Information

Expert Consensus

Management of patients with chronic retinal diseases in the current conditions of the COVID-19 pandemic in the world and in Ukraine

Moderator:

Korol Andrii R.— Doctor of Medical Sciences, The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences (NAMS) of Ukraine, Head of Laser Department (Odesa)

Members:

Bezditko Pavlo A. — Doctor of Medical Sciences, Professor, Chair of Department of Ophthalmology, Kharkiv National Medical University (Kharkiv).

Bezkorovayna Iryna M. — Doctor of Medical Sciences, Professor, Department of Otorhinolaryngology and Ophthalmology, Ukrainian Medical Stomatological Academy (Poltava)

Zhaboyedov Dmytro G. — Doctor of Medical Sciences, Professor, Chair of Department of Ophthalmology, Bogomolets National Medical University; Medical Ophthalmological Center «Zir 100%» (Kyiv).

Zaychenko Ganna V. — Doctor of Medical Sciences, Professor, Chair of Department of Pharmacology, Bogomolets National Medical University (Kyiv).

Lutsenko Nina S. — Doctor of Medical Sciences, Professor, Chair of Department of Eye Diseases, Zaporizhzhia Medical Academy of Postgraduate Education (Zaporizhzhia).

Sergienko Andrii M. — Doctor of Medical Sciences, Professor, Department of Ophthalmology, National Pirogov Memorial Medical University; “Ophthalmology Clinic of Professor Sergienko” (Vinnytsya).

Ulyanova Nadiya A. — Doctor of Medical Sciences, Professor, Chair of Regional Ophthalmological Center in Volyn Regional Clinical Hospital (Lutsk).

Karliychuk Maryna A. — Doctor of Medical Sciences, Department of Ophthalmology named after B.L. Radzikhovskyi, Bukovinian State Medical University; Chair of Department of Vitreoretinal and Laser Microsurgery, Center of Eye Microsurgery “Vash Zir” (Chernivtsi).

Pavliv Oleksandra B. — MD, PhD, Head of the Ophthalmological Department, Lviv Regional Clinical Hospital, Chief Out-of-Staff Expert in Ophthalmology of the Department of Health Care of the Lviv Regional State Administration (Lviv).

Shevchyk Vasyl I. — MD, PhD, Surgeon-In-Chief, “Vasyl Shevchyk Eye Microsurgery” Clinic (Chernigiv).

On November 18, 2020, the Advisory Board was held in virtual format to discuss the specifics of management of patients with chronic retinal diseases in the current conditions of the COVID-19 pandemic in the world and in Ukraine.

The COVID-19 pandemic has led to a significant decrease in visits to ophthalmology clinics and a reduction in the number of required intravitreal injections in patients with retinal diseases worldwide (El Hamichi S. et al., 2020).

Quarantine restrictions will continue to affect the work of ophthalmologists in varying degrees for a long time ahead. Inadequate ophthalmologic care for patients with chronic retinal diseases can result in partial or complete loss of autonomy for these patients and a significant decline in quality of life (Royal College of Ophthalmologists, 2020).

According to experts, the actual and complete guideline for the management of patients with retinal diseases during the pandemic is Medical Retinal Management Plans during COVID-19 (Royal College of Ophthalmologists, 2020), which was last revised on September 22, 2020. Having analyzed the Medical Retinal Management Plans during COVID-19, the experts made their recommendations, considering the specifics of patient management in the current pandemic conditions in Ukraine.

Thus, according to the Royal College of Ophthalmologists (RCO), in patients with neovascular age-related macular degeneration (nAMD), as a capacity of most clinics has improved, consider moving pre-pandemic protocols. In most cases, this would be a Treat and Extend (T&E) or individualized anti-VEGF treatment regimen. In rare situations, where clinic is still constrained by capacity issues, maintain all patients on fixed 8 weekly anti-VEGF therapy. Such patients may need Optical Coherence Tomography (OCT) and visual acuity assessments and management changed, if deemed appropriate.

Members of the workgroup agreed that in the current pandemic conditions in Ukraine, the use of aflibercept has its advantages in both T&E and fixed protocols. Treatment of patients with nAMD is recommended to start with 3 initial monthly injections of aflibercept, followed by extension of the interval between injections up to two months. If there are no constraints in the clinic and the patient compliance is good, consider switching to T&E to adjust the interval between injections based on each patient's individual need.

Experts disagreed with the RCO recommendation to postpone treatment of patients with diabetic macular edema (DME) for 4-6 months because, according to expert panel members, diabetic patients in Ukraine are much more likely to have insufficient glycemic control compared to patients in the UK. In most cases of patients with visual impairment due to DME, treatment approaches and protocols that were used before the pandemic should be followed. Deciding to initiate treatment, the perceived benefit of treatment / potential risk of SARS-CoV-2 infection should be balanced on an individual basis for each patient. When aflibercept is indicated in patients with DME, treatment should start with 5 monthly consecutive injections followed by injections every two months with the possibility of a further proactive extension of the intervals between injections after 1 year of treatment.

The workgroup endorsed the RCO recommendations for patients with visual impairment due to macular edema secondary to central retinal vein occlusion. Once patient general condition is clarified and medical correction of the cause of the occlusion has been initiated, treatment should be started promptly with monthly anti-VEGF injections until maximum visual acuity and/or disappearance of the disease activity is achieved. However, according to the Advisory Board members, in the current pandemic conditions in Ukraine this approach should also be used in patients with branch retinal vein occlusion. The experts emphasized that aflibercept treatment is effective in patients both with non-ischemic and ischemic types of retinal vein occlusion.

Additionally, the expert group highlighted that anti-VEGF injections should be considered an urgent procedure for diseases such as neovascular age-related macular degeneration, diabetic macular edema, and macular edema due to retinal vein occlusion. In patients with these conditions, it is unacceptable to delay the required intravitreal injections, even in the face of medical facility restrictions.

The experts also consider Guidance on Restarting Medical Retina Services (Royal College of Ophthalmologists, 2020) to be applicable in the current pandemic conditions in Ukraine, according to which, if there are significant limitations in ophthalmological clinic or department services, treatment of patients with nAMD should be considered a priority. There is no need for additional monitoring visits to the clinic between aflibercept injections.

Aflibercept (VEGF Trap-Eye) is an artificial trap-receptor that has multitargeted mode of action, blocking all isoforms of VEGF-A as well as Placental Growth Factor (PGF), unlike other anti-VEGF agents that block only VEGF-A (Papadopoulos N. et al., 2012). The mode of action of aflibercept results in a higher binding affinity to VEGF compared to native receptors and other anti-VEGF agents (Papadopoulos N. et al., 2012).

Aflibercept is known for its long-lasting action: duration of intraocular VEGF suppression with aflibercept is 71±18 days, range: 41-109 days (Fauser S. et al., 2014), that is twice as long as with ranibizumab, 36.4±6.7 days (Muether P.S. et al., 2013). Sustained VEGF-A suppression with aflibercept supports its use in a proactive regimen with intervals of more than 8 weeks (the duration of VEGF suppression is up to 16 weeks) (Fauser S. et al., 2014).

Taking into account the nature of anti-VEGF drugs, it is crucial to maintain temperature storage conditions from 2 to 8 °C. Drug properties may change with freezing, so freezing is not allowed. To preserve the efficacy and safety of anti-VEGF drugs, it is crucial to make sure that

the "cold chain" technology (2 to 8 °C) is maintained by the supplier during transportation as well as during further storage. Warming the drug to room temperature is possible prior to administration, but not for more than 24 hours.

The duration of VEGF suppression during anti-VEGF treatment is unique to each patient, suggesting using of individualized, proactive regimen such as T&E. Considering the differences in the features of anti-VEGF drugs, the proportion of patients with nAMD who, according to the randomized clinical trials data, were able to reach ≥ 12-week interval between injections in T&E regimen also differs.

In LUCAS study, only 17% patients who received ranibizumab T&E and 10% patients who received bevacizumab T&E were able to reach 12 weeks interval between injections by the end of 24 months of treatment (Berg K et al., 2016). In HAWK and HARRIER studies, only 39-45% patients receiving brolucizumab 6 mg were able to maintain a 12-week interval by 96 weeks of treatment (Dugel P et al., 2021).

In ALTAIR study by 96 weeks ~60% patients had an injection interval of 12 weeks or longer, and >40% patients had an interval of 16 weeks (Ohji M. et al., 2020).

Considering the ability to achieve injection intervals of 12-16 weeks in a large proportion of patients, the long experience of use in routine practice, and the known safety profile, the experts of the workgroup unanimously reached a consensus that to date, aflibercept is the optimal anti-VEGF drug to treat patients with retinal diseases in the current pandemic conditions in our country.

Experts reached a consensus regarding management of patients with chronic retinal diseases in the current conditions of the COVID-19 pandemic in the world and in Ukraine:

1. Maintaining maximal visual acuity is the main priority in the treatment of patients with retinal diseases in current pandemic conditions. Inadequate ophthalmologic care for patients with chronic retinal diseases can result in partial or complete loss of autonomy for these patients and a significant decline in quality of life.

2. Ophthalmological clinics and departments should aim to resume routine activities while respecting all safety measures and returning to pre-pandemic approaches to the treatment of patients with retinal diseases.

3. Injections of anti-VEGF agents should be considered an urgent procedure for diseases such as neovascular age-related macular degeneration, diabetic macular edema, and macular edema secondary to retinal vein occlusion. In patients with these conditions, it is unacceptable to delay the required intravitreal injections, even in the face of medical facility restrictions.

4. Due to the distinctive features of the aflibercept molecule, such as the longer period of VEGF suppression, the multitargeted mode of action (VEGF and PGF blocking) and the higher affinity to VEGF compared to other anti-VEGF agents, it is possible to achieve 12-16 week injection intervals in a larger proportion of patients treated with aflibercept. Combined with a long experience of use in routine practice, and the known safety profile, this makes aflibercept the optimal anti-VEGF drug to treat patients with retinal diseases in the current pandemic conditions.

5. In current pandemic conditions the recommended approaches in treating patients with retinal diseases are:
   - Treatment of patients with nAMD is recommended to start with 3 initial monthly injections of aflibercept, followed by extension of the interval between injections up to two months. If there are no constraints in the clinic and the patient compliance is good, consider switching to T&E to adjust the interval between injections based on each patient's individual need.
   - In most cases of patients with visual impairment due to DME, treatment approaches and protocols that were used before the pandemic should be followed. Deciding to initiate treatment, the perceived benefit of treatment / potential risk of SARS-CoV-2 infection should be balanced on an individual basis for each patient. When aflibercept is indicated in patients with DME, treatment should start with 5 monthly consecutive injections followed by injections every two months.
   - In patients with visual impairment due to macular edema secondary to central retinal vein occlusion or branch retinal vein occlusion, after clarifying patient's general condition and initiating medical correction of the cause of the occlusion, treatment should be started promptly with monthly aflibercept injections until maximum visual acuity and/or disappearance of the disease activity is achieved. Aflibercept can be used in patients both with non-ischemic and ischemic types of retinal vein occlusion.
   - If there are significant limitations in ophthalmological clinic or department services, treatment of patients with nAMD should be considered a priority.
   - There is no need for additional monitoring visits to the clinic between aflibercept injections.

6. To preserve the efficacy and safety of anti-VEGF drugs experts strongly recommend to choose a drug supplier that guarantees compliance with the "cold chain" technology during transportation, also, do not allow the drug to be warmed to room temperature for more than 24 hours prior to injection and eliminate its freezing, even for a short period of time.

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