Retina Roundup

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The inflammatory potential of diet is associated with the risk of age-related eye diseases

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Background & aims: Inflammation is involved in the pathogenesis of cataract, age-related macular degeneration (AMD), and possibly open-angle glaucoma (OAG). We assessed whether the inflammatory potential of diet (quantified using the dietary inflammatory index; DII) affects the incidence of these common blinding age-related eye diseases. Serum inflammation markers were investigated as possible mediators.

Methods: Participants aged >45 years were selected from the prospective, population-based Rotterdam Study. From 1991 onwards, every 4-5 years, participants underwent extensive eye examinations. At baseline, blood samples and dietary data (using food frequency questionnaires) were collected. The DII was adapted based on the data available. Of the 7436 participants free of eye diseases at baseline, 4036 developed incident eye diseases during follow-up (cataract = 2895, early-intermediate AMD = 891, late AMD = 81, OAG = 169).

Results: The adapted DII (aDII) ranged from -4.26 (i.e., anti-inflammatory) to 4.53 (i.e., pro-inflammatory). A higher aDII was significantly associated with increased inflammation. A higher neutrophil-lymphocyte ratio (NLR) was associated with an increased risk of cataract and AMD. Additionally, complement component 3c (C3c) and systemic immune-inflammation index (SII) were associated with increased risks of cataract and late AMD, respectively. Every point increase in the aDII was associated with a 9% increased risk of cataract (Odds ratio [95% confidence interval]: 1.09 [1.04-1.14]). The NLR and C3c partly mediated this association. We also identified associations of the aDII with risk of AMD (early-intermediate AMD, OR [95% CI]: 1.11 [1.03-1.19]; late AMD, OR [95% CI]: 1.24 [1.02-1.53]). The NLR partly mediated these associations. The aDII was not associated with OAG.

Conclusions: A pro-inflammatory diet was associated with increased risks of cataract and AMD. Particularly the NLR, a marker of subclinical inflammation, appears to be implicated. These findings are relevant for patients with AMD and substantiate the current recommendations to strive for a healthy lifestyle to prevent blindness.

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Pegcetacoplan for the treatment of geographic atrophy secondary to age-related macular degeneration (OAKS and DERBY): two multicentre, randomised, double-masked, sham-controlled, phase 3 trials

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Background: Geographic atrophy is a leading cause of progressive, irreversible vision loss. The objectives of OAKS and DERBY were to assess the efficacy and safety of pegcetacoplan compared with sham treatment in patients with geographic atrophy.

Methods: OAKS and DERBY were two 24-month, multicentre, randomised, double-masked, sham-controlled, phase 3 studies, in which patients aged 60 years and older with geographic atrophy secondary to age-related macular degeneration were enrolled at 110 clinical sites and 122 clinical sites worldwide, respectively. Patients were randomly assigned (2:2:1:1) by central web-based randomisation system to intravitreal 15 mg per 0·1 mL pegcetacoplan monthly or every other month, or sham monthly or every other month using stratified permuted block randomisation (stratified by geographic atrophy lesion area at screening, history or presence of active choroidal neovascularisation in the eye not under assessment, and block size of six). Study site staff, patients, reading centre personnel, evaluating physicians, and the funder were masked to group assignment. Sham groups were pooled for the analyses. The primary endpoint was the change from baseline to month 12 in the total area of geographic atrophy lesions in the study eye based on fundus autofluorescence imaging, in the modified intention-to-treat population (ie, all patients who received one or more injections of pegcetacoplan or sham and had a baseline and at least one post-baseline value of lesion area). Key secondary endpoints (measured at 24 months) were change in monocular maximum reading speed of the study eye, change from baseline in mean functional reading independence index score, change from baseline in normal luminance best-corrected visual acuity score, and change from baseline in the mean threshold sensitivity of all points in the study eye by mesopic microperimetry (OAKS only). Safety analyses included patients who were randomly assigned and received at least one injection of pegcetacoplan or sham. The now completed studies are registered with ClinicalTrials.gov, NCT03525613 (OAKS) and NCT03525600 (DERBY).

Findings: Between Aug 30, 2018, and July 3, 2020, 1258 patients were enrolled in OAKS and DERBY. The modified intention-to-treat populations comprised 614 (96%) of 637 patients in OAKS (202 receiving pegcetacoplan monthly, 205 pegcetacoplan every other month, and 207 sham) and 597 (96%) of 621 patients in DERBY (201 receiving pegcetacoplan monthly, 201 pegcetacoplan every other month, and 195 sham). In OAKS, pegcetacoplan monthly and pegcetacoplan every other month significantly slowed geographic atrophy lesion growth by 21% (absolute difference in least-squares mean -0·41 mm2, 95% CI -0·64 to -0·18; p=0·0004) and 16% (-0·32 mm2, -0·54 to -0·09; p=0·0055), respectively, compared with sham at 12 months. In DERBY, pegcetacoplan monthly and pegcetacoplan every other month slowed geographic atrophy lesion growth, although it did not reach significance, by 12% (-0·23 mm2, -0·47 to 0·01; p=0·062) and 11% (-0·21 mm2, -0·44 to 0·03; p=0·085), respectively, compared with sham at 12 months. At 24 months, pegcetacoplan monthly and pegcetacoplan every other month slowed geographic atrophy lesion growth by 22% (-0·90 mm2, -1·30 to -0·50; p<0·0001) and 18% (-0·74 mm2, -1·13 to -0·36; p=0·0002) in OAKS, and by 19% (-0·75 mm2, -1·15 to -0·34; p=0·0004) and 16% (-0·63 mm2, -1·05 to -0·22; p=0·0030) in DERBY, respectively, compared with sham. There were no differences in key secondary visual function endpoints at 24 months. Serious ocular treatment-emergent adverse events were reported in five (2%) of 213, four (2%) of 212, and one (<1%) of 211 patients in OAKS, and in four (2%) of 206, two (1%) of 208, and two (1%) of 206 patients in DERBY receiving pegcetacoplan monthly, pegcetacoplan every other month, and sham, respectively, at 24 months. New-onset exudative age-related macular degeneration was reported in 24 (11%), 16 (8%), and four (2%) patients in OAKS, and in 27 (13%), 12 (6%), and nine (4%) patients in DERBY receiving pegcetacoplan monthly, pegcetacoplan every other month, and sham, respectively, at 24 months.

Interpretation: Pegcetacoplan, the first treatment approved by the US Food and Drug Administration for geographic atrophy, slowed geographic atrophy lesion growth with an acceptable safety profile.

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Efficacy and safety of avacincaptad pegol in patients with geographic atrophy (GATHER2): 12-month results from a randomised, double-masked, phase 3 trial

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Background: Geographic atrophy is an advanced form of dry age-related macular degeneration that can lead to irreversible vision loss and high burden of disease. We aimed to assess efficacy and safety of avacincaptad pegol 2 mg in reducing geographic atrophy lesion growth.

Methods: GATHER2 is a randomised, double-masked, sham-controlled, 24-month, phase 3 trial across 205 retina clinics, research hospitals, and academic institutions globally. To be eligible, patients had to be aged 50 years or older with non-centrepoint-involving geographic atrophy and best corrected visual acuity between 20/25 and 20/320 in the study eye. Eligible patients were randomly assigned (1:1) to monthly avacincaptad pegol 2 mg administered as a 100 µL intravitreal injection or sham for the first 12 months. Randomisation was performed using an interactive response technology system with stratification by factors known to be of prognostic importance in age-related macular degeneration. Patients, investigators, study centre staff, sponsor personnel, and data analysts were masked to treatment allocation. The primary endpoint was geographic atrophy lesion size measured by fundus autofluorescence at baseline, month 6, and month 12. Efficacy and safety analyses were done in the modified intention-to-treat and safety populations, respectively. This trial is registered with ClinicalTrials.gov, NCT04435366.

Findings: Between June 22, 2020, and July 23, 2021, 1422 patients were screened for eligibility, of whom 448 were enrolled and randomly assigned to avacincaptad pegol 2 mg (n=225) or sham (n=223). One patient in the sham group did not receive study treatment and was excluded from analyses. There were 154 (68%) female patients and 71 (32%) male patients in the avacincaptad pegol 2 mg group, and 156 (70%) female patients and 66 (30%) male patients in the sham group. From baseline to month 12, the mean rate of square-root-transformed geographic atrophy area growth was 0·336 mm/year (SE 0·032) with avacincaptad pegol 2 mg and 0·392 mm/year (0·033) with sham, a difference in growth of 0·056 mm/year (95% CI

0·016-0·096; p=0·0064), representing a 14% difference between the avacincaptad pegol 2 mg group and the sham group. Ocular treatment-emergent adverse events in the study eye occurred in 110 (49%) patients in the avacincaptad pegol 2 mg group and 83 (37%) in the sham group. There were no endophthalmitis, intraocular inflammation, or ischaemic optic neuropathy events over 12 months. To month 12, macular neovascularisation in the study eye occurred in 15 (7%) patients in the avacincaptad pegol 2 mg group and nine (4%) in the sham group, with exudative macular neovascularisation occurring in 11 (5%) in the avacincaptad pegol 2 mg group and seven (3%) in the sham group.

Interpretation: Monthly avacincaptad pegol 2 mg was well tolerated and showed significantly slower geographic atrophy growth over 12 months than sham treatment, suggesting that avacincaptad pegol might slow disease progression and potentially change the trajectory of disease for patients with geographic atrophy.

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Early surgical displacement of submacular hemorrhage without tissue plasminogen activator use: one-year outcomes

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Objective: This study evaluated changes in best-corrected visual acuity and submacular hemorrhage (SMH) resolution in eyes after a single rapid subretinal displacement surgery using subretinal balanced saline solution and sterile air without tissue plasminogen activator (tPA).

Design: A retrospective comparative interventional analysis.

Participants: Twenty-six eyes with thick SMH who underwent pars plana vitrectomy and subretinal fluid displacement without tPA from 2015 and 2021 and at least 1-year of follow-up.

Methods: Surgical intervention included a standard small-gauge pars plana vitrectomy with subretinal displacement using balanced saline solution with subretinal sterile air and partial gas-air fluid exchange. Main outcome measures included degree of subfoveal SMH displacement, best and final postoperative visual acuities, and adverse events. Snellen acuity was converted to logMARs for statistical analysis.

Results: The most common etiology associated with thick SMH (92.3%) was neovascular age-related macular degeneration. Within 1 month postoperatively, 21 patients (80.8%) saw complete subfoveal blood displacement. Most of the SMH surgical displacements were done within 1 week of presenting symptoms. Average preoperative duration of SMH was 3.60 ± 2.78 days (range, 1-12 days). Mean logMAR best-corrected visual acuity improved from 1.63 ± 0.58 (Snellen 20/800 baseline) to 0.90 ± 0.42 letters (Snellen 20/160) at last follow-up ($p = 0.001$). This study's visual acuity improvement is comparable with that of prior studies using tPA. Early postoperative complications included 1 retinal detachment, 1 vitreous hemorrhage, and 1 macular hole.

Conclusion: Rapid surgery with subretinal balanced saline solution-sterile air injection without tPA was found to be effective for displacement of thick SMH with retinal function, visual acuity, and corneal refractive therapy improvement.

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5) Medicine (Baltimore). 2023 Nov 3;102(44):e35888.
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Effect of microaneurysms on the anti-VEGF treatment for diabetic macular edema: A retrospective cross-sectional study

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Abstract: Although anti-vascular endothelial growth factor (VEGF) treatment is effective for treating diabetic macular edema (DME), the effect of the microaneurysm (MA) status on the therapeutic efficacy of an anti-VEGF treatment remains unclear. Our current study investigated the effects of the number and the presence or absence of leaking MAs on DME and the efficacy of anti-VEGF therapy. A total of 51 eyes of 47 DME patients were administered anti-VEGF treatment. Fluorescence angiography results were used to determine the number of MAs and the presence or absence of leakage, with these findings matched to the optical coherence tomography maps. The correlation between the number of MAs and the retinal thicknesses and the influence of the leaking MAs was examined in order to definitively determine the effect of the anti-VEGF treatment. There was a correlation between the number of MAs and the retinal thickness of the sector in both the 6 mm (correlation coefficients: 0.42) and 3 mm (0.34) sectors ($P < .001$). There was also a correlation between the number of MAs and the retinal thickness in both the 6 mm (0.31) and 3 mm (0.24) sectors after undergoing the treatment ($P < .01$). There was a significant difference between the mean thickness of the leaking versus the non-leaking MAs in the 6 mm (388 ± 87 μm) and 3 mm (477 ± 108 μm) sectors before treatment ($P < .01$). There was also a significant difference for the retinal thickness between the sectors with and without leaking MAs after the treatment ($P < .01$). The degree of retinal edema before treatment is associated with the number of MAs and the presence of leaking MAs. Anti-VEGF treatment is less effective for focal macular edema with large numbers of MAs, which includes leaking MAs.PMCID: PMC10627656

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