Plain Language Summary

Trial of N-acetyl-L-leucine in Niemann-Pick disease type C

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Plain Language Summary: Results of randomized, double blind, placebo-controlled, cross-over trial of N-acetyl-L-leucine in NPC

What was this study about? This study investigated a medicine called N-acetyl-L-leucine (NALL) for people with Niemann-Pick Disease Type C (NPC). NPC is a rare, serious genetic disease that causes fats to build up in cells, leading to problems, especially in the brain. Patients with NPC often experience issues with balance, coordination, and other neurological symptoms. The main goal of this study was to see if NALL was safe and if it could improve these neurological symptoms.

Who participated in the study? The study included 60 patients with genetically confirmed NPC, ranging in age from 5 to 67 years. These patients had mild to severe neurological symptoms, as measured by a specific scale.

What was tested? The researchers tested N-acetyl-L-leucine (NALL). This medicine is thought to help cells by improving how they produce energy and by correcting problems with lysosomes (the cell's recycling centers). This could potentially help protect and restore nerve cell function, which might improve neurological symptoms in NPC.

How was the study done? This was a "double-blind, placebo-controlled, crossover" study. This means:

- **Randomized:** Patients were randomly assigned to start with either NALL or a placebo.
- **Double-blind:** Neither the patients nor their doctors knew if they were getting the actual medicine (NALL) or a placebo (a dummy pill with no medicine).
- **Placebo-controlled:** One group received NALL, and the other received the placebo for 12 weeks.
- **Crossover:** After the first 12 weeks, patients switched treatments. Those who started with NALL received the placebo, and those who started with the placebo received NALL for another 12 weeks. This allowed each patient to act as their own comparison, strengthening the results. Patients took their assigned medicine orally two to three times a day. Doses were adjusted for younger, lighter patients, while older patients received 4 grams per day.

What were the main findings? The study found that:

- **Improved Neurological Status:** NALL significantly improved neurological status, as measured by the Scale for the Assessment and Rating of Ataxia (SARA). Patients' SARA scores improved by an average of 1.97 points after 12 weeks on NALL, compared to a smaller improvement of 0.60 points after 12 weeks on placebo. A lower SARA score indicates better neurological status.
- **Symptom Worsening After Stopping NALL:** When patients switched from NALL to placebo, their neurological symptoms tended to worsen, suggesting that NALL was actively helping to manage symptoms.
- **Supportive Secondary Findings:** Other measures of improvement, such as overall clinical impression and functional abilities, generally supported the main finding, though these were not statistically adjusted for multiple comparisons.
- **Safety:** NALL was generally safe and well-tolerated. The number of side effects was similar between NALL and placebo, and no serious side effects were considered related to the treatment. There was a small increase the in the number of respiratory tract infections in the group of patients receiving NALL.

What do these findings mean? The results of this study suggest that N-acetyl-L-leucine (NALL) can significantly improve neurological symptoms in patients with Niemann-Pick disease type C over a 12-week period. The crossover design provides strong evidence for NALL's symptomatic effect.