Supplementary Table 1 Most frequent genotypes recorded at enrollment in the overall population

Genotype, *n* (%)	**Overall (*N* = 5894)**
Val30Met (p.Val50Met)[a]	2924 (49.6)
Wild-type	1386 (23.5)
Val122Ile (p.Val142Ile)	354 (6.0)
Glu89Gln (p.Glu109Gln)	147 (2.5)
Thr60Ala (p.Thr80Ala)	141 (2.4)
Ser50Arg (p.Ser70Arg)	94 (1.6)
Ile68Leu (p.Ile88Leu)	76 (1.3)
Phe64Leu (p.Phe84Leu)	74 (1.3)
Ser77Tyr (p.Ser97Tyr)	72 (1.2)
Ile107Val (p.Ile127Val)	45 (0.8)
Asp38Ala (p.Asp58Ala)	36 (0.6)
Glu89Lys (p.Glu109Lys)	32 (0.5)
Gly47Ala (p.Gly67Ala)	31 (0.5)
Val20Ile (p.Val40Ile)	28 (0.5)
Ala97Ser (p.Ala117Ser)	24 (0.4)
Leu111Met (p.Leu131Met)	22 (0.4)
Val28Met (p.Val48Met)	21 (0.4)
delVal122 (p.delVal142)	19 (0.3)
Glu54Gln (p.Glu74Gln)	17 (0.3)
His88Arg (p.His108Arg)	17 (0.3)
Val122Ala (p.Val142Ala)	16 (0.3)
Ser77Phe (p.Ser97Phe)	15 (0.3)
Thr49Ala (p.Thr69Ala)	15 (0.3)
Ser52Pro (p.Ser72Pro)	12 (0.2)
Pro24Ser (p.Pro44Ser)	11 (0.2)
Thr59Lys (p.Thr79Lys)	10 (0.2)
Tyr114Cys (p.Tyr134Cys)	10 (0.2)

Genotypes recorded in ≥10 patients at enrollment shown

[a] Includes 82 patients with Gly6Ser (p.Gly26Ser)/Val30Met (p.Val50Met) mutations

Supplementary Table 2 Distribution of phenotype at enrollment in symptomatic patients according to genotype category

Phenotype category, *n* (%)	**Overall (*n* = 3779)**	**ATTRwt amyloidosis (*n* = 1156)**	**Val30Met overall (*n* = 1542)**	**Val30Met early onset (*n* = 826)**	**Val30Met late onset (*n* = 588)**	**Cardiac mutations (*n* = 384)**	**Non-Val30Met excluding cardiac (*n* = 697)**
All symptomatic patients							
Predominantly cardiac	1539 (40.7)	1029 (89.0)	100 (6.5)	27 (3.3)	64 (10.9)	241 (62.8)	169 (24.2)
Predominantly neurologic	1516 (40.1)	7 (0.6)	1123 (72.8)	675 (81.7)	369 (62.8)	64 (16.7)	322 (46.2)
Mixed	628 (16.6)	113 (9.8)	277 (18.0)	112 (13.6)	142 (24.1)	66 (17.2)	172 (24.7)
No phenotype	96 (2.5)	7 (0.6)	42 (2.7)	12 (1.5)	13 (2.2)	13 (3.4)	34 (4.9)
North America, *n*	1136	668	29	1	25	256	183
Predominantly cardiac	830 (73.1)	612 (91.6)	8 (27.6)	0	8 (32.0)	167 (65.2)	43 (23.5)
Predominantly neurologic	151 (13.3)	3 (0.4)	14 (48.3)	1 (100.0)	11 (44.0)	42 (16.4)	92 (50.3)
Mixed	131 (11.5)	50 (7.5)	6 (20.7)	0	5 (20.0)	39 (15.2)	36 (19.7)
No phenotype	24 (2.1)	3 (0.4)	1 (3.4)	0	1 (4.0)	8 (3.1)	12 (6.6)
South America, *n*	235	8	190	117	53	18	19
Predominantly cardiac	18 (7.7)	6 (75.0)	1 (0.5)	0	1 (1.9)	8 (44.4)	3 (15.8)
Predominantly neurologic	156 (66.4)	1 (12.5)	145 (76.3)	96 (82.1)	34 (64.2)	3 (16.7)	7 (36.8)
Mixed	58 (24.7)	1 (12.5)	41 (21.6)	20 (17.1)	17 (32.1)	7 (38.9)	9 (47.4)
No phenotype	3 (1.3)	0	3 (1.6)	1 (0.9)	1 (1.9)	0	0
Europe, *n*	2188	462	1212	668	477	108	406
Predominantly cardiac	640 (29.3)	397 (85.9)	79 (6.5)	22 (3.3)	51 (10.7)	65 (60.2)	99 (24.4)
Predominantly neurologic	1106 (50.5)	2 (0.4)	897 (74.0)	550 (82.3)	309 (64.8)	19 (17.6)	188 (46.3)
Mixed	377 (17.2)	59 (12.8)	200 (16.5)	86 (12.8)	107 (22.4)	19 (17.6)	99 (24.4)
No phenotype	65 (3.0)	4 (0.9)	36 (3.0)	10 (1.5)	10 (2.1)	5 (4.6)	20 (4.9)
Japan, *n*	145	7	108	39	31	1	29
Predominantly cardiac	25 (17.2)	5 (71.4)	12 (11.1)	5 (12.8)	4 (12.9)	0	8 (27.6)
Predominantly neurologic	80 (55.2)	1 (14.3)	66 (61.1)	28 (71.8)	14 (45.2)	0	13 (44.8)
Mixed	39 (26.9)	1 (14.3)	29 (26.9)	6 (15.4)	12 (38.7)	1 (100.0)	8 (27.6)
No phenotype	1 (0.7)	0	1 (0.9)	0	1 (3.2)	0	0
Other Asia, *n*	75	11	3	1	2	1	60
Predominantly cardiac	26 (34.7)	9 (81.8)	0	0	0	1 (100.0)	16 (26.7)
Predominantly neurologic	23 (30.7)	0	1 (33.3)	0	1 (50.0)	0	22 (36.7)
Mixed	23 (30.7)	2 (18.2)	1 (33.3)	0	1 (50.0)	0	20 (33.3)
No phenotype	3 (4.0)	0	1 (33.3)	1 (100.0)	0	0	2 (3.3)

Val30Met early onset and late onset *n* based on all patients with available data for disease diagnosis; 128 patients with the Val30Met mutation were missing date of diagnosis. Cardiac mutations include Val122Ile, Leu111Met, Thr60Ala, and Ile68Leu. Patients with no phenotype were symptomatic patients who did fulfill criteria for any of the other phenotype categories.

ATTRwt amyloidosis = wild-type transthyretin amyloidosis

Supplementary Table 3 Clinical characteristics and patient-reported outcomes at enrollment in symptomatic patients according to genotype category

	Overall (*n* = 3779)	**ATTRwt amyloidosis (*n* = 1156)**	**Val30Met early onset (*n* = 826)**	**Val30Met late onset (*n* = 588)**	**Cardiac mutations (*n* = 384)**	**Non-Val30Met excluding cardiac (*n* = 697)**
BMI (kg/m^2), *n*	3658	1125	820	577	365	675
Mean (SD)	25.8 (13.7)	28.1 (19.1)	22.9 (4.7)	25.5 (12.3)	27.6 (17.9)	24.9 (7.3)
Modified BMI[a] (g/L), *n*	2462	715	654	436	167	426
Mean (SD)	1027.5 (230.5)	1072.2 (204.7)	992.4 (235.7)	1013.6 (226.4)	1057.3 (227.3)	995.5 (244.5)
Sitting systolic BP, *n*	3636	1118	814	572	360	672
Mean (SD)	121.9 (18.8)	120.3 (17.2)	123.0 (15.1)	132.8 (20.3)	116.5 (18.0)	116.7 (19.9)
Sitting diastolic BP, *n*	3634	1118	814	571	359	672
Mean (SD)	75.1 (12.0)	72.6 (11.6)	78.5 (11.3)	78.2 (11.3)	72.5 (11.2)	73.8 (12.8)
Derived NIS-LL score, *n*	1505	143	616	277	74	335
Mean (SD)	17.9 (21.2)	4.3 (6.2)	17.6 (20.0)	29.8 (24.0)	7.1 (9.2)	17.7 (21.2)
Reflex score, *n*	2359	298	773	469	170	560
Mean (SD)	7.7 (3.3)	9.3 (1.8)	8.5 (2.4)	6.1 (3.7)	8.6 (2.5)	6.8 (3.8)
Motor score, *n*	2243	393	736	385	157	489
Mean (SD)	151.0 (20.0)	158.5 (11.9)	151.2 (18.9)	143.9 (23.9)	155.8 (17.7)	149.2 (20.6)
Sensory score, *n*	1295	103	548	245	58	287
Mean (SD)	101.6 (26.7)	121.8 (6.5)	98.6 (25.4)	87.3 (31.1)	117.1 (13.0)	108.6 (21.5)
LV septum thickness (mm), *n*	1993	880	182	237	215	432
Mean (SD)	15.9 (5.3)	17.4 (3.5)	9.9 (1.8)	15.1(4.3)	16.8 (4.1)	16.0 (7.8)
LV ejection fraction (%), *n*	1869	885	153	160	230	409
Mean (SD)	52.2 (13.9)	48.1 (12.5)	63.3 (10.0)	60.5 (10.0)	46.3 (15.2)	56.0 (13.6)
EQ-5D-3L: VAS overall health, *n*	2423	743	645	376	206	390
Mean (SD)	65.2 (20.5)	65.5 (19.3)	69.4 (18.5)	59.7 (22.0)	65.0 (22.2)	62.6 (22.0)
EQ-5D-3L: Derived index, *n*	2461	753	651	378	214	400
Mean (SD)	0.7 (0.2)	0.8 (0.2)	0.8 (0.2)	0.7 (0.2)	0.8 (0.2)	0.7 (0.2)
Norfolk Total QoL	2472	742	656	390	210	411
Mean (SD)	33.3 (29.2)	23.9 (20.9)	30.7 (26.6)	48.8 (33.5)	29.2 (27.4)	42.2 (33.9)
Karnofsky Performance Status, *n* (%)						
10–30	10 (0.2)	2 (0.2)	0	0	3 (0.8)	4 (0.6)
40–60	429 (11.4)	82 (7.1)	71 (8.6)	125 (21.3)	40 (10.4)	101 (14.5)
70–90	1904 (50.4)	375 (32.4)	642 (77.7)	346 (58.8)	149 (38.8)	355 (50.9)
100	212 (5.6)	31 (2.7)	39 (4.7)	23 (3.9)	13 (3.4)	81 (11.6)

Val30Met early onset and late onset *n* based on all patients with available data for disease diagnosis; 128 patients with the Val30Met mutation were missing date of diagnosis. Cardiac mutations included Val122Ile, Leu111Met, Thr60Ala, and Ile68Leu

[a] Calculated by multiplying BMI by serum albumin levels to compensate for fluid accumulation

ATTR amyloidosis = transthyretin amyloidosis; ATTRwt amyloidosis = wild-type transthyretin amyloidosis; BMI = body mass index; BP = blood pressure; LV = left ventricular; mPND = modified Polyneuropathy Disability; NIS-LL = Neuropathy Impairment Score in the Lower Limbs; QoL = quality of life; VAS = visual analog scale

Supplementary Table 4 Neurologic characteristics at enrollment in symptomatic patients with a predominantly neurologic or mixed phenotype

	Overall (*n* = 2144)	**ATTRwt amyloidosis (*n* = 120)**	**Val30Met early onset (*n* = 787)**	**Val30Met late onset (*n* = 511)**	**Cardiac mutations (*n* = 130)**	**Non-Val30Met excluding cardiac (*n* = 494)**
Patients with data available, *n*	1755	50	739	437	81	359
mPND score at enrollment, *n* (%)						
0	165 (9.4)	20 (40.0)	46 (6.2)	11 (2.5)	18 (22.2)	57 (15.9)
I	914 (52.1)	13 (26.0)	485 (65.6)	184 (42.1)	37 (45.7)	148 (41.2)
II	364 (20.7)	10 (20.0)	149 (20.2)	118 (27.0)	6 (7.4)	69 (19.2)
IIIa	138 (7.9)	4 (8.0)	33 (4.5)	56 (12.8)	10 (12.3)	27 (7.5)
IIIb	106 (6.0)	2 (4.0)	15 (2.0)	39 (8.9)	8 (9.9)	37 (10.3)
IV	68 (3.9)	1 (2.0)	11 (1.5)	29 (6.6)	2 (2.5)	21 (5.8)

Val30Met early onset and late onset *n* based on all patients with available data for disease diagnosis; 128 patients with the Val30Met mutation were missing date of diagnosis.
ATTRwt amyloidosis = wild-type transthyretin amyloidosis; mPND = modified Polyneuropathy Disability