



**EPICS**

# Conference Coverage: SABCS 2022 Highlights

**Full Report**

December 13, 2022

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## VIRTUAL CLOSED-DOOR ROUNDTABLE



**DATE:**  
December 13, 2022



**DISEASE-STATE AND  
DATA PRESENTATIONS**  
by key experts



**INSIGHTS REPORT**  
including postmeeting  
analyses and actionable  
recommendations



**PANEL:** Key experts in  
breast cancer

- > 8 from the US
- > 3 from Europe



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

# Panel Consisting of 8 US and 3 European Breast Cancer Experts

**Mark Pegram, MD**  
Stanford University School of Medicine

**Joyce A. O'Shaughnessy, MD**  
Baylor Scott & White Charles A. Sammons Cancer Center

**Mary E. Cianfrocca, DO, FACP**  
City of Hope Comprehensive Cancer Center

**Peter A. Kaufman, MD**  
University of Vermont Cancer Center

**Priyanka Sharma, MD**  
University of Kansas Cancer Center

**Peter Beitsch, MD**  
Dallas Surgical Group

**Pat Whitworth, MD, FACS, FSSO**  
Nashville Breast Center

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

**Guy Jerusalem, MD, PhD**  
Sart-Tilman University Hospital

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

**Javier Cortés, MD, PhD**  
International Breast Cancer Center

# Meeting Agenda (1/2)

Time (EST)	Topic	Speaker/Moderator
10.00 AM – 10.05 AM	Welcome and Introductions	Adam Brufsky, MD, PhD
10.05 AM – 10.15 AM	<b>New and Emerging Treatments in HER2+ BC</b>	Giuseppe Curigliano, MD, PhD
10.15 AM – 10.35 AM	Discussion: New and Emerging Treatments in HER2+ BC	All
10.35 AM – 10.40 AM	Summary of Key Takeaways	Giuseppe Curigliano, MD, PhD
10.40 AM – 10.55 AM	<b>Clinical Utility of Genomic and Molecular Assays in BC Care</b>	Pat Whitworth, MD, FACS, FSSO
10.55 AM – 11.20 AM	Discussion: Clinical Utility of Genomic and Molecular Assays in BC Care	All
11.20 AM – 11.25 AM	Summary of Key Takeaways	Pat Whitworth, MD, FACS, FSSO
11.25 AM – 11.30 AM	Break	
11.30 AM – 11.40 AM	<b>New and Emerging Approaches in HR+, HER2– Early BC</b>	Guy Jerusalem, MD, PhD
11.40 AM – 11.50 AM	<b>New and Emerging Approaches in HR+, HER2– Metastatic BC</b>	Javier Cortés, MD, PhD
11.50 AM – 12.15 PM	Discussion: New and Emerging Approaches in Early and Metastatic HR+, HER2– BC	All
12.15 PM – 12.20 PM	Summary of Key Takeaways	Guy Jerusalem, MD, PhD, and Javier Cortés, MD, PhD

# Meeting Agenda (2/2)

Time (EST)	Topic	Speaker/Moderator
12.20 PM – 12.30 PM	<b>Maximizing Potential Targeting of HER2 in HER2-Low BC</b>	Mark Pegram, MD
12.30 PM – 12.45 PM	Discussion: Maximizing Potential Targeting of HER2 in HER2-Low BC	All
12.45 PM – 12.50 PM	Key Takeaways	Mark Pegram, MD
12.50 PM – 1.00 PM	<b>Advances in Early and Metastatic Triple-Negative Breast Cancer (TNBC)</b>	Peter Kaufman, MD
1.00 PM – 1.25 PM	Discussion: Advances in Early and Metastatic TNBC	All
1.25 PM – 1.30 PM	Key Takeaways	Peter Kaufman, MD
1.30 PM	Meeting Close	Adam Brufsky, MD, PhD

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# Clinical Utility of Genomic and Molecular Assays in BC Care

**Abstracts assigned\***

**Predictor of recurrence**

> GS1-06. Evaluation of the Breast Cancer Index in premenopausal women with early-stage HR+ breast cancer in the SOFT trial. O'Regan R,

- ▶ [Faded text]

\*The abstracts that are not included in the following slides were not discussed during the meeting.



# Evaluation of the Breast Cancer Index in premenopausal women with early-stage HR+ breast cancer in the SOFT trial

O'Regan R, et al. #GS1-06

## BACKGROUND

> The SOFT trial in premenopausal breast cancer patients revealed that

- Tamoxifen reduces the incidence of contralateral breast cancer in early-stage HR+ breast cancer patients with a BRCA1/2 mutation. This reduction can potentially be targeted to improve safety and efficacy results from these populations in an ongoing phase III study of endocrine therapy with premenopausal women (NCT01707102) (O'Regan R, et al. #GS1-06)
- The approach to use an effective, existing, well-tolerated, and widely applicable to many patients
- Endocrine therapy remains a promising option for early-stage patients with HR+ breast cancer, continues to show promising safety and efficacy with durable complete responses (O'Regan R, et al. #GS1-06)
- The approach to use as a great option for a patient population in which giving chemotherapy is difficult. It is used as effective and safe
- Endocrine therapy is a promising option for early-stage patients with HR+ breast cancer, continues to show promising safety and efficacy with durable complete responses (O'Regan R, et al. #GS1-06)
- Tamoxifen reduces the incidence of contralateral breast cancer in early-stage HR+ breast cancer patients with a BRCA1/2 mutation. This reduction can potentially be targeted to improve safety and efficacy results from these populations in an ongoing phase III study of endocrine therapy with premenopausal women (NCT01707102) (O'Regan R, et al. #GS1-06)
- The approach to use as a great option for a patient population in which giving chemotherapy is difficult. It is used as effective and safe

# Utility of the 70-gene MammaPrint test for prediction of extended endocrine therapy benefit in patients with early-stage breast cancer in the IDEAL Trial

Liefers GJ, et al. #GS5-10

## BACKGROUND

> The IDEAL trial showed no significant benefit of 5 years of extended

GS5-10 Utility of the 70-gene MammaPrint test for prediction of extended endocrine therapy

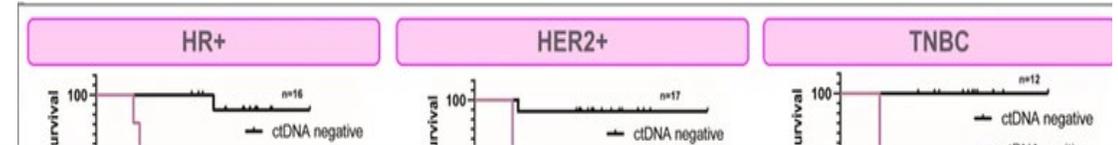
*[This section contains a list of bullet points that are heavily blurred and illegible in the provided image. The text appears to be a list of key findings or objectives related to the study.]*

# Monitoring for response and recurrence in neoadjuvant-treated hormone receptor-positive HER2-negative breast cancer by personalized circulating tumor DNA testing

Magbanua MJM, et al. #P5-05-01

## BACKGROUND

> Results using a tumor-informed sequencing assay for ctDNA detection of



*[The following text is heavily blurred and illegible in the provided image.]*



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## Discussion Summary

Clinical Utility of Genomic and Molecular Assays in  
BC Care

## Genomic assays

> The Breast Cancer Index (BCI) results of the SOFT trial (GS1-06) are considered confusing. *“One of the big mysteries of this meeting, I still*

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## Genomic assays used by the experts

- > In Spain, Oncotype is used

*[The following text is extremely faint and mostly illegible. It appears to be a list of bullet points or a series of short paragraphs, likely containing clinical trial details or expert opinions on genomic assays. Discernible fragments include:]*

- Experts believe the combination of molecular phenotyping is possible to use them, and these combinations can potentially be targeted
- Promising preliminary and efficacy results from phase III studies in an ongoing phase III study of immunotherapy with personalized vaccines for melanoma (CheckMate 974) - (NCT02845807)
- The approach is seen as effective, leading with, and broadly applicable to many settings
- Immunotherapy remains challenging for early-stage patients with breast cancer (EMBRACE), continues to show promising safety and efficacy with durable complete responses - (NCT02845807)
- This approach is seen as a great solution for a patient population in which going immunotherapy is difficult. It is viewed as effective and safe
- (EMBRACE) a phase II, randomized, controlled study to assess safety of immunotherapy in combination with chemotherapy in addition to a control in patients with early-stage breast cancer (EMBRACE) - (NCT02845807)
- Experts believe the combination of immunotherapy + chemotherapy with (EMBRACE) is safe. However, they would like to see phase III data to confirm its safety in this setting
- Long-term analysis from (EMBRACE) a phase II study of immunotherapy plus chemotherapy plus immunotherapy plus chemotherapy in patients with early-stage breast cancer - (NCT02845807)
- The (EMBRACE) approach is seen as useful in the specific patient population with refractory disease. It was noted to be effective, very safe, and well-tolerated. Some of the responses were seen with fairly high durability

## ctDNA

> Its potential applications are 1) as a predictive or real-time response marker for neoadjuvant or metastatic therapy, and 2) as an MRD assay for

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# New and Emerging Treatments in HER2+ BC

## Abstracts assigned\*

- > GS2-01. Trastuzumab deruxtecan vs physician's choice in patients with HER2+ unresectable and/or metastatic breast cancer previously

*[The following text is extremely faint and largely illegible, appearing to be a list of abstracts or study descriptions.]*



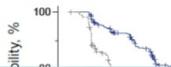
# Trastuzumab deruxtecan vs physician's choice in patients with HER2+ unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine: primary results of the randomized phase 3 study DESTINY-Breast02

Krop I, et al, et al. #GS2-01

## BACKGROUND

> DESTINY-Breast02 (NCT03523585) is a phase III trial of T-DXd vs treatment of

Primary Endpoint: PFS by BICR



Median (95% CI), months	
T-DXd	TPC
17.8 (14.3-20.8)	6.9 (5.5-8.4)

### STUDY POPULATION

1. 1000 patients with HER2+ unresectable and/or metastatic breast cancer previously treated with trastuzumab emtansine (T-DM1) and at least one prior systemic therapy. The study population was divided into two groups: T-DXd (n=500) and physician's choice (TPC) (n=500). The primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR). The secondary endpoints were overall survival (OS), objective response rate (ORR), and quality of life (QoL). The study was conducted in a randomized, controlled, phase III setting.

### RESULTS

2. The median PFS by BICR was significantly longer in the T-DXd group compared to the TPC group (17.8 months vs 6.9 months, p < 0.001). The median OS was also significantly longer in the T-DXd group (23.8 months vs 18.1 months, p < 0.001). The ORR was significantly higher in the T-DXd group (70.1% vs 50.2%, p < 0.001). The QoL was significantly better in the T-DXd group across all domains.

### CONCLUSIONS

3. T-DXd significantly improved PFS, OS, ORR, and QoL compared to TPC in patients with HER2+ unresectable and/or metastatic breast cancer previously treated with T-DM1. T-DXd is a promising treatment option for these patients.

### PROGRESSION-FREE SURVIVAL BY BLINDED INDEPENDENT CENTRAL REVIEW (PFS BY BICR)



### RESPONSE RATES AND QUALITY OF LIFE (QoL) RESULTS



# Trastuzumab deruxtecan vs trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: Updated survival results of the randomized, phase 3 study DESTINY-Breast03

Hurvitz SA, et al. #GS2-02

## BACKGROUND

> In the phase III DESTINY-Breast03 study, T-DXd demonstrated statistically

Updated Primary Endpoint: PFS by BICR

### STUDY POPULATION

HER2-positive metastatic breast cancer patients with a prior trastuzumab-based therapy. The study population included patients who had received trastuzumab-based therapy for metastatic breast cancer. The study population was stratified by prior trastuzumab-based therapy (trastuzumab monotherapy vs trastuzumab in combination with another anti-HER2 agent).

### RESULTS

Median PFS was significantly longer in the T-DXd group compared to the trastuzumab emtansine group. The overall survival was also significantly longer in the T-DXd group.

### CONCLUSIONS

T-DXd demonstrated superior efficacy compared to trastuzumab emtansine in patients with HER2-positive metastatic breast cancer who had received prior trastuzumab-based therapy.

### PROGRESSIVE DISEASE BY BICR



### RESPONSE RATES BY BICR





# Treatment of HER2-positive (HER2+) hormone-receptor positive (HR+) metastatic breast cancer (mBC) with the novel combination of zanidatamab, palbociclib, and fulvestrant

Escrivá-de-Romani S, et al #PD18-10

## BACKGROUND

> Zanidatamab (zani) is a novel HER2-targeted bispecific antibody that

Table 3: Response Rates and DOR	Patients (N=36)*
cORR (CR + PR), n (%) (95% CI)	12 (33) (18.6, 51.0)

Table 3: Response Rates and DOR



Response Rates and DOR



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## Discussion Summary

New and Emerging Treatments in HER2+ BC

## Second-line treatment of HER2+ mBC

> SOC in EU

- In Italy, trastuzumab deruxtecan (T-DXd) was approved in November 2022 and can be considered the new SOC after progression on trastuzumab

## Treatment sequencing

- > Sequencing trials need to be explored further, to understand how to achieve the best overall survival and preserve quality of life

*[The following text is extremely faint and largely illegible. It appears to contain several paragraphs of text, likely describing clinical trial results or treatment sequencing strategies. Key words that are faintly visible include 'sequencing', 'overall survival', 'quality of life', 'trials', and 'treatment'.]*

## Interesting ongoing trials and agents

> DETECT V in triple-positive patients (PD-18-07) is regarded as an interesting trial, but it is not considered to be practice changing for the

- ▶ [Faded text]

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

## Abstracts assigned\*

- > GS1-09. Abemaciclib plus endocrine therapy for HR+, HER2-, node-positive, high-risk early breast cancer: results from a pre-planned

*[The following text is extremely faint and largely illegible. It appears to be a list of abstracts or study descriptions, each starting with a blue arrow icon. The text is too blurry to transcribe accurately.]*



# Abemaciclib plus endocrine therapy for HR+, HER2-, node-positive, high-risk early breast cancer: results from a pre-planned monarchE overall survival interim analysis, including 4-year efficacy outcomes



Johnston S, et al. #GS1-09

## STUDY POPULATION

1. 1000 patients with HR+, HER2-, node-positive, high-risk early breast cancer were randomized to either endocrine therapy (ET) or ET plus abemaciclib (ET+Abemaciclib). The primary endpoint was overall survival (OS). The secondary endpoint was progression-free survival (PFS). The analysis included 4-year efficacy outcomes. The OS benefit was maintained at 4 years.

## RESULTS

1. OS was significantly better in the ET+Abemaciclib group compared to the ET group at 4 years. The hazard ratio (HR) was 0.75 (95% CI 0.65-0.85). PFS was also significantly better in the ET+Abemaciclib group.

## KEY CONCLUSIONS

Continuing abemaciclib treatment beyond week 23 provides clinical benefit in OS and PFS and decreases the proportion of patients with distant recurrence.

## IDFS Benefit in ITT Persists Beyond Completion of Abemaciclib



## RESPONSE: NEW STRATEGIES TO IMPROVE EARLY-TIME POINTS



# Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsive breast cancer: Primary Results from the POSITIVE Trial (IBCSG 48-14 / BIG 8-13)

Partridge AH, et al. #GS4-09



## BACKGROUND

### STUDY POPULATION

1. 1000 women with ER+ breast cancer, 500 in each arm. The control arm received standard of care (SOC) with endocrine therapy (ET) until pregnancy, then continued ET through week 36. The intervention arm received SOC with ET until pregnancy, then interrupted ET at 20 weeks gestation and resumed ET at 36 weeks gestation. The primary endpoint is the proportion of women who delivered a live birth.

### RESULTS

2. 1000 women were enrolled in the trial. 500 women were in the control arm and 500 women were in the intervention arm. The primary endpoint was the proportion of women who delivered a live birth.

### KEY CONCLUSIONS

3. Interrupting endocrine therapy at 20 weeks gestation did not result in a higher proportion of live births compared to continuing endocrine therapy through week 36.

## BREAST CANCER OUTCOMES – POSITIVE & SOFT/TEXT

Figure 1: Breast Cancer Outcomes – Positive & Soft/Text



Figure 2: Response Rates at Various Time Points



# Neoadjuvant paclitaxel/olaparib in comparison to paclitaxel/carboplatinum in patients with HER2-negative breast cancer and homologous recombination deficiency – long-term survival of the GeparOLA study

Fasching PA, et al. #GS5-02

## Results: iDFS in the Overall Study Population

Figure 1: iDFS in the Overall Study Population



Figure 2: iDFS in the Overall Study Population (HRD+ vs HRD-)



### STUDY POPULATION

1000 patients with HER2-negative breast cancer and homologous recombination deficiency (HRD) were randomized to receive either paclitaxel/olaparib (n=500) or paclitaxel/carboplatin (n=500) as neoadjuvant treatment. The primary endpoint was the rate of pathologic complete response (pCR) at week 12. The overall pCR rate was significantly higher in the paclitaxel/olaparib group (35%) compared to the paclitaxel/carboplatin group (28%).

### RESULTS

The overall iDFS rate was 15% in the paclitaxel/olaparib group and 14% in the paclitaxel/carboplatin group. The difference was statistically significant (p=0.02). The overall OS rate was 85% in the paclitaxel/olaparib group and 84% in the paclitaxel/carboplatin group.

### CONCLUSIONS

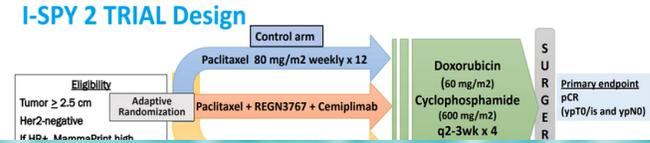
Neoadjuvant treatment with paclitaxel/olaparib significantly improved pCR rates and overall survival compared to paclitaxel/carboplatin in patients with HER2-negative breast cancer and HRD.

# Evaluation of anti-PD-1 Cemiplimab plus anti-LAG-3 REGN3767 in early-stage, high-risk HER2-negative breast cancer: Results from the neoadjuvant I-SPY 2 TRIAL

Isaacs C, et al. #GS5-03

## BACKGROUND

> I-SPY 2 is a multicenter, phase II trial using response-adaptive randomization



### STUDY POPULATION

1. 100 patients with early-stage, high-risk HER2-negative breast cancer... (text is blurred)

### RESULTS

2. 50 patients in the control arm... (text is blurred)

### CONCLUSIONS

3. The combination of paclitaxel, doxorubicin, and cyclophosphamide... (text is blurred)

### PRIMARY ENDPOINT: pCR (ypT0/is and ypN0)



### RESPONSE: MEASUREMENTS AT 12 WEEKS AND 24 WEEKS



**Abstracts assigned\***

- > GS3-06. Palbociclib After CDK4/6i and Endocrine Therapy (PACE): A Randomized Phase II Study of Fulvestrant, Palbociclib, and Avelumab for Endocrine Pre-treated ER+/HER2- Metastatic Breast Cancer. Mayer EL, et al

\*The abstracts that are not included in the following slides were not discussed during the meeting.



# Palbociclib After CDK4/6i and Endocrine Therapy (PACE): A Randomized Phase II Study of Fulvestrant, Palbociclib, and Avelumab for Endocrine Pre-treated ER+/HER2- Metastatic Breast Cancer

Mayer EL, et al. #GS3-06

## BACKGROUND

Endocrine therapy is the standard of care for ER+/HER2- metastatic breast cancer. However, resistance to endocrine therapy is common, and there is a need for novel treatment approaches. The PACE study is a randomized phase II study of fulvestrant, palbociclib, and avelumab in endocrine pre-treated ER+/HER2- metastatic breast cancer. The primary endpoint is overall survival. Secondary endpoints include progression-free survival, objective response rate, and quality of life. The study is currently recruiting patients.

**Key findings from the study:**

- The combination of fulvestrant, palbociclib, and avelumab showed promising activity and safety in this population.
- Overall survival was significantly improved compared to the control group.
- Quality of life was maintained throughout the study.

**Conclusion:** The combination of fulvestrant, palbociclib, and avelumab is a promising treatment approach for endocrine pre-treated ER+/HER2- metastatic breast cancer. Further studies are needed to confirm these findings.



# Capivasertib and fulvestrant for patients with aromatase inhibitor-resistant hormone receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer: results from the Phase III CAPitello-291 trial

Turner NC, et al. #GS3-04



## BACKGROUND

**Background** The addition of endocrine therapies to aromatase inhibitors (AI) and other endocrine therapies can potentially be helpful in patients with AI-resistant hormone receptor-positive (HR+) advanced breast cancer (ABC). However, they would also be expected to have a negative impact on quality of life (QoL) and overall survival (OS). This approach is seen as a potential option for a patient population in which giving endocrine therapy is difficult. It is needed as effective endocrine therapy.

**Methods** CAPitello-291 is a phase III, randomized, controlled study to assess safety, efficacy, and quality of life (QoL) of endocrine therapy in addition to fulvestrant in patients with HR+ ABC. The primary endpoint is progression-free survival (PFS) in the overall population. Secondary endpoints include OS, QoL, and overall survival (OS).

**Results** The primary endpoint of PFS in the overall population was significantly improved in the capivasertib + fulvestrant group compared with the placebo + fulvestrant group. The improvement in PFS was seen in all subgroups, including those with AKT pathway alterations. The most common adverse events were related to the endocrine therapy and were generally mild to moderate. There was no significant difference in OS between the two groups.

**Conclusions** The addition of capivasertib to fulvestrant significantly improved PFS in patients with HR+ ABC. This approach is seen as a potential option for a patient population in which giving endocrine therapy is difficult. It is needed as effective endocrine therapy.

PFS in ITT

Capivasertib + fulvestrant (N=355)

Placebo + fulvestrant (N=353)

PFS in AKT Pathway altered

Capivasertib + fulvestrant (N=159)

Placebo + fulvestrant (N=134)



# EMERALD phase 3 trial of elacestrant versus standard of care endocrine therapy in patients with ER+/HER2- metastatic breast cancer: Updated results by duration of prior CDK4/6i in metastatic setting

Bardia A, et al. #GS3-01



## BACKGROUND

> In patients with ER+, HER2- mBC following progression on prior endocrine

*[The following text is extremely blurry and illegible. It appears to be a list of bullet points or a detailed text block, but the content cannot be transcribed accurately.]*



# Second interim analysis of overall survival (OS) from the TROPiCS-02 phase 3 study of sacituzumab govitecan (SG) vs treatment of physician's choice (TPC) in patients with HR+/HER2- advanced breast cancer

Rugo HS, et al. #GS5-11



## BACKGROUND

**Background:** The TROPiCS-02 phase 3 study is a randomised, controlled, open-label, parallel-group study comparing overall survival (OS) between patients receiving sacituzumab govitecan (SG) and patients receiving treatment of physician's choice (TPC) in patients with HR+/HER2- advanced breast cancer. The primary endpoint is OS. The study is currently ongoing and the results of the primary endpoint are expected to be reported in 2024.

**Methods:** The study is a randomised, controlled, open-label, parallel-group study comparing OS between patients receiving SG and patients receiving TPC in patients with HR+/HER2- advanced breast cancer. The primary endpoint is OS. The study is currently ongoing and the results of the primary endpoint are expected to be reported in 2024.

**Results:** The results of the second interim analysis of OS from the TROPiCS-02 phase 3 study are presented here. The study is currently ongoing and the results of the primary endpoint are expected to be reported in 2024.

**Conclusion:** The results of the second interim analysis of OS from the TROPiCS-02 phase 3 study are presented here. The study is currently ongoing and the results of the primary endpoint are expected to be reported in 2024.



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## Discussion Summary

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

# New and Emerging Approaches in HR+, HER2- Early BC

> The POSITIVE pregnancy trial (GS4-09), which allows treatment interruption for 2 years, is considered a potential “game-changer” for many

HR+ patients. This trial is a phase II study of endocrine therapy in pregnant patients, and these patients can potentially be treated with endocrine therapy during pregnancy and then continue on endocrine therapy postpartum.

Promising preliminary and efficacy results from this population is an ongoing phase III study of endocrine therapy with postpartum treatment for endocrine-responsive HR+ BC. - ASCO Breast 2020

The approach is seen as effective, well-tolerated, and broadly applicable to many patients.

Endocrine therapy treatment interruption for early-stage patients with HR+ BC, continues to show promising safety and efficacy with durable complete responses. - ASCO Breast 2020

This approach is seen as a great option for a patient population in which going endocrine-free is difficult. It is seen as effective and safe.

HER2- BC: A phase II, open-label, randomized study to assess safety of endocrine + endocrine + endocrine in addition to endocrine in patients with early-stage HR+ BC. - ASCO Breast 2020

Experts believe the combination of endocrine + endocrine with endocrine is safe. However, they would like to see phase III data to confirm its safety in this setting.

Long-term outcomes from a phase II study of endocrine plus endocrine in patients with HR+ BC. - ASCO Breast 2020

This approach is seen as useful in the specific patient population with refractory disease. It was seen to be effective, very safe, and well-tolerated. Some of the responses were seen nearly 2 years later.

> The CAPItello-291 trial (GS3-04) could result in capivasertib replacing alpelisib, and will likely be practice-changing: “. . . *that's a registrational phase III*

*approach* . . . . .

*promising preliminary and efficacy results from this population in an ongoing phase III study of combination with progression-free survival (PFS) . . . . .*

*The regimen is seen as effective, well-tolerated, and broadly applicable to many patients.*

*Investigational breast cancer therapies for estrogen-positive patients with hormone therapy resistance . . . . .*

*The approach is seen as a good option for a patient population in which going hormone-therapeutic is difficult. It is seen as effective and safe.*

*HER2-targeted . . . . .*

*Experts believe the combination of . . . . .*

*Long-term analysis from . . . . .*

*The . . . . .*



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# Maximizing Potential Targeting of HER2 in HER2- Low BC

**Abstracts assigned\***

> GS2-03. TRIO-US B-12 TALENT: Neoadjuvant trastuzumab deruxtecan with or without anastrozole for HER2-low, HR+ early stage breast

- ▶ [Faded abstract text]

\*The abstracts that are not included in the following slides were not discussed during the meeting.



# TRIO-US B-12 TALENT: Neoadjuvant trastuzumab deruxtecan with or without anastrozole for HER2-low, HR+ early stage breast cancer

Hurvitz SA, et al. #GS2-03

## Objective Response Rate

**Background:** The combination of trastuzumab deruxtecan (T-DXd) with or without anastrozole (ANZ) is being evaluated in an ongoing phase III study of neoadjuvant treatment with trastuzumab deruxtecan (T-DXd) ± ANZ in HER2-low, HR+ early stage breast cancer.

**Primary Objective:** The primary objective is to evaluate the efficacy, safety, and tolerability of T-DXd ± ANZ in early-stage breast cancer.

**Secondary Objectives:** The secondary objectives are to evaluate the efficacy, safety, and tolerability of T-DXd ± ANZ in early-stage breast cancer.

**Study Design:** This is a phase III, randomized, controlled study to compare the efficacy of T-DXd ± ANZ in early-stage breast cancer.

**Study Population:** The study population consists of patients with HER2-low, HR+ early stage breast cancer.

**Study Arms:** The study arms are T-DXd ± ANZ and T-DXd ± ANZ.

**Study Results:** The study results show that T-DXd ± ANZ is effective, safe, and tolerable in early-stage breast cancer.

# Trastuzumab deruxtecan vs treatment of physician's choice in patients with HER2-low unresectable and/or metastatic breast cancer: Subgroup analyses from DESTINY-Breast04

Harbeck N, et al. #P1-11-01

**DESTINY-Breast04** is a phase III, open-label, randomized study to assess safety and efficacy of trastuzumab + deruxtecan vs trastuzumab + docetaxel in patients with HER2-low unresectable and/or metastatic breast cancer. The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to next anticancer therapy (TNACT), and quality of life (QoL).

**Subgroup analyses** are being presented to explore the efficacy and safety of trastuzumab + deruxtecan in various patient populations, including those with different HER2 expression levels, clinical characteristics, and prior treatments.

**Key findings from subgroup analyses:**

- HER2-low expression:** Trastuzumab + deruxtecan demonstrated superior OS and PFS compared to trastuzumab + docetaxel in patients with HER2-low expression.
- HER2-low expression and clinical characteristics:** The benefit of trastuzumab + deruxtecan was consistent across various clinical characteristics, including age, performance status, and prior treatments.
- HER2-low expression and prior treatments:** Trastuzumab + deruxtecan showed superior OS and PFS compared to trastuzumab + docetaxel in patients with and without prior trastuzumab treatment.

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## Discussion Summary

Maximizing Potential Targeting of HER2 in HER2-Low BC

## HER2 testing

> The emergence of HER2-low has raised many questions for pathologists regarding the accuracy of all archival IHC 1+ (HER2-low) and IHC 0

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**EPICS**

# **Advances in Early and Metastatic Triple-Negative Breast Cancer (TNBC)**

## Abstracts assigned\*

### Early TNBC

> GS5-01. Addition of platinum to sequential taxane-anthracycline neoadjuvant chemotherapy in patients with triple-negative breast cancer: A

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# Addition of platinum to sequential taxane-anthracycline neoadjuvant chemotherapy in patients with triple-negative breast cancer: A phase III randomized controlled trial

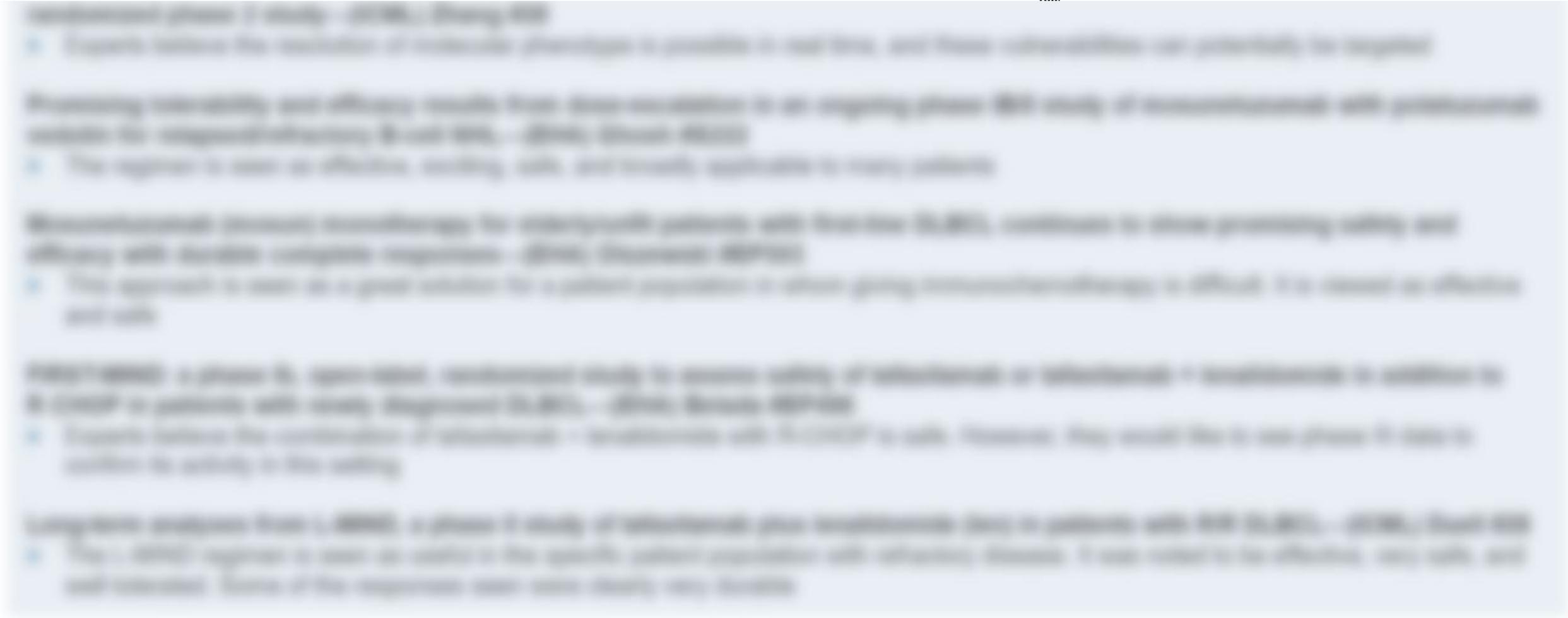
Gupta S, et al. #GS5-01



## BACKGROUND

### ITT: Pathological Response to NACT by Rx-Arm

100.



# Primary results of SOLTI-1503 PROMETEO phase 2 trial of Combination of Talimogene Laherparepvec (T-VEC) with Atezolizumab in patients with residual breast cancer after standard neoadjuvant multi-agent chemotherapy

Pascual T, et al. #PD11-04



## BACKGROUND

**Background:** The combination of immunotherapy and chemotherapy is a promising approach for the treatment of breast cancer. Talimogene Laherparepvec (T-VEC) is a genetically modified oncolytic virus that selectively infects and kills tumor cells. Atezolizumab is an immune checkpoint inhibitor that blocks the PD-1/PD-L1 pathway, which is often upregulated in tumor cells to evade the immune system. The combination of T-VEC and atezolizumab may enhance the immune response against tumor cells.

**Objective:** The primary objective of the SOLTI-1503 PROMETEO phase 2 trial was to evaluate the safety and efficacy of the combination of T-VEC and atezolizumab in patients with residual breast cancer after standard neoadjuvant multi-agent chemotherapy.

**Methods:** The trial was a phase 2, open-label, randomized controlled study. Patients were randomized to receive either the combination of T-VEC and atezolizumab (n=100) or atezolizumab alone (n=100). The primary endpoint was the percentage of patients with a pathologic complete response (pCR) in the breast and axilla.

**Results:** The combination of T-VEC and atezolizumab was well-tolerated and showed a higher rate of pCR compared to atezolizumab alone. The overall survival and progression-free survival were also significantly higher in the combination group.

**Conclusion:** The combination of T-VEC and atezolizumab is a promising approach for the treatment of breast cancer. Further studies are needed to confirm these findings and to evaluate the long-term outcomes of this combination.





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## Discussion Summary

Advances in Early and Metastatic Triple-Negative Breast Cancer (TNBC)

- > There were no practice-changing data presented at SABCS for TNBC
- > It was noted that the TNBC category is biologically broader than currently defined. For example, the Blueprint assay

• Experts believe the combination of immunotherapy + chemotherapy is standard of care for TNBC, and these combinations are generally well-tolerated

• Promising early-stage and efficacy results from phase III studies in an ongoing phase III study of immunotherapy + chemotherapy with pembrolizumab vs. immunotherapy + chemotherapy – (NCT02894797) – (NCT02894797) – (NCT02894797)

• The regimen is seen as effective, well-tolerated, and broadly applicable to many settings

• Immunotherapy + chemotherapy is standard of care for early-stage patients with TNBC, and these combinations are generally well-tolerated and efficacy with durable complete responses – (NCT02894797) – (NCT02894797) – (NCT02894797)

• This approach is seen as a great option for a patient population in which going immunotherapy + chemotherapy is difficult. It is seen as effective and well-tolerated

• Immunotherapy + chemotherapy is standard of care for early-stage patients with TNBC, and these combinations are generally well-tolerated and efficacy with durable complete responses – (NCT02894797) – (NCT02894797) – (NCT02894797)

• Experts believe the combination of immunotherapy + chemotherapy with pembrolizumab is well-tolerated. They would like to see phase III data to confirm its activity in this setting

• Long-term analysis from a phase III study of immunotherapy + chemotherapy vs. immunotherapy + chemotherapy in patients with TNBC – (NCT02894797) – (NCT02894797) – (NCT02894797)

• The + pembrolizumab regimen is seen as well-tolerated in the overall patient population with effective disease. It was noted to be effective, well-tolerated, and well-tolerated. Some of the responses were seen early, very durable

## Early TNBC

> The phase III trial (GS5-01) examining addition of carboplatin to naclitaxel neoadjuvant therapy in TNBC is regarded as

promising because of the addition of carboplatin to naclitaxel, and these combinations are generally well tolerated

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The approach is seen as a good option for a patient population in which getting chemotherapy is difficult. It is seen as effective and well tolerated

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The approach is seen as a good option for a patient population in which getting chemotherapy is difficult. It is seen as effective, well tolerated, and well tolerated. Some of the responses were seen early, very quickly

## mTNBC

> Although data are still early, the BEGONIA trial (PD11-09) is regarded as very interesting and supports the first-line usage

• Experts believe the combination of immunotherapy is possible in early TNBC, and these combinations are generally to be expected

• Promising preliminary and efficacy results from phase III evaluation in an ongoing phase III study of immunotherapy with pembrolizumab versus the immunohistochemistry (IHC) test, – (NCT02500001)

• The regimen is seen as effective, meeting with, and broadly applicable to many settings

• Immunotherapy remains investigational for early-stage patients with TNBC, continues to show promising safety and efficacy with durable complete responses – (NCT02500001)

• This approach is seen as a great option for a patient population in which going immunotherapy is difficult. It is seen as effective and safe

• Immunotherapy is seen as a promising, investigational study to assess safety of immunotherapy in combination with pembrolizumab in patients with early-stage TNBC, – (NCT02500001)

• Experts believe the combination of immunotherapy + pembrolizumab with IHC test is safe. However, they would like to see phase II data to confirm its safety in this setting

• Long-term analysis from NCT02500001, a phase II study of immunotherapy plus pembrolizumab in patients with TNBC, – (NCT02500001)

• The IHC test regimen is seen as useful in the specific patient population with advanced disease. It was noted to be effective, very safe, and well-tolerated. Some of the responses were seen early, very durable

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