Table 1a. Baseline clinical characteristics classified by inheritance pattern and age of onset in 179 patients with pathogenic and likely pathogenic dominant variants (AD-CMT2A) and 17 patients with AR-CMT2A. Out of the total of 179 patients with pathogenic and likely pathogenic dominant variants, five were asymptomatic at the age of assessment and four patients had an unknown age of onset of symptoms. Continuous and categorical data that are highlighted yellow in the inheritance pattern group and orange in the age of onset AD-CMT2A group, indicate a statistically significant difference ($p < 0.05$) between the observed values within those groups. The CMTPedS was only performed in patients aged $\leq$ 20yrs at the time of assessment. Data in the last five rows showing the clinical outcome scores represent mean $\pm$ SD, (n). All percentage values are rounded to the nearest point.

Clinical characteristics	Inheritance pattern		Onset in AD-CMT2A	
	AD-CMT2A	AR-CMT2A	Childhood onset (1 – 20yrs)	Adult onset (>20yrs)
No. of patients	179	17	144	26
Age of symptom onset, mean $\pm$ SD, yrs	11.61 $\pm$ 15.07 (range 1.0 – 81)	8.06 $\pm$ 10.92 (range 1.5 – 48)	6.15 $\pm$ 4.82 (range 1 - 20)	41.88 $\pm$ 16.63 (range 23 - 81)
Disease duration, mean $\pm$ SD, yrs	19.98 $\pm$ 14.84 (range 0.1 – 65.2)	25.35 $\pm$ 12.36 (range 4.3 – 46.1)	20.86 $\pm$ 15.56 (range 0.1 – 65.2)	15.15 $\pm$ 8.67 (range 0.7 – 33.3)
Delayed walking (> 15months), n	22/148 (15%)	3/10 (30%)	18/126 (14%)	2/15 (13%)
Foot deformities, n	127/160 (79%)	8/15 (53%)	102/128 (80%)	19/25 (76%)
Ankle-foot orthoses, n	104/166 (63%)	14/15 (93%)	91/133 (68%)	10/25 (40%)
Walking aids, n	46/161 (29%)	7/15 (47%)	38/130 (29%)	8/23 (35%)
Wheelchair-dependent, n	43/163 (26%)	3/15 (20%)	41/132 (31%)	1/23 (4%)
Foot surgery, n	42/166 (25%)	8/15 (53%)	39/134 (29%)	3/25 (12%)
Dexterity difficulties, n	106/166 (64%)	11/14 (79%)	92/132 (70%)	12/26 (46%)
Optic nerve atrophy, n	12/168 (7%)	3/15 (20%)	12/134 (9%)	0/25 (0%)
Hearing loss, n	11/159 (7%)	1/14 (7%)	8/126 (6%)	3/25 (12%)
Scoliosis, n	19/162 (12%)	4/14 (29%)	16/131 (12%)	3/24 (13%)
CMTESv2	10.75 $\pm$ 6.90, (157)	14.57 $\pm$ 6.07, (14)	12.06 $\pm$ 6.82, (122)	6.50 $\pm$ 3.42, (26)
CMTESv2-R	14.27 $\pm$ 8.05, (157)	19.14 $\pm$ 6.56, (14)	15.82 $\pm$ 7.71, (122)	9.42 $\pm$ 5.15, (26)
CMTNSv2	15.27 $\pm$ 9.71, (90)	21.00 $\pm$ 5.20, (7)	17.20 $\pm$ 9.79, (71)	8.47 $\pm$ 4.93, (15)
CMTNSv2-R	19.13 $\pm$ 10.73, (90)	26.14 $\pm$ 5.61, (7)	21.42 $\pm$ 10.47, (71)	11.13 $\pm$ 6.45, (15)
CMTPedS	26.45 $\pm$ 10.26, (47)	27.00 $\pm$ 11.31, (2)	27.31 $\pm$ 9.57, (45)	n/a

Table 1b. Baseline clinical characteristics classified by variant topology and biological effect of the variant in patients with pathogenic and likely pathogenic dominant variants (AD-CMT2A). The amino acid positions used for the dynamin-GTPase domain are 93-342. Variants shown to cause mitochondrial hypofusion in non-human disease models are p.Arg94Gln (R94Q) and p.Thr105Met (T105M), whereas variants shown to cause mitochondrial hyperfusion are p.Leu76Pro (L76P) and p.Arg364Trp (R364W). Categorical data that are highlighted yellow in the variant topology group indicate a statistically significant difference ($p < 0.05$) between the observed values within that group. The CMTPedS was only performed in patients aged $\leq$ 20yrs at the time of assessment. Data in the last five rows showing the clinical outcome scores represent mean $\pm$ SD, (n). All percentage values are rounded to the nearest point.

Clinical characteristics	Variant topology (AD-CMT2A)		Biological effect of variants	
	GTPase domain variants	Non-GTPase domain variants	Mitochondrial hypofusion (R94Q, T105M)	Mitochondrial hyperfusion (L76P, R364W)
No. of patients	104	75	11	17
Age of symptom onset, mean $\pm$ SD, yrs	11.79 $\pm$ 15.35 (range 1 – 81)	11.37 $\pm$ 14.76 (range 1 – 70)	5.55 $\pm$ 2.97 (range 2.5 – 12)	5.71 $\pm$ 14.85 (range 1 – 63)
Disease duration, mean $\pm$ SD, yrs	19.03 $\pm$ 13.99 (range 0.1 – 53.1)	21.31 $\pm$ 15.96 (range 2.6 – 65.2)	19.19 $\pm$ 12.67 (range 3.6 – 43.7)	17.51 $\pm$ 16.68 (range 2.7 – 49.3)
Foot deformities, n	73/93 (78%)	54/67 (81%)	7/8 (88%)	11/14 (79%)
Ankle-foot orthoses, n	67/96 (70%)	37/70 (53%)	9/10 (90%)	14/16 (88%)
Walking aids, n	24/93 (26%)	22/68 (32%)	4/10 (40%)	8/16 (50%)
Wheelchair-dependent, n	25/96 (26%)	18/67 (27%)	4/10 (40%)	9/16 (56%)
Foot surgery, n	29/95 (31%)	13/71 (18%)	5/10 (50%)	2/17 (12%)
Dexterity difficulties, n	68/97 (70%)	38/69 (55%)	8/10 (80%)	11/15 (73%)
Optic nerve atrophy, n	10/99 (10%)	2/69 (3%)	0/11 (0%)	2/14 (14%)
Hearing loss, n	3/90 (3%)	8/69 (12%)	0/10 (0%)	2/13 (15%)
Scoliosis, n	15/94 (16%)	4/68 (6%)	0/9 (0%)	3/16 (19%)
CMTESv2	11.31 $\pm$ 7.06, (87)	10.06 $\pm$ 6.68, (70)	12.13 $\pm$ 7.02, (8)	16.73 $\pm$ 7.81, (15)
CMTESv2-R	15.15 $\pm$ 8.16, (87)	13.19 $\pm$ 7.82, (70)	16.25 $\pm$ 8.00, (8)	20.07 $\pm$ 8.46, (15)
CMTNSv2	16.68 $\pm$ 10.38, (47)	13.72 $\pm$ 8.79, (43)	20.50 $\pm$ 16.26, (2)	26.00 $\pm$ 8.26, (10)
CMTNSv2-R	20.98 $\pm$ 11.30, (47)	17.12 $\pm$ 9.81, (43)	25.00 $\pm$ 16.97, (2)	29.90 $\pm$ 8.20, (10)
CMTPedS	27.88 $\pm$ 8.17, (24)	24.96 $\pm$ 12.06, (23)	27.00 $\pm$ 7.07, (2)	34.78 $\pm$ 5.97, (9)

Table 2. Mean change and standardised response mean (SRM) of the CMTESv2 and its weighted version (CMTESv2-Rasch) and the CMT Pediatric Scale (CMTPedS) in autosomal dominant (AD)-CMT2A and AR-CMT2A at 1 and 2 years follow-up. The CMTESv2 changed significantly over 1 and 2 years in patients with AD-CMT2A, whereas the CMTESv2-R changed significantly over 2 years. The CMTPedS (all cases grouped) changed significantly both over 1 and 2 years. There was no significant change in cases with AR-CMT2A over 1 and 2 years. Mean changes that are statistically significance have their p values and SRMs coloured in red. Data shown represent mean ± SD.

		Follow-up (yrs)	n	Baseline	Change	p	SRM
Autosomal dominant (AD)	CMTESv2	1	38	10.66 ± 5.94	0.84 ± 2.42	**0.039**	**0.35**
	CMTESv2 - Rasch	1	38	14.53 ± 6.96	0.63 ± 3.19	0.230	0.20
	CMTESv2	2	34	9.47 ± 6.26	0.97 ± 1.77	**0.003**	**0.55**
	CMTESv2 - Rasch	2	34	13.00 ± 7.68	1.21 ± 2.52	**0.009**	**0.48**
Autosomal recessive (AR)	CMTESv2	1	6	12.33 ± 6.65	0.17 ± 3.06	0.900	0.05
	CMTESv2 - Rasch	1	6	17.00 ± 7.21	-0.33 ± 2.73	0.777	-0.12
	CMTESv2	2	4	10.25 ± 7.23	0.25 ± 1.26	0.718	0.20
	CMTESv2 - Rasch	2	4	14.75 ± 7.63	0 ± 1.41	1.000	0
	CMTESv2	4	5	13.40 ± 6.66	1.80 ± 3.11	0.266	0.58
	CMTESv2 - Rasch	4	5	17.60 ± 7.23	1.40 ± 3.91	0.468	0.36
AD and AR	CMTPedS	1	17	25.41 ± 8.01	2.24 ± 3.09	**0.009**	**0.72**
	CMTPedS	2	7	28.86 ± 7.82	4.00 ± 3.79	**0.031**	**1.06**