

Study

Prospective Phase I/II **S**tudy to Evaluate Effects **o**f Sodium **P**henylbutyrate in Pre-symptomatic Infants with **S**pinal **M**uscular **A**trophy (**STOP SMA**)

Purpose

The purpose of this study is to evaluate early treatment intervention in moderating SMA symptoms in presymptomatic infants.

Condition	Intervention	Phase
Spinal Muscular Atrophy	Drug: sodium phenylbutyrate	I/II

Study Type: Interventional

Study Design: Treatment, Non-Randomized, Open Label

Official Title: Prospective Phase I/II **S**tudy to Evaluate Effects **o**f Sodium **P**henylbutyrate in in Pre-symptomatic Infants with **S**pinal **M**uscular **A**trophy (STOP SMA)

Primary Outcomes: The study will assess the safety, tolerability and potential efficacy of sodium phenylbutyrate (NaPB) in presymptomatic infants genetically confirmed to have SMA. It will also determine selected pharmacokinetic parameters.

Secondary Outcomes: The study will determine potential benefit of NaPB on lean body mass; overall motor function; potential cellular response to NaPB; and drug compliance.

Expected Total Enrollment: 12

Study start: June 2007

Spinal muscular atrophy (SMA) is a genetic disorder that results in severe muscle weakness. It is one of the most common conditions causing muscle weakness in children. Patients with SMA most often develop weakness as babies or young children. Most people with SMA gradually lose muscle strength and abilities over time. Babies with the worst form of SMA, SMA type I, sometimes lose abilities and strength quickly over a few weeks or months. Patients with milder forms of SMA, SMA types II and III, often have more slowly progressive weakness over years.

Sodium phenylbutyrate (NaPB) is a medicine that has been used for many years to treat patients with urea cycle disorders. Recent research suggests that NaPB may be able to prolong survival in animal models of motor-neuron disease. In addition, pilot data in human infants have suggested a possible benefit of early administration of NaPB. Since significant motor-neuron loss occurs in the first few weeks to months of life in the most severely affected infants, the earlier that NaPB treatment can be started, the greater the potential benefit in delaying onset and lessening severity of SMA symptoms.

In this single-center trial, we will evaluate the effects of NaPB on presymptomatic SMA type I (cohort 1) and presymptomatic SMA type II (cohort 2) infants. A variety of outcome measures will be performed at each study visit to follow the course of the disease. Total duration of the study for type I infants will be 18 months, for type II infants, 24 months.

Eligibility

Ages Eligible for Study:

- Cohort 1, 0-3 months
- Cohort 2, 0-6 months

Inclusion Criteria:

- Laboratory documentation of homozygous absence of SMN1 exon 7
- Confirmation of no more than 3 *SMN2* copies for cohort 1; no more than 4 copies for cohort 2
- Family history of affected sibling with SMA type I for cohort 1 and SMA type II for cohort 2
- Age \leq 3 months, cohort 1; Age \leq 6 months, cohort 2
- Written informed consent of parents/guardian
- Laboratory results demonstrating normal values for age.

Exclusion Criteria:

- Evidence of hepatic insufficiency, renal insufficiency, edema with sodium retention, known seizure disorder, urea cycle disorder, cardiac arrhythmia, congenital heart defect, hypertension, significant central nervous system (CNS) impairment, or neurodegenerative or neuromuscular disease other than SMA.
- History of allergy/sensitivity to sodium phenylbutyrate (NaPB)
- Use of NaPB within 30 days of study entry.
- Serious illness requiring hospitalization \leq 14 days prior to study entry
- Use of medications intended for the treatment of SMA including riluzole, valproic acid, hydroxyurea, oral use of albuterol, NaPB, butyrate derivatives, creatine, growth hormone, anabolic steroids, probenecid, oral or parenteral use of corticosteroids at entry, or agents anticipated to increase or decrease muscle strength or agents with presumed histone deacetylase (HDAC) inhibition within 30 days prior to study entry
- Unwillingness to travel for study assessments.

Location and Contact Information

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