XIPERE InXights

XIPERE Patient Case Study Series

AN IN-DEPTH DISCUSSION ON THE APPROPRIATE PATIENT TYPE FOR XIPERE®

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This supplement summarizes a roundtable discussion that took place on September 30, 2022, at the American Academy of Ophthalmology (AAO) annual meeting in Chicago, Illinois.

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Participants of this roundtable are paid consultants of Bausch + Lomb.

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 full Prescribing Information here.

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

Overview

In this roundtable discussion, **8 faculty shared their perspectives on the XIPERE® clinical data and shared their clinical experiences with XIPERE®.** These insights could help define the appropriate patient type in your practice for XIPERE®.

Macular edema (ME)—the accumulation of extracellular fluid in the intraretinal and/or subretinal spaces due to chronic ocular inflammation—is the most common sight-threatening complication of uveitis.[1] Ocular corticosteroids are the mainstay of treatment of macular edema associated with uveitis, and diverse corticosteroid formulations are available, including topical, injectable, and implantable therapies.[2] The diverse etiologies of uveitis, the presence of ocular and/or systemic comorbidities, and patients' preferences can all help inform corticosteroid selection for macular edema associated with uveitis.[1,2]

XIPERE® (triamcinolone acetonide injectable suspension) 40 mg/mL, for suprachoroidal use, is a corticosteroid indicated for the treatment of macular edema associated with uveitis.[3] The efficacy and safety of XIPERE® were evaluated in the 24-week PEACHTREE trial, as well as an additional 24-week extension study (MAGNOLIA), which demonstrated that XIPERE® delivers sustained visual and anatomic improvements in patients with macular edema associated with uveitis, with a low incidence of intraocular pressure (IOP) elevation.[3-5]

How do the PEACHTREE trial outcomes compare to real-world clinical practice?

Dr. Anesi: The PEACHTREE trial enrolled patients 18 years of age or older who had a diagnosis of noninfectious uveitis of any cause and had macular edema secondary to uveitis, which was defined as having intraretinal or subretinal fluid along with a central subfield thickness (CST) of ≥300 µm, as measured by spectral-domain optical coherence tomography (SD-OCT).[4] I'm grateful that PEACHTREE did not restrict enrollment to patients with exclusively posterior uveitis. A large proportion of the noninfectious uveitis that I encounter in my practice is anterior uveitis, much of which is associated with macular edema. For these reasons, I believe the patient enrollment of PEACHTREE aligns well with my real-world practice.

> *I believe the patient enrollment of PEACHTREE aligns well with my real-world practice.*
>
> *Stephen Anesi, MD*

Dr. Modi: I manage a fair amount of intermediate and posterior uveitis. I appreciate the relatively unrestricted enrollment of noninfectious uveitis patients into PEACHTREE, which Dr. Anesi described. This provides rationale for using XIPERE® in relatively heterogenous disease states. Among these enrollees, XIPERE® showed strong efficacy, with 47% of patients receiving XIPERE® showing a ≥15-letter improvement in best corrected visual acuity (BCVA) from baseline at Week 24, compared to just 16% of patients receiving sham control injection showing such improvement (P<0.001; N=96 vs N=64, respectively; **Figure 1**).[3] I'm excited to see how I could expand my XIPERE® usage to other appropriate patient types.

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

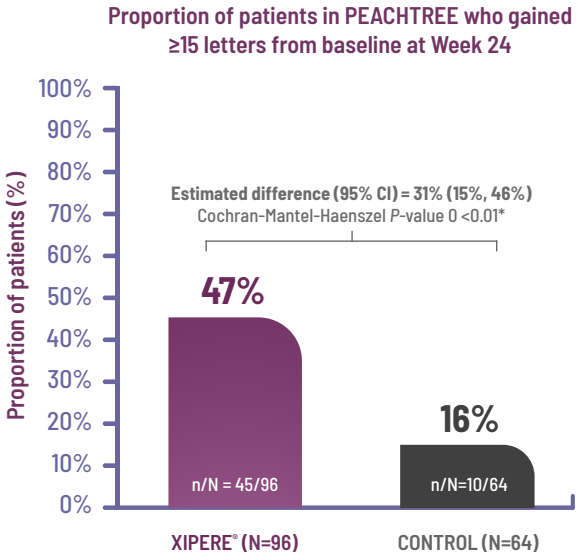

Figure 1. Proportion of patients in whom BCVA improved by ≥15 letters from baseline after 24 weeks of follow-up.[3]

Study Design: The efficacy of XIPERE® was assessed in a 6-month, randomized, multicenter, double-masked, sham-controlled study in patients with macular edema associated with anterior-, intermediate-, posterior-, or pan-uveitis.

Patients were treated at baseline and Week 12.

*The *P*-value was based on a Cochran-Mantel-Haenszel test for general association between treatment and response with stratification by country.

Dr. Walter: An important outcome of PEACHTREE was the low rate of IOP elevation with XIPERE®. Nonacute IOP elevation was reported in 14% of patients receiving XIPERE® vs 14% of patients receiving sham control. Acute increases in IOP following the suprachoroidal injection procedure were reported in 6% of patients receiving XIPERE® vs 0% of patients receiving sham control (N=96 vs N=64, respectively).[3] It would be interesting and informative if, in the future, head-to-head trials were to be conducted comparing rates of IOP elevation with XIPERE® vs other ocular corticosteroids, such as intravitreal triamcinolone acetonide injections and intravitreal dexamethasone implants.

> *An important outcome of PEACHTREE was the low rate of IOP elevation with XIPERE®.*
>
> *Scott Walter, MD*

Dr. Dacey: With regard to the efficacy of XIPERE®, I was also interested to learn about the observed reduction in CST with XIPERE®—a secondary efficacy assessment in PEACHTREE. At post-treatment Week 4, the mean change from baseline in CST was -148.5 µm with XIPERE® injection vs -4.2 µm with sham control injection (N=94 vs N=61, respectively; **Figure 2**).[3] This anatomical response occurred much faster than I would have expected before the PEACHTREE results were released. However, now that I'm using XIPERE® in my practice, I no longer find it unusual when a patient's uveitic macular edema resolves in a week or two. The speed at which XIPERE® exerts its therapeutic effect is impressive.

> *The speed at which XIPERE® exerts its therapeutic effect is impressive.*
>
> *Mark Dacey, MD*

Dr. Raiji: In my practice, I monitor the angiographic response to XIPERE® in addition to the change in CST. I observe that diffuse vascular leakage improves on a time-scale consistent with the reduction from baseline in CST.[6] However, additional studies are needed to formally evaluate these anecdotal observations.

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.
- XIPERE® is contraindicated in patients with known **hypersensitivity to triamcinolone acetonide** or any other components of this product.

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

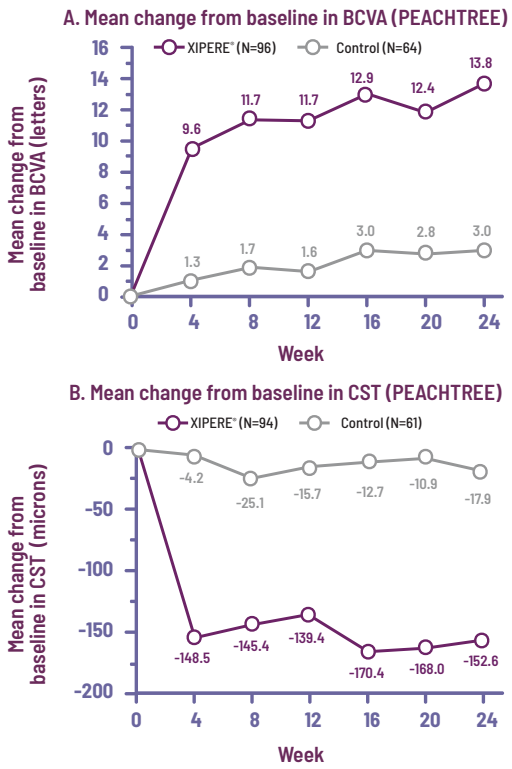

Figure 2. Mean change from baseline in (A) BCVA and (B) CST at different visits over 24 weeks of follow-up.[3]

Study Design: The efficacy of XIPERE® was assessed in a 6-month, randomized, multicenter, double-masked, sham-controlled study in patients with macular edema associated with anterior-, intermediate-, posterior-, or pan-uveitis. Patients were treated at baseline and Week 12.

Dr. Walter: With some other ocular corticosteroids I've administered, I've observed rapid reduction of macular edema immediately after treatment initiation, but this was followed by regression of the treatment effect starting occasionally around 8-12 weeks post-treatment and often by post-treatment Week 24. With XIPERE® (triamcinolone acetonide injectable suspension), the mean change from baseline in CST was -152.6 µm at 24 weeks post-injection vs -17.9 µm with sham control injection (N=94 vs N=61, respectively; **Figures 2 & 3**).[3] The reductions in CST at 24 weeks are similar to the CST reductions observed at Week 4, indicating a sustained CST response.

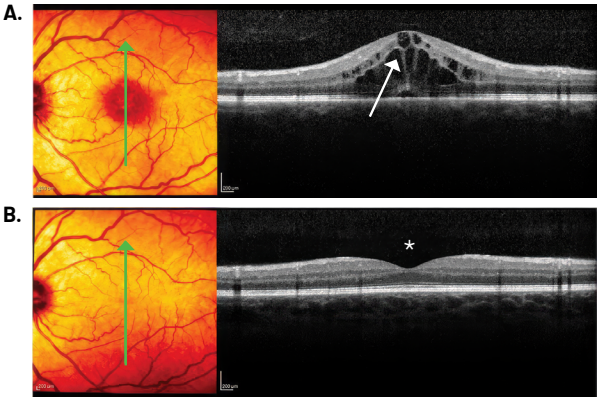

Figure 3. Examples of SD-OCT images of a patient (A) before and (B) 24 weeks after treatment with XIPERE®. Note the presence of macular edema associated with uveitis (arrow), which resolved after treatment (*). Images courtesy of Robert Wang, MD.

How do you communicate the safety profile of XIPERE® to your patients?

Dr. Dacey: Familiarity with the risk-benefit profile of XIPERE® is especially beneficial when working with uveitis patients suffering from injection fatigue. When I have a patient with uveitic macular edema who has a history of multiple intravitreal corticosteroid injections, I tell them, "I'm going to perform one XIPERE® injection today, and I'm going to perform another in 3 months. This treatment plan will potentially take us out to 1 year." It is important that the patient be made aware that, based on the MAGNOLIA extension data, two suprachoroidal injections are sufficient for 1 year of control.[3,5]

Dr. Walter: Recently, I had a patient who was terrified of the prospect of an ocular corticosteroid injection because her husband had developed endophthalmitis after an intravitreal anti-VEGF injection and suffered a loss in visual function as a result. I explained to her that while there is always a risk within the class of ocular injections, in the three phase 3 XIPERE® trials, no patients experienced endophthalmitis or suprachoroidal hemorrhage.[7] Moreover, endophthalmitis is not included in the list of ocular adverse reactions reported in ≥2% of patients in PEACHTREE, as described in the XIPERE® full Prescribing Information. By comparison, in controlled studies, the most common adverse reactions reported by ≥10% of patients and at a rate greater than control included elevated IOP and eye pain (**Figure 4**).[3]

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

Dr. Chang: In my surgical experience with patients with chronic uveitis, I find that the vitreous base can at times be fibrotic, and the vitreoretinal interface adherent. These anomalies may pose a challenge with the various intravitreal corticosteroid injectors currently on the market. I have seen patients in whom intravitreal injections were done perfectly yet return a week later with retinal detachment secondary to traction caused by the intravitreal needle penetration. In such instances of retinal detachment secondary to traction, I will use silicone oil to repair the detachment. In the three phase 3 trials, no treatment-related* retinal detachments were reported.[7] Like endophthalmitis, retinal detachment is not included in the list of ocular adverse reactions reported in ≥2% of patients in PEACHTREE, as described in the XIPERE® full Prescribing Information.[3]

* One patient in the XIPERE® group experienced retinal detachment, which occurred 8 weeks after the injection and was deemed by the investigator to not be treatment related.

> *In the three phase 3 trials...no treatment-related retinal detachments were reported.*
>
> *Peter Chang, MD*

Dr. Uchiyama: I always inform my patients about the risk-benefit profile of XIPERE®, which allows them to make an informed decision as to whether they would like to proceed with therapy. As consistent with any ocular injection, I instruct patients that if they experience any symptoms suggestive of endophthalmitis or retinal detachment, then the patient should report those symptoms without delay.[3]

> *I always inform my patients about the risk-benefit profile of XIPERE®, which allows them to make an informed decision.*
>
> *Eduardo Uchiyama, MD*

PEACHTREE

Ocular adverse reactions reported in ≥2% of patients[4]

Adverse reaction	XIPERE® (N=96) N (%)	CONTROL (N=64) N (%)
Increased intraocular pressure (IOP), nonacute*†	13 (14)	9 (14)
Eye pain, nonacute†	11 (12)	0 (0)
Cataract‡	7 (7)	4 (6)
Increased IOP, acute*§	6 (6)	0 (0)
Vitreous detachment	5 (5)	1 (2)
Injection site pain	4 (4)	2 (3)
Conjunctival hemorrhage	4 (4)	2 (3)
Visual acuity reduced	4 (4)	1 (2)
Dry eye	3 (3)	1 (2)
Eye pain, acute	3 (3)	0 (0)
Photophobia	3 (3)	0 (0)
Vitreous floaters	3 (3)	0 (0)
Uveitis	2 (2)	7 (11)
Conjunctival hyperemia	2 (2)	2 (3)
Punctate keratitis	2 (2)	1 (2)
Conjunctival edema	2 (2)	0 (0)
Meibomianitis	2 (2)	0 (0)
Anterior capsule contraction	2 (2)	0 (0)
Chalazion	2 (2)	0 (0)
Eye irritation	2 (2)	0 (0)
Eye pruritus	2 (2)	0 (0)
Eyelid ptosis	2 (2)	0 (0)
Photopsia	2 (2)	0 (0)
Vision blurred	2 (2)	0 (0)

*Includes intraocular pressure increased and ocular hypertension.
†Defined as not occurring on the day of the injection procedure or occurring on the day of the injection procedure and not resolving the same day.
‡Includes cataract, cataract cortical, and cataract subcapsular.
§Defined as occurring on the day of the injection procedure and resolving the same day.

Figure 4. Ocular Adverse Reactions Reported in ≥ 2% of Patients and Non-ocular Adverse Reactions Reported by ≥ 5% of Patients.

Non-ocular adverse reactions reported in ≥5% of patients consisted of headache: XIPERE®, 5% (n=5/96); control, 3% (n=2/64)[4]

Who is an appropriate candidate for XIPERE®?

Dr. Modi: I feel that there are many types of patients with uveitic macular edema for whom XIPERE® would be appropriate. This may be due to potentially increased therapeutic duration after the first two injections and a proven safety profile. I counsel my patients that they might feel pressure or discomfort during the suprachoroidal injection due to the introduction of the medication into the suprachoroidal space. To mitigate this, I use subconjunctival lidocaine. Additionally, I make sure

IMPORTANT SAFETY INFORMATION (CONT'D)

- 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.

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to administer slowly, taking at least 7 seconds to inject. Another aspect to take into consideration when it comes to XIPERE® (triamcinolone acetonide injectable suspension) is the injection itself into the suprachoroidal space. Retina specialists are accustomed to intravitreal injections and find them familiar to administer. As for suprachoroidal injections, there is a learning curve that requires patience. However, the more we perform suprachoroidal injections, the more second nature it will become.

> *I feel that there are many types of patients with uveitic macular edema for whom XIPERE® would be appropriate.*
>
> *Yasha Modi, MD*

Dr. Anesi: A physician might be rightfully concerned about the risk of an acute increase in IOP that may occur when the medication enters the patient's eye, as evidenced by a 6% rate of acute increases in IOP reported in the XIPERE® full Prescribing Information.[3] However, in my experience, if this should occur, it is typically a self-limiting phenomenon and resolves within a few minutes post injection. In this regard, I actually prefer the suprachoroidal route over the intravitreal route.

Dr. Raiji: I appreciate the suprachoroidal route because the likelihood of developing corticosteroid-induced cataract is low. According to the adverse event findings of PEACHTREE, the rate of cataract in the XIPERE® arm was similar to that in the sham control arm.[3] Based on the PEACHTREE data, I am less concerned about my phakic patients with uveitic macular edema requiring imminent cataract surgery. However, it is important to monitor patients for cataract formation over the long term, as the risk of cataract may increase over time.

Dr. Dacey: I believe there are a few different subcategories of patients with macular edema associated with uveitis for whom XIPERE® would be especially beneficial. The first group is patients with prior vitrectomy. Vitrectomy has considerable impact on the pharmacokinetics of triamcinolone acetonide delivered by intravitreal injection, with a mean elimination half-life of 18.6 days in nonvitrectomized eyes vs a half-life of approximately 3.2 days in a patient who had undergone a vitrectomy.[8] It seems unlikely that vitrectomy would have a meaningful impact on the pharmacokinetics of triamcinolone acetonide delivered via the suprachoroidal route, although there are currently no data in support of this hypothesis, which would need to be rigorously tested in preclinical or clinical studies. The second subgroup of patients for whom XIPERE® would be beneficial are those who live far away from their retina specialist. Many of us see patients who drive 4, 5, or even 10 hours to see us and they can't come into the retina clinic often. Based on the MAGNOLIA extension data, 50% of patients treated with XIPERE® reached 48 weeks without the need for rescue medication. This demonstrated durable efficacy which may be beneficial for these patients.[5]

Dr. Wang: Something to keep in mind, before administering XIPERE®, is to check for preexisting scarring in the suprachoroidal space. I recently administered XIPERE® to a monocular patient with uveitic macular edema caused by sympathetic ophthalmia, and I was mindful about the patient's preexisting scarring potentially interfering with the suprachoroidal injection but the injection was performed without any difficulties. Regardless, suprachoroidal scarring is a potential concern that we all need to be cognizant of.

> *I was mindful of the patient's preexisting scarring...the XIPERE® injection was performed without any difficulties. Regardless, preexisting scarring is a potential concern that we all need to be cognizant of.*
>
> *Robert Wang, MD*

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How does XIPERE® fit into the broader treatment landscape?

Dr. Dacey: I often have conversations with patients where I explain that I need to use a combination of therapies to treat their uveitis. For example, I might have a patient where immunosuppressive or immunomodulatory therapy might be effective at quieting their uveitis, but the patient could still have smoldering, persistent macular edema. This type of patient represents an excellent candidate for XIPERE®.

Dr. Raiji: In my view, the real value of XIPERE® is that it's a local therapy that is compartmentalized in the suprachoroidal space. This makes XIPERE® different from systemic immuno-suppressants, and from other ocular corticosteroids.

> *The real value of XIPERE® is that it's a local therapy that is compartmentalized in the suprachoroidal space. This makes XIPERE® different from systemic immunosuppressants, and from other ocular corticosteroids.*
>
> *Veena Raiji, MD*

Dr. Walter: As a retina specialist, I prefer to avoid systemic immunosuppression in my uveitis patients and use local therapy whenever it's appropriate. XIPERE® is an excellent addition to our armamentarium for local corticosteroid therapy.

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.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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

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