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Huntington's Disease Clinical Trials Corner: April 2020

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Abstract. In this edition of the Huntington's Disease Clinical Trials Corner we expand on the UniQure AMT-130 and on the Neurocrine Biosciences KINECT-HD trials, and list all currently registered and ongoing clinical trials in Huntington's disease.

Keywords: Huntington disease, clinical trials

INTRODUCTION

The Huntington's Disease Clinical Trials Corner is a regular section devoted to highlighting ongoing and recently completed clinical trials in Huntington's disease (HD). Clinical trials previously reviewed by the Huntington's Disease Clinical Trials Corner are listed in Table 1.

In this edition, we highlight the UniQure AMT-130 (NCT04120493) [1], and the Neurocrine Biosciences KINECT-HD trial (NCT04102579) [2]. We tabulate all currently registered and ongoing clinical trials in Tables 2 to 4. For further details on the methodology used, please refer to the first edition of Huntington's Disease Clinical Trials Corner [3].

If you would like to draw attention to specific trials, please feel free to email us at: f.rodrigues@ucl.ac.uk and e.wild@ucl.ac.uk.

ONGOING CLINICAL TRIALS

A list of all ongoing clinical trials is given in Tables 2, 3 and 4.

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In addition to the trials covered below, it is worth mentioning that Wave Life Sciences made a preliminary announcement of results from their ongoing PRECISION-HD2 trial (NCT03225846) [4]. This is a phase 1b/2a trial investigating WVE-120102, an intrathecal allele-selective antisense oligonucleotide (ASO). When compared with placebo, this drug was shown to reduce CSF mutant huntingtin by 12.4% (95% CI 0.40 to 24.58), while CSF total huntingtin and neurofilament light (NfL) remained unchanged. Whist statistically significant, this reduction was derived from a comparison of all ASO doses pooled together (mean change from baseline –6.0% [95% CI –9.57 to 4.85]) against a placebo arm showing a somewhat larger change than might be expected due to disease progression from natural history studies (mean change from baseline 9.5% [95% CI 1.77 to 20.38]). The ASO was also considered to be "generally safe and well tolerated among patients receiving doses up to 16 mg". No results were disclosed about the PRECISION-HD1 trial (NCT03225833) [5], testing WVE-120101, another intrathecal allele-selective ASO targeting a different single-nucleotide polymorphism. As a result, a new 32 mg dosage cohort will added to both trials and further updates are awaited from the broader program [6].

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Table 1
Clinical trials previously reviewed by the Huntington's Disease Clinical Trials Corner. IONIS-HTT_{Rx}, RG6042 and tominersen refer to the same molecule

	Trial name	Intervention	Edition
NCT02519036	IONIS-HTTRx	IONIS-HTT_{Rx}*	September 2017 [3]
NCT02215616	LEGATO-HD	Laquinimod	
NCT02197130	Amaryllis	PF-02545920	
NCT02006472	PRIDE-HD	Pridopidine	
NCT03225833	PRECISION-HD1	WVE-120101	February 2018 [13]
NCT03225846	PRECISION-HD2	WVE-120102	
NCT01795859	FIRST-HD	Deutetrabenazine	
NCT02481674	SIGNAL	VX15/2503	August 2018 [14]
NCT00712426	CREST-E	Creatine	
NCT03761849	GENERATION-HD1	RG6042*	January 2019 [15]
NCT03344601	PACE-HD	Physical activity	
NCT02535884	HD-DBS	Deep brain stimulation	June 2019 [16]
NCT02453061	TRIHEP3	Triheptanoin	
NCT04120493	AMT-130	AAV5-miHTT	April 2020
NCT04102579	KINECT-HD	Valbenazine	

AMT-130 (NCT04120493)

Study title: A Phase I/II, Randomized, Double-blind, Sham Control Study to Explore Safety, Tolerability, and Efficacy Signals of Multiple Ascending Doses of Striatally-Administered rAAV5-miHTT Total Huntingtin Gene (HTT) Lowering Therapy (AMT-130) in Early Manifest Huntington Disease [1].

Intervention: Single-time intrastriatal injection of AAV5-miHTT [7].

Description: The AMT-130 trial, sponsored by UniQure, aims to evaluate the safety, tolerability and proof-of-concept of a single-time bilateral intrastriatal injection of AAV5-miHTT in adults (25 to 65 years of age) with manifest HD (i.e. clinically symptomatic and genetically confirmed [CAG $\geq$ 44]) and early disease stage, comparing with sham injection, for disease progression.

Individuals who have received any experimental agent or participation in the following are not eligible for this study: any investigational trial within 60 days or five half-lives prior to screening; with a deep brain stimulator *in situ*; with history of gene therapy, RNA or DNA targeted HD specific investigational agent, cell transplantation or other experimental cerebral surgery; contraindications for lumbar punctures or 3 Tesla MRI; putaminal and caudate volumes per side inferior to 2.5 and 2.0 cm^3, respectively; brain or spinal cord pathology that may interfere with CSF homeostasis and circulation, increased intracranial pressure, malformations or tumours; hospitalization for major medical reason or major surgical procedure involving general anaesthesia within 12 weeks of screening; current use of medications to treat or that can aggravate chorea, or unstable concomitant medication within 3 months of screening.

This trial is an US-based, multi-centre, randomized, sham-controlled, double-blind, parallel study. It will have 3 study arms: the low dose group, where participants will receive a single total dose of 6×10^{12} genome copies of AAV5-miHTT via a MRI-guided convection-enhanced delivery; the high dose group, where participants will receive a single total dose of 6×10^{13} genome copies of AAV5-miHTT via a MRI-guided convection-enhanced delivery; and the imitation surgery arm, where participants will receive bilateral partial thickness burr holes with no intrastriatal injections. The study will last 5 years, where participants will be blind to treatment allocation for 18 months, followed by an unblinded period of 3.5 years.

The trial has already started recruitment [8], and has a recruitment target of 26 participants, across 4 sites. It will follow a multiple ascending dose design, with a first cohort of 10 participants (stage 2 HD; 6 randomized to low dose and 4 to sham surgery) and a second cohort of 16 participants (stage 1-2 HD; 10 randomized to high dose and 6 to sham surgery).

The primary outcome will be safety, measured at 18 months, and the secondary outcome will be CSF biomarkers, namely levels of the vector DNA and miRNA expression at 60 months. Other outcomes include: biofluid and imaging biomarkers; clinical scales such as the UHDRS motor, cognitive, behaviour and functional subscales, the Huntington's Disease Cognitive Assessment Battery (HD-CAB),

Table 2
Ongoing pharmacological clinical trials registered at the World Health Organization (WHO) International Clinical Trials Research Platform (ICTRP) for people with Huntington's disease (HD). N/S, not specified; PD, Parkinson's disease; VMAT2, Vesicular Monoamine Transporter 2. Note: IONIS-HTT_{Rx}, ISIS 443139, RG6042 and tominersen refer to the same molecule. New trials since the last Clinical Trials Corner are indicated by *

Registration ID	Trial name	Intervention	Mechanism of Action	Population	Comparison	Main outcome	Study design	Estimated Enrolment	Sponsor	Location
NCT04201834*	–	Risperidone	Dopamine antagonist	Early and moderate HD with chorea	None	Change in motor scales at 12 weeks	Non-randomized, open label (assessor-blind), uncontrolled trial	12	University of Rochester	USA (single centre)
NCT04071639*	–	Haloperidol, risperidone, sertraline and coenzyme Q10	Multiple (dopamine antagonists, selective serotonin reuptake inhibitor, dietary supplement)	Early and moderate HD	Coenzyme Q10	Efficacy at 5 years	Randomized, open label, controlled, parallel trial	100	Second Affiliated Hospital, School of Medicine, Zhejiang University	China (single centre)
NCT04120493*	AMT-130	rAAV5-miHTT	Nonselective miRNA	Early HD	Sham intervention	Safety at 18 months	Randomized, double-blind, sham-controlled, parallel trial	26	UniQure Biopharma B.V.	USA (multi-centre)
NCT04102579*	KINECT-HD	Valbenazine	VMAT2 inhibitor	HD with chorea	Placebo	Efficacy at 12 weeks	Randomized, double-blind, placebo-controlled, parallel trial	120	Neurocrine Biosciences, Huntington Study Group	USA (multi-centre)
EUCTR2019-002178-30-DK*	–	WVE-120102	Allele-selective antisense oligonu-cleotide	HD	None	Safety and tolerability at 97 weeks	Open-label extension	70	Wave Life Sciences Ltd.	Australia, Canada, Denmark, France, Poland and United Kingdom (multi-centre)

(*Continued*)

Table 2
(*Continued*)

Registration ID	Trial name	Intervention	Mechanism of Action	Population	Comparison	Main outcome	Study design	Estimated Enrolment	Sponsor	Location
NCT04000594*	GEN-PEAK	RG6042	Allele-nonselective antisense oligonucleotide	HD	None	Pharmacodynamics and pharmacokinetics at multiple timepoints until 6 months	Non-randomized. open-label, multiple-dose, parallel trial	20	Hoffmann-La Roche	The Netherlands and UK (multi-centre)
NCT03980938*	–	Neflamapimod	p38α MAPK inhibitor	Early HD	Placebo	Change in cognitive scales at 10 weeks	Randomized, double-blind, placebo-controlled, cross-over trial	16	EIP Pharma Inc, Voisin Consulting, Inc.	UK (single centre)
NCT03842969	GEN-EXTEND	RG6042	Allele-nonselective antisense oligonucleotide	HD	None	Safety and tolerability at up to 5 years	Open-label extension	1050	Hoffmann-La Roche	USA, Canada, Europe (multi-centre)
NCT03761849	GENERATION-HD1	RG6042	Allele-nonselective antisense oligonucleotide	HD	Placebo	Clinical efficacy at 101 weeks	Randomized, double-blind, placebo-controlled, parallel trial	909	Hoffmann-La Roche	USA, Canada, Europe (multi-centre)
NCT03515213	–	Fenofibrate	PPARα agonist	HD	Placebo	Pharmacodynamics at 6 months	Randomized, double-blind, placebo-controlled, parallel trial	20	University of California, Irvine	USA (single centre)
NCT03764215	Tasigna HD	Nilotinib	Selective Bcr-Abl tyrosine kinase inihbitor	HD	None	Safety, tolerability and pharmacodynamics at 3 months	Open label, multiple ascending dose	20	Georgetown University	USA (single centre)

NCT03225833	PRECISION-HD1	WVE-120101	Allele-selective antisense oligonu-cleotide	HD	Placebo	Safety and tolerability at 1 and 120 days	Randomized, double-blind, placebo-controlled, combined single ascending dose/multiple ascending dose trial	48	Wave Life Sciences Ltd.	Australia, Canada, Denmark, France, Poland and United Kingdom (multi-centre)
NCT03225846	PRECISION-HD2	WVE-120102	Allele-selective antisense oligonu-cleotide	HD	Placebo	Safety and tolerability at 1 and 120 days	Randomized, double-blind, placebo-controlled, combined single ascending dose/multiple ascending dose trial	60	Wave Life Sciences Ltd.	Australia, Canada, Denmark, France, Poland and United Kingdom (multi-centre)
NCT02453061	TRIHEP 3	Triheptanoin	Anaplerotic therapy	HD	Safflower oil	Pharmaco-dynamic efficacy at 6 months	Randomized, double-blind, controlled, parallel trial	100	Institut National de la Santé Et de la Recherche Médicale, Ultragenyx Pharmaceuti-cal Inc	France, Netherlands (multi-centre)
NCT02509793	–	Tetrabenazine	VMAT2 inhibitor	HD with impulsivity	None	Cognitive and behavioural effects at 8 weeks	Single group, open-label trial	20	University of Texas Health Science Center, and H. Lundbeck A/S	USA (single centre)

(*Continued*)

Table 2
(*Continued*)

Registration ID	Trial name	Intervention	Mechanism of Action	Population	Comparison	Main outcome	Study design	Estimated Enrolment	Sponsor	Location
NCT02481674	SIGNAL	VX15/2503	Anti-semaphorin 4D monoclonal antibody	Late premanifest or early HD	Placebo	Safety and tolerability at 15 and 21 months	Randomized, double-blind, placebo-controlled, parallel trial	240	Vaccinex Inc., Huntington Study Group	USA (multi-centre)
EUCTR2013-002545-10-SE	OSU6162Open1300(-)-OSU616		Monoaminergic stabilizer	HD, PD, brain trauma, stroke, myalgic encephalomyeli-tis and narcolepsy	None	Safety at 3, 6 and 12 months	Single group, open-label trial	240	A. Carlsson Research AB	Sweden (multi-centre)
NCT00514774	UDCA-HD	Ursodiol	Bile acid	HD	Placebo	Safety, tolerability and pharma-cokinetics at 35 days	Randomized, double-blind, placebo-controlled, parallel trial	21	Oregon Health and Science University, Huntington Study Group, Huntington Society of Canada	N/S

Table 3
Ongoing invasive non-pharmacological clinical trials registered at the World Health Organization (WHO) International Clinical Trials Research Platform (ICTRP) for people with Huntington's disease (HD). AD, Alzheimer's disease, CBD; Corticobasal Degeneration; DBS, deep brain stimulation; ET, Essential Tremor; GP, Globus pallidus; HT, Holmes Tremor; MNC, mononuclear cells; MS, Multiple Sclerosis; PD, Parkinson's disease; TD, Tardive dyskinesia; WD, Wilson's disease. New trials since the last Clinical Trials Corner are indicated by *

Registration ID	Trial name	Intervention	Mechanism of Action	Population	Comparison	Main outcome	Study design	Esimated Enrolment	Sponsor	Location
NCT04244513*	–	GPi DBS	Deep brain stimulation	HD with chorea	Sham intervention	Efficacy at 3 and 6 months	Randomized, double-blind, sham-controlled, cross-over trial	40	Beijing Municipal Administration of Hospitals, Medtronic	China (multi-centre)
NCT04219241*	ADORE-EXT	Cellavita	Stem cell therapy	HD	None	Efficacy and safety at 2 years	Open label extension	35	Azidus Brasil, Cellavita Pesquisa Científica Ltda	Brazil (single centre)
ISRCTN52651778	TRIDENT	Foetal stem cell transplant	Stem cell therapy	Early stage HD	Usual care	Safety at 4 weeks	Randomized, open label, controlled, parallel trial	30	Cardiff University	UK (single centre)
NCT02728115	SAVE-DH	Cellavita	Stem cell therapy	HD	None	Safety at 5 years	Non-randomized, open label, uncontrolled, parallel trial	6	Azidus Brasil	Brazil (single centre)
NCT03252535	ADORE-HD	Cellavita	Stem cell therapy	HD	Placebo	Efficacy at 120 days	Randomized, double-blind, placebo-controlled, parallel trial	35	Azidus Brasil	Brazil (single centre)
NCT03297177	–	Autologous stem/stromal cells	Autologous stem/stromal cell injection	HD, AD, PD, CBD, MS	None	Safety at 5 years	Single group, open-label trial	300	Healeon Medical Inc, Global Alliance for Regenerative Medicine, Regeneris Medical	USA and Honduras (multi-centre)

(*Continued*)

Table 3
(*Continued*)

Registration ID	Trial name	Intervention	Mechanism of Action	Population	Comparison	Main outcome	Study design	Esimated Enrolment	Sponsor	Location
NCT02535884	HD-DBS	GP DBS	Deep brain stimulation	Moderate HD with chorea	Sham intervention	Efficacy at 12 months	Randomized, double-blind, sham-controlled, parallel trial	50	Heinrich-Heine University, KKS Netzwerk, Medtronic, The George Institute, EHDN, CHDI Foundation, Inc.	Austria, France Germany, Switzerland (multi-centre)
NCT01834053	BMACHC	Bone Marrow Derived MNC transplant	Bone marrow transplant	HD with chorea	None	Cognitive and behavioural effects at 6 months	Single group, open-label trial	50	Chaitanya Hospital, Pune	India (single centre)
NCT02252380	–	Magnetic Resonance Guided Focused Ultrasound	Extracranial stereotactic radioablation	HD, ET, HT, PD, WD, dystonia, TD, or orofacial dyskinesias	None	Adverse events after the procedure	Single group, open-label trial	10	InSightec	Canada (single centre)

Table 4
Ongoing non-invasive non-pharmacological clinical trials registered at the World Health Organization (WHO) International Clinical Trials Research Platform (ICTRP) for people with Huntington's disease (HD). AD, Alzheimer's disease; ALS, Amyotrophic Lateral Sclerosis; ET, Essential Tremor; HT, Holmes Tremor; MS, Multiple Sclerosis; PD, Parkinson's disease; TD, Tardive dyskinesia. New trials since the last Clinical Trials Corner are indicated by *

Registration ID	Trial name	Intervention	Mechanism of Action	Population	Comparison	Main outcome	Study design	Esimated Enrolment	Sponsor	Location
ACTRN12620000281998*	–	Ketogenic diet	–	HD	None	Change in cognition and motor scores at 12 weeks	Non-randomized, open label, single group trial	10	Waikato Hospital	New Zealand (-)
ACTRN12619000870156*	–	Transcranial alternating current stimulation	Transcranial magnetic stimulation	Premanifest and early HD	Sham intervention	Biomarkers	Randomized, open-label, cross-over trials	60	Monash University, Epworth Centre for Innovation in Mental Health	Australia (single centre)
ACTRN12618001717246	–	Multidisciplinary therapy program	Exercise, cognitive training, lifestyle guidance and social activities	Premanifest HD	Standard of care	Feasibility and safety	Clustered, non-randomized, open label, parallel trial	40	Edith Cowan University, Deakin University and Lotterywest	Australia (two centres)
NCT03417583	–	Neuropsychiatric treatment protocol	Multidisciplinary intervention	HD with neuropsychiatric symptoms	Standard of care	Change in quality of life at 18 months	Non-randomized, assessor-blinded, parallel trial	100	Vanderbilt University Medical Center and Teva Pharmaceuticals USA	USA (single centre)
CTRI/2018/01/011359	–	Repetitive transcranial magnetic stimulation	Transcranial magnetic stimulation	Early to moderate HD and PD	Sham stimulation	Efficacy at 5 days	Randomized, single-blind, placebo-controlled, parallel trial	40	Vinay Goyal	India (single centre)

(*Continued*)

Table 4
(*Continued*)

Registration ID	Trial name	Intervention	Mechanism of Action	Population	Comparison	Main outcome	Study design	Esimated Enrolment	Sponsor	Location
NCT03344601	PACE-HD	Supported structured aerobic exercise training program	Physiotherapy	HD	Activity as usual	Data completeness, recruitment, retention, safety, adherence, fidelity and acceptability at 12 months	Nested open-label, randomized controlled parallel trial	120	Cardiff University and CHDI Foundation, Inc	Germany, Spain and USA (multi-centre)
ACTRN126170 01269325	–	Swallowing skill training	Speech and language therapy	HD and ALS	None	Swallowing function and quality of life at 2 weeks	Single group, open-label trial	54	University of Canterbury	New Zealand (single centre)

the Neuro-QoL, HDQLIFE and Hospital Anxiety and Depression Scale (HADS); and quantitate motor assessments (i.e. Q-Motor).

Sponsors/funders: UniQure Biopharma B.V..

Comments: The AAV5-miHTT is an engineered microRNA (miRNA) targeting both human wild-type and mutant huntingtin for degradation. It is delivered via an adeno-associated viral vector serotype 5 (AAV5). This is the first human trial of an AAV-mediated gene therapy in Huntington's disease.

If it functions as intended, upon injection into the brain parenchyma using MRI-guided convection-enhanced delivery, the AAV5-miHTT will bind to cell receptors and will be internalised by neurons and transported to the nucleus. There, the miRNA will be uncoated from the viral vector and remains episomal. After expression and processing of the miHTT transgene by the endogenous RNA interference machinery into a hairpin structure, the miRNA is transported into the cytoplasm. There the mature miRNA will load in the RNA-induced silencing complex and bind huntingtin mRNA, targeting it for cleavage and degradation. In theory, this mechanism of action makes this method irreversible, and animal models have demonstrated long-lasting miRNA expression over time after a single injection.

The efficacy and safety of this miRNA and vector has been assessed in cultured human neurons, and in vivo in multiple animal models such as mice, non-human primates and transgenic minipigs. Transgene expression accompanied by huntingtin lowering has been seen in the injected and distant structures such as the cortex.

The selected vector – AAV5 – has been tested in 4 clinical studies across haematological and metabolic disorders. When given intravenously it appears safe and tolerable, showing low activity to pre-existing neutralizing antibodies. However this is the first time it has been used for intraparenchymal delivery into the brain.

The AAV5-miHTT will be injected to the caudate and putamen bilaterally via MRI-guided convection-enhanced delivery. This approach involves surgical exposure of the brain tissue, and insertion of small diameter catheters into the injected structures. Injection usually takes long time periods (several hours) and a pressure gradient in order to saturate the targeted tissues. Even with these techniques, there is limited tissue distribution after injection. In non-human models both the vector and huntingtin lowering have been demonstrated to be present in distant structures, such as the cortex. It is unclear whether this occurs via axonal transport or by some other mechanism such as secretion and absorption of miRNA-containing exosomes.

This is a challenging trial using a novel therapeutic approach. The community will be looking forward to learning more about the feasibility of the approach, its safety, and efficacy.

KINECT-HD (NCT04102579)

Study title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy, Safety, and Tolerability of Valbenazine for the Treatment of Chorea Associated With Huntington Disease [2].

Intervention: Once daily valbenazine, [9] a VMAT2 inhibitor.

Description: The KINECT-HD trial, sponsored by Neurocrine Biosciences and the Huntington Study Group, aims to evaluate the efficacy, safety and tolerability of valbenazine in adults (18 to 75 years of age) with a clinical diagnosis of HD with chorea, compared with placebo. The purpose is to assess whether valbenazine is more effective than placebo in reducing chorea associated with HD.

Individuals with the following are not eligible: a history of prior VMAT2 inhibitor therapy; swallowing difficulties; who are pregnant or breastfeeding; or with a history of long QT syndrome, cardiac tachyarrhythmia, left bundle-branch block, atrioventricular block, bradycardia or hear failure; unstable or serious medical or psychiatric illness; significant suicidal risk; substance dependence or abuse; unstable antidepressant regimen; previous history of gene therapy; receiving an investigational drug within 30 days of baseline visit; and blood donation or significant blood loss ($\geq$550 mL) within 30 days of baseline visit.

KINECT-HD is an international, multi-centre, randomized, double-blind, controlled, parallel phase 3 trial. It has 2 study arms: the active group, where participants will receive valbenazine once daily up to 80 mg based on tolerability for 12 weeks; and the comparator group, where participants will receive a placebo capsule once daily for 12 weeks.

The study will last around 15 weeks, with an 8-week dose adjustment (i.e. 40 mg > 60 mg > 80 mg) based on tolerability followed by 4 weeks of dose

maintenance, and will enrol 120 participants equally distributed across groups. Recruitment is currently ongoing, and approximately 55 centres across the US and Canada will be involved.

The primary outcome measure is change in chorea at 12 weeks measured as a sum of the chorea items of the UHDRS Total Motor Score. Secondary outcomes include subjective impression of change; quality of life and digital biomarkers.

Sponsors/funders: Neurocrine Biosciences and the Huntington Study Group.

Comments: Valbenazine is a vesicular monoamine transporter 2 (VMAT2) inhibitor previously approved by FDA for tardive dyskinesia. It is a prodrug of dihydrotetrabenazine that reduces dopamine release into the synaptic cleft by selectively inhibiting presynaptic VMAT2.

There are two other VMAT2 inhibitors on the market: tetrabenazine (3-times daily) and deutatrabenazine (twice-daily), both of them approved by FDA for chorea associated with HD. Apart from dosage regimen, it is unclear if there are differences between these two modestly effective drugs, which have comparable safety profiles with risks of suicidality, parkinsonism and QT prolongation [10–12].

Currently, valbenazine is FDA-approved for tardive dyskinesia (40 mg daily for one week followed by 80 mg daily thereafter) and has had an unsuccessful trial in paediatric Tourette's syndrome.

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CONFLICTS OF INTEREST

FBR and EJW were sub-investigators on LEGATO-HD (NCT02215616), IONIS HTT_{Rx} (NCT02519036) and IONIS HTT_{Rx} OLE (NCT03 342053), are sub-investigators on the Roche GENERATION-HD (NCT03761849), Roche Natural History Study (NCT03664804) and Roche GEN-EXTEND (NCT03842969) trials, and EJW was a sub-investigator on the Amaryllis (NCT02197130). EJW is the chief investigator of the Roche GEN-PEAK trial (NCT04000594) and FBR is a sub-investigator. The authors did not make use of confidential or privileged information: all materials included in this manuscript were collected from publicly available sources. FBR has provided consultancy services to GLG. EJW has participated in scientific advisory boards with Hoffmann-La Roche Ltd, Ionis, Shire, GSK, Wave Life Sciences, PTC Therapeutics, Takeda and Mitoconix. All honoraria were paid through UCL Consultants Ltd, a wholly owned subsidiary of UCL. Their Host Institution, University College London Hospitals NHS Foundation Trust, has received funds as compensation for conducting clinical trials for Ionis Pharmaceuticals, Pfizer and Teva Pharmaceuticals. Hoffman La Roche Ltd has supported UCL with research funding for EJW.

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