COMPOSITIONS AND METHODS TO TREAT BIETTI CRYSTALLINE DYSTROPHY

CROSS-REFERENCE TO RELATED APPLICATION AND INCORPORATION OF SEQUENCE LISTING

This application claims benefit under 35 U.S.C. § 119(e) of U.S. Provisional Appln. No. 62/810,250, filed February 25, 2019, herein incorporated by reference in its entirety. The sequence listing that is contained in the file named "PAT058467-WO-PCT_SL.pdf", which is 712,266 bytes (measured in operating system MS-Windows) and was created on August 27, 2021, is filed herewith and incorporated herein by reference.

BACKGROUND

Bietti crystalline dystrophy (BCD) is an autosomal recessive disorder in which numerous small, yellow or white crystalline-like deposits of lipid accumulate in the retina, which is followed by chorioretinal atrophy and progressive vision loss. Subjects with BCD typically begin noticing vision problems in their teens or twenties. They often experience night blindness in addition to a reduction in visual acuity. They also usually lose areas of vision, most often peripheral vision. Color vision may also be impaired.

The vision problems may worsen at different rates in each eye, and the severity and progression of symptoms varies widely among affected subjects, even within the same family. However, most subjects with BCD become legally blind by 40 or 50 years of age. Most affected subjects retain some degree of vision, usually in the center of the visual field, although it is typically blurry and cannot be corrected by prescription lenses.

BCD is caused by mutations in the CYP4V2 gene. The gene, located on the long arm of human chromosome 4, encodes cytochrome P450 family 4 subfamily V member 2. As a member of the cytochrome P450 family of enzymes, the ω-hydroxylase is involved in lipid metabolism, specifically oxidation of polyunsaturated fatty acids such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). At least 80 different CYP4V2 gene mutations have been identified in subjects with BCD (Zhang et al., Mol Vis 24:700-711, 2018). CYP4V2 gene mutations that cause BCD impair or eliminate the function of the enzyme and are believed to affect lipid breakdown. However, it is unknown how they lead to the specific signs and symptoms of BCD.

BCD is estimated to affect approximately 65,000 people worldwide (Xiao et al., Biochem Biophys Res Comm 409:181-186, 2011; and Mataftsi et al., Retina 24:416-426,