

SUPPLEMENTARY TABLES**Table S1: Non-compartmental PK parameters of oral SENS-111 in the SAD study, arithmetic mean±SD**

Dose (mg)	C _{max} (ng/mL)	T _{max} [†] (h)	AUC ₀₋₇₂ (ng/mL*h)	AUC _{0-inf} (ng/mL*h)	t _{1/2} (h)	Cl/F (L/h)	Vd/F (L)
100	105 ± 38	1.8 (1.5, 6.0)	1935 ± 294	2276 ± 274	29.9 ± 3.4	44.4 ± 4.7	1922 ± 332
200	286 ± 78	1.5 (1.0, 2.0)	4158 ± 417	4519 ± 440	22.2 ± 2.0	44.6 ± 4.3	1430 ± 182
300	456 ± 108	1.5 (0.5, 2.0)	6709 ± 1421	7566 ± 1829	26.3 ± 4.0	41.2 ± 7.8	1545 ± 287
400	960 ± 574	1.5 (0.5, 4.0)	11351 ± 3009	12284 ± 3405	21.8 ± 1.6	34.4 ± 8.2	1068 ± 204
500	1135 ± 430	0.5 (0.5, 2.0)	15361 ± 3536	17419 ± 3936	27.8 ± 3.3	29.9 ± 6.5	1198 ± 271

† Median (min, max)

Table S2: Non-compartmental PK parameters of oral SENS-111 in the MAD studies, arithmetic mean±SD

Dose (mg)	Day	C _{max} (ng/mL)	T _{max} [†] (h)	AUC ₀₋₂₄ (ng/mL*h)	AUC _{0-inf} (ng/mL*h)	t _{1/2} (h)	R [#]
50 (N=9)	1	35.1 ± 12.9	4.0 (1.0, 6.0)	457 ± 94.6	713 ± 105	15.6 ± 3.2	2.0 ± 0.4
	4	57.2 ± 13.4	4.0 (1.0, 8.0)	913 ± 183	1889 ± 483	27.8 ± 3.1	
100 (N=9)	1	96.9 ± 15.3	1.5 (1.0, 6.0)	1256 ± 127	1745 ± 228	12.4 ± 1.7	2.0 ± 0.4
	4	171 ± 35.2	1.5 (1.0, 8.0)	2449 ± 502	4534 ± 1570	25.3 ± 5.5	
150 (N=9)	1	198 ± 70.9	1.0 (0.5, 4.0)	1772 ± 418	2354 ± 593	11.6 ± 1.1	1.8 ± 0.2
	4	261 ± 87.0	1.5 (1.0, 6.0)	3152 ± 727	5727 ± 1421	24.8 ± 2.1	
200 (N=9)	1	296 ± 102	2.0 (1.0, 6.0)	3416 ± 653	4920 ± 1174	13.2 ± 2.3	2.7 ± 0.7
	7	644 ± 275	1.5 (1.0, 6.0)	9390 ± 3684	23513 ± 12367	47.6 ± 7.1	
250 (N=9)	1	517 ± 182	1.0 (0.5, 6.0)	4662 ± 1019	6442 ± 1541	12.7 ± 1.8	2.6 ± 0.4
	7	1088 ± 467	1.0 (0.5, 4.0)	12174 ± 3345	28231 ± 9414	55.9 ± 13.5	

† median (range)

#accumulation ratio (AUC₀₋₂₄ at D4or D7/AUC₀₋₂₄ at D1)

Table S3: Non-compartmental PK parameters of SENS-111 metabolites in the SAD study, arithmetic mean±SD

Metabolite	Dose (mg)	C _{max} (ng/mL)	T _{max} [†] (h)	AUC ₀₋₇₂ (ng•h/mL)	AUC _{0-inf} (ng•h/mL)	t _{1/2} (h)
UR-64167	100 (N=6)	6.4 ± 2.0	2.0 (1.5, 6.0)	128 ± 31	164 ± 37	36.9 ± 19.9
	200 (N=6)	14.0 ± 4.6	1.5 (1.0, 2.0)	254 ± 41	280 ± 49	22.3 ± 4.3
	300 (N=6)	16.5 ± 2.6	1.8 (1.0, 2.0)	308 ± 45	356 ± 58	28.2 ± 5.5
	400 (N=6)	37.3 ± 24.5	1.5 (0.5, 8.0)	542 ± 85	598 ± 87	23.7 ± 3.3
	500 (N=6)	43.8 ± 25.9	1.0 (0.5, 2.0)	769 ± 383	869 ± 396	27.6 ± 5.0
UR-64250	100 (N=6)	-	-	-	-	-
	200 (N=6)	1.5 ± 1.4	2.0 (1.5, 4.0)	13.7 ± 16.6	31 ± 19	45.3 ± 20.3
	300 (N=6)	2.5 ± 2.1	3.0 (1.5, 6.0)	35 ± 38	61 ± 39	29.8 ± 24.5
	400 (N=6)	2.8 ± 1.8	3.0 (1.0, 8.0)	41 ± 37	55 ± 40	30.9 ± 18.7
	500 (N=6)	6.6 ± 8.3	2.0 (1.5, 4.0)	112 ± 162	134 ± 174	36.0 ± 30.0

† Median (min, max)

Table S4: Non-compartmental PK parameters of SENS-111 metabolites in the MAD study, arithmetic mean±SD

Metabolite	Dose (mg)	Day	C _{max} (ng/mL)	T _{max} (h)	AUC _{0-t*} (ng•h/mL)	AUC _{0-inf} (ng•h/mL)	t _{1/2} (h)
UR-64167	50 (N=9)	1	2.0 ± 0.3	4.0 (1.0, 6.0)	28.0 ± 2.9	41.4 ± 5.1	13.8 ± 1.7
		4	3.3 ± 0.7	4.0 (1.0, 6.0)	79.3 ± 22.7	104 ± 32.5	26.3 ± 8.0
	100 (N=9)	1	4.9 ± 1.2	1.5 (1.5, 6.0)	66.4 ± 18.2	93.1 ± 28.0	12.5 ± 1.6
		4	8.4 ± 2.6	2.0 (1.0, 8.0)	202 ± 83.3	236 ± 112	24.3 ± 6.0
	150 (N=9)	1	8.2 ± 2.7	1.5 (1.0, 4.0)	90.8 ± 19.6	127 ± 30.3	12.9 ± 1.8
		4	11.7 ± 3.5	2.0 (1.0, 6.0)	266 ± 74.4	310 ± 89.3	27.1 ± 3.1
	200 (N=9)	1	15.5 ± 7.1	2.0 (1.0, 6.0)	193 ± 76	285 ± 119	13.9 ± 2.9
		7	30.4 ± 15.9	1.5 (1.0, 8.0)	1174 ± 816	1269 ± 870	44.1 ± 15.3
	250 (N=9)	1	22.7 ± 15.3	1.5 (1.0, 6.0)	240 ± 97	341 ± 122	13.4 ± 2.9
		7	30.4 ± 15.9	1.5 (1.0, 8.0)	1174 ± 816	1269 ± 870	44.1 ± 15.3
UR-64250	50 (N=9)	1	0.6 ± 0.04	8.0 (4.0, 8.0)	1.3 ± 2.0	NC	NC
		4	0.8 ± 0.2	4.0 (1.5, 6.0)	4.2 ± 5.2	NR	NR
	100 (N=9)	1	1.3 ± 0.6	4.0 (1.5, 4.0)	4.4 ± 6.0	NR	NR
		4	1.5 ± 0.9	4.0 (2.0, 4.0)	10.6 ± 14.3	NR	NR
	150 (N=9)	1	1.2 ± 0.5	2.0 (1.5, 4.0)	6.1 ± 8.3	NR	NR
		4	1.3 ± 1.0	4.0 (1.5, 6.0)	17.0 ± 22.7	NR	NR
	200 (N=9)	1	3.8 ± 5.2	4.0 (1.5, 6.0)	45.8 ± 67.3	NR	NR
		7	8.2 ± 13.0	4.0 (1.5, 4.0)	292 ± 559	368 ± 622	26.7 ± 12.3
	250 (N=9)	1	1.6 ± 0.7	2.0 (1.5, 6.0)	16.6 ± 11.3	NR	NR
		7	3.6 ± 1.4	4.0 (1.0, 4.0)	86.0 ± 53.2	117 ± 64.5	26.3 ± 12.9

† Median (min, max)

NC, not calculated; NR, not reached

*AUC_{0-t} t= 24 h for Day 1, 72 h for Day 4, 196 h for Day 7

SUPPLEMENTARY FIGURES

Figure S1: Mean (SD) plasma concentration-time profiles for SENS-111. (A) for the SAD study on day 1; (B) for the 4-day MAD study after 1 day (dotted lines) and 4 days (solid lines); and (C) for the 7-day MAD study after 1 day (dotted lines) and 7 days (solid lines).

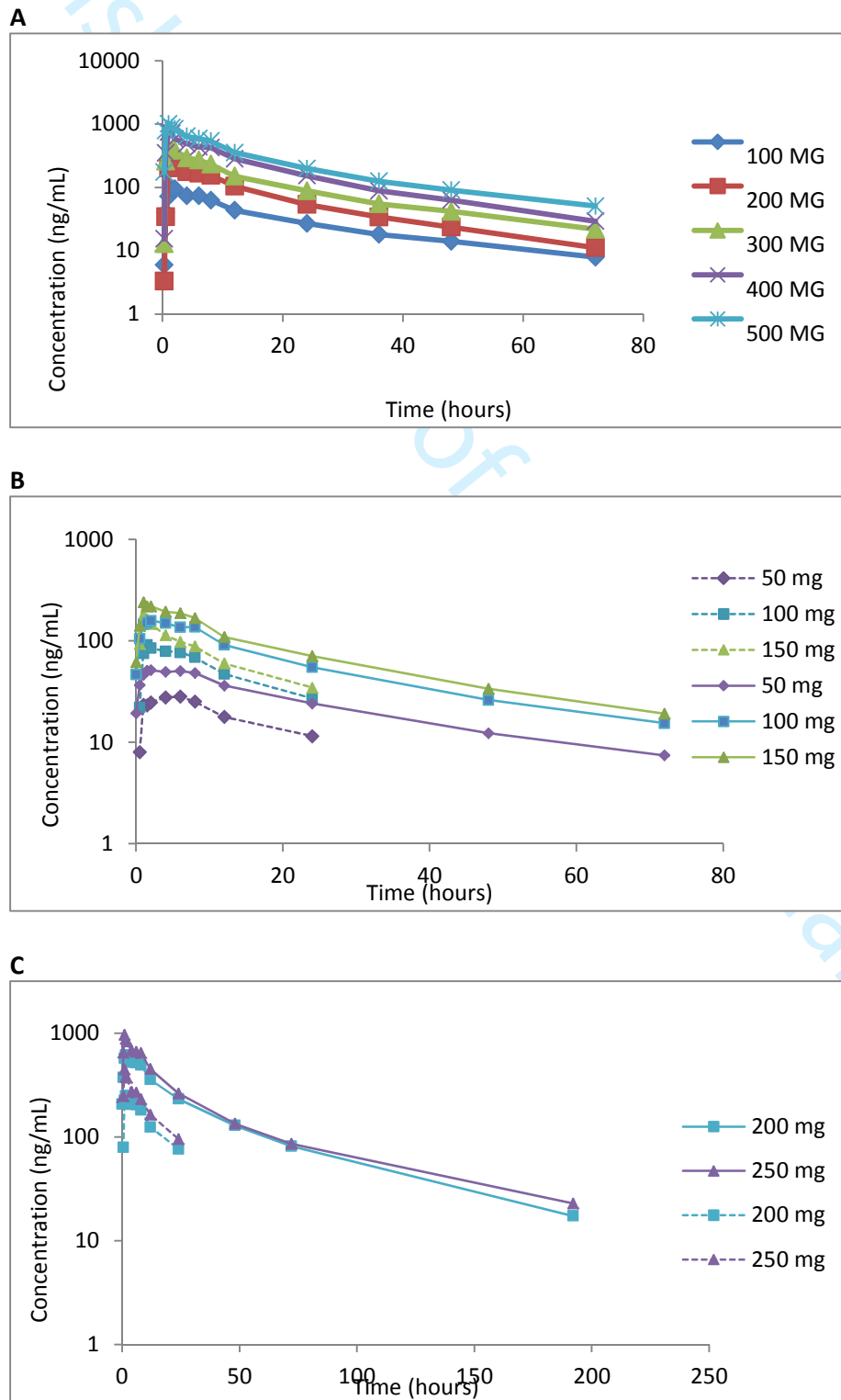


Figure S2: Goodness of fit plots for SENS-111.

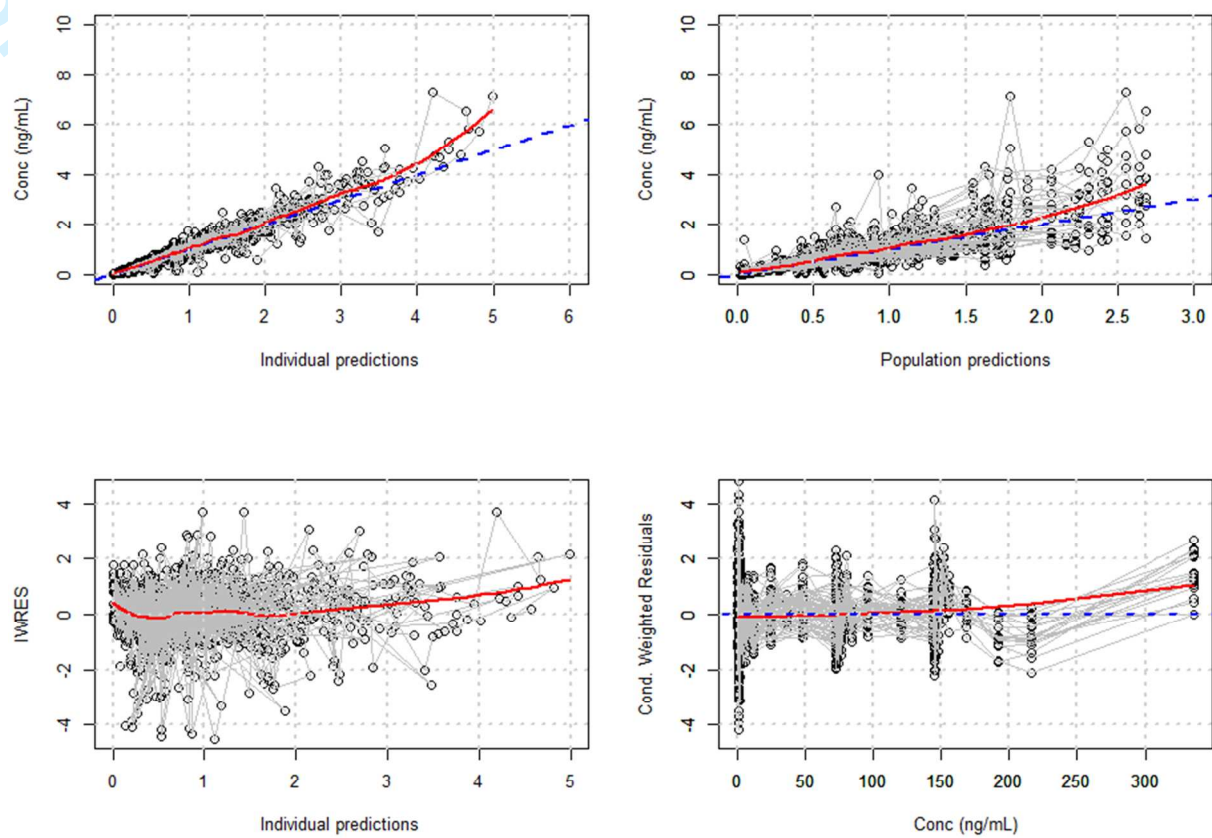


Figure S3: Visual predictive checks (VPCs) using untransformed data to estimate the time-varying change in SENS-111 exposure (200 mg on day 1 versus day 7) and dose-dependent SENS-111 exposure

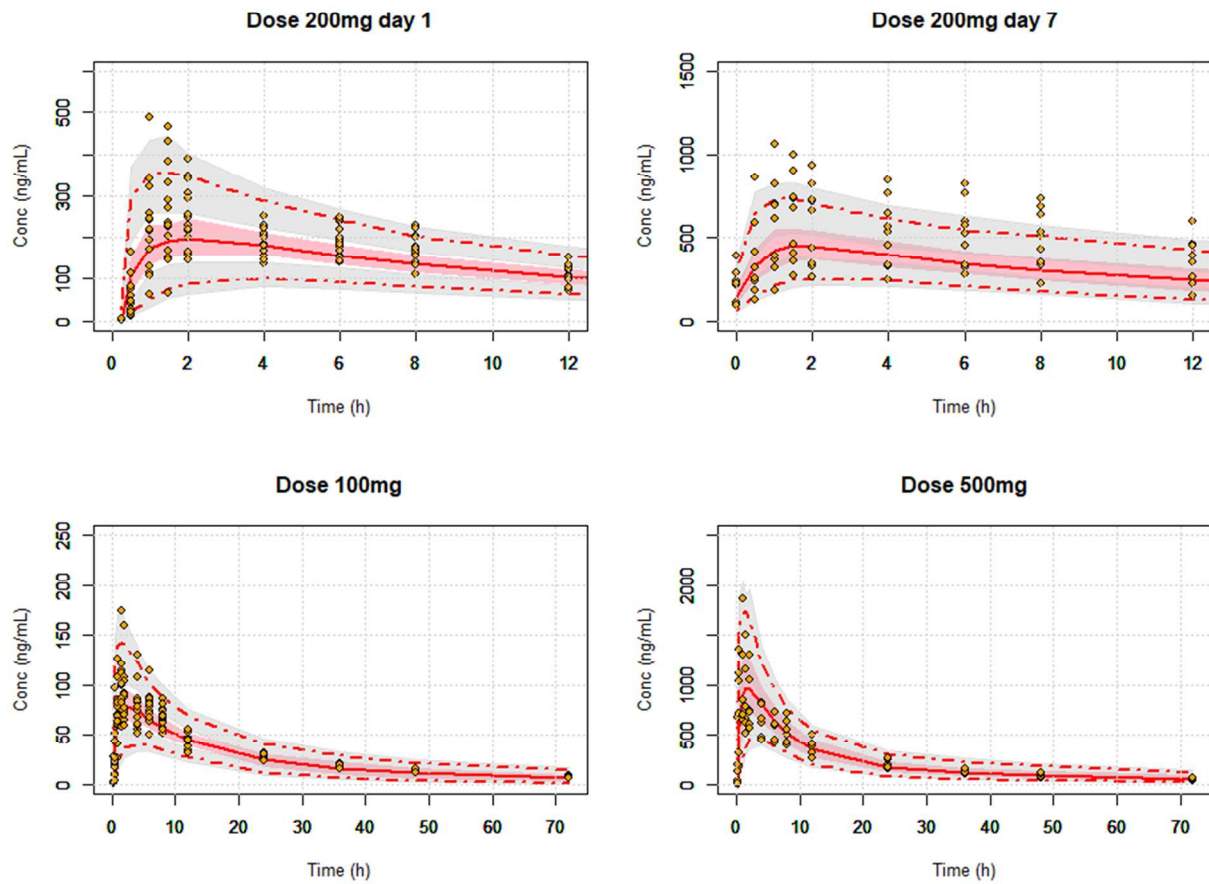


Figure S4: Mean absolute and relative change from baseline over time with placebo treatment are shown for duration of vertigo, and latency of appearance and disappearance.

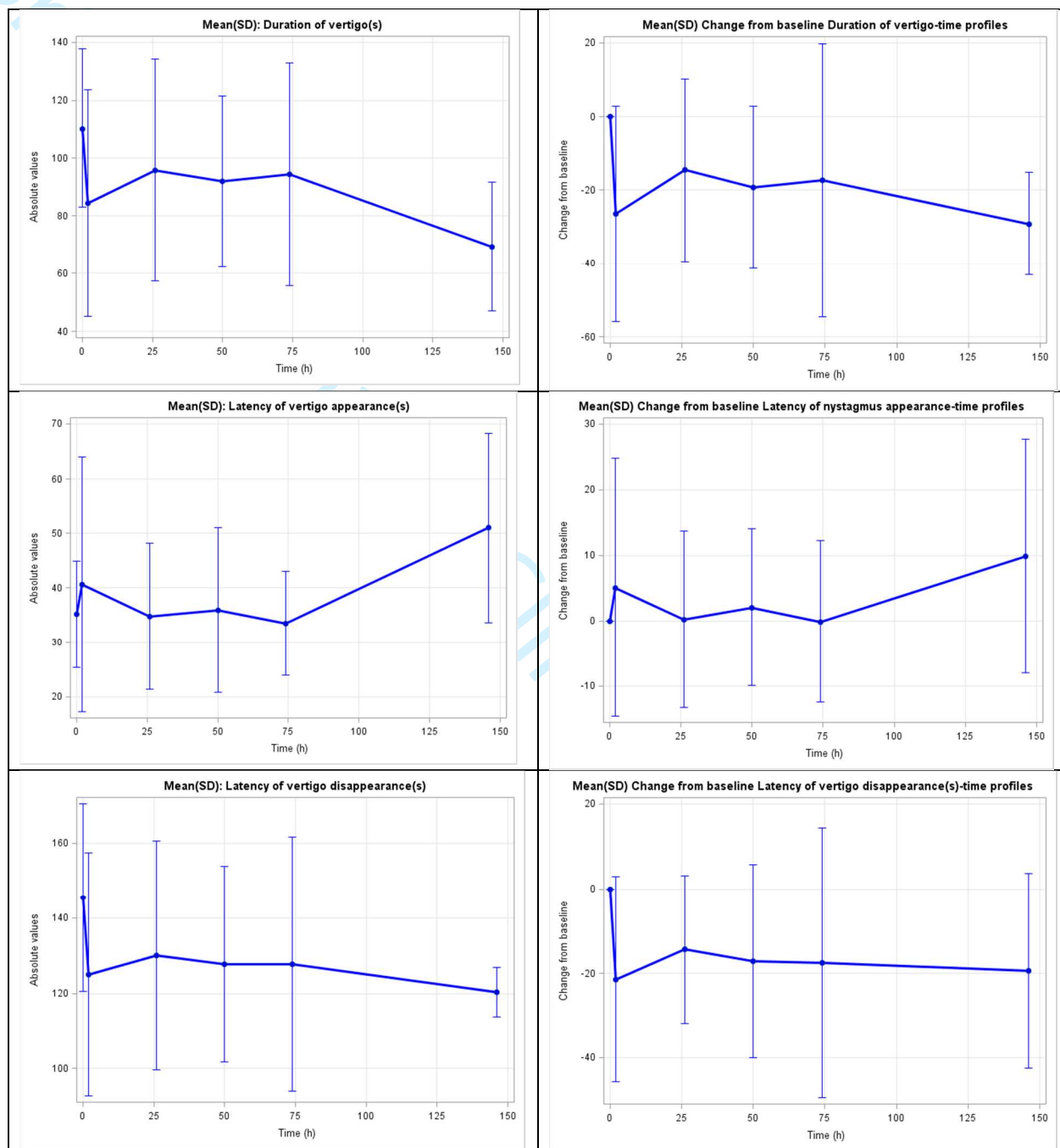


Figure S5: Boxplots of showing the relationship between vertigo duration, and latency of appearance and disappearance with level of SENS-111 exposure.

