

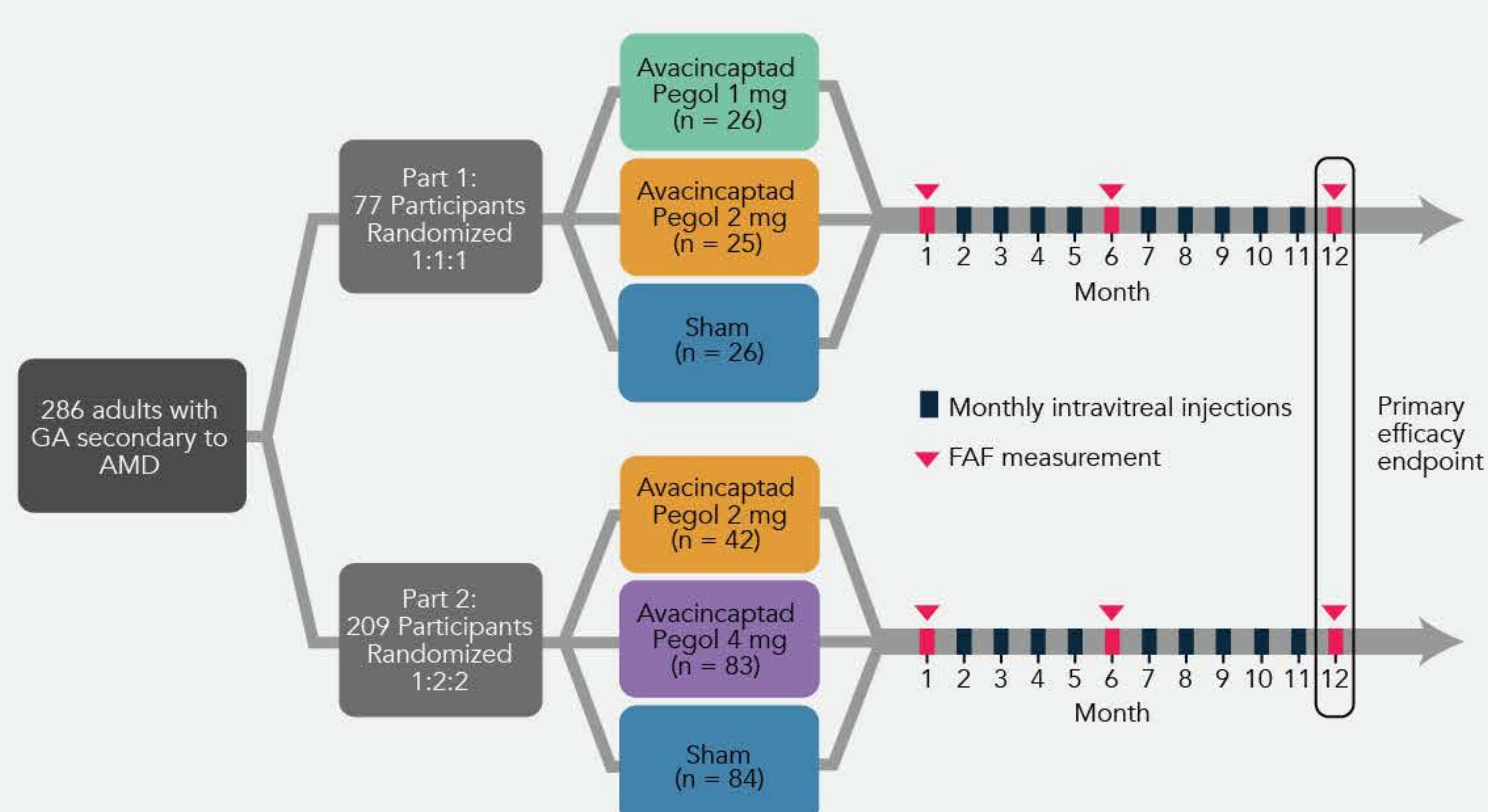
C5 Inhibitor Avacincaptad Pegol for Geographic Atrophy Due to Age-Related Macular Degeneration

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The complement cascade is thought to play a key role in retinal degeneration secondary to age-related macular degeneration (AMD). Studies have shown that complement is deposited in human eyes with AMD, as well as suggest that polymorphisms are present in complement regulatory proteins in ~50% of eyes with non-neovascular, or dry AMD. Polymorphisms in genes coding for complement or complement regulatory proteins are associated with an increased risk for AMD, and greater than 7-times more likely of developing AMD with homozygous alleles. This study investigated avacincaptad pegol, an inhibitor of complement C5, whose terminal fragments C5a and C5b may activate the immune system and lead to cell death. By preventing the formation of terminal fragments of C5, it is thought that the progression of retinal cell degeneration may be slowed.



286 participants enrolled in this international, prospective, randomized, double-masked, sham-controlled phase 2/3 pivotal clinical trial between January 2016 and October 2018.

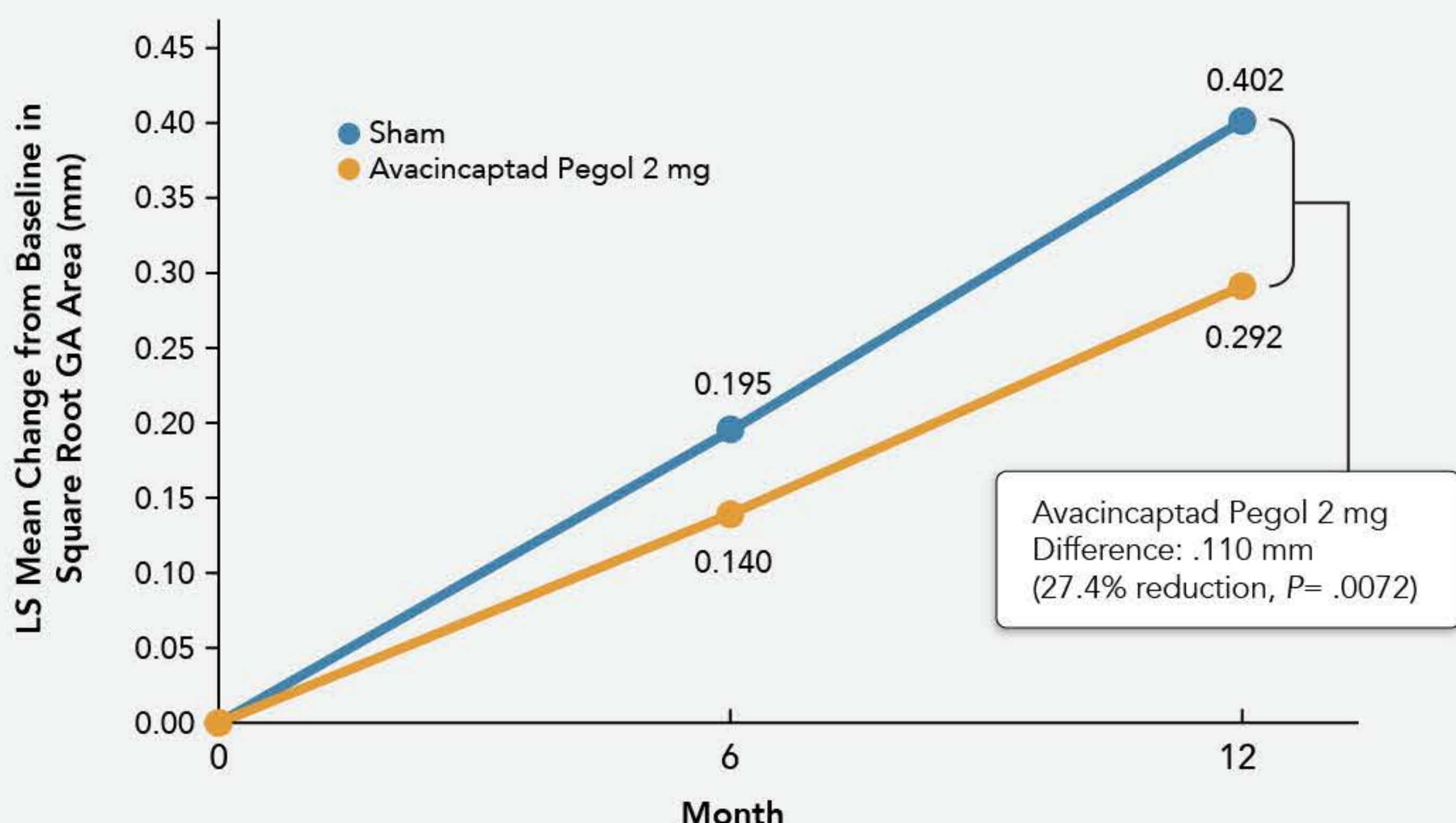


Main Outcome Measures: The primary efficacy endpoint was the mean rate of change in GA area over 12 months measured by fundus autofluorescence (FAF) at three timepoints: baseline, month 6, and month 12



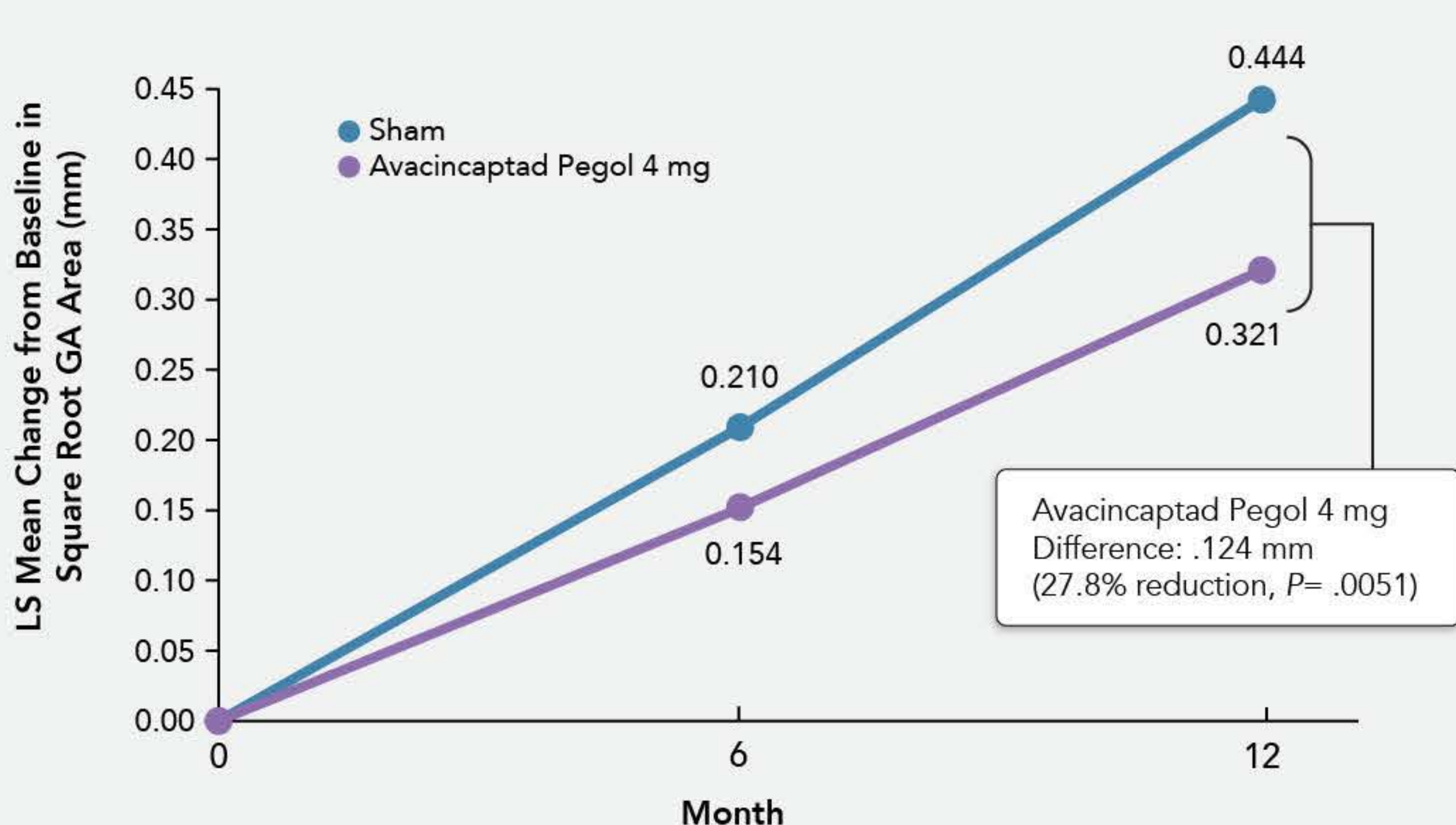
There was a statistically significant reduction in the mean rate of GA growth over 12 month in the avacincaptad pegol cohorts.

Mean Rate of Change in Square Root of GA Area



Based on LS means from MMRM model; ITT Population; Hochberg procedure used for significance texting. The LS means is an estimate of the MMRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data. Sham: Corresponding sham for the 2 mg arm.

Mean Rate of Change in Square Root of GA Area



Based on LS means from MMRM model; ITT Population; Hochberg procedure used for significance texting. Sham: Corresponding sham for the 4 mg arm.

LS = least squares; MMRM = mixed model repeated measures; ITT = intention to treat; GA = geographic atrophy.

The reduction in the mean rate of GA growth (square root transformation) over 12 months was 27.4% ($P = .0072$) for the **avacincaptad pegol 2 mg** cohort and 27.8% ($P = .0051$) for the **avacincaptad pegol 4 mg** cohort compared with their corresponding sham cohorts.



Avacincaptad pegol was generally well tolerated after monthly administration over 12 months.



There were no avacincaptad pegol-related adverse events (AEs) or inflammation.



The most frequent ocular AEs were related to the injection procedure.



There were no ocular serious AEs (SAEs) and no cases of endophthalmitis.



Conclusions

Intravitreal administration of avacincaptad pegol 2 mg and 4 mg led to a significant reduction of GA growth in eyes with AMD over a 12-month period. Because C5 inhibition theoretically preserves C3 activity, it may offer additional safety advantages. A second confirmatory pivotal clinical trial is underway to confirm the efficacy and safety of avacincaptad pegol in slowing the GA growth (GATHER2 Study).