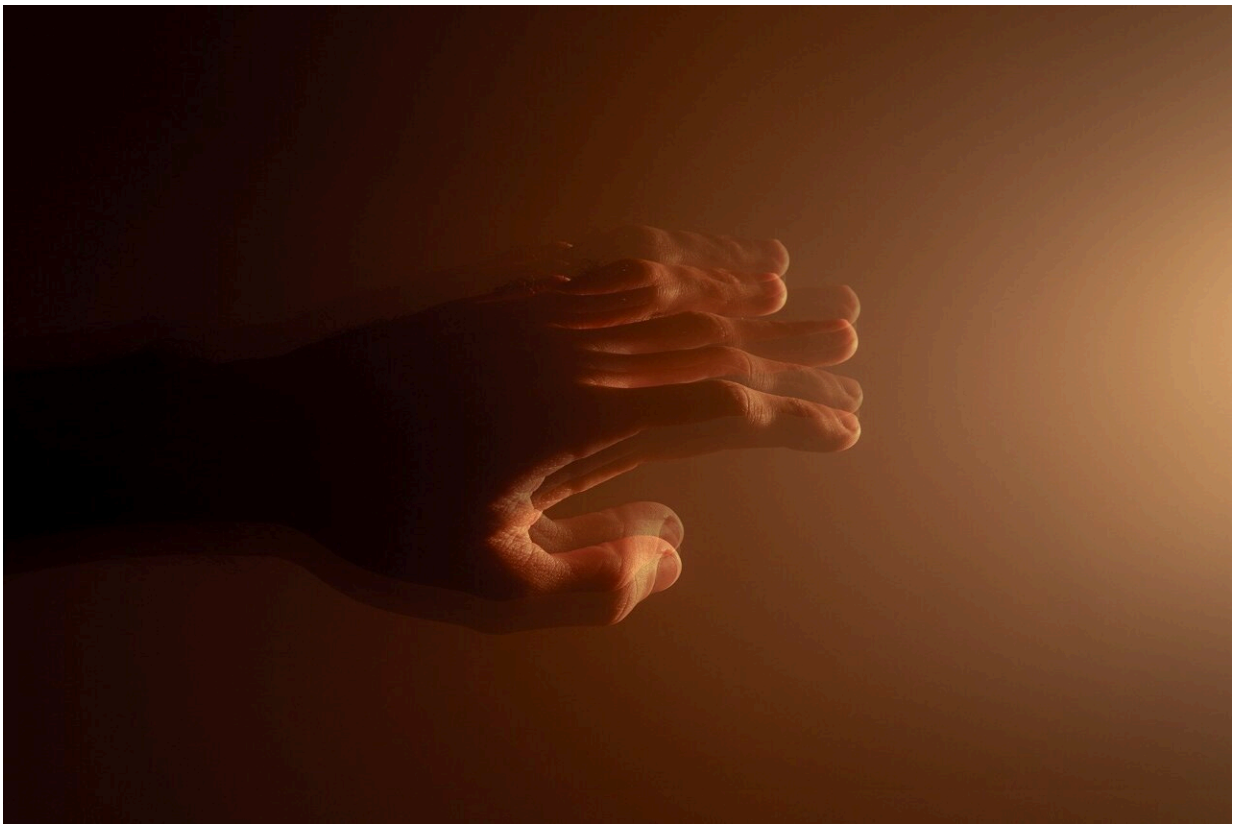
New drug may slow rapid progression of Parkinson's disease

April 16 2024



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Prasinezumab, a monoclonal antibody, is shown to reduce signs of motor deterioration in individuals with Parkinson's disease (PD) who have rapidly progressing disease, as reported in an exploratory analysis of data from a large phase 2 clinical trial published in *Nature Medicine*.

There are currently no disease-modifying treatments for PD, a neurodegenerative disorder characterized by worsening of both motor and non-motor symptoms over time. Aggregation of alpha-synuclein in the brain is a hallmark of PD, and several preclinical studies have suggested that this pathology is a key driver of disease progression.

Prasinezumab is the first experimental therapeutic monoclonal antibody designed to bind aggregated alpha-synuclein, allowing it to be degraded. The antibody was recently investigated in 316 patients with early-stage PD in the phase 2 PASADENA clinical trial, but was found to have no meaningful effect on disease progression in this cohort. However, participants in the trial had highly variable disease progression.

Gennaro Pagano and colleagues analyzed the potential effects of prasinezumab on motor progression in four pre-specified subpopulations who had rapidly progressing motor symptoms in the phase 2 PASADENA trial. These rapidly progressing subgroups were defined by the use of monoamine oxidase B (MAO-B) inhibitors at baseline, the staging of their disease on the Hoehn and Yahr scale, the presence of rapid eye movement sleep behavior disorder, or the presence of diffuse malignant phenotypes.

Researchers found that prasinezumab treatment reduced motor symptom worsening in all rapidly progressing subpopulations after 52 weeks, compared with the motor symptoms of those treated with a placebo. This effect was not seen in treated subpopulations characterized as slow

progressors. Assessment of motor symptoms was done using part III of the Movement Disorder Society Unified PD rating scale (MDS-UPDRS), which is the standard clinical assessment tool for quantifying motor symptoms in PD.

These findings suggest that the clinical efficacy of prasinezumab is seen only at one year in treated patients with rapidly progressing PD. Further research is needed to determine if prasinezumab may be effective in patients with slower progression of disease after longer treatment duration periods; this is being explored in an extended open-label phase of the PASEDENA trial. Further trials are also needed to confirm these effects in patients with rapidly progressing PD, and this is currently being investigated in a large phase 2 trial (the PADOVA study).

More information: Gennaro Pagano et al, Prasinezumab slows motor progression in rapidly progressing early-stage Parkinson's disease, *Nature Medicine* (2024). DOI: 10.1038/s41591-024-02886-y

Provided by Nature Publishing Group