

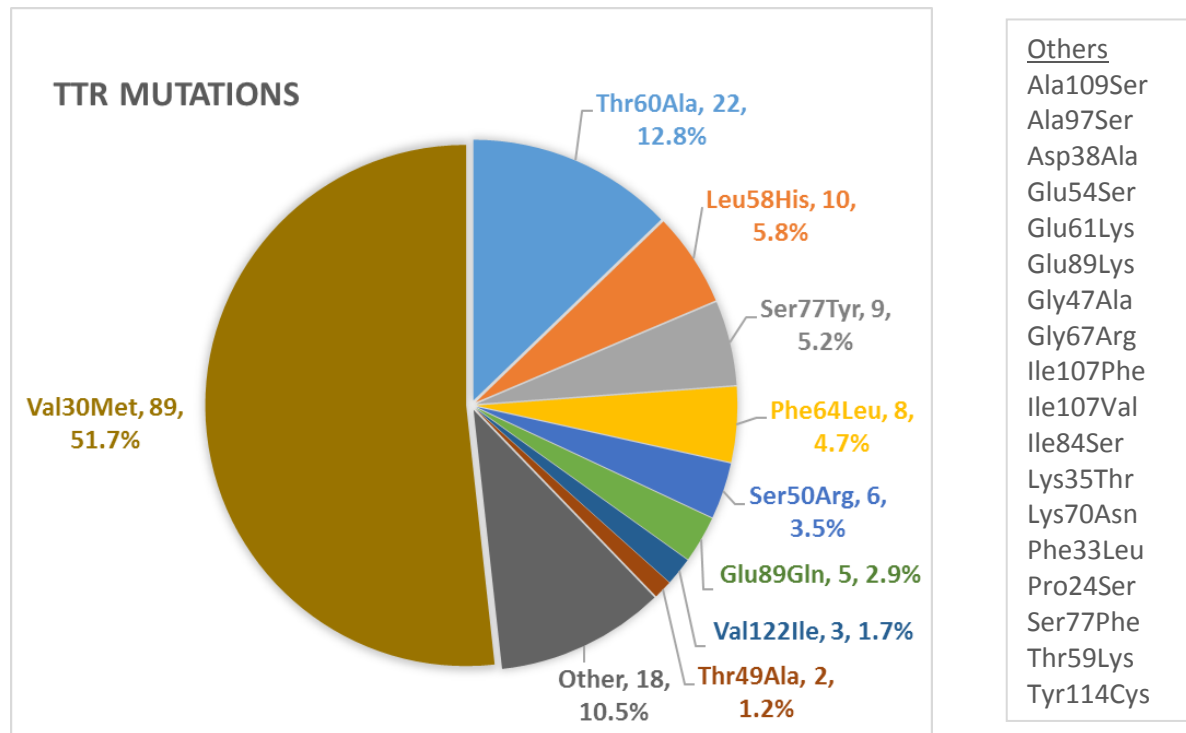
SUPPLEMENTAL DATA

Hereditary Transthyretin Amyloidosis: Baseline Characteristics of Patients in the NEURO-TTR Trial

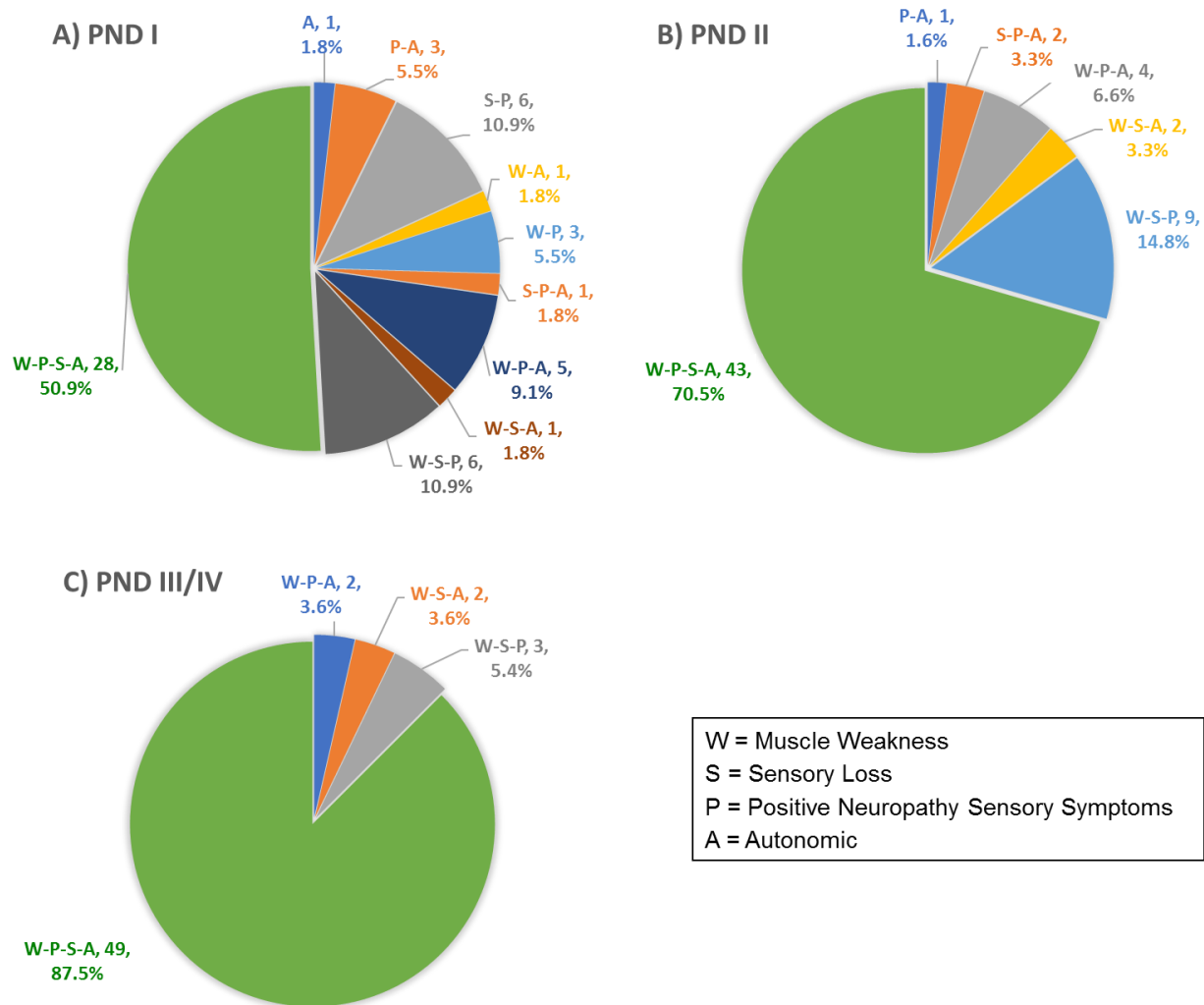
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Supplemental Figure S1: Prevalence of TTR Mutations in the NEURO-TTR Trial. Number and percentage of patients (N=172) exhibiting each observed mutation. Val30Met (52%) was the most common TTR mutation, followed by Thr60Ala (13%). Mutations categorized under Others were each represented by one patient.



Supplemental Figure S2: Symptoms Dysfunction by PND Score. Presence of symptoms as measured by NSC score becomes increasingly broader as disease stage (PND score) progresses. (A) PND I (N=55). (B) PND II (N=61). (C) PND III/IV (N=56). Chart labels show symptom categories, number of subjects, percentage subjects. Symptom categories are as follows: Muscle weakness (W), sensory loss (S), Positive neuropathy sensory symptoms (P), and autonomic (A).



Supplemental Table S1: Baseline Laboratory Tests by Region, Disease Onset, and Prior Treatment with TTR Stabilizers

	Total (n=172)	Region			Disease Onset		Prior Treatment	
		US (n=82)	Europe (n=60)	SA (n=30)	Early (n=56)	Late (n=116)	Stabilizers (n=99)	Naïve (n=73)
SERUM CHEMISTRY								
Albumin (g/L)								
Mean (SD)	42.6 (3.3)	42.9 (2.6)	42.3 (3.6)	42.1 (4.3)	42.8 (3.9)	42.5 (3.0)	42.9 (3.2)	42.2 (3.4)
Median	42.7	43.2	42.1	42.5	42.7	42.7	43.0	42.3
(Min – Max)	(32-50)	(35-48)	(32-50)	(32-48)	(32-50)	(32-49)	(32-50)	(32-48)
Creatine Kinase (U/L)								
Mean (SD)	196.6 (123.4)	196.2 (115.8)	193.4 (118.2)	204.1 (154.6)	208.6 (136.9)	190.8 (116.6)	204.5 (128.6)	185.9 (116.2)
Median	171.2	171.8	187.8	162.0	181.5	168.9	173.3	163.3
(Min – Max)	(40-689)	(47-536)	(40-557)	(51-689)	(43-689)	(40-544)	(40-689)	(43-536)
Creatinine (μmol/L)								
Mean (SD)	76.6 (19.1)	80.6 (20.2)	71.0 (16.8)	76.6 (18.2)	72.4 (14.3)	78.6 (20.8)	76.8 (18.6)	76.2 (19.9)
Median	74.3	77.0	70.3	80.0	74.3	74.7	75.0	73.0
(Min – Max)	(38-142)	(43-142)	(38-124)	(43-122)	(43-101)	(38-142)	(38-142)	(43-122)
eGFR (mL/min/1.72m²)								
Mean (SD)	88.4 (18.6)	82.7 (17.5)	93.8 (17.6)	93.0 (19.4)	100.4 (16.3)	82.6 (16.8)	88.2 (18.3)	88.7 (19.1)
Median	89.3	86.5	95.5	95.3	101.8	85.8	89.0	90.3
(Min – Max)	(41-133)	(41-123)	(52-133)	(53-126)	(59-133)	(41-124)	(42-133)	(41-126)

		Region			Disease Onset		Prior Treatment	
	Total (n=172)	US (n=82)	Europe (n=60)	SA (n=30)	Early (n=56)	Late (n=116)	Stabilizers (n=99)	Naïve (n=73)
HEMATOLOGY								
Platelets (10 ⁹ /L)								
Mean (SD)	219.5 (56.1)	209.6 (50.9)	219.5 (56.3)	246.5 (61.8)	241.1 (63.5)	209.0 (49.1)	215.3 (51.3)	225.2 (61.9)
Median	215.8	202.3	209.5	239.8	240.8	200.7	212.0	222.5
(Min – Max)	(117-406)	(117-406)	(130-387)	(133-381)	(138-387)	(117-406)	(117-381)	(138-406)
Red Blood Cell Count (10 ¹² /L)								
Mean (SD)	4.489 (0.511)	4.495 (0.544)	4.397 (0.448)	4.653 (0.508)	4.553 (0.554)	4.458 (0.488)	4.479 (0.458)	4.501 (0.577)
Median	4.500	4.473	4.413	4.735	4.578	4.463	4.475	4.530
(Min – Max)	(3.16-6.31)	(3.16-6.31)	(3.42-5.17)	(3.20-5.36)	(3.20-6.31)	(3.16-5.55)	(3.42-5.55)	(3.16-6.31)
Hemoglobin (g/L)								
Mean (SD)	136.6 (14.2)	138.7 (14.9)	132.9 (12.3)	138.1 (14.4)	135.4 (15.0)	137.1 (13.8)	136.4 (13.6)	136.9 (14.9)
Median	137.2	140.0	133.8	139.3	137.0	137.4	136.5	139.0
(Min – Max)	(97-181)	(103-181)	(103-156)	(97-157)	(97-181)	(103-165)	(112-165)	(97-181)
OTHER SERUM LAB TESTS								
RBP4 (µg/mL)								
Mean (SD)	35.49 (10.49)	33.87 (10.26)	37.68 (11.29)	35.56 (8.84)	35.85 (10.91)	35.32 (10.33)	36.64 (10.63)	33.93 (10.16)
Median	34.79	34.03	37.36	34.72	35.58	34.55	36.62	33.88
(Min – Max)	(10.96-64.21)	(10.96-58.10)	(15.86-64.21)	(15.01-54.29)	(10.96-63.11)	(13.88-64.21)	(10.96-64.21)	(13.88-55.08)
Vitamin A (µg/dL)								

		Region			Disease Onset		Prior Treatment	
	Total (n=172)	US (n=82)	Europe (n=60)	SA (n=30)	Early (n=56)	Late (n=116)	Stabilizers (n=99)	Naïve (n=73)
Mean (SD)	51.1 (15.4)	46.8 (14.1)	55.0 (16.0)	54.9 (15.4)	53.2 (15.9)	50.0 (15.2)	52.7 (14.6)	48.9 (16.3)
Median	50.8	47.5	54.3	52.8	52.0	50.0	52.5	47.0
(Min – Max)	(13-92)	(13-87)	(25-92)	(24-91)	(13-91)	(23-92)	(13-92)	(24-91)
hsCRP (mg/L)								
Mean (SD)	3.78 (11.07)	2.26 (3.99)	3.63 (8.79)	8.17 (22.21)	6.07 (17.23)	2.65 (5.91)	3.99 (12.53)	3.47 (8.64)
Median	0.90	0.90	0.90	0.80	0.80	0.90	0.90	0.90
(Min – Max)	(0.2-105.0)	(0.2-24.6)	(0.2-51.4)	(0.2-105.0)	(0.2-105.0)	(0.2-51.4)	(0.2-105.0)	(0.2-64.6)
URINALYSIS								
Protein Excretion Rate (mg/day)								
Mean (SD)	165.9 (172.4)	144.6 (147.4)	176.1 (185.9)	194.0 (196.8)	183.6 (202.4)	157.3 (156.1)	169.0 (168.0)	162.2 (178.8)
Median	110.0	103.5	112.0	138.5	120.0	107.5	109.0	114.0
(Min – Max)	(44-936)	(44-884)	(46-936)	(60-912)	(46-936)	(44-884)	(44-936)	(49-912)
A/C (mg/mmol)								
Mean (SD)	5.84 (14.11)	5.10 (15.81)	5.52 (10.54)	8.32 (16.60)	8.78 (18.03)	4.35 (11.47)	4.48 (9.40)	7.76 (18.79)
Median	1.24	1.13	1.47	0.90	1.13	1.24	1.24	1.24
(Min – Max)	(0.23-91.76)	(0.33-91.76)	(0.45-53.22)	(0.23-60.23)	(0.23-91.76)	(0.33-88.82)	(0.34-53.22)	(0.23-91.76)
P/C (mg/mmol)								
Mean (SD)	21.23 (28.48)	18.84 (29.25)	21.26 (23.42)	27.73 (34.89)	25.51 (30.34)	19.17 (27.43)	18.46 (19.91)	25.00 (36.90)
Median	12.83	12.33	14.33	14.33	13.05	12.33	12.67	13.11

		Region			Disease Onset		Prior Treatment	
	Total (n=172)	US (n=82)	Europe (n=60)	SA (n=30)	Early (n=56)	Late (n=116)	Stabilizers (n=99)	Naïve (n=73)
(Min – Max)	(5.50-205.67)	(5.50-205.67)	(5.67-152.00)	(6.33-168.33)	(5.67-177.33)	(5.50-205.67)	(5.50-152.00)	(6.67-205.67)

US denotes United States; SA, South America/Australasia.

Lab Test (LLN-ULN): Albumin, serum (35-55 g/L); Creatine Kinase (25-210 U/L); Creatinine, serum (44-124 µmol/L); eGFR (CKD-EPI formula) (>60 mL/min/1.73m²); Platelets (140-400 10⁹/L); Red Blood Cell Count (RBCs) (4.30-6.00 10¹²/L); Hemoglobin (136-180 g/L); Retinol Binding Protein 4 (RBP4) (11.9-48.3 µg/mL); Vitamin A (24-128 ug/dL); High-sensitivity C-reactive protein (hsCRP) (0-3 mg/L); Protein Excretion Rate, urine (0-299 mg/day); Albumin/Creatinine Ratio (A/C) (0-1.8 mg/mmol); Protein/Creatinine Ratio (P/C) (0-23 mg/mmol).

Supplemental Table S2. Baseline Laboratory Tests by TTR Mutation ($\geq 5\%$ Prevalence in NEURO-TTR)

	Total (n=172)	Val30Met (n=89)	Non- Val30Met (n=83)	Thr60Ala (n=22)	Leu58His (n=10)	Ser77Tyr (n=9)	Phe64Leu (n=8)
SERUM CHEMISTRY							
Albumin (g/L)							
Mean (SD)	42.6 (3.3)	42.5 (3.8)	42.7 (2.8)	41.7 (3.1)	44.1 (2.4)	43.2 (2.6)	43.8 (3.0)
Median	42.7	42.7	42.7	42.3	44.8	42.7	44.0
(Min – Max)	(32-50)	(32-50)	(35-49)	(35-47)	(39-47)	(40-49)	(38-48)
Creatine Kinase (U/L)							
Mean (SD)	196.6 (123.4)	220.5 (137.1)	170.9 (101.6)	129.9 (63.9)	181.8 (137.4)	119.0 (43.7)	233.7 (121.3)
Median	171.2	202.0	158.3	115.7	136.7	107.0	243.5
(Min – Max)	(40-689)	(40-689)	(47-536)	(50-279)	(64-448)	(69-173)	(92-386)
Creatinine ($\mu\text{mol/L}$)							
Mean (SD)	76.6 (19.1)	78.4 (18.7)	74.6 (19.4)	80.3 (18.7)	74.0 (17.4)	67.5 (16.0)	72.0 (15.6)
Median	74.3	77.3	71.0	77.7	76.3	63.3	70.7
(Min – Max)	(38-142)	(43-124)	(38-142)	(53-120)	(43-103)	(39-94)	(55-105)
eGFR (mL/min/1.73m^2)							
Mean (SD)	88.4 (18.6)	89.5 (19.9)	87.2 (17.2)	82.3 (16.6)	85.1 (12.1)	91.7 (15.1)	89.0 (13.3)
Median	89.3	90.0	89.0	83.8	88.0	94.0	89.3
(Min – Max)	(41-133)	(48-133)	(41-124)	(42-109)	(62-98)	(57-108)	(62-108)
HEMATOLOGY							

	Total (n=172)	Val30Met (n=89)	Non- Val30Met (n=83)	Thr60Ala (n=22)	Leu58His (n=10)	Ser77Tyr (n=9)	Phe64Leu (n=8)
Platelets (10 ⁹ /L)							
Mean (SD)	219.5 (56.1)	228.8 (57.1)	209.5 (53.5)	210.8 (60.7)	226.4 (39.3)	205.5 (59.4)	203.2 (56.1)
Median	215.8	225.5	201.0	192.0	229.5	186.5	201.8
(Min – Max)	(117-406)	(123-387)	(117-406)	(133-406)	(159-273)	(150-338)	(117-276)
RBCs (10 ¹² /L)							
Mean (SD)	4.489 (0.511)	4.529 (0.534)	4.446 (0.483)	4.370 (0.617)	4.728 (0.433)	4.466 (0.390)	4.574 (0.540)
Median	4.500	4.565	4.450	4.333	4.665	4.430	4.695
(Min – Max)	(3.16-6.31)	(3.20-6.31)	(3.16-5.41)	(3.16-5.41)	(4.16-5.38)	(3.77-5.15)	(3.46-5.09)
Hemoglobin (g/L)							
Mean (SD)	136.6 (14.2)	136.4 (14.3)	136.8 (14.1)	135.8 (16.1)	145.9 (14.8)	136.7 (12.1)	137.4 (17.3)
Median	137.2	137.5	137.0	138.3	142.7	135.5	143.5
(Min – Max)	(97-181)	(97-181)	(103-165)	(106-164)	(124-165)	(120-158)	(103-156)
OTHER SERUM LAB TESTS							
RBP4 (µg/mL)							
Mean (SD)	35.49 (10.49)	39.91 (8.89)	30.75 (10.04)	32.00 (11.46)	36.29 (6.31)	32.56 (13.24)	28.83 (6.37)
Median	34.79	40.01	28.27	28.22	37.24	30.42	28.05
(Min – Max)	(10.96-64.21)	(15.01-63.11)	(10.96-64.21)	(13.88-57.38)	(26.67-42.85)	(15.86-64.21)	(21.33-40.76)
Vitamin A (µg/dL)							
Mean (SD)	51.1 (15.4)	58.2 (14.0)	43.4 (13.1)	43.7 (14.0)	51.9 (8.9)	44.8 (17.2)	40.5 (7.3)

	Total (n=172)	Val30Met (n=89)	Non- Val30Met (n=83)	Thr60Ala (n=22)	Leu58His (n=10)	Ser77Tyr (n=9)	Phe64Leu (n=8)
Median	50.8	56.5	42.5	42.0	50.3	39.5	41.0
(Min – Max)	(13-92)	(24-92)	(13-85)	(23-80)	(41-68)	(25-85)	(31-53)
hsCRP (mg/L)							
Mean (SD)	3.78 (11.07)	4.78 (13.94)	2.71 (6.74)	2.59 (3.64)	4.42 (7.90)	6.29 (16.92)	1.76 (1.05)
Median	0.90	1.00	0.70	0.80	0.90	0.60	1.90
(Min – Max)	(0.2-105.0)	(0.2-105.0)	(0.2-51.4)	(0.2-13.1)	(0.2-24.6)	(0.2-51.4)	(0.2-3.1)
URINALYSIS							
Protein Excretion Rate (mg/day)							
Mean (SD)	165.9 (172.4)	185.4 (186.5)	141.0 (150.2)	129.3 (106.9)	84.5 (17.1)	104.3 (70.8)	263.6 (347.1)
Median	110.0	120.0	94.0	102.0	81.0	83.0	111.0
(Min – Max)	(44-936)	(46-936)	(44-884)	(44-540)	(68-108)	(60-273)	(90-884)
A/C (mg/mmol)							
Mean (SD)	5.84 (14.11)	7.29 (13.34)	4.22 (14.85)	1.79 (2.02)	0.90 (0.57)	1.61 (1.36)	13.32 (33.29)
Median	1.24	1.64	0.96	1.02	0.74	1.13	0.57
(Min – Max)	(0.23-91.76)	(0.23-60.23)	(0.33-91.76)	(0.33-9.61)	(0.34-2.03)	(0.57-4.63)	(0.57-88.82)
P/C (mg/mmol)							
Mean (SD)	21.23 (28.48)	23.80 (28.30)	18.48 (28.58)	15.44 (10.86)	11.08 (3.40)	12.22 (4.73)	34.33 (69.25)
Median	12.83	14.00	12.33	13.22	10.83	11.67	10.33
(Min – Max)	(5.50-205.67)	(5.67-168.33)	(5.50-205.67)	(5.50-59.50)	(6.50-18.00)	(7.00-20.33)	(6.67-205.67)

Total (n=172)	Val30Met (n=89)	Non- Val30Met (n=83)	Thr60Ala (n=22)	Leu58His (n=10)	Ser77Tyr (n=9)	Phe64Leu (n=8)
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Lab Test (LLN-ULN): Albumin, serum (35-55 g/L); Creatine Kinase (25-210 U/L); Creatinine, serum (44-124 $\mu\text{mol/L}$); eGFR (CKD-EPI formula) (>60 mL/min/1.73m²); Platelets (140-400 $10^9/\text{L}$); Red Blood Cell Count (RBCs) (4.30-6.00 $10^{12}/\text{L}$); Hemoglobin (136-180 g/L); Retinol Binding Protein 4 (RBP4) (11.9-48.3 $\mu\text{g/mL}$); Vitamin A (24-128 ug/dL); High-sensitivity C-Reactive protein (hsCRP) (0-3 mg/L); Protein Excretion Rate, urine (0-299 mg/day); Albumin/Creatinine Ratio (A/C) (0-1.8 mg/mmol); Protein/Creatinine Ratio (P/C) (0-23 mg/mmol).