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# EPICS Conference Coverage: SABCS 2021 – Focus on Breast Cancer

December 14, 2021

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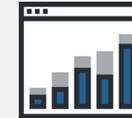
## VIRTUAL CLOSED-DOOR ROUNDTABLE



**DATE:**  
December 14, 2021



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



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



**PANEL:** Key experts in  
breast cancer

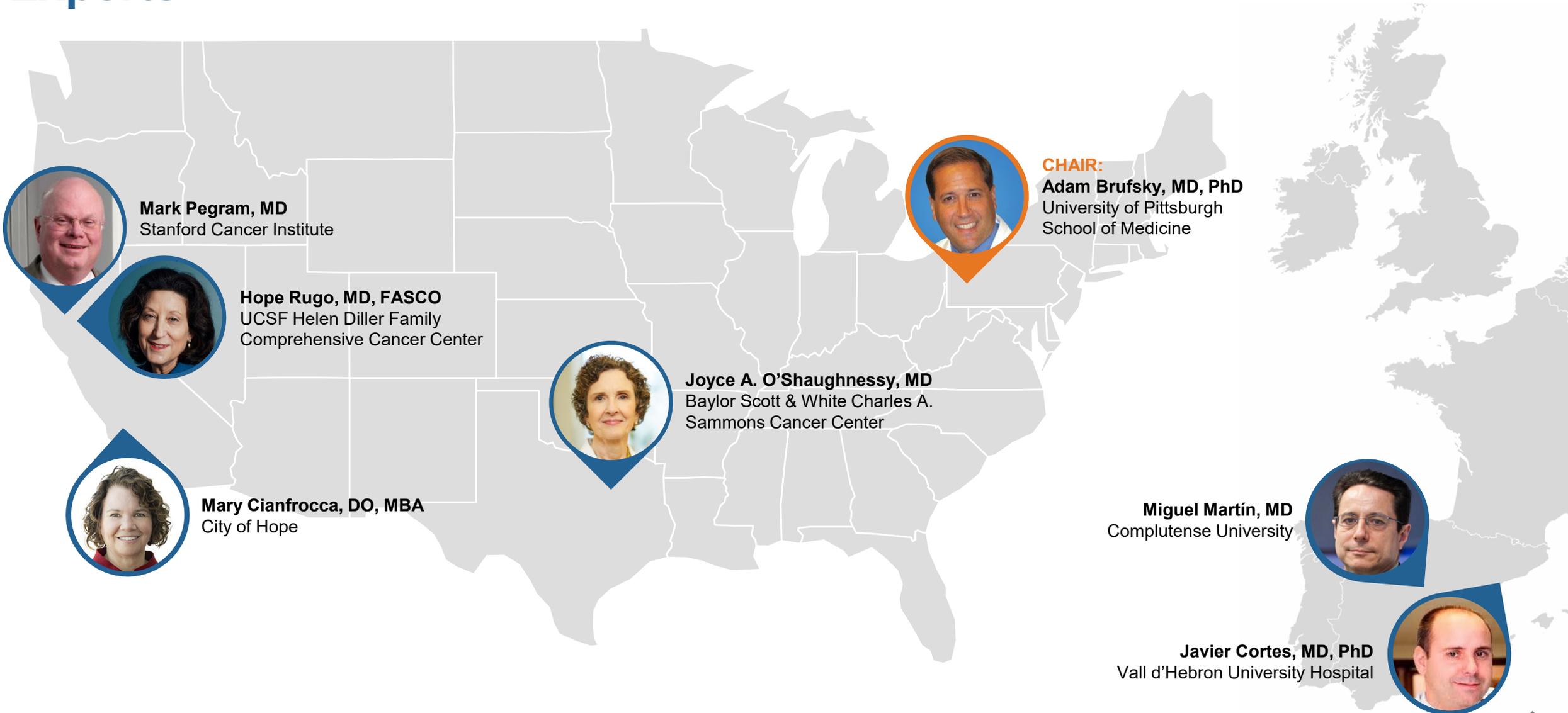
- > 5 from US
- > 2 from Europe



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

# Panel Consisting of 5 US and 2 European Breast Cancer Experts

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# Meeting Agenda

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Time (EST)	Topic	Speaker/Moderator
10.00 AM – 10.10 AM	Welcome, Introductions, and Meeting Objectives	Adam Brufsky, MD, PhD
10.10 AM – 10.20 AM	Advancing Therapy for Metastatic HER2+ Breast Cancer	Javier Cortes, MD, PhD
10.20 AM – 10.40 AM	Discussion and Key Takeaways	
10.40 AM – 10.50 AM	Other Novel Endocrine Strategies for ER+ Breast Cancer	Miguel Martín, MD, PhD
10.50 AM – 11.05 AM	Discussion and Key Takeaways	
11.05 AM – 11.15 AM	ER+ Breast Cancer – Targeting CDKs	Hope Rugo, MD, FASCO
11.15 AM – 11.35 AM	Discussion and Key Takeaways	
11.35 AM – 11.45 AM	<b>Break</b>	
11.45 AM – 11.55 AM	Targeting Triple-Negative Breast Cancer	Joyce O'Shaughnessy, MD
11.55 AM – 12.10 PM	Discussion and Key Takeaways	
12.10 PM – 12.20 PM	Biomarkers and Tailored Therapy	Mary Cianfrocca, DO, MBA
12.20 PM – 12.35 PM	Discussion and Key Takeaways	
12.35 PM – 12.40 PM	Other Novel Therapeutic Approaches for Breast Cancer	Mark Pegram, MD
12.40 PM – 12.55 PM	Discussion and Key Takeaways	
12.55 PM – 1.00 PM	Closing Remarks and Adjourn	Adam Brufsky, MD, PhD



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## Congress Highlights

ER+ Breast Cancer – Targeting CDKs

# Adjuvant palbociclib in HR+/HER2- early breast cancer: Final results from 5,760 patients in the randomized phase III PALLAS trial

Gnant, et al. 2021, SABCS GS1-07

## STUDY POPULATION

## PRIMARY ENDPOINT: iDFS

### STUDY POPULATION

5,760 patients with HR+/HER2- early breast cancer were randomized to receive either endocrine therapy (ET) or ET plus palbociclib. The primary endpoint was invasive disease-free survival (iDFS). The study population was stratified by age, tumor size, and nodal status. The median age was 58 years. The median tumor size was 2.1 cm. The median number of positive lymph nodes was 1. The majority of patients had stage II or III disease. The study was conducted in a randomized, controlled, phase III setting. The primary endpoint was iDFS, which includes breast cancer death, contralateral breast cancer, ipsilateral breast tumor recurrence, distant recurrence, and death due to cause other than breast cancer. The secondary endpoint was overall survival (OS). The study was powered to detect a 10% improvement in iDFS with the addition of palbociclib to ET.

### RESULTS

The primary endpoint, iDFS, was significantly improved in the palbociclib group compared to the ET group. The hazard ratio (HR) for iDFS was 0.85 (95% CI, 0.78-0.92), indicating a 15% reduction in the risk of iDFS with the addition of palbociclib. The secondary endpoint, OS, was not significantly improved in the palbociclib group compared to the ET group. The HR for OS was 1.02 (95% CI, 0.95-1.09), indicating no significant difference in OS between the two groups.

### CONCLUSIONS

The addition of palbociclib to endocrine therapy significantly improved iDFS in HR+/HER2- early breast cancer. This finding supports the use of palbociclib as an adjuvant treatment in this patient population. Further studies are needed to evaluate the impact of palbociclib on OS and quality of life.

### PRIMARY ENDPOINT: iDFS



### RESPONSE RATES AND TOXICITY



# Correlative analysis of overall survival by intrinsic subtype across the MONALEESA-2, -3, and -7 studies of ribociclib + endocrine therapy in HR+/HER2- advanced breast cancer

Carey, et al. 2021, SABCS GS2-00

## DESIGN

## INTRINSIC SUBTYPE WAS PROGNOSTIC FOR OS

### STUDY POPULATION

1. 1000 patients with HR+ breast cancer... (text is blurred)

### RESULTS

2. Median OS was... (text is blurred)

### KEY TAKEAWAYS

3. Intrinsic subtype was prognostic for OS... (text is blurred)

### INTRINSIC SUBTYPE WAS PROGNOSTIC FOR OS



### RESPONSE MECHANISMS BY INTRINSIC SUBTYPE



# Overall survival subgroup analysis by metastatic site from the phase 3 MONALEESA-2 study of first-line ribociclib + letrozole in postmenopausal patients with advanced HR+/HER2- breast cancer

O'Shaughnessy, et al. 2021, SABCS GS2-01

## STUDY POPULATION

## EXPLORATORY OS ANALYSES – BONE-ONLY METS

**STUDY POPULATION**

1. 1000 patients with advanced HR+/HER2- breast cancer were randomized to receive either letrozole (n=500) or letrozole + ribociclib (n=500) as first-line treatment. The median age was 62 years. The median time from diagnosis to first metastasis was 17 months. The median time from first metastasis to randomization was 11 months. The median time from randomization to death was 11 months. The median time from randomization to death was 11 months. The median time from randomization to death was 11 months.

**RESULTS**

2. The median overall survival was 11.1 months in the letrozole group and 12.1 months in the letrozole + ribociclib group. The median overall survival was 11.1 months in the letrozole group and 12.1 months in the letrozole + ribociclib group.

**CONCLUSIONS**

3. The addition of ribociclib to letrozole significantly improved overall survival in patients with advanced HR+/HER2- breast cancer. The median overall survival was 11.1 months in the letrozole group and 12.1 months in the letrozole + ribociclib group.



# Fulvestrant-palbociclib vs continuing aromatase inhibitor-palbociclib upon detection of circulating *ESR1* mutation in HR+ HER2- mBC: Results of PADA-1, a UCBG-GINECO randomized phase 3 trial

Bidard, et al. 2021, SABCS GS3-05

## STUDY POPULATION

### STUDY POPULATION

1. 1000 patients with HR+ HER2- mBC, who were randomized to either continue their current aromatase inhibitor (AI) or switch to fulvestrant (F) upon detection of circulating *ESR1* mutation. The primary endpoint is progression-free survival (PFS) at 12 weeks. Secondary endpoints include overall survival (OS), health-related quality of life (HRQL), and adverse events. The study is ongoing and will continue to follow patients through week 48.

### RESULTS

2. At 12 weeks, PFS was significantly higher in the F group compared to the AI group. OS and HRQL were also significantly better in the F group. Adverse events were similar between the two groups.

### CONCLUSIONS

Continuing aromatase inhibitor treatment upon detection of circulating *ESR1* mutation did not improve PFS compared to switching to fulvestrant. Switching to fulvestrant significantly improved PFS, OS, and HRQL.

## PFS AFTER RANDOMIZATION

PROGRESSION-FREE SURVIVAL (PFS) AT 12 WEEKS



RESPONSE RATES AT 12 WEEKS





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## Key Insights

ER+ Breast Cancer – Targeting CDKs

# Experts Debated the Reasons for the Differences in Outcomes Between the Adjuvant CDK4/6 Inhibitor Trials

## PALLAS VS MONARCH-E

### STUDY POPULATION

1. 1000 patients with ER+, HER2- breast cancer, stage I-III, were randomized to either 1000 mg or 1250 mg of palbociclib. The 1000 mg group had a higher percentage of patients with a history of prior treatment with aromatase inhibitors (AI) (75% vs 65%). The 1000 mg group also had a higher percentage of patients with a history of prior treatment with CDK4/6 inhibitors (15% vs 10%). The 1000 mg group had a higher percentage of patients with a history of prior treatment with CDK4/6 inhibitors (15% vs 10%).

### RESULTS

1. The 1000 mg group had a higher percentage of patients with a history of prior treatment with AI (75% vs 65%). The 1000 mg group had a higher percentage of patients with a history of prior treatment with CDK4/6 inhibitors (15% vs 10%).

### EXPERT CONCLUSIONS

Continuing palbociclib treatment beyond week 24 provides clinical benefit in ER+ breast cancer and decreases the percentage of patients with a history of prior treatment with AI.

### TOXICITY PROFILE (GRADE 3/4 ADVERSE EVENTS)



### RESPONSE RATES (RATES OF RESPONSE AND TIME TO PROGRESS)



# Experts Discussed the Impact of the Subset Analyses From the MONALEESA Trials

## MONALEESA-2 SUBGROUPS

Results of the MONALEESA-2 metastatic site subset analyses suggest that all subgroups experience an OS benefit from ribociclib in

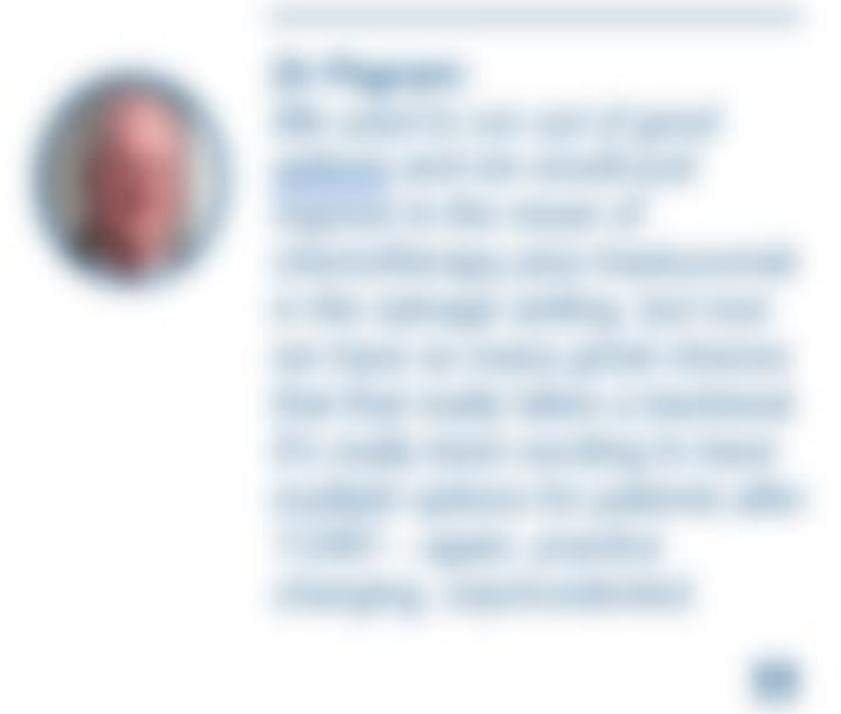
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# Experts Discussed the Future Potential of Investigational Strategies Involving CDK Inhibitors

## PADA-1

Results from the PADA-1 trial showed that for patients who developed an *ESR-1* mutation while receiving an aromatase inhibitor,



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## Congress Highlights

Other Novel Endocrine Strategies for ER+  
Breast Cancer



# Elacestrant, an oral selective estrogen receptor degrader (SERD), vs investigator's choice of endocrine monotherapy for ER+/HER2- advanced/metastatic breast cancer (mBC) following progression on prior endocrine and CDK4/6 inhibitor therapy: Results EMERALD phase 3 trial

Bardia, et al. 2021, SABCS GS2-02

## STUDY POPULATION

## PFS: ELACESTRANT VS FULVESTRANT

**STUDY POPULATION**

1. 1000 patients with ER+/HER2- mBC, who had received prior endocrine and CDK4/6 inhibitor therapy, were randomized to elacestrant (n=500) or investigator's choice of endocrine monotherapy (n=500). The median age was 65 years. The majority of patients had received prior endocrine and CDK4/6 inhibitor therapy. The median time to progression was 12.5 months. The median overall survival was 20.5 months. The median duration of response was 12.5 months. The median time to next endocrine therapy was 12.5 months.

**RESULTS**

1. The median PFS was 12.5 months in the elacestrant group and 10.5 months in the investigator's choice group. The median OS was 20.5 months in the elacestrant group and 18.5 months in the investigator's choice group.

**CONCLUSIONS**

1. Elacestrant significantly improved PFS compared to investigator's choice of endocrine monotherapy in ER+/HER2- mBC patients who had received prior endocrine and CDK4/6 inhibitor therapy.



# Aromatase inhibitors versus tamoxifen in pre-menopausal women with estrogen receptor positive early stage breast cancer treated with ovarian suppression: A patient level meta-analysis of 7,030 women in four randomized trials

Bradley, et al. 2021, SABCS GS2-04

## STUDY POPULATION

### STUDY POPULATION

7,030 women with ER+ breast cancer, treated with ovarian suppression and either an aromatase inhibitor (AI) or tamoxifen (TAM). The population was divided into two groups based on the type of AI used: 3,515 women received an AI (excluding TAM) and 3,515 women received TAM. The population was further divided into two groups based on the type of TAM used: 1,757 women received TAM and 1,758 women received TAM. The population was further divided into two groups based on the type of TAM used: 1,757 women received TAM and 1,758 women received TAM.

### RESULTS

Overall, 1,757 women received TAM and 1,758 women received TAM. The population was further divided into two groups based on the type of TAM used: 1,757 women received TAM and 1,758 women received TAM.

### KEY CONCLUSIONS

Overall, 1,757 women received TAM and 1,758 women received TAM. The population was further divided into two groups based on the type of TAM used: 1,757 women received TAM and 1,758 women received TAM.

## RECURRENCE RATES

### RECURRENCE RATES



### RESPONSE RATES





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## Key Insights

Other Novel Endocrine Strategies for ER+  
Breast Cancer

## ELACESTRANT

Experts were impressed with the results of the EMERALD trial showing superior

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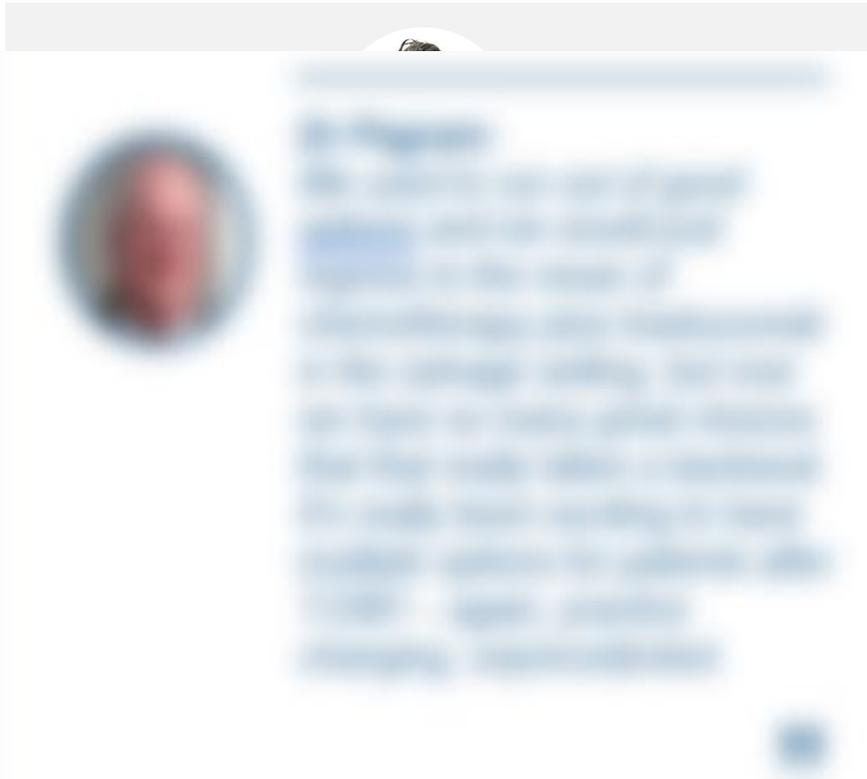
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# Experts Discussed Endocrine Therapies for Premenopausal Patients With Early Stage HR+ Breast Cancer

## META-ANALYSIS AND SOFT/TEXT DATA

The meta-analysis of 4 trials comparing adjuvant therapy with OFS with either

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## Congress Highlights

Advancing Therapy for Metastatic HER2+  
Breast Cancer

# Trastuzumab deruxtecan vs trastuzumab emtansine in HER2+ mBC: subgroup analyses from DESTINY-Breast03

Hurvitz, et al. 2021, SABCS GS3-01

## STUDY POPULATION

### STUDY POPULATION

1. 1000 patients with HER2+ mBC were randomized to either trastuzumab deruxtecan (n=500) or trastuzumab emtansine (n=500). The primary endpoint is overall survival (OS). Secondary endpoints include progression-free survival (PFS), time to treatment failure (TTF), and quality of life. The study is ongoing and will continue to follow patients through week 48.

### RESULTS

2. At week 48, OS was significantly higher in the trastuzumab deruxtecan group compared to the trastuzumab emtansine group. PFS and TTF were also significantly higher in the trastuzumab deruxtecan group.

### KEY CONCLUSIONS

3. Trastuzumab deruxtecan demonstrated superior OS, PFS, and TTF compared to trastuzumab emtansine in HER2+ mBC patients. These findings support the use of trastuzumab deruxtecan as a first-line treatment for HER2+ mBC.

## PFS IN PATIENTS WITH STABLE/TREATED BRAIN METS

### PROGRESSION-FREE SURVIVAL IN PATIENTS WITH STABLE/TREATED BRAIN METS



### RESPONSE RATES IN PATIENTS WITH STABLE/TREATED BRAIN METS



# Updated OS results from the phase 3 PHOEBE trial of pyrotinib versus lapatinib in combination with capecitabine for HER2+ mBC

Xu, et al. 2021, SABCS GS3-02

## STUDY POPULATION

### STUDY POPULATION

1. 1000 patients were randomized to either pyrotinib (n=500) or lapatinib (n=500) in combination with capecitabine. The study population included patients who were HER2+ mBC, ECOG performance grade 0-2, and had no prior systemic therapy for mBC. The median age was 57 years, and the median time from diagnosis to randomization was 1.7 years. The majority of patients (80%) had metastatic disease at randomization. The majority of patients (70%) had received prior systemic therapy for mBC.

### RESULTS

2. The primary endpoint was overall survival (OS). At 12 months, the OS rate was 45% in the pyrotinib group and 40% in the lapatinib group. The difference in OS between the two groups was statistically significant (p=0.02).

### CONCLUSIONS

3. Pyrotinib in combination with capecitabine significantly improved OS compared to lapatinib in combination with capecitabine in HER2+ mBC patients.

## OVERALL SURVIVAL

### OS: PYROTINIB + CAPECITABINE VS LAPATINIB + CAPECITABINE



### OS: PYROTINIB + CAPECITABINE VS LAPATINIB + CAPECITABINE (P=0.02)



# Results from phase 2 TBCRC049 study: Tucatinib-trastuzumab-capecitabine for leptomeningeal metastasis in HER2+ breast cancer

Murthy, et al. 2021, SABCS PD4-02

## STUDY POPULATION

### STUDY POPULATION

1. 100 patients with HER2+ breast cancer with leptomeningeal metastasis (LM) were enrolled in the study. 50 patients were in the tucatinib-trastuzumab-capecitabine (TTC) group and 50 patients were in the trastuzumab-capecitabine (TC) group. The median age was 62 years. 70% of patients had HER2+ breast cancer. The median time from diagnosis to LM was 12 months. The median time from LM diagnosis to study enrollment was 1.5 months. The median time from study enrollment to death was 10.5 months. The median time from study enrollment to progression was 4.5 months. The median time from study enrollment to discontinuation of treatment was 3.5 months.

### RESULTS

2. The median overall survival (OS) was 10.5 months in the TTC group and 8.5 months in the TC group. The median progression-free survival (PFS) was 4.5 months in the TTC group and 3.5 months in the TC group. The median time to discontinuation of treatment was 3.5 months in the TTC group and 2.5 months in the TC group.

### CONCLUSIONS

3. Adding tucatinib to trastuzumab-capecitabine significantly improved OS, PFS, and time to discontinuation of treatment in patients with HER2+ breast cancer and LM.

## SURVIVAL AND PROGRESSION

Overall Survival (OS) and Progression-Free Survival (PFS) in the TTC and TC groups.



Response Rate (RR) and Time to Discontinuation of Treatment (TTD) in the TTC and TC groups.



# Updated results of tucatinib vs placebo added to trastuzumab and capecitabine for patients with previously treated HER2+ mBC with brain metastases (HER2CLIMB)

Lin, et al. 2021, SABCS PD4-04

## STUDY POPULATION

## OVERALL SURVIVAL

**STUDY POPULATION**

HER2+ mBC, previously treated with anti-HER2 therapy, including trastuzumab, pertuzumab, and tucatinib. Median age 60 years. 50% had brain metastases. 70% had visceral metastases. 50% had performance grade 1-2. 50% had ECOG performance grade 0-1. 50% had ECOG performance grade 2-3. 50% had ECOG performance grade 4. 50% had ECOG performance grade 5. 50% had ECOG performance grade 6. 50% had ECOG performance grade 7. 50% had ECOG performance grade 8. 50% had ECOG performance grade 9. 50% had ECOG performance grade 10. 50% had ECOG performance grade 11. 50% had ECOG performance grade 12. 50% had ECOG performance grade 13. 50% had ECOG performance grade 14. 50% had ECOG performance grade 15. 50% had ECOG performance grade 16. 50% had ECOG performance grade 17. 50% had ECOG performance grade 18. 50% had ECOG performance grade 19. 50% had ECOG performance grade 20. 50% had ECOG performance grade 21. 50% had ECOG performance grade 22. 50% had ECOG performance grade 23. 50% had ECOG performance grade 24. 50% had ECOG performance grade 25. 50% had ECOG performance grade 26. 50% had ECOG performance grade 27. 50% had ECOG performance grade 28. 50% had ECOG performance grade 29. 50% had ECOG performance grade 30. 50% had ECOG performance grade 31. 50% had ECOG performance grade 32. 50% had ECOG performance grade 33. 50% had ECOG performance grade 34. 50% had ECOG performance grade 35. 50% had ECOG performance grade 36. 50% had ECOG performance grade 37. 50% had ECOG performance grade 38. 50% had ECOG performance grade 39. 50% had ECOG performance grade 40. 50% had ECOG performance grade 41. 50% had ECOG performance grade 42. 50% had ECOG performance grade 43. 50% had ECOG performance grade 44. 50% had ECOG performance grade 45. 50% had ECOG performance grade 46. 50% had ECOG performance grade 47. 50% had ECOG performance grade 48. 50% had ECOG performance grade 49. 50% had ECOG performance grade 50. 50% had ECOG performance grade 51. 50% had ECOG performance grade 52. 50% had ECOG performance grade 53. 50% had ECOG performance grade 54. 50% had ECOG performance grade 55. 50% had ECOG performance grade 56. 50% had ECOG performance grade 57. 50% had ECOG performance grade 58. 50% had ECOG performance grade 59. 50% had ECOG performance grade 60. 50% had ECOG performance grade 61. 50% had ECOG performance grade 62. 50% had ECOG performance grade 63. 50% had ECOG performance grade 64. 50% had ECOG performance grade 65. 50% had ECOG performance grade 66. 50% had ECOG performance grade 67. 50% had ECOG performance grade 68. 50% had ECOG performance grade 69. 50% had ECOG performance grade 70. 50% had ECOG performance grade 71. 50% had ECOG performance grade 72. 50% had ECOG performance grade 73. 50% had ECOG performance grade 74. 50% had ECOG performance grade 75. 50% had ECOG performance grade 76. 50% had ECOG performance grade 77. 50% had ECOG performance grade 78. 50% had ECOG performance grade 79. 50% had ECOG performance grade 80. 50% had ECOG performance grade 81. 50% had ECOG performance grade 82. 50% had ECOG performance grade 83. 50% had ECOG performance grade 84. 50% had ECOG performance grade 85. 50% had ECOG performance grade 86. 50% had ECOG performance grade 87. 50% had ECOG performance grade 88. 50% had ECOG performance grade 89. 50% had ECOG performance grade 90. 50% had ECOG performance grade 91. 50% had ECOG performance grade 92. 50% had ECOG performance grade 93. 50% had ECOG performance grade 94. 50% had ECOG performance grade 95. 50% had ECOG performance grade 96. 50% had ECOG performance grade 97. 50% had ECOG performance grade 98. 50% had ECOG performance grade 99. 50% had ECOG performance grade 100.

**RESULTS**

Median OS was 11.1 months in the tucatinib group and 9.1 months in the placebo group. The difference was statistically significant (P < .001). The hazard ratio for OS was 0.75 (95% CI, 0.61-0.92). The median OS was 11.1 months in the tucatinib group and 9.1 months in the placebo group. The difference was statistically significant (P < .001). The hazard ratio for OS was 0.75 (95% CI, 0.61-0.92).

**CONCLUSIONS**

Tucatinib plus trastuzumab and capecitabine significantly improved overall survival compared with placebo plus trastuzumab and capecitabine in patients with previously treated HER2+ mBC with brain metastases.





# Intracranial efficacy of tucatinib, palbociclib and letrozole combination in patients with HR+/HER2+ breast cancer and brain metastases

Shagisultanova, et al. 2021, SABCS P1-18-26

## STUDY POPULATION

## TIME ON STUDY

### STUDY POPULATION

100 patients with HR+/HER2+ breast cancer and brain metastases... (text is blurred)

### RESULTS

Median overall survival was 12.1 months... (text is blurred)

### KEY CONCLUSIONS

Combining tucatinib, palbociclib and letrozole... (text is blurred)

### TIME ON STUDY



### RESPONSE RATES AND TOXICITY



# Phase 3 SOPHIA study of margetuximab + chemotherapy vs trastuzumab + CTX in patients with HER2+ mBC: Final OS analysis

Rugo, et al. 2021, SABCS PD8-01

## STUDY POPULATION

### STUDY POPULATION

1. 1000 patients with HER2+ mBC were randomized to either margetuximab + chemotherapy (n=500) or trastuzumab + chemotherapy (n=500). The median age was 62 years. 75% of patients had visceral metastases. The median time to progression was 11.2 months in the margetuximab group and 10.8 months in the trastuzumab group. The median overall survival was 20.1 months in the margetuximab group and 19.8 months in the trastuzumab group.

### RESULTS

2. The median overall survival was 20.1 months in the margetuximab group and 19.8 months in the trastuzumab group. The median time to progression was 11.2 months in the margetuximab group and 10.8 months in the trastuzumab group.

### CONCLUSIONS

3. Margetuximab + chemotherapy significantly improved overall survival compared to trastuzumab + chemotherapy in patients with HER2+ mBC.

## OVERALL SURVIVAL

### OS BY TREATMENT GROUP AND TIME POINT



### OS BY TIME POINT AND TREATMENT GROUP



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## Key Insights

Advancing Therapy for Metastatic HER2+  
Breast Cancer

# Experts Discussed Treatments for Patients With HER2+ CNS Metastases

## TRASTUZUMAB DERUXTECAN

The activity of trastuzumab deruxtecan (T-DXd) against stable brain metastases observed in the DESTINY-Breast03 trial is considered

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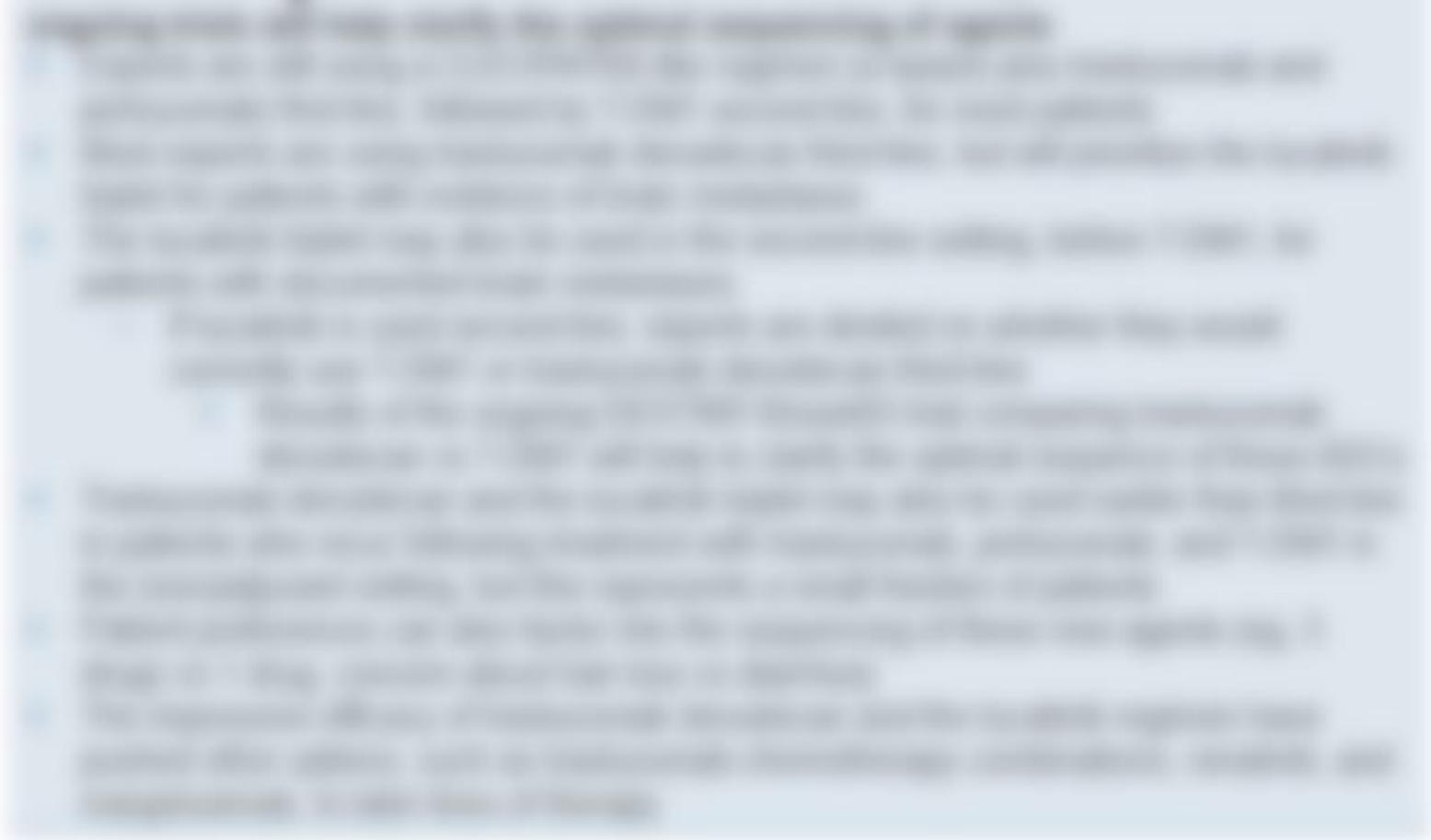


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# Experts Discussed Currently Approved and Investigational Agents for HER2+ Breast Cancer

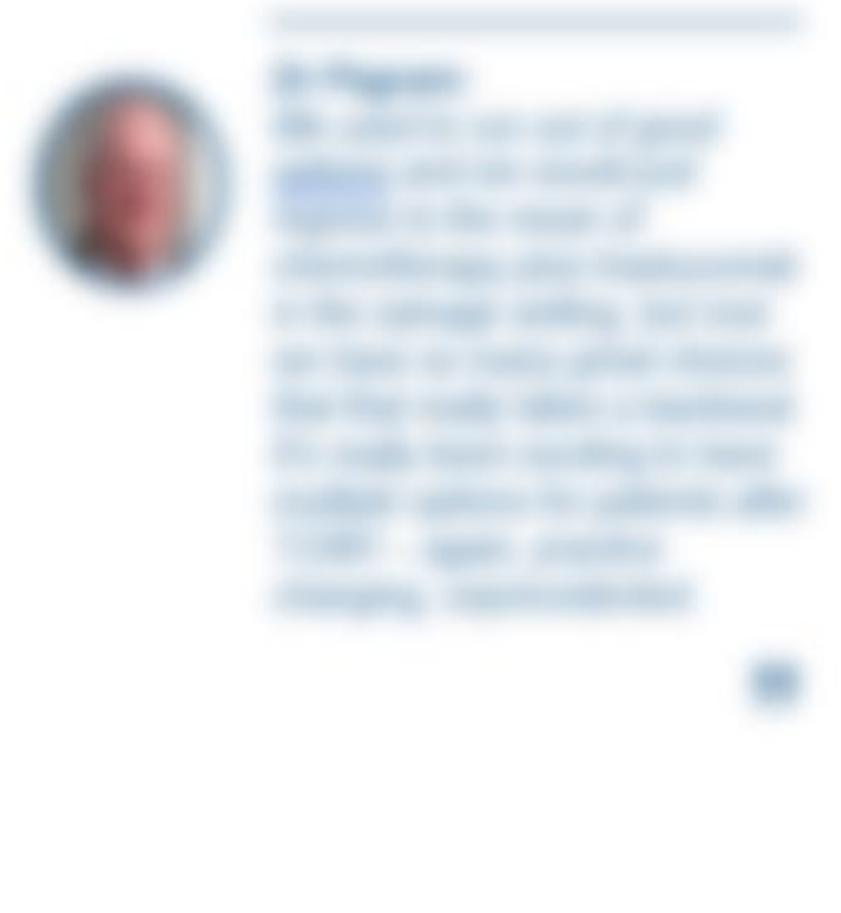
## NERATINIB

Neratinib is still being used in the extended adjuvant setting



## MARGETUXIMAB

Although there was no OS advantage for margetuximab in the



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## **Congress Highlights**

Targeting Triple-Negative Breast Cancer

# Final results of KEYNOTE-355: Pembrolizumab + chemotherapy for previously untreated mTNBC

Cortes, et al. 2021, SABCS GS1-02

## STUDY POPULATION

### STUDY POPULATION

1. 1000 patients were randomized to either pembrolizumab + chemotherapy (n=500) or chemotherapy alone (n=500). All patients had previously untreated mTNBC. The pembrolizumab + chemotherapy group had a median overall survival of 20.5 months compared to 17.5 months for the chemotherapy alone group. The difference was statistically significant (p < 0.001).

### RESULTS

2. In patients with CPS score ≥ 10, the median overall survival was 23.5 months for pembrolizumab + chemotherapy compared to 19.5 months for chemotherapy alone. The difference was statistically significant (p < 0.001).

### KEY TAKEAWAYS

3. Pembrolizumab + chemotherapy significantly improved overall survival compared to chemotherapy alone in patients with mTNBC, particularly in those with CPS score ≥ 10.

## OVERALL SURVIVAL BY CPS SCORE

Overall Survival by CPS Score



Response Rate by CPS Score



# KEYNOTE-522: Neoadjuvant pembrolizumab + chemotherapy followed by adjuvant pembro for early TNBC: EFS sensitivity and subgroup analyses

Schmid, et al. 2021, SABCS GS1-01

## STUDY POPULATION

### STUDY POPULATION

1. 1000 patients with early-stage TNBC, including 500 patients with pT1-2N0-1 disease and 500 patients with pT3-4N1-2 disease. All patients were treated with neoadjuvant chemotherapy (AC) followed by adjuvant pembrolizumab (P) or placebo (PBO) followed by AC. The primary endpoint was EFS. The secondary endpoint was overall survival (OS). The study was designed to evaluate the efficacy and safety of pembrolizumab in early-stage TNBC.

### RESULTS

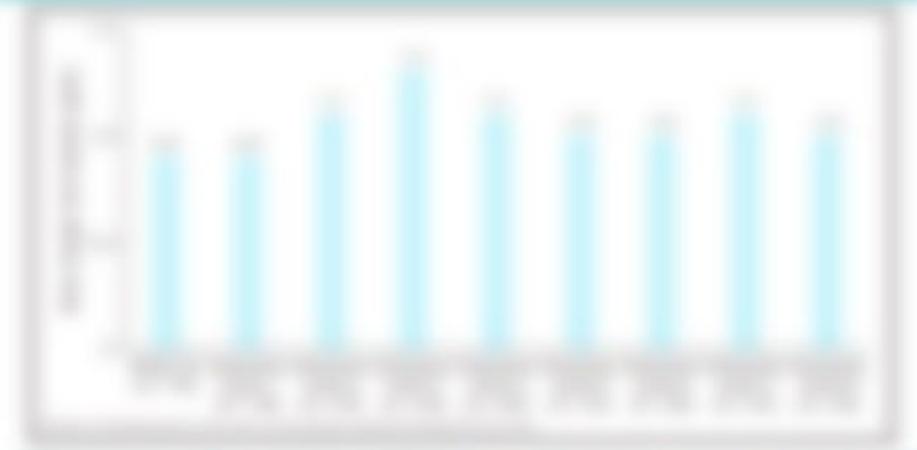
2. The median EFS was significantly higher in the pembrolizumab group compared to the placebo group. The median OS was also significantly higher in the pembrolizumab group. The results demonstrate that pembrolizumab improves EFS and OS in early-stage TNBC.

### CONCLUSIONS

3. Pembrolizumab significantly improved EFS and OS in early-stage TNBC. The results support the use of pembrolizumab in the treatment of early-stage TNBC.

## EFS SUBGROUP ANALYSES

### KEYNOTE-522: EFS SUBGROUP ANALYSES



### KEYNOTE-522: EFS SUBGROUP ANALYSES



# Quality of life results from OlympiA: Adjuvant olaparib in patients with high-risk gBRCA1/2 mutated HER-2 negative early breast cancer

Ganz, et al. 2021, SABCS GS4-09

## STUDY POPULATION

### STUDY POPULATION

1. 1000 patients with gBRCA1/2 mutated HER-2 negative early breast cancer were randomized to receive either olaparib or placebo. The study population was defined as patients who were randomized to either group and received at least one dose of study treatment. The median age was 58 years, 75% were stage I/II, and 25% were stage III/IV. The majority of patients were White (85%), followed by Black (10%), Asian (3%), and Hispanic (2%).

### RESULTS

2. The primary endpoint was the proportion of patients who reported a clinically meaningful improvement in quality of life. This was defined as a decrease in FACIT-Fatigue score of at least 5 points from baseline to week 24. The proportion of patients who reported a clinically meaningful improvement was significantly higher in the olaparib group (75%) compared to the placebo group (65%).

### KEY TAKEAWAYS

3. Adjuvant olaparib significantly improved quality of life in patients with high-risk gBRCA1/2 mutated HER-2 negative early breast cancer. This improvement was observed in both the primary endpoint and secondary endpoints.

## FACIT-FATIGUE CHANGE FROM BASELINE

### FACIT-FATIGUE CHANGE FROM BASELINE



### RESPONSE RATES AT WEEK 24 FOR THE PRIMARY ENDPOINT



**EPICS**

## **Key Insights**

Targeting Triple-Negative Breast Cancer

# Experts Discussed Treatments for Patients With Early Stage TNBC and Residual Disease After Neoadjuvant Therapy

OLYMPIA

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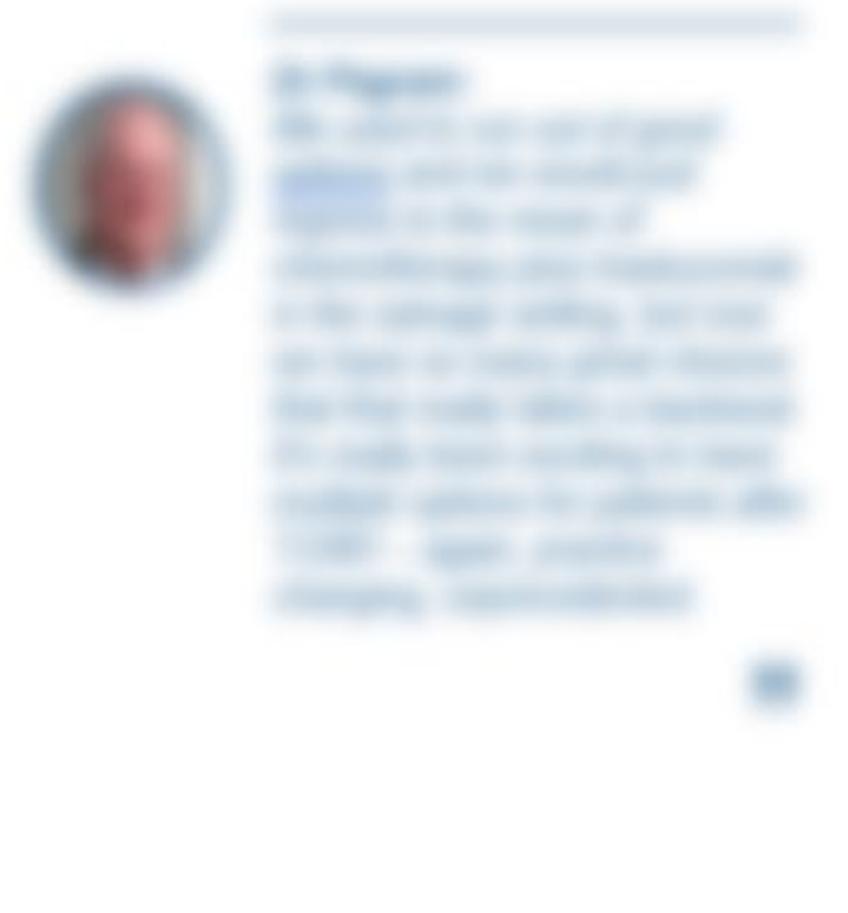
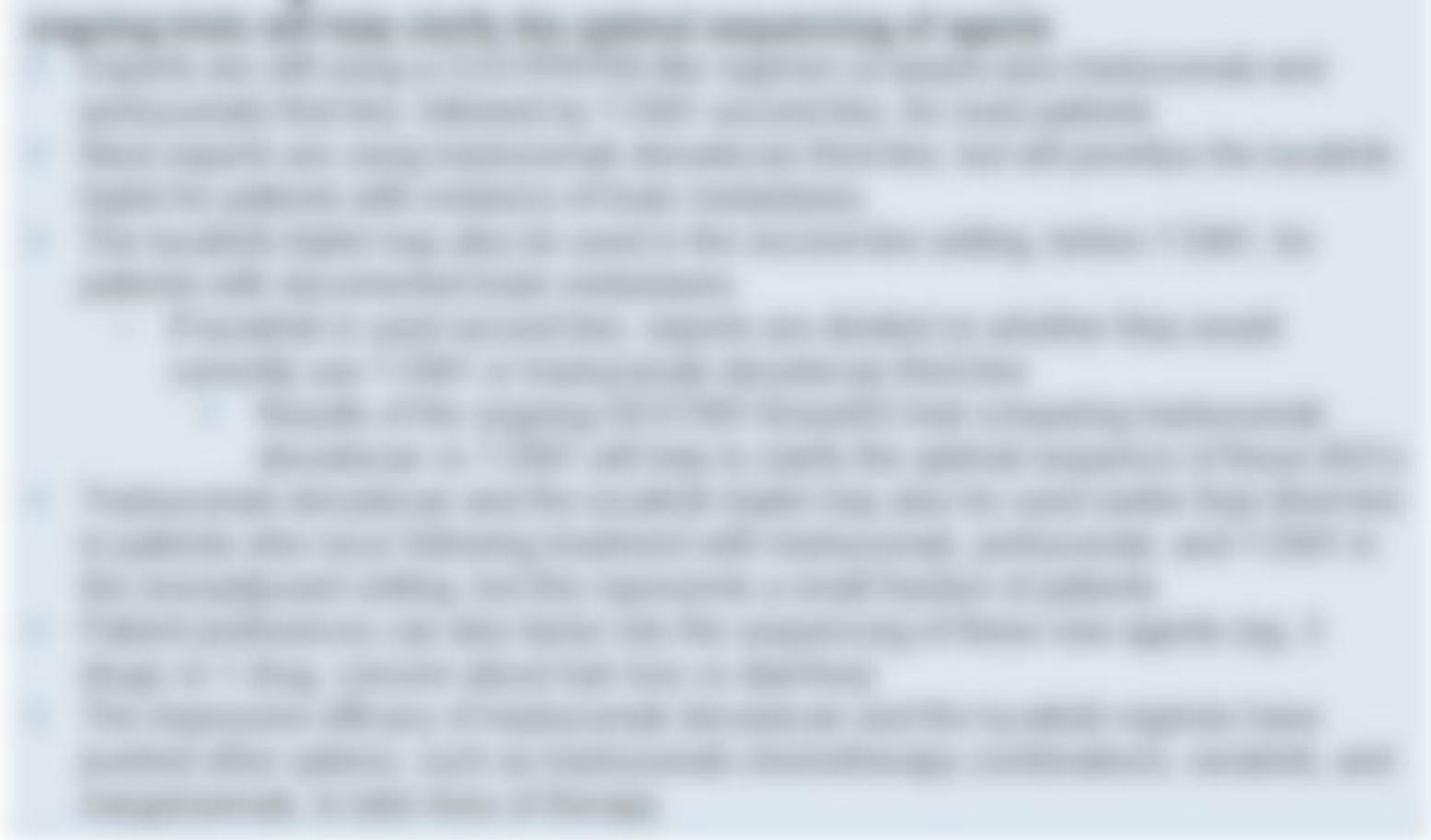


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# Experts Discussed Pembrolizumab for Early Stage and Metastatic TNBC

## KEYNOTE-522

The subset analyses of the KEYNOTE-522 trial confirmed that all subsets of patients benefited from the addition of pembrolizumab to



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## Congress Highlights

Biomarkers and Tailored Therapy

# Clinical utility of molecular tumor profiling: Results from the randomized trial SAFIR02-BREAST

Andre, et al. 2021, SABCS GS1-10

## STUDY POPULATION AND DESIGN

*[This section contains a blurred list of bullet points detailing the study population and design.]*

## ESCAT CLASSIFICATION FRAMEWORK



# cTRAK TN: Utilising ctDNA mutation tracking to detect MRD and trigger intervention in patients with moderate and high risk early stage TNBC

Turner, et al. 2021, SABCS GS3-06

## STUDY POPULATION

*[Blurred text describing the study population, including details on patient characteristics and study design.]*

## OBSERVATION GROUP – LEAD TIME TO RECURRENCE



# RxPONDER Update: Endocrine therapy +/- chemotherapy for HR+/HER2- BC with 1–3 positive lymph nodes with an RS $\leq 25$

Kalinsky, et al. 2021, SABCS GS2-07

## STUDY POPULATION

*[Blurred text describing the study population and inclusion/exclusion criteria]*

## PREMENOPAUSAL SUBSET ANALYSES



EPICS

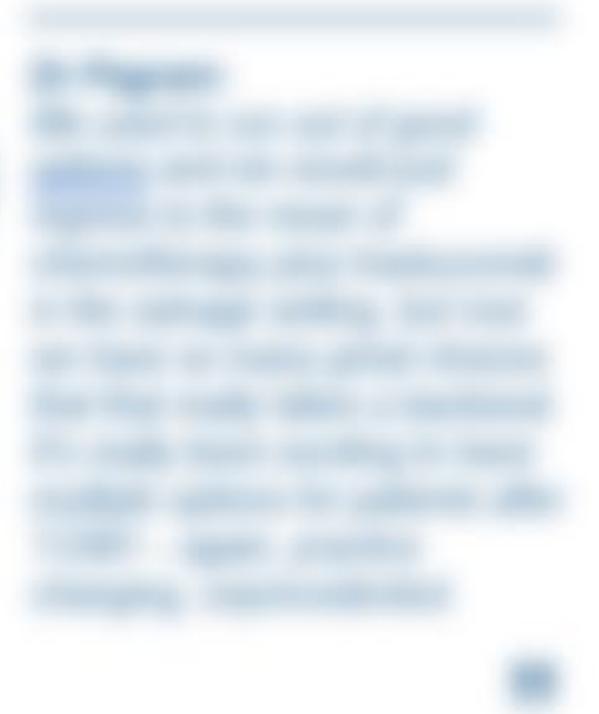
## Key Insights

Biomarkers and Tailored Therapy

# Experts Discussed Results From Trials Exploring the Use of Molecular Testing in Breast Cancer

SAFIR02

The SAFIR02 trial evaluated whether matching targeted therapies to molecular alterations compared with standard chemotherapy in



# Experts Reviewed Updated Results From the RxPONDER Trial



## RxPONDER

The Oncotype DX Recurrence Score (RS) is perceived to be useful in the

*[Blurred text area]*



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**EPICS**

## **Congress Highlights**

Other Novel Therapeutic Approaches for  
Breast Cancer

# Datopotamab deruxtecan in advanced/metastatic HER2- breast cancer: Results from the phase 1 TROPION-PanTumor01 study

Krop, et al. 2021, SABCS GS1-05

### STUDY POPULATION

1. 100 patients with advanced/metastatic HER2- breast cancer, including 50 patients with HER2- breast cancer and 50 patients with HER2- breast cancer. The study population included patients with HER2- breast cancer who had received prior systemic therapy for advanced/metastatic disease. The study population included patients with HER2- breast cancer who had received prior systemic therapy for advanced/metastatic disease. The study population included patients with HER2- breast cancer who had received prior systemic therapy for advanced/metastatic disease.

### DESIGN

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### KEY CONCLUSIONS

Continuing treatment beyond week 25 provides clinical benefit in HER2- breast cancer and decreases the proportion of patients with HER2- breast cancer who have received prior systemic therapy for advanced/metastatic disease.



# CCTG MA.32, a phase III trial of adjuvant metformin vs placebo in early breast cancer: Primary efficacy analysis

Goodwin, et al. 2021, SABCS GS1-08

## STUDY POPULATION

1. 1800 patients, 900 in each arm, with a 10% risk of relapse or death at 5 years. Median age 62 years. 85% were in breast cancer, 15% were in breast cancer with lymph node metastases. Median time to relapse or death was 2.5 years. All patients were treated with standard of care including surgery, chemotherapy, and endocrine therapy. The primary endpoint was overall survival at 5 years. The secondary endpoint was overall survival at 10 years. The study was powered to detect a 10% difference in overall survival at 5 years. All patients were treated through week 48.

## RESULTS

1. Overall survival at 5 years was 85% in the metformin arm and 84% in the placebo arm. Overall survival at 10 years was 75% in the metformin arm and 74% in the placebo arm. The difference in overall survival at 5 years was statistically significant (p=0.02).

## KEY CONCLUSIONS

Continuing metformin treatment beyond week 24 provides clinical benefit in overall survival and decreases the number of deaths in patients.

## OVERALL SURVIVAL FROM STARTLINE TO END OF STUDY (WEEK 48)



## RESPONSE: METFORMIN VS PLACEBO ANALYSIS PERIODS



# Nimbus: A phase 2 trial of nivolumab plus ipilimumab for patients with hypermutated her2-negative mBC

Barroso-Sousa, et al. 2021, SABCS GS2-10

## STUDY POPULATION

100 patients with mBC, 50% patients with a HER2-negative, hypermutated mBC, 50% patients with a HER2-negative, non-hypermutated mBC. Median age 68 years, 90% patients with a ECOG performance grade 0-1. The median time to treatment discontinuation was 11.2 weeks. The median overall survival was 11.2 months. The median time to treatment discontinuation was 11.2 weeks. The median overall survival was 11.2 months.

## RESULTS

100 patients with mBC, 50% patients with a HER2-negative, hypermutated mBC, 50% patients with a HER2-negative, non-hypermutated mBC. Median age 68 years, 90% patients with a ECOG performance grade 0-1. The median time to treatment discontinuation was 11.2 weeks. The median overall survival was 11.2 months.

## KEY CONCLUSIONS

Combining nivolumab plus ipilimumab showed a trend towards improved overall survival and decreased the proportion of patients with treatment discontinuation.

## TOXICITY PROFILE (GRADE 3/4 ADVERSE EVENTS)



## RESPONSE RATE (RR) BY BIOMARKER STATUS



# Neratinib + fulvestrant + trastuzumab for HR+, *HER2*-mutant mBC and neratinib + trastuzumab for TNBC: SUMMIT trial updates

Jhaveri, et al. 2021, SABCS GS4-10

### STUDY POPULATION

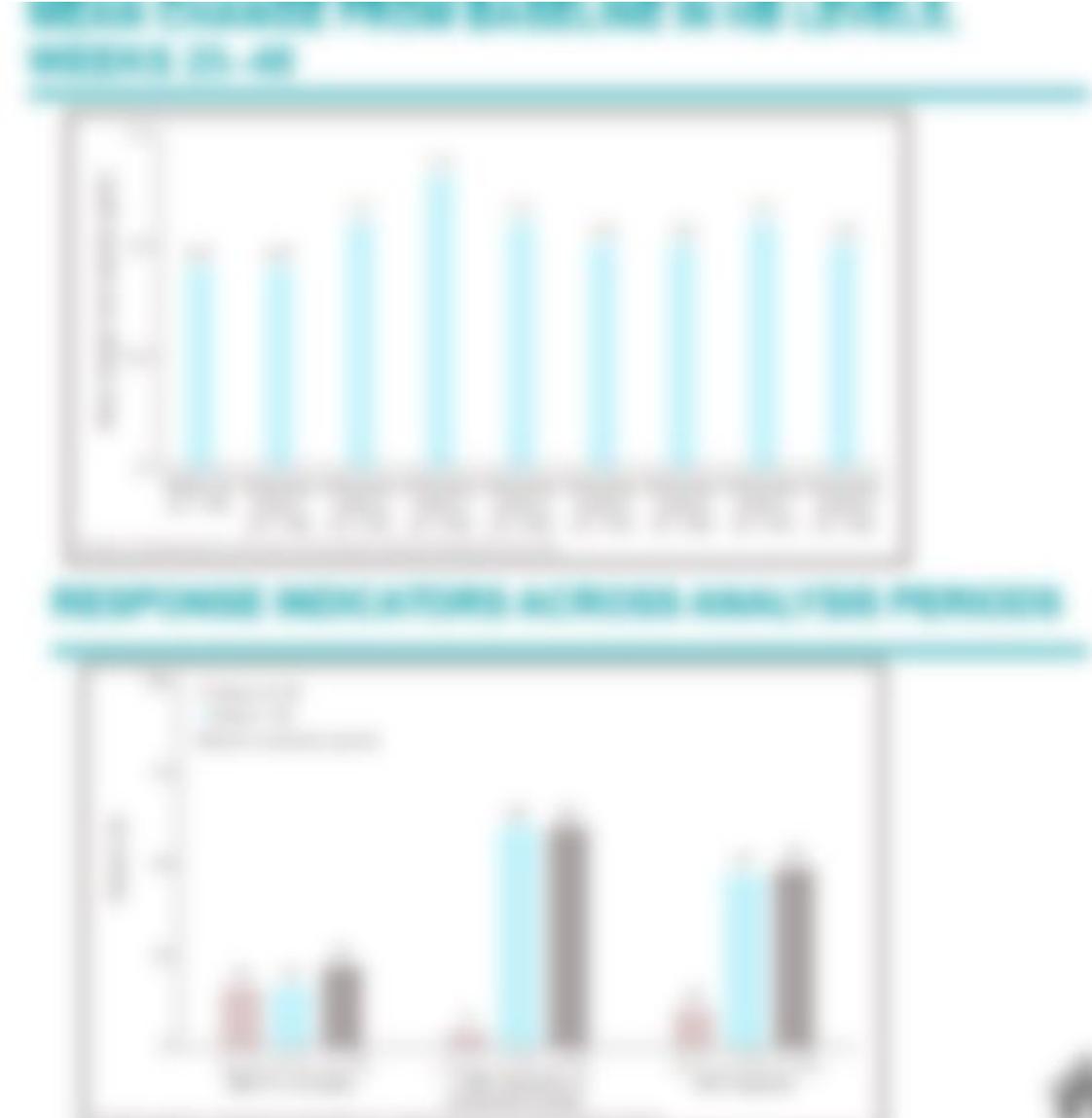
1. 1000 patients with HR+, *HER2*-mutant mBC or TNBC, who were not on systemic anti-*HER2* therapy, were randomized to receive either neratinib + fulvestrant + trastuzumab (NFT) or fulvestrant + trastuzumab (FT). The primary endpoint is overall survival (OS) at 24 weeks. Secondary endpoints include progression-free survival (PFS), time to next anti-*HER2* therapy (TNT), and quality of life (QoL). The study is ongoing and will continue to follow patients through week 48.

### RESULTS

1. OS at 24 weeks was significantly higher in the NFT group compared to the FT group (p < 0.001). PFS and TNT were also significantly higher in the NFT group (p < 0.001). QoL was similar between groups.

### KEY CONCLUSIONS

Combining neratinib with fulvestrant and trastuzumab significantly improved OS, PFS, and TNT in patients with HR+, *HER2*-mutant mBC and TNBC.



**EPICS**

## **Key Insights**

Other Novel Therapeutic Approaches for  
Breast Cancer

# Experts Assessed Phase I Data With Novel Agents for mBC

## DATOPOTAMAB DERUXTECAN

*[Blurred text area containing detailed information about the clinical trial, likely including objectives, design, and results.]*



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# Experts Discussed Data From Trials in *HER2+* or *HER2-* Mutated Breast Cancer

## SUMMIT

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