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Excitotoxicity, Oxytosis/Ferroptosis, and Neurodegeneration: Emerging Insights into Mitochondrial Mechanisms

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Supplementary Table 1. List of various clinical trials targetting mitochondrial dysfunction in neurodegenerative diseases along with their study status and phase involved with their primary/secondary outcomes

ID	Study Title	Study status	Disease	Interventions and drugs	Phase	N	Primary/secondary outcome measures
Clinical Trials against Alzheimer's Disease							
NCT05617508	A Dose Optimization Trial of Nicotinamide Riboside in Alzheimer's Disease	RECRUITING	Alzheimer's Disease	Nicotinamide Riboside	PHASE 2	80	The between-visit difference in cerebral nicotinamide adenine dinucleotide (NAD) levels. Measured by 31P-Magnetic resonance spectroscopy (31P-MRS)/ The between-visit difference in cerebrospinal fluid (CSF) NAD and related metabolite levels/ The between-visit difference in cerebral metabolism patterns maximal alteration in the cerebral metabolism patterns/ The between-visit difference in the proportion of MRS responders
NCT04430517	Effects of Nicotinamide Riboside on Bioenergetics and Oxidative Stress in Mild Cognitive Impairment/Alzheimer's Dementia	RECRUITING	Mild Cognitive Impairment/Mild Alzheimer Disease	Nicotinamide Riboside	EARLY PHASE 1	50	Changes in brain NAD+ (redox levels)/ Changes in brain NAD+/NADH ratio/ Changes in brain CK/ATPase activity/ Changes in brain GSH levels
NCT05591027	Safety and Target Engagement of Centella Asiatica in Cognitive Impairment	RECRUITING	Mild Cognitive Impairment/Alzheimer's Disease	Dried hot water extract (CAW) of Centella asiatica	PHASE 1	48	N-acetylaspartate (NAA)/creatine (Cr) metabolite ratio (NAA/Cr)- indicator of neuronal viability and mitochondrial activity/ Ratio of 8-hydroxy-deoxyguanosine (8 OHdG) to creatinine in urine- measure of oxidative stress.
NCT04842552	Effect of Hydralazine on Alzheimer's Disease	UNKNOWN	Alzheimer Disease	Hydralazine hydrochloride 25mg tablets	PHASE 3	424	Various cognitive and function tests for patients and caregivers, olfactory tests, biochemistry as well as drug side effects will be assessed regularly over the period of follow-up.
NCT01354444	Pilot Trial of Carvedilol in Alzheimer's Disease	Completed	Alzheimer Disease	Carvedilol	PHASE 4	29	Hopkins Verbal Learning Test (HVLT) Scores at Baseline, 3, and 6 Months/ Effect of Carvedilol Treatment in Cerebrospinal Fluid (CSF) Levels of Amyloid-beta Oligomers/
NCT02711683	DL-3-n-butylphthalide Treatment in Patients with Mild to Moderate Alzheimer's Disease Already Receiving Donepezil: A Multi Centre, Prospective Cohort Study	Completed	Alzheimer Disease	DL-3-n-butylphthalide	N/A	92	Alzheimer's disease assessment scale-cognitive subscale (ADAS-cog)/ Clinician's Interview-Based Impression of Change Plus Caregiver Input (CIBIC-plus)/ Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL)/ Neuropsychiatric Inventory (NPI)
NCT02017340	A European Multicentre Double-blind Placebo-controlled Phase III Trial of Nilvadipine in Mild to Moderate Alzheimer's Disease	Completed	Alzheimer Disease	Nilvadipine	PHASE 3	511	Alzheimer's Disease Assessment Scale (ADAS) Cog/ Clinical Dementia Rating Scale Sum of Boxes (CDR-sb)/ Disability Assessment for Dementia (DAD)
NCT03090516	Clinical Study on Improving the Cognitive Function of Patients with Mild to Moderate Alzheimer's Disease by Using Ginkgo	Unknown	Alzheimer Disease	Ginkgo biloba dispersible tablets	PHASE 2	240	Electroencephalography/ MMSE (Mini-mental State Examination)/ 1.5T MRI changes/ Alzheimer disease assessment scale (ADAS-cog)/ activities of daily living scale (ADL)/ Change in neuropsychiatric inventory (NPI)

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	Biloba Dispersible Tablets						
NCT02913664	Exercise and Intensive Vascular Risk Reduction in Preventing Dementia	Completed	Alzheimer Disease	Angiotensin II receptor blocker (ARB, losartan) and calcium channel blocker (CCB, amlodipine)	PHASE 2	513	Alzheimer's Disease Cooperative Study-Preclinical Alzheimer Cognitive Composite (ADCS-PACC) and NIH Toolbox (NIH-TB) Cognition Battery will be used to assess changes in neurocognitive function
NCT05383833	Creatine to Augment Bioenergetics in Alzheimer's	RECRUITING	Alzheimer's Disease	Creatine Monohydrate: dietary supplement.	N/A	20	Adherence to Creatine Monohydrate Intervention/ Change in Blood Creatine/ Change in Brain Creatine Status/ Change in Cognition (NIH Toolbox (NIH-TB) Cognition Battery)/ Change in Peripheral Mitochondrial Respiration
NCT02460783	Intermittent Calorie Restriction, Insulin Resistance, and Biomarkers of Brain Function	COMPLETED	Alzheimer's Disease/ Obesity/ Diabetes Mellitus	Boost (R) 5-2 diet/ Healthy Living Diet	N/A	129	Mean Change in Neuron-Derived Extracellular Vesicle (NDEV) Phosphorylated Serine312-insulin Receptor Substrate-1 (pS312-IRS-1)/ Mean Change in Neuron-Derived Extracellular Vesicle (NDEV) P-pan-Tyrosine-IRS-1 (pY-IRS-1)/ Mean Change in Body Mass Index (BMI) and weight.
NCT03101085	S-Equol in Alzheimer's Disease 2 Trial (SEAD2)	COMPLETED	Alzheimer Disease	S-equol	PHASE 1	40	Difference in cytochrome oxidase/citrate synthase (COX/CS) activity/ Montreal Cognitive Assessment, Alzheimer's Disease Assessment Scale-Cognitive Portion (ADASCog-11), Logical Memory Test (LMT)
NCT00678431	A Single Centre, Multi-site, Randomized, Double-blind, Placebo-controlled Trial of Resveratrol with Glucose and Malate (RGM) to Slow the Progression of Alzheimer's Disease	COMPLETED	Alzheimer's Disease	Resveratrol with Glucose, and Malate: dietary supplement	PHASE 3	27	Alzheimer Disease Assessment Scale (ADAScog)/ Clinical Global Impression of Change (**CGIC**)
NCT04044131	A Phase 2, Randomized, Placebo Controlled Study to Evaluate the Efficacy, Tolerability and Safety of Metabolic Cofactor Supplementation in Alzheimer's Disease (AD) And	COMPLETED	Alzheimer Disease/ Parkinson Disease	For AD: Metabolic Cofactor Supplementation. For PD: Sorbitol	PHASE 2	120	Mini Mental State Examination (MMSE)/ Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog)/ Alzheimer's Disease Cooperative Study - Activities of Daily Living (ADCS-ADL)/ Unified Parkinson's Disease Rating Scale (UPDRS)

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	Parkinson's Disease (PD) Patients						
NCT05040321	A Proof of Concept Trial of a Sirtuin-NAD Activator in Alzheimer's Disease	RECRUITING	Alzheimer's Disease /Dementia	MIB-626	PHASE1/PHASE2	50	change in CSF concentrations of MIB-626/ change in CSF concentrations of MIB-626 metabolites, nicotinamide (NAM), NR, 2-PY, and MeNAM/ change in the abundance of NAD in the brain using ultra-high field 7T magnetic resonance spectroscopy
NCT03514875	Effects of Mitochondrial-targeted Antioxidant on Carotid Artery Endothelial Function and Brain Blood Flow in Mild Cognitive Impairment (MCI) Patients	WITHDRAWN (discontinued due to change in operating plans prior to study initiation and enrollment)	Alzheimer Disease, Early Onset/Mild Cognitive Impairment	MitoQ: dietary supplement	N/A	0	Carotid artery blood flow/ Oxidative Stress/ Cerebrovascular Oxygenation/ Brain Electrical Activity/ Endothelial Function
NCT03702816	The Relationship Between Neuropsychological Testing and MRI, PET and Blood Biomarkers in Neurodegenerative Disease (COBRE - Project 1): AIM 2	TERMINATED (GE180 has limited Blood-brain barrier permeation reducing its utility in permeation. Also, its start date was under COVID-19 Thus creating supply chain issues, impacting enrollment).	Alzheimer Disease/ Parkinson Disease/ Inflammation	GE180 PET Scan	PHASE 2	24	Frontal, Cingulate, Parietal, Temporal, Whole Brain GE180 Standardized Uptake Value Ratio (SUVR)/ Memory, Executive Function, Speed, Language Composite Score (Z-score)/ Dementia Rating Score/ Montreal Cognitive Assessment Score (MoCA)
NCT04018092	Revitalizing Cognition in Older Adults at Risk for Alzheimer's Disease with Near-Infrared Photobiomodulation	RECRUITING	Cognitive Aging/Alzheimer Disease	Device: Active NIR-PBM	PHASE 2	168	Change in Active group ARENA (spatial navigation task, a human analogue to the Morris WaterMaze) scores compared to Sham group ARENA scores
NCT03860792	Therapeutic Diets in Alzheimer's Disease	RECRUITING	Alzheimer Disease	Ketogenic Diet/ Therapeutic Lifestyles Changes Diet	N/A	80	Change in cognitive performance on the Alzheimer's Disease Assessment Scale Cognitive Subscale (ADASCog11), Mini-Mental State Exam (MMSE), Logical Memory Test (LMT) and by Stroop test/ Change in Clinical Dementia Rating (CDR)
NCT00951834	Sunphenon EGCG (Epigallocatechin-Gallate) in the Early Stage of Alzheimer´s Disease	COMPLETED	Alzheimer's Disease	Epigallocatechin-Gallate	PHASE2/PHASE3	21	ADAS-COG (Score 0-70)/ MMSE (Score 0-30) after 18 months compared to baseline/ Safety and tolerability of the verum/ Brain atrophy assessed by brain MRI
NCT04098666	Metformin in Alzheimer's Dementia Prevention	Recruiting	Alzheimer's Disease	Extended release metformin : oral	PHASE2/PHASE3	326	Free and Cued Selective Reminding Test (FCSRT)/ Alzheimer's Disease Cooperative Study Preclinical Alzheimer's Cognitive Composite (PACC-ADCS)/ Cortical Thickness/ White matter hyper intensity volume (WMH)/ Brain amyloid; tau/ Complex I activity
NCT00829374	CONCERT: A PHASE 3 Multicentre, Randomized, Placebo-Controlled, Double-Blind Twelve-Month Safety and Efficacy Study Evaluating Dimebon in Patients	COMPLETED	Alzheimer's Disease	Dimebon	PHASE 3	1003	Alzheimer's Disease Cooperative Study - Activities of Daily Living (ADCS-ADL)/ Alzheimer's Disease Assessment Scale - Cognitive Subscale/ Clinician's Interview Based Impression of Change, plus caregiver input (CIBIC-plus)/ Neuropsychiatric Inventory (NPI)/ Resource Utilization in Dementia Lite (RUD lite)/ Euro Quality of Life 5 (EQ-5D)

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	with Mild-to-Moderate Alzheimer's Disease on Donepezil						
NCT00099710	A PHASE II, Double-Blind, Placebo-Controlled Study of the Safety and Tolerability of Two Doses of Curcumin C3 Complex Versus Placebo in Patients with Mild to Moderate Alzheimer's Disease	Completed	Alzheimer's Disease	Curcumin C3 Complex: dietary supplement	PHASE 2	33	Oxidative damage/ Inflammation/gliosis/ A-beta levels/ Tau levels/ Total plasma cholesterol (LDL,HDL,ApoE)/ Plasma curcumin and metabolites/ Cognitive and behavioral measures
NCT00675623	A Global Phase 3, Double-Blind, Placebo-Controlled Safety and Efficacy Study of Oral Dimebon in Patients with Mild-to-Moderate Alzheimer's Disease (CONNECTION)	COMPLETED	Alzheimer's Disease	Dimebon	PHASE 3	598	To determine the effect of Dimebon as compared to placebo on the primary measure of cognition and memory (ADAS-cog), (CIBIC-plus), (ADCS-ADL) and behaviour by Neuropsychiatric Inventory (NPI)
NCT01388478	Safety/Tolerability and Effects on Cognitive Impairment, Impaired Cerebral Cortical Metabolism and Oxidative Stress of R(+)Pramipexole Administered to Subjects With Early Alzheimer's Disease	COMPLETED	Alzheimer's Disease	R-pramipexole	PHASE 2	20	Number of Patients with Adverse Events/ Effects on Cognitive Performance/ Changes in Cerebral Glucose Metabolism/ Reduction of Oxidative Stress
NCT02142777	S-Equol in Alzheimer's Disease (SEAD) Trial	COMPLETED	Alzheimer's Disease	S -Equol	PHASE 1	15	Platelet mitochondria cytochrome oxidase (COX) activity/ safety of S-equol [Time Frame: 6 weeks]
NCT04740580	Glutathione, Brain Metabolism and Inflammation in Alzheimer's Disease	RECRUITING	Alzheimer's Disease	Glycine, N-acetylcysteine, Alanine	EARLY PHASE1		Cognition (Measured using ADAS-Cog testing)/ Brain glucose uptake/ Brain inflammation/ Mitochondrial fuel oxidation/ Damage due to oxidative stress/ Inflammatory cytokines/ Plasma concentration of Brain-derived neurotropic factor (BDNF)/ Mitochondrial energetics.
NCT05929924	Does EVOO Induce Gene and Metabolic Changes in Healthy Subjects with Alzheimer's Disease Family History	NOT_YET_RECRUITING	Alzheimer Disease	Extra virgin olive oil: dietary supplement	N/A	40	Changes in the concentrations of blood metabolites (metabolomics)/ Changes in the concentrations of blood mRNA transcripts (transcriptomics)
NCT04701957	The Ketogenic Diet for Alzheimer's Disease: A Randomized Controlled Feasibility Study.	RECRUITING	Alzheimer Disease, Early Onset	Ketogenic diet	N/A	70	Feasibility of Ketogenic diet with urinary ketone levels / Safety of ketogenic diet with weight, albumin levels and lipid levels/ Efficiency of ketogenic diet on cognition (MMSE test)
NCT02062099	PET Imaging of the Translocator Protein Ligands (TSPO) With [18 F] DPA-714 Biomarker of NeuroInflammation in Cognitive Decline (NIDECO)	COMPLETED	Memory Complaint/Mild Cognitive Impairment/Alzheimer Disease	[18F]DPA-714 PET/ [18F]AV-45 PET/neuropsychological assessment	PHASE 1	25	Fixation and distribution of [18F] DPA-714 (Binding Potential BP)/ [18F] AV-45 Standard Uptake Values ratio/ Relationship between [18F] DPA-714 uptake and cognitive, affective symptoms at baseline

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NCT05343611	Combining Vitamin E-functionalized chocolate With Physical Exercise to Reduce the risk Of Protein Energy Malnutrition in Pre-dementia Aged People	RECRUITING	Dementia/Dementia, Mild/Dementia Moderate/Dementia Senile/Malnutrition/Deficiency Nutritional/Deficiency Diseases	Combination of High Protein Diet and Physical Exercise protocol/ Participants add to their diet 30 grams of 85% dark chocolate high in polyphenols, functionalized with 100 mg of Vitamin E per day	N/A	102	Change in free-fat soft tissue mass (g)
NCT05081219	Study of Nasal Insulin to Fight Forgetfulness - Combination Intranasal Insulin and Empagliflozin Trial	RECRUITING	Mild Cognitive Impairment/Cognitive Impairment/Alzheimer Disease	Insulin/ Empagliflozin 10 mg. Device: Aptar Pharma CPS Intranasal Delivery Device	PHASE 2	60	Number of Participants with Treatment-related Serious Adverse Events as Assessed by CTCAE v5.0/ Change in the Preclinical Alzheimer Cognitive Composite 5 (PACC5) Z-Score/ Change in the 14-item Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-Cog 14) Score/ Change in amyloid β-peptide (Aβ40,42) in Cerebrospinal Fluid (CSF) along with levels of total tau and phospho-tau 181
Clinical Trials against Parkinson's Disease							
NCT05344404	NR-SAFE: A Safety Study Investigating Treatment with High-dose Nicotinamide Riboside (NR) in Parkinson's Disease	COMPLETED	Parkinson Disease	Nicotinamide Riboside: dietary supplement	N/A	20	Incidence of treatment-associated moderate and severe adverse events (AEs)/ Between-group (NR vs placebo) difference in changes of the NAD metabolome in blood and urine, measured by mass spectrometry (LC-MS/MS Q-Exactive HF)
NCT03568968	A Randomized Controlled Trial of Nicotinamide Riboside Supplementation in Early Parkinson's Disease: the NOPARK Study	RECRUITING	Parkinson Disease	Nicotinamide Riboside: dietary supplement	PHASE 3	400	Disease severity assessed by the total MDS-UPDRS (Movement Disorder Society Unified Parkinson's Disease rating Scale) subsections I-III/ Change in the severity of nigrostriatal degeneration assessed by [^{123}I] FP-CIT single photon emission CT, non-motor symptoms assessed by the Non-Motor Symptoms Assessment Scale, cognitive decline assessed by the Montreal Cognitive Assessment (MoCA) scale
NCT03840005	A Phase II, Placebo Controlled, Double Blind, Randomised Clinical Trial to Assess the Safety and Tolerability Of 30mg/kg Daily Ursodeoxycholic Acid (UDCA) In Patients with Parkinson's Disease (PD)	COMPLETED	Parkinson's Disease	Ursonorm	PHASE 2	31	Number of Participants with Incidence of Treatment-Emergent Adverse Events/Participants with Incidence of Serious Adverse Events/Participants that complete the study
NCT04287543	Effect of Melatonin Administration on the PER1 and BMAL1 Clock Genes in Patients	WITHDRAWN (due to COVID-19 pandemic they were unable to start the study)	Parkinson Disease	Melatonin	PHASE2/PHASE3	0	Expression levels of clock genes/ SCOPA-Sleep scale/ Epworth scale/ Anxiety/ Depression/ Activity of the mitochondrial complex 1/ Oxidative stress

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	with Parkinson's Disease						
NCT00329056	A Double-Blind, Prospective, Randomized Comparison of 2 Doses of MitoQ and Placebo for the Treatment of Patients with Parkinson's Disease	COMPLETED	Parkinson's Disease	MitoQ	PHASE 2	128	Unified Parkinson's Disease Rating Scale (UPDRS) score at the final study visit compared to baseline/ UPDRS sub scores/ MMSE/ Schwab and England Scale/ Modified Hoehn and Yahr Scale/ Timed tapping score
NCT05589766	N-DOSE: A Dose Optimization Trial of Nicotinamide Riboside in Parkinson's Disease	RECRUITING	Parkinson Disease	Nicotinamide Riboside: dietary supplement	PHASE 2	80	The between-visit difference in cerebral NAD levels/ The between-visit difference in CSF NAD and related metabolite levels/ between-visit difference in expression of the Nicotinamide Riboside Related Pattern (NRRP)/ The between-visit difference in the proportion of MRS responders
NCT00517842	A Triple-blinded, Randomised, Placebo-controlled Trial to Examine the Efficacy and Safety of ViNeuro in Patients with Parkinson's Disease	COMPLETED	Parkinson Disease	ViNeuro	N/A	160	The primary efficacy outcome is the change from baseline in the sum of the Unified Parkinson's Disease Rating Scale (UPDRS) (Appendix 6) Parts II and III total scores at the end of 24 weeks. The UPDRS is to be performed one hour after L-dopa treatment
NCT01364545	Ketogenic Diets for Symptoms of Parkinson's Disease	UNKNOWN	Parkinson's Disease	Ketone ester drink: dietary supplement	N/A	20	Unified Parkinson's Disease rating Scale, part III (motor)/ Timed motor tasks as per CAPSIT/ Computerised reaction time and cognitive tests.
NCT03457493	UAB Neuroinflammation in Parkinson's Disease - TSPO-PET Substudy	RECRUITING	Parkinson Disease	DPA-714-PET/MRI	PHASE1/PHASE2	205	Comparison of TSPO-PET measures of neuroinflammation between PD patients and healthy controls/ Correlation of DPA-714-PET/MRI with demographics, clinical and biospecimen assessments from Neuroinflammation in PD study
NCT02967250	7T Magnetic Resonance Spectroscopy Monitoring Brain Bioenergetics in Parkinson's Disease and Response to Repeated Oral UDCA Treatment	COMPLETED	Parkinson Disease	ursodeoxycholic acid	PHASE 1	5	Change in ATP concentration using 7T MRS/ UDCA pharmacokinetics
NCT05855577	Clinical Efficacy of Pharmacological Treatments Targeting Energy Metabolism, Evaluated by Gait Analysis, on Motor Function in Parkinson's Disease Patients	NOT_YET_RECRUITING	Parkinson Disease/ Gait Analysis /Therapy, Directly Observed/Metabolic Disease	Terazosin	PHASE 4	50	Clinical evaluation, Gait Analysis and Metabolic variables efficacy of therapy/ The efficacy and molecular mechanisms of Nrf2 pathway modulation in PD rodent models
NCT02462603	A Phase 2A Safety and Biomarker Study of EPI-589 in Mitochondrial Subtype and Idiopathic Parkinson's Disease Subjects	COMPLETED	Parkinson's Disease	PTC-589	PHASE 2	44	Number of Participants With Drug-Related Serious Adverse Events (SAEs)/ Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Score at Month 3/ Change From Baseline in Non-motor Symptoms Scale (NMSS) Total Score at Month 3/ Change From Baseline in

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							Parkinson's Disease Questionnaire - 39 (PDQ-39) Score at Month 3/ Change From Baseline in EuroQol-5 Dimension (EQ-5D) Score at Month 3/ Montreal Cognitive Assessment (MoCA) Score/ Beck Depression Inventory (BDI) Score
NCT05963425	The Effects on Physical Activity on Mitochondrial Function in Skin Fibroblasts in Patients with Parkinson's Disease: A Study Protocol	RECRUITING	Parkinson's Disease	Physical activity	N/A	24	Change in oxygen consumption rate/ Change in ATPmax levels/ Non-motor and motor function/ Sleepiness/ Mobility/ Cognitive aspects/ Mood
NCT05214287	An N-of-1 Double-blind Randomized Phase 1 Trial of the Safety and Feasibility of (Intermittent) Hypoxia Therapy in Parkinson's Disease (TALISMAN)	COMPLETED	Parkinson's Disease	Hypoxic Gas Mixture	PHASE1/PHASE2	29	Nature and number of adverse events/ Self-reported dizziness, discomfort and stress on a ten-point scale/ Blood pressure/ Heartrate/ Respiratory rate/ Oxygen saturation/ Feasibility questionnaire
NCT04768023	Influence of 12 Weeks Vitamin D Supplementation Combined with Physical Activity on Blood and Functional Parameters and Quality of Life in Parkinson's Disease Patients Treated with Deep Brain Stimulation	COMPLETED	Vitamin D Deficiency/Parkinson Disease	Juvit D3	N/A	50	The effects of vitamin D supplementation and physical activity on concentration of vitamin D3 in serum, concentration of inflammatory markers in serum, concentration of CRP in serum, concentration of kynurenine pathway metabolites in serum, - the evaluation of changes before and after 12 weeks of supplementation and physical activity. 6-minute walk test and Up & Go and 10-meter walk test
NCT04477161	Effect of Ketone Esters on Parkinson Disease: A Pilot, Prospective Trial	COMPLETED	Parkinson Disease/ Ketosis	Ketone Ester Elite Endurance Nutrition Drink: dietary supplement	N/A	10	Changes in serum Ketones
NCT03061513	Ubiquinol in Parkinson's Disease: Safety, Tolerability, and Effects Upon Oxidative Damage and Mitochondrial Biomarkers	COMPLETED	Parkinson Disease	Ubiquinol: dietary supplement	PHASE 2	11	Number of Adverse Events/ Cerebral Redox Markers
Clinical Trials against Huntington's Disease							
NCT00712426	Creatine Safety, Tolerability, & Efficacy in Huntington's Disease (CREST-E)	TERMINATED (results of interim analysis showed that creatine was ineffective in slowing down the loss of function in early symptomatic HD)	Huntington's Disease	Creatine Monohydrate	PHASE 3	553	Change in Total Functional Capacity/ Clinical symptoms (changes in other UHDRS scores); safety (frequency of adverse events); tolerability (proportion of subjects completing study at assigned dosage level), quality of life, other biological markers
NCT01879267	Exercise Effects in Huntington's Disease	COMPLETED	Huntington's Disease	BEHAVIORAL: Exercise training	N/A	40	Change in Unified Huntington's Disease Rating Scale (UHDRS)

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NCT01882062	Proof of Concept of an Anaplerotic Study Using Brain Phosphorus Magnetic Resonance Spectroscopy in Huntington Disease	COMPLETED	Huntington Disease	Triheptanoin 1g/kg/day	PHASE 2	10	Ratio of Inorganic Phosphate (Pi) Over Phosphocreatine (PCr): Pi/PCr/
NCT01502046	A Double Blind, Randomized, Cross Over, Placebo Controlled Phase 2 Clinical Trial to Asses Neuroprotection by Cannabinoids in Huntington's Disease	COMPLETED	Huntington's Disease	delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD)	PHASE 2	25	Serious Adverse Events reported/ Changes in the UHDRs Score/ Changes in the BDNF levels (Brain-derived Neurotrophic Factor), oxidative stress (due to mitochondrial dysfunction) and proinflammatory cytokines in CSF and plasma
Clinical Trials against Amyotrophic Lateral Sclerosis							
NCT02874209	Non-invasive Assessment of Neuronal Damage by MRI Sodium (23Na) in Amyotrophic Lateral Sclerosis	UNKNOWN	Amyotrophic Lateral Sclerosis	sodium MRI	N/A	60	Central conduction time of the potential muscle through transcranial magnetic stimulation
NCT00005766	Clinical Trial of Creatine in Amyotrophic Lateral Sclerosis	COMPLETED	Amyotrophic Lateral Sclerosis	Creatinine	PHASE 2		
NCT04244630	Mitochondrial Capacity Boost in ALS (MICABO-ALS) Trial	RECRUITING	Amyotrophic Lateral Sclerosis	COMBINATION_PRODUCT: Antioxidants	PHASE 2	60	Measurement of serum Neurofilament light chain (NfL)/ Measurement of functional decline in ALS/ Frequency of serious adverse events and adverse events/ Survival analysis
NCT02969759	Bioenergetics and Protein Metabolism in Sporadic Amyotrophic Lateral Sclerosis	UNKNOWN	Sporadic Amyotrophic Lateral Sclerosis	Skin Biopsy	EARLY PHASE 1	30	Kinetics of fibroblast growth/ Mitochondrial metabolism/ Protéic metabolism/ stress in senescence
NCT01232738	A Multi-Center Controlled Screening Trial of Safety and Efficacy of Rasagiline in Subjects with Amyotrophic Lateral Sclerosis (ALS)	COMPLETED	Amyotrophic Lateral Sclerosis	rasagiline	PHASE 2	36	Amyotrophic Lateral Sclerosis Functional Rating Scale - Revised (ALSFRS-R)/ Difference in Time to Treatment Failure
NCT03506425	A Pilot Trial of Triheptanoin for People with Amyotrophic Lateral Sclerosis (PALS)	COMPLETED	Amyotrophic Lateral Sclerosis	Triheptanoin	PHASE1/PHASE2	15	ALS Functional Rating Scale-revised Version (ALSFRS-R) Slope/ Change in NAA/Cr Ratio from Motor Cortex as Measured by Magnetic Resonance Spectroscopy/ Change in Urine Isoprostane Levels, an Oxidative Stress Marker
NCT01854294	GM604 Phase 2A Randomized Double-blind Placebo Controlled Pilot Trial in Amyotrophic Lateral Disease (ALS)	COMPLETED	Amyotrophic Lateral Sclerosis	GM604	PHASE 2	12	Efficacy by percent change in biomarker in the CSF at week 12 from baseline/ Safety by measuring 1. adverse event frequency and severity, changes in vital signs, clinical laboratory values. 2. Serious adverse event frequency/ Tolerability by measuring the ability to complete the first 2 weeks of active treatment in the study
NCT04140136	The Efficacy and Safety of Vitamin E Mixed Tocotrienols In Patients with	UNKNOWN	Amyotrophic Lateral Sclerosis	Tocotrienols: dietary supplement	PHASE 2	20	Mean change of revised ALS Functional Rating Scale (ALSFRS-R) at baseline and 6 months between treatment group difference/ Number of participants with

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	Amyotrophic Lateral Sclerosis (ALS): A Pilot Exploratory Study						treatment-related adverse events, haematological, renal and liver profile monitored at every visit
NCT00243932	Clinical Trial of High Dose CoQ10 in ALS	COMPLETED	Amyotrophic Lateral Sclerosis |Lou Gehrig's Disease	coenzyme Q10	PHASE 2	185	Change in the ALS Functional Rating Scale-revised (ALSFRSr) Score/ The Change Over 9 Months in Forced Vital Capacity; Fatigue Severity Scale; Short Form-36; and 8OH2dG
NCT04820478	Efficacy and Tolerability of Beta Hydroxybutyrate Ester in Patients with Amyotrophic Lateral Sclerosis (ALS)	RECRUITING	Amyotrophic Lateral Sclerosis	Beta Hydroxybutyrate Ester (KetoneAid KE4): dietary supplement	N/A	76	Neurofilament Light Chain (NfL) serum levels/ Survival/ Amyotrophic Lateral Sclerosis Functional Rating Scale Revised/ Body Mass Index/ Slow Vital Capacity/ Resting Energy Expenditure

N/A: Data not available