

Supplemental Tables for:
Tamoxifen Dose Escalation in Patients with Diminished Cyp2d6 Activity Normalizes Endoxifen Concentrations Without Increasing Toxicity
Daniel L Hertz et al.

Table S1. Baseline Endoxifen Concentrations by Race, Across and Within CYP2D6 Phenotype Groups (n=344)

Phenotype	n	White	Black	p-value (white vs. black)
		Mean (ng/mL)	Mean (ng/mL)	
Combined	292	7.90	7.51	0.63
UM	4	6.85	14.58	0.14
EM	105	10.07	9.69	0.86
IM	167	6.97	7.09	0.88
PM	16	3.58	0.8	0.34

¹p-value for comparison of endoxifen concentration is based on the two group t-test

Abbreviations: EM: extensive metabolizer, UM: ultra-rapid metabolizer, IM: intermediate metabolizer, PM: poor metabolizer

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Table S2. Differences in Toxicity Across Phenotype Groups at Baseline

	Maximum score	EM/UM Mean	IM Mean	PM Mean	p-value*
FACT					
INDIVIDUAL TOXICITIES					
Hot flashes	4	1.83	1.78	1.86	0.9041
Cold sweats	4	0.55	0.50	0.62	0.8941
Night sweats	4	1.39	1.37	1.11	0.4755
Vaginal discharge	4	0.73	0.75	0.69	0.9901
Vaginal itching/irritation	4	0.47	0.36	0.45	0.3755
Vaginal bleeding	4	0.09	0.11	0.34	0.0480
Vaginal dryness	4	1.06	0.85	0.76	0.0497
Pain/discomfort with intercourse	4	0.66	0.60	0.96	0.6527
Lost interest in sex	4	1.39	1.25	1.67	0.9318
Weight gain	4	1.10	1.21	1.07	0.6246
Lightheaded/dizzy	4	0.38	0.35	0.38	0.7147
Vomiting	4	0.03	0.00	0.00	0.0097
Diarrhea	4	0.13	0.17	0.07	0.9388
Headaches	4	0.63	0.46	0.52	0.0896
Bloated	4	0.48	0.63	0.57	0.1785
Mood swings	4	0.76	0.75	1.14	0.2585
Breast tenderness	4	0.74	0.58	0.31	0.0157
Irritable	4	0.70	0.65	1.00	0.5248
SUBSCALE					
Physical Well-Being	28	24.75	24.91	24.89	0.6548
Social/Family Well-Being	28	23.60	23.54	23.26	0.7507
Emotional Well-Being	24	20.37	20.54	19.90	0.9279
Functional Well-Being	28	22.49	23.22	22.79	0.2314
Breast Cancer Subscale	36	25.75	26.30	25.72	0.5197
Endocrine Subscale	72	58.90	59.56	58.61	0.6736
Endocrine Subscale Total	220	175.73	178.06	175.16	0.5373
SCALE					
FACT-B Trial Outcome Index	92	73.10	74.44	73.40	0.3807
FACT-B Total	144	116.90	118.52	116.55	0.5546
FACT-G Total	108	91.18	92.25	90.83	0.6262
BCPT-MSS					
INDIVIDUAL TOXICITIES					

Hot flashes	4	1.75	1.69	1.69	0.6285
Nausea	4	0.21	0.21	0.14	0.6738
Vomiting	4	0.04	0.04	0.00	0.6040
Difficulty w/bladder control when laugh/cry	4	0.50	0.48	0.34	0.4345
Difficulty w/bladder control at other times	4	0.49	0.52	0.48	0.8568
Vaginal dryness	4	0.98	0.87	0.78	0.2539
Pain with intercourse	4	0.66	0.58	0.82	0.9657
General aches and pains	4	1.23	1.11	1.21	0.4207
Joint pains	4	1.16	1.13	1.07	0.6995
Muscle stiffness	4	1.01	0.94	0.86	0.3813
Weight gain	4	0.99	1.11	1.17	0.2685
Unhappy with appearance of body	4	1.21	1.23	1.21	0.9425
Forgetfulness	4	1.19	1.11	1.34	0.9996
Night sweats	4	1.34	1.30	1.14	0.5471
Difficulty concentrating	4	0.96	0.91	0.97	0.8062
Easily distracted	4	0.89	0.91	0.90	0.9322
Arm swelling	4	0.33	0.29	0.28	0.5868
Decreased range of motion in arm on surgery side	4	0.48	0.49	0.48	0.9942
SUBSCALE					
Hot flashes	4	1.54	1.50	1.43	0.5779
Nausea	4	0.12	0.12	0.07	0.5547
Bladder Control	4	0.50	0.50	0.41	0.7287
Vaginal Problems	4	0.84	0.73	0.84	0.4864
Musculoskeletal	4	1.13	1.06	1.05	0.4518
Cognitive Problems	4	1.01	0.98	1.07	0.9725
Weight Problems	4	1.10	1.17	1.19	0.4999
Arm Problems	4	0.41	0.39	0.38	0.7552
SCALES					
MSS	4	0.86	0.83	0.82	0.5895

*p-value using linear regression assuming an additive genetic effect

Abbreviations:

FACT-B: Functional Assessment of Cancer Therapy-Breast

BCPT-MSS: Breast Cancer Prevention Trial Menopausal Symptom Scale

Note: higher scores indicate better QOL for all FACT summary scores. Higher scores indicate worse symptoms for individual items on both the FACT and BCPT, and for the BCPT summary scores.

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Table S3. Change in Overall Toxicity and Toxicity Subscales from Baseline to 4 Months

	EM/UM			IM			PM		
	Change	95% CI	p-value	Change	95% CI	p-value	Change	95% CI	p-value
FACT-Physical Well-Being	-0.05	-0.54, 0.44	0.85	0.09	-0.24, 0.41	0.61	-0.47	-1.44, 0.50	0.33
FACT-Social/Family Well-Being	-0.28	-0.87, 0.30	0.34	-0.16	-0.66, 0.34	0.53	-0.28	-2.00, 1.44	0.74
FACT-Emotional Well-Being	0.00	-0.44, 0.43	0.99	0.27	-0.01, 0.55	0.06	0.38	-0.10, 0.86	0.11
FACT-Functional Well-Being	-0.19	-0.79, 0.40	0.52	0.06	-0.31, 0.43	0.75	-1.21	-3.47, 1.05	0.28
FACT-Breast Cancer Subscale	0.09	-0.50, 0.67	0.77	0.67	0.24, 1.09	0.002	-0.24	-1.74, 1.25	0.74
FACT-Endocrine Subscale	0.44	-0.41, 1.29	0.31	-0.05	-0.71, 0.60	0.87	1.66	-0.56, 3.88	0.13
FACT-B Trial Outcome Index	-0.17	-1.34, 1.00	0.77	0.85	0.08, 1.63	0.031	-1.93	-5.31, 1.46	0.25
FACT-B Total	-0.59	-2.30, 1.12	0.50	1.04	-0.10, 2.18	0.07	-1.82	-6.43, 2.79	0.42
FACT-G Total	-0.62	-2.05, 0.80	0.39	0.28	-0.68, 1.23	0.57	-1.58	-5.77, 2.62	0.44
BCPT-Hot Flashes	-0.14	-0.26, -0.02	0.027	-0.01	-0.12, 0.11	0.89	-0.04	-0.51, 0.43	0.86
BCPT-Nausea	0.03	-0.03, 0.09	0.36	-0.01	-0.05, 0.03	0.64	0.04	-0.04, 0.13	0.33
BCPT-Bladder Control	0.01	-0.09, 0.10	0.89	0.05	-0.04, 0.14	0.27	0.29	-0.02, 0.60	0.06
BCPT-Vaginal Problems	0.00	-0.14, 0.13	0.96	0.08	-0.02, 0.19	0.12	-0.33	-0.61, -0.06	0.020
BCPT-Musculoskeletal	0.05	-0.09, 0.20	0.46	-0.03	-0.13, 0.08	0.60	-0.17	-0.44, 0.10	0.21
BCPT-Cognitive Problems	0.08	-0.01, 0.18	0.09	-0.04	-0.13, 0.06	0.45	0.15	-0.07, 0.38	0.17
BCPT-Weight Problems	0.02	-0.12, 0.15	0.81	-0.04	-0.16, 0.07	0.44	-0.08	-0.41, 0.24	0.60
BCPT-Arm Problems	-0.02	-0.12, 0.07	0.65	-0.10	-0.16, -0.04	0.001	-0.06	-0.22, 0.09	0.42
BCPT-MSS Total	0.01	-0.05, 0.07	0.73	-0.02	-0.06, 0.03	0.47	-0.01	-0.14, 0.11	0.80

Abbreviations: FACT-B: Functional Assessment of Cancer Therapy-Breast; BCPT-MSS: Breast Cancer Prevention Trial Menopausal Symptom Scale
 p-value based on paired t-test

Note: increase in FACT scores indicate improvement in QOL, and decreases in BCPT scores indicate improvement in symptoms.

Table S4. Change in individual toxicities on the FACT-B and/or BCPT-MSS

	EM/UM				IM				PM			
	FACT-B		BCPT-MSS		FACT-B		BCPT-MSS		FACT-B		BCPT-MSS	
	Change	p-value	Change	p-value	Change	p-value	Change	p-value	Change	p-value	Change	p-value
Hot flashes	-0.10	0.16	-0.08	0.28	0.00	0.95	0.00	0.95	-0.26	0.25	-0.21	0.38
Cold sweats	-0.02	0.75	---	---	-0.06	0.26	---	---	-0.30	0.26	---	---
Night sweats	-0.18	0.018	-0.20	0.007	-0.04	0.58	0.00	0.95	0.23	0.45	0.22	0.41
Vaginal discharge	-0.09	0.15	---	---	0.12	0.029	---	---	0.00	1.00	---	---
Vaginal itching/irritation	0.04	0.61	---	---	0.06	0.16	---	---	-0.17	0.38	---	---
Vaginal bleeding	0.04	0.26	---	---	-0.01	0.80	---	---	-0.17	0.33	---	---
Vaginal dryness	-0.09	0.29	-0.02	0.81	0.07	0.18	0.08	0.17	-0.17	0.30	-0.09	0.54
Pain/discomfort with intercourse	0.02	0.73	0.00	1.00	0.08	0.09	0.08	0.16	-0.55	0.004	-0.48	0.002
Lost interest in sex	-0.01	0.94	---	---	0.09	0.20	---	---	-0.23	0.13	---	---
Weight gain	0.03	0.75	0.06	0.45	0.02	0.81	0.03	0.63	0.09	0.60	-0.08	0.72
Lightheaded/dizzy	-0.02	0.73	---	---	0.05	0.29	---	---	0.00	1.00	---	---
Vomiting	-0.01	0.57	0.02	0.47	0.03	0.08	-0.02	0.29	0.00	1.00	0.00	1.00
Diarrhea	-0.01	0.71	---	---	-0.02	0.52	---	---	0.00	1.00	---	---
Headaches	-0.08	0.21	---	---	0.05	0.29	---	---	0.00	1.00	---	---
Bloated	0.10	0.10	---	---	0.03	0.55	---	---	0.05	0.67	---	---
Mood swings	0.00	1.00	---	---	-0.10	0.10	---	---	-0.30	0.031	---	---
Breast tenderness	-0.10	0.22	---	---	-0.11	0.06	---	---	0.13	0.45	---	---
Irritable	-0.01	0.83	---	---	-0.13	0.015	---	---	-0.13	0.33	---	---
Nausea	---	---	0.03	0.59	---	---	0.00	0.91	---	---	0.08	0.33
Difficulty w/bladder control when laugh/cry	---	---	0.08	0.16	---	---	0.04	0.43	---	---	0.42	0.038
Difficulty w/bladder control at other times	---	---	-0.07	0.21	---	---	0.03	0.61	---	---	0.17	0.33
General aches and pains	---	---	-0.03	0.70	---	---	-0.05	0.47	---	---	-0.38	0.06
Joint pains	---	---	0.08	0.35	---	---	0.00	0.95	---	---	-0.08	0.57
Muscle stiffness	---	---	0.11	0.24	---	---	-0.06	0.34	---	---	-0.04	0.79
Unhappy with appearance of	---	---	-0.03	0.67	---	---	-0.11	0.11	---	---	-0.08	0.65

body												
Forgetfulness	---	---	-0.01	0.83	---	---	-0.01	0.89	---	---	-0.17	0.38
Difficulty concentrating	---	---	0.10	0.12	---	---	-0.07	0.18	---	---	0.21	0.06
Easily distracted	---	---	0.16	0.011	---	---	-0.02	0.69	---	---	0.42	0.002
Arm swelling	---	---	-0.03	0.66	---	---	-0.02	0.47	---	---	0.04	0.66
Decreased ROM in arm on surgery side	---	---	-0.02	0.79	---	---	-0.19	<.0001	---	---	-0.17	0.33

Average of score (0-4) at 4 months minus baseline for all patients in phenotype group.

p-value based on paired t-test

--- Indicates toxicity not collected on that scale

Note: decreases in all items indicate improvements in symptoms

FACT-B: Functional Assessment of Cancer Therapy-Breast

BCPT-MSS: Breast Cancer Prevention Trial Menopausal Symptom Scale