

## Supplementary data

**Supplemental Table 1** Baseline circulating concentrations of sex steroid hormones by *COMT* genotype activity regardless of treatment group in postmenopausal women (*n*= 937)

<b>Sex hormone</b>	<b><i>G/G COMT</i> Genotype (<i>n</i> = 248)</b>	<b><i>A/A COMT</i> Genotype (<i>n</i>= 300)</b>	<b><i>G/A COMT</i> Genotype (<i>n</i>= 389)</b>	<b><i>P</i><sup>1</sup></b>
<b>Estrone, pg/mL</b>	23.8 (22.2, 25.5)	22.2 (20.9, 23.7)	23.6 (22.3, 25.0)	0.29
<b>Estradiol, pg/mL</b>	3.3 (2.8, 3.7)	3.6 (3.2, 4.1)	3.7 (3.3, 4.1)	0.41
<b>Bioavailable estradiol, pg/mL</b>	1.5 (1.3, 1.7)	1.6 (1.4, 1.8)	1.7 (1.5, 1.9)	0.42
<b>Androstenedione, pg/mL</b>	485 (458, 513)	492 (467, 518)	501 (478, 524)	0.70
<b>Testosterone, pg/mL</b>	165 (153, 178)	151 (141, 162)	155 (146, 165)	0.24
<b>Bioavailable testosterone, pg/mL</b>	42.1 (38.7, 45.9)	38.0 (35.2, 41.1)	40.4 (37.8, 43.2)	0.22
<b>SHBG, nmol/L</b>	69.8 (65.5, 74.4)	70.1 (66.1, 74.3)	66.7 (63.3, 70.2)	0.35

Values are geometric means (95% CIs). Abbreviations: *COMT*, catechol-O-methyltransferase; SHBG, sex hormone binding globulin.

<sup>1</sup> *P* value for difference across *G/G* vs *A/A* vs *G/A COMT* genotype groups based on one-way ANOVA test.

## Supplementary data

**Supplemental Table 2** Baseline circulating concentrations of sex steroid hormones and IGF-1 and IGFBP-3 by age (years) regardless of treatment group in postmenopausal women (*n*= 937)

<b>Sex hormone and IGF protein</b>	<b>50- 54 (<i>n</i>= 127)</b>	<b>55- 59 (<i>n</i>= 312)</b>	<b>60- 64 (<i>n</i>= 277)</b>	<b>65- 70 (<i>n</i>= 221)</b>	<b><i>P</i><sup>1</sup></b>
<b>Estrone, pg/mL</b>	26.0 (23.6, 28.6)	22.9 (21.5, 24.3)	22.8 (21.4, 24.4)	22.7 (21.1, 24.4)	0.08
<b>Estradiol, pg/mL</b>	5.6 (4.6, 6.8)	3.3 (2.9, 3.8)	3.3 (2.9, 3.7)	3.2 (2.8, 3.7)	0.0005
<b>Bioavailable estradiol, pg/mL</b>	2.5 (2.0, 3.1)	1.5 (1.3, 1.7)	1.5 (1.3, 1.7)	1.4 (1.2, 1.7)	0.0005
<b>Androstenedione, pg/mL</b>	520 (479, 565)	518 (491, 546)	485 (459, 513)	457 (429, 487)	0.002
<b>Testosterone, pg/mL</b>	144 (129, 160)	154 (144, 165)	153 (143, 165)	171 (158, 186)	0.01
<b>Bioavailable testosterone, pg/mL</b>	36.7 (32.6, 41.3)	39.9 (37.0, 43.0)	39.7 (36.7, 43.0)	42.9 (39.2, 46.9)	0.06
<b>SHBG, nmol/L</b>	69.7 (64.3, 75.6)	67.8 (64.4, 71.4)	67.1 (63.5, 70.9)	70.9 (66.7, 75.4)	0.64
<b>IGF-1, ng/mL</b>	96.5 (92.0, 101.2)	90.9 (88.2, 93.7)	85.6 (82.9, 88.4)	82.0 (79.1, 85.1)	<0.0001
<b>IGFBP-3, ng/mL</b>	2064 (1990, 2141)	2087 (2039, 2136)	2021 (1971, 2072)	2018 (1963, 2075)	0.08

Values are geometric means (95% CIs). Abbreviations: IGF-1, insulin-like growth factor; IGFBP-3, insulin-like growth factor binding protein 3; SHBG, sex hormone binding globulin.

<sup>1</sup> *P* values derived from ANOVA test across four age groups with adjustment for BMI at baseline.

## Supplementary data

<b>Supplemental Table 3</b> Circulating levels of sex hormones by age (years) in postmenopausal women randomly assigned to GTE or placebo group ( $n = 937$ )									
<b>Sex hormone</b>	<b>50- 54 (<math>n = 127</math>)</b>		<b>55- 59 (<math>n = 312</math>)</b>		<b>60- 64 (<math>n = 277</math>)</b>		<b>65- 70 (<math>n = 221</math>)</b>		<b><math>P^1</math></b>
<b>Time point</b>	GTE ( $n = 56$ )	PLC ( $n = 71$ )	GTE ( $n = 151$ )	PLC ( $n = 161$ )	GTE ( $n = 145$ )	PLC ( $n = 132$ )	GTE ( $n = 111$ )	PLC ( $n = 110$ )	
<b>Estrone, pg/mL</b>									
Month 0	23.5 (20.3, 27.1)	28.2 (24.8, 32.0)	21.5 (19.7, 23.5)	24.2 (22.2, 26.4)	22.2 (20.3, 24.3)	23.5 (21.4, 25.8)	24.9 (22.4, 27.6)	20.7 (18.7, 22.9)	0.009
Month 12	26.2 (22.7, 30.3)	24.0 (21.1, 27.3)	21.1 (19.3, 23.1)	21.0 (19.3, 22.9)	21.7 (19.8, 23.7)	23.9 (21.7, 26.2)	23.5 (21.2, 26.0)	22.2 (20.0, 24.6)	
<b>Estradiol, pg/mL</b>									
Month 0	5.0 (3.7, 6.6)	6.1 (4.7, 7.9)	2.9 (2.4, 3.5)	3.8 (3.2, 4.5)	3.2 (2.7, 3.8)	3.4 (2.8, 4.1)	3.6 (2.9, 4.4)	2.9 (2.4, 3.6)	0.13
Month 12	5.6 (4.2, 7.4)	3.6 (2.8, 4.6)	3.2 (2.7, 3.8)	3.1 (2.6, 3.7)	3.7 (3.1, 4.4)	3.0 (2.5, 3.6)	3.7 (3.0, 4.5)	3.1 (2.5, 3.8)	
<b>Bioavailable estradiol, pg/mL</b>									
Month 0	2.1 (1.6, 2.9)	2.8 (2.2, 3.7)	1.3 (1.1, 1.6)	1.7 (1.4, 2.1)	1.4 (1.2, 1.7)	1.5 (1.3, 1.9)	1.6 (1.3, 2.0)	1.3 (1.0, 1.6)	0.13
Month 12	2.5 (1.9, 3.3)	1.7 (1.3, 2.2)	1.5 (1.2, 1.8)	1.4 (1.2, 1.7)	1.7 (1.4, 2.0)	1.4 (1.1, 1.7)	1.6 (1.3, 2.0)	1.4 (1.1, 1.7)	
<b>Androstenedione, pg/mL</b>									
Month 0	525 (464, 595)	516 (462, 577)	504 (467, 543)	532 (494, 573)	459 (425, 496)	515 (475, 559)	454 (415, 496)	460 (421, 503)	0.50
Month 12	547 (487, 613)	512 (463, 568)	485 (452, 520)	503 (470, 538)	453 (422, 487)	502 (465, 541)	433 (399, 470)	407 (374, 441)	
<b>Testosterone, pg/mL</b>									
Month 0	156 (133, 184)	135 (117, 156)	144 (131, 159)	163 (149, 180)	148 (134, 164)	160 (144, 178)	162 (144, 182)	181 (161, 203)	0.79
Month 12	165 (142, 193)	138 (120, 158)	149 (136, 164)	155 (142, 170)	159 (144, 175)	152 (137, 168)	167 (149, 186)	172 (154, 192)	
<b>Bioavailable testosterone, pg/mL</b>									
Month 0	38.0 (31.8, 45.4)	35.7 (30.5, 41.8)	37.2 (33.4, 41.5)	42.6 (38.3, 47.3)	37.9 (34.0, 42.4)	41.8 (37.2, 46.9)	41.1 (36.2, 46.7)	44.8 (39.4, 50.8)	0.81
Month 12	41.9 (35.4, 49.7)	37.2 (32.0, 43.3)	39.2 (35.3, 43.5)	40.9 (37.0, 45.2)	40.9 (36.8, 45.5)	39.6 (35.4, 44.2)	41.9 (37.1, 47.3)	42.4 (37.6, 47.9)	
<b>SHBG, nmol/L</b>									
Month 0	74.4 (65.8, 84.0)	66.3 (59.5, 73.9)	67.1 (62.3, 72.3)	68.4 (63.7, 73.6)	66.8 (61.9, 72.1)	67.4 (62.3, 73.0)	69.2 (63.4, 75.5)	72.6 (66.6, 79.3)	0.90
Month 12	69.8 (61.5, 79.3)	64.8 (57.9, 72.5)	67.3 (62.3, 72.7)	67.7 (62.8, 72.9)	68.7 (63.5, 74.4)	67.6 (62.2, 73.4)	71.2 (65.1, 78.0)	72.7 (66.4, 79.6)	

Values are geometric means (95% CIs). Abbreviations: GTE, green tea extract; PLC, placebo; SHBG, sex hormone binding globulin.

<sup>1</sup>  $P$  values for the interaction between treatment and age based on relative changes of hormones from baseline derived from generalized linear model with adjustment for BMI and hormone levels at baseline.