

Clinical Breast Cancer

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Illustration by Erin Moore

Original Studies

- 1 A Randomized Phase II Study of Eribulin/Cyclophosphamide or Docetaxel/Cyclophosphamide as Neoadjuvant Therapy in Operable HER2-negative Breast Cancer**
Denise A. Yardley, Dianna Shipley, John Zubkus, Gail L. Wright, Patrick J. Ward, Aruna Mani, Mythili Shastry, Lindsey Finney, Laura DeBusk, John D. Hainsworth

The present phase II study compared the combination of eribulin plus cyclophosphamide (ErC) to docetaxel plus cyclophosphamide (TC) as neoadjuvant therapy for HER2⁻ breast cancer patients. Patients received either eribulin 1.4 mg/m² on days 1 and 8 plus cyclophosphamide 600 mg/m² on day 1 or docetaxel 75 mg/m² plus cyclophosphamide 600 mg/m² on day 1 for 6 cycles before surgery. Neoadjuvant ErC showed no greater efficacy than TC.
- 10 Phase II Study of S-1 Combined With Low-Dose Docetaxel as Neoadjuvant Chemotherapy for Operable Breast Cancer Patients (N-1 Study)**
Misako Nakagawa, Mayumi Ikeuchi, Masami Morimoto, Hirokazu Takechi, Hiroaki Toba, Takahiro Yoshida, Kazumasa Okumura, Naoki Hino, Aya Nishisho, Akira Tangoku

Efficacy of S-1 (Taiho Pharmaceutical Co, Tokyo, Japan) used in combination with docetaxel (S-1+DOC) for breast cancer was evaluated. After 4 cycles of S-1+DOC, patients with a complete response (CR) underwent surgery, and those with partial response underwent 4 more cycles. Patients with stable disease or progressive disease received epirubicin and cyclophosphamide or trastuzumab and paclitaxel. The pathological CR rate was 29 patients [34.9%], and 8 patients [19.5%] for patients with luminal type breast cancer. S-1+DOC was expected to be an effective chemotherapy for luminal type breast cancer.
- 17 EarlyR: A Robust Gene Expression Signature for Predicting Outcomes of Estrogen Receptor–Positive Breast Cancer**
Steven A. Buechler, Yesim Gökmen-Polar, Sunil S. Badve

Currently available molecular signatures assess the risk of recurrence and the benefit of chemotherapy; however, these tests may have large intermediate risk groups, limiting their usefulness. We describe a novel 5-gene signature that is a robust prognostic assay that performed similarly to currently available signatures in concordance analyses. However, it identified significantly fewer patients as intermediate risk and more as low risk than currently available assays.

- 27 **Patterns of Relative Telomere Length is Associated With *hTERT* Gene Expression in the Tissue of Patients With Breast Cancer**
Karuvaje Thriveni, Anisha Raju, Rekha V. Kumar, Swamyvelu Krishnamurthy, Ramesh Chaluvayaswamy
Leukocyte telomere length is one of the prognostic factors in breast cancer. In this study, we analyzed the telomere length from breast cancer tissue, which is relatively increased with *hTERT* mRNA expression, in 98 patients. The results showed shortened tissue telomere in early stages and elongated telomere in advanced stages, in contrast to the leukocyte telomere length pattern, indicating different dynamics in breast cancer tissue.
- 35 **Including the Ductal Carcinoma-In-Situ (DCIS) Score in the Development of a Multivariable Prediction Model for Recurrence After Excision of DCIS**
Lawrence Paszat, Rinku Sutradhar, Limei Zhou, Sharon Nofech-Mozes, Eileen Rakovitch
Clinical care for women who have undergone breast-conserving surgery for ductal carcinoma-in-situ (DCIS) is controversial. Accurate prediction of the risks of recurrence would help inform decision making. Predictive models including the DCIS score multigene expression assay were developed using a complete case series of 1102 women; results indicate that such a model allows computation of more accurate risk of recurrence.
- 47 **Phase 1b Study of Trebananib Plus Paclitaxel and Trastuzumab in Patients With HER2-Positive Locally Recurrent or Metastatic Breast Cancer**
Peter A. Kaufman, Hans Wildiers, Gilles Freyer, Margaret Kemeny, Anthony Gonçalves, Guy Jerusalem, Alison Stopeck, Nandagopal Vrindavanam, Florence Dalenc, Nuwan Nanayakkara, Benjamin Wu, Cheryl A. Pickett
Given the potential interactions between human epidermal growth factor receptor 2 (HER2) signaling and angiogenesis, we investigated the angiopoietin (Ang) 1/Ang2 inhibitor trebananib plus trastuzumab and paclitaxel in HER2-positive breast cancer. Forty women received trebananib (10 or 30 mg/kg) plus trastuzumab and paclitaxel. The combination demonstrated acceptable toxicity and antitumor response in HER2-positive locally recurrent/metastatic breast cancer.
- 58 **Risk Factors for Local Relapse and Inferior Disease-free Survival After Breast-conserving Management of Breast Cancer: Recursive Partitioning Analysis of 2161 Patients**
Josef Hammer, Hans Geinitz, Carsten Nieder, Christine Track, Howard D. Thames, Dietmar H. Seewald, Andreas L. Petzer, Ruth Helfgott, Kurt J. Spiegel, Dietmar Heck, Elisabeth Bräutigam
Recursive partitioning analysis was found to be a suitable method to assign patients with early stage breast cancer to different risk groups who had considerable variation in local relapse rates and disease-free survival. Lymph node ratio was associated with both endpoints.
- 63 **Individualized Prediction of Menses Recovery After Chemotherapy for Early-stage Breast Cancer: A Nomogram Developed From UNICANCER PACS04 and PACS05 Trials**
Barbara Pistilli, Chafika Mazouni, Anna Zingarello, Matthieu Faron, Mahasti Saghatchian, Michael Grynberg, Marc Spielmann, Paul Kerbrat, Henri Roché, Veronique Lorgis, Thomas Bachelot, Mario Campone, Christelle Levy, Anthony Gonçalves, Anne Lesur, Corinne Veyret, Laurence Vanlemmens, Jerome Lemonnier, Suzette Delaloue
An accurate and individualized prediction of menses recovery is feasible for premenopausal patients eligible for adjuvant chemotherapy for early-stage breast cancer to better inform the chemotherapy discussion and individualize fertility counseling.
- 71 **Magnetic Resonance Imaging Combined With Second-look Ultrasonography in Predicting Pathologic Complete Response After Neoadjuvant Chemotherapy in Primary Breast Cancer Patients**
Naoki Hayashi, Hiroko Tsunoda, Maki Namura, Tomohiro Ochi, Koyu Suzuki, Hideko Yamauchi, Seigo Nakamura
Magnetic resonance imaging (MRI) or ultrasonography (US) alone is limited in the ability to predict the pathologic complete response (pCR) accurately after neoadjuvant chemotherapy. We found that MRI combined with second-look US for predicting pCR was useful compared with MRI alone, especially for estrogen receptor-negative/human epidermal growth factor receptor-positive tumors. However, it was difficult to predict the residual in situ component.

- 78 **Role of Elective Nodal Irradiation in Patients With ypN0 After Neoadjuvant Chemotherapy Followed by Breast-Conserving Surgery (KROG 16-16)**
Won Kyung Cho, Won Park, Doo Ho Choi, Yong Bae Kim, Jin Ho Kim, Su Ssan Kim, Kyubo Kim, Jin Hee Kim, Sung Ja Ahn, Sun Young Lee, Jeongshim Lee, Sang-Won Kim, Jeanny Kwon, Ki Jung Ahn
This multi-institutional study aimed to investigate the role of elective nodal irradiation (ENI) in ypN0 patients following neoadjuvant chemotherapy and breast-conserving surgery according to subtype and primary tumor response. We analyzed 261 patients and found that ENI does not improve survival regardless of subtype or primary tumor response. Whole-breast irradiation might be sufficient in ypN0 patients.

Corrigendum

- 87 Corrigendum

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- e1 **Fibroepithelial Breast Lesion: When Sequencing Can Help to Make a Clinical Decision. A Case Report**
Giacomo Montagna, Charlotte K.Y. Ng, Tatjana Vlajnic, Viola Paradiso, Sophie Dellas, Hubertina Reina, André Kind, Walter P. Weber, Salvatore Piscuoglio, Christian Kurzeder
- e7 **Metastatic Breast Cancer Patient With Activating *HER2* Exon 20 Insertion Mutation With Response to Pozitotinib: Case Report of Compassionate Drug Use**
Apurva Pandey, Adam M. Brufsky
- e12 **Interdisciplinary Management of Transgender Individuals at Risk for Breast Cancer: Case Reports and Review of the Literature**
Julia Eismann, Yujing J. Heng, Kristin Fleischmann-Rose, Adam M. Tobias, Jordana Phillips, Gerburg M. Wulf, Kari J. Kansal
- e20 **Breast Cancer Screening Awareness and Practices Among Women Attending Primary Health Care Centers in the Ghail Bawazir District of Yemen**
Amen Bawazir, Najla Bashateh, Hoda Jradi, Ahlam Bin Breik
This cross-sectional study aimed to assess breast cancer screening awareness and practices among women attending primary health care centers in the Ghail-Bawazir district of Yemen. A significant association between marital status, level of education, working status, and level of knowledge and breast screening practice was reported. Health care providers play a very limited role in providing awareness to their patients.
- e30 **Factors Affecting Sexual Function and Body Image of Early-Stage Breast Cancer Survivors in Poland: A Short-Term Observation**
Robert Kowalczyk, Krzysztof Nowosielski, Ida Cedrych, Marek Krzystanek, Iwona Glogowska, Joanna Streb, Jakub Kucharz, Zbigniew Lew-Starowicz
This study aimed to evaluate correlates and impact factors of sexual function and body image of female breast cancer survivors. A total of 128 women aged 18 to 65 who were free of disease and who underwent surgical treatment for breast cancer were evaluated. The results indicated that the role of the partner and/or family support is important in maintaining sexual health and restoring body image.
- e40 **Physician Survey of Timing of Adjuvant Endocrine Therapy Relative to Radiotherapy in Early Stage Breast Cancer Patients**
Sharon F. McGee, Lisa Vandermeer, Sasha Mazzarello, Marta Sienkiewicz, Carol Stober, Brian Hutton, Dean Fergusson, John Hilton, Jean-Michel Caudrelier, Phillip Blanchette, Mark Clemons
The optimal timing of adjuvant endocrine therapy with respect to radiotherapy in early breast cancer is unknown. We conducted a multicenter survey of oncologists to evaluate institutional and personal practices. Results showed that decisions around the timing of therapies were being based on personal opinion and preference. In the absence of data to support these decisions, appropriately powered trials are needed.

- e48 Risk Reduction and Survival Benefit of Risk-Reducing Salpingo-oophorectomy in Hereditary Breast Cancer: Meta-analysis and Systematic Review**
Ye-Lei Xiao, Kang Wang, Qiang Liu, Jie Li, Xiang Zhang, Hong-Yuan Li
We performed a meta-analysis to examine the relationship between risk-reducing salpingo-oophorectomy (RRSO) and breast cancer (BC) risk and mortality. RRSO was associated with a significant reduction in the incidence of BC in women with *BRCA1/2* mutations, regardless of history of BC. RRSO could improve the survival of women with BC.
- e66 Predictors for Survival and Distribution of 21-Gene Recurrence Score in Patients With Pure Mucinous Breast Cancer: A SEER Population-Based Retrospective Analysis**
Shuning Ding, Jiayi Wu, Caijin Lin, Weiguo Chen, Yafen Li, Kunwei Shen, Li Zhu
This study retrospectively analyzed prognostic factors and distribution of the 21-gene recurrence score (RS) in 8048 patients with pure mucinous breast cancer. Molecular phenotype as well as age, race, tumor size, and lymph node status were independent prognostic factors. RS correlated significantly with age, progesterone receptor status, and grade.
- e74 Impact of Chemotherapy-induced Menopause in Women of Childbearing Age With Non-metastatic Breast Cancer – Preliminary Results From the MENOCOR Study**
Judith Passildas, Olivier Collard, Aude-Marie Savoye, Joyce Dohou, Angeline Ginzac, Emilie Thivat, Xavier Durando, Fabrice Kwiatkowski, Frédérique Penault-Llorca, Catherine Abrial, Marie-Ange Mouret-Reynier
In our study, we evaluated the quality of life of young women experiencing chemotherapy-induced menopause. Our results underline that age and pre-treatment anti-Müllerian hormone level could be helpful to predict the menopause but these results have to be confirmed in further studies. At 6 months post-chemotherapy, the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Breast 23 (QLQ-BR23) questionnaire tended to highlight an impaired quality of life in menopausal patients.
- e85 Comprehensive Validation Study of Quality-of-Life Questionnaire Using Objective Clinical Measures: Breast Cancer Treatment Outcome Scale (BCTOS), Brazilian Portuguese Version**
Fabiola Cristina Brandini da Silva, Jonathas José da Silva, Almir José Sarri, Carlos Eduardo Paiva, René Aloisio da Costa Vieira
Quality-of-life questionnaires (QLQs) do not correlate with objective measurements of treatment sequelae. We performed a comprehensive validation study of the Brazilian Portuguese version of the Breast Cancer Treatment Outcome Scale (BCTOS), adding physical evaluations of the main sequelae related to breast-conserving therapy (BCT). Three hundred patients were evaluated. BCTOS represented a good QLQ for BCT patients, which correlated with objective measurements.
- e101 Long-Term Survival Differences Between T1-2 Invasive Lobular Breast Cancer and Corresponding Ductal Carcinoma After Breast-Conserving Surgery: A Propensity-Scored Matched Longitudinal Cohort Study**
Kang Wang, Gui-Qi Zhu, Yang Shi, Zhu-Yue Li, Xiang Zhang, Hong-Yuan Li
The Surveillance, Epidemiology, and End Results (SEER) Program was used to compare survival and local recurrence risk (LR) in patients with 2 histologic types of disease—invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC)—receiving breast-conserving surgery (BCS). Patients with T1-2 ILC were less likely to undergo BCS and had better overall survival compared to patients with IDC, but they had worse second primary cancer-free survival and higher LR than those of patients with IDC in the nuclear grade III subgroup. Continuing efforts to identify a subset of subjects with T1-2 ILC of nuclear grade III is contraindicated for BCS in further clinical trials.

e116 Beliefs About Medication and Uptake of Preventive Therapy in Women at Increased Risk of Breast Cancer: Results From a Multicenter Prospective Study

Rachael Jane Thorneloe, Rob Horne, Lucy Side, Michael Scott Wolf, Samuel George Smith, on behalf of the ENGAGE Investigators

Preventive therapies, such as tamoxifen, are a risk reduction option for women at increased risk of breast cancer. Little is known about the psychological factors influencing the decision to use chemoprevention. Using latent profile analysis, women who reported a low need for preventive therapy and strong medication concerns were less likely to initiate tamoxifen treatment. Medication beliefs are targets for supporting informed decision-making.

e127 Dietary Habits and Physical Activity are Associated With the Risk of Breast Cancer Among Young Iranian Women: A Case-control Study on 1010 Premenopausal Women

Mohammad Fararouei, Aqsa Iqbal, Shahab Rezaian, Zahra Gheibi, Aria Dianatinasab, Saba Shakarami, Mostafa Dianatinasab

This case-control study was conducted on 1010 women to examine the association of several dietary and behavioral factors with the risk of breast cancer. It was revealed that physical activity and dietary pattern are important factors in the incidence of breast cancer. This helps in providing more pragmatic approaches in cancer prevention.

e135 Immediate Breast Reconstruction in De Novo Metastatic Breast Cancer: An Analysis of 563 Cases Based on the SEER Database

Hongliang Chen, Mingdi Zhang, Maoli Wang, Peng Zhang, Fang Bai, Kejin Wu

Controversy exists regarding the appropriateness of immediate breast reconstruction (IBR) in patients with metastatic breast cancer (MBC). An analysis of the SEER database found that 5.2% of patients with de novo MBC undergoing mastectomy received IBR between 1998 and 2015, and that the rate of IBR increased significantly. There were no statistically significant differences in survival outcomes between IBR and mastectomy in the well-matched analysis.

e142 Role of Clinical and Imaging Risk Factors in Predicting Breast Cancer Diagnosis Among BI-RADS 4 Cases

William Hsu, Xinkai Zhou, Antonia Petruse, Ngan Chau, Stephanie Lee-Felker, Anne Hoyt, Neil Wenger, David Elashoff, Arash Naeim

Overdiagnosis of breast cancer is an ongoing concern, particularly in women who receive a Breast Imaging Reporting and Data System (BI-RADS) 4 assessment. Using a population-based quality improvement registry of 1978 women (2138 examinations), we examined clinical and imaging risk factors using cross-validated logistic regression models, identifying significant predictors such as age, the presence of a lump, history of breast cancer, the number of high-risk triggers, BI-RADS score, and qualitative breast density. This analysis supports the potential added value of utilizing relevant information from the patient's medical history when deciding between active surveillance and biopsy.

e152 Characteristics and Outcomes of BI-RADS 3 Lesions on Breast MRI

Babita Panigrahi, Susan C. Harvey, Lisa A. Mullen, Eniola Falomo, Philip Di Carlo, Bonmyong Lee, Kelly S. Myers

In a study of the imaging findings prompting a Breast Imaging Reporting and Data System (BI-RADS) 3 assessment and reports of their outcomes, we assessed 199 breast MRI lesions assigned a BI-RADS 3 assessment. Of these, 80 (40%) of 199 were non-mass enhancement, 61 (31%) of 199 were a single focus and 58 (29%) of 199 were masses; of the 131 lesions with appropriate follow-up, 4 (3%) were diagnosed as malignant within a 2-year follow-up period. Despite limited data on the use of BI-RADS 3 at breast MRI, there is a low malignancy rate of 3%.

- e160 Radical Mastectomy Increases Psychological Distress in Young Breast Cancer Patients: Results of A Cross-sectional Study**
Soufiane Berhili, Asmae Ouabdelmoumen, Ali Sbai, Tayeb Kebdani, Noureddine Benjaafar, Loubna Mezouar
The present cross-sectional study aimed to detect the effect of breast cancer surgery on the psychological state of 122 young women aged < 45 years. We found that mastectomy was an independent factor associated with greater rates of psychological distress, increasing the interest of early detection in third world countries to allow for more breast conservative procedures.
- e166 Breast Cancer: Metastasis, Molecular Subtypes, and Overweight and Obesity in Veracruz, Mexico**
Carlos Adrián Alarcón Rojas, María Teresa Alvarez-Bañuelos, Jaime Morales-Romero, Héctor Suárez-Díaz, Juan Carlos Hernández-Fonseca, Guillermo Contreras-Alarcón
The high prevalence of both obesity and breast cancer has had a major impact in Mexico. We performed a cross-sectional study with a considerably larger sample size. The results showed that obese and morbidly obese women are affected by more aggressive subtypes and concomitant pathologic features. These findings reinforce the hypothesis of a greater incidence of the triple-negative type with premenopause.
- e172 Meta-analysis of the Correlation Between Schizophrenia and Breast Cancer**
Zhang Xiping, Zhao Shuai, Yu Feijiang, Chen Bo, Yang Shifeng, Cheng Qihui
In this meta-analysis on correlation between schizophrenia and breast cancer (BC), we found that the incidence of schizophrenia is positively correlated with BC, and the incidence of BC in schizophrenia patients is increased in a certain degree. Because of the effects of potential bias and publication bias, the conclusion needs more high-quality studies to increase the strength of evidence.
- e186 Real-World Experience of Palbociclib-Induced Adverse Events and Compliance With Complete Blood Count Monitoring in Women With Hormone Receptor–Positive/HER2-Negative Metastatic Breast Cancer**
Geoffrey Alan Watson, Oana Deac, Razia Aslam, Richard O'Dwyer, Antonia Tierney, Sue Sukor, John Kennedy
Palbociclib therapy in hormone receptor–positive metastatic breast cancer patients may result in adverse events such as neutropenia, and stringent monitoring of complete blood count is advised. The current study found good compliance with guidelines and demonstrated that dose adjustments are not associated with progressive disease. We also report a high incidence of thromboembolic events.
- e195 STEAP1 Inhibits Breast Cancer Metastasis and Is Associated With Epithelial–Mesenchymal Transition Procession**
Jie Xie, Yan Yang, Jiali Sun, Zhi Jiao, Haozheng Zhang, Jie Chen
To evaluate the role of 6-transmembrane epithelial antigen of prostate 1 (STEAP1) in breast cancer, we tested the expressions of STEAP1 in breast cancer and normal tissues and cells, as well as the functions of STEAP1 in breast cancer cell invasion and proliferation. Results revealed that STEAP1 was down-regulated in breast cancer, inhibited metastasis of breast cancer, and hampered the levels of epithelial–mesenchymal transition markers.
- e208 Longer Times of Receipt of Adjuvant Endocrine Therapy Correspond to Improved Functional Capacity and Lower Adiposity in Women Receiving Adjuvant Therapy**
Kamila Pires de Carvalho, Mariana Tavares Miranda Lima, Fernanda Silva Mazzutti, Isis Danyelle Dias Custódio, Paula Philbert Lajolo Canto, Carlos Eduardo Paiva, Yara Cristina de Paiva Maia
This clinical research studied functional capacity level, length of time of receipt of therapy with aromatase inhibitors (AIs), and adiposity parameters. Women with breast cancer in the first years of the use of AIs showed greater functional disability and worse adiposity parameters, thus reinforcing the need for special attention during this time and emphasizing the importance of multiprofessional follow-up.

e220 Association of SNP-SNP Interactions Between *RANKL*, *OPG*, *CHI3L1*, and *VDR* Genes With Breast Cancer Risk in Egyptian Women

Olfat G. Shaker, Mahmoud A. Senousy

Genetic susceptibility for breast cancer (BC) is still poorly understood. We investigated the association of single nucleotide polymorphism (SNP)-SNP interactions of 6 SNPs in *RANKL*, *OPG*, *CHI3L1*, and *VDR* genes with BC risk in 115 BC patients and 120 controls using logistic regression models. A stronger combined effect of SNPs via gene–gene interaction may predict BC risk. Our data have implications in genetic counseling, BC screening, and prognosis.

e239 Detection of HER2-positive Circulating Tumor Cells Using the LiquidBiopsy System in Breast Cancer

Weirong Chen, Juncheng Zhang, Lijian Huang, Lin Chen, Yanling Zhou, Dongjiang Tang, Yingming Xie, Hong Wang, Chuoji Huang

This study aimed to use the LiquidBiopsy system and immunofluorescence to measure human epidermal growth factor receptor 2 in circulating breast cancer cells. Seventy-one patients with breast cancer and 107 control provided blood samples. The results indicated that the LiquidBiopsy system may be useful for detecting human epidermal growth factor receptor 2 expression levels on CTC as it was positively correlated with pathologic examination.

e247 Palliative Local Surgery for Locally Advanced Breast Cancer Depending on Hormone Receptor Status in Elderly Patients

Hong Pan, Kai Zhang, Ming Wang, Lijun Ling, Wenbin Zhou, Shui Wang

Many elderly breast cancer patients receive palliative local surgery to control potential physical symptoms and avert potential emotional symptoms. Elderly patients with locally advanced breast cancer were identified in the Surveillance, Epidemiology, and End Results cancer database. Mastectomy strongly improved survival within hormone receptor-negative patients, but lumpectomy and mastectomy were not associated with overall survival within hormone receptor-positive patients.

e261 Impact of 21-Gene Expression Assay on Staging Estrogen Receptor–Positive HER2-Negative Breast Cancer

Andrea Breaux, Bradley Turner, Xiaoyong Wu, Shesh N. Rai, Elizabeth C. Riley, Mounika Mandadi, Mary Ann Sanders

This retrospective study investigated the impact of Oncotype DX (ODX) on the newly updated breast cancer staging system. Of the 816 cases reviewed, ODX rarely affected stage, thus supporting the American Joint Committee on Cancer 8th edition expert panel's statement that ODX is not required for staging.