

Supplementary Table e-3. Summary of the multi-level analysis of the longitudinal NfL patterns.

Cohort/Sample type	Outcome	Exposure Groups	Estimate (95% CI) [#]	P-value for difference compared with ALS-Slow	Exposure Groups	Estimate (95% CI) [#]	P-value for difference compared with ALS-BM	
		A [§] (n)			B [§] (n)			
London/Plasma	NfL levels at baseline* (pg/mL)	ALS-Slow (30)	79.1 (59.6, 104.8)	-	ALS-BM (33)	73.8 (56.6, 96.3)	-	
		ALS-Intermediate (22)	99.0 (71.4, 137.2)	0.29		ALS-AM (34)	118.2 (91.0, 153.7)	0.01
		ALS-Fast (15)	122.0 (82.5, 180.3)	0.07				
	Change in NfL levels during the first 15 months of F/U** (% change per month)	ALS-Slow (30)	0.3 (-1.0, 1.6) P†=0.68	-	ALS-BM (33)	0.5 (-0.8, 1.8) P=0.46†	-	
		ALS-Intermediate (22)	1.3 (-0.4, 3.0) P†=0.13	0.35	ALS-AM (34)	0.6 (-0.8, 2.1)	0.89	
		ALS-Fast (15)	-0.1 (-2.4, 2.2) P†=0.91	0.76		P=0.41†		
Oxford/Serum	NfL levels at baseline* (pg/mL)	ALS-Slow (21)	55.8 (41.1, 75.7)	-	ALS-BM (21)	56.6 (41.3, 77.6)	-	
		ALS-Intermediate (12)	92.7 (62.1, 138.4)	0.05	ALS-AM (22)	107.2 (78.8, 146.0)	0.004	
		ALS-Fast (10)	125 (80.5, 194.2)	0.003				

	Change in NfL0 levels during the first 15 months of F/U** (% change per month)	ALS-Slow (21)	-0.1 (-1.2, 1.1) P†=0.93	-	ALS-BM (21)	-0.1 (-1.3, 1.2) P=0.93†	-
		ALS-Intermediate (12)	-0.7 (-2.3, 0.9) P†=0.39	0.51			
		ALS-Fast (10)	4.6 (1.6, 7.7) P†=0.003	0.005	ALS-AM (22)	0.5 (-1.0, 2.0) P=0.54†	0.59
Oxford/CSF	NfL levels at baseline* (pg/mL)	ALS-Slow (9)	2882 (2014, 4125)	-	ALS-BM (11)	2993 (2038, 4395)	-
		ALS-Intermediate (8)	6294 (4326, 9156)	0.003			
		ALS-Fast (7)	10917 (7164, 16634)	<0.001	ALS-AM (11)	8024 (5936, 10846)	<0.001
	Change in NfL levels during the first 15 months of F/U** (% change per month)	ALS-Slow (9)	1.3 (0.4, 2.1) P†=0.003	-	ALS-BM (11)	1.3 (0.3, 2.2) P=0.007†	-
		ALS-Intermediate (8)	-0.3 (-1.1, 0.4) P†=0.39	0.005			
		ALS-Fast (7)	3.3 (0.8, 5.9) P†=0.01	0.14	ALS-AM (11)	-0.1 (-0.9, 0.8) P=0.89†	0.04

[§]Exposure groups: categorised by progression rate at the last visit (PRL)

A: PRL<0.5 point/month: ALS-Slow, PRL 0.5-1.0 point/month: ALS-Intermediate, PRL >1.0 point/month: ALS-Fast

B: PRL with median cut-off. AM: above median; BM: below median.

Median PRL in London cohort: 0.54

Median PRL in Oxford cohort: 0.52

#CI: Confidential Interval

*The estimate presented is the geometric mean NfL level at baseline in each exposure group

The estimate presented is the percentage change in NfL per month in each exposure group

†P-value for the rate of change in NfL over time being different from 0 in the exposure group