GM604 Phase 2A Randomized Double-blind Placebo Controlled Pilot Trial in Amyotrophic Lateral Disease (ALS) (GALS)

This study is not yet open for participant recruitment.

Verified May 2013 by Genervon Biopharmaceuticals, LLC

Sponsor:
Genervon Biopharmaceuticals, LLC

Collaborators:
Columbia University
Massachusetts General Hospital

Information provided by (Responsible Party):
Genervon Biopharmaceuticals, LLC

ClinicalTrials.gov Identifier:
NCT01854294

First received: May 8, 2013
Last updated: May 29, 2013
Last verified: May 2013
History of Changes

Purpose

GM604 is an endogenous human embryonic stage neural regulatory and signaling peptide that controls the development, monitoring and correction of the human nervous system. Neurological diseases are multisystem, multifactorial, and single target drugs are ineffective. **Genervon**'s Master Regulators play a significant role in embryonic/fetal nervous system development and are potent disease modification drug candidates modulating many pathways including inflammation, apoptotic, hypoxia... The study drug is an regulatory peptide with a sequence identical to one of the active sites of human Motoneuronotrophic Factor and is manufactured by solid phase synthesis. Pre-clinical research indicates it to be a neuro-protective agent in animal models of ALS, motorneuron diseases, PD, other neuro-degenerative diseases and stroke. GM604 controls and modulates over many known and significant ALS genes with positive effects interactively and dynamically through multiple pathways, and up to twenty-two biological processes, including neuro-protection, neurogenesis, neural development, neuronal signaling, neural transport, and other processes. GM6 is not a cocktail of drugs, but one master regulator peptide drug that functions through multiple pathways. **Genervon** hypothesized that studying the biomarkers of protein expressions of these ALS genes such as SOD1 and the protein expression of substances such as tau, NF-H, Cystatin C which were indications of degeneration of neuron in the CSF collected from ALS patients will provide information of the possible GM604's mechanisms of action in treating ALS. 1. This pilot trial is designed to test proof of principle, i.e. determine if a 2-week IV bolus treatment with this agent can (1) change ALS protein expression (target biomarkers and efficacy biomarkers) after treatment (2) have preliminary effects measures of ALS disease clinical progression.

Study Objectives are:

1. To test the safety and tolerability of GM604 in a population of ALS patients.
2. To test for changes in ALS biomarkers before and after treatment.
3. To determine preliminary effects of injections of GM604 on measures of ALS disease biomarkers and clinical progression

Condition	Intervention	Phase
Amyotrophic Lateral Sclerosis	Drug: GM604	Phase 2

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Treatment

Official Title: GM604 Phase 2A Randomized Double-blind Placebo Controlled Pilot Trial in Amyotrophic Lateral Disease (ALS)

Resource links provided by NLM:

Genetics Home Reference related topics: amyotrophic lateral sclerosis

MedlinePlus related topics: Amyotrophic Lateral Sclerosis

U.S. FDA Resources

Further study details as provided by Genervon Biopharmaceuticals, LLC:

Primary Outcome Measures:

- Efficacy by percent change in biomarker in th CSF at week 12 from baseline [Time Frame: baseline, week 2, week 12]
  [Designated as safety issue: No]

  Efficacy by percent change in biomarker in the CSF at week 12 from baseline: (a) Efficacy biomarkers (b) Target biomarkers (c) Efficacy/target biomarkers

- Safety [Time Frame: baseline, week 2, week 12] [Designated as safety issue: Yes]

  Safety: 1. adverse event frequency and severity, changes in vital signs, clinical laboratory values. 2. Serious adverse event frequency

- Tolerability [Time Frame: Baseline, week 2, week 12] [Designated as safety issue: Yes]

  Tolerability: The ability to complete the first 2 weeks of active treatment in the study

Secondary Outcome Measures:

- Efficacy by percentage change of other biomarkers not as primary endpoint in the CSF at week 12 from baseline [Time Frame: baseline, week 2, week 12] [Designated as safety issue: No]
- Efficacy by percentage change of biomarker in CSF at end of week 2 from baseline [Time Frame: baseline, week 2]
  [Designated as safety issue: No]
- ALSFRS-R [Time Frame: Symptom onset, screening, baseline, week 2, week 6, week 12] [Designated as safety issue: No]

  Progressive change in ALSFRS-R of each patient determined from the following data points:1) symptom onset, 2) baseline, 3) end of week 2 examination, 4) end of week 6 examination and 5) end of week 12 examination.

- Forced Vital Capacity (FVC) [Time Frame: Symptom onset, baseline, week 2, week 6, week 12] [Designated as safety issue: No]

  Progressive change in Forced Vital Capacity (FVC) from the following data points: 1) symptom onset, 2) baseline, 3) end of week 2 examination, 4) end of week 6 examination and 5) end of week 12 examination.

- Time Up and Go (TUG) [Time Frame: Symptom onset, baseline, week 2, week 6, week 12] [Designated as safety issue: No]

  Progressive change in Forced Vital Capacity (FVC) from the following data points: 1) symptom onset, 2) baseline, 3) end of week 2 examination, 4) end of week 6 examination and 5) end of week 12 examination.

- muscle strength [Time Frame: Symptom onset, baseline, week 2, week 6, week 12] [Designated as safety issue: No]

  Progressive muscle strength change measured by HHD (handheld dynamometry testing score) from the following data points: 1) symptom onset, 2) baseline, 3) end of week 2 examination, 4) end of week 6 examination and 5) end of week 12 examination.

- Biomarker in blood [Time Frame: baseline, week 2, week 6, week 12] [Designated as safety issue: No]

  Percentage change in Biomarkers in blood between baseline and 1) the ends of weeks 2, 2) week 2 and week 6 and 3) week 6 and week 12. Comparing the changes encompassing the entire cohort of 10 subjects.

- Mortality rate [Time Frame: baseline, week 2, week 6, week 12] [Designated as safety issue: No]

Other Outcome Measures:

- comparison of slopes (change in the rate of decline)of disease progression [Time Frame: Symptom onset, baseline, week 2, week 6, week 12] [Designated as safety issue: No]

  Secondary analyses may consider a comparison of slopes (change in the rate of decline) for any hint of disease modification using placebo outcomes in patients matched for baseline features from a large database of recent clinical trials by NEALS showing stable rates of decline as historical controls.

- stratification of patients by symptoms [Time Frame: Symptom onset, baseline, week 2, week 6, week 12] [Designated as safety issue: No]

Secondary analysis to allow a-priori stratification of patients by their symptoms if available

a. predominantly lower motor neuron
b. predominantly upper motor neuron
c. predominantly bulbar

Estimated Enrollment:	12
Study Start Date:	July 2013
Estimated Study Completion Date:	June 2014
Estimated Primary Completion Date:	March 2014 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: GM604 treated Each subject will receive a slow IV bolus injection (~1min) of 6.4 mL (320mg @50 mg/mL=6.4 mL) for each dose. A total of 6 doses will be administered over two weeks (on Mondays, Wednesdays and Fridays for the first 2 weeks).	Drug: GM604 GM604 treated group subject will receive a slow IV bolus injection (~1min) of 6.4 mL (320mg @50 mg/mL=6.4 mL) for each dose. A total of 6 doses will be administered over two weeks (on Mondays, Wednesdays and Fridays for the first 2 weeks). Other Name: GM6, GM602, GM608
Placebo Comparator: Placebo treated 6.4 mL Bacteriostatic saline will be used for the Placebo group.Injections will be given to the subject in the same manner as in GM604 treated group. A total of 6 doses will be administered over two weeks (on Mondays, Wednesdays and Fridays for the first 2 weeks).	

Show Detailed Description

Eligibility

Ages Eligible for Study:	18 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Patients with ALS: Familial and Sporadic ALS, with symptom onset < or equal to 24 months.
2. At least 18 years of age
3. Subjects meet the El Escorial criteria of definite criteria for a diagnosis of ALS.
4. Subjects can be on a stable dose of riluzole for at least a month or not taking or initiating riluzole for the duration of the trial.
5. Not on any experimental medication for the last 1 month or five times the half-life of experimental medication.
6. At screening, must have a Forced Vital Capacity (FVC) ≥ 65% of predicted capacity for age, height and gender.
7. Have fully completed informed consent form
8. Ability to comply with study procedures
9. Women of child-bearing age must be on birth control. Pregnancy test should be done in women in child bearing age.
10. Medically safe to have lumbar puncture to collect CSF

Exclusion Criteria:

1. History of liver disease, severe renal failure, diabetes, coronary heart disease, cancer
2. Clinically significant EKG abnormality at screening
3. Any comorbid condition which would make completion of the trial unlikely
4. FVC < 65%
5. Presence of a bleeding disorder
6. Allergy to local anesthetics
7. Problem with CSF pressure
8. Topical or other skin infection at the lumbar puncture site

9. BMI > 32 kg/m2
10. Medical or surgical conditions in which a lumbar puncture is contraindicated
11. Use of any anti-platelet or anticoagulant drugs, such as plavix, aggrenox, ticlid, warfarin or coumadin -

Contacts and Locations

Please refer to this study by its ClinicalTrials.gov identifier: NCT01854294

Locations

United States, Massachusetts

Massachusetts General Hospital — **Not yet recruiting**
Boston, Massachusetts, United States, 02114
Contact: Michele Parkinson, RN 617-643-6249 mparkinson@partners.org
Principal Investigator: Nazem Atassi, MD
Sub-Investigator: Merit Cudkowicz, MD

United States, New York

Columbia Medical Center NY — **Not yet recruiting**
New York, New York, United States, 10032
Contact: Nicole Armstrong, Research Coordinator 212-305-8148 na2398@columbia.edu
Principal Investigator: Hiroshi Misumoto, MD

Sponsors and Collaborators

Genervon Biopharmaceuticals, LLC

Columbia University

Massachusetts General Hospital

Investigators

Principal Investigator: Hiroshi Mitsumoto, MD Columbia Medical Center NY

Principal Investigator: Merit Cudkowicz, MD Massachusetts General Hospital

More Information

No publications provided

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ClinicalTrials.gov Identifier:	NCT01854294 History of Changes
Other Study ID Numbers:	GALS 001
Study First Received:	May 8, 2013
Last Updated:	May 29, 2013
Health Authority:	United States: Food and Drug Administration

Keywords provided by Genervon Biopharmaceuticals, LLC:

ALS	in silico analysis
motorneuron disease	active site
Central Nervous System (CNS) disease	protein
neurodegeneration	peptide
neuroprotective	embryonic stage
mechanisms of action	endogenous
pathways	master regulators
biomarkers	fetal development
Cerebral Spinal Fluid (CSF)	embryonic development
blood biomarkers	common pathways
multi-factorial	Blood Brain Barrier (BBB)
multisystem	anti-inflammatory
single target	anti-apoptotic
pathogenic mechanisms	anti-oxidative
Protein Bands Selection by Function	regenerative

Additional relevant MeSH terms:

Amyotrophic Lateral Sclerosis	Neurodegenerative Diseases

Sclerosis
Motor Neuron Disease
Spinal Cord Diseases
Central Nervous System Diseases
Nervous System Diseases

TDP-43 Proteinopathies
Neuromuscular Diseases
Proteostasis Deficiencies
Metabolic Diseases
Pathologic Processes

ClinicalTrials.gov processed this record on June 06, 2013