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Betreff: NIH Announces Kennedy's Disease Clinical Trial
Wichtigkeit: Hoch

KDA RESEARCH UPDATE

An official announcement by the
Kennedy's Disease Association

Date: **March 19, 2006**

To: **All KDA Associates**

Subject: **National Institute of Health Announces Clinical Trial**

Please review the announcement below concerning the clinical trial for Kennedy's Disease. This is the same trial that the KDA announced a couple of months ago. **If you sent an email to the following email address** (kdareply@earthlink.net) **in February or March, than you do not need to reapply.** Your information has already been given to the researchers and you should be contacted shortly.

You are being sent this email because you, or someone in your family, joined the Kennedy's Disease Association and provided your email address. If you do not wish to receive future e-mails from the KDA, you can send an email message to info@kennedysdisease.org with the word "Remove" in the subject line and we will stop sending you electronic correspondence.

Phase II

Clinical Trial to Examine the Efficacy and Safety of Dutasteride in Patients With Kennedy's Disease (Spinal and Bulbar Muscular Atrophy)

Verified by National Institutes of Health Clinical Center (CC) March 8, 2006

Sponsored by: National Institute of Neurological Disorders and Stroke (NINDS)

Information provided by: National Institutes of Health Clinical Center (CC)

ClinicalTrials.gov Identifier: NCT00303446

Purpose

Background:

Spinal and bulbar muscular atrophy (SBMA) or Kennedy's disease is a slowly progressive, X-linked motor neuron disease for which there is currently no treatment. It is caused by a mutation in the androgen receptor that results in a polyglutamine repeat expansion. Recent animal studies have demonstrated that decreasing endogenous androgen levels leads to functional improvement and increased survival. Studies have also shown that high levels of 5 alpha-reductase, the enzyme that converts testosterone to the more potent dihydrotestosterone (DHT), are present in the ventral spinal cord, while low levels of this enzyme are found within skeletal muscle. Thus, by selectively decreasing levels of DHT with dutasteride, a 5 alpha-reducatse inhibitor, it is hypothesized that there will be a selective protection of motor neurons, without the adverse effects of reducing the anabolic effects of androgen on muscle.

Objective:

This will be a phase II, double-blind, placebo-controlled trial examining the safety and efficacy of the 5 alpha-reductase inhibitor dutasteride in inhibiting the progression of neurodegeneration in patients with Kennedy's disease. Natural history data will also be obtained from the placebo control arm.

Study Population:

We aim to enroll 50 men with genetically confirmed Kennedy's disease.

Design:

Our objective is to examine the safety and efficacy of dutasteride given at a dose of 0.5 mg a day for 2 years in an outpatient setting. This will be a randomized, double-blind, placebo-controlled trial with 25 subjects in each arm. The subjects will be evaluated neurologically and endocrinologically every 6 months at the NIH Clinical Center. In addition to their clinical visits at the NIH, subjects will also be examined by their primary physician after 3, 9, 15, and 21 months of treatment. The primary objective is to examine the effects of dutasteride on inhibiting or reversing the rate of progression of weakness as measured by quantitative muscle testing. Following informed consent, patients will undergo an initial medical history and physical followed by testing of specific neurological and endocrinological measures over a two-day outpatient visit. Patients will provide blood samples for analysis of hormonal levels and extent of muscle damage every three months. In addition, at the initial, one-year, and two-year follow-up visits patients will have nerve conduction studies as well as quantitative and functional strength evaluation. Each patient will be randomized to the treatment or placebo arm and will be given a 3 month supply of the study drug or a matched placebo at each visit. In between clinic visits, the NIH clinical pharmacy will send an additional 3 month supply to each subject until the subsequent visit.

Outcome Measures:

The primary outcome measure used will be quantitative muscle testing (QMT). Secondary outcome measures include the Adult Myositis Assessment Tool (AMAT), 2-minute walk, a quality of life measure (SF-36v2TM), neurophysiological testing (sensory nerve action potentials, and statistical motor unit number estimation). Changes in hormone levels (testosterone, dihydrotestosterone, androstenedione, estradiol), and creatine kinase levels will also be measured and correlated with changes in strength. Evaluation of disease severity and course as related to CAG repeat length and androgen levels will also be assessed.

Future Directions:

The results of this phase II study will assist us in developing a multi-center, double-blind, placebo-controlled phase III trial. In addition, natural history data will be obtained from the control arm that will be important in future clinical trials of SBMA.

Study Type: Interventional
Study Design: Treatment, Safety/Efficacy
Further study details as provided by National Institutes of Health Clinical Center (CC):

Expected Total Enrollment: 50

Study start: March 13, 2006

Eligibility

Genders Eligible for Study: Male

Criteria

INCLUSION CIRTERIA:

Genetically confirmed SBMA.

Neurological symptoms of SBMA.

Ability to ambulate 100 feet with or without the use of assistive devices.

Willingness to participate in all aspects of trial design and follow-up.

Male sex.

EXCLUSION CRITERIA:

Age less than 18 years.

Female sex.

A history of hypersensitivity to dutasteride or 5 alpha-reductase inhibitors

Exposure to 5 alpha-reductase inhibitors, anti-androgens, testosterone, or steroids in the preceding 6 months.

Patients who are taking potent CYP3A4 inhibitors for over 4 weeks.

Patients with any pre-existing liver disease

Alkaline phosphatase, SGOT, SGPT, or total bilirubin greater than 1.5 X the upper limit of normal.

Creatinine greater than 1.5 X the upper limit of normal.

Platelet count, white blood cell count or hemoglobin below the lower limit of normal.

Other clinically significant medical disease that, in the judgment of the investigators, would expose the patient to undue risk of harm or prevent the patient from completing the

study.

Maryland

National Institute of Neurological Disorders and Stroke (NINDS), 9000 Rockville Pike, Bethesda, Maryland, 20892, United States; Recruiting

Patient Recruitment and Public Liaison Office 1-800-411-1222 prpl@mail.cc.nih.gov
TTY 1-866-411-1010

More Information

Publications

Kennedy WR, Alter M, Sung JH. Progressive proximal spinal and bulbar muscular atrophy of late onset. A sex-linked recessive trait. Neurology. 1968 Jul;18(7):671-80. No abstract available.

Harding AE, Thomas PK, Baraitser M, Bradbury PG, Morgan-Hughes JA, Ponsford JR. X-linked recessive bulbospinal neuronopathy: a report of ten cases. J Neurol Neurosurg Psychiatry. 1982 Nov;45(11):1012-9.

Olney RK, Aminoff MJ, So YT. Clinical and electrodiagnostic features of X-linked recessive bulbospinal neuronopathy. Neurology. 1991 Jun;41(6):823-8.

Study ID Numbers: 060113; 06-N-0113
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