

Multicenter trial

Long-acting azithromycin safe, effective in treating bacterial conjunctivitis

Novel formulation offers convenient, minimal-frequency dosing schedule

By Cheryl Guttman

Reviewed by Mark B. Abelson, MD

Fort Lauderdale, FL—An investigational long-acting solution of 1.0% azithromycin (AzaSite™, InSite Vision) is safe, well tolerated, and effective for the treatment of bacterial conjunctivitis in pediatric patients and adults, according to the results of pivotal phase III clinical trial involving placebo and active controls.



Dr. Abelson

The active ingredient in this novel product has been formulated into a solution that contains a controlled-release ophthalmic drug delivery system (DuraSite®, InSite Vision). It remains in the eye for up to several hours to enhance antibiotic exposure to

target tissues while permitting reduced dosing frequency, said Mark B. Abelson, MD, during the annual meeting of the Association for Research in Vision and Ophthalmology.

Dr. Abelson reported the results from the multicenter, double-masked, active-controlled study in which patients were randomly assigned to 5-day courses of the azithromycin product or tobramycin 0.3%. The long-acting azithromycin solution was administered twice daily (morning and bedtime) for 2 days and then once in the morning for the last 3 days of treatment. Tobramycin was administered on a q.i.d. dosing schedule on all 5 days. Patients in the AzaSite group were given additional bottles of vehicle to use each day in order to maintain the blind study.

Follow-up visits were scheduled on days 3 and 6. The results showed the two anti-infectives were similarly safe and well tolerated. They were equivalent in terms of achieving bacterial eradication and clinical resolution of the ocular signs of bacterial conjunctivitis.

“Options for treatment of ocular infections have been limited to a few classes of antibiotics,” said Dr. Abelson, associate clinical professor of ophthalmology, Harvard Medical School, Boston. “However, having a broader range of agents available would be valuable to avoid overuse that promotes development of resistance and thereby can limit the utility of available agents for treating serious infections.

“In particular, it would be useful to have an alternative that could be used to treat bacterial conjunctivitis, which is the most common bacterial ocular infection, so that other, more potent agents could be reserved for managing ker-

atitis or endophthalmitis,” he said.

“Azithromycin offers an antimicrobial spectrum that targets the most common gram-positive and gram-negative causes of bacterial conjunctivitis and has a long-standing safety history established through years of systemic use,” Dr. Abelson continued. “Clinical trial results demonstrate it is effective in treating bacterial conjunctivitis, and this unique formulation with its convenient once- and twice-daily dosing schedule should facilitate compliance. Considering all of its attributes, I expect that once available, this 1% azithromycin product should become the treatment of choice for bacterial conjunctivitis.”

Study enrollment

The active-controlled study enrolled 746 subjects at 47 clinical centers. Eligible patients, who were at least 1 year old, were required to have grade 1 ocular discharge and grade 1 bulbar or palpebral conjunctival injection in at least 1 eye with a duration of no more than 3 days. The injection scales used for guiding the clinical evaluation were developed by Ophthalmic Research Associates Inc. (ORA), CRO for the study.

Of the enrolled subjects, 316 patients had positive bacterial cultures, and 170 (54%) of those individuals were pediatric patients (up to 11 years old). The most common pathogens included *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and other *Streptococcus viridans*.

Clinical resolution, defined as absence of ocular discharge, bulbar conjunctival injection, and palpebral conjunctival injection, was evaluated as the primary efficacy endpoint. At the last visit in the per protocol analysis, clinical resolution rates were nearly identical in the azithromycin and tobramycin groups, 79.9% versus 78.3%, respectively. Overall bacterial eradication rates were 88.1% for azithromycin (86.1% for all gram-positive bacteria, 92.9% for all gram-negative bacteria) and 94.3% for tobramycin (92.2% for all gram-positive bacteria, 98.4% for all gram-negative bacteria). The differences between treatments were not statistically significant for any of those endpoints.

In separate studies, the azithromycin 1% product was also compared against placebo in a randomized, double-masked, vehicle-controlled trial performed at 42 centers. That study had similar inclusion criteria and used the same administration schedule for the study medications. It enrolled 685 subjects.

The long-acting azithromycin product has been very well tolerated in clinical trial experience. In the active-controlled study, the most

Take-Home Message

A long-acting formulation of 1.0% azithromycin (AzaSite, InSite Vision) has demonstrated efficacy and safety in the treatment of bacterial conjunctivitis in children and adults. When administered twice daily for 2 days followed by once daily for 3 days, it achieved clinical resolution and bacterial eradication rates comparable to tobramycin 0.3% q.i.d. and significantly superior to vehicle control.

commonly reported ocular adverse event was eye irritation (1.9%). The rate of that event was similar in patients using tobramycin and may be related to the infection itself rather than the treatment, noted Dr. Abelson.

“Overall, patients seem to find that the azithromycin solution is very comfortable on instillation,” he said.

Although bacterial conjunctivitis is generally self-limiting, prompt initiation of antibiotic therapy is recommended to hasten resolution, limit infection transmission, and reduce the risk of progression to a more serious infection that can occur if corneal integrity becomes compromised. The dosing schedule of the long-acting azithromycin product makes it a convenient alternative for treatment, but may also have implications for cost savings.

“Children using a medication that needs to be administered four times a day may need to be treated during school,” Dr. Abelson said. “However, transport of a prescription medication to school is prohibited in some states. In those situations, children need to have duplicate product—one for use at home and the other to keep at school. With a medication that is administered once or twice daily, only a single prescription is necessary.”

It is expected that InSite Vision will submit the NDA for AzaSite to the FDA later this summer, he said. **OT**

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Dr. Abelson is the chief executive officer of Ophthalmic Research Associates Inc., CRO that conducted the azithromycin phase III studies.