Abstract Title: #005 - A phase 2, placebo-controlled, randomized, double-blind trial of tozadenant (SYN-115) in patients with Parkinson’s disease with wearing-off fluctuations on levodopa

Press Release Title: New Drugs May Improve Quality of Life for People with Parkinson’s Disease

Objective: To evaluate the safety and efficacy of tozadenant as an adjunct to levodopa in PD patients with wearing-off fluctuations and determine dosages for phase 3 trials.

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Background: Tozadenant is an oral, selective adenosine 2-alpha receptor antagonist.

Design/Methods: This was an international, 12-week, double-blind, phase 2 trial in which patients on stable dosages of levodopa with at least 2.5 hr of OFF time/day were randomized to tozadenant 60, 120, 180 or 240 mg BID, or matching placebo. Primary outcome measure was change from baseline to Week 12 in hr/day spent in the OFF state. A mixed-model repeated-measures ANCOVA was used for analyses with a prespecified hierarchical step-down approach to test multiple dose groups.

Results: Of 420 patients randomized, 337 completed treatment: mean age, 63.3 yr; PD duration, 8.7 yr; baseline OFF time, ~6 hr. Significant reductions in mean placebo-corrected change from baseline in OFF time were observed with tozadenant (mITT population) 120 mg BID (-1.1 hr, p=0.0039) and 180 mg BID (-1.2 hr, p=0.0039). ON time with troublesome dyskinesia was not significantly increased in any tozadenant group. Mean placebo-corrected UPDRS III scores significantly improved with tozadenant 120 mg BID (-2.2, p=0.0325) and 180 mg BID (-2.5, p=0.0325). Mean placebo-corrected UPDRS I-III scores improved significantly in all tozadenant groups (all groups, p≤ 0.03) as did mean placebo-corrected CGI-I and CGI-S scores. PGI-I scores significantly improved in the 120 mg BID group. Most common AEs in the combined tozadenant groups were dyskinesia, nausea, dizziness, constipation, PD worsening, insomnia, and falls.

Conclusions: Tozadenant, at a daily dosage of 120 or 180 mg BID, was generally well tolerated and demonstrated efficacy in reducing OFF time and improving motor signs without significantly increasing troublesome dyskinesia. These two dosages can be considered for future trials.
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