Plain Language Summary

Efficacy and safety of efavirenz in adult patients diagnosed with NPC that had cognitive impairment

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Plain Language Summary: Results of a clinical trial on the efficacy and safety of efavirenz in adult patients diagnosed with NPC that had cognitive impairment.

What was this study about? This study investigated a medicine called efavirenz as a potential treatment for Niemann-Pick disease type C (NPC). NPC is a rare, genetic, and progressive brain disorder where cholesterol and other fats build up abnormally inside cells, particularly in the brain. This leads to severe neurological problems like issues with movement, speech, and thinking (dementia). This study aimed to see if efavirenz, which is known to affect how the brain handles cholesterol, could be a safe and effective way to slow down the disease's progression.

Who participated in the study? The study enrolled 16 patients with genetically confirmed NPC, ranging in age from 15 to 60 years. These patients had adult or late juvenile-onset NPC and were already receiving standard care, including miglustat.

What was tested? The researchers tested efavirenz. This medicine is typically used to treat HIV, but at much lower doses, it's thought to activate an enzyme in the brain called CYP46A1. This enzyme helps the brain process and remove cholesterol. The hypothesis was that by improving cholesterol handling, efavirenz could help correct problems with brain cell connections (synapses) and improve cognitive and psychiatric symptoms in NPC.

How was the study done? This was a "single-center, phase II, single-arm clinical trial." This means:

- **Single-center:** The study was conducted at one hospital.
- **Phase II:** This is an early-stage study to further evaluate the safety and initial effectiveness of the medicine.
- **Single-arm:** All enrolled patients received efavirenz in addition to their standard care. There was no separate control group receiving a placebo. Patients received efavirenz orally for 52 weeks (1 year). The dose started at 25 mg per day for the first 26 weeks and then increased to 100 mg per day for the remaining 26 weeks. Researchers regularly assessed cognitive performance, neurological signs, and biological markers using various tests and imaging.

What were the main findings? The study found that:

- **Cognitive Response:** All 16 patients (100%) met the primary goal of the study, meaning they showed no deterioration in a combined measure of cognitive performance after 52 weeks of treatment.
- **Neuropsychological Outcomes:** While the overall cognitive decline was halted, more detailed tests showed varied results. Learning, memory, and executive control were relatively preserved, but some subtle impairments in verbal fluency, attention, and cognitive inhibition were still observed.

- **Earlier Treatment Benefits:** The study identified two subgroups of patients based on their response. Patients who started treatment earlier in their disease course (shorter time since symptom onset) tended to show more favorable responses.
- **Neurological Outcomes:** Some neurological symptoms like dysphagia (swallowing difficulties) improved, particularly in patients with longer disease durations. Ataxia (coordination problems) and overall disability remained relatively stable but were generally better in those who started treatment earlier.
- **Safety:** No efavirenz-related or serious side effects were reported, indicating that the medicine was safe and well-tolerated at the doses used, even when combined with miglustat.

What do these findings mean? This study suggests that efavirenz appears to be a safe and promising new treatment option for Niemann-Pick disease type C, particularly for slowing the rate of cognitive decline. The findings highlight that starting treatment earlier in the disease course may lead to greater benefits. While this was a small, uncontrolled study, the positive results warrant further investigation in larger, longer-term clinical trials (Phase III) to confirm these findings and fully understand efavirenz's long-term impact on NPC progression.