HHS Public Access

Author manuscript

Ophthalmology. Author manuscript; available in PMC 2017 March 01.

Published in final edited form as:

Ophthalmology. 2016 March ; 123(3): 609–616. doi:10.1016/j.ophtha.2015.10.034.

Outcomes in Eyes with Retinal Angiomatous Proliferation in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT)

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Abstract

Objective—To compare baseline characteristics, visual acuity (VA) and morphological outcomes between eyes with retinal angiomatous proliferation (RAP) and all other eyes among patients with neovascular age-related macular degeneration (NVAMD) treated with anti-vascular endothelial growth factor (anti-VEGF) drugs.

Design—Prospective cohort study within the Comparison of AMD Treatments Trials (CATT).

Participants—Patients with NVAMD

Methods—Reading Center staff evaluated baseline and follow-up digital color fundus photographs (CFP), fluorescein angiograms (FA), and optical coherence tomograms (OCT) of eyes having NVAMD treated with either ranibizumab or bevacizumab over a 2-year period. RAP was identified by the intense intra-retinal leakage of fluorescein in combination with other associated features.

Main outcome measures—VA, fluorescein leakage, scar, geographic atrophy (GA) on FA and retinal thickness, fluid and subretinal hyperreflective material (SHRM) on OCT, and number of intravitreal anti-VEGF injections at 1 and 2 years.

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Meeting Presentation: ARVO 2015

Financial Disclosure(s): The author(s) have made the following disclosure(s): Dr Jaffe has a consultancy relationship with Heidelberg Engineering, Alcon/Novartis, Genentech/Roche, and Neurotech. Dr. Ying is a consultant for Janssen R & D. Other members of the writing committee have no financial relationships to declare

Online Material: This article contains online-only material. The following should appear online-only: Figure 3.

Results—RAP was present in 126 of 1183 (10.7%) study eyes at baseline. Mean VA improvement from baseline was greater (10.6 vs 6.9 letters; p=0.01) at one year but similar at 2 years (7.8 vs 6.2; p=0.34). At 1 year, eyes with RAP were more likely to have: no fluid (46 vs 26%; p<0.001) on OCT, no leakage on FA (61 vs 50%; p=0.03), and greater reduction in foveal thickness (-240 vs -161u, p<0.001). They were more likely to develop GA (24 vs 15%; p=0.01), and less likely to develop scar (17 vs 36%; p<0.001), or SHRM (36 vs 48%; p=0.01). These results were similar at 2 years. The mean change in lesion size at 1 year differed (-0.27 vs 0.27 DA; p=0.02) but was similar at 2 years (0.49 vs 0.79; p=0.26). Among eyes treated PRN, eyes with RAP received a lower mean number of injections in year 1 (6.1 vs 7.4; p=0.003) and year 2 (5.4 vs 6.6; p=0.025).

Conclusions—At both 1 and 2 years after initiation of anti-VEGF treatment in CATT, eyes with RAP were less likely to have fluid, FA leakage, scar, and SHRM and more likely to have GA than eyes without RAP. Mean improvement in VA was similar at 2 years.

Retinal angiomatous proliferation (RAP), also termed type 3 choroidal neovacularization, is a distinct form of neovascular age-related macular degeneration (NVAMD) whose intraretinal pathology differentiates it from classic and occult CNV. Depending to a large extent upon imaging modalities used (fluorescein angiograms (FA), indocyanine green angiogram (IGA) and optical coherence tomogram (OCT)), the prevalence of RAP among eyes presenting with treatment - naïve neovascular age-related macular degeneration is between 10% and 40%, the majority of them occurring among Caucasians.[1-5] Untreated, eyes with RAP often develop poor visual acuity. For example, one study showed that more than one-third of patients with RAP followed up for 20 months became legally blind.[6] Prior to the introduction of intravitreal anti-VEGF for RAP, several modes of treatment that included direct laser photocoagulation of the vascular lesion, laser photocoagulation of the feeder retinal arteriole, scatter “grid like” laser photocoagulation, photodynamic therapy, transpupillary thermotherapy and intravitreal triamcinolone acetonide were used, yielding only marginally better visual acuity and/or short term visual acuity improvement.[7-9] In contrast, better visual outcomes can be achieved by treating RAP with intravitreal anti-VEGF injections.[10-14] However, there are no prospective studies that describe visual and anatomical outcomes at one and two years in eyes with RAP treated with anti-VEGF therapy.

The Comparison of Age-related Macular Degeneration Treatments Trials (CATT) study followed up a large cohort of patients with treatment-naïve NVAMD eyes treated with randomly assigned ranibizumab or bevacizumab through two years. The cohort included eyes with classic and occult CNV and RAP, occurring alone or in varying combinations. Herein, we compared the baseline characteristics, 2-year visual and morphological outcomes between eyes having RAP and eyes without RAP.

Methods

The methods used to grade CATT study images have been previously described.[15,16] Briefly, the CATT cohort consisted of patients with treatment-naïve NVAMD who were randomly assigned for treatment with ranibizumab or bevacizumab on a monthly or as needed basis. Patients were recruited from 43 clinical centers in the United States between

February 2008 and December 2009 and needed to be over 50 years old. Institutional review boards associated with each center approved the clinical trial protocol. All patients provided written informed consent. The study was compliant with Health Insurance Portability and Accountability Act regulations and adhered to the tenets of the Declaration of Helsinki. CATT was registered with ClinicalTrials.gov (NCT00593450). Study eyes had to have active neovascularization associated with age-related macular degeneration and visual acuities between 20/25 and 20/320. The neovascularization could be subfoveal or extrafoveal but if extrafoveal a sequelae of neovascularization such as fluid, serous pigment epithelial detachment, blocked fluorescence, or hemorrhage had to be located under the foveal center. Active neovascularization was defined by the presence of leakage on fluorescein angiography and fluid on OCT.

Grading of color and FA images at baseline and years 1 and 2 were performed at the CATT Fundus Photograph Reading Center of the University of Pennsylvania. Two trained certified graders independently assessed the images and discrepant results were adjudicated. Morphological features identified on these images included active leakage of fluorescein on FA, fibrotic scar, non-fibrotic scar, type of CNV (classic, occult and RAP), type of total CNV lesion, hemorrhage, blocked fluorescence contiguous with the CNV, serous pigment epithelial detachment, non-geographic atrophy, geographic atrophy, retinal pigment epithelial tear, and pathology in the foveal center. OCT scans were graded at the CATT OCT Reading Center of Duke University by two independent certified readers. Discrepant data were arbitrated by an independent Senior Reader. Readers assessed the following parameters on OCT images: intraretinal fluid (IRF), subretinal fluid (SRF), and subretinal pigment epithelium (RPE) fluid, vitreomacular adhesions (VMA) and sub-retinal hyper reflective material (SHRM). In addition, the center point retinal thickness, subretinal fluid thickness, and sub-retinal tissue complex thickness were measured.[17]

RAP lesions were identified by FA and color fundus photograph findings (Figure 1). To be considered a RAP lesion, a focal area of intense intra-retinal hyperfluorescence (hot spot) in the early phase of the FA was required, along with one or more of the following signs on FA: focal intraretinal superficial hemorrhages, lipid, serous or fibro-vascular pigment epithelial detachment, retinal vascular abnormality such as an anastomosis between retinal vessels, between retinal and choroidal vessels or retinal vessels with the underlying CNV complex.[1,2]

Statistical Methods

We performed the statistical comparison of baseline characteristics and outcomes at Year 1 and Year 2 between eyes with baseline RAP and eyes without baseline RAP. The two group independent t-test was used to compare means of continuous variables and Fisher's exact test for comparison of proportions of categorical variables. A P-value<0.05 was considered to be statistically significant. All the statistical comparisons were made using SAS v9.2 (SAS Institute, Inc).

Results

Baseline Characteristics

At enrollment, RAP was present in 126 of 1183 (10.7%) CATT patients who had sufficient image quality. The frequencies of specific RAP features are listed in Table 1. Superficial hemorrhage was present in 91% of RAP eyes, 12% had serous pigment epithelial detachment, 14% had fibrovascular pigment epithelial detachment, 22% had hard exudates, 20% had retina vessel – CNV lesion anastomosis and 1% had retinal vessel – retinal vessel anastomosis.

Comparison of baseline characteristics between patients with and without RAP is shown in Table 2. Patients who had RAP were older (mean 81.7 years) than patients without RAP lesions (mean 79 years) ($p<0.001$). There was a lower percentage of past or current cigarette smokers in the RAP group (45% vs 59%, $p=0.004$). Systemic diseases such as hypertension and diabetes mellitus were similar in the two groups. The baseline visual acuity (VA) was similar in eyes with and without RAP (60.1 letters vs 60.6 letters, $p=0.47$). The CNV lesion size in Disc Areas (DA) was smaller in eyes with RAP (1.22 DA vs 1.85 DA, $p<0.001$) and the total CNV lesion area showed a similar difference (1.59 DA vs 2.59 DA, $p<0.001$) between the two groups. RAP eyes had CNV that was more commonly located away from the foveal center in comparison to eyes with no RAP (40% vs 60%, $p<0.001$). RAP lesions were almost always associated with the occult-only type of CNV (93% vs 56%, $p<0.001$); classic-only type of CNV was uncommon when RAP was present (4% vs 25%, $p<0.001$). CNV-associated hemorrhages were more frequent in eyes with RAP (93% vs 59%) but tended to be smaller (91% with <1DA vs 47% with <1DA, $p<0.001$). Serous pigment epithelial detachments identified on FA were more common in eyes with RAP than in eyes that had no RAP (13% vs 4%, $p<0.001$). The mean retinal thickness did not differ between the two groups (191 vs 211μ, $p=0.23$) but there was more intraretinal fluid (93% vs 73%, $p<0.001$) and sub-RPE fluid (60% vs 47%, $p=0.08$) and less sub-retinal fluid (67% vs 84%, $p<0.001$) in eyes with RAP when compared to eyes without RAP. Sub-retinal hyper-reflective material was similar between the two groups (71% vs 77%, $p=0.14$).

One – Year Outcomes

Greater VA improvement from baseline was seen in eyes with RAP (10.6 letters vs 6.9 letters, $p=0.01$) than in eyes without RAP, and more eyes with RAP had a ≥15 letters increase from baseline (41% vs 28%, $p=0.005$). Foveal total thickness decreased to a greater extent in eyes with RAP (-240μ vs -161μ, $p<0.001$) than those without RAP. On OCT, more eyes with RAP had complete fluid resolution (46% vs 26%, $p<0.001$) than eyes without RAP. The proportion of eyes with no active fluorescein leakage on FA was higher in the RAP group than in the non-RAP group (61% vs 50%, $p=0.03$). Total CNV lesion size decreased in eyes with RAP while it increased in those with CNV but no RAP (-0.27 DA vs 0.27 DA, $p=0.02$). A greater proportion of eyes developed geographic atrophy (24% vs 15%, $p=0.01$) in the RAP group while a lesser proportion developed scar (17% vs 36%, $p<0.001$) and SHRM (36% vs 48%, $p=0.01$) at 1 year. Among PRN-treated eyes (60 eyes with RAP, 497 without RAP), fewer injections were required in eyes that had RAP (mean 6.1 injections vs 7.4 injections, $p=0.003$) than in eyes that did not have RAP. (Table 3). Within the RAP

group, more eyes treated monthly had complete fluid resolution (63% vs. 31%, p<0.001) and no leakage on FA (73% vs. 56%, p=0.08) than eyes treated PRN.

Two – Year Outcomes

At 2 years, the mean VA improvement from baseline (7.8 letters vs 6.2 letters, p=0.34) and a ≥15 letter increase from baseline (33% vs 29%, p=0.51) were not significantly different between eyes with and without RAP lesions. The change in mean VA from baseline through two years of follow up is shown in Figure 2. The total foveal thickness reduction from baseline continued to be greater in eyes that had RAP (-223μ vs -156μ, p<0.001). A greater proportion of eyes with RAP had no fluid on OCT (36% vs 22%, p=0.002) and no leakage on FA (78% vs 68%, p=0.02). The mean change in area of the total CNV lesion from baseline did not differ significantly between the groups (0.49 DA vs 0.79 DA, p=0.26) at 2 years. Eyes with RAP continued to develop more geographic atrophy (32% vs 19%, p=0.004) and less scar (31% vs 44%, p=0.01) and less SHRM (35% vs 44%, p=0.001). In the PRN treatment group, fewer injections in year 2 were required in eyes with RAP (5.4 injections vs 6.6 injections; p=0.025). (Table 4). Within the RAP group, more eyes treated monthly for 2 years had complete fluid resolution (55%) than eyes treated PRN for 2 years (29%) or switched from monthly in year 1 to PRN in year 2 (33%, p=0.06).

Discussion

This study reports the visual acuity and morphological outcomes from anti-VEGF treatment in eyes with RAP compared to eyes with CNV but no RAP. There are few reports of visual acuity in eyes with RAP treated for more than one year with anti-VEGF drugs. The studies that do exist are difficult to compare to the CATT since most have a small number of patients (<25) and did not have a comparison group of treated eyes without RAP.[13,18-22] The few retrospective studies that had follow-up periods extending up to 3 years showed there was improvement and stabilization of visual acuity in the anti-VEGF-treated eyes with RAP. However, one small retrospective study showed that although all 20 study eyes had improved or had stable VA at months 1 and 3, only 63% had similar stability or improvement at 2 years of follow-up.[22] Similar to these studies, our study showed a rapid improvement in VA within the first three months of intravitreal anti-VEGF therapy that continued to improve and then stabilize during the first year (Tables 3 and 4 and Figure 2). However, in the second year, VA began to decline modestly such that there was no statistically significant difference between eyes with or without RAP in overall VA gain at the end of two years of treatment. When eyes that developed GA by 2 years were excluded from the analysis, the pattern of a modest decline in VA gain during year 2 among eyes with RAP and of stable VA in eyes without RAP persisted (Figure 3 available at http://aaojournal.org) indicating that the decline was not due solely to the higher incidence of GA among eyes with RAP.

Our study also showed that among eyes assigned to the PRN treatment, the eyes with RAP needed fewer anti-VEGF injections than eyes without RAP in year 1. In a smaller study, which included 11 eyes with RAP given anti-VEGF therapy, the mean number of injections required for eyes with RAP was 7 in the first year, 6 in the second year, and 7 in the third

year.[19] In another slightly larger study, ranibizumab was given monthly for 3 months, and then PRN thereafter to treat eyes with RAP. The mean number of injections in this study was 5.5 and 7.7 at 12 and 24 months, respectively.[21] In the CATT cohort the mean reduction in total foveal thickness at both 1 and 2 years and the proportion of eyes without intraretinal, subretinal and sub-RPE fluid was significantly greater in eyes with RAP than in treatment-naïve NVAMD eyes without RAP. These data from our clinical trial suggest that the response of RAP lesions to anti-VEGF treatment is more rapid at the start of therapy and is similar to that of other types of NVAMD at the end of two years. The rapid response of RAP lesions to anti-VEGF therapy could be attributed to the smaller baseline NVAMD lesion that is known to have a more favorable prognostic outcome in exudative AMD with anti-VEGF treatment. Other baseline features such as the preponderance of RAP associated occult CNV as well as the not sub-foveal location of CNV in almost half of the eyes with RAP also could have contributed to a more favorable morphological outcome. Within the RAP group, more eyes with RAP became fluid free and had less fluorescein leakage during follow up years 1 and 2 on the monthly regimen when compared with eyes on the PRN and the switched regimen; these differences among dosing regimens are consistent with the overall results of CATT.[15]

Our study corroborated many of the findings from previous studies of treatment-naïve eyes with RAP. For example, patients who present with untreated RAP and NVAMD tend to be older than patients with NVAMD without RAP.[23,24] However patients who were past or present cigarette smokers tended to have lower risk of RAP, a finding that has was not identified in the one other study that evaluated smoking.[24] As reported in other anti-VEGF studies, in our study a relatively high proportion of eyes with RAP lesions developed geographic atrophy by 2 years. The increased GA development may be related to baseline subfoveal choroidal thinning, reticular pseudodrusen, and GA in the fellow eye.[25-27] On the other hand, a lower proportion of eyes with RAP developed scar. This finding may be related to the strong association of RAP lesions with occult type of CNV which is known to produce fewer scars than classic or mixed CNV lesions and also to fewer number of eyes with RAP having SHRM during the 2 years of follow up. SHRM, a morphologic feature seen on optical coherence tomography (OCT) as hyperreflective material located external to the retina and internal to the retinal pigment epithelium (RPE), is associated with reduced VA and increased scar formation.[28,29] The CATT cohort had either CNV or its sequelae in the foveal center and eyes with RAP tended to have CNV that was predominantly extra-foveal. As a result deleterious morphological outcomes such as GA and scar tended to occur in an extra-foveal location.

The large number of treatment-naïve eyes with RAP was a major study strength. The method used to identify RAP was a relative study limitation. The diagnosis of RAP lesions in this study was based on the fluorescein angiographic appearance supported by color fundus photographic features and correlated well with the fluid observed on OCT. ICGA is useful to diagnose RAP, particularly in the later stages, but was not available in this study. Accordingly, RAP may have been underdiagnosed, and, therefore, the actual number of eyes with RAP may have been higher than what we have reported.[5,30,31]

In summary, approximately 10% of treatment-naïve eyes in our cohort had RAP. Eyes with RAP treated with anti-VEGF drugs in CATT were less likely to have fluid, FA leakage, scar, and SHRM and more likely to have GA at 1 or 2 years than other types of CNV. Although VA gain was greater and lesion growth was less in eyes with RAP at 1 year, by 2 years they were similar to eyes without RAP. Fewer injections were needed to treat RAP than the other types of CNV.

Acknowledgments

Financial Support: This study was supported by cooperative agreements U10 EY017823, U10 EY017825, U10 EY017826, U10 EY017828 and R21EY023689 from the National Eye Institute, National Institutes of Health, Department of Health and Human Services. ClinicalTrials.gov number, NCT00593450.

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Although more geographic atrophy developed after treatment of retinal angiomatous proliferation with anti-vascular endothelial growth factor drugs, visual acuity improvement at 2 years was similar to eyes with other forms of neovascular age-related macular degeneration.

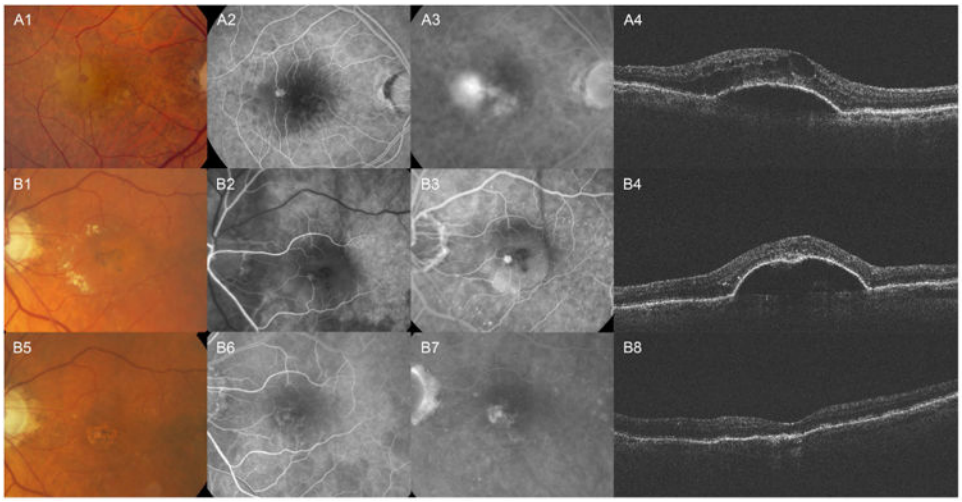

Figure 1.

Color image of the study eye at baseline (A1). Intra-retinal hyperfluorescence (hot spot) that leaks intensely in late phase-angiogram (A2). Petaloid hyperfluorescence is observed in the fovea (A3) corresponding to the large intraretinal cysts noted on OCT (A4). Sub-RPE fluid (serous pigment epithelial detachment) is also seen on OCT. Color image of another patient at baseline with intraretinal lipid (B1) and an intense hyperfluorescent spot (B2, B3) surrounded by hyperfluorescence in the sub-RPE space consistent with a serous pigment epithelial detachment. The OCT (B4) shows sub-RPE fluid (serous pigment epithelial detachment). At two years, atrophic areas are seen (B5, B6 and B7) with corresponding signal penetration into the choroid on OCT (B8).

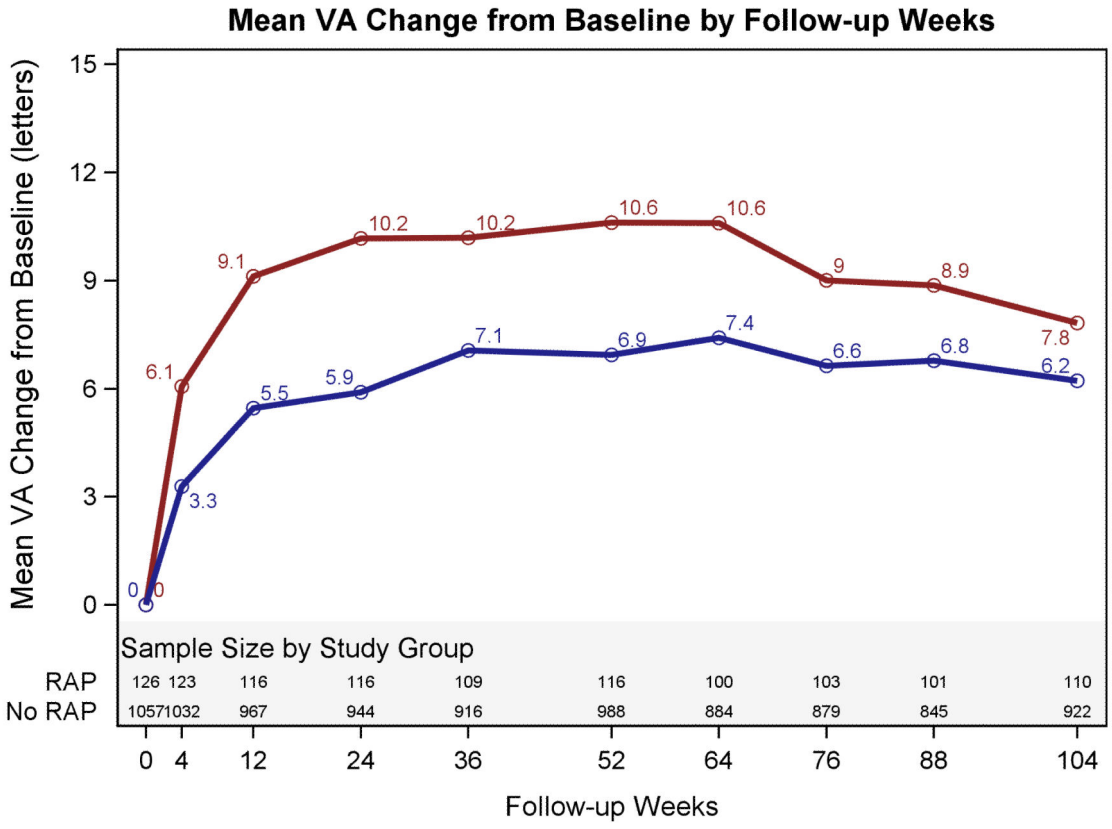

Figure 2.

Mean visual acuity (VA) change from baseline through two years. Red line = Eyes with Retinal Angiomatous Proliferation (RAP). Blue line = Eyes without RAP.

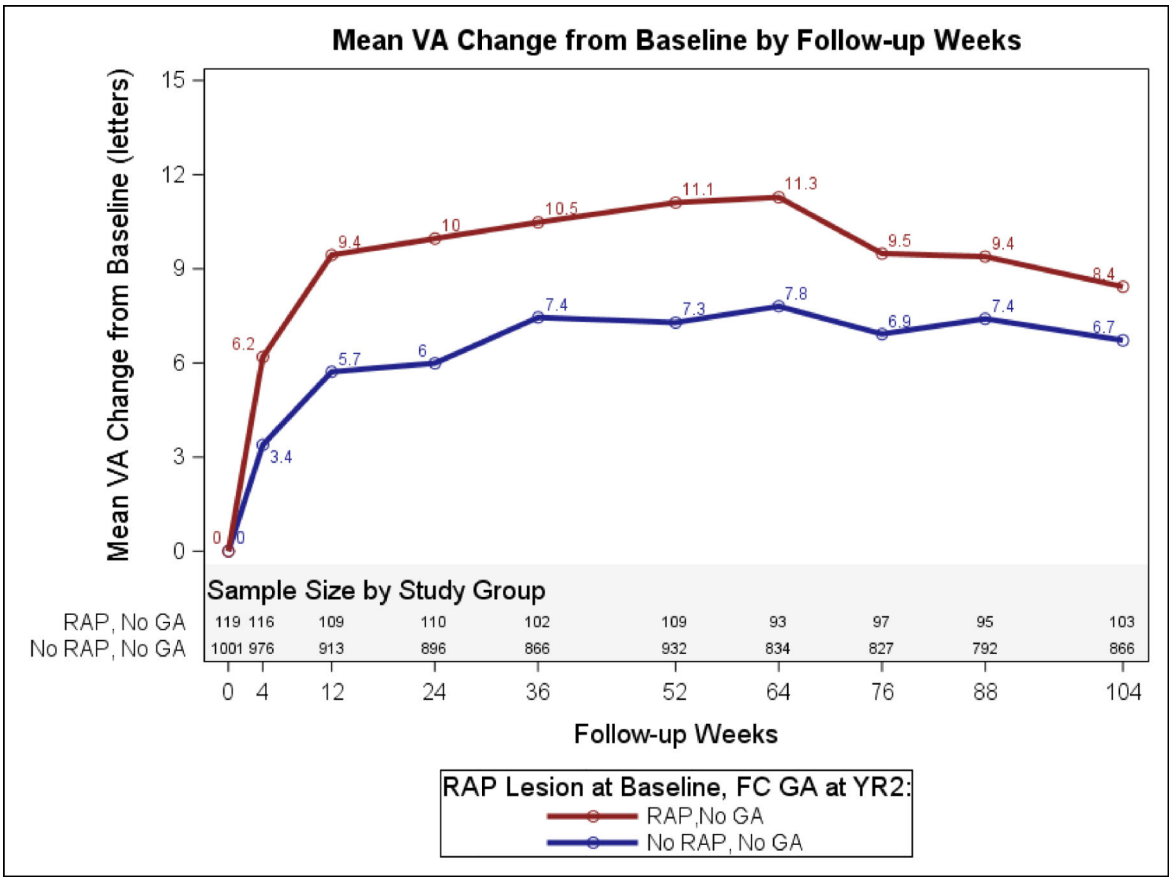

Figure 3.

Mean visual acuity change from baseline through two years in eyes without foveal center geographic atrophy at 2 years.

VA=Visual Acuity, RAP=Retinal Angiomatous Proliferation, GA=Geographic atrophy, YR2 =Year 2, FC=Foveal Center.

Table 1

Features of retinal angiomatous proliferation.

Retinal angiomatous proliferation components	**Number (%)**
Area of intense intraretinal hyperfluorescence (hot spot)	126 (100.0)
Superficial intra-retinal hemorrhages	114 (90.5)
Associated serous pigment epithelial detachment (SPED)	15 (11.9)
Associated lipid (hard exudates)	28 (22.2)
Associated fibrovascular pigment epithelial detachment (FV-PED)	18 (14.3)
Associated retinal anastomosis	
None	100 (79.4)
Retina-retina	1 (0.8)
Retina-lesion	25 (19.8)

Table 2

Baseline characteristics of groups based on the presence of retinal angiomatous proliferation (RAP).

Baseline characteristics	With RAP Lesion N=126 (%)	Without RAP Lesion N=1057 (%)	P Value**
Patients (N=1183§)			
Age, years Mean (SE†)	81.7 (0.65)	79.0 (0.23)	<0.001
Female	87 (69.1)	644 (60.9)	0.08
Former or current cigarette smoker	57 (45.2)	620 (58.7)	0.004
Presence of hypertension	80 (63.5)	742 (70.2)	0.13
Presence of Diabetes mellitus	22 (17.5)	184 (17.4)	1.00
Geographic atrophy in fellow eye	21 (16.7)	122 (11.5)	0.11
CNV or scar in fellow eye	40 (31.8)	308 (29.1)	0.47
Study eye			
Visual acuity, letters: Mean (SE†)	60.1 (1.09)	60.6 (.042)	0.70
Area of choroidal neovascularization, disc areas: Mean (SE†)	1.22 (0.13)	1.85 (0.06)	<0.001
Baseline total area of lesion, disc areas: Mean (SE†)	1.59 (0.15)	2.59 (0.08)	<0.001
Pathology in foveal center			<0.001
Fluid only	60 (47.6)	254 (24.0)	
Choroidal neovascularization	50 (39.7)	637 (60.3)	
Hemorrhage	5 (3.97)	88 (8.33)	
Other (pigment, drusen etc)	11 (8.73)	69 (6.53)	
Location of lesion (does not include fluid)			<0.001
Sub-foveal	65 (51.6)	777 (73.5)	
Not Sub-foveal	61 (48.4)	261 (24.7)	
CNV			<0.001
Occult only	117 (92.86)	577 (55.91)	
Classic only	4 (3.97)	258 (25.0)	
Occult and classic	5 (3.97)	197 (19.1)	
None/Cannot grade/Cannot decide	0 (0.00)	25 (2.37)	
Hemorrhage (associated with the lesion)			<0.001
None	9 (7.14)	432 (40.87)	
≤ 1 Disc area	114 (90.5)	495 (46.8)	
≤ 2 Disc area	1 (0.79)	58 (5.49)	
> 2 Disc area	2 (1.59)	52 (4.92)	
Geographic atrophy	5 (3.97)	77 (7.28)	0.20
Scar	1 (0.79)	45 (4.26)	0.05
Serous pigment epithelial detachment	16 (12.7)	46 (4.35)	<0.001
Cystoid macular edema on fluorescein angiogram	11 (8.73)	88 (8.33)	0.86
OCT Features			
Retinal thickness, microns: Mean (SE†)	191 (14.2)	211 (5.40)	0.23
Total thickness, microns: Mean (SE†)	476 (16.4)	458 (5.78)	0.30
Intra-retinal fluid	117 (92.9)	768 (72.7)	<0.001

Baseline characteristics	With RAP Lesion N=126 (%)	Without RAP Lesion N=1057 (%)	P Value**
Sub-retinal fluid	84 (66.7)	885 (83.7)	<0.001
Sub-retinal pigment epithelium fluid	76 (60.3)	495 (46.8)	0.08
Vitreo-macular adhesion/traction	10 (7.94)	133 (12.6)	0.15
Sub-retinal hyper-reflective material	90 (71.4)	817 (77.3)	0.14

§ 2 subjects excluded due to poor image quality.

** From independent t-test for continuous variables and Fisher's exact test for categorical variables.

† SE is standard error

Table 3

Year 1 outcomes of groups based on presence of baseline retinal angiomatous proliferation. (N=1104[§])

Year 1 Outcomes	With RAP Lesion (N=116) (%)	Without RAP Lesion (N=988) (%)	P Value*
Visual acuity, letters: Mean (SE°)	70.9 (1.19)	67.7 (0.58)	0.07
Visual acuity change from baseline, letters: Mean (SE°)	10.6 (1.00)	6.93 (0.48)	0.011
≥ 15 letters increase from baseline	48 (41.4)	279 (28.2)	0.005
Hemorrhage contiguous with lesion	2 (1.72)	19 (1.92)	1.00
Retinal thickness at fovea, microns			0.20
<120	27 (23.3)	208 (21.1)	
120-212	82 (70.7)	651 (65.9)	
>212	7 (6.03)	112 (11.3)	
Change in total foveal thickness from baseline, microns: Mean (SE°)	-240 (17.8)	-161 (5.7)	<0.001
No fluid on OCT	53 (45.7)	260 (26.3)	<0.001
No Leakage on FA	71 (61.2)	491 (49.7)	.027
Change in lesion size from baseline, disc areas: Mean (SE°)	-0.27 (0.14)	0.27 (0.08)	0.019
Pathology in fovea center			<0.001
No pathology	51 (44.0)	161 (16.3)	
Fluid only	19 (16.4)	66 (6.68)	
Choroidal neovascularization	8 (6.90)	251 (25.4)	
Scar	5 (4.31)	197 (19.9)	
Geographic atrophy	2 (1.72)	20 (2.02)	
Non-geographic atrophy	13 (11.2)	138 (14.0)	
Other	18 (15.5)	155 (15.7)	
RPE†† tear involving macula (n, %)	1 (0.86)	17 (1.79)	0.71
Mean number of injections, PRN† only: Mean (SE°)	6.07 (0.38)	7.42 (0.15)	0.003
Geographic Atrophy	28 (24.1)	144 (14.6)	0.014
Scar	20 (17.2)	359 (36.3)	<0.001
Sub-retinal hyper reflective material	42 (36.2)	472 (47.8)	0.013

§ Number of patients with Year 1 visual acuity outcome.

* From independent t-test for continuous variables and Fisher's exact test for categorical variables.

† 60 patients with RAP Lesion and 497 patients without RAP Lesion were in PRN groups.

° SE is standard error.

†† RPE is retinal pigment epithelium

Table 4

Year 2 outcomes of groups based on presence of baseline retinal angiomatous proliferation (N=1032[§])

Year 2 Outcomes	With RAP lesion (N=110) (%)	Without RAP lesion (N=922) (%)	P Value[*]
Visual acuity, letters: Mean (SE[°])	68.0 (1.57)	67.3 (0.61)	0.72
Visual acuity change from baseline, letters: Mean (SE[°])	7.82 (1.60)	6.21 (0.54)	0.34
≥ 15 letters increase from baseline	36 (32.7)	271 (29.4)	0.51
Hemorrhage contiguous with lesion	2 (1.82)	28 (3.04)	0.76
Retinal thickness at fovea, microns			0.83
<120	25 (22.7)	220 (23.9)	
120-212	72 (65.5)	570 (61.8)	
>212	12 (10.9)	116 (12.6)	
Change in total foveal thickness from baseline, microns: Mean (SE[°])	-223 (20.5)	-156 (6.22)	<0.001
No fluid on OCT	40 (36.4)	200 (21.7)	0.002
No Leakage on FA	86 (78.2)	624 (67.7)	0.023
Change in lesion size from baseline, disc areas: Mean (SE[°])	0.49 (0.19)	0.79 (0.09)	0.26
Pathology in fovea center			<0.001
No pathology	41 (37.3)	162 (17.6)	
Fluid only	5 (4.55)	28 (3.04)	
Choroidal neovascularization	13 (11.82)	164 (17.8)	
Scar	7 (6.36)	222 (24.1)	
Geographic atrophy	7 (6.36)	56 (6.07)	
Non-geographic atrophy	20 (19.2)	168 (18.2)	
Other	17 (15.5)	122 (13.2)	
Mean number of injections, PRN[†] only: Mean (SE[°])	5.36 (0.43)	6.57 (0.18)	0.025
Geographic Atrophy	35 (31.8)	179 (19.4)	0.004
Scar	34 (30.9)	405 (43.9)	0.010
Sub-retinal hyper reflective material	38 (34.5)	428 (43.8)	0.014

[§] Number of patients with Year 2 visual acuity outcome.

[*] From independent t-test for continuous variables and Fisher's exact test for categorical variables.

[†] 56 patients with RAP lesion and 460 patients without RAP lesion were in PRN groups.

[°] SE is standard error.

[††] RAP is retinal pigment epithelium