Abstract

Purpose: Since size of the subretinal hyperreflective material (SRHM) on OCT imaging has been correlated with long-term visual outcome in exudative age-related macular degeneration (eAMD) treated with intravitreal anti-vascular endothelial growth factor (VEGF), we tested the hypothesis that low dose proton beam treatment (PBT) with anti-VEGF reduced the volume of SRHM by reducing the fibrotic part in the choroidal neovascular membrane associated with eAMD.

Methods: Baseline 1 and 2 year OCT images of eyes completing 24 months of a prospective phase I/II randomized, prospective, sham-controlled study of PBT combined with antiVEGF therapy were analyzed using the automated volume measure of subRPE lesion (Cirrus). Our analysis was on 14 eyes with SRHM volume greater than 0.01 mm$^3$ at baseline (n=5 24GyE, n=3 16GyE, n=6 sham).

Results: Among 30 eyes, interim analysis showed 15 completed 24 months of the study, and had OCT images. All showed SRHM, ranging 0.01 to 2.05 millimeters cubed (mm$^3$) at baseline (mean 0.48 mm$^3$ ± 0.62 mm$^3$), 0.2-76 mm$^3$ at 12 months (mean 0.38 mm$^3$ ± 0.77 mm$^3$), and 0.01-3.84 mm$^3$ at 24 months (mean 0.51 mm$^3$ ± 1.04 mm$^3$). No significant difference in mean volume was noted among groups at 12 and 24 months. As measure of very small volume SRHM (< 0.01 mm$^3$) has limited accuracy, further analysis was on 14 eyes with SRHM volume of > 0.01 mm$^3$ at baseline (n=5 24GyE, n=3 16GyE, n=6 sham). The proportion with SRHM volume decreases by > 50% from baseline at 12 months was 3/5 in 24GyE, 3/3 in 16GyE, and 1/6 in sham, with a significant difference between PBT versus sham at 12 months (p = 0.03 by X2) and a trend at 24 months (p = 0.057 by X2, 2/5 in 24GyE, 2/5 in 16GyE, and 0/5 in sham due to 1 eye not having 24-month imaging). Eyes with > 50% decrease in SRHM at 24 months had significant reduction in SRHM at 12 months.

Conclusions: Interim OCT analysis of eyes in this small prospective phase I/II sham controlled study of eAMD show a significantly higher proportion of eyes with greater than halving in volume of SRHM among eyes with eAMD treated with PBT and antiVEGF therapy as compared to antiVEGF monotherapy. This supports the hypothesis that low dose radiation with intravitreal antiVEGF may reduce the size of SRHM in eAMD. A larger study may be warranted to further characterize this effect.

Methods:

Interim analysis of baseline, 1 and 2 year OCT images of human eyes completing the 24 months follow-up as part of a prospective phase I/II randomized, prospective, sham-controlled study of PBT combined with antiVEGF therapy were analyzed for SRHM volume using the automated volume measure of subRPE lesion (Cirrus).

Eyes were randomized 1:1 to 24GyE PBT, 16GyE PBT or sham radiation and followed for antiVEGF treatment as needed based on new OCT fluid and/or macular hemorrhage after three monthly antiVEGF.

Results:

Among 30 eyes, interim analysis showed 15 completed 24 months of the study, and had OCT images. All showed SRHM, ranging 0.01 to 2.05 millimeters cubed (mm$^3$) at baseline (mean 0.48 mm$^3$ ± 0.62 mm$^3$), 0.2-76 mm$^3$ at 12 months (mean 0.38 mm$^3$ ± 0.77 mm$^3$), and 0.01-3.84 mm$^3$ at 24 months (mean 0.51 mm$^3$ ± 1.04 mm$^3$). No significant difference in mean volume was noted among groups at 12 and 24 months. As measure of very small volume SRHM (< 0.01 mm$^3$) has limited accuracy, further analysis was on 14 eyes with SRHM volume of > 0.01 mm$^3$ at baseline (n=5 24GyE, n=3 16GyE, n=6 sham). The proportion with SRHM volume decreases by > 50% from baseline at 12 months was 3/5 in 24GyE, 3/3 in 16GyE, and 1/6 in sham, with a significant difference between PBT versus sham at 12 months (p = 0.03 by X2) and a trend at 24 months (p = 0.057 by X2, 2/5 in 24GyE, 2/5 in 16GyE, and 0/5 in sham due to 1 eye not having 24-month imaging). Eyes with > 50% decrease in SRHM at 24 months had significant reduction in SRHM at 12 months.

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