

# SMA Research Update – Providing Hope!

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## Currently, there are (7) active studies within Columbia University Medical Center:

### Clinical Study of Spinal Muscular Atrophy

**\*\*Ongoing, not recruiting\*\***

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Spinal Muscular Atrophy (SMA) is one of the most devastating neurological diseases of childhood. Affected infants and children suffer from progressive muscle weakness caused by degeneration of lower motor neurons in the spinal cord and brainstem. Clinically, four phenotypes are distinguished within the continuous spectrum of disease severity based on the age of onset and the highest motor milestone ever achieved. SMA is caused by homozygous deletion of the survival motor neuron-1 (SMN1) gene. A related gene, SMN2, produces low levels of full-length SMN protein due to inefficient splicing. There is an inverse correlation between SMN copy number and disease severity, presumably mediated by levels of full length SMN protein. Therefore, increasing the amount of full-length SMN protein is a promising treatment strategy. Several drugs targeting splicing efficiency have resulted in increased SMN protein in preclinical assays and are now awaiting clinical testing.

With the future objective to conduct clinical trials in SMA, the proposed project has 3 specific aims: 1) To establish a web-based database that will serve to enroll the patient population and that will facilitate timely recruitment for future clinical trials; (2) to plan for clinical trials by a) developing reliable outcome measures, and (b) establishing the infrastructure needed to carry out efficient clinical trials, (c) convening meetings of preclinical and clinical researchers involved in SMA drug development to select candidate drugs, and (3) to characterize the patient population from a clinical and molecular point of view.

We have established a Pediatric Neuromuscular Clinical Research Network (PNCr) to evaluate patients at three sites: New York, Boston and Philadelphia. Data management (including fully web-based data repository) and statistical analyses will be carried out at the University of Rochester by the "Muscle Study Group Data Center", which is a group experienced in clinical trials of neuromuscular disease. We will characterize the patient population using selected outcome measures, standardized among sites. The clinical trial planning phase will focus on developing the necessary infrastructure between sites, critically evaluating candidate outcome measures, obtaining pilot data using those outcome measures, and establishing their reliability. In parallel to the proposed study we will work closely with the preclinical units of the Columbia University SMA research center to identify and prioritize candidate drugs for future clinical trials. Finally, based on the observational data from the proposed study, and discussions among the network's clinical experts we will develop efficient phase I/II clinical trial designs to test candidate drugs. This clinical research is timely and relevant, because laboratory research has identified candidate drugs for SMA. There is currently no effective treatment for this devastating disease. All activities of the Network will conform to established regulations that govern clinical research and patient privacy (HIPAA).

This is an observational study with an observational model: case-only.

#### Eligibility

<b>Ages Eligible for Study:</b>	Child, Adult, Senior
<b>Sexes Eligible for Study:</b>	All
<b>Accepts Healthy Volunteers:</b>	No
<b>Sampling Method:</b>	Non-Probability Sample

**Study Population**

People diagnosed with Spinal Muscular Atrophy types I, II, or III before the age of 17.

**Criteria**

## Inclusion Criteria

- Clinical diagnosis of Spinal Muscular Atrophy
- Genetic diagnosis of SMN gene deletion
- Parents or if applicable subjects must give informed consent
- must be capable of complying with the study procedures
- Female subjects of child-bearing potential must agree to undergo pregnancy test prior to radiological studies
- Diagnosis of SMA before age 19 years

## Exclusion Criteria:

- Unstable medical condition precluding participation
- Significant respiratory compromise that would interfere with safe travel to site of evaluation. (The clinical site PI decides when air travel is not recommended and when the patient's location is not within a reasonably safe driving distance (upper limit 150-250 miles))

**Further study details as provided by Darryl C. De Vivo, Columbia University:****Primary Outcome Measures:**

- Hammersmith Functional Motor Scale Expanded (HFMS) [ Time Frame: Up to 36 months ]  
For SMAII/III patients over 2 years of age, we will additionally administer the Hammersmith SMA functional motor scale (H-SMA-FMS), a disease-specific instrument.
- Gross Motor Function Scale (GMFM) [ Time Frame: Up to 36 months ]  
The GMFM contains 88 items in 5 dimensions: (A) lying and rolling, (B) sitting, (C) crawling, (D) standing, and (E) walking.

Biospecimen Retention: Samples With DNA blood and skin tissue

Enrollment:	120
Study Start Date:	May 2005
Estimated Study Completion Date:	December 2022