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EPICS

Conference Coverage: ASCO 2022 – Focus on Breast Cancer

June 14, 2022

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Report Contents

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Meeting Snapshot

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VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
June 14, 2022

DISEASE-STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

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

BREAST CANCER-SPECIFIC DISCUSSIONS on latest research updates, therapeutic advances, and their application in clinical decision-making

Panel Consisting of 3 US and 3 EU Breast Cancer Experts

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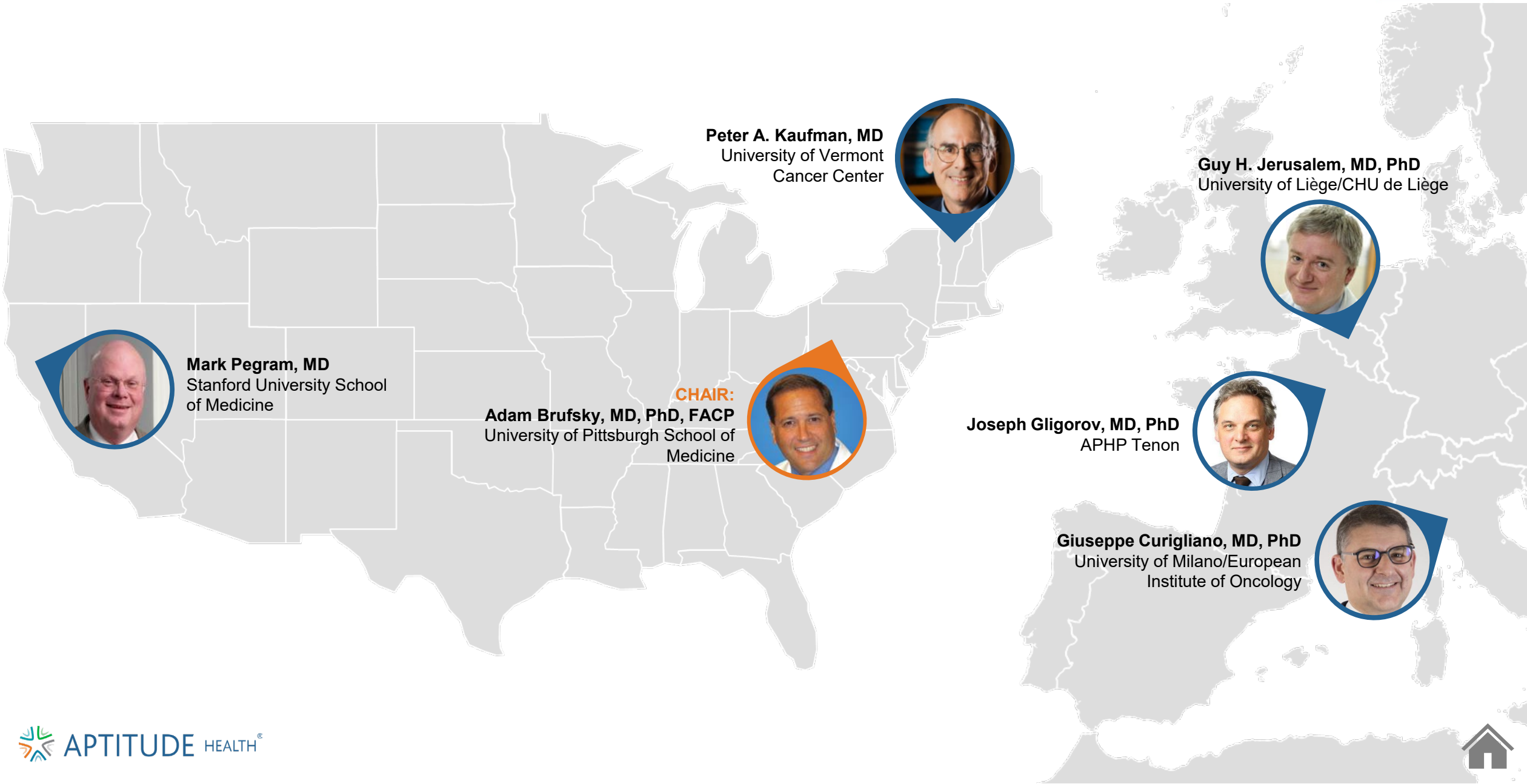

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Meeting Agenda

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Time	Topic	Speaker/Moderator
10.00 AM – 10.05 AM	Welcome and Introductions	Adam Brufsky, MD, PhD, FACP
10.05 AM – 10.15 AM	Updates on Neoadjuvant Therapies for Breast Cancer	Mark Pegram, MD
10.15 AM – 10.30 AM	Discussion	All
10.30 AM – 10.35 AM	Key Takeaways	Mark Pegram, MD
10.35 AM – 10.45 AM	CDK4/6 Inhibitors in the Treatment of HR+, HER2– Breast Cancer	Guy H. Jerusalem, MD, PhD
10.45 AM – 11.05 AM	Discussion	All
11.05 AM – 11.10 AM	Key Takeaways	Guy H. Jerusalem, MD, PhD
11.10 AM – 11.20 AM	Novel Therapeutic Approaches for HR+, HER2– Breast Cancer	Giuseppe Curigliano, MD, PhD
11.20 AM – 11.40 AM	Discussion	All
11.40 AM – 11.45 AM	Key Takeaways	Giuseppe Curigliano, MD, PhD
11.45 AM – 11.55 AM	Advances in TNBC	Peter Kaufman, MD
11.55 AM – 12.15 PM	Discussion	All
12.15 PM – 12.20 PM	Key Takeaways	Peter Kaufman, MD
12.20 PM – 12.30 PM	Evolving Treatments for HER2+, HR–, and HER2-Low Breast Cancer	Joseph Gligorov, MD, PhD
12.30 PM – 12.50 PM	Discussion	All
12.50 PM – 12.55 PM	Key Takeaways	Joseph Gligorov, MD, PhD
12.55 PM – 1.00 PM	Closing Remarks	Adam Brufsky, MD, PhD, FACP

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Updates on Neoadjuvant Therapies for Breast Cancer

Congress Highlights From ASCO 2022

Phase II MUKDEN 01: Primary Analysis of Neoadjuvant Pyrotinib and Letrozole Plus Dalpiciclib in TNBC

Nan Niu, et al. 2022. ASCO #588

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STUDY POPULATION

> Treatment-naive patients with stage II–III triple-positive BC

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Phase II coopERA BC: Final Analysis of Neoadjuvant Giredestrant Plus Palbociclib in Postmenopausal Women With ER+, HER2– eBC

Peter Fasching, et al. 2022. ASCO #589

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STUDY DESIGN

2-week neoadjuvant single-agent window-of-opportunity phase

16-week neoadjuvant combination (ET + palbociclib) phase

EFFICACY

Figure 2: Relative reduction in Ki67 at week 2[8] and at surgery

Phase II NeoSTAR: Response-Guided Neoadjuvant Sacituzumab Govitecan in Localized TNBC

Laura Spring, et al. 2022. ASCO #512

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STUDY POPULATION AND DESIGN

> Patients with localized TNBC (tumor size ≥1cm, or any size if

EFFICACY

> pCR: 30% with sacituzumab govitecan alone

Phase II NeoPACT: Clinical and Biomarker Results of Pembrolizumab and Carboplatin Plus Docetaxel in TNBC

Priyanka Sharma, et al. 2022. ASCO #513

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STUDY POPULATION

> 115 patients with stage I–III TNBC were enrolled, of which 109

EFFICACY: PATHOLOGIC RESPONSE

Phase II: Neoadjuvant Ipilimumab and Nivolumab Plus Paclitaxel Following Anthracycline-Based Chemotherapy for Treatment Resistant Early-Stage TNBC

Sherene Loi, et al. 2022. ASCO #602

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STUDY POPULATION

> Previously untreated stage III TNBC with ≥15 mm of tumor remaining or 10 mm of tumor with 1 positive node after 4 cycles of anthracycline-

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Updates on Neoadjuvant Therapies for Breast Cancer

Key Takeaways

Key Takeaways: Updates on Neoadjuvant Therapies for BC (1/3)

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Strategies emerge for chemotherapy de-escalation, but are not yet practice changing (1/2)

#508: Primary analysis of MUKDEN 01: A multicenter, single-arm, prospective, phase 2 study of neoadjuvant

Key Takeaways: Updates on Neoadjuvant Therapies for BC (2/3)

EPICS

Strategies emerge for chemotherapy de-escalation, but are not yet practice-changing (2/2)

#589: Neoadjuvant giredestrant (GDC-9545) plus palbociclib (P) vs anastrozole (A) plus P in postmenopausal women with estrogen

Key Takeaways: Updates on Neoadjuvant Therapies for BC (3/3)

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There is a need for robust biomarkers to predict response to immune checkpoint inhibitors beyond PD-L1

With the approval of pembrolizumab based on the KEYNOTE-522 trial, immunotherapies have arrived in early BC. However, a need

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CDK4/6 Inhibitors in the Treatment of HR+, HER2– Breast Cancer

Congress Highlights From ASCO 2022

Phase III PALOMA-2: OS Analysis of First-Line Palbociclib Plus Letrozole in ER+/HER2– Advanced BC

Richard Finn, et al. 2022. ASCO LBA1003

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STUDY POPULATION

OUTCOME

EXPERT CONCLUSIONE

Phase II MAINTAIN: Fulvestrant or Exemestane ± Ribociclib After Progression on Antiestrogen Therapy Plus CDK4/6i in Unresectable or HR+, HER2– mBC

Kevin Kalinsky, et al. 2022. ASCO LBA1004

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STUDY POPULATION

> Randomized phase II trial with ribociclib plus switch of ET vs

PRIMARY ENDPOINT: PFS

Phase I SERENA-1: Updated Analysis of Camizestrant Plus Palbociclib in ER+, HER2– Advanced BC

Mafalda Oliveira, et al. 2022. ASCO #1032

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STUDY POPULATION

> Postmenopausal women with 2 (1–5) lines of prior therapy (N = 25)

AUTHORS' CONCLUSION

Phase Ib: Dalpiciclib Plus Letrozole/Anastrozole or Fulvestrant in HR+/HER2– Advanced BC

Qingyuan Zhang, et al. 2022. ASCO #1066

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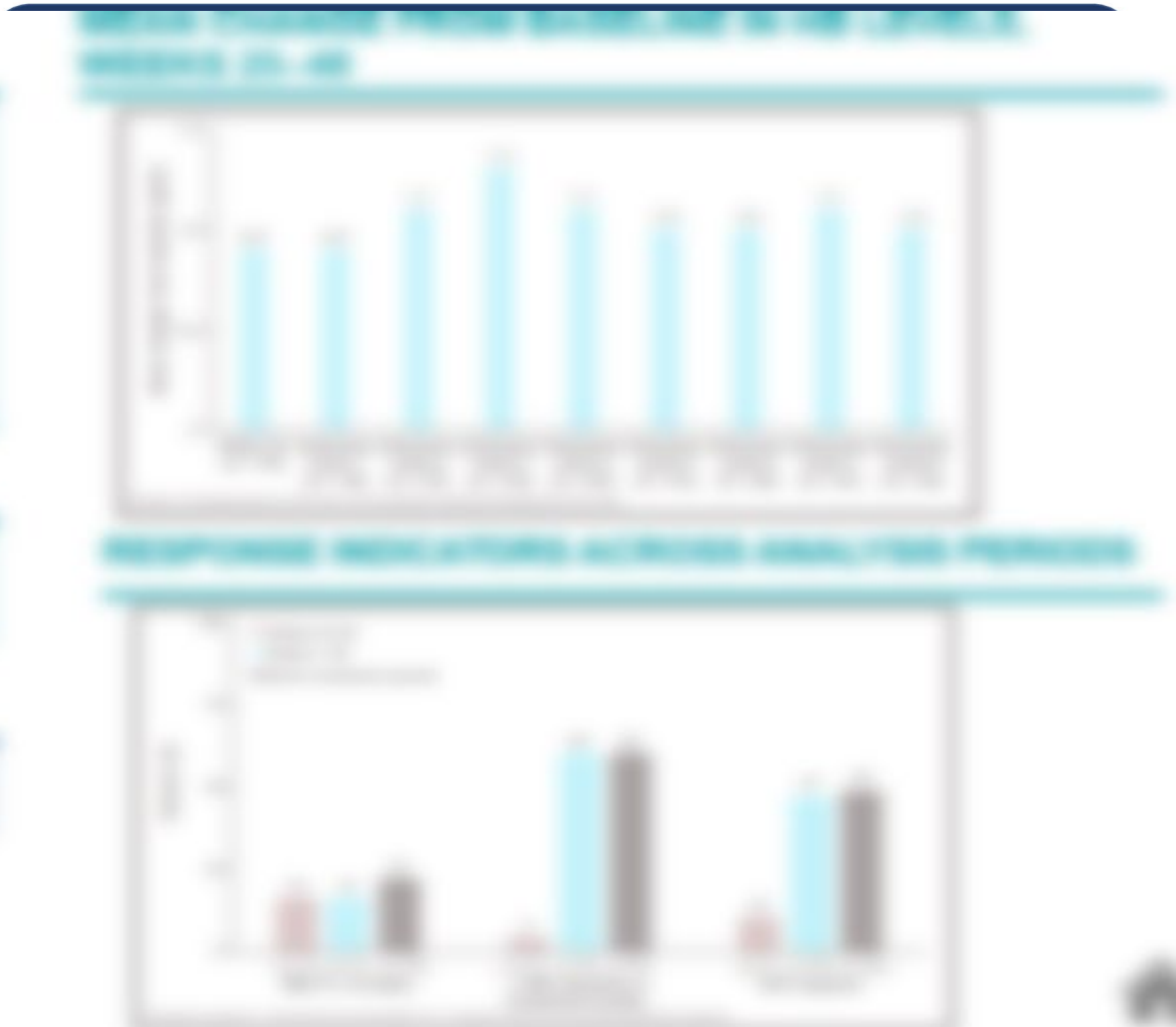
STUDY POPULATION

> Phase Ib trial with dalpiciclib plus ET

AUTHORS' CONCLUSION



Real-world: Identifying Genetic Factors of Response and Resistance to CDK4/6i in Metastatic HR+/HER2– BC

Smita Agrawal, et al. 2022. ASCO #1064

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STUDY POPULATION

> DNA sequencing database analysis to identify factors involved in

OVERALL RATIONALE

Molecular Alterations Associated With Rapid Progression Following CDK4/6i in Metastatic HR+ BC

Malinda T. West, et al. 2022. ASCO #1054

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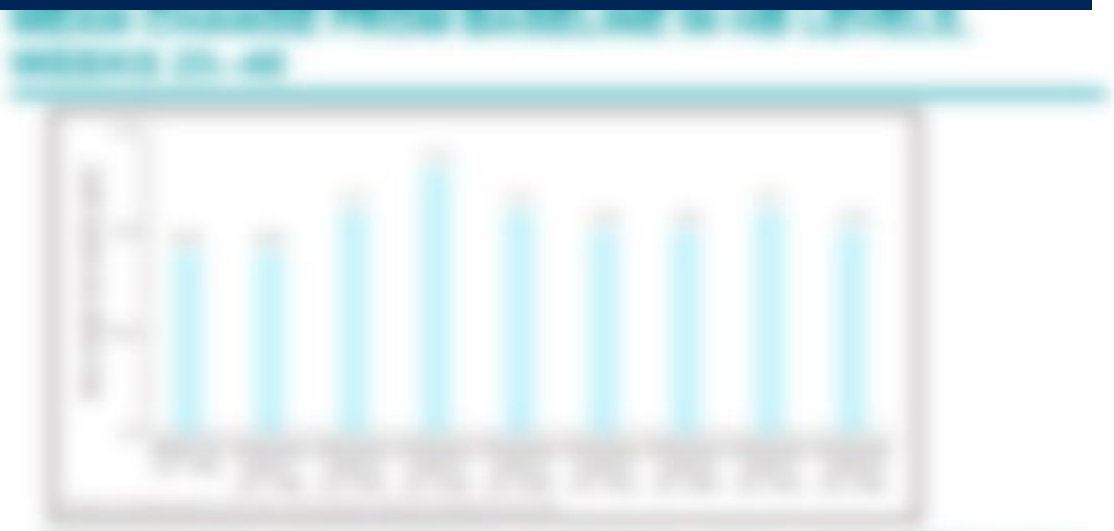
STUDY POPULATION

> Molecular alteration analysis using NGC (N = 34) to

ALTERATIONS ASSOCIATED WITH RAPID PROGRESSION



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CDK4/6 Inhibitors in the Treatment of HR+, HER2– Breast Cancer

Key Takeaways

Key Takeaways: CDK4/6 Inhibitors in the Treatment of HR+, HER2– Breast Cancer (1/3)

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The different OS outcomes from first-line trials are expected to change the market distribution of CDK4/6i

LBA1003: Overall survival (OS) with first-line palbociclib plus letrozole (PAL+LET) vs placebo plus

"

Dr Pegram:

The gold standard by which we make

[illegible]

[illegible]

[illegible]

Key Takeaways: CDK4/6 Inhibitors in the Treatment of HR+, HER2– Breast Cancer (2/3)

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Treatment of CDK4/6i-refractory ER+, HER2– BC remains an unmet need

LBA1004: A randomized, phase II trial of fulvestrant or exemestane with or without ribociclib after progression on anti-estrogen

Immunotherapies

The analysis of the tumor microenvironment (TME) in the Mpaxxon130 trial shows that immunoactivation is a prerequisite for the antitumor effect of immune checkpoint inhibitor (ICPI) in triple-negative breast cancer (TNBC).

- Patients who showed survival benefits with atezolizumab and nab-paclitaxel combination in the programmed cell death protein 1 ligand 1 positive (PD-L1+) population demonstrated immune infiltration, higher proliferation, more DNA repair deficiency, angiogenesis, and higher estrogen receptor (ER) response. More benefits were observed in patients with basal like immune-activated molecular subtype.
- The PD-L1 negative (PD-L1-) population did not benefit from the addition of atezolizumab to nab-paclitaxel in any molecular subtypes.

Immunoactivation in metastatic (m)TNBC

There are clinical trials with the aim to "heat up" the tumor, using methods to increase immunoactivation to achieve improved benefits from immunotherapies.

- The addition of an antibody drug conjugate (ADC) may provide the necessary immunogenic cell death required for the activity of ICPI in the PD-L1+ population, as shown in the BEGONIA trial. The addition of trastuzumab deruxtecan (T-DXd) to durvalumab showed clinical responses both in PD-L1+ and PD-L1- populations.
- The use of histone deacetylase inhibitors (HDACi) may increase immunogenicity, homologous recombination deficiency, and decrease DNA repair protein expression. Romidepsin in combination with cisplatin and nivolumab showed durable objective responses, supporting that HDACi can be effective in heating up a tumor.

Key Takeaways: CDK4/6 Inhibitors in the Treatment of HR+, HER2– Breast Cancer (3/3)

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New insights into the molecular mechanisms governing CDK4/6i resistance

Other CDK4/6i publications

#1032: Serena-1: Updated analyses from a phase 1 study (parts C/D) of the

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Novel Therapeutic Approaches for HR+, HER2– Breast Cancer

Congress Highlights From ASCO 2022

Phase III TROPiCS-02: Primary Results of Sacituzumab Govitecan in HR+, HER2– Advanced BC

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Hope S. Rugo, et al. 2022. ASCO LBA1001

STUDY POPULATION

> Phase III study of sacituzumab govitecan vs

PRIMARY ENDPOINT: PFS

SG demonstrated a statistically significant improvement in PFS vs TPC with a 34% reduction in the risk of disease

Phase II FAKTION: OS and Updated PFS Data With Fulvestrant Plus Capivasertib After Relapse or Progression on an AI in Metastatic ER+ BC

Robert Hugh Jones, et al. 2022. ASCO #1005

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STUDY POPULATION

> Randomized prospective trial with fulvestrant plus capivasertib vs

OS IN ITT POPULATION

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Phase III SOLAR-1: Biomarker Analysis of Alpelisib Plus Fulvestrant in HR+, HER2– Advanced BC

Dejan Juric, et al. 2022. ASCO #1006

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STUDY POPULATION

> Biomarker analysis of SOLAR-1 randomized prospective trial with

SUBGROUP ANALYSIS

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Phase II BYLieve: Baseline Biomarker Analysis of Alpelisib Plus ET in HR+, HER2– *PIK3CA*-Mutated Advanced BC

Dejan Juric, et al. 2022. ASCO #1018

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STUDY POPULATION

> Biomarker analysis of BYLieve trial with alpelisib plus ET in *PI3KCA*-

AUTHORS' CONCLUSIONS

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Phase Ia/b EMBER: Imlunestrant, an Oral SERD, in ER+ Advanced BC and Endometrial Endometrioid Cancer

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Komal L. Jhaveri, et al. 2022. ASCO #1021

STUDY POPULATION

> Phase Ia/b trial with imlunestrant in ER+, HER2– aBC

EFFICACY OUTCOMES

Figure 5A. PFS aBC All, and 2L post-CDK4/6i subgroup

Figure 5B. PFS aBC by ESR1 (ESR1m v ESR1nd)

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Phase II: Lasofoxifene Plus Abemaciclib in Pre- and Postmenopausal Women With Locally Advanced or Metastatic ER+, HER2– BC and an *ESR1* Mutation After Progression on Prior Therapies

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Senthil Damodaran, et al. 2022. ASCO #1022

STUDY POPULATION

> Open-label phase II trial in ER+ HER2– a/mBC with

EFFICACY OUTCOMES

Phase II I-SPY2: pCR Rates for HR+, HER2– BC by Molecular Subtype

Laura Ann Huppert, et al. 2022. ASCO #504

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STUDY POPULATION

> Neoadjuvant trial with multiple investigational arms

PCR RATE BY MP HIGH1/2 AND BP-BASAL VS LUMINAL

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Phase I/Ib: Long-term Safety of Inavolisib Alone or in Combination With Palbociclib and/or ET in *PIK3CA*-Mutated, HR+, HER2– Metastatic BC

Philippe L. Bedard, et al. 2022. ASCO #1052

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STUDY POPULATION

> Safety evaluation of inavolisib monotherapy alone or in

SAFETY OVERVIEW

Table 2: Most common treatment-related* AEs (any grade in >10% of patients on treatment ≥1 year)

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Novel Therapeutic Approaches for HR+, HER2– Breast Cancer

Key Takeaways

Key Takeaways: Novel Therapeutic Approaches for HR+, HER2– Breast Cancer (1/3)

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TROPiCS-02 results are not impressive but may extend FDA label of sacituzumab govitecan

LBA1001: Primary results from TROPiCS-02: A randomized phase 3 study of sacituzumab govitecan (SG) versus treatment of

Key Takeaways: Novel Therapeutic Approaches for HR+, HER2– Breast Cancer (2/3)

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Advances in targeting the PI3K/AKT/mTOR pathway

#1005: Fulvestrant plus capivasertib versus fulvestrant plus placebo after relapse or progression on an aromatase inhibitor in

Key Takeaways: Novel Therapeutic Approaches for HR+, HER2– Breast Cancer (3/3)

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Advances in ER-targeting therapies

#1021: A phase 1a/b trial of imlunestrant (LY3484356), an oral selective estrogen receptor degrader (SERD) in ER-

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Advances in TNBC

Congress Highlights From ASCO 2022

Phase II: Preliminary Results of Sitravatinib Plus Tislelizumab in Locally Recurrent or Metastatic TNBC

Lei Fan, et al. 2022. ASCO #1070

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STUDY POPULATION

> Phase II trial of TKI plus anti–PD-1 in patients with or without PD-

EFFICACY OUTCOMES

A -

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Phase III ASCENT: Final Results of Sacituzumab Govitecan in Previously Treated, Metastatic TNBC

Aditya Bardia, et al. 2022. ASCO #1071

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STUDY POPULATION

> Final results of the phase III ASCENT trial with sacituzumab

OVERALL SURVIVAL

Figure 4. Overall Survival* (BMNeg Population)

Exposure-Response Analysis of Sacituzumab Govitecan Efficacy and Safety in Metastatic TNBC

Indrajeet Singh, et al. 2022. ASCO #1076

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STUDY POPULATION

> Combined PK analysis of phase I and phase III

SERUM CONCENTRATION IN CORRELATION WITH OUTCOMES

Phase II: Lurbinectedin in Pretreated *BRCA1/2*-Associated Metastatic BC

Valentina Boni, et al. 2022. ASCO #1092

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STUDY POPULATION

> Phase II basket trial in *BRCA1/2*-mutated tumors; this analysis is

CLINICAL RESPONSES

RECIST responses (%)

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Phase II plasmaMATCH Cohort E: Olaparib Plus Ceralasertib in TNBC

Alistair E. Ring, et al. 2022. ASCO #1024

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STUDY POPULATION

> Genomic profiling using ctDNA; cohort E has no actionable

CLINICAL RESPONSES

Phase Ib/II: BET Inhibitor ZEN-3694 Plus Talazoparib in TNBC Without *gBRCA1/2* Mutations

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Philippe Georges Aftimos, et al. 2022. ASCO #1023

STUDY POPULATION

> Phase Ib/II trial in mTNBC without *BRCA1/2* or *PALB2* mutations

CLINICAL RESPONSES

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Advances in TNBC

Key Takeaways

Key Takeaways: Advances in TNBC (1/2)

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No practice-changing data, but several interesting early and hypothesis-generating signals were presented

#1070: The safety, tolerability, and preliminary antitumor activity of sitravatinib plus tislelizumab in patients with locally recurrent or metastatic triple-negative breast cancer (Lei Fan, et al)

Key Takeaways: Advances in TNBC (2/2)

EPICS

Final data from ASCENT trial confirm efficacy and QOL benefit

#1071: Sacituzumab govitecan (SG) versus treatment of physician's choice (TPC) in patients (pts) with previously treated, metastatic triple-negative breast cancer (mTNBC): Final results from the phase 3 ASCENT study (Aditya Bardia, et al)

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Evolving Treatments for HER2+, HR–, and HER2-Low Breast Cancer

Congress Highlights From ASCO 2022

Phase III DESTINY-Breast03: Safety Follow-up of T-DXd in HER2+ Unresectable and/or Metastatic BC

Erika P. Hamilton, et al. 2022. ASCO #1000

EPICS

STUDY POPULATION

> Safety follow-up of the phase III head-to-head trial between T-DXd

DRUG-RELATED TEAES

Phase Ib/2: Preliminary Results of Zanidatamab Plus Docetaxel as 1L Therapy for Patients With Advanced HER+ BC

Keun-Seok Lee, et al. 2022. ASCO #1031

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STUDY POPULATION

> Phase Ib/2 trial with a novel HER2-targeting bispecific antibody

TREATMENT DURATION AND RESPONSE

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Pooled Analysis: Pyrotinib Monotherapy or in Combination With Capecitabine in HER+ Metastatic BC

Xiuwen Guan, et al. 2022. ASCO #1034

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STUDY POPULATION

> Pyrotinib as monotherapy or in combination with capecitabine or

SURVIVAL OUTCOMES

Real-world Clinical Outcomes in Patients With Local/Regional HER2-Low BC: An NCDB Analysis

Changchuan Jiang, et al. 2022. ASCO #558

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STUDY POPULATION

> National Cancer Database analysis showing HER2 expression (N

OS SUBGROUP ANALYSIS

Hazard Ratio for OS (HER2-low vs. HER2-zero breast cancer) from Cox regressions.

Prognostic Implications of HER2Neu-Low in Metastatic BC

Shaakir Hasan, et al. 2022. ASCO #1044

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STUDY POPULATION

> Retrospective analysis of mBC data (N = 24,636)

SURVIVAL OUTCOME CORRELATIONS

Table 1. Three Year Survival

Retrospective Study to Estimate the Prevalence of HER2-Low BC and Describe Clinicopathological Characteristics

Giuseppe Viale, et al. 2022. ASCO #1087

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STUDY POPULATION

> Retrospective analysis of HER2-low expression in

TIME TO FIRST SUBSEQUENT TREATMENT

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Phase III DESTINY-Breast04: T-DXd in HER2-Low Unresectable and/or Metastatic BC

Shanu Modi, et al. 2022. ASCO LBA3

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STUDY POPULATION

> Phase III trial in HER2-low expressing (+ or ++ by IHC) patients

PFS AND OS IN HR– POPULATION

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Evolving Treatments for HER2+, HR–, and HER2-Low Breast Cancer

Key Takeaways

Key Takeaways: Evolving Treatments for HER2+, HR–, and HER2-Low Breast Cancer (1/3)

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DB-03 update strengthens safety of T-DXd

#1000: Trastuzumab deruxtecan (T-DXd) versus trastuzumab emtansine (T-DM1) in patients (pts) with HER2-positive (HER2+)

Key Takeaways: Evolving Treatments for HER2+, HR–, and HER2-Low Breast Cancer (2/3)

EPICS

Outcomes from DB-04 are redefining treatment of HER2-low mBC

LBA3: Trastuzumab deruxtecan (T-DXd) versus treatment of physician's choice (TPC) in patients (pts)

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[illegible]

[illegible]

Key Takeaways: Evolving Treatments for HER2+, HR–, and HER2-Low Breast Cancer (3/3)

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Real-world data indicate HER2-low expression may be associated with better prognosis

#558: Real-world clinical outcomes in patients with local/regional HER2-low breast cancer: An NCDB analysis. (Changchuan Jiang, et al)