Supplementary Online Content

Daniel E, Maguire MG, Grunwald JE, et al; Comparison of Age-Related Macular Degeneration Treatments Trials Research Group. Incidence and progression of nongeographic atrophy in the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT) Clinical Trial. *JAMA Ophthalmol*. Published online March 19, 2020. doi:10.1001/jamaophthalmol.2020.0437

eFigure 1. Example of non-geographic atrophy (NGA) evolution in color fundus photographs (CFP), fluorescein angiograms (FA) and OCT images in the area of baseline choroidal neovascularization at baseline, year 1, 2 and 5.

eFigure 2. Progression from non-geographic atrophy (NGA) to geographic atrophy (GA) in the Year 1 NGA cohort

eFigure 3. Progression from non-geographic atrophy (NGA) to geographic atrophy (GA) in the Year 2 Non-geographic atrophy cohort.

eFigure 4. A1, A2 Non-geographic atrophy surrounding a non-fibrotic scar at year 1 developing into geographic atrophy at year 5. B1, B2 Non-geographic atrophy at 1 year with a large fibrotic scar at year 5.

eTable 1. Univariate analysis for the baseline risk factors for incident non-geographic atrophy (NGA)

eTable 2. Univariate analysis for baseline risk factors for progression from non-geographic atrophy (NGA) to geographic atrophy (GA)

This supplementary material has been provided by the authors to give readers additional information about their work.

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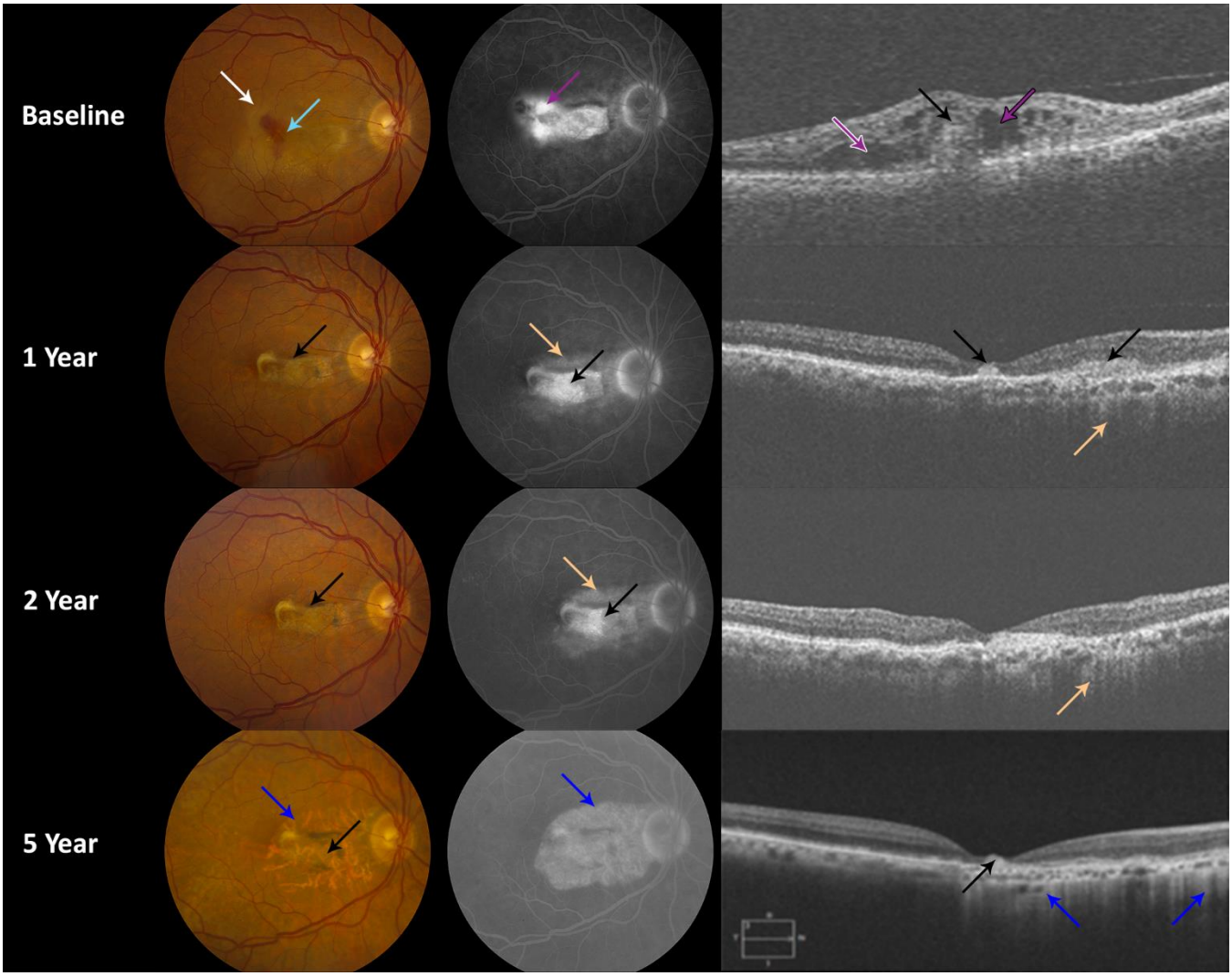
eFigure 1. Example of non-geographic atrophy (NGA) evolution in color fundus photographs (CFP), fluorescein angiograms (FA) and OCT images in the area of baseline choroidal neovascularization at baseline, year 1, 2 and 5.



Baseline images show choroidal neovascularization (CNV) (white arrow) with hemorrhage (blue arrow), leakage of dye (purple arrow) and intraretinal fluid (purple arrow with black border), subretinal fluid (purple arrow with white border) and a mass extending into the inner retina (black arrow). At year 1, a rectangular fibrotic scar with no surrounding hypopigmentation or hyperpigmentation (NGA) is observed, but FA shows mild hyperfluorescent areas (yellow arrow) peripheral to the staining fibrotic scar (black arrow) with some choroidal hypertransmission. At year 2, there are no signs of NGA around the scar on color but the peripheral hyperfluorescence has enlarged (yellow arrow) with increased choroidal hypertransmission (yellow arrow). At year 5, there is a large area geographic atrophy (GA) (blue arrow) surrounding a disintegrating fibrotic scar (black arrow) with distinct choroidal hypertransmission. This example suggests that OCT hypertransmission can detect NGA and impending GA earlier than color images.

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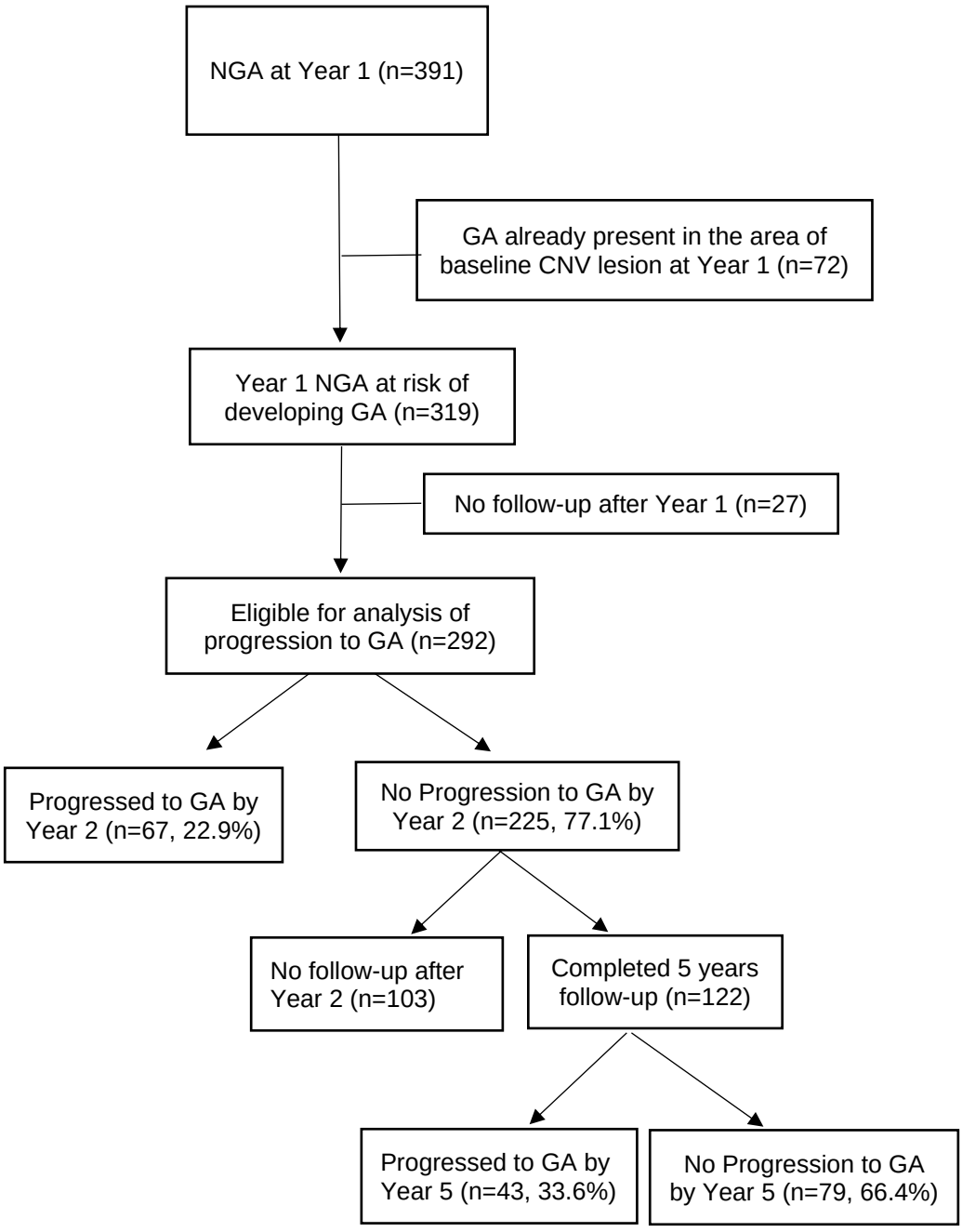
eFigure 2. Progression from non-geographic atrophy (NGA) to geographic atrophy (GA) in the Year-1 NGA cohort



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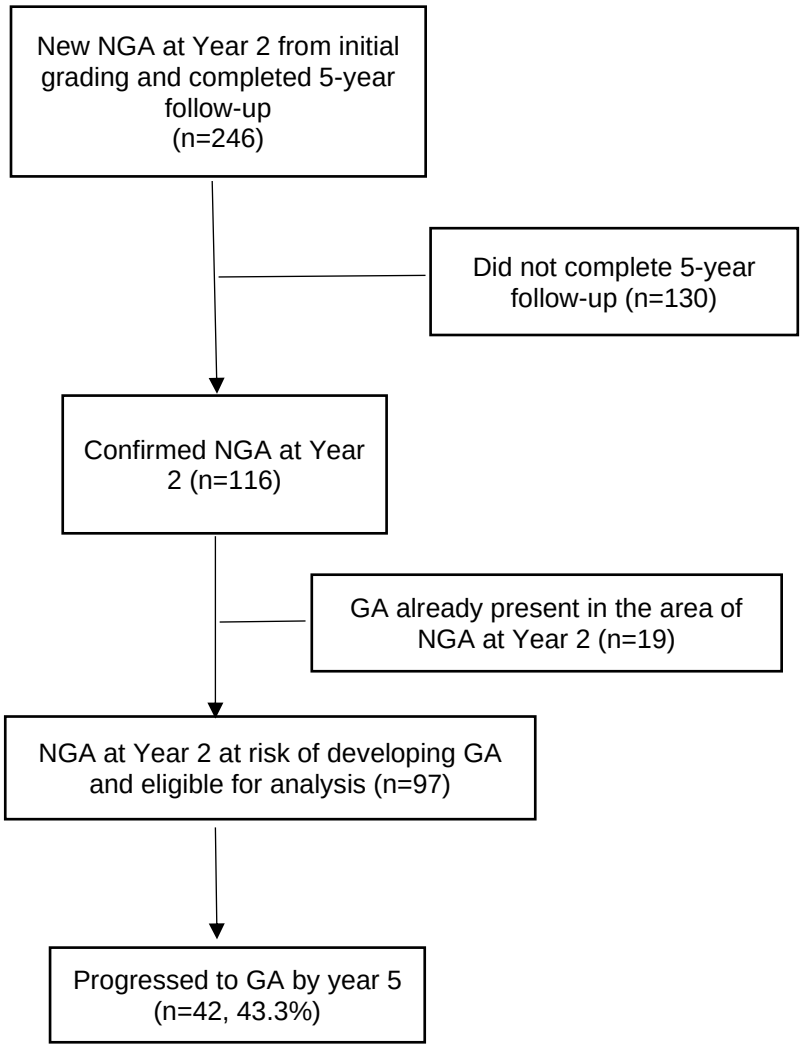
eFigure 3: Progression from non-geographic atrophy (NGA) to geographic atrophy (GA) in the Year-2 non-geographic atrophy cohort.



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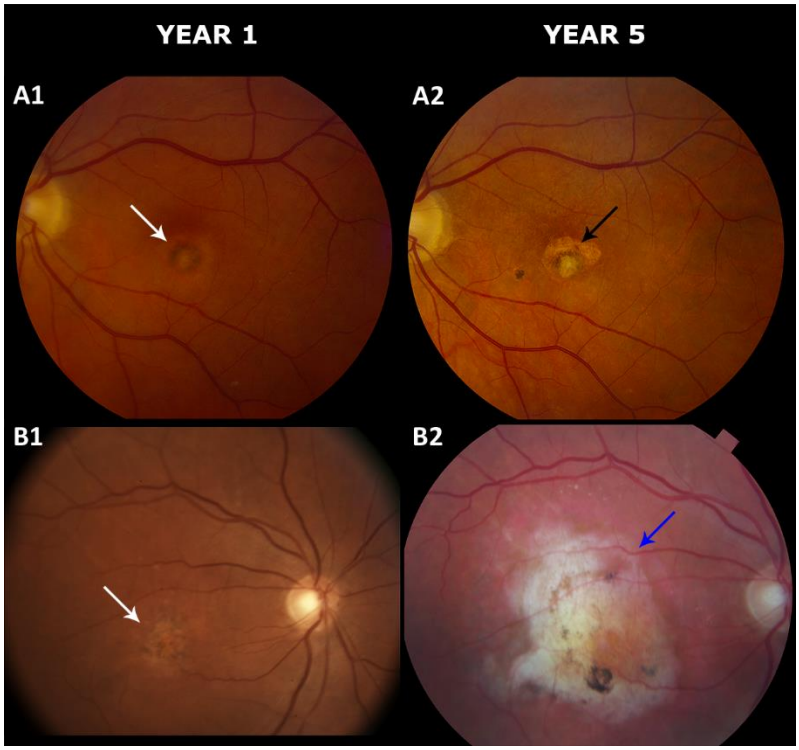
eFigure 4: Supplemental online: A1, A2 Non-geographic atrophy surrounding a non-fibrotic scar at year 1 developing into geographic atrophy at year 5. B1, B2 Non-geographic atrophy at 1 year with a large fibrotic scar at year 5.



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eTable1. Univariate analysis for the baseline risk factors for incident non-geographic atrophy

Baseline demographics	Number of patients	Non-geographic atrophy by 5 Years n (%)	Risk Ratio (95% CI)	P Value
Age (years)				**.03**
50-69	134	94(70.1%)	1.00	
70-79	387	268(69.3%)	1.08(0.85,1.37)	
80-89	511	339(66.3%)	1.12(0.89,1.41)	
>=90	75	58(77.3%)	1.60(1.15,2.24)	
Gender				.09
Female	685	474(69.2%)	1.00	
Male	422	285(67.5%)	0.99(0.85,1.15)	
Cigarette Smoking				.92
Never	474	324(68.4%)	1.00	
Quit	539	374(69.4%)	1.02(0.88,1.19)	
Current	94	61(64.9%)	0.98(0.74,1.29)	
Hypertension				.51
No	341	243(71.3%)	1.00	
Yes	766	516(67.4%)	0.95(0.81,1.11)	
Diabetes				.78
No	910	626(68.8%)	1.00	
Yes	197	133(67.5%)	0.97(0.81,1.18)	
Dietary supplement use				.94
No	111	80(72.1%)	1.00	
Beta carotene, C, E and Zinc	702	482(68.7%)	0.96(0.75,1.22)	
Other supplements	294	197(67.0%)	0.97(0.75,1.27)	
Hypercholesterolemia				.73
No	471	318(67.5%)	1.00	
Yes	636	441(69.3%)	1.03(0.89,1.19)	
Drug group				.93
Bevacizumab	537	366(68.2%)	1.00	
Ranibizumab	570	393(68.9%)	1.01(0.87,1.16)	
Regimen group				**.01**
PRN	556	369(66.4%)	1.00	
Switched	268	199(74.3%)	1.28 (1.08,1.53)	
Monthly	283	191(67.5%)	1.01 (0.85, 1.21)	

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Baseline ocular characteristics	Number of study eyes	Non-geographic atrophy by 5 years n (%)	Risk ratio (95% CI)	P-value
Baseline VA Fellow eye				.24
20/20 or better	333	230(69.1%)	1.00	
20/25-20/40	435	290(66.7%)	1.03(0.86,1.22)	
20/50 or worse	339	239(70.5%)	1.16(0.96,1.39)	
Baseline VA Study eye				**.007**
20/25-40	402	276(68.7%)	1.00	
20/50-80	413	276(66.8%)	1.07(0.90,1.26)	
20/100-160	221	151(68.3%)	1.10(0.90,1.35)	
20/200-320	71	56(78.9%)	1.68(1.25,2.26)	
Baseline total area of CNV (DA)				**.03**
<=1	446	304(68.2%)	1.00	
>1 to <=2	219	142(64.8%)	0.86(0.71,1.06)	
>2 to <=4	206	151(73.3%)	1.19(0.98,1.45)	
>4	104	76(73.1%)	1.18(0.91,1.52)	
Baseline total area of CNV lesion (DA)				**.03**
<=1	358	251(70.1%)	1.00	
>1 to <=2	239	150(62.8%)	0.81(0.66,1.00)	
>2 to <=4	266	194(72.9%)	1.13(0.93,1.36)	
>4	202	140(69.3%)	1.03(0.83,1.27)	
Location of lesion				.89
Not Subfoveal	304	212(69.7%)	1.00	
Subfoveal	786	539(68.6%)	1.01(0.86,1.19)	
Lesion type				.48
Predominantly classic	247	171(69.2%)	1.00	
Minimally classic	184	130(70.7%)	1.02(0.81,1.29)	
Occult only	653	446(68.3%)	0.92(0.77,1.10)	
Lesion Composition				.16
CNV only	564	399(70.7%)	1.00	
CNV and hemorrhage	283	190(67.1%)	1.02(0.86,1.22)	
CNV and blocked fluorescence	76	56(73.7%)	1.13(0.85,1.50)	
CNV and SPED	47	26(55.3%)	0.65(0.44,0.97)	
CNV and others	123	82(66.7%)	0.89(0.70,1.13)	
RAP Lesion				.45
No	968	662(68.4%)	1.00	

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Yes	119	87(73.1%)	1.09(0.87,1.37)	
Blocked fluorescence				.85
No	936	644(68.8%)	1.00	
Yes	159	110(69.2%)	1.02(0.83,1.25)	
SPED (proportion of total lesion)				.19
None	1030	717(69.6%)	1.00	
<50%	21	15(71.4%)	0.82(0.49,1.38)	
>=50%	40	21(52.5%)	0.69(0.44,1.06)	
Hemorrhage (associated with the lesion)				.35
None	703	490(69.7%)	1.00	
<=2 DA	310	206(66.5%)	0.98(0.83,1.15)	
>2 DA	77	56(72.7%)	1.21(0.92,1.61)	
Scar				.19
No	1050	727(69.2%)	1.00	
Yes	43	27(62.8%)	0.77(0.53,1.14)	
Glaucoma (yes/no)				.84
No	985	674(68.4%)	1.00	
Yes	122	85(69.7%)	0.98(0.78,1.23)	
CNV at fellow eye				.08
None/questionable	748	512(68.4%)	1.00	
Present	328	227(69.2%)	1.15(0.98,1.35)	
GA in fellow eye				.15
None/questionable	966	657(68.0%)	1.00	
Present	128	94(73.4%)	1.18(0.94,1.46)	
Pseudodrusen in study eye				.32
No/Questionable	840	575(68.5%)	1.00	
Yes	197	138(70.1%)	1.10(0.91,1.33)	
Pseudodrusen in fellow eye				**.02**
No/Questionable	753	507(67.3%)	1.00	
Yes	254	187(73.6%)	1.22(1.03,1.45)	
Pseudodrusen in either eye				.06
No/Questionable	772	523(67.7%)	1.00	
Yes	292	209(71.6%)	1.17(1.00,1.38)	

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Baseline OCT characteristics	Number of study eyes	Non-geographic atrophy by 5 years n (%)	Risk ratio (95% CI)	P-value
Intra-retinal thickness (µm)				.07
<120	113	67(59.3%)	1.00	
120 to 212	584	405(69.3%)	1.22(0.94,1.59)	
>212	405	285(70.4%)	1.35(1.03,1.77)	
Sub-retinal thickness (µm)				.17
0	734	507(69.1%)	1.00	
>0 to <=25	93	69(74.2%)	1.19(0.92,1.54)	
>25	275	181(65.8%)	0.91(0.77,1.08)	
Sub-RPE thickness (µm)				**<.001**
>0 to <=75	275	194(70.5%)	1.00	
>75 to <=160	261	193(73.9%)	1.16(0.94,1.42)	
>160 to <=275	282	204(72.3%)	0.99(0.81,1.21)	
>275	284	166(58.5%)	0.72(0.58,0.88)	
Retinal fluid in the fovea center				**.004**
No Fluid	266	178(66.9%)	1.00	
Fluid not in fovea center	300	193(64.3%)	0.90(0.73,1.10)	
Fluid in fovea center	523	378(72.3%)	1.20(1.00,1.43)	
Subretinal fluid in the fovea center				.24
No Fluid	187	117(62.6%)	1.00	
Fluid not in fovea center	523	373(71.3%)	1.19(0.97,1.47)	
Fluid in fovea center	387	261(67.4%)	1.11(0.89,1.38)	
Sub-RPE fluid in the fovea center				**.002**
No Fluid	483	337(69.8%)	1.00	
Fluid not in fovea center	196	148(75.5%)	1.06(0.87,1.29)	
Fluid in fovea center	343	219(63.8%)	0.76(0.64,0.91)	
Any fluid				.30
No Fluid	12	5(41.7%)	1.00	
Fluid not in fovea center	189	135(71.4%)	1.99(0.81,4.86)	
Fluid in fovea center	903	618(68.4%)	1.86(0.77,4.50)	
RPE elevation				.62
No	145	99(68.3%)	1.00	
Yes	946	648(68.5%)	0.95(0.76,1.17)	

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SPED				.09
None	1030	717(69.6%)	1.00	
Not in fovea center	27	11(40.7%)	0.52(0.29,0.94)	
In fovea center	34	25(73.5%)	0.91(0.61,1.36)	
Epiretinal Membrane				.15
No	901	609(67.6%)	1.00	
Yes	156	114(73.1%)	1.16(0.95,1.42)	
Vitreo-macular attachment				.26
No	908	628(69.2%)	1.00	
Yes	135	86(63.7%)	0.88(0.70,1.10)	
SHRM				.52
No	247	171(69.2%)	1.00	
Yes	845	578(68.4%)	1.06(0.89,1.26)	

Genetic SNP	**Number of Patients**	**Non-geographic atrophy by 5 years n (%)**	**Risk ratio (95% CI)**	**P-value**
CFH				.33
TT	173	117(67.6%)	1.00	
TC	392	288(73.5%)	1.08(0.87,1.34)	
CC	270	179(66.3%)	0.94(0.74,1.19)	
ARMS2				**.001**
GG	266	172(64.7%)	1.00	
GT	399	280(70.2%)	1.19(0.98,1.44)	
TT	170	132(77.6%)	1.53(1.22,1.93)	
C3				.89
CC	461	320(69.4%)	1.00	
CG	318	222(69.8%)	0.97(0.82,1.15)	
GG	56	42(75.0%)	1.04(0.75,1.44)	
HTRA1				**.002**
GG	274	175(63.9%)	1.00	
AG	399	284(71.2%)	1.23(1.01,1.48)	
AA	162	125(77.2%)	1.51(1.20,1.91)	
LIPC				.85
TT	48	36(75.0%)	1.00	
CT	345	246(71.3%)	0.96(0.67,1.36)	

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CC	441	302(68.5%)	0.92(0.65,1.31)	
CFB				.52
TT	786	548(69.7%)	1.00	
AT	47	34(72.3%)	1.19(0.83,1.69)	
AA	2	2(100.0%)	1.61(0.39,6.67)	
C2				.91
TT	4	3(75.0%)	1.00	
GT	149	105(70.5%)	0.92(0.29,2.92)	
GG	680	474(69.7%)	0.88(0.28,2.77)	
CFH162v				.98
TT	525	366(69.7%)	1.00	
GT	193	129(66.8%)	0.98(0.80,1.20)	
GG	14	10(71.4%)	0.99(0.52,1.87)	
TLR3				.81
CC	76	51(67.1%)	1.00	
CT	341	236(69.2%)	1.00(0.73,1.35)	
CC	418	297(71.1%)	1.05(0.78,1.42)	

PRN=pro re nata, VA=Visual Acuity, CNV=choroidal neovascularization, DA = Disc Areas, SPED = Serous pigment epithelial detachment, RAP = Retinal angiomatous proliferens, RPE = Retinal pigment epithelium, SHRM = Sub-retinal hyper-reflective material, GA = Geographic Area, SNP = Single nucleotide polymorphisms

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eTable 2. Univariate analysis for baseline risk factors for progression from Non-geographic atrophy NGA to Geographic atrophy (GA)

Baseline Features	Number of study eyes with non-geographic atrophy	Progression to geographic atrophy n (%)	Risk ratio (95% CI)	P-value
Age (years)				**.009**
50-69	50	14(28.0%)	1.00	
70-79	148	60(40.5%)	1.59(0.89,2.85)	
80-89	166	68(41.2%)	2.13(1.20,3.80)	
>=90	25	10(40.0%)	3.47(1.52,7.91)	
Gender				**.02**
Female	254	109(42.9%)	1.00	
Male	135	43(32.1%)	0.66(0.46,0.94)	
Cigarette Smoking				.87
Never	164	65(39.6%)	1.00	
Quit	192	74(38.7%)	1.02(0.73,1.42)	
Current	33	13(39.4%)	0.87(0.48,1.58)	
Hypertension				.83
No	132	54(41.2%)	1.00	
Yes	257	98(38.1%)	0.96(0.69,1.35)	
Diabetes				.73
No	321	126(39.3%)	1.00	
Yes	68	26(38.8%)	1.08(0.70,1.65)	
Dietary supplement use				.64
No	41	15(37.5%)	1.00	
Beta carotene, C, E and Zinc	252	103(40.9%)	1.17(0.68,2.02)	
Other supplements	96	34(35.4%)	0.99(0.54,1.82)	
Drug group				.21
Bevacizumab	198	73(37.1%)	1.00	
Ranibizumab	191	79(41.4%)	1.23(0.89,1.69)	
Regimen group				.12
Pro re nata (PRN)	187	67(36.0%)	1.00	
Switched	106	38(35.8%)	1.00(0.67, 1.49)	
Monthly	96	47(49.0%)	1.44(0.99, 2.10)	

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Baseline VA fellow eye				**.005**
20/20 or better	121	36(30.0%)	1.00	
20/25-20/40	154	68(44.2%)	1.76(1.17,2.64)	
20/50 or worse	114	48(42.1%)	1.97(1.28,3.06)	
Baseline VA Study eye				**.001**
20/25-40	156	54(34.8%)	1.00	
20/50-80	132	49(37.1%)	1.23(0.84,1.82)	
20/100-160	73	32(43.8%)	1.93(1.24,3.01)	
20/200-320	28	17(60.7%)	2.66(1.53,4.62)	
Baseline total area of CNV (DA)				.29
<=1	166	60(36.4%)	1.00	
>1 to <=2	64	22(34.4%)	0.83(0.51,1.35)	
>2 to <=4	79	31(39.2%)	1.14(0.74,1.76)	
>4	40	19(47.5%)	1.48(0.88,2.48)	
Baseline total area of CNV lesion (DA)				.13
<=1	138	55(39.9%)	1.00	
>1 to <=2	69	19(27.9%)	0.60(0.36,1.02)	
>2 to <=4	100	40(40.0%)	1.01(0.67,1.52)	
>4	72	33(45.8%)	1.18(0.76,1.82)	
Location of lesion				.93
Not Subfoveal	98	36(37.1%)	1.00	
Subfoveal	288	114(39.6%)	0.98(0.67,1.43)	
Lesion type				.45
Predominantly classic	87	35(40.7%)	1.00	
Minimally classic	66	24(36.4%)	0.72(0.42,1.21)	
Occult only	230	91(39.6%)	0.85(0.57,1.26)	
RAP Lesion				**.02**
No	338	126(37.4%)	1.00	
Yes	47	23(48.9%)	1.70(1.09,2.67)	
Blocked fluorescence				.37
No	332	130(39.3%)	1.00	
Yes	55	20(36.4%)	0.81(0.50,1.29)	
Hemorrhage (associated with the lesion)				.50
None	254	100(39.4%)	1.00	
<=2 DA	106	41(39.0%)	0.86(0.60,1.24)	

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>2 DA	27	9(33.3%)	0.71(0.36,1.41)	
CNV in fellow eye				.91
None/questionable	258	100(38.9%)	1.00	
Present	119	46(38.7%)	1.02(0.72,1.45)	
GA in fellow eye				**.006**
None/questionable	342	127(37.2%)	1.00	
Present	43	23(53.5%)	1.89(1.20,2.95)	
Pseudodrusen in study eye				.37
No/Questionable	292	115(39.4%)	1.00	
Yes	80	33(41.3%)	1.19(0.81,1.76)	
Pseudodrusen in fellow eye				**.001**
No/Questionable	260	88(34.0%)	1.00	
Yes	101	50(49.5%)	1.84(1.29,2.61)	
Pseudodrusen in either eye				**.007**
No/Questionable	264	95(36.1%)	1.00	
Yes	115	54(47.0%)	1.59(1.13,2.22)	
GA outside non-GA area at the visit of first non-GA observation				**.02**
Absent	372	143(38.5%)	1.00	
Present	17	9(52.9%)	2.19(1.11,4.31)	

OCT characteristics				
Intra-retinal thickness (µm)				.24
<120	35	11(31.4%)	1.00	
120 to 212	220	82(37.3%)	1.33(0.71,2.51)	
>212	134	59(44.4%)	1.64(0.86,3.12)	
Sub-retinal thickness (µm)				.11
0	252	104(41.3%)	1.00	
>0 to <=25	33	13(39.4%)	0.86(0.48,1.54)	
>25	104	35(34.0%)	0.66(0.45,0.98)	
Sub-RPE thickness (µm)				.23
>0 to <=75	99	36(36.7%)	1.00	
>75 to <=160	105	48(45.7%)	1.33(0.86,2.06)	
>160 to <=275	99	41(41.4%)	1.28(0.82,2.01)	
>275	86	27(31.4%)	0.87(0.53,1.43)	
Intraretinal fluid in the fovea center(yes/no)				**.005**
No Fluid	102	28(27.5%)	1.00	

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Fluid not in fovea center	96	41(42.7%)	1.98(1.22,3.21)	
Fluid in fovea center	185	81(44.0%)	1.99(1.29,3.07)	
Subretinal fluid in the fovea center(yes/no)				**<.001**
No Fluid	61	36(59.0%)	1.00	
Fluid not in fovea center	180	67(37.2%)	0.49(0.32,0.73)	
Fluid in fovea center	145	48(33.3%)	0.38(0.25,0.59)	
Sub-RPE fluid in the fovea center(yes/no)				.90
No Fluid	178	70(39.5%)	1.00	
Fluid not in fovea center	76	32(42.1%)	1.10(0.72,1.68)	
Fluid in fovea center	106	40(37.7%)	1.00(0.68,1.48)	
Any fluid				.80
No Fluid	4	1(25.0%)	1.00	
Fluid not in fovea center	67	25(37.3%)	1.40(0.19,10.33)	
Fluid in fovea center	318	126(39.7%)	1.56(0.22,11.21)	
RPE elevation				.49
No	59	21(36.2%)	1.00	
Yes	321	128(39.9%)	1.18(0.74,1.87)	
SPED				.33
None	368	145(39.5%)	1.00	
Not in fovea center	7	1(14.3%)	0.30(0.04,2.17)	
In fovea center	12	4(33.3%)	0.63(0.23,1.70)	
Epiretinal Membrane				.19
No	310	120(38.7%)	1.00	
Yes	59	26(44.8%)	1.33(0.87,2.04)	
Vitreo-macular attachment				.08
No	314	130(41.5%)	1.00	
Yes	54	15(27.8%)	0.62(0.36,1.06)	
SHRM				.99
No	87	37(43.0%)	1.00	
Yes	298	113(37.9%)	1.00(0.69,1.45)	

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Genotype				
CFH				.86
TT	60	23(38.3%)	1.00	
TC	154	61(39.9%)	0.95(0.59,1.54)	
CC	98	36(36.7%)	0.87(0.51,1.47)	
ARMS2				.20
GG	90	33(37.1%)	1.00	
GT	154	54(35.1%)	0.93(0.60,1.44)	
TT	68	33(48.5%)	1.37(0.84,2.23)	
C3				.49
CC	170	64(37.9%)	1.00	
CG	120	48(40.0%)	1.24(0.85,1.80)	
GG	22	8(36.4%)	0.94(0.45,1.97)	
HTRA1				.14
GG	90	32(36.0%)	1.00	
AG	158	56(35.4%)	1.03(0.66,1.59)	
AA	64	32(50.0%)	1.53(0.94,2.51)	
LIPC				.82
TT	15	4(26.7%)	1.00	
CT	134	51(38.1%)	1.38(0.50,3.84)	
CC	163	65(40.1%)	1.34(0.49,3.70)	
CFB				.84
TT	293	114(39.0%)	1.00	
AT	17	6(35.3%)	1.28(0.56,2.94)	
AA	2	0(0.0%)	0.00(0.00)	
CFH162v				.31
TT	193	66(34.4%)	1.00	
GT	78	35(44.9%)	1.38(0.91,2.08)	
GG	6	3(50.0%)	1.22(0.38,3.91)	
TLR3				.75
CC	27	10(37.0%)	1.00	
CT	127	47(37.0%)	1.11(0.56,2.21)	
CC	158	63(40.1%)	1.24(0.64,2.43)	

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PRN=pro re nata, VA=Visual Acuity, CNV=choroidal neovascularization, DA = Disc Areas, SPED = Serous pigment epithelial detachment, RAP = Retinal angiomatous proliferens, RPE = Retinal pigment epithelium, SHRM = Sub-retinal hyper-reflective material, GA = Geographic Area, SNP = Single nucleotide polymorphisms

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