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## **Exercise May Boost Quality of Life for Patients With Metastatic Breast Cancer**

*Treatment for metastatic disease may last indefinitely, amplifying the need for effective interventions*

SAN ANTONIO – Among patients with metastatic [breast cancer](#), those who took part in a nine-month structured exercise program reported less fatigue and an improved quality of life compared to those who did not undergo the exercise program, according to results from the [PREFERABLE-EFFECT](#) trial presented at the [San Antonio Breast Cancer Symposium](#), held December 5-9, 2023.

Breast cancer and its treatments can cause side effects, such as fatigue, nausea, pain, and shortness of breath, which can decrease a patient's health-related quality of life (HR-QoL). For patients with metastatic disease, optimizing the ability to function is crucial, explained study presenter Anne May, PhD, a professor at the Julius Center for Health Sciences and Primary Care at the University Medical Center, Utrecht, in the Netherlands.

"Optimizing quality of life is, of course, important for everybody, but especially for patients living with metastatic disease who undergo continuous treatment," May said. "By improving quality of life through enhanced symptom management, we can help patients better enjoy their personal, social, and, if applicable, working life."

Researchers have previously assessed the effects of exercise programs on patients with less advanced cancer, finding them to benefit patients' HR-QoL and energy levels. However, whether these benefits also apply to patients with metastatic disease has not been rigorously tested, May said. She added that a longer exercise program may be necessary for patients with metastatic disease because their treatment usually continues for much longer periods.

May and her colleagues enrolled 357 patients with metastatic breast cancer to the PREFERABLE-EFFECT trial, a collaboration between institutions in Germany, Poland, Spain, Sweden, the Netherlands, and Australia. All participants in the trial received a physical activity tracker and generic exercise advice; 178 patients were randomly assigned to twice-weekly supervised exercise sessions for nine months, involving balance, resistance, and aerobic exercises (one weekly session could be performed instead via an exercise app during the final three months).

At enrollment and after three, six, and nine months, the participants were surveyed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-30), a comprehensive questionnaire assessing patients' physical, mental, emotional, and financial quality of life. Additionally, the EORTC-FA12 questionnaire was used to assess multidimensional fatigue among the

participants. Each questionnaire was scored from 0 to 100, with higher scores on the EORTC-QLQ-30 indicating improved HR-QoL and higher scores on the EORTC-FA12 indicating higher levels of fatigue. Researchers also tested physical fitness using the steep ramp test, in which participants were asked to ride a stationary bike at increasing resistance levels until voluntary exhaustion.

At three, six, and nine months, respectively, patients assigned to the exercise intervention had average HR-QoL scores that were 3.9, 4.8, and 4.2 points higher than patients in the control arm. Patients who participated in the exercise intervention had EORTC-FA12 scores that were 3.4, 5.3, and 5.6 points lower (indicating decreased fatigue) at three, six, and nine months, respectively, compared with those of the patients in the control arm. All differences were statistically significant.

At six months, patients assigned to the exercise intervention also reported significantly better scores on important EORTC-QLQ-30 subscales, compared with those in the control arm, including a 5.5-point increase in social functioning, a 7.1-point decrease in pain, and a 7.6-point decrease in shortness of breath. In the steep ramp test, patients in the exercise arm reached an average maximum resistance that was 24.3 Watts (13%) higher than those in the control arm.

May and colleagues found that the nine-month intervention was not only effective but may have also encouraged longer-term compliance. “We think a nine-month program helps patients incorporate exercise into their routine,” she said. “Many patients continued exercising beyond nine months; exercising became part of their daily lives and cancer treatment regimens.”

Based on these findings, May suggested that physicians and nurses should routinely recommend supervised exercise to patients with metastatic breast cancer and that policymakers and insurance companies should ensure cost coverage for exercise programs.

Limitations of this study include the inability to blind participants to their respective research arms, which may have motivated patients in the control arm to voluntarily increase their physical activity levels. May noted that this may have led to an underestimation of the intervention’s effect.

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## **Abstract**

### **GS02-10**

#### **Effects of a structured and individualized exercise program on fatigue and health-related quality of life in patients with metastatic breast cancer: the multinational randomized controlled PREFERABLE-EFFECT study**

**Presenting Author:** Anne M. May, PhD

**Introduction:** Patients with metastatic breast cancer (mBC) often experience cancer- and treatment-related side effects that can impair daily life activities and health-related quality of life (HRQoL). Interventions are needed that improve HRQoL by alleviating fatigue and other side effects during palliative BC cancer treatment. Recent evidence-based international guidelines (ASCO, ACSM) recommend exercise for patients with BC during adjuvant treatment for reducing side effects. However, evidence of the effectiveness of exercise in patients with mBC is scarce. The PREFERABLE-EFFECT study (NCT04120298) was designed to assess the effects of a 9-month supervised exercise program in patients with mBC on fatigue, HRQoL, and other cancer- and treatment-related side effects.

**Methods:** PREFERABLE-EFFECT is a multinational, randomized controlled trial including patients with mBC from five European countries (Germany, Poland, Spain, Sweden, The Netherlands) and Australia. Participants were randomly assigned to usual care or an individualized, structured exercise program consisting of aerobic, resistance, and balance training. The first six months included twice weekly supervised exercise sessions of one hour. In the last three months, one supervised session was replaced by an unsupervised session, supplemented by an exercise App. All participants received general exercise advice (physical activity  $\geq 30$  min/day) and an activity tracker. Our primary outcomes, physical fatigue (subscale of the EORTC QLQ-FA12) and HRQoL (summary score of the EORTC QLQ-C30), were assessed at baseline, 3, 6, and 9 months. Among other physical fitness outcomes, maximal short exercise capacity was assessed with the Steep Ramp Test. The intervention effects (intention-to-treat) were determined by comparing the change from baseline to 3, 6 (i.e., primary endpoint) and 9 months between groups using separate mixed models for repeated measures, adjusted for baseline values of the outcome variable and stratification factors (mBC line of treatment (1<sup>st</sup>/2<sup>nd</sup> vs. 3<sup>rd</sup> or higher) and study center). A significant improvement of either or both primary outcomes (applying the Bonferroni-Holm method) was considered as successful.

**Results:** Between 2019-2022, we included 357 patients with mBC, with 178 patients randomized to the exercise intervention and 179 to usual care. Patients were, on average, 55.4 years of age (SD=11.1), most patients received 1<sup>st</sup> or 2<sup>nd</sup> line of treatment at study enrollment (74.8%) and had bone metastases (73.9%). At 6 months (primary endpoint), participation in the exercise intervention resulted in statistically significant positive effects on both primary outcomes, compared to usual care: physical fatigue was lower (mean difference: -5.3, 95% CI -10.0; -0.6,  $p=0.027$ , effect size (ES)=0.22) and HRQoL was better (+4.8, 95% CI 2.2; 7.4,  $p=0.0003$ , ES=0.33). Beneficial effects were also found at 3 months (physical fatigue: -3.4, -7.8; 1.0, ES=0.14 and QoL: 3.9, 1.5; 6.3, ES=0.27) and 9 months (physical fatigue: -5.6, -10.9; -0.4, ES=0.24 and QoL: +4.3, 1.4; 7.3, ES=0.31). Further, at the primary endpoint, we found positive exercise effects on physical fitness (+24.3 Watts, 15.5; 33.1, ES=0.42) and numerous QLQ-C30 scales, including social functioning (+5.5, 0.2; 10.8, ES=0.20), pain (-7.1, -12.1; -1.9, ES=0.28) and dyspnea (-7.6, -12.2; -3.0, ES=0.28). Two SAEs occurred (one wrist fracture and one sacral stress fracture), neither related to bone metastases.

**Conclusion:** This large multinational study demonstrated significant beneficial effects of a supervised exercise intervention offered during palliative treatment on mBC patients' fatigue, HRQoL, and other clinically relevant outcomes. Based on these findings, we recommend supervised resistance and aerobic exercise as part of supportive care regimens during palliative treatment of mBC.

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