# Retina Roundup

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1) BioDrugs (2022 Mar 1) doi: 10.1007/s40259-022-00516-y.

## EFFECT MODIFICATION BY INDICATION TO THE RISKS OF MAJOR THROMOEMBOLIC ADVERSE EVENTS IN PATIENTS RECEIVING INTRAVITREAL ANTI-VEGF TREATMENT: A POPULATION-BASED RETROSPECTIVE COHORT STUDY

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**Background:** The association between intravitreal anti-vascular endothelial growth factor (anti-VEGF) treatment and the risk of major thromboembolic adverse events (TAEs) remains under debate. This study aimed to examine associated risks of TAEs in patients receiving intravitreal anti-VEGF treatment, and effect modification by different indications.

**Methods:** This retrospective cohort study analyzed Taiwan's National Health Insurance Database during 2011-2017 to identify neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME) ,patients newly receiving intravitreal aflibercept or ranibizumab. We followed up patients for 2 years, or until the occurrence of TAEs, including ischemic heart disease, ischemic stroke, transient ischemic attack, deep vein thrombosis, and pulmonary embolism, death, or the end of the study period.We examined statistical interactions between the anti-VEGF treatment (i.e., ranibizumab and aflibercept) and indications (i.e., nAMD and DME) with regard to the outcome of TAEs.

**Results:** We included 12,215 nAMD and 7532 DME patients. Among nAMD patients, those receiving aflibercept had lower risk of TAEs (adjusted hazard ratio [HR] 0.85; 95% CI 0.77-0.94) compared with those receiving ranibizumab. However, among DME patients, those receiving aflibercept had no differences in the risk of TAEs (1.14; 0.97-1.35) compared with those receiving ranibizumab. Among patients treated with ranibizumab, the DME group had a higher risk of TAEs than the nAMD group (HR 1.15; 95% CI 1.03-1.28); similar results were observed in patients treated with aflibercept (HR 1.53; 95% CI 1.27-1.85). When DME patients were treated with aflibercept, the risk of TAEs was 31% higher than when nAMD patients were treated with ranibizumab (HR 1.31; 95% CI 1.09-1.56; $p < 0.05$).

**Conclusions:** Patients treated with aflibercept or ranibizumab for different indications may be associated with varying risk of TAEs. The findings provide evidence to support treatment selection, taking indications and TAE risk into consideration.

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## SUB-TENON'S CAPSULE TRIAMCINOLONE ACETONIDE INJECTION TO PREVENT BROLUCIZUMAB-ASSOCIATED INTRAOCULAR INFLAMMATION

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**PURPOSE:** To investigate the efficacy of sub-Tenon's capsule triamcinolone acetonide (STTA) injections for preventing development of intraocular inflammation (IOI) related to intravitreal injection (IVI) of brolucizumab for neovascular age-related macular degeneration (nAMD).

**METHODS:** Consecutive patients with nAMD treated with brolucizumab IVIs were studied retrospectively. All eyes treated with brolucizumab in the clinic were switched from another anti-vascular endothelial growth factor agent. After the fourth case of IOI related to brolucizumab IVI, all eyes treated with brolucizumab received a STTA injection. The patients were divided into two groups: brolucizumab alone and brolucizumab combined with a STTA injection.

**RESULTS:** Forty-four eyes (44 patients) treated with at least one brolucizumab IVI were studied: 14 eyes received brolucizumab IVI alone and 30 eyes received the combination therapy. IOI related to brolucizumab IVIs developed in four (28.6%) of 14 eyes in the brolucizumab group; IOI was severe in one eye, moderate in two eyes, and mild in one eye according to the HAWK and HARRIER trial definition; IOI did not develop in the 30 eyes that received combination therapy, the difference of which reached significance ($p = 0.012$). Regarding combination therapy, the intraocular pressure in three (10%) eyes increased to 22 to about 26mmHg after the STTA injection and returned to normal range within 2months without medication; no cataracts developed during this short mean follow-up period follow-up period of $7.1 \pm 0.4$ months.

**CONCLUSION:** The results indicated the possible preventative effect of a STTA injection on development of brolucizumab-associated IOI

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## EPIMACULAR BRACHYTHERAPY FOR PREVIOUSLY TREATED NEOVASCULAR AGE-RELATED MACULAR DEGENERATION: MONTH 36 RESULTS OF THE MERLOT RANDOMISED CONTROLLED TRIAL

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**BACKGROUND:** To assess the long-term safety and efficacy of epimacular brachytherapy (EMB) for chronic, active, neovascular age-related macular degeneration (nAMD).

**METHODS:** This pivotal, randomised, controlled surgical device trial recruited patients with chronic nAMD receiving intravitreal ranibizumab from 24 UK hospitals. Participants were randomised to either pars plana vitrectomy with 24 Gray EMB and (PRN) ranibizumab (n=224) or PRN ranibizumab monotherapy (n=119). Although masking was not possible, masked clinicians assessed best-corrected visual acuity (BCVA) and imaging. After month 24, participants reverted to standard care, with either ranibizumab or aflibercept, returning for a month 36 study visit.

**RESULTS:** Of 363 participants, 309 (85.1%) completed month 36. The number of injections was 12.1±8.1 in the EMB group versus 11.4±6.1 in the ranibizumab group (difference 0.7, 95% CI of difference -0.9 to 2.3, p=0.41) between months 1 and 36, and 3.6±3.3 (n=200) versus 3.9±2.7 (n=102) (difference -0.3, 95% CI of difference -1.0 to 0.4, p=0.43) between months 25 and 36 (standard care). Over 36 months, BCVA change was -19.7±18.5 letters in the EMB group and -4.8±12.5 in the ranibizumab group (difference -14.9, 95% CI of difference -18.5 to -11.2, p<0.0001). The month 36 BCVA of 20 EMB-treated participants with microvascular abnormalities (MVAs) at month 24 was similar to EMB-treated participants without MVAs (-21.8 vs -19.4 letters, p=0.65).

**CONCLUSION:** EMB does not reduce the number of anti-vascular endothelial growth factor (VEGF) injections, either within or outside of a trial setting, and is associated with worse BCVA than anti-VEGF monotherapy.

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# FINE PARTICULATE MATTER MEASURED BY SATELLITES PREDICTS THE RISK OF AGE-RELATED MACULAR DEGENERATION IN A LONGITUDINAL COHORT STUDY

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## Abstract

Although studies have revealed that ambient particulate matter (PM) has detrimental effects on the ocular surface, there have been limited reports detailing the effect of ambient PM on the posterior segment of the eye.

A large-scale longitudinal cohort study evaluating the association between fine PM, especially PM2.5, and the retina could elucidate the risk of ambient pollutants for retinal diseases. 7 they investigated the association between PM2.5 and the development of age-related macular degeneration (AMD). We conducted a population-based cohort study of 4,284,128 participants in Taiwan between 2001 and 2011.

PM2.5 was continuously measured by satellites and subsequently assigned to each geographic district along with its postcode. & evaluate the dose-response relationship between PM2.5 and AMD development. The annual mean of PM2.5 exposure was 34.23 ± 7.17 μg/m3. The PM2.5 concentrations were highest in spring, followed by those in winter, autumn, and summer. Twelve thousand ninety-five new AMD cases were reported during the study period. After adjusting for covariates, the AMD risk increased by 19% (95% confidence interval 1.13-1.25) for a 10 μg/m3 PM2.5 increase.

The present study demonstrated that chronic exposure to PM2.5 increases the risk of AMD. Almost half of the Taiwanese live in a polluted area where the PM2.5 levels are higher than the World Health Organization recommended air quality guideline of 10 μg/m3 had a 1.4-fold risk, which significantly increases concern about their visual health and social burden.

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## VITRECTOMY FOR DIABETIC COMPLICATIONS: A POOLED ANALYSIS OF RANDOMIZED CONTROLLED TRIALS UTILIZING MODERN TECHNIQUES AND EQUIPMENT

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**PURPOSE**: To report updated clinical outcomes in subjects undergoing pars plana vitrectomy (PPV) using modern techniques and equipment for the treatment of proliferative diabetic retinopathy (PDR)-related complications.

**DESIGN:** Pooled analysis of 5 randomized clinical trials conducted at the same institution and included both study and control subjects from the trials. There were 943 subjects who prospectively underwent small-gauge PPV with anti-vascular endothelial growth factor (VEGF) pretreatment for PDR-related complications and completed 6-months follow up.

**RESULTS:** The visual acuity of the study population improved from median 2.00 (IQR 1.3, 2.3) at baseline to median 1.00 (IQR 0.5, 1.3) at 6 months. One hundred eighty-four patients (19.5%) achieved 20/50 or better acuity, and 652 patients (69.1%) achieved 20/200 or better acuity at 6 months. The vision improved or remained stable in 901 patients (95.5%), and 11 patients (1.2%) developed no light perception at 6 months. Intraoperative complications occurred in 343 cases (36.4%) of cases, and 199 cases (21.1 %) experienced a postoperative complication. The most common postoperative complication was vitreous hemorrhage in 124 cases (62.3% of all complications). Unplanned secondary PPV was necessary in 86 cases (9.1 %).

**CONCLUSIONS:** This study reports updated clinical outcomes in patients undergoing PPV for PDR-related complications which compares favourably to the age prior to small-gauge PPV and anti-VEGF pre-treatment.

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