XIPERE InXights

XIPERE Patient Case Study Series

TREATMENT OF MACULAR EDEMA ASSOCIATED WITH UVEITIS IN A PHAKIC PATIENT WITH SARCOIDOSIS

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Sarcoidosis is a multisystemic inflammatory disorder of unknown etiology that is characterized by pathological granuloma formation in affected organs, especially the lungs.[1] In the United States, the majority of patients diagnosed with sarcoidosis are female and over 55 years of age.[2] The incidence and prevalence of sarcoidosis are higher amongst African American individuals (17.8 and 141.4 per 100,000, respectively) compared to White (8.1 and 49.8), Hispanic (4.3 and 21.7), and Asian (3.2 and 18.9) individuals.[2]

Approximately 30% to 60% of patients with sarcoidosis have ocular involvement, with bilateral granulomatous uveitis as a frequent presentation.[3] According to the International Workshop on Ocular Sarcoidosis (IWOS), the following clinical signs are suggestive of ocular sarcoidosis: (1) mutton-fat keratic precipitates/small granulomatous keratic precipitates and/or iris nodules (Koeppe/Busacca); (2) trabecular meshwork nodules and/or tent-shaped peripheral anterior synechiae; (3) snowballs or string-of-pearl vitreous opacities; (4) multiple chorioretinal peripheral lesions (active and/or atrophic); (5) nodular and/or segmental peri-phlebitis (± candlewax drippings) and/or retinal macroaneurysm in an inflamed eye; (6) optic disc nodule(s)/granuloma(s) and/or solitary choroidal nodule; and (7) bilaterality.[4] Moreover, IWOS recommends that, before a diagnosis of ocular sarcoidosis can be made, other causes of granulomatous uveitis must be ruled out, and a systemic investigation should be performed to confirm systemic findings consistent with suspected sarcoidosis.[4]

The Standardization of Uveitis Nomenclature (SUN) Working Group developed classification criteria for sarcoidosis-associated uveitis using a machine learning-based approach.[5] This analysis identified the key criteria for sarcoidosis-associated uveitis as: (1) a compatible uveitic syndrome of any anatomic class (anterior or intermediate or anterior/intermediate or posterior uveitis with choroiditis or multifocal choroiditis, or panuveitis with choroiditis or retinal vascular sheathing or retinal vascular occlusion); and (2) evidence of sarcoidosis (either tissue biopsy demonstrating non-caseating granulomata or bilateral hilar adenopathy on chest imaging).[5] Exclusionary criteria are positive serology for syphilis using a treponemal test, and evidence of infection with *Mycobacterium tuberculosis*.[5]

Corticosteroids have been recommended in the treatment of macular edema caused by sarcoidosis-associated uveitis.[6] Here, we describe such an instance that was treated with XIPERE® (triamcinolone acetonide injectable suspension) 40 mg/mL. This patient was phakic and demonstrated minimal cataract progression, with no rise in intraocular pressure, following XIPERE treatment.

INDICATION

XIPERE® (triamcinolone acetonide injectable suspension) for suprachoroidal use is a corticosteroid indicated for the treatment of macular edema associated with uveitis.

IMPORTANT SAFETY INFORMATION

Patients should be monitored following injection for elevated intraocular pressure. See Dosage and Administration instructions in full Prescribing Information.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

XIPERE® (triamcinolone acetonide injectable suspension) 40 mg/mL

Case Report: Macular Edema Associated With Uveitis in a Phakic Patient With Sarcoidosis

BACKGROUND: We present a 64-year-old white male, with past medical history significant for hyperlipidemia, treated with rosuvastatin, and hypothyroidism, treated with levothyroxine. Other medication use included vitamin D and calcium supplements, aspirin, and tadalafil. He is a now-retired engineering manager and nonsmoker.

The patient's past ocular history was significant for an episode of posterior uveitis approximately 4 years prior, which was treated with a single intravitreal injection of triamcinolone acetonide 40 mg/mL in each eye, spaced 3 weeks apart, by another provider.

Prior workup revealed bilateral hilar lymphadenopathy, and a biopsy was performed via bronchoscopy. Histological analysis revealed non-caseating granulomas, consistent with a diagnosis of sarcoidosis. Because the patient's systemic symptoms were mild, the patient was not treated with any systemic agents.

DIAGNOSIS: The patient was referred to Dr.Raiji with a visual acuity of 20/70 in his right eye. The patient had an intraocular pressure of 10 mm Hg, and was phakic with a grade 1+ nuclear sclerotic cataract. Examination revealed a cup-to-disc ratio of 0.1 and showed no evidence of anterior vitreous cells, but did exhibit snowballs and a few retinal hemorrhages. Fluorescein angiography revealed optic disc and macular leakage, and SD-OCT revealed cystoid macular edema with a central retinal thickness of 702 µm (**Figure 1**). Based on these findings, the patient was diagnosed with sarcoidosis-associated posterior uveitis with macular edema.

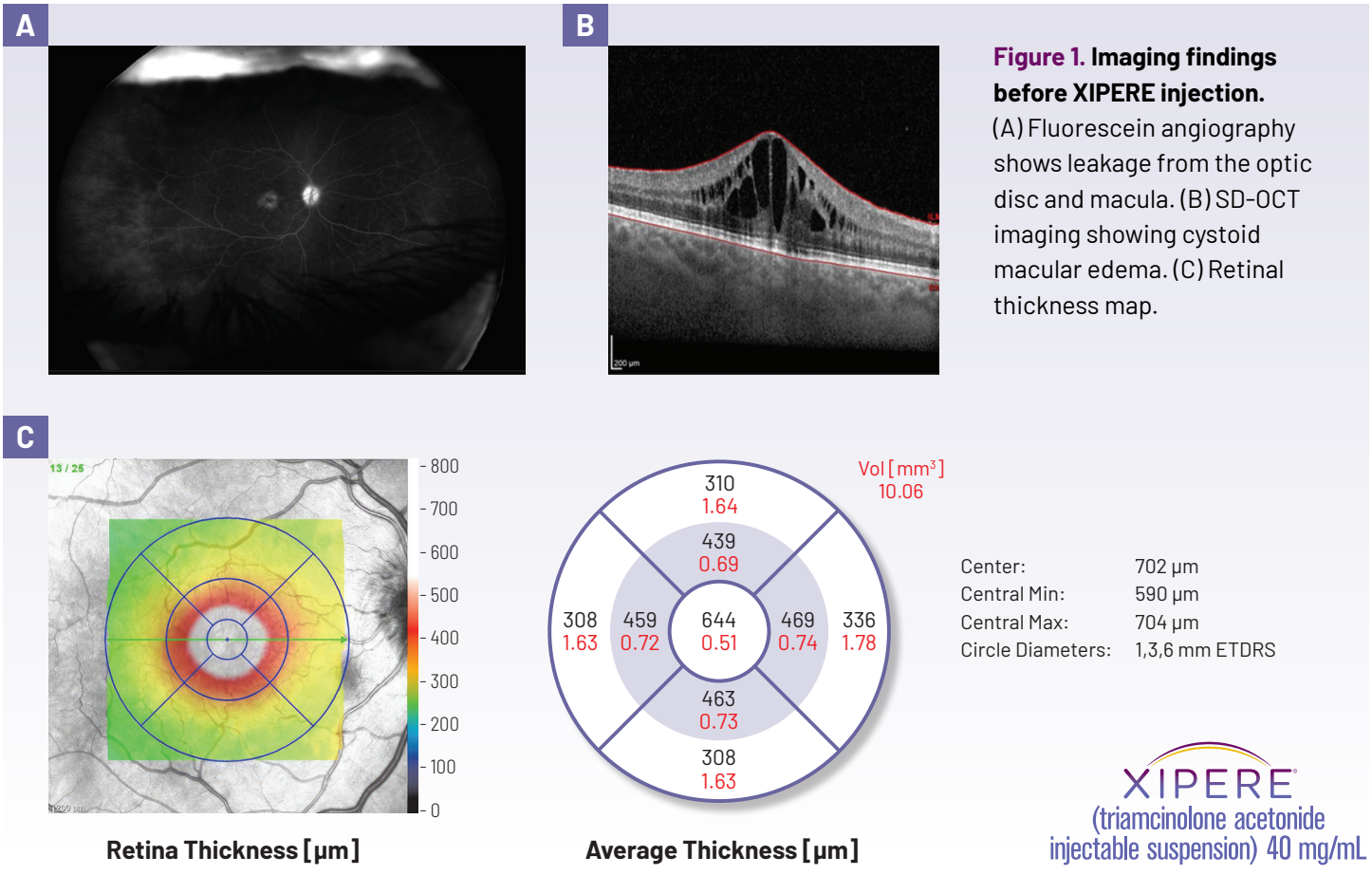

Figure 1. Imaging findings before XIPERE injection. (A) Fluorescein angiography shows leakage from the optic disc and macula. (B) SD-OCT imaging showing cystoid macular edema. (C) Retinal thickness map.

TREATMENT: A single injection of XIPERE was administered. Two weeks following treatment, the patient's visual acuity had markedly improved to 20/32, and his intraocular pressure was 12 mm Hg. His cystoid macular edema had improved significantly, with his central retinal thickness decreasing to 231 µm (67.1% reduction from baseline; **Figure 2**).

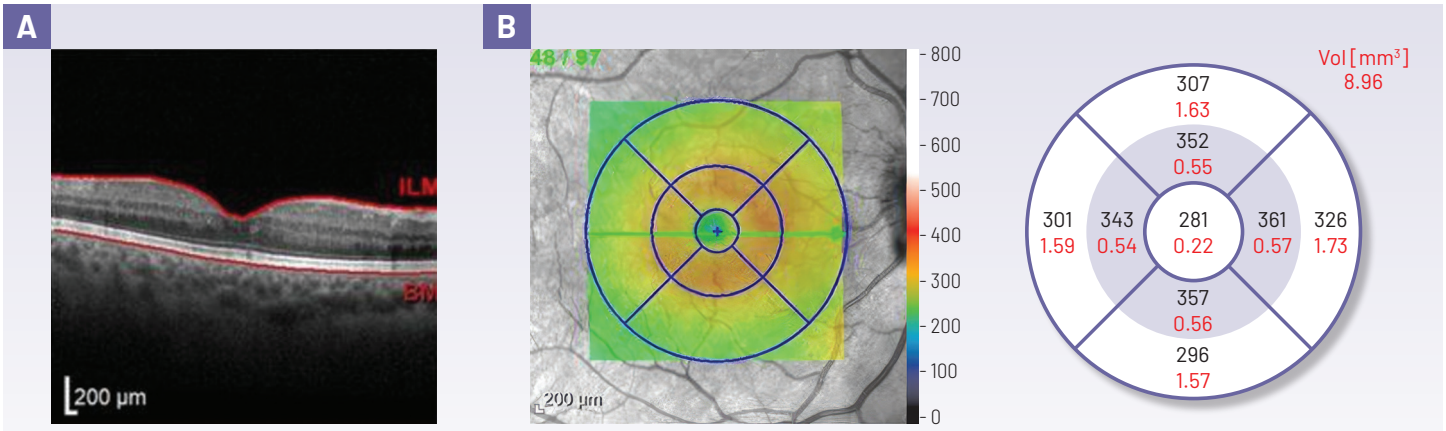

Figure 2. Imaging findings 2 weeks after XIPERE injection. (A) SD-OCT imaging showing reduction of cystoid macular edema. (B) Retinal thickness map.

Six weeks after treatment, the patient's visual acuity was 20/25, his intraocular pressure was 13 mm Hg, and there was no evidence of macular edema. OCT revealed a central retinal thickness of 220 µm (68.7% reduction from baseline; **Figure 3**).

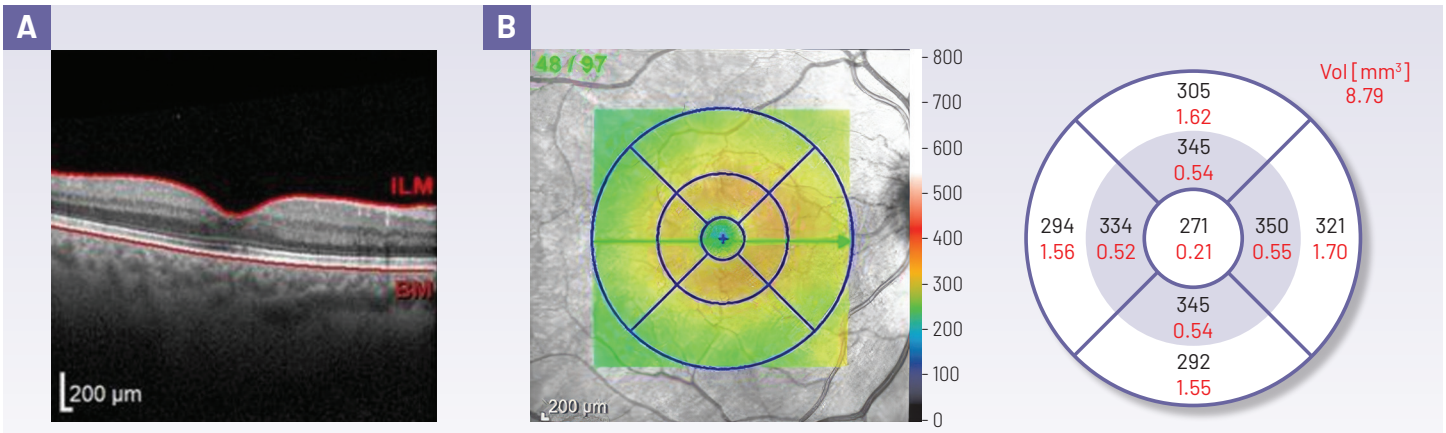

Figure 3. Imaging findings 6 weeks after XIPERE injection. (A) SD-OCT imaging showing reduction of cystoid macular edema. (B) Retinal thickness map.

IMPORTANT SAFETY INFORMATION (CONT'D)

- XIPERE® is contraindicated in patients with active or **suspected ocular or periocular infections** including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.

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Ten weeks after treatment, the patient's visual acuity was 20/32, his intraocular pressure was 14 mm Hg, and there continued to be no evidence of macular edema recurrence. Fluorescein angiography revealed reduced macular leakage. OCT revealed a central retinal thickness of 216 µm (69.2% reduction from baseline; **Figure 4**).

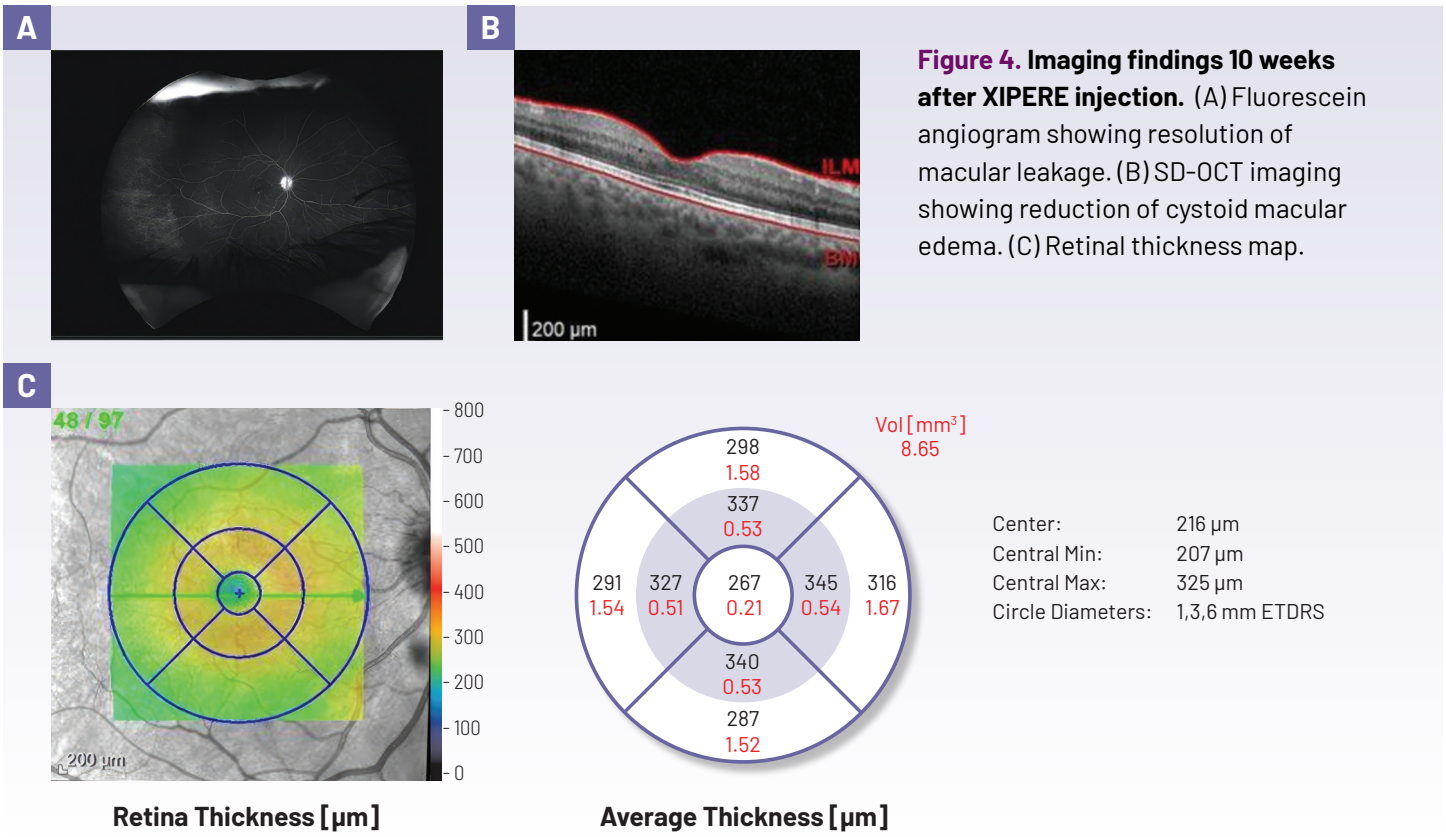

Figure 4. Imaging findings 10 weeks after XIPERE injection. (A) Fluorescein angiogram showing resolution of macular leakage. (B) SD-OCT imaging showing reduction of cystoid macular edema. (C) Retinal thickness map.

Sixteen weeks after treatment, the patient's visual acuity was 20/32^{+2}, and his intraocular pressure was 12 mm Hg. The patient's nuclear sclerotic cataract was still grade 1+, although a trace posterior subcapsular cataract had developed. There continued to be no evidence of macular edema, with a central retinal thickness of 218 µm (68.9% reduction from baseline; **Figure 5**). **When asked about his visual function, the patient replied, "I'm doing great."**

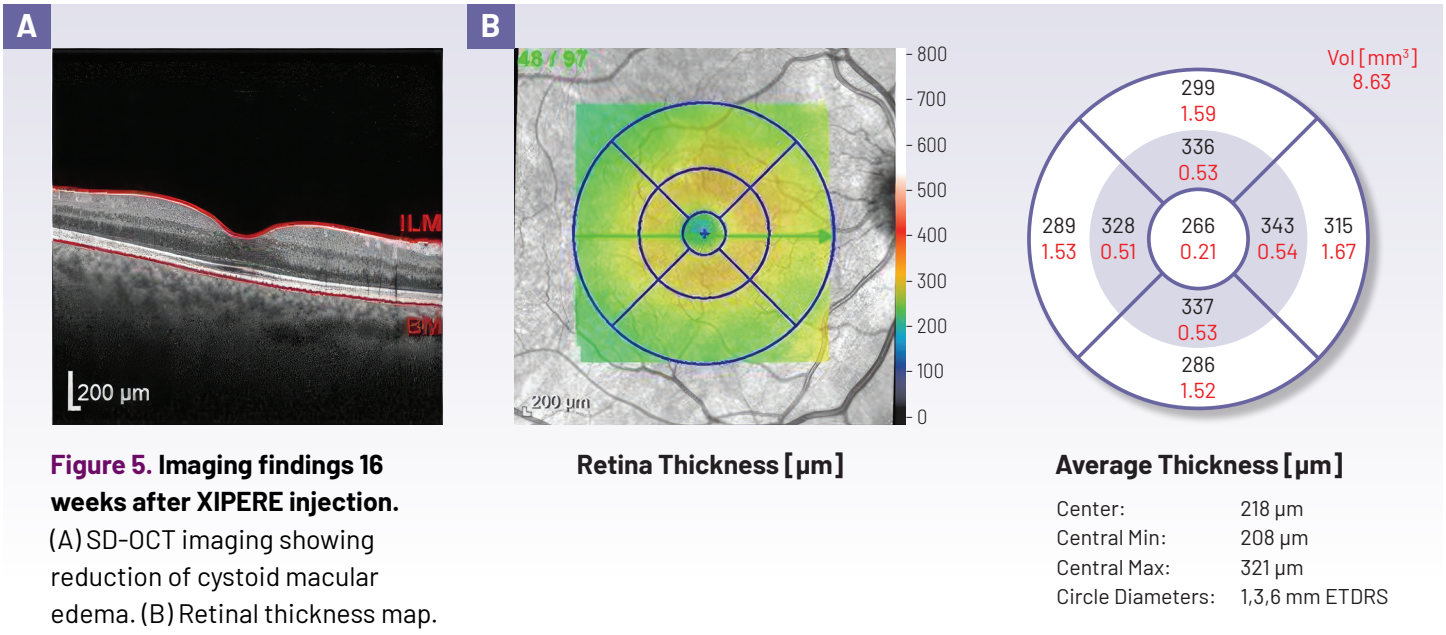

Figure 5. Imaging findings 16 weeks after XIPERE injection. (A) SD-OCT imaging showing reduction of cystoid macular edema. (B) Retinal thickness map.

Twenty-six weeks after treatment, there was still no evidence of cystoid macular edema recurrence, his visual acuity remained 20/25, and his intraocular pressure was 12 mm Hg. Central retinal thickness by OCT was 275 µm (60.8% reduction from baseline; **Figure 6**).

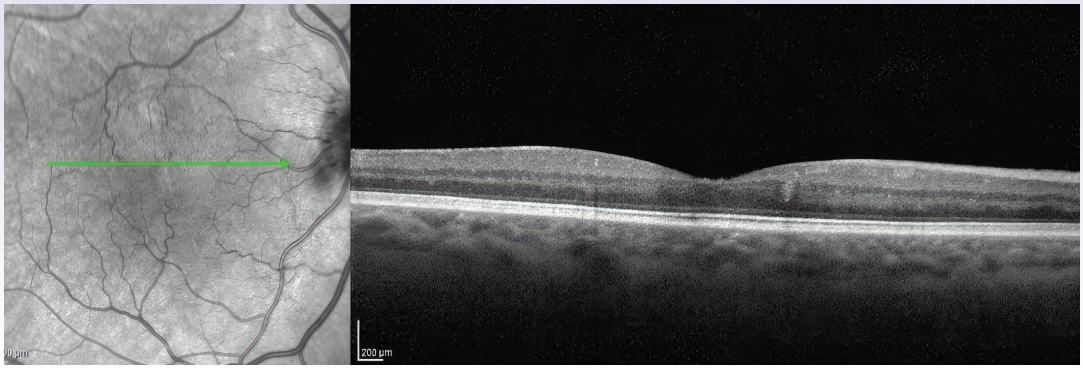

Figure 6. SD-OCT imaging findings 26 weeks after XIPERE injection. Imaging revealed no evidence of cystic macular edema recurrence.

WHY XIPERE®? Because the patient was phakic and had a grade 1+ cataract, XIPERE was selected based on its clinical profile to treat his macular edema associated with sarcoidosis-associated posterior uveitis. XIPERE was studied in a multicenter, randomized, sham-controlled, double-masked study in patients with macular edema associated with uveitis.[7] In this study, the rate of cataract (including cataract, cortical cataract, and subcapsular cataract) was 7% among patients receiving XIPERE (N=96) and 6% among patients receiving control sham treatment (N=64).[7] The most common adverse reactions reported by ≥10% of patients and at a rate greater than control included elevated intraocular pressure and eye pain.[7]

Moreover, due to the patient's desire for less frequent intravitreal injections of triamcinolone acetonide, he was motivated to try an ocular corticosteroid option that leveraged a different delivery route. In contrast to intravitreally administered drugs, XIPERE is administered as a suprachoroidal injection that delivers triamcinolone acetonide into the anatomical compartment between the choroid and sclera.[7] With this delivery route, XIPERE provides durable efficacy that has the potential to last up to a year, following 1 or 2 injections.[8]

CONCLUSIONS

Sarcoidosis is a systemic inflammatory disorder that can have ocular involvement manifesting as uveitis.[3] Ocular corticosteroids may be utilized in the treatment of macular edema caused by sarcoidosis-associated uveitis.[6] This case study describes a patient with macular edema associated with sarcoidosis-associated posterior uveitis who was treated with XIPERE. The patient demonstrated resolution of macular edema on SD-OCT, reduction of leakage on fluorescein angiography, and improvement in visual function, which were durable up to 6 months post injection. The patient exhibited minimal progression of nuclear sclerotic cataract and no sustained elevation of intraocular pressure.

IMPORTANT SAFETY INFORMATION (CONT'D)

- XIPERE® is contraindicated in patients with known **hypersensitivity to triamcinolone acetonide** or any other components of this product.
- Use of corticosteroids may produce cataracts, increased intraocular pressure, and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses, and should be used cautiously in patients with a history of ocular herpes simplex.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

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IMPORTANT SAFETY INFORMATION (CONT'D)

- Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia can occur following administration of a corticosteroid. Monitor patients for these conditions with chronic use.
- In controlled studies, the most common ocular adverse reactions were increased ocular pressure, non-acute (14%), eye pain, non-acute (12%), cataract (7%), increased intraocular pressure, acute (6%), vitreous detachment (5%), injection site pain (4%), conjunctival hemorrhage (4%), visual acuity reduced (4%), dry eye (3%), eye pain, acute (3%), photophobia (3%), and vitreous floaters (3%), and in 2% of patients: uveitis, conjunctival hyperaemia, punctate keratitis, conjunctival oedema, meibomianitis, anterior capsule contraction, chalazion, eye irritation, eye pruritus, eyelid ptosis, photopsia, and vision blurred.

  The most common non-ocular adverse event was headache (5%).
- Corticosteroids should be used during pregnancy or nursing only if the potential benefit justifies the potential risk to the fetus or nursing infant.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch + Lomb at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

Please see additional Important Safety Information throughout and full Prescribing Information here.

References: 1. Grunewald J, Grutters JC, Arkema EV, Saketkoo LA, Moller DR, Müller-Quernheim J. Sarcoidosis. *Nat Rev Dis Primers.* 2019;5(1):45. **2.** Baughman RP, Field S, Costabel U, et al. Sarcoidosis in America: analysis based on health care use. *Ann Am Thorac Soc.* 2016;13(8):1244-1252. **3.** Herbort CP, Rao NA, Mochizuki M, et al. International criteria for the diagnosis of ocular sarcoidosis: results of the first International Workshop on Ocular Sarcoidosis (IWOS). *Ocul Immunol Inflamm.* 2009;17(3):160-169. **4.** Mochizuki M, Smith JR, Takase H, et al. Revised criteria of International Workshop on Ocular Sarcoidosis (IWOS) for the diagnosis of ocular sarcoidosis. *Br J Ophthalmol.* 2019;103(10):1418-1422. **5.** Standardization of Uveitis Nomenclature (SUN) Working Group. Classification criteria for sarcoidosis-associated uveitis. *Am J Ophthalmol.* 2021;228:220-230. **6.** Takase H, Acharya NR, Babu K, et al. Recommendations for the management of ocular sarcoidosis from the International Workshop on Ocular Sarcoidosis. *Br J Ophthalmol.* 2021;105(11):1515-1519. **7.** XIPERE® (triamcinolone acetonide injectable suspension) [package insert]. Bridgewater, NJ: Bausch & Lomb Incorporated; 2022. **8.** Khurana RN, Merrill P, Yeh S, et al. Extension study of the safety and efficacy of CLS-TA for treatment of macular oedema associated with non-infectious uveitis (MAGNOLIA). *Br J Ophthalmol.* 2022;106(8):1139-1144.

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