Clinical Trial Summary

Sarcotropin®

A MEDICAL FOOD

Clinical Trial Summary

Title:
A Phase III, Randomized, Open Label,Placebo-Controlled Clinical Study To Evaluate The Efficacy And Safety of Sarcotropin® For The Treatment of Age Related Changes in Form, Function and Quality of Life In Healthy Subjects

CLINICAL RESEARCH ORGANIZATION:
Ethicare Clinical Trial Services
5/C, Vardan Tower, Nr. Vimal House,
Vithalbhai Patel Colony
Navrangpura, Ahmedabad – 380014, India

Study Initiation Date: 15/SEP/2011
Study Completion Date: 02/MAR/2012

Objectives:
Primary:
To evaluate the efficacy of Sarcotropin® in treating age-related changes in form, function and quality of life in healthy subjects.

Secondary:
To determine the safety of Sarcotropin® in healthy human subjects using vital signs as well as haematology, biochemistry and urinalysis measures.

Methodology:
This study was conducted as an open label, randomized, placebo-controlled clinical trial in healthy subjects which was conducted at three centers located in Ahmedabad. Treatments were provided and outcome measures were obtained therein. The study was conducted in accordance with the Declaration of Helsinki, current International Conference on Harmonization (ICH) Guideline for Good Clinical Practice (GCP) and Ethical Guidelines for Biomedical Research on Human Subjects. The study protocol was approved by an Independent Ethics Committee for all three sites. The study subjects received oral and written information about the

intentions and nature of the study before participating. Male and female healthy subjects aged 40 to 70 years, who met all the inclusion criteria based on history and clinical examination were recruited for the study.

On visit 1 (Day -15 to 0), after signing the informed consent document, subjects were screened for baseline determinations of following tests and measurements:

- Anatomical measurements of the forearm (flexed and widest area) and wrist, waist and hips
- Body composition including total body fat, total body water, muscle mass, bone mass and visceral body fat
- Bone mineral density as measured by DEXA
- Forced vital capacity (FVC) using a spirometer
- Grip strength of right and left hand through Hand Grip Strength Dynamometer
- Cardiovascular compliance by measurements of blood pressure, pulse rate and 12 Lead ECG
- Subjects self-administered Quality of life questionnaires

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Visit # 1 (day 0): Blood samples were collected for measurement of biochemical parameters, GH neuroendocrine axis activity and also safety markers including hematology, biochemistry and urinalysis. Intravenous Glucose Tolerance Test (IGTT) was also performed during which serum insulin and glucose were measured. Subject's eligibility was assessed based on laboratory results and also on the basis of inclusion-exclusion criteria consideration.

At Visit #2 (Day 1), eligible subjects were randomized and then assigned to receive Sarcotropin® or placebo per an oral daily dose of 10 mL every morning for 90 consecutive days. Subjects were instructed to keep daily dosing records of subjective experiences while participating in the study. Each subject was given a diary to maintain personal records. The subjects were then provided with sufficient medication for 30 days and instructed to return to the clinic with empty bottles at the next visit. During the course of the trial, each enrolled subject visited the site as follows:

Visit Schedule: V1: Screening Visit 1: Day -15 to 0

V2: Visit 2: Day 1

V3: Visit 3: Day 30 (±2 day)

V4: Visit 4: Day 45 (±2 day)

V5: End of Study Visit 5: Day 90 (±3 day)

IGTT was performed at Visit #3 (Day 30). After collection of a fasting blood sample, 25ml of 25 percent glucose in distilled water was injected intravenously over a period of 10-12 minutes and then blood samples were collected at intervals of 1 min, 5 min, 1 hour and 2 hours thereafter.

During follow-up Visit #4 (Day 45) and at the end study visit 5 (Day 90), subjects were evaluated using anatomical measurements, body composition, forced vital capacity, grip strength, cardiovascular compliance and each subject's self administered quality of life questionnaire as criteria. In addition, blood samples were collected to measure biochemical markers of GH neuroendocrine axis activity and also safety markers based upon hematology, biochemistry and. Bone mineral density was measured at the end of study visit 5 (Day 90).

Safety:

Safety / Tolerability were evaluated based on spontaneous reporting of adverse events by the healthy subjects and by the use of an open question analysis throughout the study. Also, change from pre-treatment to post treatment follow-up in vital signs (blood pressure and heart rate), hematology, biochemistry and urinalysis were used to evaluate safety of treatment.

Statistical Methods:

A total of 116 male and female healthy subjects were screened, out of which 94 were enrolled. Data from all the sites were pooled for analysis. An intention-to-treat and pre-protocol analysis was done for efficacy. For safety, intention-to-treat analysis was done. Collected data were expressed as mean, standard deviation, and standard error of mean, maximum and minimum whereas categorical data was expressed as percentages. Paired t-test was used to compare changes in each efficacy and safety parameters at baseline, day 45 and on day 90 for both treatment and placebo groups. Unpaired t-test was used to compare the treatment and placebo groups for each efficacy parameter.

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Wilcoxon Sign Rank Test was used to compare changes in QOL at baseline and at the end of the day 90 study period. Wilcoxon Two-Sample Test was used to compare outcomes of treatment and placebo groups for QOL. A "p" value less than 0.05 was considered significant for changes occurring between the groups as well as within groups.

Outcomes Summary:

A total of 94 male and female healthy subjects were enrolled of which 53 were male (56.38 %) and 41 were female (43.62 %). Of these, 75 subjects completed the study. Out of the 75 on-study subjects, 50 (M - 29 and F - 21) were in the treatment group whereas 25 subjects (M - 13 and F - 12) were in the placebo group. Nineteen subjects were discontinued from the study for personal reasons and/or due to adverse events.

The mean age of all subjects on treatment ranged from 40 to 68 years with a mean of 48.89 ± 0.992 years, mean height 163.56 ± 1.25 cm and mean weight of 71.67± 2.07 kg. The mean age of all subjects in the placebo group ranged from 40 to 62 years with a mean of 49.50 ± 1.24 years, a mean height of 159.57 ± 4.02 cm and mean weight at 72.60 ± 3.86 kg.

Efficacy Outcomes:

Insulin-like growth factor-1 (IGF-1) was significantly increased from 103.54 ± 1.94 ng/mL at baseline to 111.40 ± 2.01 ng/mL at day 45. Levels further increased to 120.47 ± 2.10 ng/mL after 90 days of treatment. In contrast, there were no significant changes in IGF-1 levels in subjects receiving placebo.

Body Mass Index (BMI) and total body water did not change significantly in either treatment or placebo groups during the course of study.

Total body fat was significantly decreased in the treatment group from 34.46 ± 1.23 % at baseline to 32.54 ± 1.04 % on day 45 and to 31.31 ± 1.11 % at the end of treatment. The decrease in body fat after 45 days of treatment was 5.57% and after 90 days it decreased 9.14%. Visceral fat decreased in the treatment group from 11.84 ± 0.66 % at baseline to 10.62 ± 0.66 % on day 45 and to 10.15 ± 0.67 % after 90 days of Sarcotropin administration. Visceral fat was reduced by 10.3% and 14.27% after 45 and 90 days of treatment, respectively. There were no changes in total or visceral body fat within the placebo group.

Muscle mass was significantly increased from 41.88 ± 1.28 Kg at baseline to 44.13 ± 1.24 Kg at the end of the 90 day treatment period. Lean body mass increased by 5.37% after 90 days treatment with Sarcotropin in comparison to placebo which was not associated with change in muscle mass.

Forced vital capacity (FVC) significantly increased by 16.61% after 90 days of Sarcotropin treatment. FVC was significantly increased from 71.84 ± 3.18 % at baseline to 73.60 ± 3.52 % on day 45 and to 83.77 ± 3.70 % on day 90. There were no changes in FVC in the placebo group throughout the course of study.

Favorable changes were measured in the treatment group for bone mass and grip strength but these did not reach the level of statistical significance. No changes in bone mineralization or cardiovascular compliance were noted in either group. It is possible that longer treatment periods are required to gain positive effects for these clinical parameters.

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Changes in Quality of Life (QoL) were measured using standardized questionnaires that were completed by all subjects at baseline and on days 45 and 90 of study. The questionnaire consisted of 15 questions that could be answered on a graded scale of 1 – 5. A lowering score trend was considered to reflect improvement in QoL. The score was reduced in treated subjects from 36.4 at baseline to 31.1 and 25.9 on days 45 and 90, respectively. These changes represented a 28.85% reduction on day 90 in the treated group. In comparison, the mean score was reduced from 37.6 to 34.1 on day 45 and to 31.5 at day 90. This represents a 16.22% reduction in the placebo group. Thus, there was a significant improvement in QoL for both the groups but the effect occurred in 96% of those receiving Sarcotropin as compared with only 60% of those receiving placebo. Of those showing improvement, most remarked about having increased energy, improved work ability/capacity, increased confidence, improved physical fitness, increased resistance towards illness, increased sleep duration and overall feelings of happiness. A few of subjects reported having reduced back pain and ankle pain while others remarked about improvement in skin texture and radiance.

Changes in pancreatic function as evaluated using the Intravenous Glucose Tolerance Test (IGTT) suggested that insulin sensitivity was increased in the treatment group. This conclusion is indicated by the fact that mean glucose levels were in the normal range at base line before glucose administration, but spiked significantly by one minute afterward. Thereafter, blood glucose returned by normal levels within two hours. A similar profile occurred after 30 days on study both in treated and placebo subjects. However, insulin levels were 24.62 % and 32.94 % lower at 1 hour and 2 hours, respectively, after glucose administration in the treatment group as compared to 3.4 % and 7.25 % lower in the placebo group. Despite the lower insulin levels in the treated individuals, their blood glucose levels were comparable to those in the placebo group suggesting the sarcotropin increased insulin sensitivity.

Safety Outcomes:

A total of twenty adverse events were reported from 94 enrolled subjects. Of those possibly related to treatment as determined by the physician in charge included soft stool, drowsiness, upset stomach and menstrual irregularity. Unrelated events as determined by the physician in charge included itching, increased osteoarthritis problems and joint pain. Of the individuals reporting such adverse events, five were discontinued from the study of their own accord or by the doctor's order. No clinically significant changes in biochemical or hematological parameters were noted except that total platelet count was increased in treatment group. However, the values were well within the normal range and therefore not considered to be clinically relevant.

There were neither unexpected adverse events nor serious adverse events reported during the course of this study.

Conclusions:

The results of this study demonstrate that Sarcotropin is safe and effective for improving body composition and quality of life in humans that are middle-aged and beyond. Statistically significant increases in lean body mass suggest that the product has value in opposing sarcopenia; the loss of muscle that underlies much of the adverse effects of aging on health, vitality and quality of life.