• Brief Report •

Intraocular inflammation after intravitreal injection of faricimab–a case series including one case of bilateral choroidal involvement

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Abstract

● **AIM:** To report and analyze cases of sterile intraocular inflammation (IOI) following intravitreal faricimab injections in patients treated for neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME).

● **METHODS:** This double-center case series included nine eyes of six patients who developed uveitis after faricimab therapy. Comprehensive clinical evaluation was performed, including slit-lamp examination, intraocular pressure (IOP) measurement, fluorescein and indocyanine green angiography (ICGA), and laboratory tests. Inflammatory responses were treated with topical or systemic corticosteroids, and patients were monitored for visual acuity and inflammatory activity.

● **RESULTS:** The incidence of IOI was 0.8% per patient (Innsbruck) and 0.23% (Czechia), with inflammation typically occurring between the third and sixth injection (mean interval: 10d post-injection). Inflammatory presentations ranged from anterior uveitis to posterior segment involvement. One notable case demonstrated novel choroidal hypofluorescent lesions on angiography, suggesting deeper ocular involvement. The mean patient age was 76y; five of six affected patients were female. All cases responded to local and systemic corticosteroids, with full recovery of initial visual acuity.

● **CONCLUSION:** Sterile IOI after faricimab appears to be a rare but relevant adverse event. Although the incidence falls within expected ranges for anti-vascular endothelial growth factor (anti-VEGF) agents, the observed choroidal involvement represents a potentially new safety signal. Prompt diagnosis and corticosteroid therapy are effective in all cases. Our findings support the need for vigilant post-marketing surveillance and further studies to better understand the underlying mechanisms and risk factors of faricimab-associated inflammation.

● **KEYWORDS:** case series; choroidal involvement; faricimab; intraocular inflammation; uveitis
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INTRODUCTION

Faricimab, a novel therapeutic agent, has recently received international approval for the treatment of neovascular age-related macular degeneration (nAMD), retinal vein occlusion (RVO) and diabetic macular edema (DME). This innovative biologic agent targets two pivotal cytokines–angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A)–that are integral to the pathophysiology of these vision-threatening conditions. Results from Phase III clinical trials have underlined the drug's efficacy and safety, establishing it as a significant advancement in retinal disease management.

The dual inhibition mechanism of faricimab, which simultaneously addresses both angiogenesis and vascular permeability, marks a potential improvement in therapeutic options available to patients. As ophthalmologists continue to explore the full potential of this treatment, it is imperative to closely monitor and report any adverse events to ensure comprehensive understanding and optimal patient care.

At the end of last year, the manufacturer issued an update to the Warnings and Precautions and Adverse Reactions-Postmarketing Experience sections of the US Prescribing Information. This update followed spontaneous post-marketing reports of retinal vasculitis with or without occlusion in patients treated with faricimab. As of the end of August 2023, with 1.5 million vials dosed globally, the estimated reporting rate of retinal vasculitis was 0.06 per 10 000 injections, for retinal vasculitis with or without occlusion: 0.17 per 10 000 injections[1].

In addition, there are isolated case reports in the literature describing intraocular inflammation (IOI) following the administration of faricimab. We have recently observed an increase in such reactions of varying severity. This case series reports on nine affected eyes that developed uveitis following faricimab injections. Our ongoing analysis and vigilance are crucial in identifying and mitigating any potential risks associated with faricimab.

PARTICIPANTS AND METHODS

Ethical Approval This study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was secured from all participants for the use of their data in analysis and publication.

This double-center case series included nine eyes of six patients who had previously undergone intravitreal therapy with faricimab for treatment of nAMD and subsequently developed uveitic reactions of varying severity. The study was conducted at the Department of Ophthalmology and Optometry at the Medical University of Innsbruck, Austria and the Department of Ophthalmology at the University Hospital Ostrava, Czechia.

RESULTS

Case 1 In December 2023, a 83-year-old male patient presented at our emergency department with complaints of cloudy vision in both eyes, which developed 16d after the most recent intravitreal injections of faricimab in both eyes.

His medical history included excision of an invasive squamous cell carcinoma in the cheek area the previous year, hypothyroidism managed with levothyroxine, and antihypertensive treatment. In terms of ophthalmological history, the patient was diagnosed with active nAMD in both eyes. From October 2018 until December 2023, he received a total of 23 injections with aflibercept (2 mg) and three injections with faricimab in the right eye. In the left eye, he received one injection of aflibercept (2 mg) in May 2023 before switching to faricimab, of which he received 3 injections by December 2023. The injections were given simultaneous bilateral.

The best corrected visual acuity (BCVA) was 0.4 logMAR (20/50 Snellen) in the right eye and 1.0 logMAR (20/200 Snellen) in the left eye. Clinical examination revealed a significantly elevated intraocular pressure (IOP) of 25 mm Hg in the right eye and 46 mm Hg in the left eye. Both eyes exhibited intraocular irritation, characterized by keratic precipitates on the left eye with inflammatory cells at 0.5+ according to the Standardization of Uveitis Nomenclature (SUN) grading system in both the anterior chamber and vitreous body of both eyes. These findings were documented using a slit lamp camera, as shown in Figure 1.

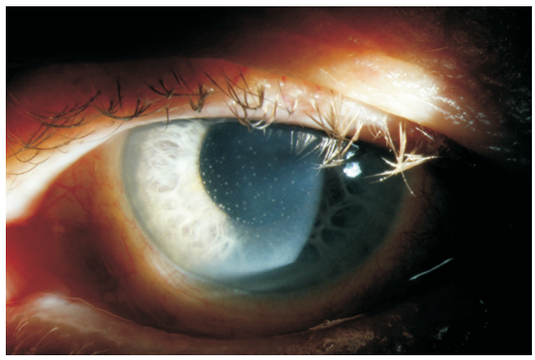

Figure 1 Slit lamp photography of keratic precipitates found in Case 1 (6.3× magnification).

The elevated IOP was managed with carbonic anhydrase inhibitor/beta blocker eye drops, alpha-2-agonist eye drops, and a single intravenous dose of a carbonic anhydrase inhibitor 500 mg, which significantly reduced the pressure to 16 mm Hg in the right and 27 mm Hg in the left eye after one hour.

Fluorescein angiography (FAG) of the retinal vessels showed no signs of vasculitis. Indocyanine green angiography (ICGA) did not reveal any pathological findings. Comprehensive blood tests, including assays for various virological antibodies, were negative.

Uveitis was addressed with topical steroid treatment. This led to a good response allowing for a gradual tapering of therapy over five weeks. Concurrently, with the reduction of inflammation, the IOP normalized, and the pressure-lowering therapy was subsequently discontinued.

Throughout the course of the disease, visual acuity deteriorated in both eyes, reaching a nadir of 0.16 logMAR (20/29 Snellen) in both eyes. However, after the latest follow-up, visual acuity had stabilized, returning to the initial values of 0.4 logMAR (20/50 Snellen) in the right eye and 1.0 logMAR (20/200 Snellen) in the left eye.

Case 2 In January 2024, a 79-year-old woman presented to our emergency department with symptoms of blurred vision in her right eye for the past two days. Her medical history included soft tissue rheumatism and antihypertensive therapy as well as beta blocker for chronic heart failure. Her type 2 diabetes was managed with a sodium-glucose cotransporter 2 (SGLT2)-inhibitor, and she was undergoing therapy with an aromatase inhibitor for post-breast cancer treatment. She was

also under blood-thinning therapy with a thrombin inhibitor, a new oral anticoagulant. Her ophthalmologic history included a diagnosis of nAMD on the right eye, for which she had received in total five intravitreal injections of faricimab, the most recent being four days prior to her presentation. The left eye showed signs of dry AMD.

At presentation her visual acuity was counting fingers (1.9 logMAR, 20/1600 Snellen). The IOP on the right eye was 18 mm Hg. Slit lamp examination revealed Descemet's membrane folds and speckled keratic precipitates, as well as cells at 0.5+SUN in the anterior chamber. No signs of retinal infiltration were observed. The subretinal fluid seen at the last visit, which initially prompted the therapy with faricimab, had noticeably improved. FAG and ICGA of the retinal vessels showed no signs of vasculitis or pathological findings in the choroid. Blood tests showed positive results for hepatitis C virus serology as an incidental finding. Both the IgM and IgG antibodies, as well as the qualitative and quantitative real-time polymerase chain reaction (PCR), were positive. The patient was referred to the gastroenterology department, where she is currently undergoing antiviral treatment. Apart from that, the blood work showed no evidence consistent with uveitis.

Topical steroid treatment was started and which lead to a notable improvement in the inflammatory response. Keratic precipitates were minimized to the Arlt's triangle so that the treatment could be gradually discontinued. Importantly, visual acuity increased to 0.5 logMAR (20/63 Snellen) surpassing even the recorded value of 1.0 logMAR from the last regular check-up prior to the onset of inflammation.

In a follow-up examination two months after tapering off cortisone therapy, signs of inflammation flared up again in the right eye. Increased keratic precipitates were observed. Therefore, prednisolone acetate eye drops were restarted.

The follow-up examination two weeks later already showed a considerable decrease in the precipitates in the right eye. The local steroid therapy was continued. Restarting intravitreal injections was not necessary, as the nAMD remained inactive.

Case 3 In December 2023, a 70-year-old woman presented to our emergency department complaining of pain in her right eye that had been present for one day.

Her medical history included treatment with a tyrosine-kinase inhibitor for non-small cell lung cancer (NSCLC) with cerebral metastasis since July 2022. In terms of ophthalmological history, she had AMD of the right eye, which had been treated with intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections since 2021. In total, she had received nine injections with aflibercept (2 mg), from 2021 until switching to faricimab in 2023. She received 5 injections of faricimab, the latest of which was administered more than a month prior to the onset of her symptoms. Additionally, the patient had a history of bilateral endocrine orbitopathy with multiple surgical orbital decompressions, which had already caused impaired visual acuity before the onset of her complaints. Her visual acuity was 1.6 logMAR (20/800 Snellen) in the right eye and 2.3 logMAR (20/4000 Snellen) in the left eye.

The clinical examination of the right eye showed hyperemia of the conjunctiva and keratic precipitates all over the cornea, making the assessment of the anterior chamber difficult. No hypopyon was observed. Angiography of retinal vessels showed no signs of retinal vasculitis. ICGA revealed no pathological findings. Blood tests showed no evidence consistent with uveitis.

Therapy with topical steroids and cyclopentolate eye drops three times a day were initiated. As the inflammation showed no improvement under local therapy and the IOP increased to 26 mm Hg, systemic treatment with corticosteroids as well as pressure lowering eye drops had to be introduced. After consultation with the oncologists, treatment with a tyrosine-kinase inhibitor could be continued.

This approach led to a steady improvement in her condition. After one month, the keratic precipitates had resolved, and the anterior chamber of the eye showed no signs of irritation, with only isolated cells at 0.5+SUN present in the vitreous humor. Consequently, both local and systemic therapies were discontinued. The IOP remained at a normal range.

Case 4 In March 2024, a 64-year-old woman presented to our emergency department reporting pain and redness in her right eye along with blurred vision. These symptoms had occurred one day after an injection with faricimab. This injection was part of her ongoing treatment regimen for macular neovascularization (MNV) secondary to chronic central serous retinopathy (CCS), a condition she had since 2000. Other than that, she had no other ophthalmological pre-existing conditions. Her medical record showed hypothyroidism–managed with levothyroxine–and a urinary retention disorder.

Her CCS was treated with intravitreal anti-VEGF injections at our clinic since 2016. Initially, she was administered with aflibercept (2 mg) of which she got in total 37 injections. Her treatment was switched to faricimab in 2023, of which she received a total of six injections before the onset of her symptoms.

Upon clinical examination BCVA was 1.9 logMAR (20/2000 Snellen) on her right eye and -0.1 logMAR (20/16 Snellen) on her left eye. IOP was found to be within normal range.

The slit-lamp examination identified conjunctival hyperemia, keratic precipitates and 0.5+ to 1+SUN cells in the anterior chamber. Additionally, up to 1+SUN cells were observed in the vitreous body. Retinal angiography showed no signs of vasculitis or choroidal changes.

Blood tests showed no evidence consistent with uveitis. The initial treatment strategy included the administration of

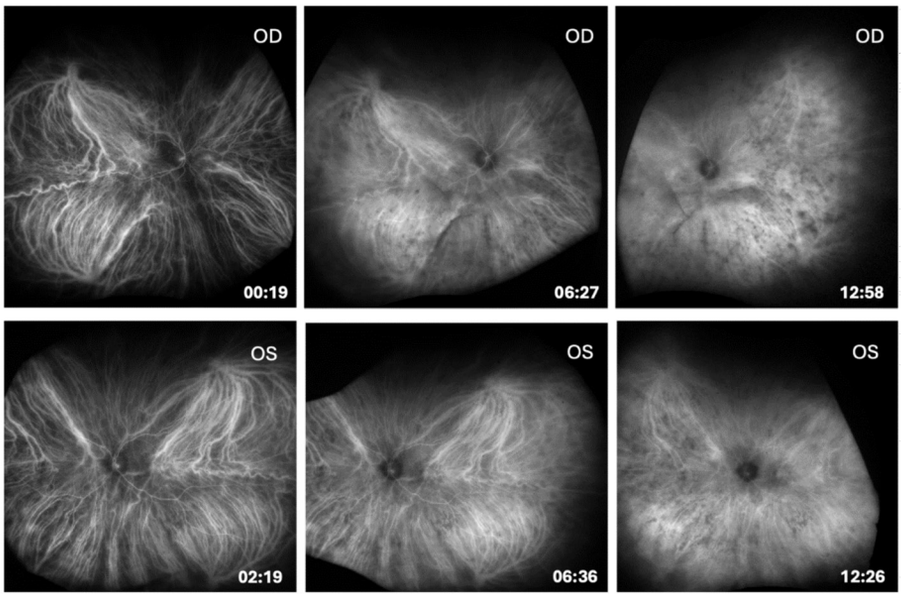

Figure 2 Indocyanine green angiography showing sharply demarcated hypofluorescent areas scattered over the entire fundus in the right eye and left eye found in Case 5 OD: Right eye; OS: Left eye.

aminoglycoside and steroid eye drops. However, this regimen was quickly modified the following day to just topical steroid therapy.

This therapeutic approach led to a gradual reduction in endothelial precipitates and inflammatory activity in both the anterior chamber and vitreous body over the subsequent two weeks. As the inflammation subsided, the frequency of cortisone-containing eye drop application was reduced. Intravitreal injection therapy for the treatment of MNV was resumed with aflibercept (2 mg) as part of the ongoing management of the MNV.

Case 5 In May 2024, a 93-year-old woman presented to our emergency department reporting cloudy vision in both eyes. Her ophthalmologic history included pseudophakia, history of posterior Yttrium Aluminum Garnet (YAG) laser capsulotomy and nAMD in both eyes. The latter was first described three months prior and at the time of presentation a therapy with intravitreal faricimab injections was indicated. By the time of her presentation, she had already received three intravitreal injections, the last one five days before the onset of symptoms. Her medical history included polymyalgia rheumatica, arterial hypertension, and hyperthyroidism.

Clinical examination revealed endothelial precipitates on the cornea, 1+SUN cells in the anterior chamber, vitreous opacities in both eyes, and 1+SUN cells in the vitreous of the left eye.

The BCVA in the right eye was 1.6 logMAR (20/800 Snellen) and in the left eye 2.3 logMAR (20/4000 Snellen). The IOP was elevated, measuring 35 mm Hg in the right eye and 31 mm Hg in the left eye, which was treated with carbonic anhydrase inhibitor/beta blocker eye drops and alpha-2-agonist eye drops to lower the pressure.

An angiography showed no vascular leakage with fluorescein. However, within 15min after indocyanine green injection, sharply demarcated hypofluorescent choroidal lesions were revealed, scattered across the entire fundus in both eyes, as shown in Figure 2. Blood tests, aside from positive CMV-IgG, showed no abnormalities. Moreover, human leukocyte antigen (HLA) testing did not demonstrate any disease-specific associations.

The inflammatory reaction was treated with topical steroid eye drops. Additionally, intravenous treatment with 64 mg of prednisolone was started. The elevated IOP was treated successfully with local therapy.

Four days after symptom onset, recombinant tissue plasminogen activator (rTPA) and sulfur hexafluoride gas were administered intravitreally into the left eye to treat a progressive macular hemorrhage.

Signs of inflammation continued to regress under systemic prednisolone therapy, which was tapered off, allowing the patient to be discharged after a total of ten days. She continued treatment with local prednisolone eye drops administered five times a day and an ointment at night.

At the last follow-up, nAMD in the right eye showed no activity. The subretinal macular hemorrhage in the left eye had significantly regressed, and intravitreal therapy was switched to aflibercept (2 mg). There were no more signs of inflammation in the anterior chamber and the vitreous. The keratic precipitates had completely regressed in both eyes. However, although the choroidal lesions observed in angiography had diminished three months after the initial examination, they had not completely resolved and remained detectable.

Case 6 In July 2024, a 68-year-old woman was sent to our clinic by her ophthalmologist, complaining of pain in both

Table 1 Overview of the clinical presentation of all cases

Case	Laterality	Uveitis form	Anterior chamber cells[a]	Hypopyon	Keratic precipitates	Hyperemia	Flare[a]	Vitreous cells[a]	CME
Case 1	OD	Intermediate	+0.5	No	Yes	Yes	+1	+0.5	Yes
	OS	Intermediate	+0.5	No	Yes	Yes	+1	+0.5	No
Case 2	OD	Anterior	+0.5	No	Yes	No	+1	0	No
Case 3	OD	Anterior	+1.5	No	Yes	Yes	+1	0	No
Case 4	OD	Intermediate	+1	No	Yes	Yes	0	+1	Yes
Case 5	OD	Panuveitis	+1	No	Yes	No	+1	0	Yes
	OS	Panuveitis	+1	No	Yes	No	+1	+1	Yes
Case 6	OD	Panuveitis	+0.5	No	Yes	Yes	+1	+0.5	No
	OS	Panuveitis	+0.5	No	Yes	Yes	+1	+1	Yes

[a]SUN grading system. SUN: Standardization of Uveitis Nomenclature; CME: Cystoid macular edema; OD: Right eye; OS: Left eye.

eyes and blurred vision four days after the fifth injection of faricimab in both eyes.

Her medical history included hypothyroidism, hypertension, and type 2 diabetes managed with insulin therapy. Her ophthalmologic history included cataract surgery in 2021 and laser photocoagulation of leaking macular microaneurysms in 2018. She was diagnosed with DME in 2023 due to moderate non-proliferative diabetic retinopathy (NPDR) and treated with faricimab.

At the time of her presentation, her BCVA was 0.6 logMAR (20/80 Snellen) in both eyes. Her IOP was 20 mm Hg in the left eye and 28 mm Hg in the right eye. The clinical examination revealed ocular irritation in both eyes, hyperemic conjunctiva, keratic precipitates, 0.5+SUN cells in the anterior chamber and 0.5+ to 1+SUN cells in the vitreous body in both eyes. Ultrasound revealed multiple small mobile hyperechoic floaters in the vitreous in both eyes as well as retinoschisis in the right eye in the lower temporal quadrant. There were no biomicroscopic signs of hypopyon. Vasculitis with extravascular leakage or choroidal alterations could be ruled out by ICGA and FAG.

Elevated IOP was managed with a combination of topical carbonic anhydrase inhibitor and beta blocker with a good response (14/15 mm Hg). Uveitis was treated with topical dexamethasone initially, but due to worsening vision to 1.0 logMAR (20/200 Snellen) in both eyes and progression of inflammatory signs, intravenous pulse therapy was started with 1 mg methylprednisolone sodium succinate once a day. Concurrently, peroral omeprazole was administered once a day to prevent gastric ulcers.

As comprehensive blood tests showed no relevance to the currently treated uveitis, inflammatory signs were reduced (especially cell activity in the anterior chamber and vitreous), and the patient's vision increased to 0.4 logMAR (20/50 Snellen) in the right eye and 0.5 logMAR (20/63 Snellen) in the left eye. Oral steroids were continued starting at 40 mg per day which were rapidly reduced over the next few weeks.

Ten days after the first signs of uveitis, we did not observe any cells in the anterior chamber or vitreous body, patient's vision was 0.3 logMAR (20/40 Snellen) on the left eye and 0 logMAR (20/20 Snellen) on the right eye, IOP was at 15 mm Hg on the right and 16 mm Hg on the left eye. OCT revealed mild DME on the right eye and few cysts on the left eye.

The Table 1 provides an overview of the clinical presentation of all cases and the individual eyes.

In our clinical observations, six cases of uveitis were reported following faricimab injections, affecting nine eyes. These cases presented with varying degrees of inflammation, ranging from mild irritation to severe vasculitis with granulomatous changes. The incidence of IOI in the Innsbruck cohort was approximately 0.8% (five affected patients out of 604 injections). The incidence of IOI in Czechia was 0.23% (one patient, both eyes, out of total 871 injections). The interval between the last faricimab injection and the IOI diagnosis varies from 1 to 30d, with a mean of 10d and a median of 5d before the inflammation occurs. The average number of faricimab injections before the occurrence of IOI was 5, ranging from 3 to 6 injections

DISCUSSION

Sterile IOI following intravitreal injections of anti-VEGF therapy is considered a rare complication, with an estimated incidence ranging from 0.005% to 4.4%, regardless of the specific medication used. Differentiating it from infectious inflammation initially can be challenging. Infectious inflammation, which occurs with an incidence between 0.02% and 0.14%, typically presents with more pronounced symptoms. Sterile IOI manifests in 65% of cases within two days of the causative event, whereas infectious IOI generally takes an average of four days to develop. Additionally, a treated sterile IOI usually resolves within five weeks[2].

There are various known and hypothesized causes that may contribute to inflammation following intravitreal injections. Individual patient factors, such as the presence of anti-drug antibodies (ADA) and the breakdown of the blood-

retina barrier in conditions like exudative AMD, can increase susceptibility to immunological reactions. The presence of ADA can trigger inflammatory responses, although this phenomenon is not uniformly observed across all anti-VEGF agents. To the best of our knowledge, no ADA tests are available for faricimab[3], according to Roche (Personal communication with Nancy Holekamp, Principal Global Medical Science Director, on August 30, 2024), who also indicated that the incidence of ADA prior to treatment with faricimab ranges between 1% and 3%.

In the clinical trials for brolucizumab for example, pre-existing ADA were detected in up to 43.7% (884/2023) of subjects. This high prevalence of positive ADA titers prior to the first injection is not unexpected and has also been observed in drug-naive subjects for various antibody fragments of similar structure, such as nanobodies and single-domain antibodies. Although European Medicines Agency (EMA) investigations revealed that a pre-existing ADA status does not increase the likelihood of a treatment-induced ADA response, a higher incidence of IOI with elevated ADA levels was reported[4].

Moreover, medication-related factors include non-infectious contaminants introduced during the manufacturing process, such as endotoxins and protein aggregates, which can induce inflammatory responses. The production process of anti-VEGF drugs can introduce such impurities, and specific formulations of these medications may inherently possess immunogenic properties. The use of siliconized syringes for drug administration has been associated with inflammation, as silicone oil (SO) microdroplets can interact with protein molecules. Syringes are often siliconized to reduce plunger resistance, but SO release can denature proteins, creating SO-protein complexes that may provoke an immune response[5]. Factors such as temperature fluctuations, light exposure, and syringe agitation during shipping and preparation can increase SO release and protein aggregation[6]. Agitation, commonly done by physicians to remove air bubbles, including a case-control study on aflibercept, have shown that syringe brand and handling practices influence the incidence of inflammation post-injection[7-9].

It is notably that at the Medical University of Innsbruck the compounding pharmacy aliquoted doses from a single vial into insulin syringes potentially increasing the risk of contamination with silicone oil. Nonetheless, initial isolated case reports of IOI following faricimab administration have already been published in clinics where only one injection per vial was used. This might explain the low number of cases, but it does not exclude the possibility of general avoidance[10].

However our observations are consistent with a recently published case series from France and Italy, which also found an incidence of 0.6% and 0.41%, respectively, per intravitreal injection of faricimab[11-12].

Furthermore, a Swiss case series reported 12 eyes from 7 patients developing noninfectious IOI after intravitreal faricimab injections over a 22-month period. Among these, two eyes exhibited retinal vasculitis, with one case progressing to occlusive vasculitis involving both arteries and veins, leading to significant vision loss from 20/80 to 20/2000. The median number of injections before IOI onset was 3.5, and the median interval between the last injection and diagnosis was 28d[13].

Additionally, a case series from Nebraska, USA, highlighted the risk of rechallenging patients with faricimab after prior IOI. In this series, three out of four eyes developed occlusive retinal vasculitis following continued faricimab treatment despite existing mild IOI symptoms. This underscores the need for extreme caution when considering re-administration of the same biologic agent in patients exhibiting even mild IOI symptoms[14].

It is also noteworthy that IOI typically did not occur immediately after the first faricimab injection but rather between the third and sixth injection. A potentiation of possible causes, such as ADA or SO, could also play a role in this phenomenon.

Another non-immunological aspect previously discussed is the preservatives used in these medications. Polysorbate is a preservative commonly used in medications for intravitreal injection. Specifically, Polysorbate-80, used in Beovu (brolucizumab), has been shown to destabilize the retinal barrier, suggesting its role in the inflammatory responses observed in patients. In contrast, Polysorbate-20, used in Lucentis (ranibizumab), did not demonstrate the same destabilizing effects. Both faricimab and aflibercept contain Polysorbate-20[15-16].

All affected patients at the Medical University of Innsbruck suffered from AMD, and it appears to be coincidental that none of the affected patients were undergoing treatment for DME. This is most likely a coincidence, as there are existing case reports of IOI occurring under faricimab therapy for DME[10,17].

Additionally, it must be noted that almost all patients had comorbidities that either inherently have a higher incidence of IOI[18] or their treatments could potentially trigger IOI. For example all our patients (except case four) suffered from an autoimmunological disease, such as thyroid dysregulation, which is known to trigger systemic immunological responses[19]. Furthermore, in case three, the patient was receiving osimertinib for the treatment of her NSCLC. According to the healthcare professional information, keratitis and uveitis is listed as a rare ophthalmologic side effect of this medication. Therefore the possibility that the ongoing cancer therapy could have influenced the inflammatory process in the eye cannot be excluded[20].

Nevertheless, our findings align with previous reports documenting the incidence of uveitis and other forms of IOI with faricimab. The Phase III TENAYA and LUCERNE studies, which compared faricimab to aflibercept, indicated that faricimab had a well-tolerated safety profile with an incidence of uveitis ranging from 0.5% to 2.0% across various studies[21-22]. While the occurrence of IOI in our cases falls within these expected complication rates, the involvement of the choroid represents a novel finding. The presence of hypofluorescent areas detected in the ICGA raises the differential diagnosis of granulomas versus a perfusion disturbance of the choriocapillaris. Regardless of which hypothesis proves to be accurate in the future, this observation underscores that the drug's effects are not limited to the retinal vasculature and retina, as previously assumed, but extend to deeper ocular layers as well.

Moreover, a recent pharmacovigilance analysis utilizing data from the FDA Adverse Event Reporting System (FAERS) and the Japanese Adverse Drug Event Report (JADER) identified new safety signals associated with faricimab. Notably, strong associations were found with macular ischemia [reporting odds ratio (ROR)=260.46], keratic precipitates (ROR=739.65), and optic nerve injury. These findings suggest a potential risk of retinal circulation impairment and highlight the need for closer monitoring of ocular complications, particularly in high-risk patient groups[23].

In conclusion, the uveitis resulting post injection could be managed with administration of local and systemic corticosteroids in all our cases and all patients regained their initial visual acuity. Inflammation following intravitreal injections is likely multifactorial, influenced by both the intrinsic properties of anti-VEGF medications and external factors related to their handling and administration. While the occurrence of IOI may fall within the expected range of complications, the involvement of the choroid is a new finding. Therefore, we suggest performing fluorescein and indocyanine angiography in cases of uveitis after faricimab injections to rule out choroidal involvement.

Further research and large-scale post-marketing studies are essential to refine our understanding of the inflammatory risks associated with faricimab and to optimize patient safety in clinical practice.

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