Patient-reported Cognitive Impairment in women participating in the RxPONDER trial (SWOG S1007) by menopausal status

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On Behalf of the RxPonder Investigators

Disclosures

- Consulting/honoraria: Gilead, Puma

Background

- Breast cancer treatment is associated with cancer-related cognitive impairment (CRCI)
- Effect of endocrine therapy (ET) vs chemotherapy followed by endocrine therapy (CET) on CRCI is not well understood
- Unknown whether menopausal status affects CRCI

Brezden JCO 2000; Ahles JCO 2012;Whittaker Sci Rep 2022

RxPONDER Schema and PRO Substudy

Key Entry Criteria

- Women age ≥ 18 yrs
- HR+HER2- breast cancer with 1-3 LN+ without distant metastasis
- Axillary staging by SLNB or ALND
- Recurrence Score 0-25

REGISTRATION

RANDOMIZATION

Arm 1:
Chemotherapy Followed by Endocrine Therapy **N = 274 pts**

Arm 2:
Endocrine Therapy Alone **N = 294 pts**

Overall N = 5,083 pts

PRO substudy
HRQoL questionnaire baseline, 6mo, 12mo and 36mo after randomization

Substudy N = 568 pts

ALND = Axillary Lymph Node Dissection, SLNB = Sentinel Lymph Node Biopsy

RxPONDER PRO Substudy

- Consecutive English-speaking US patients invited to participate from Feb 2011- Dec 2012 (goal n=500)
- HRQOL questionnaires at baseline (after randomization), and 6 mo, 12 mo, 36 mo
  - PROMIS Perceived Cognitive Function Concerns – 8 selected questions
  - Also PROMIS Anxiety & Fatigue, and EQ-5D
- Primary endpoint: Mean cognitive function score by treatment arm and menopausal status
  - T-scores: reference population with mean score 50, SD 10
  - Higher score = better cognitive function
  - Change of 3 units is clinically meaningful (0.3 SD)
- Analysis:
  - Intent to treat
  - Generalized estimating equations (GEE) model was fit to the three follow-up timepoints adjusting for baseline score, treatment arm and timepoint
  - Change from baseline and Odds of clinically meaningful worse cognitive function

VII. PROMIS Cognitive Function Concerns

Please respond to each item by marking one box per row.

In the past 7 days...	Never (0)	Rarely (Once) (1)	Sometimes (two or three times) (2)	Often (about once a day) (3)	Very Often (several times a day) (4)
I have had trouble forming thoughts	☐	☐	☐	☐	☐
My thinking has been slow	☐	☐	☐	☐	☐
I have had trouble concentrating	☐	☐	☐	☐	☐
I have had to work really hard to pay attention or I would make a mistake	☐	☐	☐	☐	☐
It has seemed like my brain was not working as well as usual	☐	☐	☐	☐	☐
I have had to work harder than usual to keep track of what I was doing	☐	☐	☐	☐	☐
I have had trouble shifting back and forth between different activities that require thinking	☐	☐	☐	☐	☐
My problems with memory, concentration, or making mental mistakes have interfered with the quality of my life	☐	☐	☐	☐	☐

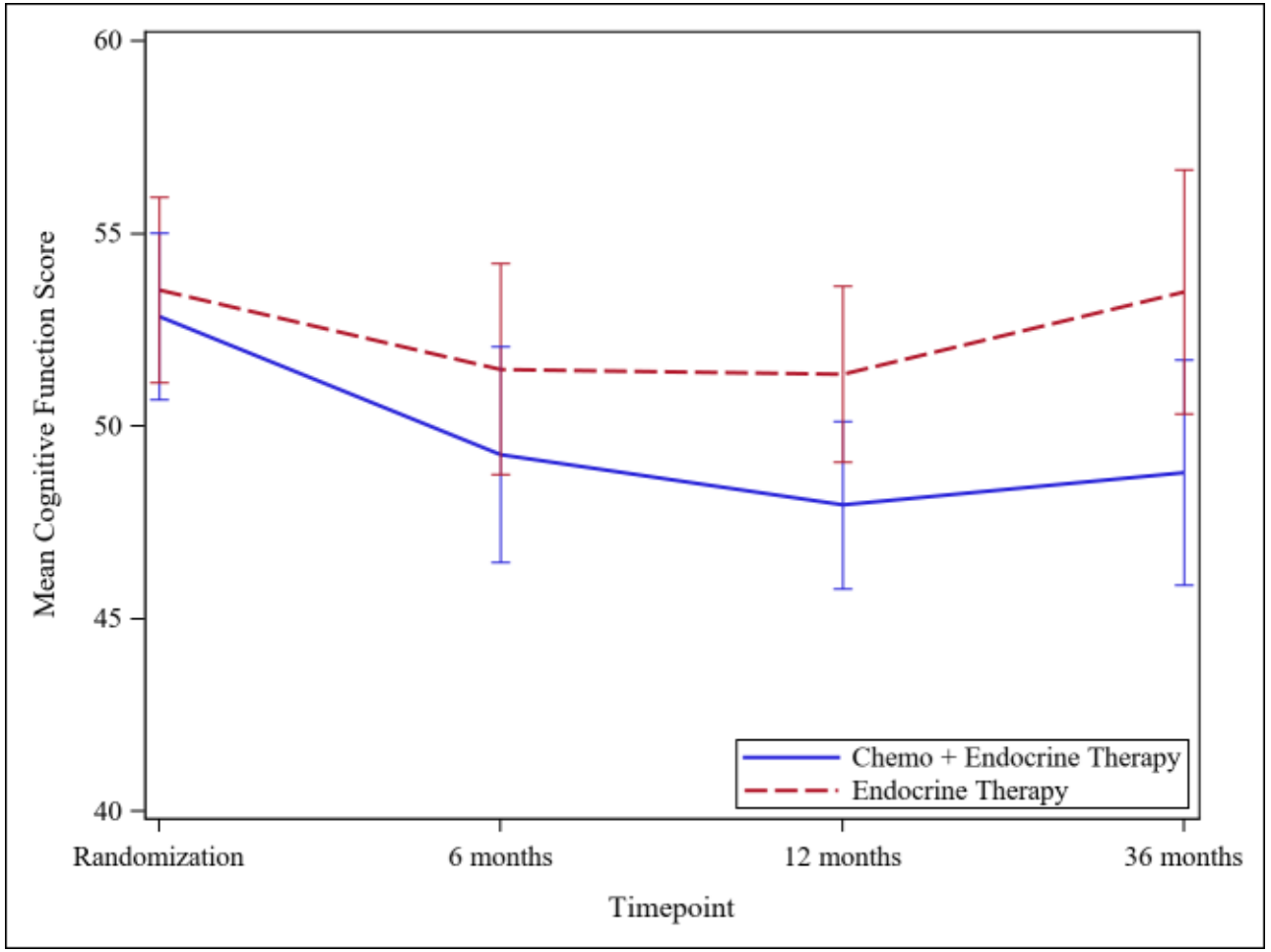
Baseline Characteristics: Premenopausal

Baseline Variable	CET (n=65)	ET (n=74)	All Participants (n=139)
Age, median (range)	48 (28-56)	47 (30-54)	48 (28-56)
Age category, n (%)			
<40	5 (7.7)	6 (8.1)	11 (7.9)
40-49	32 (49.2)	50 (67.6)	82 (59.0)
50-59	28 (43.1)	18 (24.3)	46 (33.1)
Race, n (%)			
White	54 (83.1)	61 (82.4)	115 (82.7)
Black	8 (12.3)	5 (6.8)	13 (9.4)
Asian	0 (0.0)	5 (6.8)	5 (3.6)
Unknown/not reported	3 (4.6)	3 (4.1)	6 (4.3)
Ethnicity, n(%)			
Not Hispanic	57 (87.7)	61 (82.4)	118 (84.9)
Hispanic	4 (6.2)	10 (13.5)	14 (10.1)
Unknown/not reported	4 (6.2)	3 (4.1)	7 (5.0)
Recurrence Score			
0-13	20 (30.8)	34 (46.0)	54 (38.9)
14-25	45 (69.2)	40 (54.1)	85 (61.2)

Baseline Characteristics: Postmenopausal

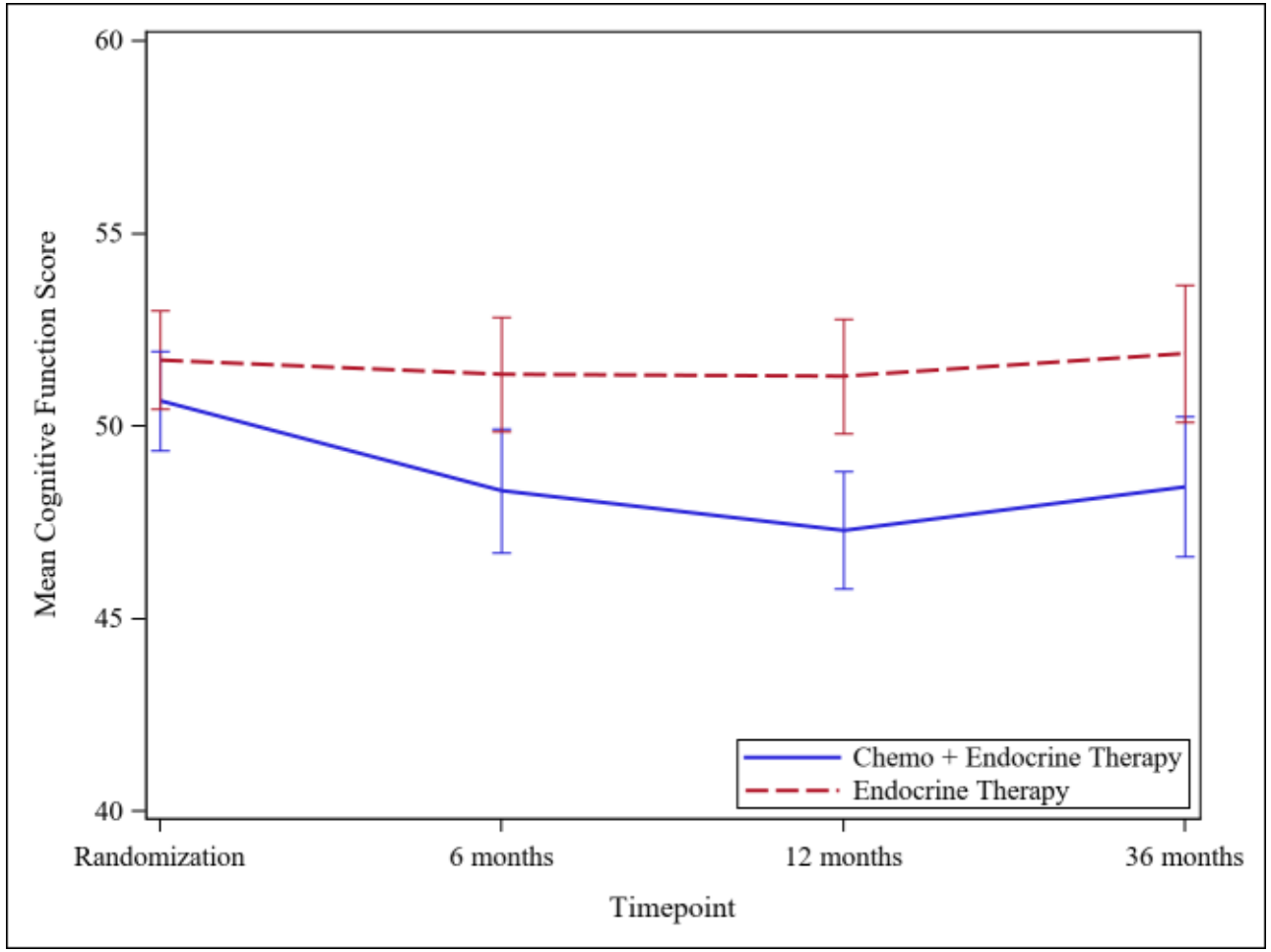
Baseline Variable	CET (n=209)	ET (n=220)	All Participants (n=429)
Age, median (range)	63 (37-88)	62 (46-86)	62 (37-88)
Age category, n (%)			
<49	5 (2.4)	4 (1.8)	9 (2.1)
50-59	71 (34.0)	85 (38.6)	156 (36.4)
≧60	133 (63.6)	131 (59.6)	264 (61.6)
Race, n (%)			
White	177 (84.7)	184 (83.6)	361 (84.2)
Black	22 (10.5)	19 (8.6)	41 (9.6)
Asian/Pacific Islander	2 (1.0)	5 (2.3)	7 (2.6)
Native American	0 (0.0)	3 (1.4)	3 (0.7)
More than one race	0 (0.0)	2 (0.9)	2 (0.5)
Unknown/not reported	8 (3.8)	7 (3.2)	15 (3.5)
Ethnicity, n(%)			
Not Hispanic	191 (91.4)	202 (91.8)	393 (91.6)
Hispanic	9 (4.3)	11 (5.0)	20 (4.7)
Unknown/not reported	9 (4.3)	7 (3.2)	16 (3.7)
Recurrence Score			
0-13	90 (43.1)	87 (39.6)	177 (41.3)
14-25	119 (56.9)	133 (60.5)	252 (58.7)

Mean Cognitive Function Score: Premenopausal



Total n=139					
	CET	65	43	44	36
	ET	74	55	56	39

Mean Cognitive Function Score - Postmenopausal

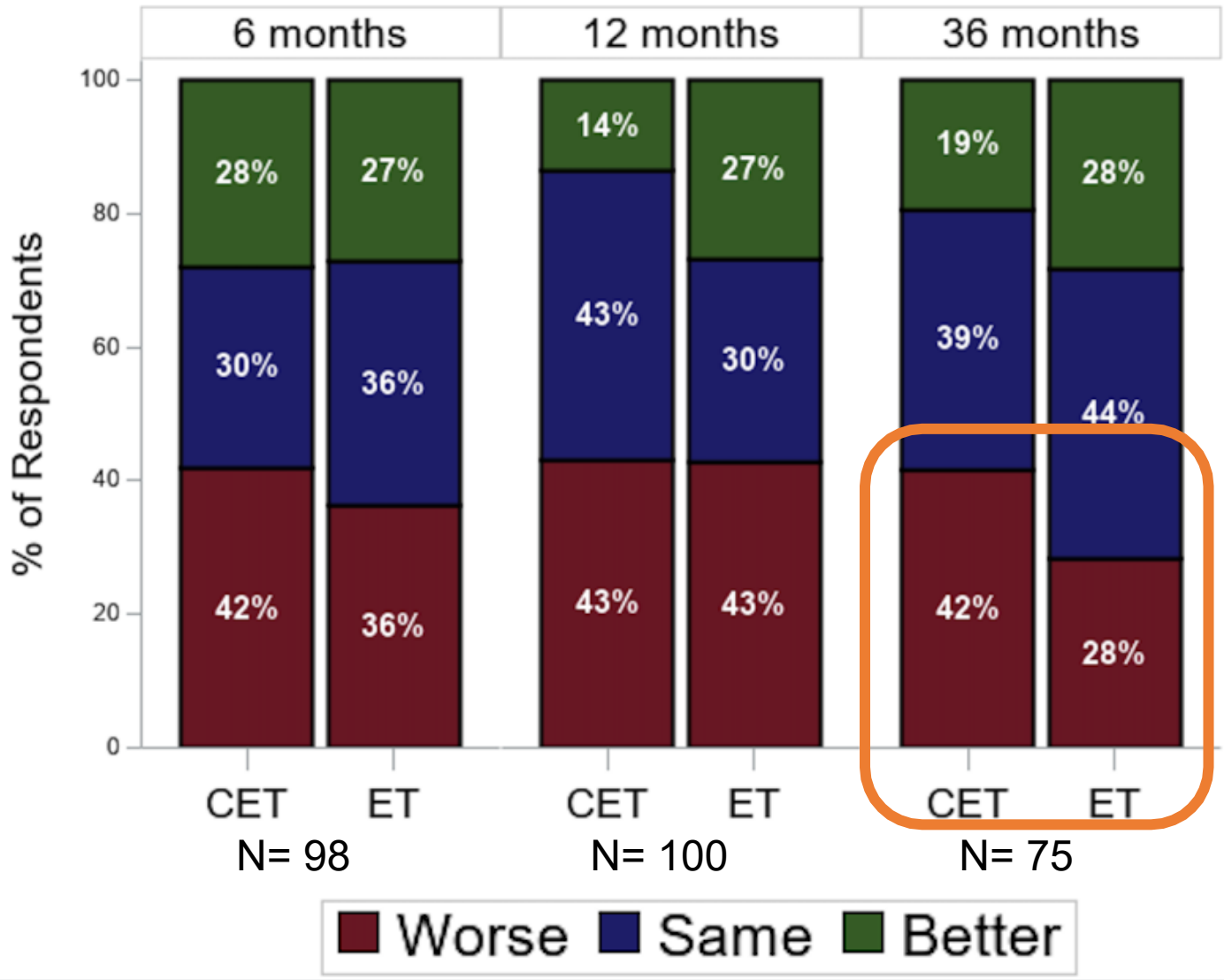


Total n=429	CET	209	159	149	122
	ET	220	184	182	137

Comparisons of Mean Cognitive Function Score by menopausal status

Menopausal status	Treatment Arm	Timepoint				Longitudinal mean score difference
		Randomi-zation	6 months	12 months	36 months	
Premenopausal	CET	52.84	49.27	47.95	48.80	-3.02 (p=0.01)
	ET	53.23	51.49	51.35	53.50	
Postmenopausal	CET	50.65	48.32	47.30	48.43	-2.36 (p<0.003)
	ET	51.73	51.35	51.30	51.89	

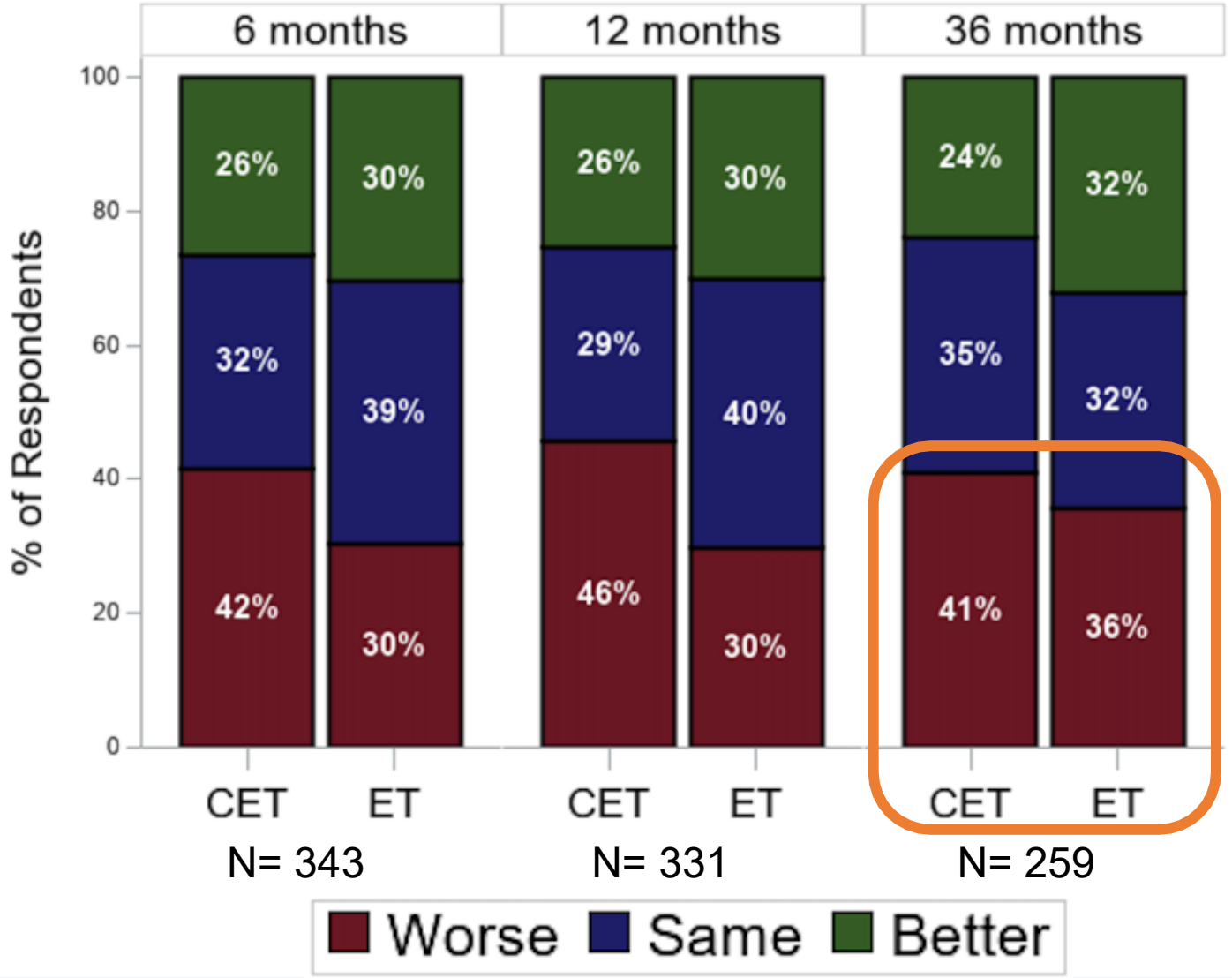
Change from baseline: Premenopausal



Clinically meaningful = Change in cognitive function score of 3 points from baseline

Increase ≥ 3 = Better
Decrease ≥ 3 = Worse

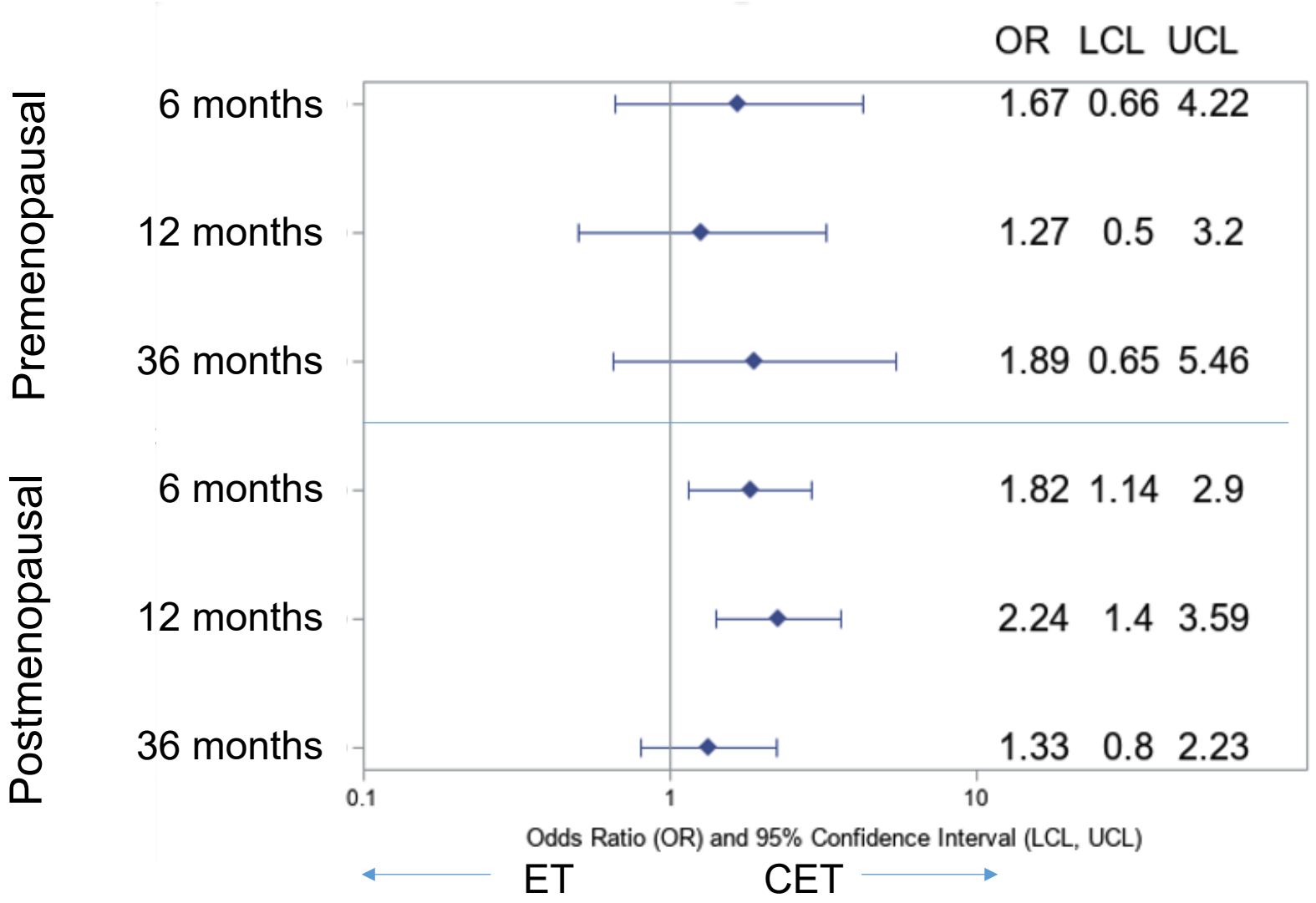
Change from baseline: Postmenopausal



Clinically meaningful = Change in cognitive function score of 3 points from baseline

Increase ≥ 3 = Better
Decrease ≥ 3 = Worse

Odds of Having Worse Cognitive Function



OR = odds ratio
LCL = lower confidence limit
UCL = upper confidence limit

Conclusion

- CET has greater negative effect on CRCI compared to ET alone in both pre- and post-menopausal women
- CRCI seems to persist over time in a significant proportion of patients
  - These findings deviate from an analysis of CRCI in participants of the TAILORx trial
- Limitations:
  - small sample size – particularly in the premenopausal group
  - drop-out over time
  - no adherence data for ET
  - unknown menopausal status change during follow-up

Wagner JCO 2020

Future Directions

- Investigate CRCI in a more diverse population
- Understand the predictors of CRCI and cognitive function recovery
- Anxiety and fatigue PRO analysis at poster session P6-05-06
  - Patient-reported anxiety and fatigue in women enrolled in the RxPONDER trial (SWOG S1007) by menopausal status
- Forthcoming analysis on interactions between anxiety, fatigue, CRCI and overall QOL

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