



JOURNAL OF CLINICAL ONCOLOGY

**1- Effects of Aerobic and Resistance Exercise on Metabolic Syndrome, Sarcopenic Obesity, and Circulating Biomarkers in Overweight or Obese Survivors of Breast Cancer: A Randomized Controlled Trial.**

Dieli-Conwright, C.M.; Courneya, K.S.; Demark-Wahnefried, W.; Sami, N.; Lee, K.; Buchanan, T.A.; Spicer, D.V.; Tripathy, D.; Bernstein, L.; Mortimer, J.E.  
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Resumen:  
Purpose Metabolic syndrome is associated with an increased risk of cardiovascular disease, type 2 diabetes, and breast cancer recurrence in survivors of breast cancer. This randomized controlled trial assessed the effects of a 16-week combined aerobic and resistance exercise intervention on metabolic syndrome, sarcopenic obesity, and serum biomarkers among ethnically diverse, sedentary, overweight, or obese survivors of breast cancer. Methods Eligible survivors of breast cancer (N = 100) were randomly assigned to exercise (n = 50) or usual care (n = 50). The exercise group participated in supervised moderate-to-vigorous-65% to 85% of heart rate maximum-aerobic and resistance exercise three times per week for 16 weeks. Metabolic syndrome z-score (primary outcome), sarcopenic obesity, and serum biomarkers were measured at baseline, postintervention (4 months), and 3-month follow-up (exercise only). Results Participants were age 53 ± 10.4 years, 46% were obese, and 74% were ethnic minorities. Adherence to the intervention was 95%, and postintervention assessments were available in 91% of participants. Postintervention metabolic syndrome z-score was significantly improved in exercise versus usual care (between-group difference, -4.4; 95% CI, -5.9 to -2.7; P < .001). Sarcopenic obesity (appendicular skeletal mass index, P = .001; body mass index, P = .001) and circulating biomarkers, including insulin (P = .002), IGF-1 (P = .001), leptin (P = .001), and adiponectin (P = .001), were significantly improved postintervention compared with usual care. At 3-month follow-up, all metabolic syndrome variables remained significantly improved compared with baseline in the exercise group (P < .01). Conclusion Combined resistance and aerobic exercise effectively attenuated metabolic syndrome, sarcopenic obesity, and relevant biomarkers in an ethnically diverse sample of sedentary, overweight, or obese survivors of breast cancer. Our findings suggest a targeted exercise prescription for improving metabolic syndrome in survivors of breast cancer and support the incorporation of supervised clinical exercise programs into breast cancer treatment and survivorship care plans.

**2- Enzalutamide for the Treatment of Androgen Receptor-Expressing Triple-Negative Breast Cancer.**

Traina, T.A.; Miller, K.; Yardley, D.A.; Eakle, J.; Schwartzberg, L.S.; O'Shaughnessy, J.; Gradishar, W.; Schmid, P.; Winer, E.; Kelly, C.; Nanda, R.; Guacal, A.; Awada, A.; Garcia-Estevéz, L.; Trudeau, M.E.; Steinberg, J.; Uppal, H.; Tudor, I.C.; Peterson, A.; Cortes, J.  
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Resumen:  
Purpose Studies suggest that a subset of patients with triple-negative breast cancer (TNBC) have tumors that express the androgen receptor (AR) and may benefit from an AR inhibitor. This phase II study evaluated the antitumor activity and safety of enzalutamide in patients with locally advanced or metastatic AR-positive TNBC. Patients and Methods Tumors were tested for AR with an immunohistochemistry assay optimized for breast cancer; nuclear AR staining > 0% was considered positive. Patients received enzalutamide 160 mg once per day until disease progression. The primary end point was clinical benefit rate (CBR) at 16 weeks. Secondary end points included CBR at 24 weeks, progression-free survival, and safety. End points were analyzed in all enrolled patients (the intent-to-treat [ITT] population) and in patients with one or more postbaseline assessment (whose tumor expression = 10% nuclear AR (the evaluable subgroup)). Results Of 118 patients enrolled, 78 were evaluable. CBR at 16 weeks was 25% (95% CI, 17% to 33%) in the ITT population and 33% (95% CI, 23% to 45%) in the evaluable subgroup. Median progression-free survival was 2.9 months (95% CI, 1.9 to 3.7 months) in the ITT population and 3.3 months (95% CI, 1.9 to 4.1 months) in the evaluable subgroup. Median overall survival was 12.7 months (95% CI, 8.5 months to not yet reached) in the ITT population and 17.6 months (95% CI, 11.6 months to not yet reached) in the evaluable subgroup. Fatigue was the only treatment-related grade 3 or higher adverse event with an incidence of > 2%. Conclusion Enzalutamide demonstrated clinical activity and was well tolerated in patients with advanced AR-positive TNBC. Adverse events related to enzalutamide were consistent with its known safety profile. This study supports additional development of enzalutamide in advanced TNBC.

**3- Racial Differences in 21-Gene Recurrence Scores Among Patients With Hormone Receptor-Positive, Node-Negative Breast Cancer.**

Holowatyj, A.N.; Cote, M.L.; Ruterbusch, J.J.; Ghanem, K.; Schwartz, A.G.; Vigneau, F.D.; Gorski, D.H.; Purrington, K.S.  
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Resumen:  
Purpose The 21-gene recurrence score (RS) breast cancer assay is clinically used to quantify risk of 10-year distant recurrence by category (low, < 18; intermediate, 18 to 30; high, = 31) for treatment management among women diagnosed with hormone receptor-positive, human epidermal growth factor receptor 2-negative, lymph node-negative breast cancer. Although non-Hispanic black (NHB) women have worse prognosis compared with non-Hispanic white (NHW) women, the equivalency of 21-gene RS across racial groups remains unknown. Patients and Methods Using the Metropolitan Detroit Cancer Surveillance System, we identified women who were diagnosed with hormone receptor-positive, human epidermal growth factor receptor 2-negative, lymph node-negative invasive breast cancer between 2010 and 2014. Multinomial logistic regression was used to quantify racial differences in 21-gene RS category. Results We identified 2,216 women (1,824 NHW and 392 NHB) with invasive breast cancer who met clinical guidelines for and underwent 21-gene RS testing. The mean RS was significantly higher in NHBs compared with NHWs (19.3 v 17.0, respectively; P = .0003), where NHBs were more likely to present with high-risk tumors compared with NHWs (14.8% v 8.3%, respectively; P = .0004). These differences were limited to patients younger than 65 years at diagnosis, among whom NHBs had significantly higher RS compared with NHWs (20 to 49 years: 23.6 v 17.3, respectively; P < .001 and 50 to 64 years: 19.6 v 17.4, respectively; P = .023). NHBs remained more likely to have high-risk tumors compared with NHWs after adjusting for age, clinical stage, tumor grade, and histology (odds ratio [OR], 1.75; 95% CI, 1.18 to 2.59). Conclusion NHBs who met clinical criteria for 21-gene RS testing had tumors with higher estimated risks of distant recurrence compared with NHWs. Further study is needed to elucidate whether differences in recurrence are observed for these women, which would have clinical implications for 21-gene RS calibration and treatment recommendations in NHB patients.

**4- Improving Breast Cancer Surgical Treatment Decision Making: The iCanDecide Randomized Clinical Trial.**

Hawley, S.T.; Li, Y.; An, L.C.; Resnicow, K.; Janz, N.K.; Sabel, M.S.; Ward, K.C.; Fagerlin, A.; Morrow, M.; Jagsi, R.; Hofer, T.P.; Katz, S.J.  
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Resumen:  
Purpose This study was conducted to determine the effect of iCanDecide, an interactive and tailored breast cancer treatment decision tool, on the rate of high-quality patient decisions-both informed and values concordant-regarding locoregional breast cancer treatment and on patient appraisal of decision making. Methods We conducted a randomized clinical trial of newly diagnosed patients with early-stage breast cancer making locoregional treatment decisions. From 22 surgical practices, 537 patients were recruited and randomly assigned online to the iCanDecide interactive and tailored Web site (intervention) or the iCanDecide static Web site (control). Participants completed a baseline survey and were mailed a follow-up survey 4 to 5 weeks after enrollment to assess the primary outcome of a high-quality decision, which consisted of two components, high knowledge and values-concordant treatment, and secondary outcomes (decision preparation, deliberation, and subjective decision quality). Results Patients in the intervention arm had higher odds of making a high-quality decision than did those in the control arm (odds ratio, 2.00; 95% CI, 1.37 to 2.92; P = .0004), which was driven primarily by differences in the rates of high knowledge between groups. The majority of patients in both arms made values-concordant treatment decisions (78.6% in the intervention arm and 81.4% in the control arm). More patients in the intervention arm had high decision preparation (estimate, 0.18; 95% CI, 0.02 to 0.34; P = .027), but there were no significant differences in the other decision appraisal outcomes. The effect of the intervention was similar for women who were leaning strongly toward a treatment option at enrollment compared with those who were not. Conclusion The tailored and interactive iCanDecide Web site, which focused on knowledge building and values clarification, positively affected high-quality decisions largely by improving knowledge compared with static online information. To be effective, future patient-facing decision tools should be integrated into the clinical workflow to improve decision making.

**5- Quality of Life From Canadian Cancer Trials Group MA.17R: A Randomized Trial of Extending Adjuvant Letrozole to 10 Years.**

Lemieux, J.; Brundage, M.D.; Parulekar, W.R.; Goss, P.E.; Ingle, J.N.; Pritchard, K.I.; Celano, P.; Muss, H.; Galow, J.; Strasser-Weippl, K.; Whelan, K.; Tu, D.; Whelan, T.J.  
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Resumen:  
Purpose MA.17R was a Canadian Cancer Trials Group-led phase III randomized controlled trial comparing letrozole to placebo after 5 years of aromatase inhibitor as adjuvant therapy for hormone receptor-positive breast cancer. Quality of life (QOL) was a secondary outcome measure of the study, and here, we report the results of these analyses. Methods QOL was measured using the Short Form-36 (SF-36; two summary scores and eight domains) and menopause-specific QOL (MENQOL; four symptom domains) at baseline and every 12 months up to 60 months. QOL assessment was mandatory for Canadian Cancer Trials Group centers but optional for centers in other groups. Mean change scores from baseline were calculated. Results One thousand nine hundred eighteen women were randomly assigned, and 1,428 women completed the baseline QOL assessment. Compliance with QOL measures was > 85%. Baseline summary scores for the SF-36 physical component summary (47.5 for letrozole and 47.9 for placebo) and mental component summary (55.5 for letrozole and 54.8 for placebo) were close to the population norms of 50. No differences were seen between groups in mean change scores for the SF-36 physical and mental component summaries and in the other eight QOL domains except for the role-physical subscale. No difference was found in any of the four domains of the MENQOL. Conclusion No clinically significant differences were seen in overall QOL measured by the SF-36 summary measures and MENQOL between the letrozole and placebo groups. The data indicate that continuation of aromatase inhibitor therapy after 5 years of prior treatment in the trial population was not associated with a deterioration of overall QOL.

**6- Interventions to Address Sexual Problems in People With Cancer: A Systematic Review of Clinical Oncology Clinical Practice Guideline Adaptation of Cancer Care Ontario Guideline.**

Carter, J.; Lacchetti, C.; Andersen, B.L.; Barton, D.L.; Bolte, S.; Damast, S.; Diefenbach, M.A.; DuHamel, K.; Florendo, J.; Ganz, P.A.; Goldfarb, S.; Hallmeyer, S.; Kushner, D.M.; Rowland, J.H.  
Vol. 36 Nr. 5 Página: 492 - 511 Fecha de publicación: 10/02/2018

Resumen:  
Purpose The adaptation of the Cancer Care Ontario (CCO) guideline Interventions to Address Sexual Problems in People With Cancer provides recommendations to manage sexual function adverse effects that occur as a result of cancer diagnosis and/or treatment. Methods ASCO staff reviewed the guideline for developmental rigor and updated the literature search. An ASCO expert Panel (Table A1) was assembled to review the guideline content and recommendations. Results The ASCO Expert Panel determined that the recommendations from the 2016 CCO guideline are clear, thorough, and based upon the most relevant scientific evidence. ASCO statements and modifications were added to adapt the CCO guideline for a broader audience. Recommendations It is recommended that there be a discussion with the patient, initiated by a member of the health care team, regarding sexual health and dysfunction resulting from cancer or its treatment. Psychosocial and/or psychosexual counseling should be offered to all patients with cancer, aiming to improve sexual response, body image, intimacy and relationship issues, and overall sexual functioning and satisfaction. Medical and treatable contributing factors should be identified and addressed first. In women with symptoms of vaginal and/or vulvar atrophy, lubricants in addition to vaginal moisturizers may be tried as a first option. Low-dose vaginal estrogen, lidocaine, and dehydroepiandrosterone may also be considered in some cases. In men, medication such as phosphodiesterase type 5 inhibitors may be beneficial, and surgery remains an option for those with symptoms or treatment complications refractory to medical management. Both women and men experiencing vasomotor symptoms should be offered interventions for symptomatic improvement, including behavioral options such as cognitive behavioral therapy, slow breathing and hypnosis, and medications such as venlafaxine and gabapentin. Additional information is available at: www.asco.org/survivorship-guidelines and www.asco.org/guidelineswiki.

**7- Randomized, Multicenter, Placebo-Controlled Clinical Trial of Duloxetine Versus Placebo for Aromatase Inhibitor-Associated Arthralgias in Early-Stage Breast Cancer: SWOG S1202.**

Henry, N.L.; Unger, J.M.; Schott, A.F.; Fehrenbacher, L.; Flynn, P.J.; Prow, D.M.; Sharer, C.W.; Burton, G.V.; Kuzma, C.S.; Moseley, A.; Lew, D.L.; Fisch, M.J.; Moinpour, C.M.; Hershman, D.L.; Wade JL, 3rd  
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Resumen:  
Purpose Adherence to aromatase inhibitor (AI) therapy for early-stage breast cancer is limited by AI-associated musculoskeletal symptoms (AIMSS). Duloxetine is US Food and Drug Administration approved for treatment of multiple chronic pain disorders. We hypothesized that treatment of AIMSS with duloxetine would improve average joint pain compared with placebo. Methods This randomized, double-blind, phase III trial included AI-treated postmenopausal women with early-stage breast cancer and who had average joint pain score of = 4 out of 10 that developed or worsened since AI therapy initiation. Patients were randomly assigned 1:1 to duloxetine or placebo for 13 weeks. The primary end point was average joint pain through 12 weeks, examined using multivariable linear mixed models, adjusted for stratification factors (baseline pain score of 4 to 6 v 7 to 10 and prior taxane use). Clinically significant change in average pain was defined as a = 2-point decrease from baseline. Results Of 299 enrolled patients, 127 patients treated with duloxetine and 128 who received placebo were evaluable for the primary analysis. By 12 weeks, the average joint pain score was 0.82 points lower for patients who received duloxetine compared with those who received placebo (95% CI, -1.24 to -0.40; P = .0002). Similar differences were observed for any joint pain, joint stiffness, pain interference, and functioning. Rates of adverse events of worst grade higher in the duloxetine-treated group (78% v 50%); rates of grade 3 adverse events were similar. Conclusion Results of treatment with duloxetine for AIMSS were superior to those of placebo among women with early-stage breast cancer, although it resulted in more frequent low-grade toxicities.

**8- Alcohol and Cancer: A Statement of the American Society of Clinical Oncology.**

LoConte, N.K.; Brewster, A.M.; Kaur, J.S.; Merrill, J.K.; Alberg, A.J.  
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Resumen:  
Alcohol drinking is an established risk factor for several malignancies, and it is a potentially modifiable risk factor for cancer. The Cancer Prevention Committee of the American Society of Clinical Oncology (ASCO) believes that a proactive strategy by the Society to minimize excessive exposure to alcohol has important implications for cancer prevention. In addition, the role of alcohol drinking on outcomes in patients with cancer is in its formative stages, and ASCO can play a key role by generating a research agenda. Also, ASCO could provide needed leadership in the cancer community on this issue. In the issuance of this statement, ASCO joins a growing number of international organizations by establishing a platform to support effective public health strategies in this area. The goals of this statement are to: Promote public education about the risks between alcohol abuse and certain types of cancer; Support policy efforts to reduce the risk of cancer through evidence-based strategies that prevent excessive use of alcohol; Provide education to oncology providers about the influence of excessive alcohol use and cancer risks and treatment complications, including clarification of conflicting evidence; and Identify areas of needed research regarding the relationship between alcohol use and cancer risk and outcomes.

**9- Impact of Preexisting Mental Illness on All-Cause and Breast Cancer-Specific Mortality in Elderly Patients With Breast Cancer.**

Iglay, K.; Santorelli, M.L.; Hirshfield, K.M.; Williams, J.M.; Rhoads, G.G.; Lin, Y.; Demissie, K.  
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Resumen:  
Purpose Limited data are available on the survival of patients with breast cancer with preexisting mental illness, and elderly women are of special interest because they experience the highest incidence of breast cancer. Therefore, we compared all-cause and breast cancer-specific mortality for elderly patients with breast cancer with and without mental illness. Methods A retrospective cohort study was conducted by using SEER-Medicare data, including 19,028 women = 68 years of age who were diagnosed with stage I to IIIa breast cancer in the United States from 2005 to 2007. Patients were classified as having severe mental illness if an International Classification of Diseases, Ninth Edition, Clinical Modification code for bipolar disorder, schizophrenia, or other psychotic disorder was recorded on at least one inpatient or two outpatient claims during the 3 years before breast cancer diagnosis. Patients were followed for up to 5 years after breast cancer diagnosis to assess survival outcomes, which were then compared with those of patients without mental illness. Results Nearly 3% of patients had preexisting severe mental illness. We observed a two-fold increase in the all-cause mortality hazard between patients with severe mental illness compared with those without mental illness after adjusting for age, income, race, ethnicity, geographic location, and marital status (adjusted hazard ratio, 2.19; 95% CI, 1.84 to 2.60). A 20% increase in breast cancer-specific mortality hazard was observed, but the association was not significant (adjusted hazard ratio, 1.20; 95% CI, 0.82 to 1.74). Patients with severe mental illness were more likely to be diagnosed with advanced breast cancer and aggressive tumor characteristics. They also had increased tobacco use and more comorbidities. Conclusion Patients with severe mental illness may need assistance with coordinating medical services.

**10- National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer.**

Childers, C.P.; Childers, K.K.; Maggard-Gibbons, M.; Macinko, J.  
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Resumen:  
Purpose In the United States, 3.8 million women have a history of breast (BC) or ovarian cancer (OC). Up to 15% of cases are attributable to heritable mutations, which, if identified, provide critical knowledge for treatment and preventive care. It is unknown how many patients who are at high risk for these mutations have not been tested and how rates vary by risk criteria. Methods We used pooled cross-sectional data from three Cancer Control Modules (2005, 2010, 2015) of the National Health Interview Survey, a national in-person household interview survey. Eligible patients were adult females with a history of BC and/or OC meeting select 2017 National Comprehensive Cancer Network eligibility criteria on the basis of age of diagnosis and family history. Outcomes included the proportion of individuals reporting a history of undergoing genetic testing with a health professional, being advised to undergo genetic testing, or undergoing genetic testing for BC or OC. Results Of 47,218 women, 2.7% had a BC history and 0.4% had an OC history. For BC, 35.6% met one or more select eligibility criteria; of those, 29.0% discussed, 20.2% were advised to undergo, and 15.3% underwent genetic testing. Testing rates for individual eligibility criteria ranged from 6.2% (relative with OC) to 18.2% (diagnosis = 45 years of age). For OC, 15.1% discussed, 13.1% were advised to undergo, and 10.5% underwent testing. Using only four BC eligibility criteria and all patients with OC, an estimated 1.2 to 1.3 million individuals failed to receive testing. Conclusion Fewer than one in five individuals with a history of BC or OC meeting select National Cancer Comprehensive Network criteria have undergone genetic testing. Most have never discussed testing with a health care provider. Large national efforts are warranted to address this unmet need.

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