

Association between mitochondrial haplogroups and ranibizumab response in neovascular age-related macular degeneration.

Francisco Ascaso; [Olivia Esteban](#); [Julio Montoya](#); [Paula Montes](#); [Javier Mateo](#); [Javier Lara](#); [Eduardo Ruiz-Pesini](#)

+ Author Affiliations & Notes

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Abstract

Purpose : The association between mitochondrial DNA (mtDNA) haplogroup and the risk of neovascular age-related macular degeneration (nAMD) has been reported. This prospective, observational clinical study analyzes the anatomical and functional outcomes after one year of intravitreal ranibizumab therapy in nAMD patients according to the mt-DNA haplogroup.

Methods : Ninety-eight eyes corresponding to 91 patients with nAMD were treated with three consecutive monthly intravitreal ranibizumab 0.5 mg followed by a flexible pro re nata (PRN). Retreatment criteria were: loss ≥ 5 ETDRS letters; increased central foveal thickness (CFT) $> 100 \mu\text{m}$; intra or subretinal fluid on OCT; new or persistent macular haemorrhages. Exclusion criteria were previous treatment with photodynamic therapy or anti-VEGF drug; vitrectomy or any other retinal disease; corneal or lens opacities. Patients were classified into four groups according to their mtDNA haplogroup determined by PCR (Hg H- m.7028C>T; Hg HV- m.14766T>C; Hg JT- m.421 6T>C and Hg U- m.12308A>G). Chi-square, Kolmogorov-Smirnov, ANOVA, Mann-Whitney, Kruskal-Wallis, analysis of variance, Wilcoxon, and Friedman tests were used. SPSS 21.0 program. A p value < 0.05 was statistically significant.

Results : Gender, age, risk factors (smoking, diabetes, arterial hypertension and dyslipidemia) and neovascular lesion type were equally distributed among four groups. There were no significant differences between groups in baseline or after loading fase

in best corrected visual acuity (BCVA) or CFT. At 4 months, BCVA was significantly higher than baseline in haplogroups HV ($p = 0.02$), JT ($p = 0.002$) and U ($p = 0.002$). CFT was significantly lower in all haplogroups (HV, $p < 0.001$; JT, $p = 0.028$; U, $p = 0.043$; Others, $p = 0.007$). Eighteen patients were excluded at 12 months because of exclusion criteria, however baseline variables were equally distributed among four groups. At 12 months, BCVA in HV and U did not show significant worsening; however, JT showed lower BCVA values than baseline. CFT values in JT were higher than baseline ($p = 1.00$), whereas HV and U were significantly lower than baseline (HV, $p < 0.001$; U, $p = 0.007$). CFT values were significantly different between JT and U ($p = 0.010$).

Conclusions : mtDNA haplogroups showed different response to ranibizumab at 12 month. It could be a potential biomarker to predict the response to this therapy in nAMD patients.

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Table 1. Demographic, clinical characteristics and response to ranibizumab therapy of the studied patient population.

Haplogroups	Total	HV	JT	U	Others
Baseline					
Patients/eyes	91/98	54/57	11/12	18/19	8/10
Gender (% F)	63	59	71	65	70
Age (year)	76.9 ± 7.5	77.3 ± 7.6	78.3 ± 7.1	75.9 ± 8.8	75.2 ± 6.7
BCVA (N° ETDRS letters)	46.1 ± 19.5	44.8 ± 20.5	40.8 ± 22.1	47.6 ± 18.4	57.0 ± 19.2
CFT (µm)	380.7 ± 99.1	391.7 ± 94.0	364.3 ± 81.9	360.1 ± 82.3	370.9 ± 82.3
4-month follow-up					
Patients/eyes	91/98	54/57	11/12	18/19	8/10
Gender (% F)	63	59	71	65	70
Age (year)	76.9 ± 7.5	77.3 ± 7.6	78.3 ± 7.1	75.9 ± 8.8	75.2 ± 6.7
BCVA (N° ETDRS letters)	55.1* ± 17.7	50.9* ± 21.7	56.3* ± 22.4	57.1* ± 17.3	60.0 ± 17.8
CFT (µm)	251.1* ± 69.7	255.4* ± 72.2	224.9* ± 33.3	250.4* ± 84.2	223.8* ± 48.0
12-month follow-up					
Patients/eyes	73/76	45/45	9/10	12/13	7/8
Gender (% F)	66	67	67	62	71
Age (year)	75.9 ± 8.1	76.1 ± 7.0	79.8 ± 8.4	74.8 ± 8.3	72.7 ± 4.0
BCVA (N° ETDRS letters)	53.9 ± 17.6	53.1 ± 18.7	40.0 ± 9.5	60.9 ± 17.1	57.9 ± 12.9
CFT (µm)	281.6* [^] ± 98.0	285.0* ± 91.6	368.0 ^a ± 123.4	216.2* ^{^a} ± 77.3	284.7 ± 43.1
IVR (N°)	6.7 ± 1.7	6.9 ± 1.9	7.1 ± 1.5	6.4 ± 1.8	6.5 ± 1.5

BCVA = best corrected visual acuity; CFT = central foveal thickness; IVR = intravitreal ranibizumab injections; N° ETDRS letters = number of early treatment diabetic retinopathy study chart letters.

Means ± standard deviations are shown for all variables, except gender, which is reported in relative frequency of females (% F).

^{^,a} indicate significantly different between groups and from the group sharing this superscript lowercase letter, respectively.

* Significantly different from the basal value of the same parameter.

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