Modafinil Versus Amphetamines for the Treatment of Narcolepsy Type 2 and Idiopathic Hypersomnia

ClinicalTrials.gov Identifier: NCT03772314

Recruitment Status : Not yet recruiting
First Posted : December 11, 2018
Last Update Posted : December 11, 2018

See Contacts and Locations

Sponsor:
Emory University

Collaborator:
American Academy of Sleep Medicine

Information provided by (Responsible Party):
Lynn Marie Trotti, Emory University

Study Description

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Brief Summary:

For diseases that cause excessive daytime sleepiness (such as narcolepsy and idiopathic hypersomnia), there are several medications that can be used to treat sleepiness. However, it can be difficult to decide which medication to use for a particular individual for several reasons: 1) there are very few studies that directly compare two medications to see which works best; 2) there are very few studies that include people with a disorder of sleepiness called idiopathic hypersomnia.

To address this gap in knowledge, the researchers propose a randomized clinical trial comparing modafinil and amphetamine salts in patients with narcolepsy type 2 or idiopathic hypersomnia. All participants will either receive modafinil or amphetamine salts -- no participant will receive placebo.

This study will evaluate which medication works better to improve sleepiness. The researchers will also see which medication is better for other symptoms including difficulty waking up and difficulty thinking, as well as seeing which medication causes fewer side. Finally, this study will see if any information about patients (such as age or sleep study features) predicts responding better to one medication or the other.

Condition or disease	Intervention/treatment	Phase
Idiopathic Hypersomnia Narcolepsy Without Cataplexy	Drug: **Modafinil** Drug: Amphetamine-Dextroamphetamine	Phase 2

Detailed Description:

Currently, there are insufficient data to guide clinical practice regarding the use of amphetamines for the treatment of narcolepsy. This may be particularly important in the case of narcolepsy type 2, for which randomized, controlled trial data show that other treatments are less beneficial than they are for participants with narcolepsy type 1. For the closely related disorder of idiopathic hypersomnia, clinical trial data to guide treatment decision-making are even more limited, with only three published controlled trials ever performed.

To address these evidence gaps, the researchers propose a randomized, active-treatment controlled trial comparing modafinil and amphetamine salts for the treatment of narcolepsy type 2 and idiopathic hypersomnia. The primary outcome will be reduction in excessive daytime sleepiness, as measured by change in Epworth Sleepiness Scale scores from baseline to week 12 on treatment. Other important patient-reported outcomes will be considered as secondary outcomes, including Patient Global Impression of Change for sleep inertia, cognitive dysfunction, and sleepiness.

In addition to directly comparing the efficacy of these two medications for hypersomnolent patients, this study will also evaluate for relatively safety in this population. Further, this study will assess clinical predictors of treatment response. All three of these aims will be complementary in informing shared decision-making about whether to treat with modafinil or amphetamine salts.

Forty-four treatment-naïve adult patients seeking evaluation at the Emory Sleep Center for narcolepsy type 2 or idiopathic hypersomnia will be invited to participate and will be randomized to one of the treatment arms upon consent. Participants will receive study treatment for 12 weeks.

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	44 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose:	Treatment
Official Title:	Informing Treatment Decisions in the Central Disorders of Hypersomnolence: A Pragmatic Clinical Trial of **Modafinil** Versus Amphetamines
Estimated Study Start Date :	March 2019
Estimated Primary Completion Date :	February 2022
Estimated Study Completion Date :	February 2022

Resource links provided by the National Library of Medicine NIH NLM

Genetics Home Reference related topics: Narcolepsy

Drug Information available for: Dextroamphetamine sulfate Dextroamphetamine Amphetamine sulfate Amphetamine Modafinil Armodafinil

Genetic and Rare Diseases Information Center resources: Narcolepsy Idiopathic Hypersomnia

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Active Comparator: **Modafinil** Participants in this study arm will take **modafinil**.	Drug: **Modafinil** Participants will received 100-400 milligrams (mg) per day of **modafinil** for 12 weeks. Other Name: **Provigil**

Experimental: Amphetamine-dextroamphetamine Participants in this study arm will take amphetamine-dextroamphetamine (amphetamine salts).	Drug: Amphetamine-Dextroamphetamine Participants will receive 10-40 mg/day of oral amphetamine salts for 12 weeks. Other Name: Adderall

Outcome Measures

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Primary Outcome Measures :

1. Change in Epworth Sleepiness Scale (ESS) Score [Time Frame: Baseline, Week 12]

   The Epworth Sleepiness Scale (ESS) asks respondents to indicate how likely they are to doze off or fall asleep during daytime situations such as reading or talking to someone. There are 8 items which are answered on a scale of 0 to 4 where 0 = would never doze and 4 = high chance of dozing. Total score can range from 0 to 24, with higher scores indicating more sleepiness. A score of 0 to 5 can be interpreted as "lower normal daytime sleepiness", a score of 6 to 10 is "higher normal daytime sleepiness", score between 11 to 12 are "mild excessive daytime sleepiness, scores of 13 to 15 are "moderate excessive daytime sleepiness" and scores of 16 to 24 indicate "severe excessive daytime sleepiness".

Secondary Outcome Measures :

1. Change in Patient Global Impression of Change (PGIc) for Sleepiness Score [Time Frame: Weeks 4, 8, 12]

   The PGIc for Sleepiness asks respondents to rate their sleepiness compared to baseline. Responses are indicated on a scale of 1 to 7 where 1 = very much improved and 7 = very much worse.

2. Change in Patient Global Impression of Change (PGIc) for Sleep Inertia Score [Time Frame: Weeks 4, 8, 12]

   The PGIc for Sleep Inertia asks respondents to rate their sleep interia compared to baseline. Sleep inertia is defined for participants as "difficulty waking up and getting out of bed in the morning because of sleepiness". Responses are indicated on a scale of 1 to 7 where 1 = very much improved and 7 = very much worse.

3. Change in Patient Global Impression of Change (PGIc) for Cognitive Dysfunction Score [Time Frame: Weeks 4, 8, 12]

   The PGIc for Cognitive Dysfunction asks respondents to rate their cognitive dysfunction compared to baseline. Cognitive dysfunction is defined for participants as "difficulty with thinking, problems with attention or concentration, and/or brain fog". Responses are indicated on a scale of 1 to 7 where 1 = very much improved and 7 = very much worse.

Eligibility Criteria

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Information from the National Library of Medicine NIH NLM

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- A diagnosis of idiopathic hypersomnia or narcolepsy type 2 (without cataplexy), according with the International Classification of Sleep Disorders, third edition (ICSD-3) criteria

Exclusion Criteria:

- Obstructive sleep apnea (Apnea-Hypopnea Index (AHI) > 5)
- Severe periodic limb movements of sleep with arousals (periodic limb movements (PLM) arousal index > 30)
- Allergy to either of the study drugs
- Contraindication to either of the study drugs
  - For modafinil, these contraindications include: history of left ventricular hypertrophy, mitral valve prolapse, severe cardiovascular disease, unstable angina, myocardial infarction, severe hepatic impairment, substance abuse history, psychosis, or unstable depression or mania
  - Contraindications to amphetamine salts, in addition to those listed above, include: other cardiac structural abnormalities, cardiomyopathy, severe arrhythmias, uncontrolled hypertension, glaucoma, Tourette's syndrome, and epilepsy
- Women who are pregnant, planning to become pregnant within 16 weeks, or breastfeeding will be excluded

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03772314***

Contacts

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Locations

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Sponsors and Collaborators

Emory University

American Academy of Sleep Medicine

Investigators

Principal Investigator: Lynn Marie Trotti, MD, MSc Emory University

More Information

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Responsible Party:	Lynn Marie Trotti, Associate Professor, Emory University
ClinicalTrials.gov Identifier:	NCT03772314 History of Changes
Other Study ID Numbers:	IRB00108167
First Posted:	December 11, 2018 Key Record Dates
Last Update Posted:	December 11, 2018
Last Verified:	December 2018

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: No

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No
Product Manufactured in and Exported from the U.S.:	No

Additional relevant MeSH terms:

Modafinil	Central Nervous System Stimulants
Armodafinil	Cytochrome P-450 CYP3A Inducers
Narcolepsy	Cytochrome P-450 Enzyme Inducers
Disorders of Excessive Somnolence	Molecular Mechanisms of Pharmacological Action
Cataplexy	Physiological Effects of Drugs
Hypersomnolence, Idiopathic	Sympathomimetics
Sleep Disorders, Intrinsic	Autonomic Agents
Dyssomnias	Peripheral Nervous System Agents
Sleep Wake Disorders	Dopamine Agents
Nervous System Diseases	Neurotransmitter Agents
Mental Disorders	Adrenergic Agents
Amphetamine	Adrenergic Uptake Inhibitors
Dextroamphetamine	Neurotransmitter Uptake Inhibitors
Adderall	Membrane Transport Modulators
Wakefulness-Promoting Agents	Dopamine Uptake Inhibitors