High-dose Ambroxol for Disease Modification and Prevention of Gba1-Related Parkinson Disease: From the Wrong Mouse to the Right *Drosophila*

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Abstract

After early skepticism, the association between Gaucher Disease (GD), a rare genetic disease and Parkinson's Disease (PD), the second most common neurodegenerative disorders, is well established, but its underlying mechanisms is controversial: loss of function (haploinsufficiency) or gain of function. Both approaches are supported

only that this is not the case, in fact, carriers of the non-N370S variant have a higher risk to develop PD than patients with GD who have two mutant alleles and double the amount of the mutant enzyme [4]. Paradoxically, venglustat clinical trial patients with GD and PD were excluded.

Literature Review

A year after our viewpoint, in February 2021, Sanofi halted the venglustat GBA1-PD clinical, citing no beneficial treatment effect compared to placebo [7]. The trial revealed more Adverse Events (AEs) in the venglustat group relative to the placebo cohort.

GBA1-PD is not .two

to halt or, ideally, reverse the prodromal changes in the population at risk, starting with carriers of GBA1 variants, could be a transformative development. It has the potential to revolutionize the management of these devastating disorders, prompting the inclusion of PD prodromal testing in routine assessments for individuals aged 40 and above, similar to current practices for preventing or early detecting various forms of cancer.

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