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GS4-08

GS4-08 10-year results of a phase 3 trial of low-dose tamoxifen in non-invasive breast cancer

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We have previously shown in a phase 3 trial that tamoxifen 5 mg/day for 3 years decreased by 52% the incidence of recurrence of invasive breast cancer or DCIS after a median follow-up of 5.1 years in women with excised non invasive breast disease, including atypical ductal hyperplasia, DCIS or LCIS (DeCensi et al. JCO 2019; 37:1629). Toxicity was negligible with only an extra hot flash per day in the tamoxifen arm compared with the placebo arm. These findings were incorporated into the ASCO clinical practice guidelines for breast cancer risk reduction as an alternative option to standard doses and duration of tamoxifen or aromatase inhibitors in women with non-invasive disease (Visvanathan et al. JCO 2019; 37:3152). In the present study we update the findings on breast cancer recurrence after a median of 9.14 years (interquartile range, IQR, 7.16-10.73) and a total of 10.57 person years of follow up to see if the treatment effect is retained with more events and after a median of approximately 6 years from treatment cessation. We conducted a national multicenter randomized trial of tamoxifen, 5 mg/d or placebo administered for 3 years after surgery in women with hormone-sensitive or unknown breast intraepithelial neoplasia, including atypical ductal hyperplasia and lobular or ductal carcinoma in situ. The primary end point was the incidence of invasive breast cancer or ductal

carcinoma in situ. Between November 1, 2008, and March 31, 2015, 1,160 women were screened and 500 aged 75 years of age or younger were included in the study. Women with high-grade or comedo/necrotic DCIS received adjuvant radiotherapy of 50 Gy in 25 courses. The mean age was 54 years (standard deviation, 9 years), and 55% of participants were postmenopausal. The mean (SD) body mass index, kg/m2, was 25.7 (4.8) on tamoxifen and 25.3 (4.2) on placebo. Twenty percent had ADH, 11% had LCIS, and the remaining 69% had DCIS. After a median follow-up of 9.14 years, there were 22 neoplastic events (invasive breast cancer or DCIS) with tamoxifen and 37 with placebo (annual rate 11.09, 95% CI, 7-30-16.84 on T vs 19.71, 95% CI, 14.28-27.21 on P per 1,000 person-years; hazard ratio, 0.56; 95% CI, 0.33 to 0.95; P = .03), which resulted in a 5-year number needed to treat of 18. Overall, 71% of the recurrences were invasive breast cancer. The follow-up was updated with the most recent visit within 12 months in two thirds of the participants, so an update of all participants will be performed by Sept 30th with full analysis of neoplastic events, annual risk rate ratio, serious adverse events and deaths. Moreover, an updated analysis of potential effect modifiers will be conducted, including menopausal status, baseline estradiol levels, menopausal symptoms, BMI, smoking status and Ki-67 of the primary lesion. In conclusion, our findings indicate that low dose tamoxifen given for 3 years still significantly prevents recurrences from non-invasive breast cancer after a median of 6 years from treatment cessation, providing a valid prevention/interception option in this disease group. Supported by Ente Ospedaliero Ospedali Galliera, Genova, Italy, the Italian Ministry of Health (RFPS-2006-1-339898), the Italian Association for Cancer Research (IG 2008 Grant No. 5611), and the Italian League against Cancer (LILT 7-08).

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