Intravitreal bevacizumab and cardiovascular risk in patients with age-related macular degeneration: systematic review and meta-analysis of randomized controlled trials and observational studies

Ivana Mikačić¹, Damir Bosnar²

¹ Department of Internal Medicine, Clinical Pharmacology Unit, University Hospital “Sveti Duh”, Zagreb, Croatia

² University Eye Clinic, University Hospital "Sveti Duh", Zagreb, Josip Juraj Strossmayer University of Osijek, Croatia
Figure S1. Forest plot summarizing meta-analysis of incidence of all-cause mortality (all-cause death) and vascular mortality (death vascular) across individual bevacizumab arms in randomized controlled trials (RCT), case-series and non-randomized controlled studies (non-rand) depicted in Table 3 in the main text. Pooled estimates were generated whenever ≥2 bevacizumab arms were available from studies with similar general design, duration and the same exclusion or non-exclusion of patients with a pre-existing cerebrovascular disease burden (CVD excl?). Study duration in months (mo) is also depicted as well as the average number of delivered doses. Random-effects meta-analysis of proportions was performed using the Freeman-Tukey double-arcsine transformation. Pooled estimates are back-transformed to proportions. When only one arm was available for the “design-by-duration-by-patient exclusion” subset, proportions with the exact Clopper-Person 95% CI are presented. Particulars of such single arms are depicted in bold font. Pooled estimates are also bolded. Studies contributing bevacizumab arms are identified by the author or study name (for brevity). All references are listed in the main text.
Figure S2. Forest plot summarizing meta-analysis of incidence of myocardial infarction (MI) and stroke across individual bevacizumab arms in randomized controlled trials (RCT), case-series and non-randomized controlled studies (non-rand) depicted in Table 3 in the main text. Pooled estimates were generated whenever ≥2 bevacizumab arms were available from studies with similar general design, duration and the same exclusion or non-exclusion of patients with a pre-existing cerebrovascular disease burden (CVD excl?). Study duration in months (mo) is also depicted as well as the average number of delivered doses. Random-effects meta-analysis of proportions was performed using the Freeman-Tukey double-arcsine transformation. Pooled estimates are back-transformed to proportions. When only one arm was available for the “design-by-duration-by-patient exclusion” subset, proportions with the exact Clopper-Person 95% CI are presented. Particulars of such single arms are depicted in bold font. Pooled estimates are also bolded. Studies contributing bevacizumab arms are identified by the author or study name (for brevity). All references are listed in the main text.
Figure S3. Forest plot summarizing meta-analysis of incidence of atherothrombotic events (ATE), venous thromboembolism (VTE), hypertension and heart failure across individual bevacizumab arms in randomized controlled trials (RCT), case-series and non-randomized controlled studies (non-rand) depicted in Table 3 in the main text. Pooled estimates were generated whenever ≥2 bevacizumab arms were available from studies with similar general design, duration and the same exclusion or non-exclusion of patients with a pre-existing cerebrovascular disease burden (CVD excl?). Study duration in months (mo) is also depicted as well as the average number of delivered doses. Random-effects meta-analysis of proportions was performed using the Freeman-Tukey double-arcsine transformation. Pooled estimates are back-transformed to proportions. When only one arm was available for the “design-by-duration-by-patient exclusion” subset, proportions with the exact Clopper-Person 95% CI are presented. Particulars of such single arms are depicted in bold font. Pooled estimates are also bolded. Studies contributing bevacizumab arms are identified by the author or study name (for brevity). All references are listed in the main text.