# Chronological changes of side effect profile of anastrozole compared with tamoxifen in Japanese women : Findings from N-SAS BC03 trial every 3 months after one year of the randomization

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Comprehensive Support Project

## Abstract

**Introduction:** Selective aromatase inhibitors (AIs) now serve as treatment of choice for hormone responsive postmenopausal early breast cancer. The difference in the toxicity profile between AIs and tamoxifen (TAM) has been noted and are derived from the clinical trials conducted in the Western countries. The ethnic difference might exist in terms of the toxicity profile, however few data concerning the difference in the toxicity profile between AIs and TAM among Asian women is available.

**Patients & Methods**: We investigated the adverse events among Japanese women who participated in Phase III Randomized Adjuvant Study of Tamoxifen Alone Versus Sequential Tamoxifen and Anastrozole in Hormone-Responsive Postmenopausal Breast cancer Patients (N-SAS BC 03 trial). Two years ago we reported the worst toxicity grade after randomization of adverse events between anastrozole and tamoxifen arm. In the present study, we show adverse events at baseline and every 3 months chronologically after one year of the randomization.

**Result & Conclusion:** Table shows that significant changes were observed in hot flash and vaginal discharge in favor of anastrozole gradually after the randomization. On the other hand, the number of arthralgia increased gradually after randomization in anastrozole arm. This change is significant. Further studies should be mandatory to reveal the similarity and difference in the toxicity profile of AIs between Western and Asian population.

## Patients Characteristics

| | | ANA | TAM |
|---|---|---|---|
| Number | | 354 | 352 |
| Stage | Ⅰ | 153 | 144 |
| | ⅡA | 124 | 134 |
| | ⅡB | 51 | 51 |
| | ⅢA | 13 | 12 |
| | ⅢB | 13 | 11 |
| Lynph node status | 0 | 212 | 212 |
| | 1-3 | 102 | 99 |
| | 4≦ | 40 | 41 |
| HER2 | 0-2+ | 166 | 165 |
| | 3+ | 14 | 14 |
| | unknown | 174 | 173 |
| Tumor size | ＜3cm | 282 | 279 |
| | 3cm≦ | 72 | 73 |
| ER/PR | ER(+) PR(+) | 253 | 250 |
| | ER(+) PR(-) | 75 | 76 |
| | ER(-) PR(+) | 26 | 26 |
| Surgery | Breast conserving | 185 | 184 |
| | Mastectomy | 169 | 168 |
| Tamoxifen treatment | 1.0-2.0years | 171 | 171 |
| | 2.0-4.0years | 183 | 181 |
| Age | ≦ 59 years old | 176 | 172 |
| | 60 years old ≦ | 178 | 180 |
| Chemotherapy | yes | 163 | 161 |
| | no | 191 | 191 |
| Performance Status | 0 | 350 | 347 |
| | 1 | 4 | 5 |

## Objective

To evaluate the side effect profile of anastrozole compared with tamoxifen in NSAS-BC03 trial

## Methods

**Study design**

The NSAS-BC03 is a phase III randomized open label adjuvant study of tamoxifen alone versus sequential tamoxifen and anastrozole in hormone-responsive postmenopausal breast cancer patients.

The NSAS-BC03 protocol compares 5 years upfront ajuvant thearpy with tamoxifen with 1 to 4 years of tamoxifen followed by anastrozole for a total 5 years. (Figure 1)

Primary endpoint: Disease free survival (DFS), adverse events

Secondary endpoint: Relapse free survival (RFS), Overall survival (OS), health related quality of life (HRQOL)

**Inclusion Criteria**

Stage I-IIIB estrogen and/or progesterone receptor positive breast cancer treated with surgery

Pathologically confirmed axlliar status

Eastern Cooperative Oncology Group performance status 0-1

Postmenopausal at randomization, define as:

Age ≥60 years

Age ≥45 years with ≥1 year amenorrhea

Bilateral Oophorectomy

No recurrence

Tmoxifen treatment for 1-4 years after surgery

Adequate hematologic, hepatic and biochemical function

**Exclusion Criteria**

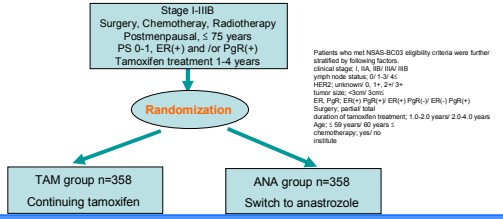
History of invasive carcinoma within 5 years, deep vein thrombosis and osteoporosis

Bilateral breast cancer

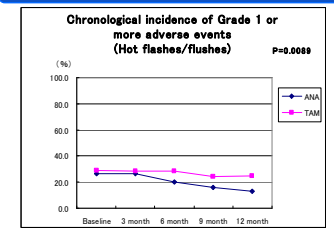
**Statistical Analyses**

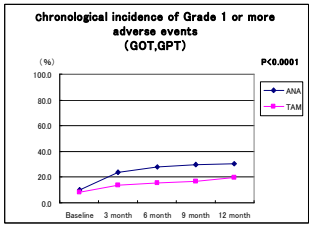
The data were expressed as difference of incidence over time course and analyzed using chi-square testsand generalized estimating equation (GEE) with the baseline value as a covariate.

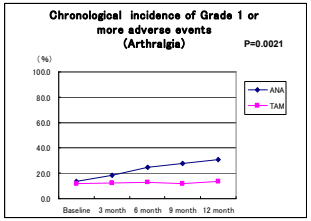
## Study Protocol

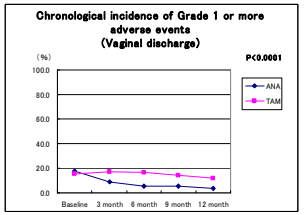



## Results




## Summary

The significant changes were observed in hot flash and vaginal discharge in favor of anastrozole gradually after the randomization. On the other hand, the number of liver dysfunction and arthralgia increased gradually after randomization in anastrozole arm. These changes are also significant.

## Discussion

In ABCSG 8 or ITA trials, there were no observed differences in adverse events such as hot flashes and vaginal discharges. There was a trend towards more reports of bone pain in the anastrozole group than in the tamoxifen group in ABCSG 8. IES trial showed the similar results about adverse event. On the other hand, our study indicated that there were significantly more incidences of arthralgia and liver dysfunction, and less incidence of hot flashes and vaginal discharge in patients treated with anastrozole than those treated with tamoxifen. The reason why there are more differences in Japanese women than in western women remains uncertain. Further studies should be mandatory.

## References

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