

Objective and subjective assessment of edema during adjuvant chemotherapy using taxane-containing regimens in a randomized controlled trial; National Surgical Adjuvant Study of Breast Cancer (NSAS-BC) 02

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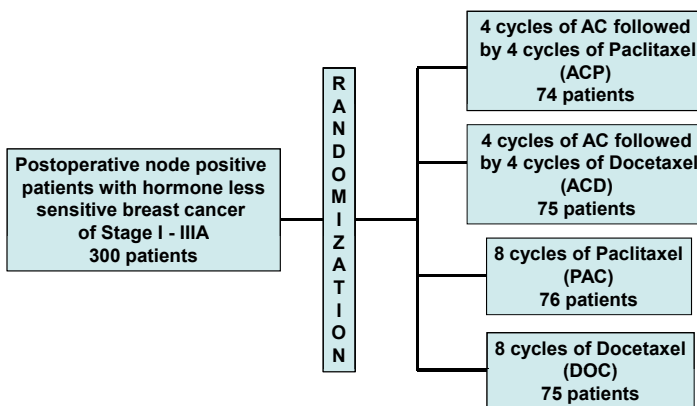
Background

Taxanes are frequently used in treatment of breast cancer (BC) patients. However, some patients treated with taxanes, especially docetaxel (DOC), experience severe edema during and following the treatment. We prospectively assessed body weight and health-related quality of life (HRQOL) related to edema in a randomized controlled trial comparing four taxane-containing regimens in an adjuvant setting.

Patients and Method

We conducted NSAS BC02 trial in which postoperative patients with node positive BC were randomly assigned to receive one of the following four adjuvant chemotherapeutic regimens; (1) ACP regimen: 4 cycles of doxorubicin 60mg/m² plus cyclophosphamide 600mg/m² q3weeks (AC) followed by 4 cycles of paclitaxel (PAC) 175 mg/m² q3weeks, (2) ACD regimen: 4 cycles of AC followed by 4 cycles of DOC 75mg/m² q3weeks, (3) PAC regimen: 8 cycles of PAC, (4) DOC regimen: 8 cycles of DOC. During the study we recorded body weight at baseline (at study entry), on day 1 of each cycle and at 7 months, and every 6 months thereafter. And we asked the patients to answer FACT-B, and -Taxane at baseline, on day 1 of cycle 3, 5, and 7, and at 7 and 12 months. We compared the change of weight and the scores of 4 items regarding edema in FACT-B (B8 (change in weight) and FACT-Taxane (Tax1 [anasarca], Tax2 [edema of hands], and Tax3 [edema of legs or feet]) among the four regimens. Data were analyzed on an intent-to-treat basis. The statistical significance of the differences among the regimens was examined with analysis of covariance and t-test.

Study design



Questions of B8, Tax1, Tax2, and Tax3 in FACT-B and -Taxane

- B8 I am bothered by a change in weight.
- Tax1 I feel bloated.
- Tax2 My hands are swollen.
- Tax3 My legs or feet are swollen.

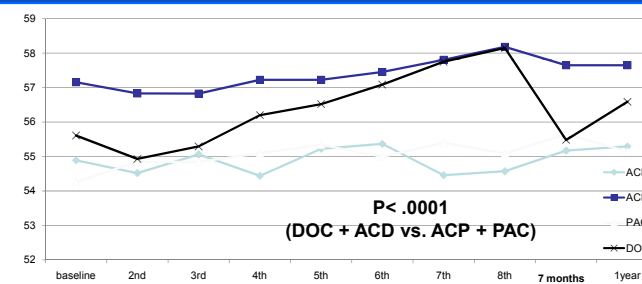
Results

Of 1060 patients who entered N-SAS BC 02 trial, first 300 patients participated in this HRQOL study (ACP 74 patients, ACD 75, PAC 76, and DOC 75). The weight increased markedly and recovered by 7 months in the patients of DTX regimen, increased slightly in those of ACD regimen, and was almost stable in those of ACP and PAC regimens. The difference in the change of weight from the baseline to the 8th cycle between the patients of DOC plus ACD regimens and those of ACP plus PAC regimens was statistically significant ($P < .0001$). The compliance of FACT-B, and -Taxane was high throughout the study period ($> 85\%$ at each point). The scores of B8, Tax1, Tax2, or Tax3 were relatively stable in ACP, ACD, and PAC regimens over the study period, but those of DOC regimen became lower (indicating worse HRQOL) up to 7 months, then recovered to the baseline levels except the scores of Tax2 which were still lower than those of other 3 regimens at 12 months. When the scores of the patients of DOC regimen were compared with those of other 3 regimens combined, the differences were statistically significant in all items of B8 ($P = .0450$), Tax1 ($P = .0016$), Tax2 ($P < .0001$), and Tax3 ($P < .0001$).

Patient and tumor characteristics

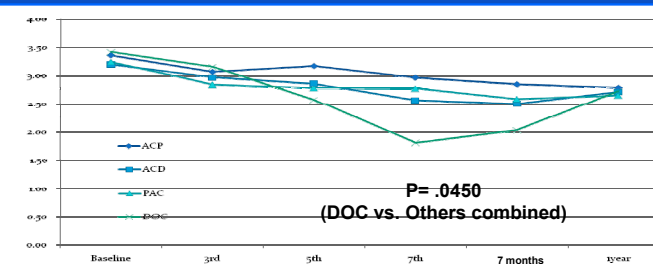
		ACP	ACD	PAC	DOC
Age at entry	mean	53.40	52.7	50.6	50.1
	standard deviation	7.7	9.2	9.9	8.5
Tumor size	range	28 - 68	28 - 70	26 - 66	30 - 67
	less than 3 cm	41	42	44	43
	3 cm or larger	33	33	32	32
Pathological nodal status	1 - 3	41	41	42	41
	4 - 9	18	20	21	21
	10 or more	15	14	13	13
Hormone receptor status	ER+ PgR+	0	0	0	0
	ER+ PgR-	21	17	18	19
	ER- PgR+	7	13	10	10
	ER- PgR-	45	45	47	46
	PgR unknown	1	0	1	0
HER2 status	0 or 1+	36	31	34	31
	2+	4	5	4	5
	3+	13	15	15	13
	unknown	21	24	23	26
Type of surgery	mastectomy	33	30	33	31
	breast conservation	41	45	43	44

Body weight change by treatment group

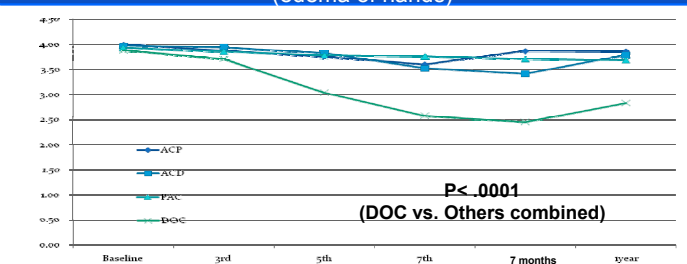


		baseline	2nd	3rd	4th	5th	6th	7th	8th	7 months	1year
ACP	mean	54.9	54.5	55.1	54.4	55.2	55.4	54.5	54.6	55.2	55.3
	sd	8.8	8.4	9.1	8.5	9.3	8.9	8.2	8.1	9.4	8.6
ACD	mean	57.2	56.1	56.5	57.2	57.2	57.5	57.8	58.2	57.7	57.7
	sd	9.4	8.4	8.2	8.6	8.8	9.5	8.7	8.5	9.4	8.6
PAC	mean	54.3	54.9	54.8	55.1	55.3	55.0	55.4	55.1	55.7	55.2
	sd	8.8	8.8	8.9	8.9	9.1	9.1	9.4	55.1	8.5	9.3
DOC	mean	55.6	54.9	55.3	56.2	56.5	57.1	57.8	58.2	55.5	56.6
	sd	8.1	8.0	8.2	8.3	8.5	8.4	8.2	8.3	8.3	8.5

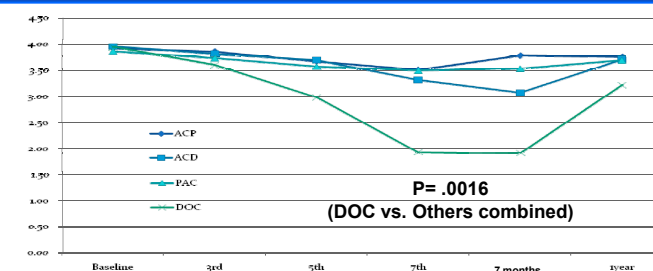
Scores of Item B8 in FACT-B (change in weight)



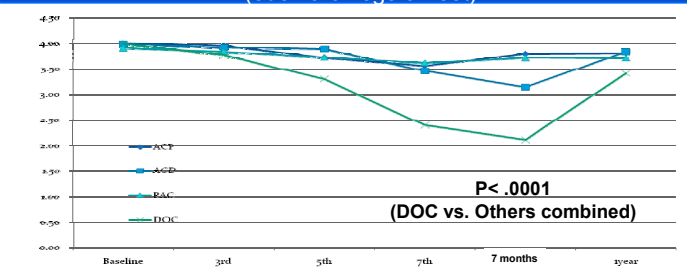
Scores of Item Tax2 in FACT-Taxane (edema of hands)



Scores of Item Tax1 in FACT-Taxane (anasarca)



Scores of Item Tax3 in FACT-Taxane (edema of legs or feet)



Discussion

The patients who received 8 cycles of DOC were agonized by chemotherapy (CT)-related edema. However, the agony seemed to disappear by 6 months after the completion of CT except for that of edema of hands. The reason why only the scores of Tax2 (edema of hands) did not recover at 12 months in the patients of DOC regimen is suspected to be the ipsilateral hand and arm edema affected by axillary dissection which might have lasted for a long time.