Allergic conjunctivitis is one of the most common maladies patients come to an ophthalmologist for, said multiple specialists during an EyeWorld Educational Symposium, “The Role of Ocular Allergy in Your Practice: Advancing Diagnostics and Treatment to Improve Outcomes,” held during the 2012 ASCRS•ASOA Symposium & Congress. The symposium was supported by an educational grant from ISTA Pharmaceuticals (Irvine, Calif.).

It’s estimated that 40% of the U.S. population will have ocular allergy symptoms at some point during the year, said Edward Holland, M.D., professor of ophthalmology, University of Cincinnati. What are the treatment options for allergic conjunctivitis? And out of these possibilities, which is the most efficacious? A distinguished panel of experts, including Dr. Holland, Richard Lindstrom, M.D., founder and attending surgeon, Minnesota Eye Consultants; Stephen Lane, M.D., adjunct clinical professor, University of Minnesota; Craig McCabe, M.D., clinical instructor, Vanderbilt Eye Center, Nashville, Tenn., and in practice, McCabe Vision Center, Murfreesboro, Tenn.; and Michael Blaiss, M.D., clinical professor of pediatrics and medicine, University of Tennessee Health Science Center, Memphis, weighed in.

Dr. Holland kicked off the session with an overview of ocular surface disease and the impact these conditions have on refractive outcomes after cataract surgery (Figure 1). Although ocular surface disease historically has been of interest only to corneal surgeons, thanks to premium IOLs, ocular surface disease has migrated to refractive surgeons’ radars in recent years.

“Aqueous tear deficiency and meibomian gland dysfunction were the leading causes of decreased vision in people with premium IOLs,” Dr. Holland said.

Ocular surface disease is an extremely common condition, he said, although the exact numbers vary widely, anywhere from 7-34% of the U.S. population. Researchers do know that ocular surface disease is more common in women than men, and the incidence increases with age.

“Dry eye is certainly under diagnosed,” he said. “Diagnosed dry eye makes up about 16 million Americans, but about 40 million Americans do not have the diagnosis and just put up with the symptoms” (Figures 2 and 3).

Allergic eye disease is the most common but least talked about ocular surface issue, said Dr. Holland. Over 50 million Americans suffer from some type of allergies, and allergic incidence...
itching, Dr. Lane said. There are a number of ways to treat this bother - some symptom, such as allergen avoidance, cold compresses, over-the-counter medications, lubricants, and prescription drugs such as mast cell stabilizers and/or antihistamines, topical steroids, and NSAIDs.

“The most popular way [to treat ocular allergies] is with a dual action antihistamine and mast cell stabilizer,” Dr. Lane said, such as Bepreve (bepotastine besilate, ISTA Pharmaceuticals), which Dr. Lane gave the clinical trial results of.

The Bepreve clinical trials utilized a Conjunctival Allergen Challenge (CAC) and included two randomized placebo-controlled studies with single-site and multi-site type characteristics. Patients with allergic conjunctivitis history underwent CAC testing. CAC testing meant patients were dosed with either the active agent (Bepreve) or a placebo and then introduced to an allergen. Symptoms of ocular itching were measured at 3, 5, and 7 minutes, and symptoms of conjunctival hyperemia were measured at 7, 15, and 20 minutes (Figure 4).

“In terms of the onset of action, there was a very quick onset of reaction of Bepreve compared to the placebo,” Dr. Lane said. “If you look at the long-lasting effect of this in terms of relief of itch, once again there’s statistically significant relief, up to 8 hours [with Bepreve]. If you took those patients who had a severe response, you can see that 68% of those patients had relief of severe symptoms with Bepreve [but] essentially none with the placebo” (Figures 5 and 6).

In regard to adverse events when taking Bepreve, dry eye was reported in about 2% of the placebo-treated patients and 1% of the Bepreve-treated patients, Dr. Lane said.

Finally, Dr. Lane stressed the tremendous value Bepreve provides patients, which is “important in this day and age when the economics of the medications we use are under such high scrutiny.”

Bepreve is supplied in 10 mL bottles, which allows for one copay for a 60-day period and means fewer trips to the pharmacy. “The combination provides for greater value as you consider the refill costs of this as [patients] continue to have symptoms throughout the year or at various times during the year,” Dr. Lane said.

“We have a medication that’s effective, we have a medication that is safe, and we have a medication that is of great value to the patient,” Dr. Lane said. “I think this combination lends this to be a very effective compound to be used in allergic conjunctivitis” (Figure 7).

Dr. Lindstrom gave his unique view on ocular allergies from both a clinician’s and a patient’s perspective,
Before pollen counts become high and bothersome, allergy season is a good time to think about prophylaxis therapy, said David Lindstrom, MD,Allergist, in Dallas. "I can't avoid allergens that well, but I can treat myself," he said.

"Post-allergen challenge:"
- Ocular itching assessed at 3, 5, 7 minutes
  - Achieved clinical significance
- Hyperemia assessed at 7, 15, 20 minutes
  - Achieved statistical significance, did not achieve clinical significance
- Efficacy compared to placebo (onset of action at 15 minutes; duration of effect at 8 hours)

Prophylaxis therapy is something to think about prior to exposure. Cold compresses can be useful to feel better and wash out the tears. Most of the antihistamines make me dry, and dry eye is one of the issues we need to deal with. I find that I only use two drugs for myself and two drugs for my patients: a mast cell stabilizer antihistamine and occasionally a topical steroid.

As Dr. Lindstrom is "extremely allergic" to cats, he can't, however, live a feline-free life as his mother-in-law has a cat.

"If I take a single drop of a mast cell stabilizer antihistamine before I [visit my mother-in-law], I'm totally asymptomatic. If I go without doing that and try to catch up afterward, it's very difficult and sometimes requires topical steroids for me," he said.

Because of this, Dr. Lindstrom is an advocate for using prescription drops such as Bepreve for prophylaxis to save patients "from a lot of trouble." He also starts the drops during the allergy season before pollen counts become high and bothersome.

"I can't avoid allergens that well, but I can treat myself," he said. "Prophylaxis therapy is something to think about prior to exposure. Cold compresses can be useful to feel better and wash out the tears. Most of the antihistamines make me dry, and dry eye is one of the issues we need to deal with. I find that I only use two drugs for myself and two drugs for my patients: a mast cell stabilizer antihistamine and occasionally a topical steroid."

The three main prescription drugs in this class are Bepreve, Pataday (olopatadine, Alcon, Forth Worth, Texas), and Lastacaft (alcaftadine, Allergan, Irvine, Calif.). Dr. Lindstrom prefers Bepreve, he said, for a number of reasons such as value, efficacy, and safety, although he acknowledged that Pataday "is a great drug" also.

"One of the key issues to look at is what do you get when you write a prescription for Bepreve?" he asked. "You get 10 mL, and with prophylaxis one drop is often enough. So 10 mL is a pretty good value versus 2.5 mL for Pataday and 3 mL for Lastacaft. The sample of Bepreve is as large as the prescription for Pataday. Value as far as cost per drop [for Bepreve] is pretty good as long as it's a potent drug, and it turns out Bepreve is a potent drug."

Bepreve is more effective than other drugs in treating nasal congestion and rhinorrhea, he said. It's also "extremely safe," Dr. Lindstrom said. "One thing I like about this drug is it doesn't seem to make dry eye worse. It's nice to have something where you don't have to worry about making dry eye worse."

Although Dr. Lindstrom acknowledged that many ophthalmologists use Pataday "with great effect," the cost per drop is significantly higher than Bepreve. Lastacaft has similar value issues and isn't as comfortable as the other two drops, he said.

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**Fast relief of ocular itch**

<table>
<thead>
<tr>
<th>% of eyes with 21 unit reduction in itching</th>
<th>Clinical success: Onset of action</th>
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<tbody>
<tr>
<td>BEPREVE</td>
<td>95%</td>
</tr>
<tr>
<td>Placebo</td>
<td>47%</td>
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\( \text{p}<0.05 \)

Dose applied 15 min prior to CAC

Clinical significance is at least a 1-unit reduction in itching score

**Long-lasting relief of ocular itch**

<table>
<thead>
<tr>
<th>% of eyes with 21 unit reduction in itching</th>
<th>Clinical success: 8 hours</th>
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</thead>
<tbody>
<tr>
<td>BEPREVE</td>
<td>90%</td>
</tr>
<tr>
<td>Placebo</td>
<td>40%</td>
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</tbody>
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\( \text{p}<0.05 \)

Dose applied 8 hours prior to CAC

Clinical significance is at least a 1-unit reduction in itching score
Clinical and safety summary

- Allergic conjunctivitis is an urgent and growing problem among Americans
- Ocular allergies affect >20% of Americans

**Bepreve:**

- **Powerful relief:**
  - Highly selective to the H1 receptor and an effective mast cell stabilizer
  - 95% of eyes had a clinically significant reduction (≥1 unit) of ocular itch at onset (p<0.05)
  - 90% of eyes had a clinically significant reduction (≥1 unit) of ocular itch at 8 hours (p<0.05)
  - 68% of patients with severe itch experienced complete relief within 3 minutes

- **Comfortable relief:**
  - Comfort equal to placebo
  - Indicated for use in patients ≥2 years of age

- **Value add:**
  - Supplied as 10 mL bottle (60 days of therapy) for 1 co-pay

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Improving the treatment of ocular allergies

“[Lastacaft] doesn’t seem to have quite the same level of potency, it causes some discomfort, and it causes redness,” Dr. Lindstrom said.

Although Bepreve and Pataday are the two most popular topical medications prescribed in the U.S., no head-to-head clinical studies have been published directly comparing the two. Because of this, Dr. McCabe took it upon himself to lead an investigator-initiated, single-center, single-masked switch patient preference study. The purpose was to compare patient perceived relief of ocular itch and ocular allergy symptoms when treating allergic conjunctivitis with Bepreve and Pataday.

Thirty patients participated in the study, which was conducted during fall allergy season. Patients took either Bepreve twice daily or Pataday once daily for 2 weeks, followed by a week-long washout period using artificial tears twice a day. After the washout period ended, patients switched to the remaining branded drop for 2 weeks.

“During the time they took these drops, they filled out a daily diary at noon and 8 p.m. where they rated how well that medication relieved various allergy symptoms. At the end of the study, they were asked which agent provided better relief of their ocular allergy symptoms and which one they would like me to write a prescription for,” Dr. McCabe said.

Bepreve “got the jumpstart on the relief of their ocular itching,” Dr. McCabe said. “By almost a 2-to-1 margin, 19 patients compared to 11 rated Bepreve as giving them better all-day relief of ocular itching. Overall patients felt that Bepreve rather than Pataday offered better relief of morning ocular allergy symptoms, however the greatest difference was seen in the first week. Our patients also reported that Bepreve provided better relief of evening ocular allergy symptoms. They rated Bepreve as more effectively improving their ocular allergy symptoms in the evening when compared to Pataday.”

Dr. McCabe concluded, “Despite all we hear about dosing and compliance, patients chose the greater efficacy of Bepreve over the once-a-day convenience of Pataday for improved relief of their multi-symptom associated allergic conjunctivitis.”

Dr. Blaiss provided his thoughts on ocular allergies from the perspective of an allergist. Most patients come to Dr. Blaiss complaining of nasal problems associated with their eyes.

“Basically every patient with ocular allergy symptoms has nasal problems,” he said.

Dr. Blaiss continued by giving an overview of what he looks at in rhinoconjunctivitis. He tries to determine if the allergies are seasonal or perennial, which makes the patient’s past history important, especially family history.

“If mom, dad, or a sibling has allergies, the chance of that person having allergies is two- to three-fold,” he said.

Environmental history is also key, he said. Questions to ask patients include are they exposed to pets or dust mites? Are mold spores in the air that can cause long-term rhinoconjunctivitis?

To manage patients with ocular allergies, Dr. Blaiss goes over avoidance procedures. For example, if a patient is allergic to pollen, Dr. Blaiss suggests the patient stay in during the early morning and evening hours, when pollen counts are at their highest. Lubricating eye drops have also been shown to help flush out the eye and remove allergens, he said.

“What we do a lot of are systemic therapies and a great deal of oral second-generation antihistamines,” Dr. Blaiss said. “The problem is even the second-generation non-sedating antihistamines are not efficacious as far as ocular allergies.”

In fact, many of the over-the-counter drugs can lead to drying of the eyes. Dr. Blaiss places almost every rhinoconjunctivitis patient he sees on an intranasal agent, an antihistamine and/or corticosteroid.

“Some of these do have a label as far as decreasing ocular symptoms associated with allergic rhinitis,” he said, but they are usually not as efficacious as topical ocular agents, especially in patients with moderate to severe allergic conjunctivitis.

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