



# Plain Language Summary

## Efficacy and safety of N-acetyl-L-leucine in Niemann-Pick disease type C

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**Plain Language Summary:** Results of an open-label study on the efficacy and safety of N-acetyl-L-leucine in NPC

Niemann-Pick disease type C (NPC) is a rare and serious genetic condition that mainly affects children, but can also appear in teens and adults. It's a progressive disease, meaning it gets worse over time, and it causes a wide range of problems, especially with the brain and nervous system. These can include issues with movement, balance, speech, and thinking, which significantly impact a person's daily life.

### About the Study:

- **What they wanted to find out:** This study aimed to see how safe and effective a new medication called N-acetyl-L-leucine (NALL) was in improving symptoms, daily functioning, and quality of life for children (age 6 and older) and adults with NPC.
- **Who participated:** 33 patients with a confirmed diagnosis of NPC, ranging in age from 7 to 64 years old. Most of these patients were already taking another medication for NPC called miglustat.
- **How it was done:** This was an "open-label, rater-blinded" study. "Open-label" means everyone knew they were getting the active drug. "Rater-blinded" means the people judging the results didn't know which part of the study the patient was in (before, during, or after treatment).
  - The study had three periods: a baseline period (before treatment), a 6-week treatment period where patients took NALL by mouth every day, and a 6-week "washout" period where they stopped taking the drug.
  - To measure changes, doctors recorded videos of patients performing specific tasks, like walking an 8-meter distance or using a 9-hole peg test (a test of fine motor skills). These videos were then randomly paired and reviewed by neurologists who didn't know the order of the videos. They used a special 7-point scale to rate how much the patient's condition had changed (improved or worsened).
- **What they measured:** The main goal was to see changes using the video-based rating scale. They also used other scales to assess balance and coordination (ataxia), overall disability, and quality of life, and monitored for any side effects.

### What the Study Found:

- **Improvements in Symptoms:**
  - NALL significantly improved symptoms, daily functioning, and quality of life during the 6-week treatment period. This was seen in the video-based ratings and other neurological scales.
  - The improvements were consistent across different patient groups (various ages, genders, and disease severities), suggesting NALL could help a wide range of NPC patients.
  - Importantly, when patients stopped taking NALL during the 6-week "washout" period, the improvements they had gained were lost, and their symptoms worsened again. This showed that the positive effects were directly due to the medication.
  - The study also noted that NALL's benefits were seen even in patients already taking Miglustat, suggesting it could offer additional help.

- **Safety:**
  - NALL was found to be safe and well-tolerated.
  - Only a few side effects were reported and these were mild, temporary, and manageable.
  - No serious side effects related to the treatment occurred, and no patients had to stop the study because of side effects.

#### **What This Means:**

This study provides strong evidence that NALL can significantly and meaningfully improve neurological symptoms, functioning, and quality of life in both children and adults with NPC. The fact that improvements were lost during the washout period showed that NALL has a positive effect on symptoms while it's being taken. The drug also has a favorable safety profile, meaning it's generally safe to use.

While this study was not placebo-controlled (which can sometimes make it harder to be sure about a drug's effects), the researchers used careful methods, like blinded video reviews and comparing each patient to themselves before and after treatment, to demonstrate the results were reliable. NALL showed great promise as a way to help manage the challenging symptoms and improve the daily lives of patients.