

Abstract GS6-03

Symptoms and health-related quality of life on endocrine therapy alone (E) versus chemoendocrine therapy (CT+E): TAILORx patient-reported outcomes results

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Background: Rationale for TAILORx Patient-Reported Outcomes (PROs)

- **TAILORx design: endocrine therapy +/- chemotherapy**
 - novel opportunity to evaluate effects of CT
 - common and distressing symptoms, including cognitive impairment, fatigue and endocrine symptoms
- **Data on the unique contribution of chemotherapy**
 - acute and long-term symptoms
 - improve understanding of mechanisms, inform clinical decision-making and inform expectations

Methods: PRO Objectives

Primary PRO Objective:

- Compare changes in patient-reported cognitive impairment between CT+E and E alone from baseline to 3 months

Secondary Objectives:

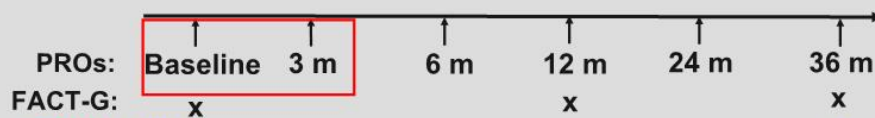
- Compare cognitive impairment change scores between CT+E and E alone at 6, 12, 24 and 36 months
- Compare key symptoms and health-related quality of life acutely and long-term
 - Fatigue
 - Endocrine symptoms
- Examine differences by treatment arm based on menopausal status

Methods: Patient-Reported Outcomes

Domain	PRO	# items	Range	Sample item	Measures
Primary outcome:					
Patient-reported Cognitive Function	Functional Assessment of Cancer Therapy (FACT) - Cognitive Function V3 (FACT-Cog) Perceived Cognitive Impairment (PCI)^{1,2}	20	0-80	Trouble concentrating Thinking has been slow Work harder than usual to keep track	
Secondary outcomes:					
Fatigue	FACT – Fatigue	13	0-52	Fatigue, Trouble finishing things	
Endocrine Symptoms	FACT – Endocrine symptoms	19	0-76	Hot flashes/hot flushes, Night sweats Vaginal dryness	
Health-related QOL	FACT – General	27	0-108	Feel ill Content with the quality of life	

- Items rated on 5-point Likert scale based on past 7 days

¹Wagner et al. J Supp Oncol 2007
²Jacobs et al. J Pain Sym Manag 2007



Methods: Primary Endpoint and Statistical Considerations

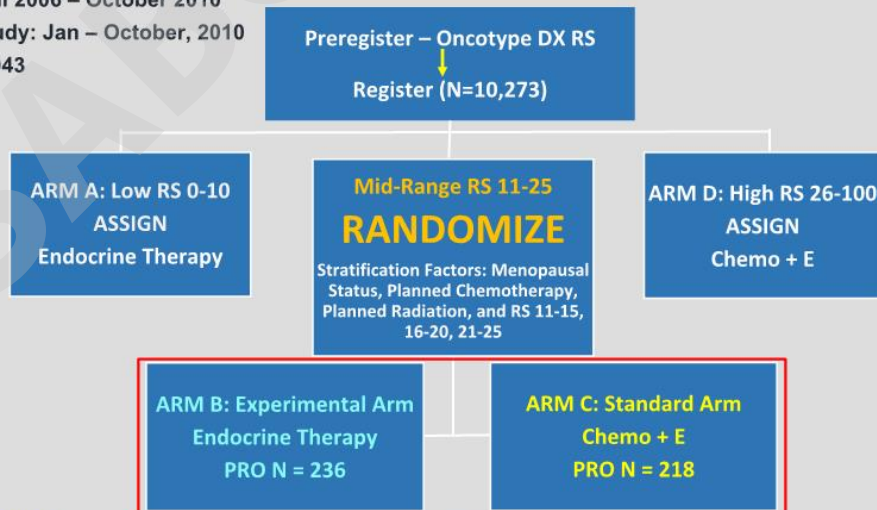
- **Primary end point**
 - FACT-Cog Perceived Cognitive Impairment scale change scores from baseline to 3 months
 - Change score > 0.3 SD defined a priori as clinically meaningful (assuming 15.0 SD = > 4.5 points)
 - Per protocol population (treatment received)
- **Statistical considerations and sample size**
 - 90% power to detect 0.3 SD (4.5-point) difference in mean change scores from baseline to 3 months between CT+E versus E alone (2-sided 5% level test)
 - Planned subset analysis for pre- and postmenopausal groups
 - 90% power to detect differences corresponding to 0.38 and 0.49 SDs
- **Accrual goal = 1000**
 - 640 randomized (RS 11-25)
 - 235 per arm/470 treated per protocol (CT+E and E alone)

TAILORx Methods: Treatment Assignment & Randomization

Accrual: April 2006 – October 2010

PRO Substudy: Jan – October, 2010

PRO N = 1,043



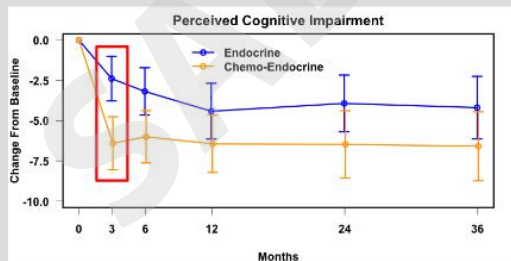
Results: Patient Characteristics and Treatment

	RS 11 to 25	
	Arm B E	Arm C Chemo+E
Sample size	236	218
Median Age (range)	56 (32, 75)	55 (35, 75)
Premenopausal	31%	36%
Initial Endocrine Therapy		
Tamoxifen	36%	38%
AI	58%	57%
OFS +/- Other	3%	0%
Other or None	2%	5%
Chemotherapy		
TC	--	70%
Anthracycline +/- taxane	--	20%
CMF	--	8%
Other	--	2%
Baseline PRO mean scores (SD)		
FACT-Cog PCI	68.0 (12.5)	69.8 (12.4)
Fatigue	39.8 (10.3)	42.4 (9.2)
Endocrine Symptoms	64.6 (9.0)	65.6 (8.3)
FACT-General	89.3 (14.2)	90.3 (12.2)

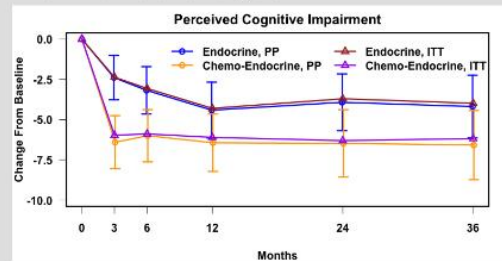
- PRO substudy sample generally comparable to TAILORx trial on demographic and clinical characteristics
- Proportion of patients age > 65 higher in E arm (19%) versus C+E (11%), p = 0.05

Results: Primary Outcome Change in Cognitive Impairment Baseline to 3 months

Per protocol analysis



Intent to treat analysis

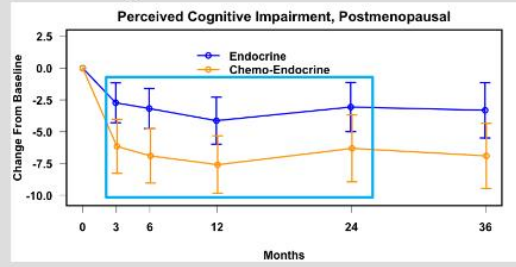
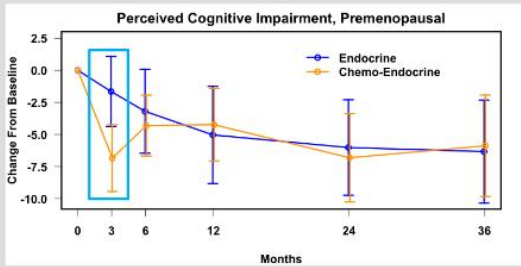


- Difference between CT+E and E change scores statistically significant³
 - 3 months: -3.82, p < 0.001
 - 6 months: -2.62, p < 0.05
- CT+E: change from baseline > 0.3 SD (observed SD = 12.5, > 3.75 CMID)
- Similar pattern of results with intent to treat analysis

³Wagner et al. ASCO 2012

Results: Secondary Objective Change in Cognitive Impairment by Menopausal Status

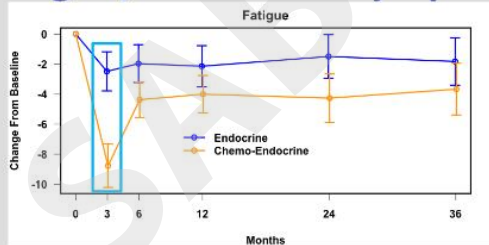
➤ Menopausal status by treatment interactions were non-significant



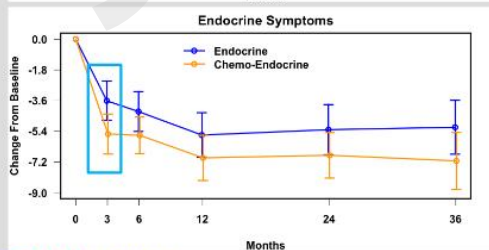
➤ Premenopausal: difference between CT+E and E change scores
- 3 months, -4.75, $p = 0.01$

➤ Postmenopausal: difference between CT+E and E change scores
- 3 months, -3.34, $p < 0.01$
- 6 months, -3.69, $p < 0.01$
- 12 months, -3.39, $p < 0.05$
- 24 months, -3.26, $p = 0.05$

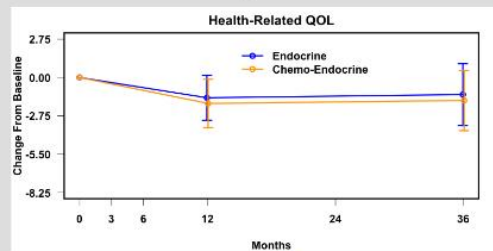
Results: Secondary Objective Fatigue, Endocrine Symptoms and HRQL



➤ Difference between CT+E and E change scores statistically significant at 3 months
- Fatigue: -5.32, $p < 0.0000001$
- Endocrine symptoms: -1.62, $p < 0.05$



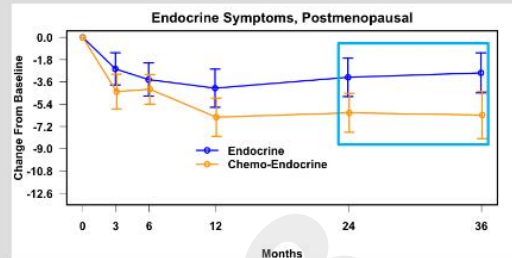
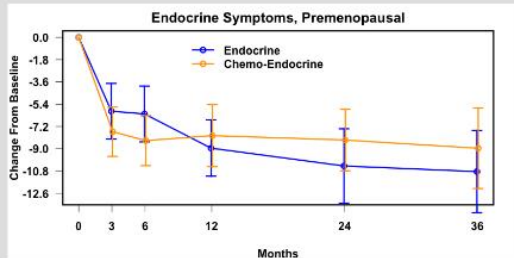
➤ Fatigue: Menopausal status by treatment interaction non-significant



Results: Secondary Objective

Change in Endocrine Symptoms by Menopausal Status

- Menopausal status by treatment interactions were significant
 - 24 months (p=0.02); 36 months (p=0.02)
- Difference between CT+E and E increases over time for postmenopausal patients



- Premenopausal women had greater increases in endocrine symptoms than postmenopausal women at all follow-up time points

Summary of Results

- First comparison of symptoms among breast cancer patients randomized to chemoendocrine therapy or endocrine therapy alone
- Patient-reported outcomes precisely capture patients' experiences with treatment and underscore the value of RS-guided treatment
- Chemotherapy associated with greater cognitive impairment, fatigue, and endocrine symptoms acutely (3-6 months) during treatment
- Cognitive impairment and fatigue comparable between treatment arms at follow-up and persist in both groups
 - Gradual increase in cognitive impairment among E alone converges with CT+E at follow-up
 - Fatigue improves among CT+E to converge with E alone at follow-up
- Premenopausal women had more long-term endocrine symptoms
- Long-term health-related quality of life comparable

Conclusions

- Women with breast cancer receiving chemotherapy will experience acute symptoms, however long-term symptom profile and HRQL is generally comparable to endocrine therapy alone
- Although both groups experience lingering symptoms, scores appear to stabilize at 12 months and beyond
- Patient-reported data on extent and duration of symptoms associated with chemotherapy can inform clinician and patient decision-making and expectations for long-term well-being

TAILORx Acknowledgments

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Joseph A. Sparano, MD, TAILORx Study Chair



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10,273 TAILORx
Volunteers
Pioneers
in Pink

Also supported by

