**10-year results of the International Breast cancer Intervention Study II (IBIS-II)**

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**Background:** Two large clinical trials have shown the benefit of aromatase inhibitors in healthy women to reduce the risk of developing breast cancer (MAP.3 and IBIS-II). Here, we report blinded 10-year median follow-up efficacy data for the IBIS-II trial, which compared anastrozole to placebo in women at increased risk of developing breast cancer.

**Material and Methods:** 3864 postmenopausal women at increased risk of developing breast cancer were recruited into a double-blind trial of anastrozole (N=1920) versus matching placebo (N=1944) for 5 years. The primary objective of this study was to determine the efficacy of anastrozole in preventing breast cancer (both invasive and ductal carcinoma in situ (DCIS)), overall and particularly in the post 5-year time period. Secondary endpoints included prevention of oestrogen receptor positive breast cancer, breast cancer mortality, non-breast cancer deaths, other cancers, cardiovascular disease, fractures, and musculoskeletal events.

**Results:** After a median follow-up of 10.9 years (IQR 8.8-13.0), a total of 241 breast cancers have been reported (HR=0.50 (0.38-0.65), P<0.0001) (Table). The reduction was larger in the first 5 years (HR=0.39 (0.27-0.58), P<0.0001), but still significant after 5 years (117 new cases (49%); HR=0.63 (0.43-0.91), P=0.015) (Table). The effects in the two time periods were not significantly different (P=0.11). Invasive estrogen receptor (ER) positive breast cancer was reduced by 54% with anastrozole (HR=0.46 (0.33-0.65), P<0.0001), with a continued significant effect observed in the post treatment follow-up period (Table). A non-significant effect was observed in invasive ER-negative breast cancer (HR=0.76 (0.39-1.45), P=0.4). A reduction in DCIS overall was observed (Table), with a very large reduction in those known to be ER-positive (HR=0.23 (0.08-0.69), P<0.0001). A total of 129 deaths have been reported, with no significant difference in all-cause mortality between the two treatment arms (63 vs. 66; HR=0.93 (0.66-1.32), P=0.7). Only 5 deaths from breast cancer (2 vs. 3) were reported, but number of events are very small and longer follow-up is needed. 321 cancers other than breast were reported, with a significant decrease observed with anastrozole (129 vs. 192, OR=0.66 (0.52-0.83), P=0.0004). Specifically, fewer endometrial cancers (4 vs. 8), ovarian cancers (5 vs. 9), lung cancers (5 vs. 12), and melanomas (9 vs. 18) were observed with anastrozole. A comprehensive adverse event profile will be reported.

**Conclusion:** This updated analysis of the IBIS-II trial confirms the significant reduction in breast cancer occurrence with anastrozole in the post-treatment follow-up period. These results indicate a long-term preventive benefit with anastrozole for ER-positive breast cancer in postmenopausal women.

**Table**: Number of events and Hazard Ratios (95% CI) according to treatment allocation and follow-up period.

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|  | **Number of events** | **HR (95% CI)** | **P-value** |
| **Overall** | 241 (81 vs. 160) | 0.50 (0.38-0.65) | <0.0001 |
| 0-5 years | 124 (35 vs. 89) | 0.39 (0.27-0.58) | <0.0001 |
| 5+ years | 117 (46 vs. 71) | 0.63 (0.43-0.91) | 0.015 |
| **Invasive ER-positive** | 151 (48 vs. 103) | 0.46 (0.33-0.65) | <0.0001 |
| 0-5 years | 72 (20 vs. 52) | 0.38 (0.23-0.64) | <0.0001 |
| 5+ years | 79 (28 vs. 51) | 0.53 (0.34-0.84) | 0.007 |
| **All DCIS** | 42 (13 vs. 29) | 0.44 (0.23-0.85) | 0.015 |
| 0-5 years | 22 (5 vs. 17) | 0.29 (0.11-0.80) | 0.011 |
| 5+ years | 20 (8 vs. 12) | 0.65 (0.26-1.59) | 0.34 |