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Pharmacogenetic influence of complement genes genotypes on the response to anti-VEGF treatment for age-related macular degeneration in a Russian population

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Age-related macular degeneration (AMD) is the leading cause of vision loss in the aging population. The current standard of care for neovascular AMD is the administration of vascular endothelial growth factor (VEGF) inhibitors. However, a high degree of variability in treatment response has been observed. The aim of the study was to determine the effect of gene polymorphisms related to the complement system on the dynamics of changes in the functional and anatomical parameters of the retina according to optical coherence tomography during anti-VEGF therapy. The genotype frequencies of the rs2285714 (CFI), rs10490924 (ARMS2), rs2230199 (C3), rs800292 (CFH), and rs6677604 (CFH) loci in the Russian cohort were determined. The height pigment epithelium detachment and neuroepithelial detachment depended on the rs2285714 genotype and were significantly higher in carriers of the risk allele initially, after 3 and after 5 doses of drug. The chances of the presence of anastomoses and loops and the activity of the neovascular membrane in the end of observation period in individuals homozygous for the risk allele of rs2285714 were significantly higher. Also association of rs2230199 with the presence of intraretinal cysts was revealed. According to the regression analysis considering gender, age, and baseline values, it was found that rs2285714 was associated with the dynamics of a decrease in the central retinal thickness (CRT) during treatment: the CRT decline was significantly less in patients with risk allele. Thus, the severity of morphological changes and the extent of macular lesions are associated with polymorphisms rs2285714 (CFI), rs2230199 (C3) in genes that play a key role in regulating the activity of the alternative pathway of the complement system. Patients with the risk allele rs2285714 poorly respond to anti-angiogenic therapy. *Acknowledgements*: Supported by RSF 21-15-00047.