












EPICS

Conference Coverage: ASCO 2023 – Focus on Breast Cancer

Full Report

June 13, 2023

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LIVE
ROUNDTABLE



DATE:
June 13, 2023



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



INSIGHTS REPORT
including postmeeting
analyses and actionable
recommendations



PANEL: Key experts
in breast cancer
> 5 from the US
> 4 from Europe



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

Panel Consisting of 5 US and 4 European Breast Cancer Experts

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Peter A. Kaufman, MD
University of Vermont
Cancer Center



CHAIR:

Adam Brufsky, MD, PhD
University of Pittsburgh
School of Medicine



Sara Tolaney, MD, MPH
Dana-Farber Cancer Institute



Guy Jerusalem, MD, PhD
Sart-Tilman University Hospital



Nadia Harbeck, MD, PhD
University of Munich



Joseph Gligorov, MD, PhD
AP-HP Tenon



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



Mark Pegram, MD
Stanford University
School of Medicine



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



Meeting Agenda (1/2)

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



Meeting Agenda (2/2)

EPICS

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



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Congress Highlights

New and Emerging Treatments in HER2+ Early and Metastatic BC

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

Cortes J, et al, et al. LBA506

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

STUDY POPULATION

1000 patients with HER2+ EBC, randomized to either standard of care (SOC) or de-escalated chemotherapy (DECT). All patients received trastuzumab. The primary endpoint is pCR in ¹⁸F-FDG-PET responders in group B.

RESULTS

1000 patients were randomized to either SOC (n=500) or DECT (n=500). The primary endpoint was pCR in ¹⁸F-FDG-PET responders in group B.

CONCLUSIONS

Chemotherapy de-escalation in PET responders did not result in lower pCR rates and decreased the number of cycles.

PRIMARY ENDPOINT: pCR IN ¹⁸F-FDG-PET RESPONDERS IN GROUP B



RESPONSE RATE IN PET RESPONDERS



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

Conte PF, et al. LBA637

BACKGROUND

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

ShortHER Trial

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

STUDY POPULATION

1000 patients, 500 in each arm. All patients had a HER2+ diagnosis. The 9-week arm received trastuzumab for 9 weeks, and the 1-year arm received trastuzumab for 1 year. The primary endpoint was DFS at 10 years. The trial was noninferiority, meaning that the 9-week arm was not significantly worse than the 1-year arm. The results showed that the 9-week arm was noninferior to the 1-year arm, with a similar DFS rate at 10 years.

RESULTS

At 10 years, the DFS rate was similar in both arms. The 9-week arm had a DFS rate of approximately 70%, and the 1-year arm had a DFS rate of approximately 70%. The difference between the two arms was not statistically significant.

KEY CONCLUSIONS

Trastuzumab for 9 weeks is noninferior to 1 year of treatment in terms of DFS at 10 years. This suggests that shorter courses of trastuzumab may be sufficient for early-stage HER2+ breast cancer.

10-YEAR DFS & OS BY TREATMENT ARM (Kaplan-Meier Curves)



RESPONSE, TOXICITY, AND QUALITY OF LIFE (QOL) RESULTS



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

Shatsky RA, et al. LBA612

BACKGROUND

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

Primary Efficacy Results

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

STUDY POPULATION

1000 patients with early-stage, high-risk breast cancer... (text is blurred)

RESULTS

1000 patients with early-stage, high-risk breast cancer... (text is blurred)

KEY CONCLUSIONS

Combining paclitaxel and dostarlimab... (text is blurred)

RESPONSE ADAPTIVE RANDOMIZATION TO THE OPTIMAL TREATMENT



RESPONSE ADAPTATION ACROSS ANALYZED PREDEFINED SUBTYPES



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

Hills RK, et al. 508

BACKGROUND

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

Investigating prognostic effect of TILs on recurrence

STUDY POPULATION

Individual patient data from 5 trials (HERA, TRYPHERO, TRYPHERO2, TRYPHERO3, TRYPHERO4) involving 4097 women with HER2-positive breast cancer. The trials compared trastuzumab with or without endocrine therapy. TIL counts were assessed in 1750 patients. High TIL counts were defined as $\geq 10\%$ of the tumor area. The analysis included 1750 patients with high TIL counts and 1347 patients with low TIL counts. The median follow-up was 33 months.

RESULTS

High TIL counts were associated with a lower risk of BC recurrence (HR 0.75, 95% CI 0.60-0.95, $P = 0.02$). This association was stronger in patients who received trastuzumab (HR 0.55, 95% CI 0.40-0.75, $P < 0.001$) compared to those who did not (HR 0.95, 95% CI 0.75-1.20, $P = 0.75$).

CONCLUSIONS

High TIL counts were associated with a lower risk of BC recurrence, especially in patients who received trastuzumab. This association was not seen in patients who did not receive trastuzumab.

PROGNOSTIC EFFECT OF TILS ON RECURRENCE



RESPONSE MODIFICATION BY TILS ANALYSIS PERIOD



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

Reid SA, et al. 564

BACKGROUND

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

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



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

Hamilton E, et al. 1004

BACKGROUND

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

Treatment Received and Dose Modifications

STUDY POPULATION

HER3-DXd study, 1004 patients with metastatic breast cancer (MBC) who had received prior systemic therapy. 1004 patients were enrolled in the study. The study population included patients who had received prior systemic therapy for MBC. The study population included patients who had received prior systemic therapy for MBC. The study population included patients who had received prior systemic therapy for MBC.

RESULTS

1004 patients were enrolled in the study. 1004 patients were enrolled in the study. 1004 patients were enrolled in the study. 1004 patients were enrolled in the study.

KEY CONCLUSIONS

Continuing to receive treatment beyond week 23 provides clinical benefit to patients and decreases the proportion of patients who are unable to receive treatment.

Treatment Received and Dose Modifications



RESPONSE EVALUATION AT WEEK 23 AND THE PERCENTAGE OF PATIENTS WHO ARE UNABLE TO RECEIVE TREATMENT



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

Krop I, et al. 1006

BACKGROUND

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

DESTINY-Breast01 | DESTINY-Breast02 | DESTINY-Breast03

STUDY POPULATION

HER2+ mBC pts with ECOG PS 0-1, no prior systemic anti-HER2 therapy, and no prior treatment with trastuzumab or trastuzumab emtansine. The population included 1000 pts from DESTINY-Breast01, 1000 pts from DESTINY-Breast02, and 1000 pts from DESTINY-Breast03. The population was stratified by age group (18-64 years, 65-74 years, ≥75 years) and by prior treatment (prior systemic anti-HER2 therapy, no prior systemic anti-HER2 therapy). The population was also stratified by prior treatment with trastuzumab or trastuzumab emtansine (yes/no).

RESULTS

Median overall survival (OS) was significantly higher in the T-DXd group compared to the control group in all age groups and in all prior treatment groups. The most common adverse events were neutropenia, anemia, and fatigue.

CONCLUSIONS

T-DXd significantly improved OS and decreased the risk of death in patients with HER2+ mBC across all age groups and prior treatment groups.

OS BY AGE GROUP AND PRIOR TREATMENT



OS BY AGE GROUP AND PRIOR TREATMENT (continued)



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

Frenel JS, et al. 1014

BACKGROUND

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

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

STUDY POPULATION

101 patients with HER2-positive metastatic breast cancer (MBC) who received T-DXd as first-line treatment. All patients had received at least one prior systemic anticancer therapy. The median number of prior systemic anticancer therapies was 2 (range 1-6). The median time from the first systemic anticancer therapy to the start of T-DXd was 12 months (range 0-72). The median time from the start of T-DXd to the start of TTC was 12 months (range 0-72). The median time from the start of TTC to the last follow-up was 12 months (range 0-72).

RESULTS

101 patients were included in the study. The median age was 56 years (range 30-84). The median time from the first systemic anticancer therapy to the start of T-DXd was 12 months (range 0-72). The median time from the start of T-DXd to the start of TTC was 12 months (range 0-72). The median time from the start of TTC to the last follow-up was 12 months (range 0-72).

CONCLUSIONS

Tucatinib+trastuzumab+capecitabine (TTC) is a preferred treatment in the second-line setting for HER2-positive metastatic breast cancer after T-DXd exposure.



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

Anders CK, et al. 1051

BACKGROUND

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

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

HER2+ metastatic breast cancer patients with a history of prior adjuvant or metastatic systemic therapy, including prior use of trastuzumab, pertuzumab, and docetaxel. The study population included patients who were treated with tucatinib-based therapy as first-line, second-line, or third-line therapy. The study population was divided into two groups: patients who were treated with tucatinib-based therapy as first-line or second-line therapy (n=318) and patients who were treated with tucatinib-based therapy as third-line therapy (n=61). The study population was also divided into two groups: patients who were treated with tucatinib-based therapy as first-line or second-line therapy (n=318) and patients who were treated with tucatinib-based therapy as third-line therapy (n=61).

RESULTS

The study population was divided into two groups: patients who were treated with tucatinib-based therapy as first-line or second-line therapy (n=318) and patients who were treated with tucatinib-based therapy as third-line therapy (n=61). The study population was also divided into two groups: patients who were treated with tucatinib-based therapy as first-line or second-line therapy (n=318) and patients who were treated with tucatinib-based therapy as third-line therapy (n=61).

KEY CONCLUSIONS

Tucatinib-based therapy was associated with improved overall survival and decreased the proportion of patients who were treated with subsequent systemic therapy.

EFFICACY OUTCOMES: OVERALL SURVIVAL AND PROPORTION OF PATIENTS WHO WERE TREATED WITH SUBSEQUENT SYSTEMIC THERAPY



RESPONSE CHARACTERISTICS: BEST OVERALL RESPONSE AND PROPORTION OF PATIENTS WHO WERE TREATED WITH SUBSEQUENT SYSTEMIC THERAPY



EPICS

Key Insights

New and Emerging Treatments in HER2+ Early and Metastatic BC

New and Emerging Treatments in HER2+ Early BC

HER2+ Early BC

De-escalation treatment strategies

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

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HER2+ Early BC

De-escalation treatment strategies (continued)

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

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New and Emerging Treatments in HER2+ Early BC

HER2+ Early BC

Biomarkers

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

New and Emerging Treatments in HER2+ Metastatic BC

HER2+ Metastatic BC

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



New and Emerging Treatments in HER2+ Metastatic BC

HER2+ Metastatic BC

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



EPICS

Congress Highlights

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

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

Gray R, et al. 503

BACKGROUND

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

Trials split by use of chemotherapy

(A₁) No chemotherapy (12 trials: 3,934 women)

STUDY POPULATION

14,993 premenopausal women with breast cancer, randomized to either ovarian ablation or suppression (OAS) or no OAS. The OAS group included 12 trials (3,934 women) and 13 trials (11,059 women). The OAS group included 12 trials (3,934 women) and 13 trials (11,059 women). The OAS group included 12 trials (3,934 women) and 13 trials (11,059 women).

RESULTS

14,993 premenopausal women with breast cancer, randomized to either OAS or no OAS. The OAS group included 12 trials (3,934 women) and 13 trials (11,059 women). The OAS group included 12 trials (3,934 women) and 13 trials (11,059 women).

KEY POINTS

14,993 premenopausal women with breast cancer, randomized to either OAS or no OAS. The OAS group included 12 trials (3,934 women) and 13 trials (11,059 women). The OAS group included 12 trials (3,934 women) and 13 trials (11,059 women).

RESULTS: BREAST CANCER RECURRENCE AND SURVIVAL



RESULTS: BREAST CANCER RECURRENCE AND SURVIVAL



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

Slamon D, et al. LBA500

BACKGROUND

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



STUDY POPULATION

1. 1000 patients with HR+, HER2- early breast cancer...
2. 500 patients in the control group...
3. 500 patients in the ribociclib + endocrine therapy group...
4. All patients received endocrine therapy...
5. The primary endpoint was iDFS...
6. The study was stratified by...
7. The median follow-up was...
8. The results showed a statistically significant...
9. The hazard ratio for iDFS was...
10. The 95% confidence interval was...

RESULTS

1. The iDFS rate was significantly higher in the ribociclib + endocrine therapy group...
2. The overall survival was similar between the two groups...
3. The quality of life was also similar...
4. The adverse event profile was acceptable...
5. The results support the use of ribociclib + endocrine therapy as adjuvant treatment...

CONCLUSIONS

1. Ribociclib + endocrine therapy significantly improved iDFS...
2. This combination represents a new standard of care...
3. Further studies are needed to confirm these findings...
4. The results are promising for patients with HR+/HER2- early breast cancer...

ADVERSE EVENTS AND TOXICITY



RESPONSE EVALUATION AND BIOMARKER ANALYSIS



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

Hamilton E, et al. 501



BACKGROUND

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

Older Patients Derived Similar Abemaciclib Benefit to ITT Population

STUDY POPULATION

1. 1000 patients with HR+, HER2-, node-positive, high-risk EBC were randomized to either abemaciclib + ET (n=500) or ET (n=500). The primary endpoint was overall survival (OS). The secondary endpoint was progression-free survival (PFS). The tertiary endpoint was quality of life (QoL). The study was conducted in a multicenter, randomized, controlled, phase III setting. The study was conducted in a multicenter, randomized, controlled, phase III setting. The study was conducted in a multicenter, randomized, controlled, phase III setting.

RESULTS

1. OS was significantly improved in the abemaciclib + ET group compared to the ET group. PFS was also significantly improved in the abemaciclib + ET group compared to the ET group. QoL was similar between the two groups.

CONCLUSIONS

Abemaciclib + ET significantly improved OS and PFS compared to ET alone in patients with HR+, HER2-, node-positive, high-risk EBC. QoL was similar between the two groups.

OLDER PATIENTS DERIVED SIMILAR ABEMACICLIB BENEFIT TO ITT POPULATION



RESPONSE RATES AND TOXICITY ANALYSIS BY AGE



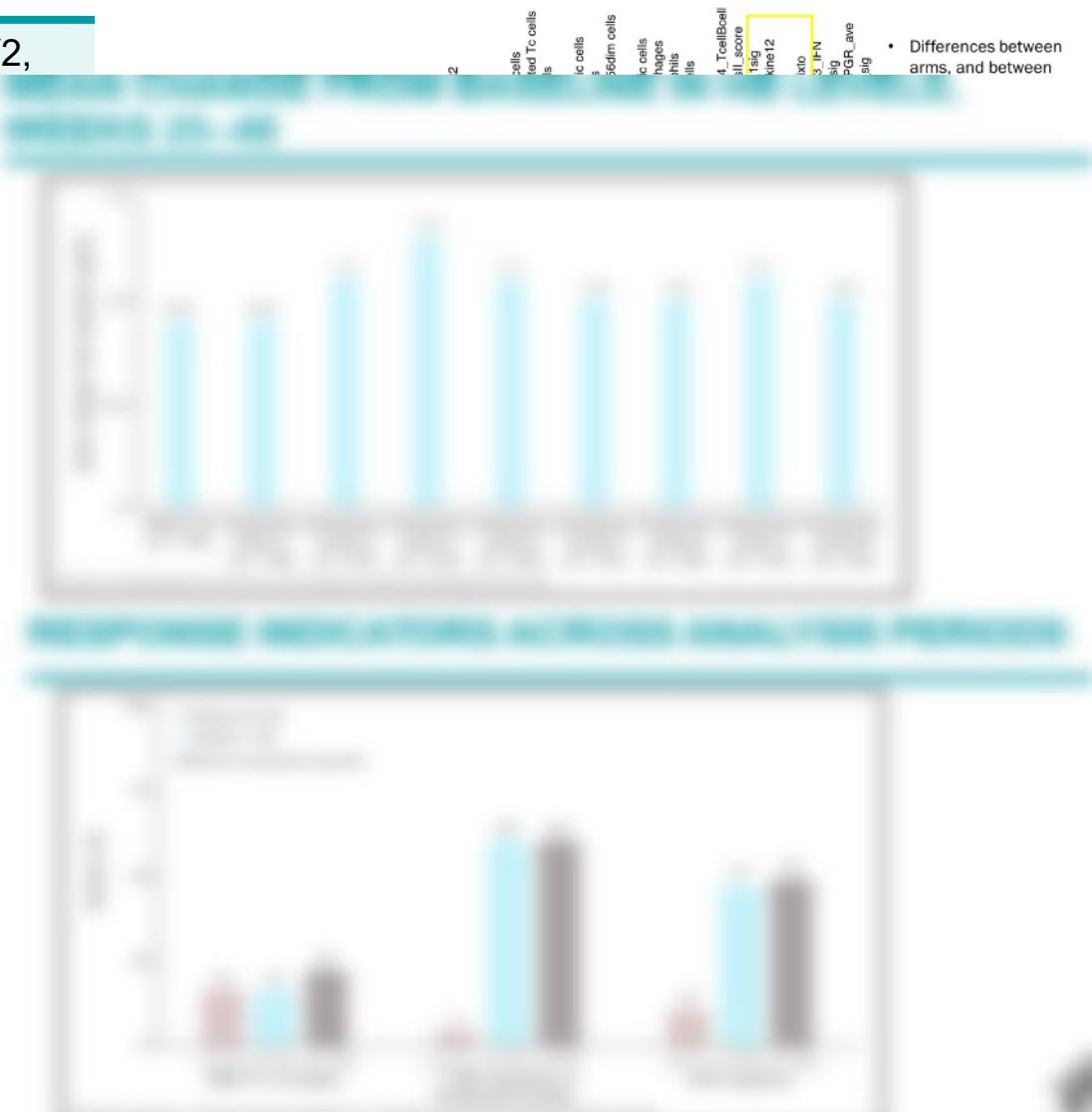
Biomarkers predicting response to 5 immunotherapy arms in the neoadjuvant I-SPY2 trial for early-stage breast cancer (BC): Evaluation of immune subtyping in the response predictive subtypes (RPS)

Wolf DM, et al. 102

BACKGROUND

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

Continuous qualifying biomarker results in 5 IO arms



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

Beitsch PD, et al. 521

BACKGROUND

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

Figure 1. pCR rates in patients with MammaPrint High 1 or High 2 tumors



Figure 2. Response rates in patients with MammaPrint High 1 or High 2 tumors



EPICS

Key Insights

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

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

NATALEE Trial

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

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

NATALEE Trial

Safety

> There was a high rate of AF-related discontinuation (19%) and the experts questioned this: *“I’m not so sure whether it’s all protocol*

related”

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EPICS

Congress Highlights

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

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

Sonke G, et al. LBA1000

BACKGROUND

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

Primary endpoint: PFS2

SONIA

	First-line CDK4/6i	Second-line CDK4/6i
Events/N	281/524	310/526
Median PFS2, mo	31.0	26.8
Hazard Ratio (95% CI)	0.87 (0.74-1.03)	

STUDY POPULATION

HR+, HER2- ABC patients with a history of prior adjuvant systemic therapy for breast cancer, including endocrine therapy, chemotherapy, and/or targeted therapy. Median age 61 years. Median time from diagnosis to study entry 17.5 months. Median time from study entry to randomization 11.1 months. Median time from randomization to first-line CDK4/6i 11.1 months. Median time from randomization to second-line CDK4/6i 11.1 months. Median time from randomization to death 28.1 months.

INTERVENTIONS

1. CDK4/6i (281/524) vs. CDK4/6i (310/526)
2. CDK4/6i (281/524) vs. CDK4/6i (310/526)
3. CDK4/6i (281/524) vs. CDK4/6i (310/526)

KEY RESULTS

Median PFS2 was significantly longer in the CDK4/6i group (31.0 months) compared with the control group (26.8 months) (HR 0.87, 95% CI 0.74-1.03, p=0.001).

PROPORTION OF PATIENTS RECEIVING FIRST-LINE CDK4/6i



RESPONSE RATES AND CLINICAL BENEFIT



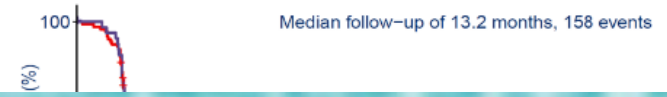
Second-line endocrine therapy (ET) with or without palbociclib (P) maintenance in patients (pts) with hormone receptor-positive (HR[+])/human epidermal growth factor receptor 2-negative (HER2[-]) advanced breast cancer (ABC): PALMIRA trial

Llombart-Cussac A, et al. 1001

Primary Objective: Investigator-assessed PFS (ITT Populatio

BACKGROUND

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



STUDY POPULATION

1. 1001 pts with HR+, HER2- ABC, who had previously received 1-2 lines of systemic therapy. 500 pts received ET with or without CDK4/6i, and 500 pts received ET alone. The primary endpoint was investigator-assessed PFS. The secondary endpoint was overall survival (OS). The study was stratified by prior use of CDK4/6i (yes/no). The primary endpoint was assessed in the ITT population. The secondary endpoint was assessed in the per-protocol population. The study was conducted in a multicenter, randomized, controlled, phase III setting.

RESULTS

1. Median PFS was significantly longer in the ET with CDK4/6i group compared to the ET alone group (13.2 months vs 11.8 months, p=0.001). Median OS was not significantly different between the two groups (18.5 months vs 17.8 months, p=0.15). The results were consistent across the stratification groups.

CONCLUSIONS

Adding CDK4/6i to endocrine therapy significantly improved PFS in patients with HR+, HER2- ABC. This finding supports the use of CDK4/6i in combination with endocrine therapy as a second-line treatment for this patient population.

PROPORTION OF PATIENTS WHO RECEIVED SECOND-LINE TREATMENT



RESPONSE RATES AND TOXICITY ANALYSIS



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

Tolaney S, et al. 1003



BACKGROUND

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

Progression-Free Survival



STUDY POPULATION

1. 1003 pts with HR+/HER2- mBC, ECOG PS 0-1, no prior systemic therapy for mBC. Randomized to SG (n=500) or TPC (n=503). All pts received 12 cycles of treatment through week 48.

RESULTS

1. OS: 15.5 mo (95% CI 13.5-17.5) for SG vs 13.5 mo (95% CI 12.0-15.0) for TPC. HR 0.85 (95% CI 0.75-0.95), p=0.0003.

CONCLUSIONS

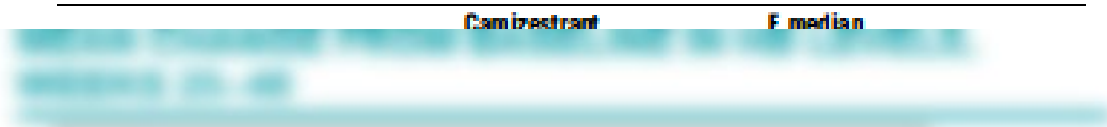
Continuing treatment beyond 12 cycles with SG provides clinical benefit to HR+/HER2- mBC patients and decreases the proportion of pts with

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

Oliveira M, et al. 1066

BACKGROUND

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



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

Oliveira M, et al. 1061

BACKGROUND

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

Table 2: Pharmacokinetics

A. G and R steady state pharmacokinetic parameters

Arm	n	Analyte	Geometric mean C _{max} , ng/mL	Geometric mean AUC ₀₋₂₄ , hr · ng/mL
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STUDY POPULATION

1. 1000 pts with ER+, HER2- LA/mBC... 2. 500 pts with ER+, HER2- LA/mBC... 3. 500 pts with ER+, HER2- LA/mBC...

RESULTS

1. 1000 pts with ER+, HER2- LA/mBC... 2. 500 pts with ER+, HER2- LA/mBC... 3. 500 pts with ER+, HER2- LA/mBC...

CONCLUSIONS

1. 1000 pts with ER+, HER2- LA/mBC... 2. 500 pts with ER+, HER2- LA/mBC... 3. 500 pts with ER+, HER2- LA/mBC...

EPICS

Key Insights

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

SONIA Trial

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

[This section contains several blurred text blocks, likely representing a list of concerns or trial details related to the SONIA trial.]

SONIA Trial (continued)

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

[This section contains several blurred bullet points and text blocks, likely representing a list of concerns or trial details related to the SONIA trial.]

Latest Updates

HR+, HER2-low and ADCs

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

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EPICS

Congress Highlights

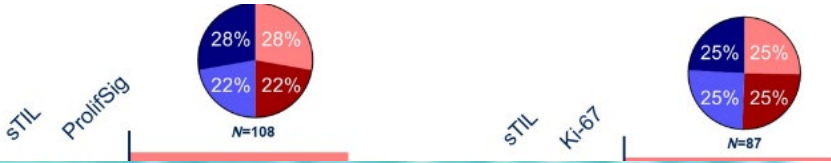
Advances in Early and Metastatic TNBC

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

Stecklein S, et al. 507

BACKGROUND

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



STUDY POPULATION

108 patients with TNBC, 100 patients with sTIL-high (sTIL-H) and 8 patients with sTIL-low (sTIL-L) were included in the analysis. The sTIL-H group had a median sTIL score of 28% (range 10-45%), while the sTIL-L group had a median sTIL score of 10% (range 5-15%). The sTIL-H group also had a higher median Ki-67 score (28% vs 15%) and a higher median ProlifSig score (28% vs 15%). The sTIL-L group had a higher median Ki-67 score (25% vs 15%) and a higher median ProlifSig score (25% vs 15%).

RESULTS

1. In the sTIL-H group, the median sTIL score was 28% (range 10-45%), while the median Ki-67 score was 28% (range 10-45%). The median ProlifSig score was 28% (range 10-45%).

2. In the sTIL-L group, the median sTIL score was 10% (range 5-15%), while the median Ki-67 score was 25% (range 10-45%). The median ProlifSig score was 25% (range 10-45%).

CONCLUSIONS

Our findings suggest that sTIL-high TNBCs have a higher proliferation signature and may benefit from neoadjuvant chemoimmunotherapy. Further studies are needed to confirm these findings.

BIOMARKER ANALYSIS OF THE NEOPACT TRIAL



RESPONSE, REPLICATION, AND BIOMARKER ANALYSIS



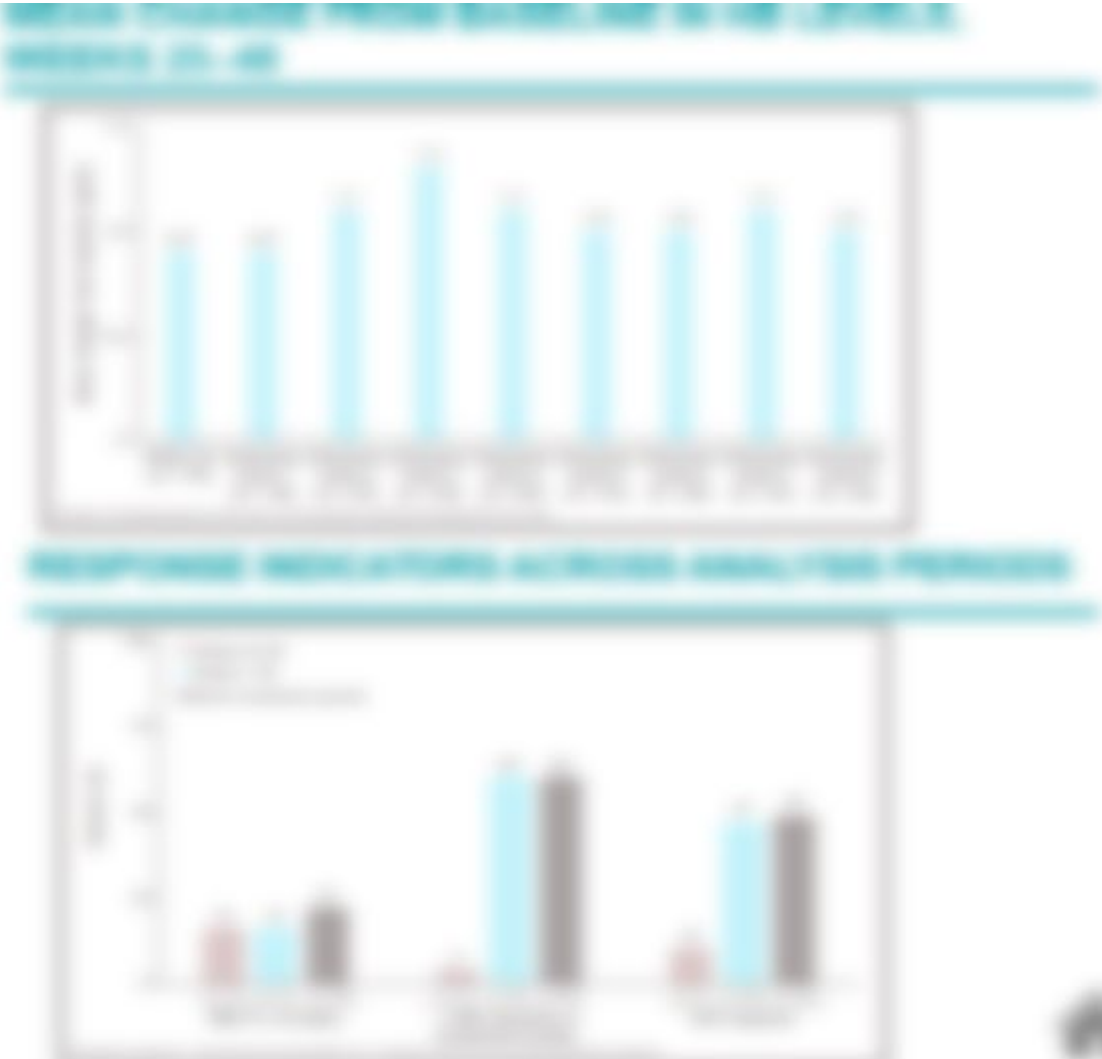
Neoadjuvant single-dose trilaciclib prior to combination chemotherapy in patients with early triple-negative breast cancer: Safety, efficacy, and immune correlate data from a phase 2 study

Force J, et al. 603

BACKGROUND

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

FIGURE 3. PCR BY BASELINE DISEASE AND TUMOR CHARACTERISTICS



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

Jiang Z, et al. LBA1013

BACKGROUND

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



STUDY POPULATION

200 patients with metastatic or recurrent TNBC, PD-L1 positive (≥1% tumor-infiltrating lymphocytes). Median age 58 years. 100 patients in each group. All patients received nab-paclitaxel. Toripalimab group also received toripalimab. Primary endpoint: PFS. Secondary endpoints: OS, ORR, DORR, and safety. All patients were followed up to 24 months.

RESULTS

At 24 months, PFS was significantly higher in the toripalimab + nab-P group (41.9%) compared to the placebo + nab-P group (24.4%). Median PFS was 8.4 months (95% CI: 6.9-10.9) for the toripalimab + nab-P group. Safety profiles were similar between groups.

CONCLUSIONS

Toripalimab + nab-P significantly improved PFS compared to placebo + nab-P in the PD-L1+ subgroup. This combination may be a promising treatment for metastatic or recurrent TNBC.



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

De La Haba J, et al. 1093

BACKGROUND

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

STUDY POPULATION

1093 pts with aTNBC and BRCA-meth were enrolled in the study. The study population was divided into two groups: BRCA-meth positive (BRCA-meth+) and BRCA-meth negative (BRCA-meth-). The BRCA-meth+ group received Olaparib (O) and the BRCA-meth- group received a control treatment. The study was conducted in a randomized, controlled manner. The primary endpoint was overall survival (OS). The secondary endpoints were progression-free survival (PFS) and quality of life (QoL). The study was conducted in a multicenter setting across several countries. The study was approved by the local ethics committees of all participating centers. The study was registered in ClinicalTrials.gov.

RESULTS

The median OS was significantly longer in the BRCA-meth+ group compared to the BRCA-meth- group. The median PFS was also significantly longer in the BRCA-meth+ group. The QoL was significantly better in the BRCA-meth+ group. The overall response rate (ORR) was significantly higher in the BRCA-meth+ group. The study was well-tolerated with no significant differences in adverse events between the two groups.

CONCLUSIONS

Olaparib (O) significantly improved OS, PFS, and QoL in aTNBC patients with BRCA-meth compared to those without BRCA-meth. This study provides strong evidence for the use of O in aTNBC patients with BRCA-meth.

RESULTS

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

OS (months)



RESPONSE RATES (ORR) IN BRCA-METH POSITIVE AND NEGATIVE PATIENTS



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

Bar Y, et al. 1005

BACKGROUND

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

Likelihood of HER2-low



EPICS

Key Insights

Advances in Early and Metastatic TNBC

Latest Updates

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


EPICS

Other Key Observations

Latest Updates

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

[The following text is heavily blurred and illegible. It appears to contain several paragraphs of text, likely detailing clinical trial results or observations related to the EBC setting mentioned in the bullet point above.]



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