Editorial

The non-responsiveness to anti-vascular endothelial growth factor agents in the treatment of neovascularage-related macular degeneration

Abstract

In this editorial, the definition and potential risk factors of the non-responsiveness to the intravitreal applications of anti-vascular endothelial growth factors in the patients with neovascular age-related macular degeneration were summarized. To know the potential risk factors for the non-responsiveness to these agents may prevent unnecessary treatment interventions and unrealistic patient expectations.

Keywords: anti-vascular endothelial growth factor, age-related macular degeneration, non-responsiveness, definition, non-responders, potential risk factors

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Abbreviations: Anti-VEGF, anti-vascular endothelial growth factor; n-AMD, neovascular age-related macular degeneration; BVCA, best corrected visual acuity; PED, pigment epithelium detachment

Editorial

The anti-vascular endothelial growth factor (anti-VEGF) agents including bevacizumab, ranibizumab, and aflibercept have been widely used in the current treatment of neovascular age-related macular degeneration (n-AMD), and they are beneficial in most n-AMD patients.[1–5] However, some patients cannot respond to the treatment as expected. In recent studies, it has been showed that the incidence for non-responsiveness to bevacizumab in treatment naïve n-AMD ranges between approximately 40 and 50% while as the percent of non-responsiveness to ranibizumab was between approximately 10-20%.[6–9] Although there is currently no more evidence in the literature, a recent report demonstrated that the rates of non-responsiveness to aflibercept in the treatment of n AMD based on best corrected visual acuity (BVCA) and fundus findings were approximately 8% and 13%, respectively.[10]

The absence of expected response to an anti-VEGF agent has been named in different forms as "incomplete response, poor response, non-response, unresponsive, tolerance, tachyphylaxis, rebound, treatment resistant, refractory to anti-VEGF, resistance to anti-VEGF" in current ophthalmology literature.[11] However, non responsiveness is exactly different from above mentioned most nomenclatures. If the mistaken diagnosis, tachyphylaxis, and complications secondary to the drug's itself or its application were excluded, the non-responsiveness to intravitreal anti-VEGF injection in the treatment of n-AMD is defined as the loss (more than 0.2 or 5 letters) or no change in BVCA compared to baseline with persistent macular hemorrhage in fundus examination, intraretinal or subretinal fluid on optical coherence tomography and the leakage in fluorescein angiography despite to a protocol including 3 or 6 consecutive monthly intravitreal anti-VEGF injections.[6–12] However, there is no consensus on the defining of the non responsiveness. In the light of the recent reports, it can be considered that the potential risk factors for non-responsiveness to anti-VEGF agent in the treatment of n-AMD are an initial lesion with subfoveal fibrosis or atrophy in retina pigment epithelium and photoreceptors, lesion in large size, type 1 choroidal neovascularization, serous pigment epithelium detachment (PED), haemorrhagic PED, fibrovascular PED, polypoidal choroidal vasculopathy, foveal scarring and vitreomacular traction, outer retinal tubulation, cystoid degeneration in outer retina, genetic disposition or an anti-VEGF resistance (Table 1).[13-22]

Table 1 The possible risk factors for non-responsiveness to anti-VEGF agents in the patients with nAMD[6–22]

Possible risk factor for non-responsiveness
Subfoveal fibrosis/scarring
Atrophy in RPE and photoreceptors
Large lesion size
Type 1 CNV
Serous PED
Hemorrhagic PED
Fibrovascular/vascular PED
PCV
VMT
ORT
Cystoid degeneration in outer retina
Genetic disposition
Anti-VEGF resistance

Table Abbreviations: RPE, retina pigment epithelium; CNV, choroidal neo-vascularization; PED, pigment epithelium detachment; PCV, polypoidal choroidal vasculopathy; VMT, vitreo-macular traction; ORT, outer retinal tubulation; Anti-VEGF, anti-vascular endothelial growth factor

Conclusion

To know the definition and the potential risk factors of the anti-VEGF non responsiveness in the treatment of n-AMD would prevent unnecessary treatment interventions, unrealistic patient expectations, and economic consumption.

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None.

Conflicts of interest

The authors declare there are no conflicts of interest.

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