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Health-related Quality-of-Life and Psychological Distress of Breast Cancer Patients after Surgery during Phase III Randomized Trial Comparing further Tamoxifen with Switching to Anastrozole after Adjuvant Tamoxifen for 1 to 4 years : N-SAS BC 03

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Abstract

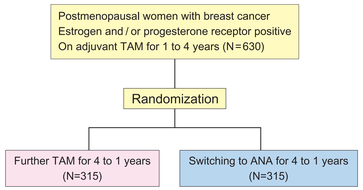
Background : Although tamoxifen (TAM) has been a standard adjuvant endocrine therapy for postmenopausal women with breast cancer for a long time, aromatase inhibitors (AIs) are regarded as alternatives of TAM now. The results of the randomized controlled trials comparing TAM with AIs in the adjuvant setting have shown better disease free survival in favor of AIs. However, very limited data have been reported regarding heath-related quality of life (HRQOL) outcomes of the patients who changed their adjuvant treatment from several years of TAM to AI.

Patients and Methods : Recurrent-free breast cancer patients were serially enrolled in a phase III randomized trial : National Surgical Adjuvant Study of Breast Cancer (N-SAS BC) 03. Primary endpoints of the N-SAS BC 03 trial were disease-free survival and adverse events. HRQOL and psychological distress were included in secondary endpoints. Eligible patients were postmenopausal women who had received definitive surgery for primary breast cancer with positive hormone receptor (s), and had been taking TAM for 1 to 4 years after the surgery. They were randomly assigned to continue TAM or to switch from TAM to anastrozole (ANA) after obtaining written informed consent. They were asked to answer patient-administered instruments to assess HRQOL (FACT-B [breast cancer scale] and FACT-ES [endocrine symptom scale]) and psychological distress (CES-D : Center for Epidemiologic Studies Depression scale) at the randomization (baseline), 3 months, and 1 year after the randomization. HRQOL and psychological distress scores during this period were compared using t-test and the general linear model with correlated errors.

Results : There was no difference in demographic and medical characteristics between the two treatment groups. The response rates of the questionnaires were 93.5% and 92.0% at baseline and 3 months, respectively. At baseline 589 patients (295 in TAM group and 294 in ANA group) answered them. The scores of FACT-G, FACT-B and FACT-ES were significantly better in TAM group than in ANA group ($P=0.012$, 0.010 and 0.015, respectively). However, any significant differences were not found between the two treatment groups for the scores of CED-D, and subscales of FACT-G, FACT-B, and FACT-ES.

Conclusion : Further TAM treatment after adjuvant TAM for 1 to 4 years may provide breast cancer patients with better HRQOL comparing with switching to ANA.

Study Design



Timing of Measurement of HRQOL and Psychological Distress

Questionnaires used : FACT-G, FACT-B, FACT-ES CES-D

Patient Characteristics

	TAM group (N=315)	ANA group (N=315)	*P* value
Age at randomization (mean±SD)	59.9 ± 7.07	59.4 ± 7.29	0.41
Tumor size (cm) (mean±SD)	2.28 ± 1.56	2.29 ± 1.27	0.96
Receptor status			
Estrogen receptor			
positive	290 (92.1%)	289 (91.7%)	0.88
negative	25 (7.9%)	26 (8.3%)	
Progesterone receptor			
positive	247 (78.4%)	247 (78.4%)	1
negative	68 (21.6%)	68 (21.6%)	
No. of involved nodes			
0	187 (59.4%)	184 (58.4%)	0.66
1-3	91 (28.9%)	94 (29.8%)	
4-9	27 (8.6%)	21 (6.7%)	
≧10	10 (3.2%)	16 (5.1%)	
Type of surgery			
Mastectomy	155 (49.2%)	155 (49.2%)	1
Breast-conserving surgery	160 (50.8%)	160 (50.8%)	
(Neo) Adjuvant chemotherapy			
yes	149 (47.3%)	147 (46.7%)	0.87
no	166 (52.7%)	168 (53.3%)	
Duration on TAM at randomization (months)			
median	25.0	25.4	0.88
range	12.2 - 48.7	12.2 - 49.6	

Compliance

	Baseline	3 months	1 year
TAM group	94%	91%	71%※
ANA group	93%	93%	71%※

※Although the minimal follow-up period of the whole cohort did not reach 1 year yet, the number of the patients in each group who entered the trial was used as a denominator.

Scores at Baseline

	TAM group	ANA group	*P* value (t-test)
FACT-G			
Physical well-being	25.0 ± 3.2	25.0 ± 3.4	0.91
Social well-being	25.0 ± 7.4	24.6 ± 8.5	0.47
Emotional well-being	18.3 ± 4.1	18.2 ± 4.2	0.75
Functional well-being	22.1 ± 5.2	21.8 ± 5.6	0.50
FACT-BCS	23.3 ± 5.3	23.7 ± 4.9	0.32
FACT-ES	59.5 ± 9.2	60.5 ± 8.5	0.13
FACT-G total	90.5 ± 13.3	89.7 ± 15.4	0.54
FACT-B total	113.7 ± 16.2	113.4 ± 17.8	0.82
FACT-ES total	149.9 ± 18.3	150.3 ± 19.4	0.80
CES-D	49.6 ± 7.1	49.3 ± 7.5	0.61
	(mean ± SD)	(mean ± SD)	

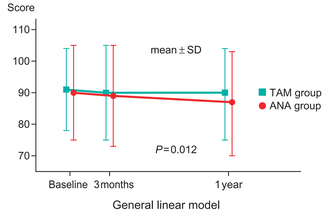
Scores at 3 months

	TAM group	ANA group	*P* value (t-test)
FACT-G			
Physical well-being	25.0 ± 3.4	24.8 ± 3.8	0.68
Social well-being	24.1 ± 8.1	23.1 ± 9.2	0.15
Emotional well-being	18.9 ± 3.9	18.8 ± 4.0	0.81
Functional well-being	21.5 ± 5.3	21.7 ± 5.7	0.65
FACT-BCS	23.7 ± 5.3	23.6 ± 5.2	0.73
FACT-ES	60.6 ± 8.8	60.5 ± 9.5	0.94
FACT-G total	89.2 ± 15.0	88.4 ± 16.0	0.50
FACT-B total	112.9 ± 17.8	112.0 ± 18.6	0.53
FACT-ES total	149.8 ± 19.8	148.8 ± 21.2	0.56
CES-D	49.6 ± 7.6	49.4 ± 7.4	0.84
	(mean ± SD)	(mean ± SD)	

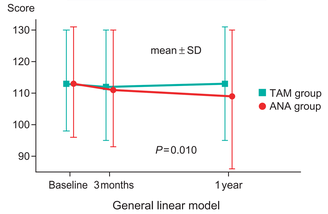
Scores at 1 year

	TAM group	ANA group	*P* value (t-test)
FACT-G			
Physical well-being	24.9 ± 3.7	24.2 ± 4.3	0.06
Social well-being	24.0 ± 8.1	23.1 ± 8.9	0.25
Emotional well-being	18.8 ± 3.9	18.4 ± 4.7	0.29
Functional well-being	22.0 ± 5.2	21.2 ± 5.4	0.14
FACT-BCS	23.8 ± 5.2	23.5 ± 5.8	0.55
FACT-ES	60.8 ± 8.3	61.2 ± 9.7	0.68
FACT-G total	**89.8 ± 14.4**	**86.8 ± 16.5**	**0.04**
FACT-B total	**113.6 ± 17.4**	**110.2 ± 19.9**	**0.05**
FACT-ES total	150.5 ± 19.4	147.8 ± 22.6	0.17
CES-D	49.5 ± 7.3	48.2 ± 8.2	0.09
	(mean ± SD)	(mean ± SD)	

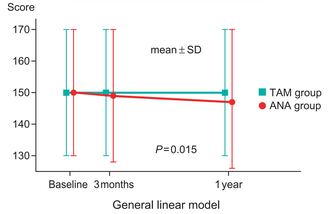
FACT-G total scores



FACT-B total scores



FACT-ES total scores



Consistency reliability

	Cronbach's alpha coefficients		
	At baseline	3 months	1 year
FACT-G			
Physical well-being	0.80	0.81	0.87
Social well-being	0.87	0.88	0.89
Emotional well-being	0.76	0.80	0.84
Functional well-being	0.90	0.90	0.89
FACT-BCS	0.63	0.63	0.70
FACT-ES	0.88	0.88	0.89
FACT-G total	0.89	0.91	0.92
FACT-B total	0.90	0.91	0.92
FACT-ES total	0.91	0.92	0.94
CES-D	0.90	0.89	0.92

Correlation Matrix at Baseline

	Phy	FACT-G Soc	FACT-G Emo	FACT-G Func	FACT -BCS	FACT -ES	FACT-G Total	FACT-B Total	FACT-ES Total	CES-D
FACT-G										
Physical	1.00	0.06	0.46	0.33	0.46	0.50	0.52	0.58	0.63	0.48
Social		1.00	0.10	0.44	0.09	0.01	0.76	0.67	0.59	0.25
Emotional			1.00	0.37	0.46	0.32	0.59	0.64	0.60	0.58
Functional				1.00	0.23	0.14	0.80	0.75	0.68	0.47
FACT-BCS					1.00	0.55	0.38	0.63	0.55	0.45
FACT-ES						1.00	0.27	0.39	0.68	0.44
FACT-G total							1.00	0.96	0.89	0.59
FACT-B total								1.00	0.92	0.64
FACT-ES total									1.00	0.67
CES-D										1.00

Pearson correlation coefficients

Correlation Matrix at 3 months

	Phy	FACT-G Soc	FACT-G Emo	FACT-G Func	FACT -BCS	FACT -ES	FACT-G Total	FACT-B Total	FACT-ES Total	CES-D
FACT-G										
Physical	1.00	0.08	0.53	0.36	0.54	0.55	0.55	0.62	0.66	0.56
Social		1.00	0.18	0.43	0.04	0.04	0.77	0.67	0.60	0.27
Emotional			1.00	0.46	0.55	0.43	0.64	0.70	0.67	0.63
Functional				1.00	0.28	0.24	0.80	0.76	0.71	0.55
FACT-BCS					1.00	0.57	0.39	0.62	0.55	0.50
FACT-ES						1.00	0.34	0.46	0.70	0.52
FACT-G total							1.00	0.96	0.91	0.64
FACT-B total								1.00	0.93	0.69
FACT-ES total									1.00	0.71
CES-D										1.00

Pearson correlation coefficients

Correlation Matrix at 1 year

	Phy	FACT-G Soc	FACT-G Emo	FACT-G Func	FACT -BCS	FACT -ES	FACT-G Total	FACT-B Total	FACT-ES Total	CES-D
FACT-G										
Physical	1.00	0.03	0.51	0.41	0.51	0.52	0.57	0.63	0.64	0.52
Social		1.00	0.11	0.44	0.08	0.07	0.74	0.64	0.57	0.25
Emotional			1.00	0.45	0.58	0.54	0.63	0.69	0.69	0.67
Functional				1.00	0.38	0.33	0.81	0.78	0.74	0.60
FACT-BCS					1.00	0.60	0.47	0.68	0.60	0.58
FACT-ES						1.00	0.43	0.53	0.75	0.55
FACT-G total							1.00	0.97	0.92	0.67
FACT-B total								1.00	0.94	0.73
FACT-ES total									1.00	0.73
CES-D										1.00

Pearson correlation coefficients

Discussion

The total scores of FACT-G, FACT-B and FACT-ES were significantly better in TAM group than in ANA group. Although the scores of TAM group were stable through 1 year, those of ANA group became worse gradually. There may have been a bias in favor of HRQOL in TAM group in this trial because the patients who entered this trial had been taking TAM for several years without severe problems, namely those who had problems by taking TAM possibly discontinued TAM before entering this trial.

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