



In cooperation with the NINDS NeuroNext program



Study Summary for NCT02507284



Official Title: An Exploratory Phase II Study to Test the Safety, Iolerability, & Activity of a Novel Vasopressin 1a Receptor Antagonist (SRX246) in Irritable Subjects with HD (STAIR)

What is SRX246?

SRX-246 is an investigational drug being developed by Azevan Pharmaceuticals for the potential treatment of symptoms related to Huntington's disease (HD). SRX246 is believed to work by blocking a receptor in the brain called the vasopressin 1a (V1a) receptor. When SRX246 binds to the V1a receptor, it prevents a small protein (peptide) normally made by the body called vasopressin, from binding to the V1a receptor. SRX246 is orally bioavailable drug that can penetrate the blood-brain barrier to get access to the brain.

Why target vasopressin in HD?

Blocking the V1a receptor is considered a novel mechanism of action for treating stress-related Central Nervous System (CNS) disorders. The V1a receptor is the primary vasopressin receptor in the CNS. The vasopressin peptide, made normally in our bodies, has been implicated in social and emotional behaviors. When a person makes too much vasopressin, this can be associated with irritable/aggressive behaviors.

Is irritability/aggression a common symptom of HD?

Yes. It is thought that irritability/aggression is observed in approximately 75% of HD patients. Symptoms like these can account for the institutionalization, poor quality of life and stress reported in HD families. Antidepressants, antipsychotics and anxiolytics that are prescribed for these symptoms are often ineffective.

How will the study drug be administered?

SRX246 will be taken orally and twice a day (BID).

What does the design of the study look like?

The study will be recruiting 108 irritable and aggressive HD patients. The 108 patients will be randomized into 3-arms:

- 1) 36 patients will be given 120 mg BID of SRX246
- 2) 36 patients will be given 160 mg BID of SRX246
- 3) The final 36 patients will be given a placebo (sugar pill)

All 72 subjects in the active SRX246 arms will receive 80 mg twice daily at baseline, then escalate to 120 mg twice daily at 2 weeks. Subjects in the 120 mg BID group will continue to take this dose of SRX246 for an additional 8 weeks. Subjects in the 160 mg BID group will increase to this level beginning at the 4 week time point. They will continue on this dose for an additional 8 weeks.

Dose escalation will occur (stepwise) if patients have *not* experienced dose-limiting adverse effects. Subjects unable to tolerate the dose escalations can be reduced to the prior dose.

Is there a chance I could receive a placebo (sugar pill)?

Yes. The STAIR study is a double-blind placebo controlled clinical study. This means that neither the patient, nor the clinician, will know if the patient is receiving SRX246. 2/3 of the subjects will receive active drug and 1/3 will receive a sugar pill.

How long is my time commitment if I enroll in STAIR?

Recruitment of the STAIR study should begin in 2Q2016. An individual's participation in this study is expected to last for about 18 weeks.

How do I know if I am a candidate for this study?

The STAIR study has very detailed inclusionary and exclusionary criteria for potential participants. Several of the major criteria are listed below. For a complete listing, please visit the "Health Professional Summary" tab in the STAIR study page on HDTrialfinder.org or go to Clinicaltrials.gov and search for "NCT02507284".

Inclusion Criteria

1. Male and female Subjects aged 18 years or older.
2. Subjects must have clinical features of HD, which can include motor, cognitive, or behavioral symptoms.
3. A confirmatory family history of HD; OR CAG repeat expansion greater than 37.
4. Total Functional Capacity (TFC) score of 5-13.
5. Evidence of irritability
6. Medications prescribed for mood, behavior, or neurologic symptoms must be stable for 30 days prior to the Baseline Visit.
7. Sufficient English skills to complete all assessments without assistance.
8. Availability of a responsible Study Partner who has good English skills, is familiar with the Subject, and is able and willing to comply with all required study procedures.

Exclusion Criteria

1. Any significant neurologic disease other than HD at screening.
2. Severe psychotic features or other severe psychiatric symptoms within the last three months which could lead to difficulty complying with the protocol.
3. History of active alcohol or substance abuse within the past two years or Subject is unable to refrain from substance abuse throughout the study.
4. Any chronic disability, significant systemic illness or unstable medical condition at screening or baseline that could lead to difficulty complying with the protocol.

5. Use of any investigational drugs within 30 days of screening.
6. Subject is currently pregnant, breast-feeding and/or lactating.
7. Subject acknowledges present use of illicit drugs at screening.
8. Active thoughts of suicide in the judgement of the Investigator.

Will study participants receive compensation for their time and travel?

The subjects and study partners receive a small amount of money at each visit. In some cases, the sponsor may be able to assist patients/partners who have to travel long distances and require hotel accommodations to attend the study visits.

What are the goals of the STAIR Study?

The *primary* goal for the STAIR study will be tolerability of the 120mg and 160mg BID doses of SRX246 in HD patients. Tolerability is defined as the proportion (percentage) of study completers. Each treatment group will be compared to the placebo group, and the statistical test of equivalence of tolerability will involve two pairwise tests (120mg vs placebo, 160mg vs placebo).

The *secondary* goal of the study is safety. Safety will be determined with an endpoint defined as the proportion of participants who experience an Adverse Event (AE).

A *final* goal of the STAIR Study is to explore several potential measures of irritability in HD Patients that can be assessed in the clinic to help us understand if SRX246 is helpful in decreasing the irritability in HD. Clinical measures such as the Unified HD Rating Scale (UHDRS); UHDRS Irritability and Aggression scale; Aberrant Behavior Checklist (ABC-I); Irritability Scale (IS), Cohen-Mansfield Agitation Inventory (CMAI); Clinical Global Impression Scale (CGI), Caregiver Burden Assessment, and even a novel eDiary will be used by participants in this trial. The “eDiary” will collect a twice daily irritability rating from subjects and observers.

Where will the study take place and how can I get involved?

The STAIR study will be conducted at 22 centers in the United States. All 22 clinical sites are NeuroNEXT study sites for the National Institutes of Health. 15 of these sites are also HDSA Centers of Excellence. For a local study coordinator contact information, please visit HDTrialfinder.org or call an HDTrialfinder Clinical Trial Navigator at 866-890-6612.

Study locations:

- Emory University - Atlanta, GA
- Massachusetts General Hospital - Boston, MA
- Northwestern University Feinberg School of Medicine - Chicago, IL
- The Ohio State University Medical Center - Columbus, OH
- Oregon Health and Science University - Portland, OR
- University of Alabama at Birmingham - Birmingham, AL
- University of California Davis - Davis, CA
- University of California Los Angeles - Los Angeles, CA
- University of Cincinnati - Cincinnati, OH
- University of Colorado Denver - Denver, CO
- University of Kansas Medical Center - Kansas City, KS
- University of Miami School of Medicine - Miami, FL
- University of Pittsburgh - Pittsburgh, PA

- University of Texas Southwestern Medical Center - Dallas, TX
- University of Utah - Salt Lake City, UT
- University of Virginia Charlottesville - Charlottesville, VA
- Vanderbilt University - Nashville, TN
- Washington University in St. Louis School of Medicine - St. Louis, MO
- SUNY Stony Brook University Medical Center - Stony Brook, NY
- Swedish Health Services/Swedish Medical Center - Seattle, WA
- New York Presbyterian Hospital/Columbia University Medical Center - New York, NY
- University of Rochester Medical Center - Rochester, NY

What is NeuroNEXT?

NeuroNEXT, is an initiative of the National Institute of Neurological Disorders and Stroke (NINDS) that supports the conduct of exploratory clinical trials for neurological conditions, such as Huntington's disease.