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Does Efficacy of Adjuvant Endocrine Therapy Correlate with Breast Cancer Patients' Ethnicity?

Hiroyuki Takei*

Division of Breast Surgery, Saitama Cancer Center, 818 Komuro Ina, Kita-Adachi, Saitama 362-0806, Japan

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Over 70% of women with breast cancer are with hormone receptor positive disease [1], and most of them are treated with an adjuvant endocrine therapy. Five years tamoxifen used to be a standard adjuvant endocrine treatment of breast cancer. It was shown by a meta-analysis that tamoxifen reduced about 40% of recurrence rates in both premenopausal and postmenopausal women with breast cancer [2].

Third generation Aromatase Inhibitors (AIs), exemestane (steroidal), anastrozole (non-steroidal), and letrozole (non-steroidal) began to be used in late 90's as an adjuvant endocrine therapy in postmenopausal women with breast cancer. A randomized controlled trial showed that 5 years adjuvant anastrozole was superior to 5 years adjuvant tamoxifen in terms of disease-free survival (DFS) rates [3]. In addition another randomized controlled trial showed that 5 years of adjuvant letrozole was superior to 5 years adjuvant tamoxifen in terms of DFS rates and overall survival (OS) rates [4]. On the other hand, randomized controlled trials showed that 5 years adjuvant therapy of letrozole or exemestane was not superior to 2 to 3 years of adjuvant tamoxifen followed by 2 to 3 years of letrozole or exemestane [4,5]. In addition, 5 years adjuvant letrozole was not superior to 2 years of adjuvant letrozole followed by tamoxifen [4]. Three AIs seemed to have a similar efficacy in the neoadjuvant setting [6]. All these results suggest that there are two standard options of adjuvant endocrine therapy for postmenopausal women with breast cancer. First is an upfront use of AIs that is intended to be treated for 5 years. Second is an upfront use of tamoxifen that is intended to be treated for 2 to 3 years followed by AIs for a total of 5 years.

The efficacy of AIs and tamoxifen partly depends on patients' characteristics. It was reported that adjuvant anastrozole was less effective in patients with higher levels of Body Mass Index (BMI) [7]. Levels of estrogen in patients receiving anastrozole or letrozole were greater at higher levels of BMI [8]. However, a steroidal AI, exemestane showed no difference in the efficacy between patients with different levels of BMI as the adjuvant setting [9]. In addition, exemestane was more effective in patients with higher levels of BMI when used as a neoadjuvant setting [10]. These results suggest that the efficacy might be different between the steroidal AI and non-steroidal AIs if patients were stratified by levels of BMI. Anyway, Asian women have lower levels of BMI than Caucasian women [7,8,10]. The efficacy and side effects of non-steroidal AIs may differ between races. In fact, side effects were different between ethnic minorities and Caucasians who took letrozole after 5 years adjuvant tamoxifen [11]. Furthermore, letrozole improved DFS in Caucasians but a definite benefit in minority women was not demonstrated [11].

Tamoxifen is converted to endoxifen by the metabolizing enzymes cytochrome P450 (CYP) 3A4 and CYP2D6 to exert its maximal effect [12]. There are genetic variant forms of CYP2D6 known to have different enzymatic activities and these variant forms of CYP2D6 distribute differently among races [13,14]. For instance, a variant allele of CYP2D6*10 having a decreased activity is found in 51% of Asians; however, it is rare in Caucasians [13]. All these results suggest that the efficacy of tamoxifen may differ between races.

Health-related Quality of Life (HRQOL) scores were higher in Japanese women with breast cancer who took adjuvant tamoxifen compared with adjuvant anastrozole or exemestane [15]. On the other hand, HRQOL scores were similar between Caucasian patients treated with adjuvant tamoxifen and adjuvant AIs [16,17]. A better HRQOL observed in Japanese patients taking tamoxifen may be due to the fact that a fatigue was significantly less frequent in Japanese patients taking tamoxifen than Caucasian patients [15]. One of the reasons for this might be due to the different metabolism of tamoxifen between Japanese patients and Caucasian patients.

From these results, the efficacy of AIs or tamoxifen may be different between patients' ethnicities. However, there have been no studies that directly compare the efficacy of these drugs between different patients' ethnicities. Therefore, in order to determine which regimen is better, the efficacy, side effects, and cost should be estimated in each patient who needs to be treated with adjuvant endocrine therapy.

As the superior efficacy of AIs to tamoxifen was shown in clinical trials, an upfront use of AIs is more preferable in breast cancer patients having higher recurrence risks. In Japanese women with breast cancer whose levels of BMI are low, non-steroidal AIs might be effective. On the other hand, an upfront use of tamoxifen is suitable in patients having low recurrence risks. In Japanese women with breast cancer, HRQOL was significantly better in patients treated with adjuvant tamoxifen than adjuvant AIs. Therefore, the upfront use of tamoxifen followed by AIs is considered appropriate in these patients.

References

1. Shibuta K, Ueo H, Furusawa H, Komaki K, Rai Y, et al. (2011) The relevance of intrinsic subtype to clinicopathological features and prognosis in 4,266 Japanese women with breast cancer. Breast Cancer 18: 292-298.

2. Davies C, Godwin J, Gray R, Clarke M, Cutter D, et al. (2011) Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet 378: 771-784.

3. Cuzick J, Sestak I, Baum M, Buzdar A, Howell A, et al. (2010) Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. Lancet Oncol 11: 1135-1141.

4. Regan MM, Neven P, Giobbie-Hurder A, Goldhirsch A, Ejlertsen B, et al. (2011) Assessment of letrozole and tamoxifen alone and in sequence for postmenopausal women with steroid hormone receptor-positive breast cancer: the BIG 1-98 randomised clinical trial at 8·1 years median follow-up. Lancet Oncol 12: 1101-1108.

***Corresponding author:** Hiroyuki Takei, Director, Division of Breast Surgery, Saitama Cancer Center, 818 Komuro Ina, Kita-Adachi, Saitama 362-0806, Japan, E-mail: h-takei@cancer-c.pref.saitama.jp

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5. van de Velde CJ, Rea D, Seynaeve C, Putter H, Hasenburg A, et al. (2011) Adjuvant tamoxifen and exemestane in early breast cancer (TEAM): a randomised phase 3 trial. Lancet 377: 321-331.

6. Ellis MJ, Suman VJ, Hoog J, Lin L, Snider J, et al. (2011) Randomized phase II neoadjuvant comparison between letrozole, anastrozole, and exemestane for postmenopausal women with estrogen receptor-rich stage 2 to 3 breast cancer: clinical and biomarker outcomes and predictive value of the baseline PAM50-based intrinsic subtype--ACOSOG Z1031. J Clin Oncol 29: 2342-2349.

7. Sestak I, Distler W, Forbes JF, Dowsett M, Howell A, et al. (2010) Effect of body mass index on recurrences in tamoxifen and anastrozole treated women: an exploratory analysis from the ATAC trial. J Clin Oncol 28: 3411-3415.

8. Folkerd EJ, Dixon JM, Renshaw L, A'hern RP, Dowsett M (2012) Suppression of plasma estrogen levels by letrozole and anastrozole is related to body mass index in patients with breast cancer. J Clin Oncol 30: 2977-2980.

9. Seynaeve C, Hille E, Hasenburg A (2010) The impact of body mass index (BMI) on the efficacy of adjuvant endocrine therapy in postmenopausal hormone sensitive breast cancer (BC) patients; exploratory analysis from the TEAM study. 33rd Annual San Antonio Breast Cancer Symposium.

10. Takada M, Saji S, Masuda N, Kuroi K, Sato N, et al. (2012) Relationship between body mass index and preoperative treatment response to aromatase inhibitor exemestane in postmenopausal patients with primary breast cancer. Breast 21: 40-45.

11. Moy B, Tu D, Pater JL, Ingle JN, Shepherd LE, et al. (2006) Clinical outcomes of ethnic minority women in MA.17: a trial of letrozole after 5 years of tamoxifen in postmenopausal women with early stage breast cancer. Ann Oncol 17: 1637-1643.

12. Stearns V, Johnson MD, Rae JM, Morocho A, Novielli A, et al. (2003) Active tamoxifen metabolite plasma concentrations after coadministration of tamoxifen and the selective serotonin reuptake inhibitor paroxetine. J Natl Cancer Inst 95: 1758-1764.

13. Ingelman-Sundberg M (2005) Genetic polymorphisms of cytochrome P450 2D6 (CYP2D6): clinical consequences, evolutionary aspects and functional diversity. Pharmacogenomics J 5: 6-13.

14. Goetz MP, Kamal A, Ames MM (2008) Tamoxifen pharmacogenomics: the role of CYP2D6 as a predictor of drug response. Clin Pharmacol Ther 83: 160-166.

15. Takei H, Ohsumi S, Shimozuma K, Takehara M, Suemasu K, et al. (2012) Health-related quality of life, psychological distress, and adverse events in postmenopausal women with breast cancer who receive tamoxifen, exemestane, or anastrozole as adjuvant endocrine therapy: National Surgical Adjuvant Study of Breast Cancer 04 (N-SAS BC 04). Breast Cancer Res Treat 133: 227-236.

16. Fallowfield L, Cella D, Cuzick J, Francis S, Locker G, et al. (2004) Quality of life of postmenopausal women in the arimidex, tamoxifen, alone or in combination (ATAC) adjuvant breast cancer trial. J Clin Oncol 22: 4261-4271.

17. Fallowfield LJ, Bliss JM, Porter LS, Price MH, Snowdon CF, et al. (2006) Quality of life in the intergroup exemestane study: a randomized trial of exemestane versus continued tamoxifen after 2 to 3 years of tamoxifen in postmenopausal women with primary breast cancer. J Clin Oncol 24: 910-917.