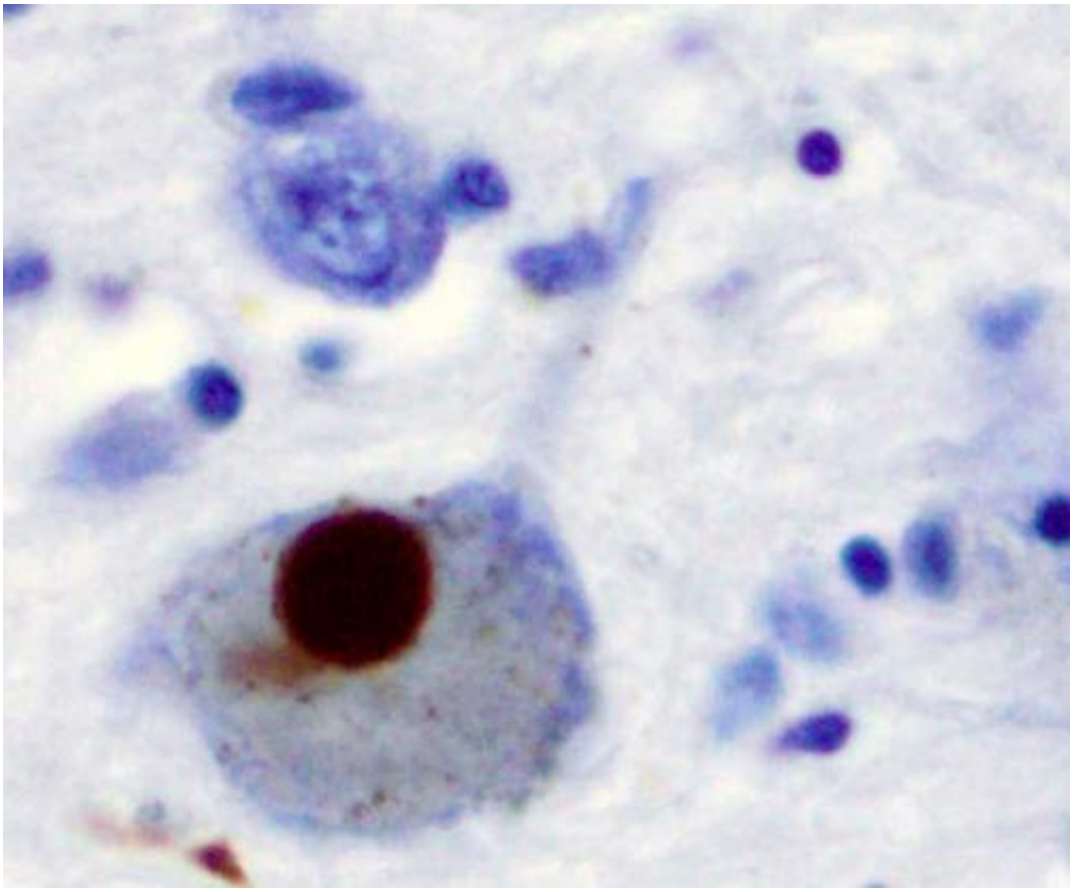
MedicalXpress

Though safe, nilotinib does not show promise for benefit for Parkinson's disease

December 5 2019



Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

Northwestern University and the Parkinson Study Group announced that

the Nilotinib in Parkinson's Disease (NILO-PD) study showed that nilotinib, an FDA-approved treatment for chronic myelogenous leukemia being tested for potential repurposing as a Parkinson's drug, was safe and tolerable in its trial population of 76 participants with moderate to advanced Parkinson's but does not exert a clinically meaningful benefit or biological effect to benefit those with Parkinson's disease.

The NILO-PD Steering Committee unanimously agreed to accelerate the announcement of these results, originally planned for 2020, in line with members' commitment to keep the Parkinson's community informed of new scientific findings as quickly as possible.

Gary Rafaloff of Marlboro, New Jersey, diagnosed with Parkinson's in 2012, served as a member of the NILO-PD steering committee. "No one wanted this trial to succeed more than I did," Rafaloff said. "If I had qualified, I would have participated as a volunteer. Instead I spent over two years working with the other committee members to ensure that the trial was designed and administered with the utmost rigor. Nevertheless, the results are what they are. The good news is that there are several other upcoming trials that we can focus on as we look forward to future success."

The randomized, placebo-controlled, double-blind study was led by principal investigator Tanya Simuni, MD, professor of neurology and head of the division of movement disorders at Northwestern University Feinberg School of Medicine. It was carried out at 25 sites through the Parkinson Study Group, the largest not-for-profit scientific network of Parkinson's disease centers in North America.

The trial was coordinated through the Clinical Trial Coordination Center at the University of Rochester, and statistical analysis was led by the University of Iowa. NILO-PD—which tested placebo, 150mg and

300mg doses of nilotinib daily over six months—was supported by an international consortium of research and patient advocacy groups: The Michael J. Fox Foundation for Parkinson's Research, The Cure Parkinson's Trust (London, United Kingdom), Van Andel Institute, The Parkinson Alliance and the Demoucelle Parkinson Charity (Brussels, Belgium). Novartis Pharmaceuticals Corporation provided the study drug and placebo for use in the trial.

"Science is a high-risk endeavor and too often strategies, even promising ones, do not prove replicable or scalable. Unfortunately, the results we observed—as measured by change in clinical symptoms and influence on biological measures—did not support testing nilotinib in a larger study," Simuni said. "This is not the outcome we hoped for, but we remain dedicated to pursuing better treatments by advancing other potential therapies in today's robust Parkinson's pipeline."

Simuni noted that it is critical that anyone considering adding nilotinib to their Parkinson's treatment regimen work closely with their health care provider before doing so. While nilotinib was seen to be safe and tolerable in the study population, the study was strict with health history, excluding those who may have heart issues or other health challenges. Therefore, its safety in a broader Parkinson's population remains unproven.

Nilotinib (marketed as Tasigna) inhibits the activity of c-Abl, a protein that has been linked to cellular pathways associated with Parkinson's disease including aggregation of alpha-synuclein protein and deactivation of parkin protein. In 2016, preliminary data from a small open-label Phase I clinical trial evaluating the safety and tolerability of nilotinib in people with advanced Parkinson's showed potential benefit in PD. The c-Abl pathway remains an important target of interest to Parkinson's researchers, with trials of other drugs in this class ongoing.

Study results were unblinded at a steering committee meeting on November 15. Study leadership and funding partners committed to broadly sharing top-line findings on an accelerated timeline—after reporting high-level results back to study participants and site investigators—in service to the Parkinson's community awaiting news from this trial and the donors who made the study possible.

NILO-PD leaders will share more detailed data with study volunteers on a call on December 12 and with the scientific community in February at the 3rd Pan American Parkinson's Disease and Movement Disorders Congress in Miami, Florida. The partners also plan to make data and biosamples available for further analysis to the wider Parkinson's research community.

"When the science doesn't pan out, it's easy to feel deflated. As a patient, I get it," said Michael J. Fox. "But even a study that doesn't show the results we hoped for ultimately gets us closer to the one that will."

Provided by Northwestern University

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