

Evaluation of Intravenous VAL-1221 Treatment for Lafora Disease

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RESEARCH SIMPLIFIED

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AIMS AND METHODS

Lafora disease (LD) is a fatal genetic disorder that causes severe seizures, loss of movement, cognitive decline, and death in young adulthood. It is caused by mutations in either the EPM2A or NHLRC1 gene, which leads to the harmful accumulation of sugars, called Lafora bodies, in the brain. There are currently no treatments that can stop or slow the disease.

VAL-1221 is an experimental drug designed to break down and clear these harmful accumulations from the brain. It had previously been tested in patients with a related condition, Pompe Disease, where it was shown to be safe. In animal studies, VAL-1221 was able to clear the sugar aggregations, also known as Lafora bodies, from the brain when injected directly into the brain. Researchers wanted to find out whether delivering the drug through a regular IV, which is directly into the bloodstream, could also allow it to reach the brain and help patients. Five LD patients between the ages of 17 and 24 received IV infusions of VAL-1221 every other week for 12 months. This was the first time any potentially disease-modifying drug had ever been given to LD patients.

RESULTS

VAL-1221 was safe and well-tolerated. A small number of patients experienced minor side effects during their infusions, such as a temporary drop in blood pressure or a mild skin rash, all of which resolved on their own or with minor treatment. None of the serious events that occurred during the study were considered related to the drug. One patient stopped treatment after eight months following a severe seizure episode. The remaining four patients completed the full 12 months.

Unfortunately, VAL-1221 did not slow the progression of the disease. Seizures, movement, cognition, and daily functioning either got worse or stayed at severely impaired levels across patients. Most importantly, when researchers tested the fluid surrounding the brain, VAL-1221 was completely undetectable, meaning the drug never actually made it through the brain's protective barrier when administered through the bloodstream. Because the drug does not reach the brain, it can not degrade the Lafora bodies.

CONCLUSION

Even though VAL-1221 did not work as hoped, this study is still an important step forward. It gives researchers critical information about what needs to happen next. The key takeaway is that for a drug like this to work in LD, **it needs to be delivered directly to the brain rather than through the bloodstream.** It also showed that a specific type of brain scan called an FDG-PET is one of the best tools available for tracking how the disease progresses, which will help design better trials in the future.