National
Multiple Sclerosis
Society
News Sheets

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RESEARCH/CLINICAL UPDATE

January 24, 2013

MS Trial Alert:
Recruiting for a Nationwide Study of an Investigational New Treatment for Spasticity

Summary: Investigators nationwide are recruiting 75 people with any type of MS for a long-term safety study of arbaclofen placarbil, an investigational oral medication that is similar to a currently approved medication, baclofen. The study is funded by XenoPort, Inc.

Rationale: Spasticity refers to feelings of muscle stiffness, tightness, and involuntary muscle spasms (sustained muscle contractions or sudden movements). It is one of the more common symptoms of people with MS. Baclofen is the most commonly used drug to treat spasticity and is a muscle relaxant. AP is an investigational medication that is similar to a currently approved medication called baclofen. Baclofen has 2 components (R- and S-baclofen) and only one of these (R-baclofen) is responsible for improving spasticity. Arbaclofen placarbil is a "prodrug" of R-baclofen, meaning it changes to R-baclofen once swallowed. In a study in people with spinal cord injury and spasticity, arbaclofen placarbil showed a significant and sustained anti-spasticity effect when taken twice daily, therefore it is believed that arbaclofen placarbil may result in less frequent daily dosing than baclofen (*Spinal Cord* 2011;49:974).

Eligibility and Details: Participants must be aged 18 to 70, diagnosed with MS and spasticity. If participants are taking a disease-modifying MS treatment, the dosage, frequency, and route of administration must be stable for at least 30 days before screening and are expected to be stable throughout the study. Further details on enrollment criteria are available via the contact information below.

Participants are being administered 45 mg of arbaclofen placarbil in tablet form, and are being followed for 26 to 36 weeks primarily to ensure the drug's safety. A secondary outcome is to determine the effectiveness of the drug on a clinical scale that measures spasticity.

Contact: To learn more about the enrollment criteria for this study, and to find out if you are eligible to participate, please visit www.CommandTrial.com.

Sites are enrolling in the following cities:
Akron, OH
Albuquerque, NM
Asheville, NC
Atlanta, GA
Bingham Farms, MI
Danbury, CT
Denver, CO
Detroit, MI
Gilbert, AZ
Golden Valley, MN
Indianapolis, IN
Lenexa, KS
Lexington, KY
Long Beach, CA
Nashville, TN
Newport Beach, CA
Patchogue, NY
Phoenix, AZ
Plainview, NY
Port Charlotte, FL
San Antonio, TX
Sarasota, FL
Seattle, WA
St. Petersburg, FL
Tacoma, WA
Tampa, FL
Toms River, NJ
Download a brochure that discusses issues to think about when considering enrolling in an MS clinical trial (PDF).

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RESEARCH/CLINICAL UPDATE

February 1, 2013

Study: Obesity is Associated with Increased Risk of MS in Girls

Researchers report that being overweight or obese was associated with an increased risk of developing MS or clinically isolated syndrome (CIS, a first clinical episode suggestive of MS, indicating increased MS risk) in girls, in a study that compared 75 children or teens with MS or CIS with the health records of more than 900,000 healthy children or teens. This finding, if confirmed, opens up the possibility that reducing obesity could reduce some risk of MS in girls. Annette Langer-Gould, MD, PhD, and colleagues (Kaiser Permanente of Southern California, Pasadena) and others report their findings in the January 30, 2013, online issue of *Neurology*. (http://www.neurology.org/content/early/2013/01/30/WNL.0b013e31828154f3.abstract)

Background: Although MS occurs most commonly in adults, it is also diagnosed in children and adolescents. While the disease is not contagious or directly inherited, epidemiologists—the scientists who study patterns of disease—have identified factors in the distribution of MS around the world that may eventually help determine what causes or triggers the disease. These factors include gender, genetics, age, geography, and ethnic background.

Because the prevalence of obesity has increased dramatically in the past several decades, and obesity is associated with an increase in immune system activity, Dr. Langer-Gould's team undertook a study to determine if there was any association between obesity and the risk for developing MS or CIS.

The Study: Investigators identified cases of MS and CIS in the database of Kaiser Permanente Southern California, a health maintenance organization with more than 900,000 members 18 years old or younger. They found 75 cases, and reviewed charts to examine body size, and compared findings with 913,172 child or teen controls without MS or CIS.

The results show that 50.6% of the children with MS or CIS were overweight or obese before their diagnosis, compared with 36.6% of the control cases. Compared to girls who were not

overweight, the risk for developing MS was about one and a half times higher for overweight adolescent girls, and over three times higher for girls who were extremely obese. The increased risk with obesity was not found in boys.

Comment: The authors suggest that the increased risk in adolescent girls in particular may be associated with increases in sex hormones such as estrogen. They comment that although one strength of the study is the large number of control cases, the primary limitation is the small number of MS cases studied.

"If further research confirms these findings, excess weight could turn out to be a modifiable risk factor that influences the development of MS in children and adolescents," says Nicholas LaRocca, PhD, Vice President of Health Care Delivery and Policy at the Society. "Finding such risk factors and addressing them is a crucial step toward ending MS."

Read more (http://www.nationalmssociety.org/about-multiple-sclerosis/pediatric-ms/index.aspx) about pediatric MS.

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RESEARCH/CLINICAL UPDATE

January 31, 2013

Clinical Trial Results Announced in Study of Peginterferon Beta-1a

Biogen Idec announced that a phase III study of peginterferon beta-1a, injected under the skin either every two or four weeks, reduced the relapse rate significantly more than placebo in a study of 1500 people with relapsing MS, reaching the primary goal of the study. Peginterferon is a new formulation of the interferon beta-1a molecule which enables it to maintain effects in the body for longer periods of time. More data from this ongoing study, also called the ADVANCE study, will be presented at the American Academy of Neurology Annual Meeting in March. According to a press release, the company is planning to file for regulatory approval in the United States and European Union in 2013.

Background: Avonex® (interferon beta-1a, Biogen Idec) is approved by the U.S. Food and Drug Administration for the treatment of people with relapsing forms of MS to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations. Peginterferon beta-1a is a "pegylated" form of the interferon beta-1a molecule. Pegylated molecules are attached to a molecule of polyethylene glycol, which enables them to maintain effects in the body for longer periods of time. Previously, the formulation has been tested in healthy individuals in two phase I clinical trials.

The Study: For this phase III, two-year trial, investigators worldwide recruited 1516 people with relapsing MS who were randomly assigned to one of three groups: placebo, peginterferon bet-1a 125 mg delivered subcutaneously (under the skin) every two weeks, or peginterferon beta-1a 125 mg delivered subcutaneously every four weeks. The primary objective of the study was to determine the effects of the drug versus placebo on the annualized relapse rate at one year. Secondary objectives included the effects on central nervous system damage as observed on MRI scans, quality of life, and disease progression as measured by the EDSS scale.

According to the press release, the annualized relapse rate was reduced significantly more that placebo, by 35.6% in the two-week dosing group, and by 27.5% in the four-week dosing group.

Similar reductions occurred in the proportion of patients who experienced relapses. The risk of disability progression (confirmed over 12 weeks), as measured by the EDSS scale, was reduced by 38% in both peginterferon groups. Disease activity on MRI scans was reduced by 67% in the two-week dosing group and by 28% in the four-week dosing group.

The most common adverse events were infections, occurring in 1% or fewer people in all three treatment groups. The most commonly reported adverse events associated with the peginterferon groups were redness at the injection site and flu-like illness. Quality of life results were not included in the press release.

The ADVANCE Study is still ongoing to finish two years. After the first year of the trial, those on placebo were transitioned into one of the active treatment arms for the second year of the study. Study participants then will have the option of enrolling in an open-label extension study called the ATTAIN study, during which they are being followed for up to four years.

Comment: "We look forward to seeing the complete data from this study," says Timothy Coetzee, PhD, Chief Research Officer of the National MS Society. "Having additional treatment options is important for people with MS, since everyone responds to therapies differently."

Read more (http://www.nationalmssociety.org/research/stop/index.aspx) about efforts to stop MS in its tracks.