IB1001-301: Effects of N-Acetyl-L-Leucine on Niemann-Pick disease type C (NPC): A Phase III, randomized, placebo-controlled, double-blind, crossover study

IntraBio is conducting a pivotal Phase III, randomized, double-blind, placebo-controlled trial with N-acetyl-L-leucine (IB1001) for patients aged 4 years and older with Niemann-Pick disease type C (NPC).

This placebo-controlled trial is being conducted principally at the request of the US Food and Drug Administration, who confirmed that placebo-data was required for approval.

Study Drug

N-acetyl-L-leucine (IB1001) is a modified amino acid that is orally administered (sachet).

IntraBio has a comprehensive body of evidence demonstrating IB1001's symptomatic and long-term neuroprotective, disease-modifying effects for NPC:

- Pre-clinical studies [Kaya et al. 2021; te Vrutche et al. 2019]
- Observational clinical studies [Bremova et al. 2015; Cortina-Borja et al. 2018; Kaya et al. 2021]
- IB1001-201 multinational, open-label, rater-blinded Phase II clinical trial [Bremova et al. 2021]. *Summary*: IB1001 met its primary and key secondary endpoints, demonstrating a statistically significant and clinical meaningfully improvement in pediatric and adult patients with NPC. Treatment was well-tolerated, with no serious adverse reactions.

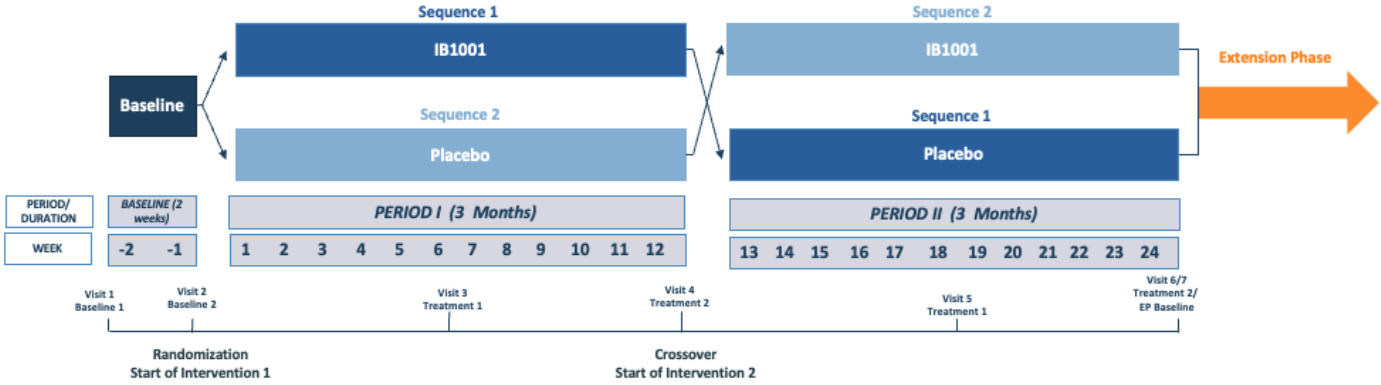
Eligibility Criteria

Patients aged 4 years + may be eligible for recruitment at sites in Australia, Europe, and the United States. Patients are required to have neurological symptoms and cannot be using any other investigational agent (including investigational drugs in expanded access programs). Patients are permitted to use a stable dose of Miglustat (Zavesca®). The full study procedures and eligibility criteria are posted on ClinicalTrials.Gov (NCT05163288).

IB1001-301 Study Design

IB1001-301 is a multinational, randomized, placebo-controlled, double-blinded, crossover Phase III study.

Patients will be assessed at 6 study visits during three study periods: a baseline period (approximately 14 days), the first intervention period ("Period I"; approximately 84 days), and the second intervention period ("Period II"; approximately 84 days). Patients will be assessed twice during each intervention period (Figure 1)



Prohibited Medications: Patients using Tanganil® (or other forms of N-acetyl-leucine not provided in IB1001-301) will be required to stop taking the medicine ("washout") for 6-weeks prior to screening (Visit 1) and must remain off Tanganil® throughout the duration of the trial.

Randomization: At **Visit 2** (Baseline 2), patients will be randomly assigned (1:1) to two randomization sequences:

- **Sequence 1**: Starting **Visit 2** (Baseline 2), patients will receive IB1001 during Period I (for approximately 84 days). At the end of Period I (Visit 4), the patient will "crossover" and immediately crossover receive placebo during Period II (for approximately 84 days).
- **Sequence 2**: Starting **Visit 2** (Baseline 2), patients will receive placebo during Period I ((for approximately 84 days). At the end of Period I (Visit 4), patients will "crossover" and immediately receive IB1001 during Period II (for approximately 84 days).

Treatment: During the trial, every patient will receive approximately 12-weeks of treatment with IB1001, and 12-weeks of placebo. Patients, their family, and the study team will not know when they are on treatment with IB1001 or placebo.

Study Assessments: Standard functional assessments (e.g., SARA, SCAFI, NPC-CSS, mDRS), will be performed, as well as quality of life questionnaires (EQ-5D, CGI). The SARA is the primary endpoint. There are no invasive procedures (i.e., lumbar punctures). Blood and urine samples will be collected, and physical examinations and 12-lead ECGs will be performed.

Extension Phase

Patients who complete the study (Visit 6) can (if their Principal Investigator determines it is in their best interest) participate in an open-label extension phase, where patients will receive treatment with IB1001 for a minimum of 1-year.

Additional Information

Trial sites are currently planned in Australia, the Czech Republic, Germany, the Netherlands, Slovakia, Switzerland, the United Kingdom, and the United States.

IntraBio will cover travel expenses (e.g. transport, hotel, food, COVID-19 tests) for the patient + 1 family member/caregiver to attend each study visit.