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HIGHLIGHTS OF ADVANCES IN MEDICAL RETINA FROM THE VIRTUAL WORLD OPHTHALMOLOGY CONGRESS 2020

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SUMMARY

The World Ophthalmology Congress (WOC) is one of the largest international ophthalmology conferences, taking place every two years. The event this year was the first of its kind, held as a virtual summit due to the Covid-19 pandemic. There were over 2000 talks from world experts, a virtual industry exhibition including free papers, e-posters, live symposia and presentations. Medical retina is a subspecialty in which exciting and innovative advances in research were presented. The topics covered included the use of Conbercept for Polypoidal Choroidal Vasculopathy, Faricimab in Diabetic Macular Oedema and neovascular Age Related Macular Degeneration (nAMD), Brolucizumab, Aflibercept and Port Delivery Systems in nAMD, amongst many others. Medical retina continues to be a rapidly advancing field within ophthalmology with new research findings having great implications for treatment burden and service delivery. This report summaries the highlights of advances within the medical retina subspecialty from free papers in WOC 2020.

Key words: ophthalmology, diabetic macular oedema; congress

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INTRODUCTION

The World Ophthalmology Congress (WOC) is one of the largest international conferences; this event takes place every two years, and this year was planned for 26-29 June. The WOC 2020 was the first of its kind, and due to the Covid-19 pandemic it took place in the form of a virtual meeting. The conference incorporated interactive symposia, free contributions, e-posters and presentations across all the sub-specialisations in the field of ophthalmology. In this report we present the exciting and innovative advances presented during the course of three days in the form of free contributions within the framework of the sub-specialisation of medical retina.

Conbercept for the treatment of polypoidal choroidal vasculopathy

Heier et al. presented the meta-analysis and trial STAR, focusing on the Conbercept preparation, a new antidote to vascular endothelial growth factor (VEGF), which is the subject of evaluation due to its potential in the treatment of polypoidal choroidal vasculopathy (PCV) [1]. With the use of Ranibizumab as the standard referential preparation, a total of 26 studies were evaluated within the framework of the meta-analysis. Best corrected visual acuity (BCVA), central retinal thickness and the degree of polyp regression were evaluated. Although no statistically significant difference was demonstrated between the preparations Conbercept and Ranibizumab, as regards central retinal thickness or BCVA, the degree of polyp regression in the 12th month was higher in the case of Conbercept ($p = 0.014$), which attests to a better long-term effect in connection with this new preparation.

The same authors further discussed the results from the 4th phase of the START study in the treatment of 246 naive patients with wet form age-related macular degeneration (wAMD) accompanied with PCV [1]. The subjects were randomised into groups with a fixed dosage of the Conbercept preparation, and with dosing in a regimen of treatment with extension of the intervals between the individual doses (T&E). Both groups attained similar results with regard to BCVA and retinal thickness in the 48th week; regression of polyps was

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greater in the T&E group, but this difference is not statistically significant. Studies document that the Conbercept preparation is not superior with regard to PCV, but it has certain long-term advantages in comparison with Ranibizumab; however, further research observing patients over a longer time period will be necessary for an assessment of these advantages.

Faricimab as a new substance in the treatment of diabetic macular edema and wet form age-related macular degeneration

Lopez et al. presented their results from the 2nd phase of the multicentric, prospective clinical trial BOULEVARD, which examined Faricimab in the treatment of 168 naive patients with diabetic macular edema (DME) [2]. Faricimab is the first bio-specific antidote for intraocular use focusing on VEGF-A and angiopoietin-2 (Ang-2). Ang-2 is a promoter of vascular destabilisation, infiltration and inflammation, leading to apoptosis of pericytes in hyperglycaemia. The patients were randomised in the ration of 1:1:1 intro groups of treatment with intravitreal Faricimab 1.5 mg, Faricimab 6.0 mg or Ranibizumab 0.3 mg, administered every four weeks (Q4W) for a period of 20 weeks. The primary results (baseline versus values in the 24th week) evaluated the change of BCVA and improvement of diabetic retinopathy (DR) with the use of the Diabetic Retinopathy Severity Scale (DRSS) from the Early Treatment Diabetic Retinopathy Study (ETDRS). The majority of patients initially had non-proliferative DR (DRSS 43/47/53). The study demonstrated that the patients who received treatment with Faricimab attained an improvement on the DRSS of > 2 degrees (27.6 % of patients, dose 1.5 mg; 38.5 % of patients, dose 6 mg) in the 24th week, in comparison with patients treated with 0.3 mg Ranibizumab (12.2%). In future, concurrent inhibition of Ang-2 and VEGF-A may play a role in improving results in patients with DR and diabetic macular edema.

Khoramnia et al. presented the results of the 2nd phase of the multicentric, randomised, controlled clinical trial STAIRWAY, which observed Faricimab and its effectiveness on patients with wAMD [3]. The trial incorporated 78 patients with wAMD and subfoveolar choroidal neovascularisation (CNV), who were randomised into groups with Faricimab and Ranibizumab. The authors demonstrated comparable results upon dosage of Faricimab in Q16W and Q12W, and Ranibizumab Q4W in terms of BCVA and the size of CNV lesions. Faricimab may be effective for an extended period in patients in comparison with Ranibizumab, which is evidence that has significant impacts for the clinical treatment of patients.

Port delivery systems for administration of pharmaceuticals in wet form age-related macular degeneration

The second phase of the LADDER trial, presented by Dhoot et al., evaluated the advantages of a port delivery system (PDS) for administering pharmaceuticals with Ranibizumab in the treatment of wAMD [4]. The trial examined 3 adjusted dosages of Ranibizumab administered by means of PDS (10, 40, 100 mg/ml) in comparison with Ranibizumab 0.5 mg administered once per month on a sample of 220 patients. It was demonstrated that PDS maintained visual and anatomical results over an average study period of 22 months. The median time for the first reapplication was 8.7 months, 13.0 months and 15.8 months in the case of the branch of PDS containing 10, 40 and 100 mg/ml respectively. In the case of the branch of PDS 100 mg/ml, 79.8 % and 59.4 % did not request reapplication within a time interval of > 6 months and > 12 months respectively. In the 22nd month the median change of BCVA against the baseline values in the case of the branch of PDS 100 mg/ml and the group of Ranibizumab administered once per month attained values of +2.9 and +2.7 letters, and the percentage of patients who maintained visual acuity (loss of < 5 letters as against the baseline value) was 87.5 % and 88.9 % respectively. Intravitreal applications of implants and reapplications were well tolerated in PDS. PDS could significantly extend the time between administration of pharmaceuticals and reduce the burden in connection with treatment of wAMD.

Brolucizumab in wet form age-related macular degeneration

Hamilton from Great Britain presented two prospective clinical trials in the 3rd phase, HARRIER and HAWK, which observed the safety and efficacy of Brolucizumab and Aflibercept in the treatment of naive patients with wAMD [5]. The activity of the pathology was evaluated for 3 mg and 6 mg of Brolucizumab with a dosing regimen of Q12W and 2 mg of Aflibercept with a dosing regimen of Q8W following a three-month saturation phase. In all three therapeutic branches, Brolucizumab had statically significantly lower activity of the pathology in comparison with Aflibercept within the framework of the HAWK and HARRIER trials ($p < 0.03$ in both). The summary findings of the authors from the HAWK and HARRIER trials indicate that patients with wAMD treated with Brolucizumab 6 mg Q12W/Q8W have better control of the pathology in comparison with Aflibercept.

Shipton et al. present a retrospective study and observe the relationship between wet form AMD and cataract surgery [6]. All the patients had a diagnosis of wet form AMD, and before cataract surgery were administered intravitreal treatment (IVT). Visual acuity and central macular thickness (CMT) were evaluated before surgery and one year after the procedure. Visual acuity was improved in patients with wet form AMD after cataract surgery (+17.7 letters, median +15, range -20 to +54). Patients to whom IVT was applied shortly before surgery showed a greater improvement of visual acuity and greater reduction of CMT. Cataract surgery does not influence the progression of wAMD, and the authors expressed the opinion that it may not be necessary to wait for the stabilisation of wAMD before embarking upon cataract surgery. Furthermore, the absence of a delay to cataract surgery may be an advantage in the sense of

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preventing complications in connection with operation on a mature cataract.

Dosage of Aflibercept preparation within treatment regimen and extension of intervals between individual doses (T&E) in wet form age-related macular degeneration

Wolf et al. presented their conclusions from the third phase of the ARIES clinical trial on patients with wAMD, who were treated with Aflibercept [7]. This multicentric, randomised, controlled global trial incorporating 271 patients evaluated two T&E regimens for Aflibercept – early commencement versus late commencement. At the outset, all patients received intravitreal administration of 2 mg Aflibercept (IVT-AFL) in a dosing regimen of Q0W, Q4W, Q8W and Q16W. The patients were then randomised into a group with a branch for early commencement (regimen IVT-AFL T&E extended by 2 or 4 weeks [maximally up to 16 weeks]) or with a branch for late commencement (IVT-AFL over a period of 1 year every 8 weeks, followed by T&E). The results in the 104th week demonstrated a virtually equivalent improvement with regard to the number of letters (+4.3 vs. +7.9 ETDRS letters), median number of injection applications (12.0 vs. 13.0), change of CMT (-162 µm and -159 µm), and last injection interval of > 12 weeks (47.2 % and 51.9 %) between the T&E regimens of early and late commencement. These results offer alternative regimens of treatment for doctors who intend to introduce a therapeutic regimen of T&E.

Prediction of hydroxycholoroquine toxicity

Hasan et al. from the United Kingdom used a logistic regression method for the diagnosis and prediction of factors influencing hydroxychloroquine-induced maculopathy [8]. The volume of the outer nuclear layer (ONL) was measured with the use of spectral optical coherence tomography (Heidelberg, spectralis) in 143 eyes of 73 patients on hydroxychloroquine (median age 62 years; 81.9 % women). A strong negative correlation was demonstrated between the volume of the ONL and the probability of toxicity with an average time of use of 6.3 years (sensitivity 94.4 %, specificity 98.8 %, odds ratio 4.1; receiver operating characteristic 0.988). The authors came to the conclusion that reduction of ONL is a precise method for predicting hydroxychloroquine-induced maculopathy, and recommend this tool for future screening.

Central serous choroidal vasculopathy

Brelen et al. presented the findings from a randomised, controlled trial which observed changes of perfusion or absence of flow in the choriocapillaris, indicating possible relative choroidal ischemia in patients with unilateral chronic serous choroiretinopathy (CSCR). A total of 33 patients were randomised into a group with multiple laser therapy (MLT) or photodynamic therapy (PDT), and optical coherence tomography angiography (OCTA) was used for evaluating the regions of non-perfusion in the choroicapillaris at 0, 1, 3 and 6 months [9]. Both groups recorded a significant reduction of average subfoveolar choroidal volume in all the above points in time. The regions signalling non-perfusion were significantly reduced at 6 months ($p = 0.005$) in the MLT group and at 1 month ($p = 0.049$) in the PDT group. However, patients in the PDT group showed smaller regions of non-perfusion than patients from the MLT group at all points in time after treatment ($p = 0.001$, dispersion analysis). This study demonstrated that PDT has a stronger influence than MLT upon normalisation of the perfusion parameters in the choriocapillaris.

CONCLUSIONS

Medical retina continues to be a rapidly developing branch in the field of ophthalmology, with significant impacts on the burdens placed both on the patient and on the centre providing this treatment. In the majority of centres, the provision of a certain level of treatment of retinal pathologies is continuing despite the COVID-19 pandemic, because this concerns continuous therapy in order to preserve sight. Recent studies have demonstrated promising potential and confirmed that several new therapies are on the horizon for the treatment of retinal pathologies. Studies incorporating these therapies and their introduction into clinical practice may now be delayed as a consequence of the unforeseeable global impacts of the COVID-19 pandemic. Despite the challenges presented to us today by COVID-19, the innovative form of organisation of the World Ophthalmology Congress 2020 ensured that research and clinical experiences can continue to be shared globally between clinical doctors.

Thanks

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