TPS10625 Poster Session

A phase II biomarker RCT in women at high risk for breast cancer: Low dose tamoxifen and lifestyle changes for breast cancer prevention (TOLERANT study).

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Background: Breast cancer (BC) prevention in high-risk women is crucial. Tamoxifen, despite its efficacy, has limited use due to its side effects. Low-dose tamoxifen (LDT) has shown much better balance between BC risk reduction and adverse effects. Additionally, lifestyle interventions (LI) like intermittent caloric restriction (ICR) and physical activity may further reduce BC risk by modulating factors such as mammographic density (MD) and sex hormone-binding globulin (SHBG) levels, which we showed is correlated with reduced breast cancer risk. This study evaluates whether LDT increases circulating SHBG more effectively than LI with or without ICR after six months. **Methods:** The TOLERANT study is a randomized, four-arm, phase II trial involving 200 high-risk women recruited from four Italian hospitals. Participants will be randomly assigned to one of four intervention arms: (1) LDT, (2) LDT + ICR, (3) LI with step counter, (4) LI with step counter + ICR. Interventions will last six months, and participants' adherence will be monitored through visits, telephone calls and diaries. Eligible women are aged 18-70 with a high risk for BC due to genetic predisposition or a history of intraepithelial neoplasia. Key exclusion criteria include history of invasive BC, BMI <18.5, and certain medical conditions. LDT involves 10 mg tamoxifen every other day. ICR follows a "5:2 diet" model, with five days of normal intake and two days at 25% of regular caloric intake. LI includes personalized advice and step counters targeting 10,000 steps per day. Primary outcome is the change in SHBG levels. Secondary outcomes include changes in metabolic and inflammatory markers, QoL, body composition, microbiome diversity, and MD. Blood and stool samples will be collected at baseline (B), three (3M), and six months (6M) to analyze biomarkers. Body composition will be assessed using bioelectrical impedance analysis, at B, 3M and 6M and MD will be measured in a subset of participants using digital mammography. As of January 20, 2025, a total of 43 participants have been enrolled, including 18 with DCIS and 25 high-risk women. The study, which has received approval from relevant ethics committees, will provide insights into the effectiveness of LDT and LI in reducing BC risk among high-risk women. The results could inform personalized prevention strategies, balancing efficacy with QoL. Trial registration: EuCT number:2023-503994-39-00; Clinical trials.gov NCT06033092 Funding: This work is funded by European Union – Next Generation EU – PNRR M6C2 – Investimento 2.1 Valorizzazione e potenziamento della ricerca biomedica del SSN – Project Code: PNRR-MAD-2022-12376567 - PI Bernardo Bonanni. Co-PI Sara Gandini. The funders had no role in study design, data collection and analysis, or abstract preparation. Reference*: Guerrieri-Gonzaga A et al. PLoS One. 2024 doi journal.pone.0309511. Clinical trial information: NCT06033092. Research Sponsor: European Union – Next Generation EU – PNRR M6C2.