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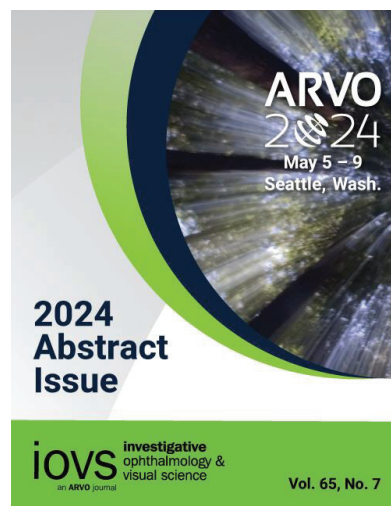
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Abstract

Purpose : We hypothesized that ildeuretinol would arrest the progression of Stargardt disease in presymptomatic individuals. Stargardt disease is the most common inherited juvenile macular dystrophy, leading to blindness. No treatment exists.

Methods : Three patients, aged 13, 17, and 18, each with 2 pathogenic *ABCA4* mutations, exhibiting early signs of maculopathy, but with 20/20 visual acuity and no complaints of visual impairment, and each with a 2-year older symptomatic sibling with Stargardt disease and identical disease-causing *ABCA4* mutations, took ildeuretinol acetate 14 mg capsules, daily for 2 to 4 years. Disease progression was monitored by best-corrected visual acuity (BCVA), fundus autofluorescence (FAF) imaging, photoreceptor density by OCT, and retinal sensitivity by microperimetry, and compared to untreated symptomatic siblings when at the same age.

Results : Ildeuretinol replaced over 80% of plasma retinol within 2 months. With treatment of up to 4 years, average BCVA was maintained at 88 ± 4 ETDRS letters (~20/20). We observed no changes by FAF imaging: no retinal flecks developed and there were no changes in hyper- or hypoautofluorescence (Fig. 1). During the first year of treatment, mean retinal sensitivity declined by an average -3.1 ± 1.5 dB/year, consistent with expected disease progression. After this initial period, there was a trend towards improvement in retinal sensitivity at an average rate of $+0.93 \pm 0.7$ dB/year. During the first 6 months of treatment, 2 patients had a reduction in photoreceptor area, consistent with disease pathophysiology. After this initial period, there was a trend towards increase in photoreceptor density. In the 2nd patient, no loss of photoreceptors was observed. There were no treatment-related adverse events. In contrast, for all 3 siblings at the same age who did not receive

gildeuretinol, visual acuity declined to 66 ± 10 letters ($\sim 20/50$), and there was year-over-year worsening in number of retinal flecks, regions of hyper- or hypo-autofluorescence, and development of retinal atrophy (Fig. 1).

Conclusions : In three individuals with presymptomatic Stargardt disease, gildeuretinol arrested vision loss and the progression of retinal pathology.

This abstract was presented at the 2024 ARVO Annual Meeting, held in Seattle, WA, May 5-9, 2024.

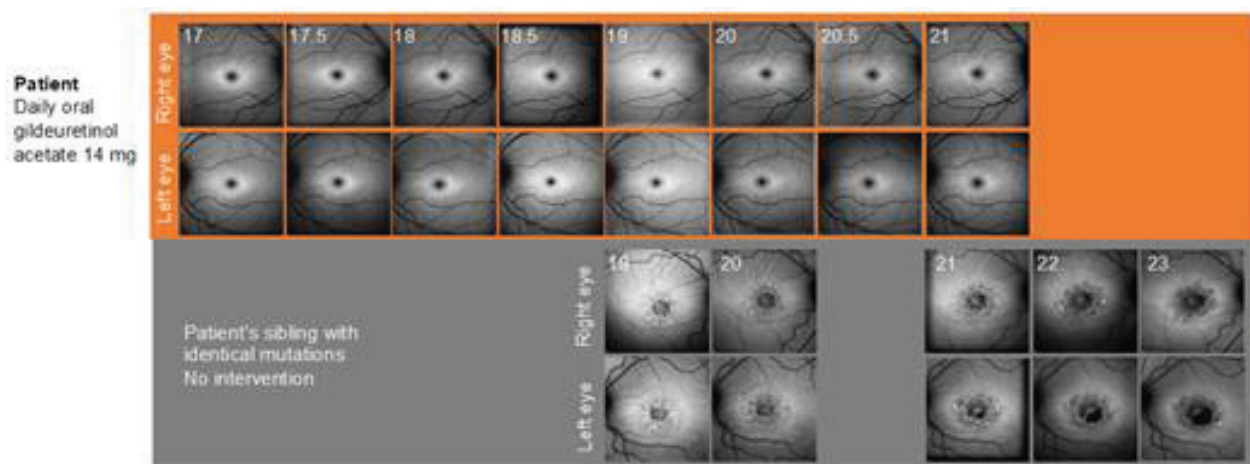


Fig. 1: Four-year progression of one of gildeuretinol-treated pre-symptomatic patients showing absence of progression (top). Untreated sibling FAF images shown (bottom). Age shown in upper left of each image. Similar results in other patient pairs.



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