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Tamoxifen for breast cancer prevention among survivors of pediatric lymphoma previously treated with chest radiation: clinical benefits, harms and tradeoffs

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Background: Survivors of pediatric lymphoma previously treated with chest radiation are at high risk for subsequent breast cancer. Although early initiation of breast cancer screening is recommended, the clinical benefits and harms of adding tamoxifen to reduce breast cancer deaths among these women are unknown.

Methods: We adapted a Cancer Intervention and Surveillance Modeling Network (CISNET) breast model using data from the Childhood Cancer Survivor Study (CCSS) to reflect the elevated risks for breast cancer and competing mortality for 5-year survivors previously treated with chest radiation (RT). Breast cancer risk was based on age, chest RT field, timing of RT relative to menarche, menopause status, anthracycline exposure, and family history. Premature menopause risk varied by cumulative ovarian RT and alkylator dose. Based on the US Preventive Services Task Force 2019 Evidence Summary, we assumed tamoxifen (20mg daily for 5 years) reduced estrogen receptor positive (ER+) breast cancer risk by 42% (RR = 0.58 [0.42-0.81]) for 20 years and increased risks for venous thromboembolism, deep vein thrombosis, coronary heart disease, stroke and endometrial cancer during treatment. Strategies included no screening or tamoxifen, annual screening with mammography and MRI starting at age 25, annual screening with mammography and MRI starting at age 25 with the addition of tamoxifen at ages 25, 30 or 35. Model outcomes included cumulative breast cancer risk, number of childbearing years before age 45 (defined as years menstruating without tamoxifen use or a breast cancer diagnosis or having survived breast cancer for at least 3 years), and number of tamoxifen-related side-effects.

Results: Among a cohort of 20-year-old 5-year lymphoma survivors previously treated with mediastinal RT without primary ovarian failure, an estimated 20% were projected to develop breast cancer and 2.6% would die from the disease before age 50 in the absence of screening or tamoxifen use. Survivors would have on average 22 childbearing years before age 45. Early initiation of breast cancer screening at age 25 would reduce breast cancer deaths before age 50 by 56.3%. Depending on age at initiation, tamoxifen would further reduce breast cancer deaths by 8.0 to 9.6 percentage points for an overall 64.3% to 65.9% reduction and reduce the average number of childbearing years by 17% to 21%. For each breast cancer death averted, a reduction of 1950 to 3740 childbearing life years and 11 to 20 side-effects would occur and varied by the tamoxifen start age compared to mammography and MRI screening.

Conclusions: Tamoxifen use for primary breast cancer prevention among pediatric lymphoma survivors may further reduce breast cancer deaths but decisions might depend on survivor preferences for side effects vs. avoiding breast cancer and consideration of timing for childbearing.