ABSTRACT

Purpose: Assess the effects of the mitochondria-targeted drug elamipretide on leakage-independent vision loss in fellow, non-study eyes with neovascular age-related macular degeneration (NV AMD) in the ReCLAIM Study, an open-label, phase 1 clinical trial to evaluate safety, tolerability, and efficacy of elamipretide in dry AMD.

Methods: Eligible participants had a single designated study eye with dry AMD (either high-risk drusen or noncentral geographic atrophy), the fellow, non-study eye could have any stage of dry or NV AMD disease. All participants received daily subcutaneous elamipretide (40 mg) for 24 weeks, and study assessments were performed for both study eye and fellow, non-study eye of participants every four weeks, with outcomes assessed at week 24. The present analysis includes only fellow, non-study eyes with either quiescent NV AMD (i.e., no fluid, leakage, or hemorrhage and stable maintenance anti-VEGF treatment regimen) or stable inactive NV AMD. Visual function studies included standard luminance best-corrected visual acuity (BCVA) and low luminance visual acuity (LLVA), defined as BCVA through a log2 neutral density filter.

Results: Of 42 participants who received study drug, a total of thirteen had fellow, non-study eyes with either quiescent NV AMD (n = 8) or stable inactive NV AMD (n = 5), with all eyes free from exudation and hemorrhage. The mean change in standard BCVA in fellow eyes with NV AMD was +6.3 ± 5.0 letters (p < 0.001) (baseline mean BCVA: 53.4 ± 21.9 letters, range: 19-66 letters), with 6/8 fellow eyes gain in 54% of fellow eyes and ≥10-letter BCVA gain in 31% of fellow eyes. The mean change in LLVA in fellow eyes with NV AMD was +6.4 ± 4.8 letters (p < 0.001) (baseline mean LLVA: 35.2 ± 22.9 letters, range: 6-74 letters), with 5/8 fellow eyes gain in 54% of fellow eyes and ≥10-letter LLVA gain in 31% of fellow eyes.

Conclusions: Subcutaneous administration of elamipretide, a mitochondria-targeted drug, was associated with improved vision in fellow, non-study eyes with NV AMD in a phase 1 clinical trial of elamipretide for dry AMD. Further study is warranted to understand the biology of retinal mitochondrial dysfunction in NV AMD and to assess the efficacy of elamipretide for treatment of leakage-independent vision loss in NV AMD.

BACKGROUND

MOA: Elamipretide, tetrapeptide drug, targets mitochondria, binding damaged cardiolipin and reversing mitochondrial dysfunction

Mitochondrial Dysfunction in Neovascular AMD?

Retinal mitochondrial dysfunction associated with AMD pathobiology (human histology; mouse models)

Study Objective

Assess effects of systemic elamipretide on fellow, non-study eyes with quiescent NV AMD in ReCLAIM study, Ph. 1 study of elamipretide for dry AMD

CONCLUSIONS

• Subcutaneous elamipretide, mitochondria-targeted drug, was associated with improved vision in fellow, non-study eyes with NV AMD in the Phase 1 ReCLAIM study for dry AMD

• Further study is warranted to assess efficacy of elamipretide as novel therapy for leakage-independent vision loss in NV AMD