LIGHTSITE III 24-Month Analysis: Evaluation of Multiwavelength Photobiomodulation in Dry Age-Related Macular Degeneration Using the LumiThera Valeda® Light Delivery System

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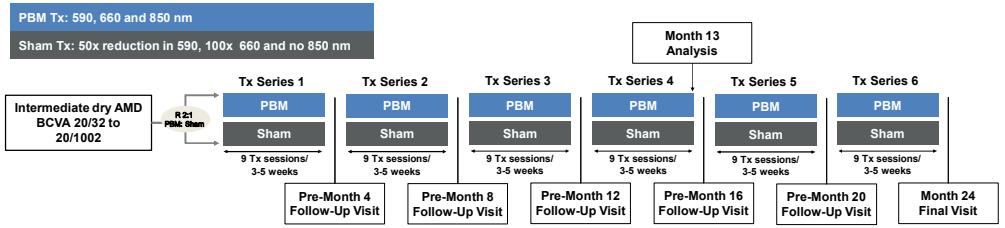
Introduction

Dry age-related macular degeneration (AMD) is a prevalent retinal disease and a leading cause of visual impairment in persons over 65. Mitochondrial dysfunction is a key contributor to disease pathology and provides a viable target for therapeutic strategies. Photobiomodulation (PBM) technology utilizes wavelengths in the 500-1000 nm range to induce cellular effects resulting in improved bioenergetics and mitochondrial output. Studies suggest the benefit of multiwavelength PBM in subjects with Dry AMD (Markowitz et al., Retina, 2020; Merry et al., Acta Ophthalmol, 2017) on clinical and anatomical outcomes. LIGHTSITE III, a randomized, double-masked, multi-center clinical trial, follows promising data from the LIGHTSITE I, LIGHTSITE II and ELECTROLIGHT studies evaluating the multiwavelength PBM using the Valeda® Light Delivery System (LumiThera Inc., Poulsbo, WA) for treatment of patients with intermediate dry AMD.

Study Design



LIGHTSITE III (NCT04065490) was a prospective, double-masked, randomized, sham-controlled, parallel group, multi-center study to assess the safety and efficacy of PBM in dry AMD. Subjects are treated with six series of PBM/Sham treatments (3x/week for 3-5 weeks) delivered over a 24-month period. Subjects were assessed for clinical and safety outcomes. Independent OCT, FAF and color fundus imaging outcomes at selected timepoints were analyzed by a masked imaging reading center (Duke Imaging Center).

LumiThera Valeda Light Delivery System

Valeda uses a multiwavelength PBM treatment comprised of 590 nm, 660 nm and 850 nm wavelengths applied to the subject's eyes for a total of < 5 minutes per treatment per eye.

Illustration of the Valeda Light Delivery System designed for the ophthalmology office setting.

Table 1. Valeda PBM Specifications

Light Source	LED
590 nm	4 mW/cm²
660 nm	65 mW/cm²
850 nm	0.6 mW/cm²
Treatment exposure	Total of 250 seconds/ eye

Results

Table 2. LIGHTSITE III Patient Demographics

Subjects	100 subjects
Eyes	Total enrolled: 148 eyes; MITT population: 145 eyes; (Randomization 2:1; PBM:Sham)
AMD Clinical Classification (Beckman's Categorization)	Early AMD: 29 eyes (20%) Intermediate AMD: 105 eyes (72%) Late AMD: 11 (8%)
Race	99% Caucasian 1% Black/African American
Gender	32 Male (32%), 68 Female (68%)
Mean Age	75 years
Time from Diagnosis	4.9 years
AREDS supplements	86 (86%) yes; 14 (14%) no

A total of 103/148 eyes (70%) had a baseline BCVA ≥ 70 letter (20/40 Snellen or better). A total of 45/148 eyes (30%) had baseline BCVA <70 letters (worse than 20/40 Snellen).

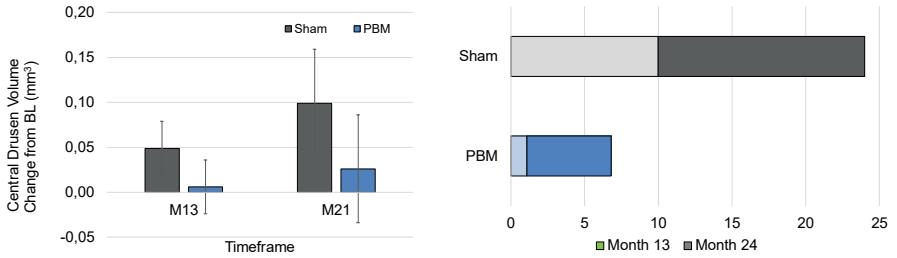


Figure 2. PBM Effect on Anatomical Outcomes. *Left.* At M13 and M21, a greater numerical increase in central drusen volume was observed in Sham eyes vs. PBM eyes. An approximate 3-4x increase in drusen volume in Sham vs PBM-treated eyes was observed at both time points. *Right.* At M13, occurrence of new geographic atrophy (GA) was observed in 5/50 (10.0%) of Sham eyes and 1/87 (1.1%) of PBM eyes. At M24, new GA occurrence progressed to 12/50 (24.0%) Sham eyes and 6/87 (6.8%) PBM eyes. New GA occurrence was significantly higher in the Sham group vs. PBM group at both time points (*Fisher exact test, M13, p = 0.024, odds ratio 9.4; M24, p = 0.007, odds ratio 4.2*).

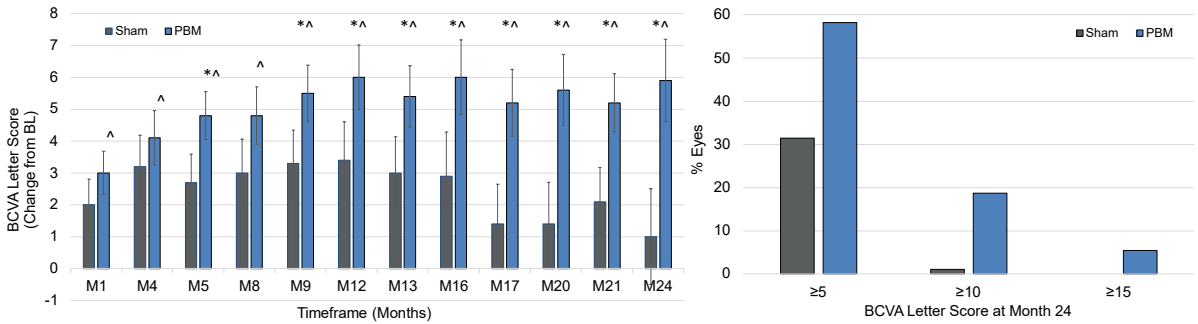


Figure 1. Photobiomodulation Improves BCVA in Intermediate Dry AMD Subjects. *Left.* A statistically significantly difference between PBM and Sham groups at Month (M) 13 (p = 0.02) and M24 (p = 0.0015) was observed. PBM improved BCVA with a mean 5.9 letter gain at M24 (p < 0.0001). *Right.* At M24, 58.2% of PBM eyes responded with a ≥5 letter gain with a mean of 8.5 ± 0.5 letters; 18.7% of PBM eyes responded with a ≥10 letter gain with a mean of 13.4 ± 0.6 letters, and 5.5% of PBM eyes showed ≥15 letter gain with a mean of 16.6 ± 0.8 letters. ^ *p < 0.0001, within group comparison (PBM); * p < 0.05, between group comparison. Post-treatment means include last observation carried forward (LOCF) data. Within group comparisons (Sham) showed significant differences at all timepoints (p < 0.0001).*

Summary and Conclusions

LIGHTSITE III provides randomized controlled trial data evaluating the effects of multiwavelength PBM in subjects with early to intermediate stage dry AMD (<5 year mean from diagnosis). Data from the 24-month analysis showed significant improvements in BCVA which were sustained throughout the duration of the study. LIGHTSITE III met the predetermined primary efficacy BCVA endpoint with a statistically significant difference between the PBM versus Sham treatment groups (*p = 0.02*) at M13. Improvements in clinical and anatomical endpoints following PBM treatment suggest disease modifying effects including a reduced progression to new GA following PBM treatment. Safety data shows a favorable safety profile with adverse events consistent with the patient population and no signs of phototoxicity. Multiwavelength PBM therapy may offer a novel, non-invasive treatment paradigm with a unique mechanism and modality for patients with dry AMD.

NIH National Eye Institute *LIGHTSITE III supported by LumiThera Inc. and the National Eye Institute (1R43EY025508-03). Presented by Dr. Diana Do at 2023 Sonoma Eye Meeting, San Diego, CA, USA.*

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