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A study to evaluate the effect of SAGE-718 on cognitive function in participants with Huntington's Disease

Submission date
12/02/2022

Recruitment status
No longer recruiting

Registration date
16/05/2022

Overall study status
Completed

Last Edited
31/01/2025

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims:
Huntington’s disease is a rare, inherited disease causing degeneration of the nerve cells in the brain, leading to gradual impairment in movement, learning abilities, and behavior.
The DIMENSION Study is evaluating the safety and effects of an experimental oral drug, SAGE-718, in adults with early Huntington’s disease (HD). This drug is being tested to see if it can specifically target cognitive symptoms associated with HD.

Who can participate?
Adults aged 25 to 65 years, with Huntington’s disease.
What does the study involve? (what interventions will be compared, will all participants receive the same treatment, what measurements will be taken)
The study lasts up to 20 weeks and includes 9 visits to the study office. The study consists of the following parts: -

a. A screening period of 28 days wherein tests will be done to check if participants are eligible to take part in the study.
b. The treatment period of 84 days wherein participants will be randomly divided into 2 groups to receive either SAGE-718 or placebo, by mouth.
c. A follow-up period of 28 days wherein participants will return to the clinic for check-up visits on Day 98 and Day 112 to help collect continued safety and effectiveness data.

What are the possible benefits and risks of participating?
Benefits:
Based on standardized interviews conducted by Sage, pre-manifest and early manifest HD patients are at high risk of losing employment, their ability to drive and to maintain financial security. In these interviews, care partners observed changes in functioning, and reported that they were beginning to assume some financial or home responsibilities that they previously held by the patient.
SAGE-718 may work to restore aberrant N-methyl-D-aspartate (NMDA) receptor activity in patients with early HD and thereby help to ameliorate cognitive deficits seen in these patients.

Risks:
• The most frequently reported side effects seen after study treatment with SAGE-718 were: Dizziness, Headache, Nausea, Vomiting, Upper respiratory tract infection (common cold), Orthostatic hypotension (drop in blood pressure when standing from laying down), Euphoric mood (feelings of physical and emotional well-being, which become excessive, all consuming, and interfere with daily living), Increased levels of alanine aminotransferase (a liver function test).
• Most side effects were reported as mild or moderate in intensity and got better or went away without stopping study treatment with SAGE-718.
• There was no selective distribution or retention of radioactive SAGE-718 to pigmented tissues and no quantifiable concentration of radioactivity was observed in the eye lens in Long Evans rats, implying that potential risk of phototoxicity is low.

Where is the study run from?
Sage Therapeutics, Inc (USA)

When is the study starting and how long is it expected to run for?
May 2021 to October 2024

Who is funding the study?
Sage Therapeutics, Inc (USA)

Who is the main contact?
Amy Bullock, PhD; amy.bullock@sagerx.com

Contact information

Type(s)
Principal investigator

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Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05107128

Clinical Trials Information System (CTIS)
2021-005577-16

Integrated Research Application System (IRAS)
1004868

Central Portfolio Management System (CPMS)
51899

Protocol serial number
718-CIH-201

Study information

Scientific Title
A randomized, placebo-controlled, double-blind study to evaluate the effect of SAGE-718 on cognitive function in participants with Huntington's Disease

Acronym
DIMENSION

Study objectives
Current study hypothesis as of 31/01/2025:

- To evaluate the effect of SAGE-718 on cognitive performance in participants with HD
- To evaluate the effect of SAGE-718 on cognition and daily function in participants with HD.
- To evaluate the safety and tolerability of SAGE-718 oral capsule in participants with HD.

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Previous study hypothesis:

- To evaluate the effect of SAGE-718 on cognitive performance in participants with HD
- To evaluate the effect of SAGE-718 on daily function in participants with HD.
- To evaluate the safety and tolerability of SAGE-718 oral capsule in participants with HD.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 05/05/2022, London-Riverside Research Ethics Committee (Temple Quay House, 2 The Square, Bristol Research Ethics Committee Centre, Bristol, BS1 6PN, UK; +44(0)207 104 8150; riverside.rec@hra.nhs.uk), ref: 22/LO/0177

Primary study design
Interventional

Study design
Interventional double-blind randomized placebo-controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Huntington's disease

Interventions
Current interventions as of 25/10/2022:

The intervention model is parallel assignment with two arms. Eligible participants will be randomized 1:1 to receive either SAGE-718 (oral softgel lipid capsules) or placebo (SAGE-718-matching oral softgel lipid capsules) for 84 days. After completing the treatment period, participants will return to the clinic for follow-up visits at on Day 98 and Day 112 to collect continued safety and efficacy data.

Participants are randomized via an IRT system.

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Previous interventions:

The intervention model is parallel assignment with two arms. Eligible participants will be randomized 1:1 to receive either SAGE-718 (oral capsules) or placebo (SAGE-718-matching oral capsules) for 84 days. After completing the treatment period, participants will return to the clinic for follow-up visits at on Day 98 and Day 112 to collect continued safety and efficacy data.

Subjects are randomized via an IRT system.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
SAGE-718

Primary outcome(s)
Current primary outcome measure as of 31/01/2025:

Change from baseline to day 84 in the cognitive function assessed using the Symbol Digit Modalities Test (SDMT)

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Previous primary outcome measure:

Change from baseline to day 84 in the cognitive function assessed using Huntington's Disease Cognitive Assessment Battery (HD-CAB) Composite Score

Key secondary outcome(s)
Current secondary outcome measures as of 31/01/2025:

1. Change from baseline to day 84 in the functional capacity assessed using Unified Huntington's Disease Rating Scale (UHDRS) - Independence Scale
2. Change from baseline to day 84 in the cognitive function assessed using the Trail Making Test Part B
3. Change from baseline to day 84 in the cognitive function assessed using the One Touch Stockings of Cambridge (OTS)
4. Change from baseline to day 84 in the motor function assessed using the Paced Tapping Test (PTAP)
5. Change from baseline to day 84 in the functioning difficulty assessed using the Huntington’s Disease Everyday Functioning (Hi-DEF) Home subdomain score
6. Change from baseline to day 84 in the cognitive function assessed using the Clinical Global Impression – Severity (CGI-S) Cognitive Status subdomain score
7. Percentage of Participants with Treatment-emergent Adverse Events (TEAEs) up to approximately 112 days

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Previous secondary outcome measures:

1. Change from baseline to day 84 in the functional capacity assessed using Unified Huntington's Disease Rating Scale (UHDRS) - Independence Scale
2. Change from baseline to day 84 in the motor function assessed using UHDRS - Total Motor Score (TMS)
3. Percentage of Participants with Treatment-emergent Adverse Events (TEAEs) up to approximately 112 days

Completion date
03/10/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 31/01/2025:

1. Meet all the following criteria for HD at Screening (Days -28 to -2):
1.1. Genetically confirmed disease with huntingtin gene CAG expansion ≥36.
1.2. At Screening, UHDRS-Total Functional Capacity (TFC) score >6 and <13 suggesting no more than a moderate level of functional impairment.

1.3. No features of juvenile HD.
2. Score of 15 to 25 (inclusive) on the Montreal Cognitive Assessment (MoCA) at screening indicating the presence of cognitive impairment.
3. Be willing to invite a study partner, if available, who is reliable, competent, and at least 18 years of age to participate in the study.
4. Be ambulatory (use of assistance devices such as a walker or cane is acceptable as is occasional use of wheelchair, as judged by the investigator. Individuals requiring a wheelchair on a regular basis are excluded), able to travel to the study center, and, as judged by the investigator, is likely to be able to continue to travel to the study center to complete study visits for the duration of the study.
5. Completion of HD-CAB Trail Making-B Test in <240 seconds at Screening (Days -28 to -2).

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Previous inclusion criteria as of 20/05/2024:

1. Meet all the following criteria for HD at Screening (Days -28 to -2):
1.1. Genetically confirmed disease with huntingtin gene CAG expansion ≥36.
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Previous inclusion criteria as of 25/10/2022:

1. Meet all the following criteria for HD:
1.1. Genetically confirmed disease with huntingtin gene CAG expansion ≥36.
1.2. UHDRS-Total Functional Capacity (TFC) score >6 and <13.
1.3. No features of juvenile HD.
2. Score <26 on the Montreal Cognitive Assessment (MoCA) at screening.
3. Be willing to invite a study partner, if available, who is reliable, competent, and at least 18 years of age to participate in the study.
4. Be ambulatory (use of assistance devices such as a walker or cane is acceptable as is occasional use of wheelchair, as judged by the investigator. Individuals requiring a wheelchair on a regular basis are excluded), able to travel to the study center, and, as judged by the investigator, is likely to be able to continue to travel to the study center to complete study visits for the duration of the study.

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4. Be ambulatory (use of assistance devices such as a walker or cane is acceptable; individuals requiring a wheelchair are excluded), able to travel to the study center, and, as judged by the investigator, is likely to be able to continue to travel to the study center to complete study visits for the duration of the study.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
25 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
189

Key exclusion criteria
Current exclusion criteria as of 20/05/2024:

1. Have participated in a previous clinical study of SAGE-718, have previous exposure to gene therapy or have participated in any HD investigational drug, biologic, or device trial within 180 days or a non-HD drug, biologic, or device trial within 30 days or 5 half-lives (whichever is longer) (Note: Participants with confirmation of enrollment in the placebo arm of these trials would not be excluded.)
2. Have a diagnosis of an ongoing neurodegenerative condition other than HD, including but not limited to, Alzheimer's Disease, vascular dementia, dementia with Lewy bodies, or Parkinson's Disease

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Previous exclusion criteria as of 25/10/2022:

1. Have participated in a previous clinical study of SAGE-718, have participated in a previous gene therapy study, or have participated in any other drug, biologic, or device trial within 30

days or 5 half-lives (whichever is longer), unless the participant participated solely in the placebo arm of the study. Additionally, participants who have received treatment with antisense oligonucleotides (ASOs) or a messenger ribonucleic acid (mRNA) splicing modifier will be excluded.
2. Have a diagnosis of an ongoing neurodegenerative condition other than HD, including but not limited to, Alzheimer's Disease, vascular dementia, dementia with Lewy bodies, or Parkinson's Disease

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Previous exclusion criteria:

1. Have participated in a previous clinical study of SAGE-718, have participated in a previous gene therapy study, or have participated in any other drug, biologic, or device trial within 180 days or 5 half-lives (whichever is longer), unless the patient participated solely in the placebo arm of the study.
2. Have a diagnosis of an ongoing neurodegenerative condition other than HD, including but not limited to, Alzheimer's Disease, vascular dementia, dementia with Lewy bodies, or Parkinson's Disease.

Date of first enrolment
05/11/2021

Date of final enrolment
11/06/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Australia

Canada

United States of America

Study participating centre
Birmingham and Solihull Mental Health NHS Foundation Trust
Unit 1
50 Summer Hill Road
Birmingham
United Kingdom
B15 2FG

Study participating centre
Re-Cognition Health
Unit 2
5 Research Way
Plymouth
United Kingdom
PL6 8BT

Study participating centre
Unit 3
Aberdeen
United Kingdom
AB25 2ZA

Study participating centre
Unit 4
Cardiff
United Kingdom
CF10 3AX

Study participating centre
Unit 5
Leeds
United Kingdom
LS1 3X

Study participating centre
Unit 6
Leeds
United Kingdom
LS7 4SA

Study participating centre
Unit 7
Newcastle Upon Tyne
United Kingdom
NE6 4QD

Study participating centre
Unit 8
Southampton
United Kingdom
SO16 6YD

Study participating centre
Unit 9
Tooting
London
United Kingdom
SW17 0QT

Sponsor information

Organisation
Sage Therapeutics, Inc.

Funder(s)

Funder type
Industry

Funder Name
Sage Therapeutics, Inc

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No