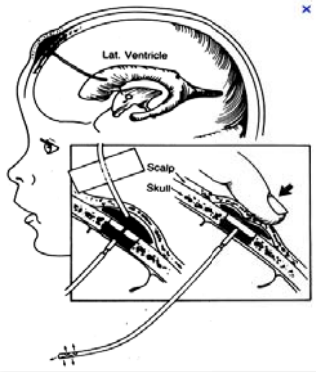
We are pleased to inform the NPC community of an upcoming clinical trial at the NIH. This trial, which will study the safety of 2-hydroxypropyl-β-cyclodextrin (HP-β-CD) in Niemann-Pick disease, type C1, is in the process of being reviewed by the FDA. We are hopeful that we will be able to start enrolling patients in January 2013.

The purpose of this study is to test the safety of a drug called 2-hydroxypropyl-β-cyclodextrin (HP-β-CD) when it is given directly into the fluid that surrounds the brain (cerebrospinal fluid, or CSF). We will also collect useful information to select a dose of HP-β-CD with the greatest potential to improve a set of laboratory tests ("biomarkers") related to cholesterol storage and neuronal damage.

This clinical trial is an open label study for 9 patients total. That means that every patient will get HP-β-CD according to the study schedule. Our current plan is to give HP-β-CD once per month through an Ommaya reservoir. The first visit to the NIH will last about 2 weeks, then patients will have to come to the NIH for about 4-5 days each month to get the study drug and for tests after they get the drug. Patients will not have to take any study medications between visits while they are at home. The duration of this study will depend greatly on the results that we obtain. However, we would predict that the study could last at least 1 year.

An Ommaya reservoir is a plastic, dome–shaped device, with a thin tube attached to the bottom of the reservoir that passes through the brain to the inside part of the brain called the ventricles. Ommaya reservoirs are used to deliver medications into the fluid that is inside and surrounding the brain. A small butterfly (blood-drawing) needle is used to access the reservoir and is removed when access to the reservoir is not needed. Ommaya reservoirs are not experimental.




In addition to safety, a goal of this study is to evaluate different doses of HP-β-CD. For this purpose each patient will be put into a "cohort." A cohort is a group of patients that will be treated the same during the study. For this study subjects will be in groups of three. Different cohorts will be started at different doses of HP-β-CD.

The first group will start at the lowest dose. After everyone in the cohort has safely received at least 2 doses of HP-β-CD, we will determine, based on biomarkers, whether the dose for everyone in that group will be maintained or increased. You may not choose which dose level of HP-β-CD you or your child receives.

Participants will be screened with a physical exam and medical history. They will provide blood and urine samples to obtain baseline information and confirm eligibility for inclusion into the protocol. Patients will also have tests of hearing, speech, swallowing, language and movement.

**Who is eligible to participate?**

To participate in this study, specific "inclusion" and "exclusion" must be met. Some of these details may still change during the FDA review. We will try to establish eligibility for this trial prior to having you make the trip to the NIH. However, laboratory tests or information may become available during the initial evaluation that would not allow us to continue.

To be eligible for this study, patients:

- Must be between 7 years and 25 years of age
- Have a documented diagnosis of NPC1 either by fibroblast testing or NPC1 mutation testing
- Have at least one neurological symptom of NPC1

- Must be healthy enough to travel to the NIH, to have surgery to place the Ommaya reservoir and to be able to comply with the requirements of the protocol
- May be on Miglustat, but may not start miglustat or change the dose of miglustat during the trial
- May **not** be taking more than one medication to control seizures
- Must be willing to stop all non-prescription supplements, except an age-appropriate multivitamin
- May **not** take anticoagulants or have a history/presence of a bleeding disorder
- May **not** have active lung disease, oxygen requirement or clinically significant history of decreased blood oxygen saturation, respiratory therapy, or requiring active suction.

**What are the risks of this study?**
The use of HP-β-CD in NPC1 is experimental, and the purpose of this protocol is to determine the safety of intraventricular HP-β-CD. While available information suggests that this can be done safely and we have tried to make this protocol as safe as possible, we simply do not know if significant problems will or will not occur.

Animals receiving high doses of HP-β-CD by injection under the skin or by injection into the spinal fluid have developed irreversible deafness with single doses. This is a concern in this study. We have some information suggesting that the hearing issue is not as severe at lower doses in the cat. We will be monitoring hearing closely in this trial.

While 9 patients is not a large number, our goal is to get useful data from a few patients quickly so we can move on to a second trial, which will be multi-center and will include more participants. We are also looking into expanding the next trial to international sites to make participation more feasible for families from outside of the US.

We are optimistic about this trial and we are eager to get started once the FDA review is complete. The encouragement and support we have received from the NPC community has been essential in getting this trial started. We will need your continued support to work toward our goal of establishing a safe and effective therapy accessible to all individuals with NPC1.

Please email nichdnpc1@mail.nih.gov if you would like more information about the study or if you are interested in participating.