

The Uveitis Pipeline



Take a look at what's next in uveitis.

AN INTERVIEW WITH STEVEN YEH, MD

Retina Today: The uveitis pipeline is busy. From a high level, what should retina specialists be aware of?

Steven Yeh, MD: There are plenty of treatment candidates in the pipeline. Intravitreal sirolimus may be an option to treat our patients in the near future, and a formulation of triamcinolone acetonide may be available soon.

RT: Can you give us an update on Clearside Biomedical's proprietary formulation of the corticosteroid triamcinolone acetonide (Xipere)?

Dr. Yeh: The phase 3 PEACHTREE study results were favorable with respect to improvement in VA in patients who were treated with the suprachoroidal preparation of preservative-free Xipere when compared with sham.¹ Low rates of cataract development and IOP elevation were noted in the phase 3 extension study MAGNOLIA.¹

The company submitted a new drug application to the US FDA in February, and it will resubmit the application in the first quarter of 2020 with stability data for the triamcinolone acetonide suspension produced using an enhanced manufacturing process.² In October, Bausch Health acquired an exclusive license for the commercialization and development of Xipere in the United States and Canada.³

RT: Where does sirolimus fit into this landscape?

Dr. Yeh: In the phase 3 SAKURA 1 study, 440 µg sirolimus intravitreal

injection (Opsiria, Santen) significantly improved ocular inflammation in patients with noninfectious uveitis (NIU) in the posterior segment.⁴

In the parallel phase 3 trial SAKURA 2, patients who received 440 µg sirolimus did not show a significant improvement in ocular inflammation compared with patients given low-dose sirolimus (44 µg).⁵ Clinical findings provide evidence of efficacy of the product, and researchers in the field have been bullish.⁵

RT: Is further research being conducted on sirolimus?

Dr. Yeh: Researchers for the LUMINA trial are evaluating the safety and efficacy of 440 µg sirolimus intravitreal injection delivered every 2 months in patients with active NIU in the posterior segment.⁶ The study will recruit 200 patients. A 6-month, single-arm, open-label period will occur first, followed by a 6-month,

double-masked, controlled period when investigators will evaluate the efficacy and safety of the drug every 2 months for a longer duration than appropriate for a sham control.

RT: The FDA approved adalimumab (Humira, AbbVie) in 2016 for the treatment of noninfectious intermediate uveitis, posterior uveitis, and panuveitis. Granted, this drug has moved beyond the pipeline, but it has certainly affected the uveitis treatment paradigm.

Dr. Yeh: Adalimumab is an anti-tumor necrosis factor alpha inhibitor. In 2016, Jaffe et al evaluated adults who showed signs of uveitis after 2 weeks of prednisone therapy.⁷ Patients were randomly assigned to receive a loading dose of 80 mg adalimumab followed by adalimumab 40 mg every 2 weeks or placebo. All patients received a prednisone burst that was tapered off for 15 weeks.

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AT A GLANCE

- ▶ The US FDA will review a new drug application for Clearside Biomedical's proprietary formulation of corticosteroid triamcinolone acetonide (Xipere) when the company files it in the first quarter of 2020.
- ▶ The LUMINA trial will assess the safety and efficacy of 440 µg sirolimus intravitreal injection (Opsiria, Santen) delivered every 2 months in patients with active noninfectious uveitis.
- ▶ Two 2019 studies evaluating adalimumab therapy showed that it was effective at preserving VA and reducing the risk of treatment failure.

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The median time to treatment failure was 24 weeks in the adalimumab group and 13 weeks in the placebo group. Adalimumab use was associated with a lower risk of uveitic flare or visual impairment.

Adalimumab has been approved for marketing for approximately 2.5 years, and we have a growing body of data on its efficacy in treating uveitis.

Adalimumab has been shown to work as an effective second-line immunosuppression drug in patients with uveitis. Patients observed in a 2019 retrospective, longitudinal study had a significantly reduced risk of treatment failure if they were treated with second-line adalimumab.⁸

In a 2019 retrospective study, researchers reviewed data from three randomized, double-masked, placebo-controlled trials to assess several anti-tumor necrosis factor alpha inhibitors in patients with uveitis.⁹ Patients with active or nonactive noninfectious uveitis who were treated with adalimumab were more likely to demonstrate VA preservation compared with patients treated with other medical interventions.

It should be noted that adalimumab is an immunosuppressant medication—an important consideration when treating patients who may have concerns about adverse events related to immunosuppression. ■

1. Merrill P. Paper presented at: American Uveitis Society Winter Symposium; November 25, 2019; Park City, UT.
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3. Bausch health licenses Clearside Biomedical's Xipere, an investigational treatment for macular edema associated with uveitis [press release]. Bausch Health; Laval, Quebec, and Alpharetta, GA; October 23, 2019.
4. Nguyen QD, Merrill PT, Clark WL; Sirolimus Study Assessing Double-Masked Uveitis Treatment (SAKURA) Study Group. Intravitreal sirolimus for noninfectious uveitis: a phase III sirolimus study assessing double-masked uveitis treatment (SAKURA). *Ophthalmology*. 2016;123(11):2413-2423.
5. Santen announces phase III SAKURA program topline results in patients with non-infectious uveitis of the posterior segment [press release]. Santen Pharmaceutical; Osaka, Japan; November 28, 2016.
6. LUMINA phase III Study assessing the efficacy and safety of intravitreal injections of 440 ug DE-109 sirolimus for the treatment of active, non-infectious uveitis of the posterior segment of the eye. ClinicalTrials.gov identifier: NCT03711929. <https://clinicaltrials.gov/ct2/show/NCT03711929>. Accessed November 25, 2019.
7. Jaffe GJ, Dick AD, Brezin AP, et al. Adalimumab in patients with active noninfectious uveitis. *N Engl J Med*. 2016;275(10):932-943.
8. Al-Janabi A, El Nokrashy A, Sharief L, Nagendran V, Lightman S, Tomkins-Netzer O. Long-term outcomes of treatment with biological agents in eyes with refractory, active, noninfectious intermediate uveitis, posterior uveitis, or panuveitis [published online ahead of print September 9, 2019]. *Ophthalmology*.
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