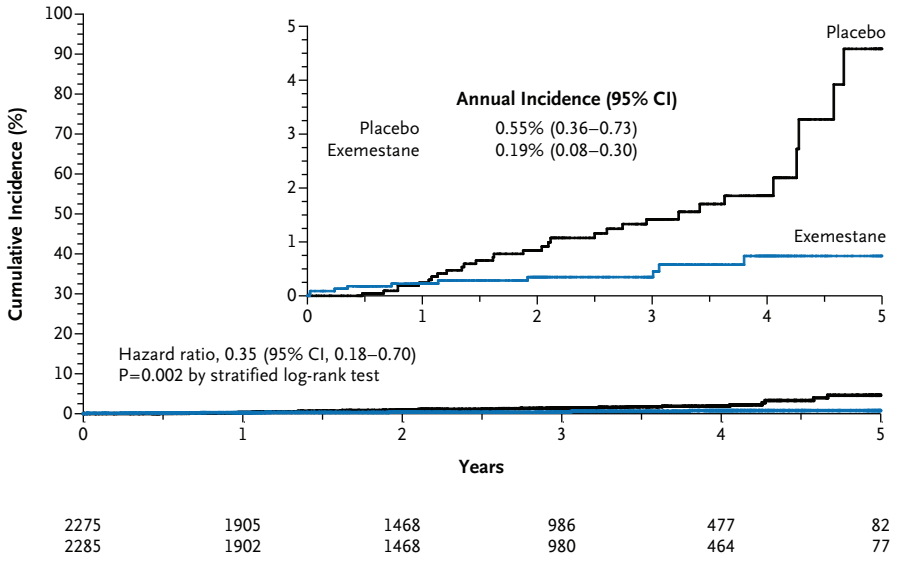

Figure 1. Cumulative Incidence of Invasive Breast Cancer.
CI denotes confidence interval.

cancer in these two groups. There were 37 ductal (10 in the exemestane groups and 27 in the placebo group) and 6 lobular (1 in the exemestane groups and 5 in the placebo group) cancers. The majority of cancers in each group were estrogen-receptor–positive, HER2/neu–negative, and node-negative (Table 2). Exemestane appeared to be superior to placebo in all prespecified subgroups defined by concurrent use of low-dose aspirin, Gail risk score, age, body-mass index, prior atypical ductal hyperplasia, atypical lobular hyperplasia, or lobular carcinoma in situ and prior ductal carcinoma in situ treated with mastectomy (Fig. 2). Exemestane also appeared to be superior in unplanned subgroups: invasive breast cancers according to prior use of menopausal hormone therapy (hazard ratio, 0.30 for prior users; 95% CI, 0.11 to 0.81; hazard ratio, 0.41 for prior nonusers; 95% CI, 0.16 to 1.05) and continent of residence (hazard ratio, 0.34 for North America; 95% CI, 0.16 to 0.71; hazard ratio, 0.39 for Europe; 95% CI, 0.07 to 1.99). The annual incidence of invasive breast cancer plus ductal carcinoma in situ (20 in the exemestane group and 44 in the placebo group) was 0.35% and 0.77% in the exemestane and placebo groups, respectively (hazard ratio, 0.47; 95% CI, 0.27 to 0.79). Combined lobular carcinoma in situ, atypical ductal hyperplasia, and atypical lobular hyperplasia occurred in 4 women (0.2%) in the exemestane group and 11 (0.5%) in the placebo group (hazard ratio, 0.36; 95% CI, 0.11 to 1.12). The number needed to treat to prevent one case of invasive breast cancer with exemestane therapy was 94 in 3 years and 26 in 5 years, but few women completed 5 years of therapy.

Table 3 (and Table 2 in the Supplementary Appendix) shows adverse events that occurred in 5% or more of women, with a difference between groups of 1% or more and prespecified secondary end points of toxicity. Symptoms and adverse events (all grades) occurred in 88% of women in the exemestane group versus 85% in the placebo group (P=0.003). Arthritis (P=0.01) and hot flashes (P<0.001) were more common in the exemestane group, but differences between the groups in the frequency of those with grade 2 or higher symptoms were modest (arthritis, 6.5% vs. 4.0%; hot flashes, 18.3% vs. 11.9%). Table 3 (and Table 2 in the Supplementary Appendix) shows no significant differences between the two groups in prespecified secondary end points, including new diagnoses of osteoporosis or cardiovascular events. Clinical fracture rates were also similar in the two groups, and the proportion of women in each group who were prescribed bisphosphonate therapy during the trial was also similar (24.5% for exemestane and 24.1% for placebo). There was no significant

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