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# GLOBAL PERSPECTIVES: CURRENT AND FUTURE MANAGEMENT OF BREAST CANCER

Virtual meeting on October 5 and 14, 2020

## FULL REPORT

# FACULTY EXPERTS

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# AGENDA – DAY 1

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| Time (CET) | Topic | Speaker/Moderator |
|---|---|---|
| 17.00 – 17.05 | Welcome and Introductions | Joyce A. O'Shaughnessy, MD |
| 17.05 – 17.20 | Current and Emerging Approaches in Triple-Negative Breast Cancer | Andreas Schneeweiss, MD |
| 17.20 – 17.50 | Key Questions and Topics for Discussion | Moderator: Joyce A. O'Shaughnessy, MD |
| 17.50 – 17.55 | Key Takeaways: TNBC | Andreas Schneeweiss, MD |
| 17.55 – 18.05 | BREAK | |
| 18.05 – 18.15 | New Standards in HER2+ Early Breast Cancer | Peter A. Kaufman, MD |
| 18.15 – 18.40 | Key Questions and Topics for Discussion | Moderator: Nadia Harbeck, MD, PhD |
| 18.40 – 18.45 | Key Takeaways: HER2+ Early BC | Peter A. Kaufman, MD |
| 18.45 – 19.00 | Current and New Treatments in HER2+ mBC | Antonio Llombart-Cussac, MD, PhD |
| 19.00 – 19.40 | Key Questions and Topics for Discussion | Moderator: Nadia Harbeck, MD, PhD |
| 19.40 – 19.45 | Key Takeaways: HER2+ mBC | Antonio Llombart-Cussac, MD, PhD |
| 19.45 – 20.00 | Conclusions and Closing | Nadia Harbeck, MD, PhD |

# AGENDA – DAY 2

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| Time (CET) | Topic | Speaker/Moderator |
|---|---|---|
| **20.00 – 20.05** | Welcome | Nadia Harbeck, MD, PhD |
| **20.05 – 20.20** | New Standards in HR+, HER2– Early Breast Cancer | Joseph Gligorov, MD, PhD |
| **20.20 – 21.00** | Key Questions and Topics for Discussion | Moderator: Nadia Harbeck, MD, PhD |
| **21.00 – 21.05** | Key Takeaways: HR+, HER2– Early BC | Joseph Gligorov, MD, PhD |
| **21.05 – 21.15** | BREAK | |
| **21.15 – 21.30** | Recent Developments and Evolving Treatments in HR+, HER2– Metastatic Breast Cancer | Adam Brufsky, MD, PhD |
| **21.30 – 22.10** | Key Questions and Topics for Discussion | Moderator: Joyce A. O'Shaughnessy, MD |
| **22.10 – 22.15** | Key Takeaways: HER2+ mBC | Adam Brufsky, MD, PhD |
| **22.15 – 22.25** | Conclusions and Closing | Joyce A. O'Shaughnessy, MD |

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# Current and Emerging Approaches in Triple-Negative Breast Cancer

ANDREAS SCHNEEWEISS, MD

# ESMO LBA16: IMpassion130: final OS analysis from the pivotal Phase III study of atezolizumab + nab-paclitaxel vs placebo + nab-paclitaxel in previously untreated locally advanced or metastatic triple-negative breast cancer. L.A. Emens, et al

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## Background

> On the basis of findings from IMpassion130, international guidelines now recommend atezolizumab (A) + *nab*-paclitaxel (nP)

# ESMO 296P: Tumour mutational burden and clinical outcomes with first-line atezolizumab and nab-paclitaxel in triple-negative breast cancer: exploratory analysis of the Phase III IMpassion130 trial. L.A. Emens, et al

## Background

> Tumor mutational burden (TMB), a surrogate for neoantigen load, is associated with improved outcomes following

# ESMO LBA15: Primary results from IMpassion131, a double-blind placebo-controlled randomised phase 3 trial of first-line paclitaxel (PAC) +/- atezolizumab (atezo) for unresectable locally advanced/metastatic triple-negative breast cancer (mTNBC). D.W. Miles, et al

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## Background

- IMpassion131 (NCT03125902) evaluated atezo + solvent-based PAC as first-line treatment for mTNBC





AESI, adverse event of special interest; ITT, intent-to-treat.

# ESMO LBA11: IMpassion031: results from a Ph 3 study of neoadjuvant (neoadj) atezolizumab + chemotherapy in early triple-negative breast cancer (TNBC). N. Harbeck, et al

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## Background

> IMpassion031 is a global phase III, multicenter, double-blind, randomized, PBO-controlled study in pts with high-risk primary





FN, febrile neutropenia; SAE, serious adverse event.

# ESMO LBA13: Tumor infiltrating lymphocytes (TILs), PD-L1 expression and their dynamics in the NeoTRIPaPDL1 trial. G. Bianchini, et al

EPICS

## Background

> NeoTRIP randomized 280 pts to 8 cycles of *nab*-paclitaxel–carbo (CT) or with atezolizumab (CT-A); 260 pts were evaluable

# ESMO LBA17: ASCENT: A randomized phase 3 study of sacituzumab govitecan (SG) vs treatment of physician's choice (TPC) in patients (pts) with previously treated metastatic triple-negative breast cancer (mTNBC). A. Bardia, et al

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## Background

> SG (TRODELVY™) is a first-in-class antibody-drug conjugate (ADC) composed of an anti–Trop-2 antibody coupled to the

# ESMO 348P: First findings from SYNERGY, a phase I/II trial testing the addition of the anti-CD73 Oleclumab (O) to the anti-PD-L1 Durvalumab (D) and Chemotherapy (ChT) as 1st line therapy for patients (pts) with metastatic triple-negative breast cancer (mTNBC). D. Eiger, et al

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## Background

> The adenosine pathway has demonstrated ability to limit antitumor activity in TNBC, making CD73, the adenosine-

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# Discussion

# CURRENT AND EMERGING APPROACHES IN TNBC (1/4)

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## Early TNBC

# CURRENT AND EMERGING APPROACHES IN TNBC (2/4)

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## mTNBC

# CURRENT AND EMERGING APPROACHES IN TNBC (3/4)

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## mTNBC

# CURRENT AND EMERGING APPROACHES IN TNBC (4/4)

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## mTNBC

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# New Standards in HER2+ Early Breast Cancer

PETER A. KAUFMAN, MD

# ESMO 165MO: Patient (pt) preference for the pertuzumab-trastuzumab fixed-dose combination for subcutaneous use (PH FDC SC) in HER2-positive early breast cancer (EBC): Primary analysis of the open-label, randomised crossover PHranceSCa study. J. O'Shaughnessy, et al

## Background

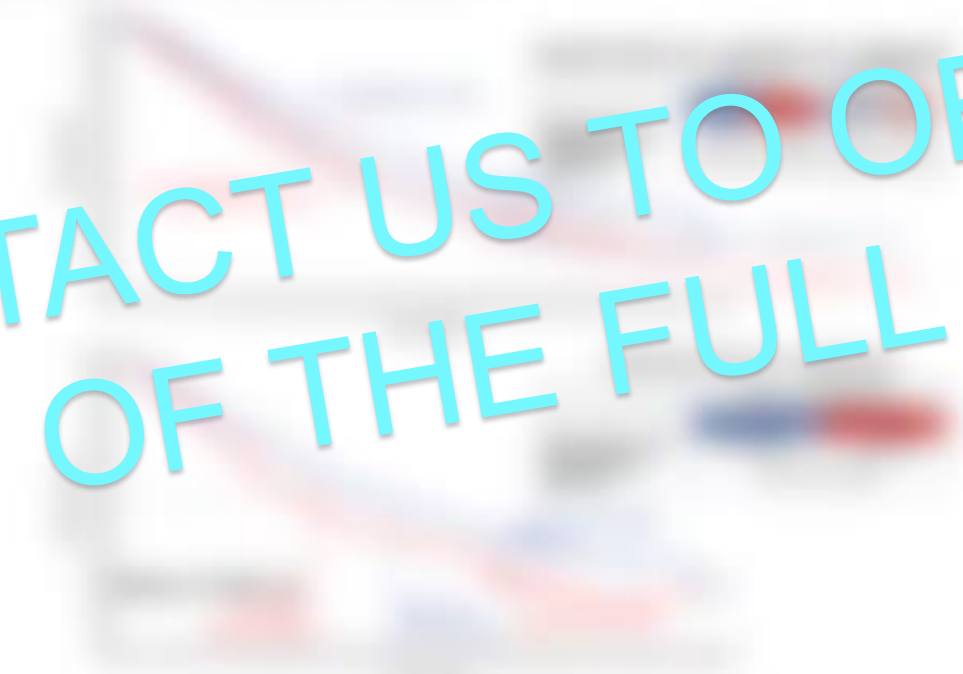
# ESMO 166MO: A phase III trial to compare the efficacy, safety, pharmacokinetics and immunogenicity of HD201 to trastuzumab in HER2+ early breast cancer patients (TROIKA). P. Xavier, et al

## Background

- HD201 is a candidate biosimilar to trastuzumab. TROIKA is a randomized, double-blind, parallel-group, equivalence

# ESMO 223P: Safety and tolerability of subcutaneous trastuzumab (H SC) self-administered at home via single-use injection device (SID) in patients (pts) with HER2-positive early breast cancer (EBC): Primary and final analysis of the open-label, phase IIIB HOMERUS study. Albert J. Ten Tije, et al

## Background



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# Discussion

# NEW STANDARDS IN HER2+ EARLY BREAST CANCER

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- The TRAIN-2 trial, presented at the American Society of Clinical Oncology 2020 Annual Meeting, provided practice-

# QUOTES – NEW STANDARDS IN HER2+ EARLY BREAST CANCER

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# Current and New Treatments in HER2+ mBC

ANTONIO LLOMBART-CUSSAC, MD, PHD

# ESMO 288P: Final results from PERUSE, a global study of pertuzumab (P), trastuzumab (H) and investigator's chosen taxane as first-line therapy for HER2-positive locally recurrent/metastatic breast cancer (LR/mBC). D.W. Miles, et al

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## Background

> P + H + docetaxel (DOC) is the standard first-line therapy for HER2-positive LR/mBC, on the basis of results from the phase

# ESMO 291P: Trastuzumab emtansine in HER2-positive metastatic breast cancer after pertuzumab and trastuzumab. TDM1RM Study. J. Martinez-Garcia, et al

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## Background

> Trastuzumab emtansine (T-DM1) is indicated for the treatment of metastatic HER2-positive BC after progression on prior

# ESMO 275O: Impact of Tucatinib on Health-Related Quality of Life (HRQoL) in Patients with HER2+ Metastatic Breast Cancer (MBC) with and without Brain Metastases (BM). V. Mueller, et al

EPICS

## Background

> Pts with HER2-positive mBC, particularly pts with brain mets, have limited tx options and increased likelihood to report

# ESMO 293P: Impact of Tucatinib on Progression Free Survival in Patients with HER2+ Metastatic Breast Cancer and Stable or Active Brain Metastases. T. Bachelot, et al

EPICS

## Background

> Up to 50% of HER2+ mBC pts will have brain mets, for which effective treatments are needed. In the HER2CLIMB (NCT02614794)

# ESMO 289P: Risk factors for interstitial lung disease in patients treated with trastuzumab deruxtecan from two interventional studies. C.A. Powell, et al

EPICS

## Background

> Trastuzumab deruxtecan (T-DXd; DS-8201) is a HER2-targeted ADC with demonstrated antitumor activity and a

# ESMO 347P: Results of the phase 1b dose escalation study of MEN1611, a PI3K Inhibitor, combined with trastuzumab (T) ± fulvestrant (F) for HER2+/PIK3CA mutant (mut) advanced or metastatic (a/m) breast cancer (BC). M. Piccart, et al

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## Background

> MEN1611 is an oral phosphoinositide 3-kinase (PI3K) inhibitor active on the p110α mutant and wild-type, β and γ isoforms.

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# Discussion

# CURRENT AND NEW TREATMENTS IN HER2+ mBC (1/4)

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- Use of the trastuzumab-pertuzumab combination as standard treatment in the frontline setting has

# CURRENT AND NEW TREATMENTS IN HER2+ mBC (2/4)

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- Sequencing of agents (cont.)

# CURRENT AND NEW TREATMENTS IN HER2+ mBC (3/4)

EPICS

- Sequencing of agents (cont.)

# CURRENT AND NEW TREATMENTS IN HER2+ mBC (4/4)

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## Novel HER2-positive agents

# MANAGEMENT OF HR+, HER2+ PATIENTS

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- In clinical practice, dual HER2 blockade + taxane chemotherapies + endocrine therapy (ET) are

# QUOTES – CURRENT AND NEW TREATMENTS IN HER2+ mBC

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# New Standards in HR+, HER2– Early Breast Cancer

JOSEPH GLIGOROV, MD, PHD

# EBCC ORAL-018: Recommendations from the European Commission Initiative on Breast Cancer on multigene tests to guide the use of adjuvant chemotherapy in patients who have hormone receptor positive, HER-2 negative, lymph node negative or up to 3 lymph nodes positive invasive breast cancer. P.G. Rossi, et al

## Background

# EBCC ORAL-007: Clinical utility of MammaPrint testing in invasive lobular carcinoma (ILC): results from the MINDACT phase III trial. O. Metzger, et al

## Background

> Chemotherapy treatment decision for pts diagnosed with ILC remains controversial. The authors investigated the clinical utility of

# EBCC LBA-001: Differential impact of prognostic parameters in hormone receptor-positive lobular early breast cancer in the WSG PlanB trial. M. Christgen, et al

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## Background

> Invasive lobular breast cancer is the second most common BC subtype. Clinicopathologic parameters associated with lobular BC

# ESMO LBA5_PR: monarchE: Abemaciclib in high risk early breast cancer. S.R. Johnston, et al

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## Background

> Superior treatment options are needed to prevent early recurrence and development of metastases for pts with HR-positive,

# ESMO LBA12: PALLAS: A randomized phase III trial of adjuvant palbociclib with endocrine therapy versus endocrine therapy alone for HR+/HER2- early breast cancer. E.L. Mayer, et al

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## Background

> Palbociclib (P) added to ET improves PFS in HR-positive, HER2-negative mBC. The global PALLAS trial (NCT02513394) was

# PENELOPE-B trial of palbociclib in early breast cancer did not meet its primary endpoint. Press release on October 9, 2020

# ESMO 176P: Germline mutation status and therapy response in patients with homologous recombination deficient, HER2-negative early breast cancer: Results of the GeparOLA study (NCT02789332). J. Hauke, et al

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## Background

> The phase II GeparOLA study randomized pts with homologous recombination deficient (HRD), HER2-negative EBC to receive

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# Discussion

# NEW STANDARDS IN HR+, HER2– EARLY BREAST CANCER (1/2)

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## CDK4/6 inhibitors in the adjuvant setting

# NEW STANDARDS IN HR+, HER2– EARLY BREAST CANCER (2/2)

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## Optimizing the use of CDK4/6 inhibitors

# KEY QUOTES – CDK4/6 INHIBITORS IN THE ADJUVANT SETTING

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# NEW STANDARDS IN HR+, HER2– EARLY BREAST CANCER (1/2)

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## Multigene tests for HR-positive EBC

# NEW STANDARDS IN HR+, HER2– EARLY BREAST CANCER (2/2)

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## Poly(ADP-ribose) polymerase (PARP) inhibitors in HRD *BRCA*-mutated pts, in the neoadjuvant setting

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# Recent Developments and Evolving Treatments in HR+, HER2– Metastatic Breast Cancer

ADAM BRUFSKY, MD, PHD

# ESMO LBA18: Overall Survival (OS) Results From SOLAR-1, a Phase 3 Study of Alpelisib (ALP) + Fulvestrant (FUL) for Hormone Receptor-Positive (HR+), Human Epidermal Growth Factor Receptor 2-Negative (HER2–) Advanced Breast Cancer (ABC). F. André, et al

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## Background

> PI3K pathway hyperactivation due to *PIK3CA* mutations contributes to poor survival in pts with HR-positive, HER2-negative

# ESMO 273O: nextMONARCH: Final overall survival analysis of abemaciclib monotherapy or in combination with tamoxifen in patients with HR+, HER2- metastatic breast cancer. E.P. Hamilton, et al

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## Background

> In the phase II nextMONARCH study, primary analysis of PFS and ORR confirmed the robust single-agent activity of abemaciclib in

# ESMO 277MO: SAR439859, an oral selective estrogen receptor (ER) degrader (SERD), in ER+/ HER2- metastatic breast cancer (mBC): Biomarker analyses from a Phase 1/2 study.
# S. Chandarlapaty, et al

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## Background

> SAR439859 has antitumor activity in pts with wild-type and mutated *ESR1* mBC. Authors described tumor molecular features and

# ESMO 278MO: cfDNA analysis from Phase 1/2 study of lerociclib (G1T38), a continuously dosed oral CDK4/6 inhibitor, with fulvestrant in HR+/HER2- advanced breast cancer patients.
# B. Krastev, et al

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## Background

> Lerociclib, dosed twice-daily with no drug holiday in combination with fulvestrant, has a favorable safety profile with low rates of

# ESMO 283MO: Ipatasertib (IPAT) + paclitaxel (PAC) for PIK3CA/AKT1/PTEN-altered hormone receptor-positive (HR+) HER2-negative advanced breast cancer (aBC): Primary results from Cohort B of the IPATunity130 randomised phase 3 trial. N. Turner, et al

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## Background

> PI3K/protein kinase B (AKT) pathway alterations occur in ~50% of HR-positive BC. In a phase II trial in advanced TNBC, adding

# ESMO 329P: Ribociclib (RIB) in patients (pts) with HR+/HER2− advanced breast cancer (ABC) and resistance to prior endocrine therapy (ET) in the MONALEESA (ML) -3 and -7 trials. S.A. Hurvitz, et al

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## Background

> ET resistance is a challenge in the treatment of pts with advanced BC. RIB + ET demonstrated significant OS benefit vs PBO in

# ESMO 337P: Efficacy of Everolimus plus Exemestane in CDK 4/6 inhibitors-pretreated or naïve HR-positive/HER2-negative breast cancer patients: a secondary analysis of the EVERMET study. F. Nichetti, et al

EPICS

## Background

> The mechanistic target of rapamycin complex 1 inhibitor everolimus (EVE) in combination with the AI exemestane (EXE) is approved

# ESMO 274O: Health-related quality of life (HRQoL) changes with veliparib in patients (pts) with metastatic or locally advanced breast cancer in the Phase 3 BROCADE 3 study. V. Dieras, et al

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## Background

> Veliparib, a PARP1/2 inhibitor, was evaluated in the phase III BROCADE 3 study for efficacy and safety in combination with

# 276O: Pooled analysis of patient (pt)-reported quality of life (QOL) in the MONALEESA (ML)-2, -3, and -7 trials of ribociclib (RIB) plus endocrine therapy (ET) to treat hormone receptor–positive, HER2-negative (HR+/HER2−) advanced breast cancer (ABC). P.A. Fasching, et al

EPICS

## Background

> Pt-reported QOL results have been presented separately for each phase III ML trial, which tested efficacy and safety of RIB with

# EBCC ORAL-009: Predictors of efficacy in patients (pts) with hormone receptor–positive/human epidermal growth factor receptor 2–negative advanced breast cancer (HR+/HER2– ABC): subgroup analyses of PALOMA-3. H. Rugo, et al

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## Background

> In PALOMA-3, ET-sensitive pts with HR-positive, HER2-negative advanced BC and disease progression on prior ET derived OS

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# Discussion

# RECENT DEVELOPMENTS AND EVOLVING TREATMENTS IN HR+, HER2– METASTATIC BREAST CANCER

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- **CDK4/6 inhibitors in the metastatic setting**

# KEY QUOTES – CDK INHIBITORS IN THE METASTATIC SETTING

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# RECENT DEVELOPMENTS AND EVOLVING TREATMENTS IN HR+, HER2– METASTATIC BREAST CANCER (1/2)

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> **Alpelisib in the metastatic setting**

# RECENT DEVELOPMENTS AND EVOLVING TREATMENTS IN HR+, HER2– METASTATIC BREAST CANCER (2/2)

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- The advent of new biomarkers in the metastatic setting calls for the need to rebiopsy pts and collect metastatic tissue

# KEY QUOTES – ORAL SERDS IN THE METASTATIC SETTING

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# RECENT DEVELOPMENTS AND EVOLVING TREATMENTS IN HR+, HER2– METASTATIC BREAST CANCER

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- **Oral taxanes in the metastatic setting**