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A study to assess the long-term safety of SAGE-718 in participants with Huntington's disease

Submission date
23/02/2023

Recruitment status
No longer recruiting

Registration date
27/10/2023

Overall study status
Stopped

Last Edited
07/02/2025

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 (HD) is a rare, inherited disease that causes progressive degeneration of the nerve cells in the brain leading to gradual impairment in movement, learning abilities, and behaviour. Health authorities have not approved SAGE-718, the study drug for the treatment of HD or any other disease.

The purpose of this study is to test the long-term safety and tolerability of SAGE-718 in participants who are in the early stages of HD.

Who can participate?
Participants who have completed previous SAGE-718 HD studies (718-CIH-201 and 718-CIH-202) and people who were not previously included in a SAGE-718 clinical study with HD aged between 25 and 65 years.

What does the study involve?
Participants will need to be a part of this study for approximately up to 4 years. The study will have three parts:

- Screening Period: Potential participants will be screened to check if they are eligible to participate in the study. Screening visit will take place up to 28 days before the study starts.

- Treatment Period: During the study period participants will self-administer SAGE-718 capsule orally once daily for 48 months. Participants will have to visit the clinic up to 15 times that is on study days 1, 30, 60, 90, 180, 270, and 365, and Months 15, 18, 21, 24, 30, 36, 42, and 48.

Participants will also have remote visits in Months 27, 33, 39, and 45.

- Follow-up Period: Participants will have a follow-up visit on Day 395 or 30 days after the last dose of the study drug or the Month 48 visit to check on their well-being.

Participants will be enrolled in three groups based on when they enter the study:
1. Group 1: Participants enter this study within 7 days of completing previous SAGE-718 studies

(718-CIH-201 and 718-CIH-202)
2. Group 2: Participants who have entered this study more than 7 days after completing previous SAGE-718 studies (718-CIH-201 and 718-CIH-202)
3. Group 3: Participants who have not participated in any previous SAGE-718 studies

What are the possible benefits and risks of participating?
Participants may not receive any direct benefit from participating in this study. This study may help the sponsor, study doctors, and scientists learn things about the study drug that may help others with HD.

Participants may experience side effects from the treatments or procedures in this study. Side effects can vary from mild to serious and may be different from person to person. As SAGE-718 is an experimental drug, all potential side effects are not known at this time.

Risks associated with SAGE-718:
The most frequently reported side effects seen after study treatment with SAGE-718 were dizziness, drowsiness, headache, nausea, vomiting, common cold, drop in blood pressure when standing from laying down (orthostatic hypotension), increased levels of some liver function test parameters(alanine aminotransferase) and decreased white blood cell (neutrophil) count.

Participants may experience allergic reactions which could be seen as rash or hives, having a hard time breathing or swallowing, wheezing when breathing, sudden change in blood pressure (making the participant feel dizzy or lightheaded), swelling around the mouth, and throat, or eyes, fast pulse, sweating.

The effect of the study drug on the unborn child or nursing infant is unknown. Female participants who are pregnant, become pregnant or are breastfeeding cannot participate in the study.

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

When is the study starting and how long is it expected to run for?
September 2022 to January 2025

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

Who is the main contact?
Dr Hugh Rickards, hugh.rickards@nhs.net

Contact information

Type(s)
Public, Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT05655520

Clinical Trials Information System (CTIS)
2022-003623-18

Integrated Research Application System (IRAS)
1007162

Protocol serial number
718-CIH-301

Study information

Scientific Title
A phase III, multicenter, open-label safety study to evaluate the long-term safety and tolerability of SAGE-718 in participants with Huntington’s disease

Study objectives
The main purpose of the study is to assess the long-term safety and tolerability of SAGE-718 softgel lipid capsule in participants with Huntington’s Disease (HD).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 26/09/2023, London – Riverside Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square , Bristol, BS1 6PN, United Kingdom; +44 207 104 8150; riverside.rec@hra.nhs.uk), ref: 23/LO/0257

Primary study design
Interventional

Study design
Interventional non-randomized Phase III open-label long-term safety study

Study type(s)
Treatment, Safety

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

Interventions
Current interventions as of 14/08/2024:
Cohort 1 (Direct Rollover): Participants from the 718-CIH-201 and 718-CIH-202 studies who will sign the informed consent for study 718-CIH-301 ≤7 days after the last day of the corresponding parent study will be enrolled in this cohort. Participants will receive SAGE-718 oral soft gel lipid capsule from Day 1 up to Month 48.

Cohort 2 (Gap Rollover): Participants from the 718-CIH-201 and 718-CIH-202 studies who will sign the informed consent for study 718-CIH-301 after a gap of >7 days after the last day of the corresponding parent study will be enrolled in this cohort. Participants will receive SAGE-718 oral soft gel lipid capsule from Day 1 up to Month 48.

Cohort 3 (De Novo): Participants who were not previously included in any SAGE-718 clinical study will be enrolled in this cohort. Participants will receive SAGE-718 oral soft gel lipid capsule from Day 1 up to Month 48.

Previous interventions:
Cohort 1 (Direct Rollover): Participants from the 718-CIH-201 study who will sign the informed consent for study 718-CIH-301 ≤7 days after the last day of the corresponding parent study will be enrolled in this cohort. Participants will receive SAGE-718 oral soft gel lipid capsule from Day 1 up to Day 365.

Cohort 2 (Gap Rollover): Participants from the 718-CIH-201 study who will sign the informed consent for study 718-CIH-301 after a gap of >7 days after the last day of the corresponding parent study will be enrolled in this cohort. Participants will receive SAGE-718 oral soft gel lipid capsule from Day 1 up to Day 365.

Cohort 3 (De Novo): Participants who were not previously included in any SAGE-718 clinical study will be enrolled in this cohort. Participants will receive SAGE-718 oral soft gel lipid capsule from Day 1 up to Day 365.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Current primary outcome measures as of 14/08/2024:
1. Percentage of participants experiencing treatment-emergent adverse events (TEAEs) and severity of TEAEs as assessed by data collected in an electronic case report form (eCRF) from initiation of the study (screening) up to follow-up visit at Month 49
2. Number of participants who withdraw due to adverse events (AEs) as assessed by data collected in eCRF from initiation of the study screening) up to follow-up visit at Month 49
3. Change from baseline in vital signs (assessed using body temperature, respiratory rate, heart rate, and blood pressure), clinical laboratory parameters (haematology, biochemistry, coagulation, and urinalysis measured using blood and urine samples), electrocardiograms (ECGs) (measured using 12-lead ECG) from initiation of the study (screening) up to follow-up visit at Month 49
4. Change from baseline in suicidality measured using Columbia Suicide Severity Rating Scale (C-SSRS) responses from initiation of the study (screening) up to follow-up visit at Month 49

Previous primary outcome measures as of 07/03/2024 to 14/08/2024:
1. Percentage of participants experiencing treatment-emergent adverse events (TEAEs) and severity of TEAEs as assessed by data collected in an electronic case report form (eCRF) from initiation of the study (screening) up to follow-up visit at Day 395
2. Number of participants who withdraw due to adverse events (AEs) as assessed by data collected in eCRF from initiation of the study screening) up to follow-up visit at Day 395
3. Change from baseline in vital signs (assessed using body temperature, respiratory rate, heart rate, and blood pressure), clinical laboratory parameters (haematology, biochemistry, coagulation, and urinalysis measured using blood and urine samples), electrocardiograms (ECGs) (measured using 12-lead ECG) from initiation of the study (screening) up to follow-up visit at Day 395
4. Change from baseline in suicidality measured using Columbia Suicide Severity Rating Scale (C-SSRS) responses from initiation of the study (screening) up to follow-up visit at Day 395

Previous primary outcome measures:
1. Percentage of participants experiencing treatment emergent adverse events (TEAEs) and severity of TEAEs as assessed by data collected in an electronic case report form (eCRF) from initiation of the study up to 13 months.
2. Number of participants who withdraw due to adverse events (AEs) as assessed by data collected in eCRF from initiation of the study up to 13 months.
3. Change from baseline in vital signs (assessed using body temperature, respiratory rate, heart rate, and blood pressure), clinical laboratory parameters (haematology, biochemistry, coagulation, and urinalysis measured using blood and urine samples), electrocardiograms (ECGs) (measured using 12-lead ECG) from initiation of the study up to 13 months.
4. Change from baseline in suicidality measured using Columbia Suicide Severity Rating Scale (C-SSRS) responses from initiation of the study up to 13 months.

Key secondary outcome(s)
There are no secondary outcome measures

Completion date
10/01/2025

Reason abandoned (if study stopped)
Internal company decision

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 14/08/2024:
For all participants:
1. Completed 718-CIH-201 (NCT05107128) or 718-CIH-202 (NCT05358821) studies or meet eligibility criteria for the de novo cohort.

Inclusion criteria for the de-novo cohort:
1. Age 25 - 65 years at the time of screening
2. Meet all of the following criteria for HD:
2.1. Genetically confirmed disease with cytosine-adenine-guanine (CAG) expansion ≥40
2.2. No features of juvenile HD.
2.3. CAG-Age-Product (CAP) score ≥90, as calculated using the CAP formula: AGE × (CAG – 30)/6.49.
3. Either Unified Huntington's Disease Rating Scale (UHDRS) -Total Functional Capacity (TFC) score=13 and Score ≤ 25 on the Montreal Cognitive Assessment (MoCA) OR UHDRS-TFC ≤12 and MoCA >25 at screening (Days -28 to -1).
4. Completion of Huntington's Disease Cognitive Assessment Battery (HD-CAB) Trail Making-B Test in <240 seconds at Screening (Days -28 to -1)
5. Ability to adhere with the study protocol.

Previous participant inclusion criteria as of 07/03/2024 to 14/08/2024:
For all participants:
1. Completed 718-CIH-201 (NCT05107128) or 718-CIH-202 (NCT05358821) studies or meet eligibility criteria for the de novo cohort.

Inclusion criteria for the de-novo cohort:
1. Age 25 - 65 years at the time of screening
2. Meet all the following criteria for HD:
2.1. Genetically confirmed disease with cytosine-adenine-guanine (CAG) expansion ≥40
2.2. No features of juvenile HD.
2.3. CAG-Age-Product (CAP) score ≥90, as calculated using the CAP formula: AGE × (CAG – 30)/6.49.
3. Either Unified Huntington's Disease Rating Scale (UHDRS) -Total Functional Capacity (TFC) score=13 or Score > 25 on the Montreal Cognitive Assessment (MoCA) at screening (one or the other; not both).
5. Ability to adhere with the study protocol.

Previous participant inclusion criteria:
For all participants:
1. Completed 718-CIH-201 (NCT05107128) or 718-CIH-202 (NCT05358821) studies or meet eligibility criteria for the de novo cohort.

Inclusion criteria for the rollover participants:
1. No significant decline in functional status since the last visit in 718-CIH-201 or 718-CIH-202, in the opinion of the investigator.

Inclusion criteria for the de-novo cohort:
1. Age 25 - 65 years at the time of screening
2. Meet all the following criteria for HD:
- Genetically confirmed disease with cytosine-adenine-guanine (CAG) expansion ≥40
- No features of juvenile HD.
3. CAG-Age-Product (CAP) score ≥90, as calculated using the CAP formula: AGE × (CAG – 30)/6.49.
4. Unified Huntington's Disease Rating Scale (UHDRS) -Total Functional Capacity (TFC) score=13 or Score > 25 on the Montreal Cognitive Assessment (MoCA) at screening.
5. Ability to adhere with the study protocol.

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
153

Key exclusion criteria
Current participant exclusion criteria as of 14/08/2024:
Exclusion criteria for all participants:
1. 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.

Exclusion criteria specific for the de-novo cohort:
1. Have previous exposure to gene therapy study, or have participated in any other HD investigational drug, biologic, or device trial within 180 days or non-HD drug, biologic or device trial within 30 days or 5 half-lives (whichever is longer). Participants with confirmation of enrollment in the placebo arm of these investigational trials would not be excluded. Additionally, participants who have received treatment with antisense oligonucleotides or a messenger ribonucleic acid (mRNA)splicing modifier will be excluded.

Exclusion criteria for the rollover participants:
1. Have one or more ongoing serious adverse events (SAEs) from the parent study.
2. Have ongoing, unresolved AE(s), which in the opinion of the investigator or sponsor, is likely to interfere with study conduct or compliance.

Previous participant exclusion criteria:
Exclusion criteria for all participants:
1. 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.

Exclusion criteria specific for the de-novo cohort:
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 patient participated solely in the placebo arm of the study. Additionally, participants who have received treatment with antisense oligonucleotides or a messenger ribonucleic acid (mRNA)splicing modifier will be excluded.

Exclusion criteria for the rollover participants:
1. Have ongoing serious adverse events (SAEs) from the parent study.
2. Have ongoing, unresolved AE(s), which in the opinion of the investigator or sponsor, is likely to interfere with study conduct or compliance.

Previous participant exclusion criteria as of 07/03/2024 to 14/08/2024:
Exclusion criteria for all participants:
1. 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.

Exclusion criteria specific for the de-novo cohort:
1. Have participated in a previous gene therapy study, or have participated in any other HD investigational drug, biologic, or device trial within 180 days or 5 half-lives (whichever is longer). Participants with confirmation of enrollment in the placebo arm of these investigational trials would not be excluded. Additionally, participants who have received treatment with antisense oligonucleotides or a messenger ribonucleic acid (mRNA)splicing modifier will be excluded.

Exclusion criteria for the rollover participants:
1. Have ongoing serious adverse events (SAEs) from the parent study.
2. Have ongoing, unresolved AE(s), which in the opinion of the investigator or sponsor, is likely to interfere with study conduct or compliance.

Previous participant exclusion criteria:
Exclusion criteria for all participants:
1. 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.

Exclusion criteria specific for the de-novo cohort:
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 patient participated solely in the placebo arm of the study. Additionally, participants who have received treatment with antisense oligonucleotides or a messenger ribonucleic acid (mRNA)splicing modifier will be excluded.

Exclusion criteria for the rollover participants:
1. Have ongoing serious adverse events (SAEs) from the parent study.
2. Have ongoing, unresolved AE(s), which in the opinion of the investigator or sponsor, is likely to interfere with study conduct or compliance.

Date of first enrolment
14/12/2022

Date of final enrolment
21/11/2024

Locations

Countries of recruitment
United Kingdom

Australia

Canada

United States of America

Study participating centre
Sage Investigational Site
United States of America
80113

Study participating centre
Sage Investigational Site
United States of America
38157

Study participating centre
Sage Investigational Site
United States of America
99202

Sponsor information

Organisation
Sage Therapeutics (United States)

ROR
https://ror.org/03t9rxt77

Funder(s)

Funder type
Industry

Funder Name
Sage Therapeutics

Alternative Name(s)
Sage Therapeutics, Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

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