Breast Care
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**Table 1.** Summary of randomized controlled studies for medical breast cancer prevention

| Study [Ref.] | Study design | Median FUP | n | Inclusion criteria | All IBC HR/RR (95% CI) | ER + IBC HR/RR (95% CI) | Breast cancer incidence (per 1,000 per year) | Side effects | No. breast cancer cases and no. of breast cancer related deaths in the study arms | Comments |
|---|---|---|---|---|---|---|---|---|---|---|
| NSABP-P1 [14] | Tam 20 mg vs. Placebo 5 years | 54.6 months | 13.388 | > 60y, or 35-59y with increased BC risk (≥1,66% in 5y Gail model) | RR 0.51 (0.39-0.66) | RR 0.31 (0.22-0.45) | | EC RR 2.53 (1.35-4.97) DVT RR 1.60 (0.91-92.86) PE RR 3.10(1.15-19.27) | | no signif. difference for development of ER- BC, after stopping tam was offered to placebo group! |
| NSABP-P1 [15] | Tam 20 mg vs. Placebo 5 years | 74.0 months | 13.207 | > 60y, or 35-59y with increased BC risk (≥1,66% in 5y Gail model) | RR 0.57 (0.46-0.70) | | 6.29 vs. 3.59 | fractures RR = 0.68 (0.51-0.92) EC RR 3.28 (1.87-6.03) PE RR 2.15 (1.08-4.51) DVT RR 1.44 (0.91-2.30) cataract RR 1.21 (1.10-1.34) | BC 250:145 death 11:12 | study unblinded when difference was significant, then tam was offered placebo group |
| Italian Tamoxifen Prevention Study [16] | Tam 20 mg vs. Placebo 5 years | 11.2 years | 5.408 | average BC risk, hysterectomy | RR 0.84 (0.60-1.17) high risk women RR 0.24 (0.10-0.59) | | all patients 2.48 vs. 2.07 high risk 6.26 vs. 1.50 | thromboembolic events RR 1.63 (1.02-2.62) | BC 74:62 death 2:2 | 53% with bilateral ovariectomy, 39.2% interrupted treatment before completion (similar in both groups), hormonal therapy was allowed high risk group (n=702): women taller than 160 cm, at least one intact ovary, < 14 years at menarche, no full-term pregnancy before 24 years |
| Royal Marsden Hospital Tamoxifen Chemoprevention Trial [19] | Tam 20 mg vs. Placebo 8 years | 13y 2 months | 2.471 | positive family history of BC | HR 0.78 (0.58-1.04) | HR 0.61 (0.43-0.86) | 6.1 vs. 4.8 | EC 13 *vs.* 5 (P=0.06) cataract 9 *vs.* 1 (P=0.02) thromboembolic events 8 vs. 3 (P=0.2) fractures 9 *vs.* 22 (P=0.6) | BC 104:82 | |

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| IBIS-I [20] | Tam 20 mg vs. Placebo 5 years | 96 months | 7.154 | women with increased BC risk | RR 0.74 (0.58-0.94) | RR 0.66 (0.50-0.87) | 5.88 vs. 4.34 | EC RR 1.55 (0.68-3.65) DVT/PE RR 1.84 (1.21-2.82) fractures RR 1.02 (0.86-1.21) cataracts RR 1.24 (0.87-1.77) | BC 168:124 Death 13:11 | |
| MORE [24, 25] | Raloxifen 60 or 120 mg/d vs. Placebo 4 years | 47.4 months | 7.705 | postmenopausal women with osteoporosis | RR 0.28 (0.17-0.46) | RR 0.16 (0.09-0.30) | 4.7 *vs.* 1.3 | EC RR 0.8 (0.2-2.7) DVT/PE 3.1 (1.5-6.2) | BC 39:22 | secondary endpoint: breast cancer risk |
| CORE [26] | 4 additional years of raloxifene 60 mg/d vs. placebo | 8 years | 4.011 | continuing trial of MORE study | HR 0.34 (0.22-0.50) | HR 0.24 (0.15-0.40) | 4.2 vs. 1.4 | thromboembolic events RR 2.17 (0.83 to 5.70) | BC 58:40 | |
| STAR (NSABP-P2) [31] | Tam 20 mg vs. raloxifene 60 mg | 81 months | 19.490 | postmenopausal, ≥35y with increased BC risk (≥1,66% in 5y Gail model) | RR 1.24 (1.05-1.47) | | 4.04 (tam) vs. 5.02 (raloxifene) | EC RR 0.55 (0.36-0.83) PE RR 0.80 (0.57-1.11) DVT RR 0.72 (0.54-0.95) cataract RR 0.80 (0.72-0.89) | BC 310 (raloxifene):247 (tamoxifen) death 4 (raloxifene):11 (tam) | raloxifene about 76% effective as tamoxifen but with less side effects |
| RUTH [23] | aloxifene 60 mg vs. placebo | 5.6 years | 10.101 | postmenopausal, ≥55y with cardiovascular risk | HR 0.56 (0.38-0.83) | HR 0.45 (0.28–0.72) | 1.5 (raloxifene) vs. 2.7 (placebo) | vertebral fractures HR 0.65 (0.47-0.89) thromboembolic event HR 1.44 (1.06-1.95) fatal stroke HR 1.49 (1.00-2.24) | BC 70:40 death (all cancers) 103:97 | no effect on cardiovascular disease |

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| PEARL [27, 28] | lasofoxifene 0.25 mg or 0.5 mg *vs.* placebo | 60 months | 8.556 | 59-80 years, osteoporosis (T-score ≤2.5) | HR 0.82 (0.45-0.49) (0.25mg) HR 0.21 (0.08-0.55) (0.5mg) | HR 0.50 (0.22–1.11) (0.25 mg) HR 0.17 (0.05-0.57) (0.5 mg) | 1.97 (placebo) vs. 1.64 (0.25 mg) vs. 0.41 (0.5 mg) | vertebral fractures HR 0.58 (0.47-0.70) nonvertebral fractures HR 0.76 (0.64-0.91) coronary heart disease events HR 0.68(0.50-0.93) thromboembolic event HR 2.06 (1.17-3.60) stroke HR 0.64 (0.41-0.99) | BC 24 (placebo): 20 (0.25mg) : 5 (0.5mg) | no increased risk for endometrial cancer |
| GENERATIONS [29, 30] | arzoxifene 20 mg vs. placebo | 54 months | 9354 | 60-86 years, osteoporosis or osteopenia | HR 0.44 (0.26-0.76) | HR 0.30 (0.14–0.63) | 2.28 (placebo) vs. 1.01 (azoxifene) | fractures RR 0.97 (0.84-1.12) thromboembolic events RR 2.3 (1.5-3.7) | BC 43 (placebo): 19 (arzoxifene) | no increased risk for endometrial cancer |
| NCIC CTG MAP.3 [35] | exemestane 25 mg vs. placebo | 35 months | 4560 | ≥35 years, postmenopausal, increased BC risk (Gail model >1,66% in 5y) | HR 0.35 (0.18-0.70) | HR 0.27 (0.12-0.60) | 1.9 (exemestane) vs. 5.5 (placebo) | arthritis 6.5% vs. 4.0% (P=0.01) hot flashes 18.3% vs. 11.9% (P<0.001) | BC 11 (exemestane) : 32 (placebo) BC death 1 (exemestane):0 (placebo) total death 19:19 | no significant differences in frequencies of cardiovascular events, fractures, osteoporosis or colrorectal and endometrial cancers |

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|---|---|---|---|---|---|---|---|---|---|---|
| IBIS-II [36] | anastrozole 1 mg vs. placebo 5 years | 5 years | 3864 | 40-70 years, postmenopausal increased BC risk (10y risk > 5%, Tyrer-Cuzick model) | HR 0.50 (0.32-0.76) | HR 0.42 (0.25–0.71) | 8.0 vs. 4.0 | fractures HR 1.00 (0.98-1.03)<br>colorectal cancer HR 0.28 (0.08-0.99)<br>arthralgia HR 1.10 (1.03-1.18)<br>joint stiffness HR 1.51 (1.17-1.94)<br>carpal tunnel syndrome HR 1.58 (1.08-2.30)<br>hypertension HR 1.64 (1.18-2.28) | BC 40 (anastrozole) : 85 (placebo)<br>BC death 2 (anastrolzole) : 0 (placebo)<br>total death 18:17 | no significant differences in frequencies of thromboembolic and cerebrovascular events or myocardial infarction and endometrial cancer |