COMPARISON OF EQ-5D SCORE BETWEEN TREATMENT WITH 4 CYCLES OF ANTHRACYCLINE FOLLOWED BY 4 CYCLES OF TAXANE AND 8 CYCLES OF TAXANE FOR NODE POSITIVE BREAST CANCER PATIENTS AFTER SURGERY: N-SAS BC 02 TRIAL

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OBJECTIVE

To examine the health-related quality of life (HRQOL), we investigated the effect of adjuvant chemotherapy regimens on utility scores assessed by the EQ-5D instrument in a randomized controlled trial for breast cancer patients after surgery.

METHODS

The N-SAS BC 02 trial included the following eligibility criteria: age 18 to 70, node-positive disease, no metastasis (Stage I - IIIA), absence of prior hormone or chemotherapy, and an Eastern Cooperative Oncology Group (ECOG) PS of 0 – 1.

Based on the 2x2 factorial design, the 1,060 eligible patients were randomly assigned to receive one of the following four regimens: (a, the ACP group) four cycles of anthracycline-containing regimens (doxorubicin 60 mg/m2 or epirubicin 75 mg/m2 + cyclophosphamide 600 mg/m2, q3 wks x 4) followed by paclitaxel (175 mg/m2, q3 wks x 4), (b, the ACD group) four cycles of anthracycline followed by docetaxel (75 mg/m2 q3, wks x 4), (c, the PTX group) eight cycles of paclitaxel (175 mg/m2, q3 wks x 8), and (d, the DTX group) eight cycles of docetaxel (75 mg/m2, q3 wks x 8).

The first 300 consecutive patients of the randomized patients from the N-SAS BC 02 trial were included in this HRQOL study (Figure 1). The primary end point was disease-free survival, defined as time from randomization to the first occurrence of any of the defined events. HRQOL and cost-effectiveness were two of the secondary end points.

We performed baseline assessments of the FACT-G, -B, -Taxane and EQ-5D between the time of patient random assignments and the start of chemotherapy. Follow-up assessments were performed before administration of chemotherapy at cycle 3, cycle 5, cycle 7, 7 months and 1 year after starting adjuvant chemotherapy.

To detect differences in utility scores between chemotherapy regimens, longitudinal utility scores from EQ-5D were analyzed based on a linear mixed model using the MIXED procedure in SAS 9.1 (SAS Institute, Cary, NC). Utility scores were analyzed by the model with the baseline scores as the covariate, and group, time and the interaction of time and group as fixed effects

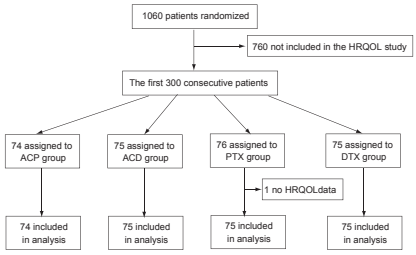

Figure 1: Study design and allocation of patients into treatment groups

RESULTS

Between November 2001 and May 2003, 300 patients were enrolled at 64 centers in Japan. Because there were no HRQOL data for one patient in the PTX group (withdrawal of consent). The baseline characteristics of 299 patients are shown in Table 1.

Numbers and percentages of 299 patients completing the EQ-5D at cycles 3, 5 and 7, at 7 months and 1 year after initiation of treatment were 294 (98%), 287 (96%), 275 (92%), 262 (88%), and 228 (76%), respectively. The percentage of missing values (at least one of the five EQ-5D responses was blank) was approximately 2 percent at each time point.

Mean utility scores and differences from baseline are shown longitudinally by group in Figure 2. The results show that utility scores measured by EQ-5D in the DTX group were lower than in other groups. In addition, the lowest score in the DTX group occurred at 7 months from the start of treatment, although utility scores of the other three groups were lowest at cycle 7 or earlier.

The analysis showed there were significant differences in the “interaction between time and group” , and “group” effects (P-values were 0.0061 and 0.0002, respectively; Table 2). Compared with the DTX group, the utility scores of the ACP and ACD groups were significantly higher (P-values were 0.0048 and <0.0001, respectively), but those of the PTX group were not significantly different (P=0.269).

Table 1: Baseline characteristics of patients shown as number

		ACP (n=74)	ACD (n=75)	PTX (n=75)	DTX (n=75)
Age (years)	Median	54	53	53	51
PS	0	64	63	65	62
	1	5	9	8	7
	Unknown	5	3	2	6
Tumor size	<3	41	42	43	43
	≥3	33	33	32	32
Number of positive lymph nodes	1-3	41	41	41	41
	4-9	18	20	21	21
	>10	15	14	13	13
Surgery	Conserving	31	30	32	31
	Mastectomy	41	45	42	44
	Others	2	0	1	0
Hormone receptor	Positive	29	31	28	29
	Negative	45	44	47	46
HER2 receptor	Positive	17	20	19	18
	Negative	36	31	33	31
	Unknown	21	24	23	26

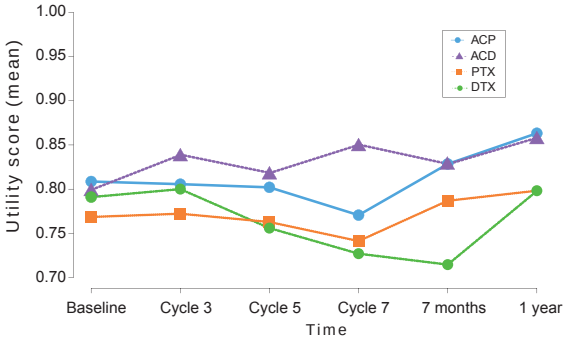

Figure 2: Longitudinal patterns of utility scores by treatment group

Table 2: Results of the linear mixed model analysis

Effect	F-value	P-value
BASELINE	45.75	<.0001 *
GROUP	6.67	0.0002 *
TIME	8.4	<.0001 *
TIME*GROUP	2.33	0.0061 *

Comparison	Difference	P-value	95% CI
ACP vs DTX	0.052	0.0048 *	[0.016 - 0.089]
ACD vs DTX	0.077	<.0001 *	[0.040 - 0.113]
PTX vs DTX	0.021	0.269	[-0.016 - 0.057]
AC followed by taxane vs taxane alone	0.054	<.0001 *	[0.028 - 0.080]
Paclitaxel vs Docetaxel	-0.002	0.889	[-0.028 - 0.024]

CONCLUSION

Our study examined longitudinal utility scores of breast cancer patients during and after four types of chemotherapy in a randomized controlled trial. Although they were similar regimens that include taxane, the mean utility scores and longitudinal patterns of utility scores were different. The results of this study will be beneficial not only for clinical decision-making, but also for appropriate allocation of medical resources.