/human epidermal growth factor receptor 2-negative (HER2[-]) advanced breast cancer (ABC): PALMIRA trial

Llombart-Cussac A, et al. 1001

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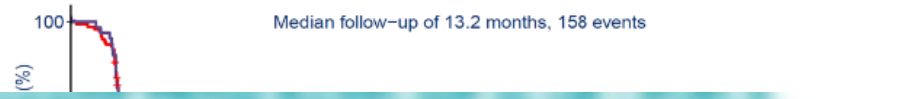
BACKGROUND

> The optimal treatment after progression on a CDK4/6i remains unknown. This

Primary Objective: Investigator-assessed PFS (ITT Populatio



Final overall survival (OS) analysis from the phase 3 TROPiCS-02 study of sacituzumab govitecan (SG) in patients (pts) with hormone receptor–positive/HER2-negative (HR+/HER2–) metastatic breast cancer (mBC)

Tolaney S, et al. 1003

BACKGROUND

> The results of an exploratory analysis of OS from the phase III TROPiCS-02 study,

Progression-Free Survival

Clinical activity of camizestrant, a next-generation SERD, versus fulvestrant in patients with a detectable *ESR1* mutation: Exploratory analysis of the SERENA-2 phase 2 trial

Oliveira M, et al. 1066

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BACKGROUND

- Camizestrant, a next-generation oral selective estrogen receptor antagonist and degrader (ngSERD), demonstrated statistically significant

Interim analyses (IA) of the giredestrant (G), G + abemaciclib (A), and G + ribociclib (R) arms in MORPHEUS Breast Cancer (BC): A phase I/II study of G treatment (tx) combinations in patients (pts) with estrogen receptor-positive, HER2-negative locally advanced/metastatic BC (ER+, HER2– LA/mBC)

Oliveira M, et al. 1061

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BACKGROUND

> MORPHEUS BC is a phase I/II study evaluating the safety and efficacy of

Table 2: Pharmacokinetics

A. G and R steady state pharmacokinetic parameters

Arm	n	Analyte	Geometric mean C_{max}, ng/mL	Geometric mean AUC_{0-24}, hr·ng/mL

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Key Insights

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

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

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SONIA Trial

- SONIA is an academic trial that addressed an important question regarding treatment with CDK4/6 inhibitors in the first and second line. However, it raised a number of concerns among the experts

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

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SONIA Trial (continued)

- SONIA is an academic trial that addressed an important question regarding treatment with CDK4/6 inhibitors in the first and second line. However, it raised a number of concerns among the experts

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

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Latest Updates

HR+, HER2-low and ADCs

> The ESMO Clinical Practice Guidelines established the use of T-DXd in HER2-low patients after at least 1 line of chemotherapy, and the data

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Congress Highlights

Advances in Early and Metastatic TNBC

Differential impact of proliferation signature on efficacy of neoadjuvant chemoimmunotherapy in sTIL-high and sTIL-low triple-negative breast cancer (TNBC): Biomarker analysis of the NeoPACT trial

Stecklein S, et al. 507

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BACKGROUND

> TNBCs with enrichment of stromal TILs (sTILs) and/or immune gene expression

Neoadjuvant single-dose trilaciclib prior to combination chemotherapy in patients with early triple-negative breast cancer: Safety, efficacy, and immune correlate data from a phase 2 study

Force J, et al. 603

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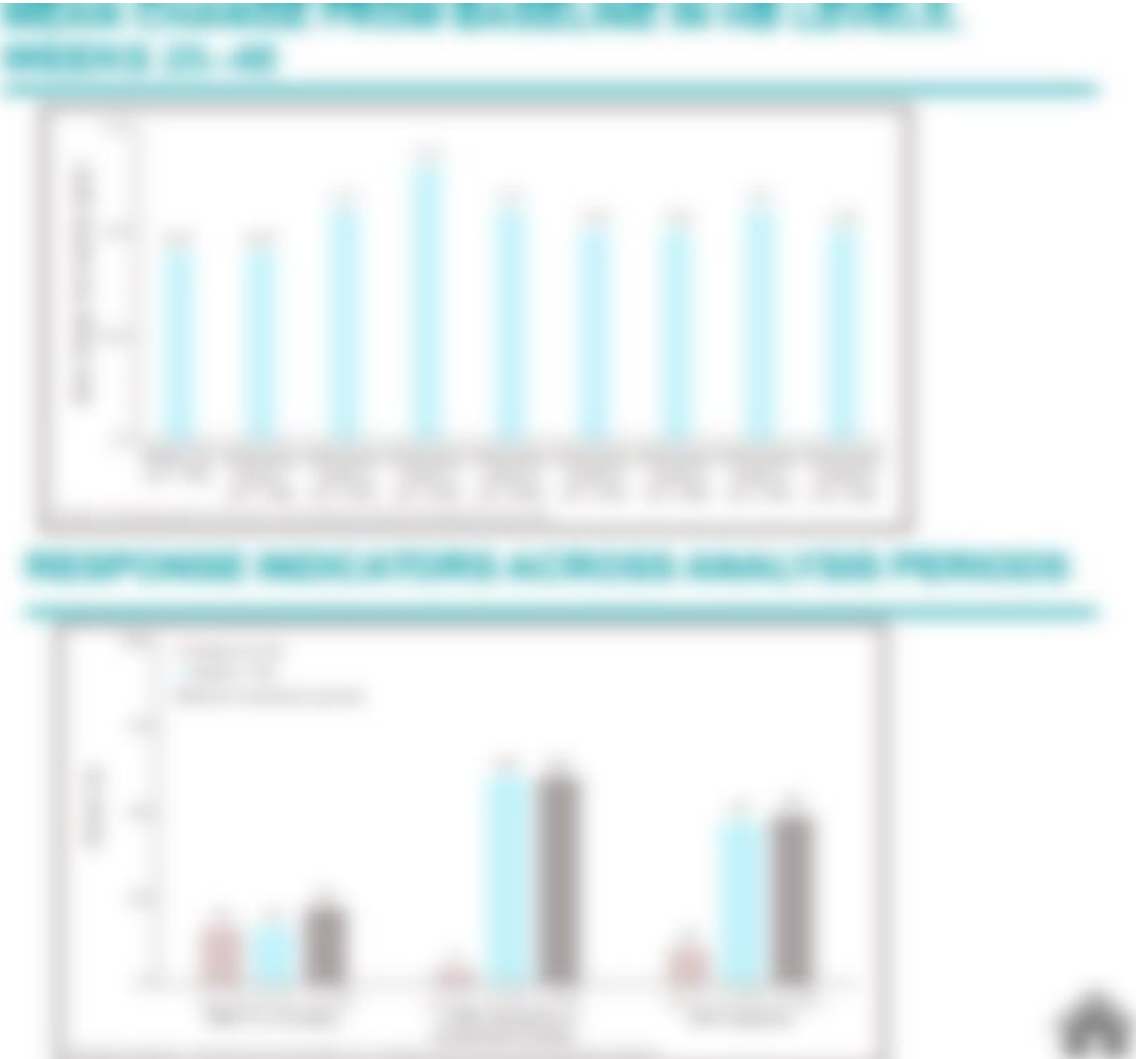
BACKGROUND

- Trilaciclib is an IV CDK4/6 inhibitor. Preliminary data from a phase II, single-arm, open-label study of neoadjuvant trilaciclib in TNBC showed

FIGURE 3. PCR BY BASELINE DISEASE AND TUMOR CHARACTERISTICS



TORCHLIGHT: A randomized, double-blind, phase III trial of toripalimab versus placebo, in combination with nab-paclitaxel(nab-P) for patients with metastatic or recurrent triple-negative breast cancer (TNBC)

Jiang Z, et al. LBA1013

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BACKGROUND

> This phase III study compares the efficacy and safety of toripalimab vs

Olaparib (O) in advanced triple negative breast cancer (aTNBC) patients (pts) with BRCA1/2 promoter methylation: GEICAM/2015-06 study (COMETA-Breast)

De La Haba J, et al. 1093

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BACKGROUND

- *BRCA1/2* promoter methylation (*BRCA*-meth) can be responsible for a dysfunctional BRCA protein. *BRCA*-meth occurs in 15%–57% of TNBC

RESULTS

- Median O exposure duration was 8 (1-88) weeks and relative dose-intensity was 90% (30-114), with any dose modifications in 6 pts. Nine pts discontinued O due to BC progressive disease (PD).
- 18% of pts experienced a related grade ≥ 3 treatment-emergent adverse events (TEAEs). Overall rates of TEAEs are shown in Tables 3a y 3b.

Dynamic HER2-low status among patients with triple negative breast cancer (TNBC): The impact of repeat biopsies

Bar Y, et al. 1005

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BACKGROUND

- T-DXd is FDA approved for HER2-low, but not HER2-0 TNBC and HR+ BC. Therefore, identifying HER2-low status is of great clinical importance. Prior

Likelihood of HER2-low

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Key Insights

Advances in Early and Metastatic TNBC

Advances in Early and Metastatic TNBC

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Latest Updates

- No practice-changing data were presented at ASCO
- Repeat biopsies as a means to increase the number of patients with HER2-low status is not considered feasible: experts were not impressed

[redacted]

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Other Key Observations

Other Key Observations

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Latest Updates

- In the EBC setting, more studies are needed on patients with residual disease following neoadjuvant immune checkpoint inhibitors and chemotherapy

[redacted]

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