

Supplementary Table 1. Drop-out patterns for the Sequential, Exemestane and control group.

Drop-out pattern	Sequential group	Exemestane group	Control group
	N (%)	N (%)	N (%)
Completed Baseline only	11 (12)	14 (12)	4 (3)
Completed Baseline+FU1	45 (50)	42 (37)	57 (46)
Completed Baseline+FU1+FU2	35 (39)	57 (50)	62 (50)

Abbreviations: FU, follow-up.

Supplementary Table 2. Results of the intention-to-treat analyses of the Sequential, the Exemestane and the control group.

Cognitive domain/test	P-value overall group-by-time interaction	Group	Adjusted mean Z-scores						Sequential group and exemestane vs control						AIC	BIC		
			T0		T1		T2		T0-T1		T0-T2							
			Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean difference in change over time	95% CI	p	ES ^a	Mean difference in change over time	95% CI			p	ES ^a
Verbal memory ^b	.02	Sequential	0.06	-0.11 to 0.22	0.03	-0.14 to 0.20	-0.32	-0.55 to -0.09	-0.21	-0.38 to -0.05	.01	-0.26	-0.44	-0.72 to -0.15	.003	-0.34	1375.19	1498.98
		Exemestane	-0.09	-0.24 to 0.05	0.03	-0.12 to 0.18	-0.16	-0.35 to 0.02	-0.06	-0.21 to 0.09	.42	-0.08	-0.13	-0.39 to 0.12	.31	-0.12		
		Control	-0.09	-0.23 to 0.06	0.10	-0.04 to 0.24	-0.02	-0.22 to 0.18										
RAVLT IR ^c	.04	Sequential	0.04	-0.15 to 0.24	0.03	-0.18 to 0.24	-0.27	-0.54 to -0.01	-0.13	-0.37 to 0.11	.28	-0.11	-0.52	-0.87 to -0.18	.003	-0.36	1832.08	1979.97
		Exemestane	-0.18	-0.36 to 0.00	-0.02	-0.20 to 0.16	-0.25	-0.47 to -0.03	0.04	-0.18 to 0.26	.73	0.03	-0.28	-0.60 to 0.04	.09	-0.21		
		Control	-0.09	-0.25 to 0.08	0.04	-0.13 to 0.21	0.12	-0.12 to 0.36										
RAVLT DR ^c	.12	Sequential	0.09	-0.11 to 0.28	0.03	-0.17 to 0.24	-0.08	-0.33 to 0.18	-0.28	-0.50 to -0.06	.01	-0.25	-0.32	-0.66 to 0.01	.06	-0.22	1767.07	1914.96
		Exemestane	-0.06	-0.23 to 0.12	0.06	-0.12 to 0.24	-0.01	-0.23 to 0.20	-0.11	-0.31 to 0.09	.27	-0.11	-0.12	-0.43 to 0.20	.47	-0.09		
		Control	-0.08	-0.25 to 0.09	0.15	-0.02 to 0.32	0.08	-0.15 to 0.31										
VAT ^d	.45	Sequential	0.07	-0.17 to 0.31	0.05	-0.21 to 0.31	-0.39	-0.76 to -0.02	-0.22	-0.51 to 0.06	.12	-0.16	-0.36	-0.85 to 0.12	.14	-0.15	2061.17	2184.96
		Exemestane	-0.12	-0.33 to 0.10	0.05	-0.17 to 0.27	-0.25	-0.54 to 0.04	-0.04	-0.30 to 0.22	.74	-0.03	-0.04	-0.47 to 0.39	.85	-0.02		
		Control	-0.04	-0.24 to 0.17	0.17	-0.04 to 0.39	-0.13	-0.43 to 0.18										
Visual memory ^b	.12	Sequential	-0.38	-0.58 to -0.19	-0.36	-0.57 to -0.15	-0.37	-0.63 to -0.11	0.03	-0.18 to 0.23	.80	0.03	-0.19	-0.51 to 0.13	.24	-0.14	1724.22	1848.96
		Exemestane	-0.33	-0.51 to -0.15	-0.20	-0.38 to -0.02	-0.35	-0.56 to -0.13	0.13	-0.06 to 0.32	.17	0.14	-0.22	-0.51 to 0.07	.14	-0.18		
		Control	-0.08	-0.25 to 0.09	-0.09	-0.26 to 0.09	0.12	-0.11 to 0.35										
WMS Visual Memory IR ^b	.73	Sequential	-0.35	-0.55 to -0.14	-0.40	-0.62 to -0.18	-0.38	-0.66 to -0.10	-0.01	-0.24 to 0.22	.94	-0.01	-0.16	-0.51 to 0.20	.38	-0.10	1860.15	1985.00
		Exemestane	-0.31	-0.49 to -0.12	-0.28	-0.47 to -0.09	-0.32	-0.55 to -0.09	0.06	-0.15 to 0.28	.57	0.06	-0.14	-0.46 to 0.19	.40	-0.10		
		Control	-0.10	-0.28 to 0.08	-0.14	-0.32 to 0.04	0.03	-0.22 to 0.27										
WMS Visual Memory DR ^b	.046	Sequential	-0.46	-0.67 to -0.25	-0.35	-0.58 to -0.13	-0.36	-0.65 to -0.08	0.08	-0.17 to 0.32	.53	0.06	-0.19	-0.55 to 0.18	.31	-0.12	1902.66	2027.40
		Exemestane	-0.36	-0.55 to -0.17	-0.12	-0.32 to 0.07	-0.35	-0.59 to -0.12	0.21	-0.02 to 0.43	.07	0.18	-0.27	-0.60 to 0.06	.10	-0.20		
		Control	-0.07	-0.25 to 0.11	-0.04	-0.22 to 0.15	0.21	-0.04 to 0.47										
Information processing speed ^b	.04	Sequential	-0.24	-0.39 to -0.09	-0.28	-0.44 to -0.12	-0.44	-0.64 to -0.25	-0.05	-0.19 to 0.09	.50	-0.07	-0.05	-0.29 to 0.18	.67	-0.05	1261.08	1385.96
		Exemestane	-0.23	-0.36 to -0.09	-0.06	-0.20 to 0.08	-0.35	-0.51 to -0.19	0.15	0.02 to 0.28	.02	0.22	0.02	-0.19 to 0.24	.82	0.03		
		Control	-0.03	-0.16 to 0.10	-0.02	-0.15 to 0.11	-0.18	-0.35 to -0.01										
Stroop card 1 ^c	.70	Sequential	-0.29	-0.50 to -0.08	-0.30	-0.52 to -0.07	-0.67	-0.95 to -0.39	0.11	-0.13 to 0.35	.36	0.09	-0.03	-0.40 to 0.34	.89	-0.02	1893.65	2041.67
		Exemestane	-0.21	-0.40 to -0.03	-0.19	-0.38 to 0.01	-0.52	-0.75 to -0.28	0.14	-0.07 to 0.36	.19	0.13	0.05	-0.29 to 0.39	.78	0.03		
		Control	-0.05	-0.22 to 0.13	-0.16	-0.34 to 0.02	-0.40	-0.65 to -0.15										
Stroop card 2 ^b	.35	Sequential	-0.20	-0.40 to -0.01	-0.23	-0.43 to -0.02	-0.28	-0.52 to -0.03	-0.08	-0.26 to 0.10	.38	-0.08	0.01	-0.27 to 0.30	.92	0.01	1645.12	1770.11
		Exemestane	-0.17	-0.35 to 0.01	-0.02	-0.20 to 0.16	-0.22	-0.42 to -0.01	0.10	-0.06 to 0.27	.23	0.12	0.04	-0.22 to 0.31	.74	0.04		
		Control	0.00	-0.17 to 0.17	0.05	-0.12 to 0.22	-0.09	-0.30 to 0.13										
Trail Making Test A ^c	.006	Sequential	-0.21	-0.40 to -0.03	-0.26	-0.46 to -0.07	-0.36	-0.61 to -0.11	-0.17	-0.38 to 0.05	.13	-0.15	-0.23	-0.57 to 0.10	.17	-0.16	1724.82	1872.70
		Exemestane	-0.30	-0.47 to -0.14	0.02	-0.15 to 0.19	-0.34	-0.55 to -0.13	0.21	0.01 to 0.41	.04	0.21	-0.12	-0.43 to 0.18	.43	-0.09		
		Control	-0.05	-0.21 to 0.11	0.06	-0.10 to 0.22	0.03	-0.20 to 0.26										
Executive functioning ^c	.005	Sequential	-0.22	-0.41 to -0.04	-0.33	-0.52 to -0.14	-0.55	-0.77 to -0.32	-0.22	-0.37 to -0.06	.007	-0.27	-0.41	-0.68 to -0.15	.002	-0.38	1475.47	1623.23
		Exemestane	-0.35	-0.51 to -0.18	-0.21	-0.38 to -0.04	-0.41	-0.60 to -0.21	0.03	-0.11 to 0.17	.69	0.04	-0.15	-0.39 to 0.09	.22	-0.15		
		Control	-0.05	-0.20 to 0.11	0.06	-0.10 to 0.22	0.04	-0.16 to 0.24										
Stroop card 3 ^c	.07	Sequential	-0.24	-0.44 to -0.03	-0.35	-0.56 to -0.13	-0.53	-0.80 to -0.25	-0.22	-0.45 to 0.00	.05	-0.19	-0.38	-0.75 to 0.00	.047	-0.17	1843.34	1986.69
		Exemestane	-0.36	-0.55 to -0.18	-0.22	-0.41 to -0.03	-0.17	-0.40 to 0.06	0.03	-0.18 to 0.24	.79	0.03	0.10	-0.24 to 0.45	.55	0.05		
		Control	-0.05	-0.22 to 0.13	0.07	-0.11 to 0.24	0.04	-0.20 to 0.29										
Table continues																		
Trail Making Test B ^c	.005	Sequential	-0.19	-0.45 to 0.08	-0.30	-0.53 to -0.07	-0.35	-0.68 to -0.01	-0.20	-0.41 to 0.00	.049	-0.20	-0.49	-0.84 to -0.13	.007	-0.24	1800.92	1976.44
		Exemestane	-0.47	-0.71 to -0.23	-0.18	-0.39 to 0.02	-0.52	-0.79 to -0.26	0.02	-0.17 to 0.20	.87	0.02	-0.43	-0.75 to -0.10	.01	-0.23		
		Control	-0.03	-0.43 to 0.37	0.05	-0.14 to 0.24	0.02	-0.27 to 0.31										
Motor speed ^f		Sequential	-0.02	-0.18 to 0.14	-0.01	-0.17 to 0.16	-0.22	-0.41 to -0.02	-0.08	-0.22 to 0.06	.25	-0.11	-0.21	-0.43 to 0.02	.07	-0.22		

	.31	Exemestane	-0.05	-0.20 to 0.09	0.01	-0.14 to 0.16	-0.22	-0.39 to -0.06	-0.03	-0.16 to 0.10	.62	-0.05	-0.18	-0.39 to 0.02	.08	-0.22	1292.93	1417.82
		Control	-0.08	-0.21 to 0.06	0.02	-0.12 to 0.16	-0.07	-0.23 to 0.10										
FePsy Fingertapping dominant hand ^f	.24	Exemestane	-0.01	-0.17 to 0.15	0.03	-0.13 to 0.20	-0.18	-0.38 to 0.02	-0.04	-0.19 to 0.11	.58	-0.05	-0.22	-0.46 to 0.03	.08	-0.21		
		Control	-0.08	-0.22 to 0.06	0.01	-0.13 to 0.15	-0.03	-0.20 to 0.14									1357.80	1482.73
FePsy Fingertapping non-dominant hand ^f	.44	Exemestane	-0.02	-0.19 to 0.16	-0.03	-0.22 to 0.15	-0.24	-0.45 to -0.02	-0.12	-0.27 to 0.03	.13	-0.15	-0.17	-0.41 to 0.07	.16	-0.18		
		Control	-0.13	-0.28 to 0.03	-0.04	-0.20 to 0.12	-0.29	-0.47 to -0.11	-0.02	-0.16 to 0.12	.80	-0.03	-0.12	-0.34 to 0.10	.28	-0.14	1437.64	1562.53
Verbal fluency ^g	.76	Exemestane	-0.39	-0.53 to -0.25	-0.39	-0.54 to -0.25	-0.39	-0.57 to -0.21	-0.02	-0.15 to 0.10	.70	-0.04	0.06	-0.12 to 0.25	.49	0.09		
		Control	-0.42	-0.54 to -0.29	-0.37	-0.50 to -0.24	-0.48	-0.63 to -0.34	0.03	-0.09 to 0.14	.66	0.04	0.00	-0.16 to 0.16	>.99	0.00	1140.02	1242.04
Letterfluency ^b	.78	Exemestane	-0.09	-0.21 to 0.03	-0.07	-0.19 to 0.05	-0.16	-0.30 to -0.01										
		Control	-0.37	-0.55 to -0.19	-0.35	-0.54 to -0.16	-0.22	-0.44 to 0.01	-0.09	-0.26 to 0.08	.29	-0.11	0.02	-0.24 to 0.27	.90	0.02		
		Exemestane	-0.41	-0.57 to -0.25	-0.31	-0.47 to -0.14	-0.27	-0.46 to -0.08	-0.01	-0.16 to 0.15	.94	-0.01	0.00	-0.23 to 0.24	.97	0.00	1490.45	1615.23
		Control	-0.07	-0.22 to 0.09	0.05	-0.11 to 0.20	0.07	-0.12 to 0.27										
Category fluency - Animals ^b	.91	Exemestane	-0.35	-0.54 to -0.16	-0.41	-0.61 to -0.21	-0.51	-0.77 to -0.25	-0.06	-0.30 to 0.18	.62	-0.05	-0.11	-0.45 to 0.23	.52	-0.07		
		Control	-0.34	-0.50 to -0.17	-0.36	-0.54 to -0.19	-0.52	-0.73 to -0.31	-0.03	-0.25 to 0.19	.81	-0.02	-0.14	-0.45 to 0.17	.38	-0.10	1793.08	1917.96
		Exemestane	-0.06	-0.22 to 0.10	-0.06	-0.23 to 0.10	-0.11	-0.34 to 0.12										
Category fluency - Professions ^c	.22	Exemestane	-0.43	-0.64 to -0.22	-0.38	-0.57 to -0.20	-0.26	-0.53 to 0.00	0.10	-0.12 to 0.32	.38	-0.02	0.16	-0.21 to 0.53	.38	0.13		
		Control	-0.52	-0.71 to -0.33	-0.40	-0.56 to -0.23	-0.53	-0.75 to -0.32	0.18	-0.02 to 0.39	.08	-0.06	-0.01	-0.35 to 0.32	.93	-0.13	1684.64	1860.20
		Exemestane	-0.27	-0.47 to -0.06	-0.40	-0.62 to -0.18	-0.27	-0.55 to 0.00	-0.12	-0.35 to 0.11	.305	-0.10	0.05	-0.30 to 0.40	.76	0.04		
Reaction speed ^b	.523	Control	-0.22	-0.40 to -0.03	-0.16	-0.36 to 0.03	-0.25	-0.49 to -0.02	0.06	-0.15 to 0.27	.573	0.06	0.02	-0.30 to 0.35	.89	0.02	1813.94	1938.06
		Exemestane	0.02	-0.16 to 0.19	0.01	-0.17 to 0.19	-0.05	-0.30 to 0.20										
FePsy Reaction Time dominant hand ^b	.04	Exemestane	-0.17	-0.39 to 0.06	-0.47	-0.71 to -0.23	-0.22	-0.53 to 0.08	-0.39	-0.68 to -0.10	.008	-0.28	-0.10	-0.50 to 0.30	.62	-0.07		
		Control	-0.23	-0.44 to -0.03	-0.11	-0.32 to 0.10	-0.22	-0.48 to 0.04	0.03	-0.24 to 0.30	.83	0.02	-0.03	-0.40 to 0.34	.87	-0.02	2026.97	2151.20
		Exemestane	0.02	-0.17 to 0.22	0.12	-0.08 to 0.31	0.07	-0.22 to 0.35										
FePsy Reaction Times non- dominant hand ^b	.84	Exemestane	-0.33	-0.56 to -0.11	-0.31	-0.55 to -0.08	-0.29	-0.58 to 0.01	0.13	-0.14 to 0.40	.33	0.10	0.17	-0.23 to 0.57	.41	0.11		
		Control	-0.20	-0.40 to 0.00	-0.22	-0.43 to -0.01	-0.28	-0.54 to -0.03	0.09	-0.16 to 0.33	.49	0.07	0.04	-0.34 to 0.41	.84	0.03	1961.66	2085.78
		Exemestane	0.01	-0.18 to 0.19	-0.10	-0.30 to 0.09	-0.12	-0.39 to 0.16										
Working memory ^g	.21	Exemestane	-0.33	-0.51 to -0.15	-0.16	-0.35 to 0.03	-0.43	-0.70 to -0.15	0.12	-0.14 to 0.38	.36	0.09	-0.23	-0.62 to 0.16	.24	-0.13		
		Control	-0.30	-0.46 to -0.13	-0.20	-0.37 to -0.03	-0.45	-0.67 to -0.24	0.04	-0.20 to 0.29	.72	0.03	-0.30	-0.65 to 0.05	.10	-0.19	1833.39	1935.06
		Exemestane	-0.06	-0.21 to 0.10	-0.01	-0.16 to 0.15	0.08	-0.14 to 0.31										

Abbreviations: T0, baseline; T1; 1 year follow-up; T2, 5 year follow-up; CI, confidence interval; ES, effect size; RAVLT, Rey Auditory Verbal Learning Test; VAT, Visual Association Test; WMS, Wechsler Memory Scale; IR, immediate recall; DR, delayed recall; AIC, Akaike information criterion; BIC, Bayesian information criterion.

^a Effect sizes: .20 small effect, .50 moderate effect, .80 large effect.

^b Adjusted for age, IQ, FACT-ES.

^c Adjusted for age, IQ, HSCL, FACT-ES.

^d Adjusted for age, HSCL, FACT-ES.

^e Adjusted for pattern missing, age, IQ, HSCL, FACT-ES.

^f Adjusted for age, IQ, HSCL.

^g Adjusted for age, IQ.

^h Adjusted for IQ, HSCL, FACT-ES.

Table
continues

Motor speed ^c	.15	Sequential	0.04	-0.15 to 0.21	0.02	-0.17 to 0.20	-0.24	-0.47 to -0.01	-0.11	-0.25 to 0.04	.14	-0.15	-0.29	-0.54 to -0.04	.02	-0.22	1089.61	1205.85
		Exemestane	-0.09	-0.25 to 0.07	0.04	-0.13 to 0.20	-0.15	-0.34 to 0.05	0.03	-0.10 to 0.16	.63	0.05	-0.07	-0.30 to 0.15	.52	-0.06		
		Control	-0.06	-0.19 to 0.08	0.04	-0.10 to 0.17	-0.04	-0.20 to 0.12										
FePsy Fingertapping dominant hand ^d	.32	Sequential	0.03	-0.15 to 0.21	0.05	-0.13 to 0.24	-0.19	-0.43 to 0.05	-0.06	-0.22 to 0.09	.42	-0.08	-0.27	-0.53 to 0.00	.05	-0.18	1139.89	1256.17
		Exemestane	-0.02	-0.17 to 0.15	0.09	-0.07 to 0.25	-0.08	-0.28 to 0.12	0.02	-0.12 to 0.16	.79	0.03	-0.11	-0.35 to 0.13	.36	-0.09		
		Control	-0.06	-0.19 to 0.08	0.03	-0.11 to 0.16	-0.01	-0.18 to 0.15										
FePsy Fingertapping non-dominant hand ^d	.12	Sequential	0.05	-0.15 to 0.24	-0.01	-0.21 to 0.20	-0.27	-0.53 to -0.02	-0.16	-0.32 to 0.01	.06	-0.19	-0.31	-0.59 to -0.02	.03	-0.20	1224.24	1340.48
		Exemestane	-0.16	-0.34 to 0.01	-0.02	-0.20 to 0.16	-0.21	-0.42 to 0.01	0.04	-0.10 to 0.19	.55	0.06	-0.03	-0.28 to 0.22	.81	-0.02		
		Control	-0.05	-0.20 to 0.09	0.05	-0.10 to 0.19	-0.07	-0.25 to 0.11										
Verbal fluency ^e	.82	Sequential	-1.16	-1.63 to -0.68	-1.11	-1.61 to -0.61	-1.08	-1.73 to -0.43	0.01	-0.42 to 0.44	.97	0.00	0.19	-0.50 to 0.89	.59	0.07	2409.68	2530.31
		Exemestane	-1.31	-1.73 to -0.88	-1.15	-1.58 to -0.71	-1.51	-2.04 to -0.98	0.12	-0.27 to 0.51	.54	0.07	-0.09	-0.70 to 0.52	.76	-0.04		
		Control	-0.14	-0.50 to 0.22	-0.10	-0.47 to 0.26	-0.26	-0.72 to 0.21										
Letterfluency ^e	.75	Sequential	-0.36	-0.56 to -0.16	-0.34	-0.55 to -0.13	-0.18	-0.45 to 0.09	-0.10	-0.28 to 0.08	.27	-0.12	-0.01	-0.31 to 0.28	.93	-0.01	1283.05	1403.59
		Exemestane	-0.45	-0.63 to -0.27	-0.33	-0.51 to -0.15	-0.30	-0.52 to -0.08	0.00	-0.16 to 0.16	.96	0.00	-0.04	-0.30 to 0.23	.78	-0.04		
		Control	-0.05	-0.20 to 0.10	0.07	-0.08 to 0.22	0.14	-0.06 to 0.34										
Category fluency - Animals ^e	.99	Sequential	-0.39	-0.60 to -0.18	-0.41	-0.63 to -0.18	-0.55	-0.87 to -0.23	-0.01	-0.27 to 0.25	.93	-0.01	-0.08	-0.47 to 0.31	.70	-0.05	1551.23	1671.94
		Exemestane	-0.36	-0.55 to -0.18	-0.42	-0.61 to -0.22	-0.53	-0.80 to -0.27	-0.05	-0.28 to 0.19	.70	-0.04	-0.09	-0.44 to 0.26	.62	-0.06		
		Control	-0.04	-0.20 to 0.12	-0.05	-0.21 to 0.12	-0.12	-0.35 to 0.11										
Category fluency - Professions ^f	.34	Sequential	-0.42	-0.64 to -0.19	-0.34	-0.56 to -0.13	-0.17	-0.50 to 0.16	0.12	-0.12 to 0.37	.32	0.11	0.17	-0.19 to 0.54	.36	0.13	1445.47	1619.53
		Exemestane	-0.48	-0.67 to -0.28	-0.40	-0.58 to -0.22	-0.57	-0.84 to -0.30	0.17	-0.05 to 0.40	.13	0.17	-0.05	-0.38 to 0.27	.74	-0.05		
		Control	-0.10	-0.41 to 0.22	-0.14	-0.28 to 0.01	-0.13	-0.37 to 0.10										
Reaction speed ^e	>.99	Sequential	0.28	0.02 to 0.55	0.27	-0.02 to 0.55	0.08	-0.29 to 0.45	0.06	-0.24 to 0.36	.70	0.04	0.03	-0.41 to 0.47	.89	0.01	1727.05	1842.60
		Exemestane	0.22	-0.01 to 0.46	0.17	-0.07 to 0.42	-0.02	-0.33 to 0.29	0.02	-0.25 to 0.30	.86	0.02	-0.01	-0.41 to 0.39	.95	-0.01		
		Control	0.03	-0.17 to 0.22	-0.05	-0.25 to 0.15	-0.21	-0.49 to 0.08										
FePsy Reaction Time dominant hand ^b	.84	Sequential	0.17	-0.12 to 0.47	0.25	-0.07 to 0.57	-0.15	-0.59 to 0.29	0.23	-0.15 to 0.60	.24	0.12	0.07	-0.48 to 0.63	.80	0.03	1944.56	2082.28
		Exemestane	0.24	-0.02 to 0.50	0.20	-0.07 to 0.48	-0.09	-0.46 to 0.29	0.11	-0.24 to 0.45	.55	0.06	0.07	-0.44 to 0.58	.79	0.03		
		Control	0.05	-0.17 to 0.27	-0.10	-0.32 to 0.13	-0.35	-0.69 to 0.00										
FePsy Reaction Times non- dominant hand ^b	.71	Sequential	0.59	0.31 to 0.87	0.42	0.11 to 0.72	0.41	0.01 to 0.82	-0.20	-0.53 to 0.13	.23	-0.13	-0.16	-0.63 to 0.31	.50	-0.07	1846.77	1917.87
		Exemestane	0.34	0.09 to 0.60	0.23	-0.04 to 0.49	0.12	-0.22 to 0.47	-0.14	-0.44 to 0.16	.35	-0.10	-0.20	-0.63 to 0.23	.35	-0.09		
		Control	-0.03	-0.24 to 0.19	0.00	-0.22 to 0.22	-0.05	-0.34 to 0.25										
Working memory ^b	.13	Sequential	-0.41	-0.61 to -0.20	-0.20	-0.42 to 0.02	-0.56	-0.89 to -0.22	0.13	-0.15 to 0.40	.36	0.10	-0.33	-0.77 to 0.10	.13	-0.17	1578.58	1654.56
		Exemestane	-0.30	-0.48 to -0.12	-0.19	-0.38 to 0.00	-0.45	-0.72 to -0.19	0.04	-0.22 to 0.29	.77	0.03	-0.33	-0.72 to 0.05	.09	-0.21		
		Control	-0.03	-0.18 to 0.13	0.05	-0.11 to 0.20	0.15	-0.07 to 0.38										

Abbreviations: T0, baseline; T1; 1 year follow-up; T2, 5 year follow-up; CI, confidence interval; ES, effect size; RAVLT, Rey Auditory Verbal Learning Test; IR, immediate recall; DR, delayed recall; VAT, Visual Association Test; WMS, Wechsler Memory Scale; AIC, Akaike information criterion; BIC, Bayesian information criterion.

^a Effect sizes: .20 small effect, .50 moderate effect, .80 large effect.

^b Adjusted for age, IQ, HSCL, FACT-ES.

^c Adjusted for age, IQ, FACT-ES.

^d Adjusted for age, FACT-ES.

^e Adjusted for age, IQ, HSCL.

^f Adjusted for pattern missing, age, IQ, HSCL, FACT-ES.

^g Adjusted for FACT-ES.

^h Adjusted for IQ.

Supplementary Table 4. Results of the intention-to-treat analyses of the Sequential and the Exemestane group.

Table
continues

Category fluency - Professions ^d	.16	Sequential	-0.54	-0.69 to -0.38	-0.51	-0.68 to -0.34	-0.44	-0.67 to -0.21	-0.09	-0.31 to 0.12	.41	-0.10	0.18	-0.14 to 0.51	.27	0.11	993.84	1076.46
		Exemestane	-0.57	-0.72 to -0.43	-0.46	-0.61 to -0.30	-0.66	-0.85 to -0.47										
Reaction speed ^h	.24	Sequential	-0.33	-0.55 to -0.11	-0.43	-0.66 to -0.20	-0.32	-0.61 to -0.02	-0.18	-0.44 to 0.07	.15	-0.19	0.03	-0.33 to 0.39	.87	0.03	1178.79	1265.04
		Exemestane	-0.25	-0.46 to -0.05	-0.17	-0.38 to 0.03	-0.27	-0.52 to -0.02										
FePsy Reaction Time dominant hand ^b	.03	Sequential	-0.22	-0.46 to 0.02	-0.50	-0.76 to -0.25	-0.25	-0.57 to 0.08	-0.43	-0.76 to - 0.10	.01	-0.35	-0.06	-0.46 to 0.34	.78	-0.05	1326.08	1412.47
		Exemestane	-0.26	-0.48 to -0.04	-0.12	-0.34 to 0.11	-0.23	-0.51 to 0.04										
FePsy Reaction Times non- dominant hand ^b	.83	Sequential	-0.41	-0.64 to -0.17	-0.35	-0.59 to -0.10	-0.32	-0.64 to 0.00	0.04	-0.24 to 0.33	.76	0.04	0.13	-0.29 to 0.55	.55	0.10	1266.74	1352.99
		Exemestane	-0.25	-0.46 to -0.03	-0.23	-0.45 to -0.01	-0.29	-0.56 to -0.02										
Working memory ^b	.87	Sequential	-0.43	-0.61 to -0.25	-0.27	-0.46 to -0.08	-0.56	-0.84 to -0.28	0.07	-0.20 to 0.34	.61	0.06	0.06	-0.34 to 0.45	.78	0.04	1133.66	1203.85
		Exemestane	-0.39	-0.55 to -0.23	-0.30	-0.47 to -0.13	-0.58	-0.79 to -0.36										

Abbreviations: T0, baseline; T1; 1 year follow-up; T2, 5 year follow-up; CI, confidence interval; ES, effect size; RAVLT, Rey Auditory Verbal Learning Test; IR, immediate recall; DR, delayed recall; VAT, Visual Association Test; WMS, Wechsler Memory Scale; AIC, Akaike information criterion; BIC, Bayesian information criterion.

^a Effect sizes: .20 small effect, .50 moderate effect, .80 large effect.

^b Adjusted for age, IQ.

^c Adjusted for age, IQ, HSCL, FACT-ES.

^d Adjusted for age, IQ, FACT-ES.

^e Adjusted for age, HSCL, FACT-ES.

^f Adjusted for pattern missing, age, IQ, FACT-ES.

^g Adjusted for age, IQ, HSCL.

^h Adjusted for IQ, HSCL, FACT-ES.

Supplementary Table 5. Results of the per-protocol analyses of the Sequential and the Exemestane group.

Adjusted mean Z-scores			Sequential group vs exemestane	
T0	T1	T2	T0-T1	T0-T2

Cognitive domain/test	P-value overall group-by-time interaction	Group	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean difference in change over time	95% CI	p	ES ^a	Mean difference in change over time	95% CI	p	ES ^a	AIC	BIC
Verbal memory ^b	.03	Sequential	0.03	-0.54 to 0.59	-0.09	-0.68 to 0.49	-1.16	-2.02 to -0.30	-0.59	-1.13 to -0.05	.03	-0.32	-1.19	-2.20 to -0.19	.02	-0.42	1448.41	1544.35
		Exemestane	-0.66	-1.17 to -0.14	-0.19	-0.72 to 0.34	-0.65	-1.33 to 0.03										
RAVLT IR ^c	.12	Sequential	0.01	-0.21 to 0.23	-0.06	-0.29 to 0.18	-0.38	-0.71 to -0.05	-0.22	-0.50 to 0.05	.11	-0.23	-0.38	-0.79 to 0.03	.07	-0.36	903.49	984.86
		Exemestane	-0.33	-0.53 to -0.14	-0.17	-0.38 to 0.03	-0.35	-0.62 to -0.07										
RAVLT DR ^d	.19	Sequential	0.07	-0.16 to 0.30	-0.02	-0.27 to 0.22	-0.18	-0.49 to 0.13	-0.20	-0.45 to 0.04	.11	-0.24	-0.24	-0.59 to 0.11	.17	-0.31	859.85	925.53
		Exemestane	-0.13	-0.34 to 0.08	-0.02	-0.24 to 0.20	-0.14	-0.40 to 0.13										
VAT ^d	.40	Sequential	0.01	-0.28 to 0.30	0.00	-0.31 to 0.31	-0.19	-0.67 to 0.29	-0.23	-0.57 to 0.11	.19	-0.20	-0.07	-0.67 to 0.54	.83	-0.04	1037.77	1102.97
		Exemestane	-0.19	-0.46 to 0.07	0.02	-0.25 to 0.29	-0.32	-0.70 to 0.05										
Visual memory ^b	.45	Sequential	-0.94	-1.38 to -0.50	-0.90	-1.36 to -0.44	-0.93	-1.52 to -0.33	-0.22	-0.65 to 0.21	.32	-0.15	0.12	-0.55 to 0.80	.72	0.07	1303.54	1400.06
		Exemestane	-0.97	-1.37 to -0.57	-0.72	-1.13 to -0.31	-1.08	-1.60 to -0.57										
WMS Visual Memory IR ^c	.55	Sequential	-0.42	-0.66 to -0.18	-0.49	-0.74 to -0.24	-0.54	-0.89 to -0.20	-0.11	-0.37 to 0.14	.38	-0.13	-0.20	-0.61 to 0.21	.34	-0.16	908.40	989.54
		Exemestane	-0.46	-0.68 to -0.24	-0.41	-0.64 to -0.19	-0.38	-0.67 to -0.10										
WMS Visual Memory DR ^c	.06	Sequential	-0.53	-0.77 to -0.29	-0.46	-0.71 to -0.20	-0.33	-0.65 to 0.00	-0.13	-0.39 to 0.13	.33	-0.15	0.32	-0.04 to 0.68	.08	0.37	882.07	963.02
		Exemestane	-0.49	-0.70 to -0.27	-0.28	-0.50 to -0.06	-0.60	-0.87 to -0.33										
Information processing speed ^e	<.001	Sequential	-0.32	-0.49 to -0.15	-0.39	-0.57 to -0.21	-0.47	-0.70 to -0.23	-0.27	-0.44 to -0.10	.002	-0.46	0.06	-0.23 to 0.35	.69	0.05	638.50	715.77
		Exemestane	-0.38	-0.53 to -0.22	-0.18	-0.34 to -0.02	-0.59	-0.79 to -0.39										
Stroop card 1 ^c	.21	Sequential	-0.34	-0.57 to -0.11	-0.42	-0.67 to -0.18	-0.62	-0.95 to -0.29	-0.17	-0.42 to 0.08	.18	-0.19	0.10	-0.33 to 0.52	.66	0.07	889.67	970.87
		Exemestane	-0.33	-0.54 to -0.12	-0.24	-0.46 to -0.03	-0.70	-0.98 to -0.42										
Stroop card 2 ^c	.04	Sequential	-0.28	-0.49 to -0.06	-0.30	-0.52 to -0.08	-0.27	-0.56 to 0.02	-0.22	-0.43 to -0.01	.04	-0.30	0.08	-0.28 to 0.43	.67	0.09	791.12	872.31
		Exemestane	-0.34	-0.53 to -0.15	-0.15	-0.34 to 0.05	-0.41	-0.65 to -0.16										
Trail Making Test A ^d	.005	Sequential	-0.34	-0.58 to -0.10	-0.43	-0.68 to -0.17	-0.49	-0.84 to -0.13	-0.41	-0.69 to -0.14	.003	-0.44	0.02	-0.43 to 0.46	.94	0.01	922.64	988.32
		Exemestane	-0.48	-0.70 to -0.26	-0.15	-0.38 to 0.07	-0.64	-0.94 to -0.35										
Executive functioning ^e	.08	Sequential	-0.35	-0.59 to -0.11	-0.46	-0.71 to -0.21	-0.65	-0.97 to -0.32	-0.24	-0.45 to -0.03	.03	-0.32	-0.30	-0.68 to 0.07	.11	-0.22	834.05	911.21
		Exemestane	-0.55	-0.76 to -0.33	-0.42	-0.64 to -0.20	-0.54	-0.81 to -0.27										
Stroop card 3 ^b	.050	Sequential	-0.33	-0.59 to -0.07	-0.45	-0.73 to -0.17	-0.59	-0.97 to -0.20	-0.29	-0.59 to 0.01	.06	-0.28	-0.59	-1.10 to -0.08	.02	-0.29	993.04	1085.70
		Exemestane	-0.60	-0.83 to -0.36	-0.43	-0.68 to -0.18	-0.26	-0.59 to 0.07										
Trail Making Test B ^e	.20	Sequential	-0.37	-0.65 to -0.10	-0.47	-0.75 to -0.18	-0.66	-1.02 to -0.30	-0.17	-0.42 to 0.08	.18	-0.21	0.12	-0.26 to 0.50	.54	0.15	931.29	1012.31
		Exemestane	-0.50	-0.75 to -0.25	-0.42	-0.68 to -0.17	-0.90	-1.20 to -0.60										
Motor speed ^e	.17	Sequential	-0.07	-0.25 to 0.10	-0.08	-0.27 to 0.10	-0.34	-0.58 to -0.11	-0.13	-0.29 to 0.02	.09	-0.25	-0.21	-0.48 to 0.06	.12	-0.21	610.00	687.16
		Exemestane	-0.17	-0.33 to -0.01	-0.05	-0.21 to 0.12	-0.23	-0.42 to -0.03										
FePsy Fingertapping dominant hand ^e	.47	Sequential	-0.07	-0.25 to 0.10	-0.04	-0.22 to 0.14	-0.29	-0.52 to -0.06	-0.08	-0.24 to 0.07	.30	-0.15	-0.15	-0.43 to 0.12	.28	-0.14	616.09	693.30
		Exemestane	-0.11	-0.26 to 0.05	0.01	-0.15 to 0.16	-0.17	-0.37 to 0.02										
FePsy Fingertapping non-dominant hand ^f	.10	Sequential	-0.08	-0.28 to 0.12	-0.13	-0.34 to 0.08	-0.38	-0.65 to -0.12	-0.19	-0.36 to -0.01	.04	-0.29	-0.26	-0.57 to 0.05	.10	-0.22	707.65	769.38
		Exemestane	-0.24	-0.43 to -0.06	-0.10	-0.29 to 0.08	-0.29	-0.51 to -0.06										
Verbal fluency ^c	.43	Sequential	-1.46	-1.91 to -1.01	-1.43	-1.90 to -0.95	-1.39	-2.04 to -0.74	-0.12	-0.59 to 0.35	.62	-0.07	0.35	-0.43 to 1.14	.37	0.15	1338.65	1419.72
		Exemestane	-1.68	-2.09 to -1.27	-1.53	-1.95 to -1.11	-1.96	-2.50 to -1.43										
Letterfluency ^g	.49	Sequential	-0.50	-0.69 to -0.30	-0.50	-0.70 to -0.29	-0.37	-0.63 to -0.11	-0.10	-0.28 to 0.08	.28	-0.16	0.01	-0.27 to 0.30	.93	0.02	721.58	787.45
		Exemestane	-0.57	-0.74 to -0.39	-0.46	-0.64 to -0.28	-0.45	-0.67 to -0.24										
Category fluency - Animals ^c	.96	Sequential	-0.48	-0.67 to -0.29	-0.51	-0.71 to -0.30	-0.66	-0.97 to -0.36	0.04	-0.23 to 0.31	.78	0.04	0.03	-0.38 to 0.43	.89	0.02	826.66	907.73
		Exemestane	-0.49	-0.66 to -0.32	-0.55	-0.73 to -0.37	-0.70	-0.95 to -0.45										
Category fluency - Professions ^c	.44	Sequential	-0.55	-0.73 to -0.38	-0.51	-0.70 to -0.32	-0.45	-0.73 to -0.16	-0.05	-0.30 to 0.20	.70	-0.06	0.19	-0.19 to 0.57	.32	0.18	769.99	851.07
		Exemestane	-0.61	-0.77 to -0.45	-0.51	-0.68 to -0.35	-0.69	-0.93 to -0.46										

Table continues

Reaction speed ^c	.92	Sequential	0.45	0.14 to 0.75	0.40	0.07 to 0.73	0.22	-0.15 to 0.60	0.04	-0.37 to 0.45	.86	0.03	0.07	-0.28 to 0.42	.69	0.11	1053.04	1133.69
		Exemestane	0.32	0.05 to 0.60	0.24	-0.05 to 0.52	0.03	-0.29 to 0.35										
FePsy Reaction Time dominant hand ^b	.89	Sequential	0.36	0.02 to 0.69	0.39	0.03 to 0.75	-0.05	-0.56 to 0.47	0.11	-0.37 to 0.59	.65	0.06	-0.01	-0.69 to 0.67	.97	-0.01	1198.88	1291.06
		Exemestane	0.35	0.04 to 0.66	0.27	-0.05 to 0.59	-0.04	-0.49 to 0.41										
FePsy Reaction Times non-dominant hand ^b	.60	Sequential	0.53	0.21 to 0.86	0.37	0.02 to 0.72	0.51	0.11 to 0.91	-0.07	-0.50 to 0.36	.74	-0.05	0.17	-0.22 to 0.56	.39	0.24	1122.75	1173.01
		Exemestane	0.31	0.02 to 0.60	0.22	-0.08 to 0.53	0.12	-0.23 to 0.47										
Working memory ⁱ	.77	Sequential	-0.51	-0.71 to -0.31	-0.31	-0.53 to -0.09	-0.69	-1.02 to -0.35	0.09	-0.21 to 0.39	.56	0.08	-0.03	-0.50 to 0.45	.91	-0.02	875.68	925.94
		Exemestane	-0.39	-0.57 to -0.21	-0.28	-0.47 to -0.09	-0.54	-0.80 to -0.27										

Abbreviations: T0, baseline; T1; 1 year follow-up; T2, 5 year follow-up; CI, confidence interval; ES, effect size; RAVLT, Rey Auditory Verbal Learning Test; IR, immediate recall; DR, delayed recall; VAT, Visual Association Test; WMS, Wechsler Memory Scale; AIC, Akaike information criteria; BIC, Bayesian information criteria.

^a Effect sizes: .20 small effect, .50 moderate effect, .80 large effect.

^b Adjusted for age, IQ, HSCL, FACT-ES.

^c Adjusted for age, IQ, HSCL.

^d Adjusted for age, FACT-ES.

^e Adjusted for age, IQ, FACT-ES.

^f Adjusted for age, HSCL.

^g Adjusted for age, IQ.

^h Adjusted for age.

ⁱ Adjusted for IQ.

Supplemental Figure Legend

Supplementary Figure 1. Flow-chart inclusion per-protocol analyses

Abbreviations: ET, endocrine therapy; T1, 1 year follow-up assessment; T2, 5 year follow-up assessment.

Supplementary Figure 2. Summary of results that differed before and after correction.

Abbreviations: ITT, Intention-to-treat analyses; PP, Per-protocol analyses; ST, short-term; LT, long-term; Seq, Sequential group; Exe, Exemestane group; RAVLT, Rey Auditory Verbal Learning Test; IR, Immediate recall; DR, Delayed recall; TMT, Trail Making Test; ndom, non-dominant hand; dom, dominant hand.

NOTE. Blue is effect that arose after correction. Yellow is effect that disappeared after correction. Green remained the same. All other domains, and all other tests have been omitted from this table, as results were identical before and after correction.

Supplementary Figure 3. Adjusted standardized change over time between patients and controls for each cognitive domain.

Mean z-scores are depicted per cognitive domain.



