

Stargardt disease ALK-001 phase 2 clinical trial: 12-month interim data

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Abstract

Purpose : Stargardt disease (STGD1) is the most prevalent inherited macular dystrophy. In the absence of an approved treatment, there is a growing interest and need for well-designed and controlled clinical trials. We present the design, baseline data, and one-year interim safety and pharmacokinetics of the prospective “TEASE” clinical trial.

Methods : TEASE is a two-year Phase 2 double-masked placebo-controlled study enrolling 50 subjects with *ABCA4*-related STGD1 and a well-delineated area of atrophy (Fig 1). The study drug ALK-001, is a selectively deuterated vitamin A used as vitamin A replacement and taken orally once-a-day. Deuterium slows vitamin A dimerization 4-5 fold without inhibiting the visual cycle. Subjects are randomized 2:1 ALK-001:placebo. After one year of treatment, 50% of placebo subjects crossover to ALK-001 in a masked and randomized fashion to compare atrophy progression before and after crossover. The primary endpoint is safety of two dose levels of ALK-001, while efficacy outcomes include atrophy lesion size by fundus autofluorescence (FAF), best-corrected visual acuity (BCVA), reading speed, dark adaptation and retinal sensitivity (microperimetry).

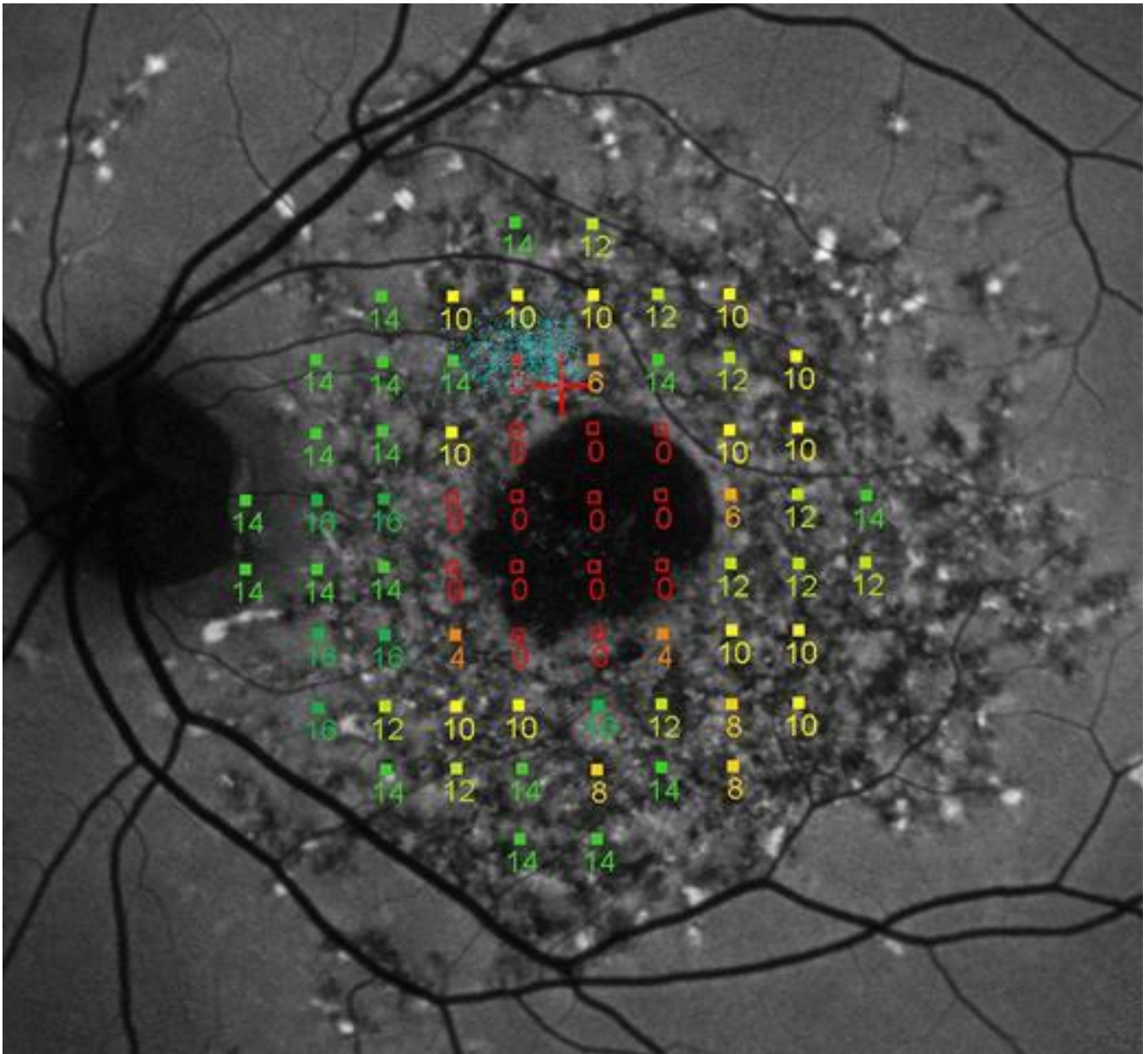
Results : 50 subjects (38 white; 28 female) have been randomized at 7 clinical sites. Median age was 46 years (range, 18-60) and disease duration 9 years (0-36). 48 of 50 subjects have completed the one-year follow-up visit. On average, 90% of vitamin A was replaced with deuterated vitamin A, which was maintained over time. ALK-001 was well-

tolerated with no unexpected adverse reactions, no report of night blindness or impaired dark adaptation, and no clinically-significant increases in liver function tests or in total vitamin A (natural + deuterated). Atrophic lesions at baseline were bilateral in 74% of cases with a 5.1 mm² (0.3-31.6) median area. 46% and 52% of subjects had BCVA better than 20/40 or worse than 20/100, respectively. Mean retinal sensitivity was 8.3 dB (SD: 4.8). Deep scotomatous areas covered approximately 32% of a 20-deg disc centered on the fovea (approx. 8 mm², n=75 eyes).

Conclusions : The TEASE study is currently the largest, fully-enrolled clinical effort to slow or prevent the progression of STGD1. This feasible study design opens the avenue to similar studies. An expanded study, TEASE-2, is currently enrolling new participants (≥ 12 years old) in the USA.

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Fig 1. FAF of a TEASE subject, displaying foveal retinal sensitivity

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