LumiThera

Dry Age-Related Macular Degeneration (AMD)
Reduced New Geographic Atrophy

Dry AMD leading cause of blindness in the developed world projected to affect 196 million by 2020

100 patients (145 eyes)
Randomised 2:1
A 10-site multi-center RCT

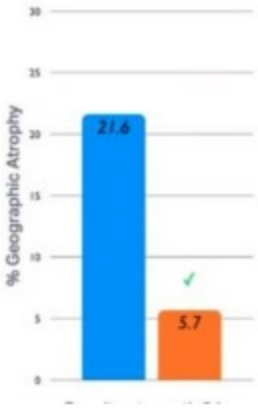
Early to intermediate dry AMD
Treated with the Lumithera Valeda PBM system
Active PBM vs Low dose PBM
Primary endpoint Best Corrected Visual Acuity (BCVA)

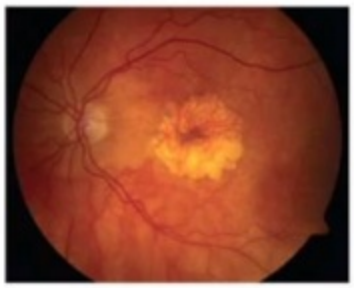
Treatment three times a week for three weeks
Every 4 months
Last treatment month 21
Follow-up at month 24

GA RESULTS 24 MONTHS FOLLOW UP
11 of 51 (21.6%) of Sham eyes
5 of 88 (5.7 %) of PBM eyes
Developed new Geographic Atrophy
p = 0.003, Fisher exact test, odds ratio 4.5

SUMMARY OF FIVE STUDIES
Total 298 eyes total

RESULTS:
- Improved visual acuity (up to 16.6 letter gain)
- Reduced drusen
- Reduced geographic atrophy
- [illegible] contrast sensitivity
- [illegible] retinal fluid and





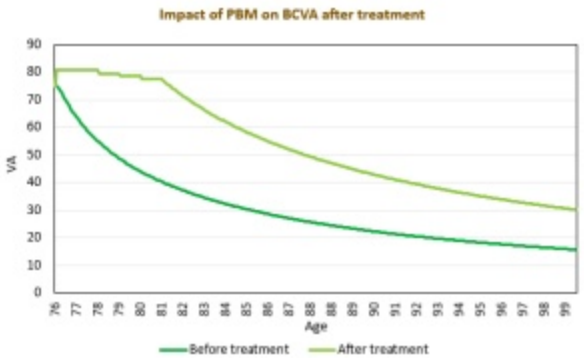
43

LumiThera

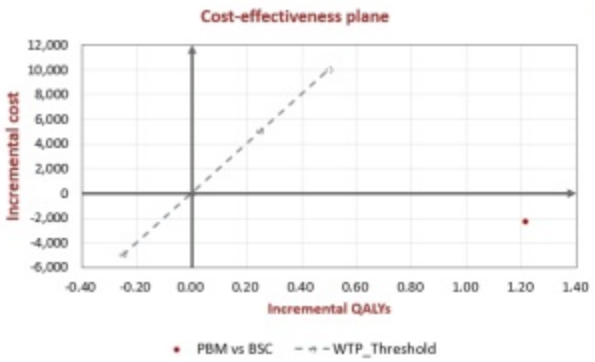
Reimbursement QALYs Analysis

PBM dominates basic standard care in the treatment of dry AMD in NHS health care model

Impact of PBM Treatment on BCVA



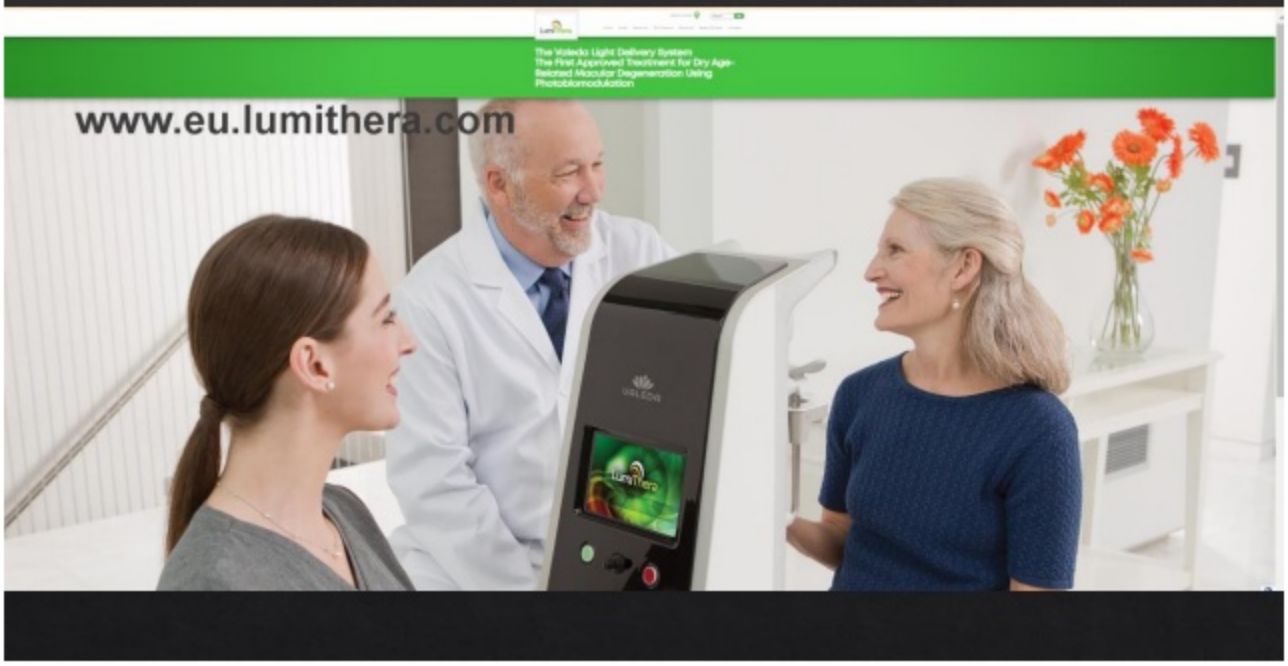
QALYs Improvement with PBM



Note: Patients starting at 75 years of age and receiving a 5.9 letter gain in 24 months of PBM and diminishing benefits over the next 4 years

29

44



45

LIGHTSITE III met the primary efficacy endpoint with a statistically significant improvement in BCVA in the PBM versus the Sham group at Month 13 (p = 0.02), with maintained significance at Month 24 (p = 0.0015)

- More patients lost BCVA in the Sham group compared to the PBM group at Month 13 and 24
- A numerical increase in drusen volume was observed in the Sham group versus no increase in the PBM group at Month 13 and 24 (~4-fold increase over PBM)
- Occurrence of new GA was observed in 24.0% of Sham versus 9.8% of PBM-treated eyes. Occurrence of new GA was significantly higher in the Sham group versus the PBM group (p = 0.007, Fisher exact test, odds ratio 4.2 at Month 24)
- A favorable safety profile was observed with no signs of phototoxicity
- LIGHTSITE III showed significant improvements in clinical and anatomical outcomes suggesting a disease modifying benefit

Individual Patient Results

This patient presented with reduction of drusen volume without progressive outer retinal degeneration. At Month 13, a significant reduction in drusen volume and no visible loss of photoreceptor/retinal pigment epithelium cells was observed.

Age: 71 years
Sex: Female
Baseline BCVA: 73 letters
Month 13 BCVA: 79 letters
Month 24 BCVA: 80 letters

Baseline

Month 13

Individual patient results may vary

INDICATIONS FOR USE

The indicated use is for treatment of ocular damage and disease using photobiomodulation, including inhibition of inflammatory mediators, edema or drusen deposition, improvement of wound healing following ocular trauma or surgery, and increase in visual acuity and contrast sensitivity in patients with degenerative diseases such as dry age-related macular degeneration.

VALEDA | Not for sale in the US | LumiThera

First Approved Treatment for Dry Age-Related Macular Degeneration Using Photobiomodulation

LIGHTSITE III Month 24 Trial Results

VALEDA

- Improves and Sustains Visual Acuity in Early to Intermediate Dry AMD Patients
- Reduces Development of Geographic Atrophy
- Slows Progression of Disease

46

47

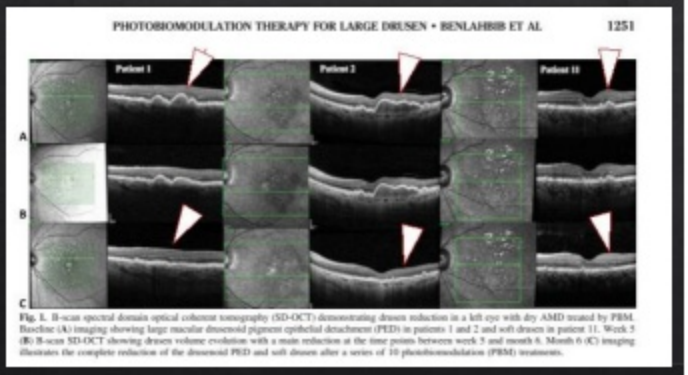
Valeda Treatment

Clinical Practice

- Valeda treatment CE licensed for dry AMD in Europe and UK
- FDA Approval awaited following LightSight Phase 3 trial.
- 4 Consultants in UK able to offer Valeda including our President of RCOphth.
- Some Opticians practices around UK have invested in equipment
- Widely available in Europe.
- Further information at www.lumithera.com

48

Paris Independent Paper



PHOTOBIOMODULATION THERAPY FOR LARGE DRUSEN • BENLAHBIB ET AL 1251

Patient 1 Patient 2 Patient 11

A B C

Fig. 1. B-scan spectral domain optical coherent tomography (SD-OCT) demonstrating drusen reduction in a left eye with dry AMD treated by PBM. Baseline (A) imaging showing large macular drusenoid pigment epithelial detachment (PED) in patients 1 and 2 and soft drusen in patient 11. Week 5 (B) B-scan SD-OCT showing drusen volume evolution with a main reduction at the time points between week 5 and month 6. Month 6 (C) imaging illustrates the complete reduction of the drusenoid PED and soft drusen after a series of 10 photobiomodulation (PBM) treatments.

PHOTOBIOMODULATION THERAPY FOR LARGE SOFT DRUSEN AND DRUSENOID PIGMENT EPITHELIAL DETACHMENT IN AGE-RELATED MACULAR DEGENERATION

A Single-Center Prospective Pilot Study

MANAL BENLAHBIB, MD,* SALOMON YVES COHEN, MD, PhD,*† NURIA TORRELL, MD,* DONATO COLANTUONO, MD,* EMANUELE CRINCOLI, MD,* FRANCESCA AMOROSO, MD,* OUDY SEMOUN, MD,* CAMILLE JUNG, MD,‡ ERIC H. SOUIED, MD, PhD*

Purpose: To evaluate visual acuity and morphologic changes after photobiomodulation (PBM) for patients affected with large soft drusen and/or drusenoid pigment epithelial detachment associated with dry age-related macular degeneration.

Method: Twenty eyes with large soft drusen and/or drusenoid pigment epithelial detachment age-related macular degeneration were included and treated using the LumiThera Valeda Light Delivery System. All patients underwent two treatments per week for 5 weeks. Outcome measures included best-corrected visual acuity, microperimetry-scotopic testing, drusen volume, central drusen thickness, and quality of life score at baseline and month 6 (M6) follow-up. Data of best-corrected visual acuity, drusen volume, and central drusen thickness were also recorded at week 5 (W5).

Results: Best-corrected visual acuity significantly improved at M6 with a mean score gain of 5.5 letters ($P = 0.007$). Retinal sensitivity decreased by 0.1 dB ($P = 0.17$). The mean fixation stability increased by 0.45% ($P = 0.72$). Drusen volume decreased by 0.11 mm^3 ($P = 0.03$). Central drusen thickness was reduced by a mean of 17.09 μm ($P = 0.01$). Geographic atrophy area increased by 0.06 mm^2 ($P = 0.07$) over a 6-month follow-up, and quality of life score increased by 3.37 points on average ($P = 0.05$). One patient presented a drusenoid pigment epithelial detachment rupture at M6 after PBM treatment.

Conclusion: The visual and anatomical improvements in our patients support previous reports on PBM. PBM may provide a valid therapeutic option for large soft drusen and drusenoid pigment epithelial detachment age-related macular degeneration and may potentially slow the natural course of the disease.

RETINA 43:1216–1224, 2023

Age-related macular degeneration (AMD) accounts for approximately 10% of blindness in developed countries.[1] Disease progression unavoidably leads to significant visual loss and severely affects quality of life (QoL).[2] Early stages of AMD are characterized by accumulation of neurotransmit lipidoproteic debris, including lipofuscin, extracellular material, and complement deposition.[3] The advanced late-stages of AMD are usually divided into exudative AMD (also called wet AMD) or geographic atrophy (GA) (also called dry AMD).[4] Dry AMD is characterized by complete or incomplete retinal pigment epithelium (RPE) and complete or incomplete outer retinal atrophy.[1,2] The pathogenesis of AMD is mainly genetically driven but remains partly understood.[5] Nevertheless, there is evidence that RPE dysfunction is involved in dry

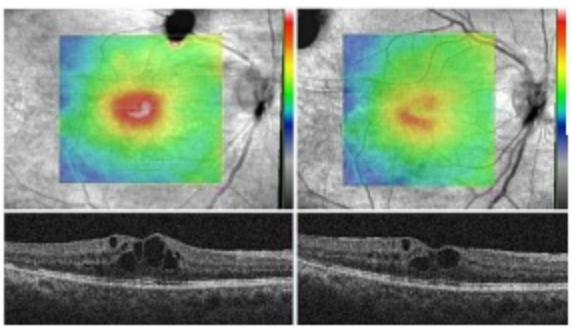
From the * Department of Ophthalmology, Department of Ophthalmology, Centre Hospitalier Intercommunal de Créteil, University of Paris Est-Creteil, Créteil, France; † Ophthalmology Center for Imaging and Laser, Paris, France; and ‡ Clinical Research Center, Centre Hospitalier Intercommunal de Créteil, Créteil, France.

None of the authors has any financial/conflicting interests to disclose.

Reprint requests: Eric H. Souied, MD, PhD, Department of Ophthalmology, University of Paris Est—Créteil, 40 Avenue de Verdun, 94010 Créteil Cedex, France; e-mail: ossoied@hotmail.com

49

Diabetic retinopathy



Clinical Ophthalmology Dovepress

ORIGINAL RESEARCH

Non-Invasive Treatment of Early Diabetic Macular Edema by Multiwavelength Photobiomodulation with the Valeda Light Delivery System

Hakan Kaymak[1,2], Marion R Munk[3–5], Stephanie E Tedford[6], Cindy L Croissant[6], Clark E Tedford[6], Rene Ruckert[4,6], Hartmut Schwahn[1]

A specific Phase 2 randomized clinical trial aimed to determine if treatment with a PBM device results in greater improvement in central subfield thickness in eyes with center-involved diabetic macular edema (CI-DME) compared to a placebo. This trial is part of the growing body of research exploring the efficacy of PBM in diabetic retinopathy.

These studies and reviews collectively indicate that photobiomodulation is a novel and potentially effective treatment for diabetic retinopathy, with ongoing research and clinical trials further investigating its efficacy and applications.

50

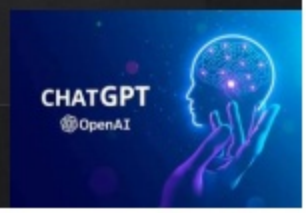
Thank you for Listening

Future for Dry AMD

- Stop smoking
- Diet
- Vitamins
- Amsler
- PhotoBioModulation for Early to intermediate dry AMD – Drusen stage.
- NICE – Very Low Qualy
- FDA Assessing Class II
- NHI grant to extend LIGHTSITE trial 3 years
- Geographic atrophy NEW drugs
  - **Pegcetacoplan (Syfovre)** First medication approved for the treatment of GA
  - **Izervay (avacincaptad pegol) – FDA approved**

Future for Wet AMD

- IVT Anti-VEGF since 2007 – Highly
  - Bevacizumab Avastin
  - Ranibizumab Lucentis
  - Aflibercept Eylea
  - Faricimab Vabysmo– New
- 30+ other drugs in development
- More durable drugs or delivery systems
- Genetic drugs for the retina to make anti-VEGF drugs



51