



Cornea Day highlights global hot topics, corneal complications, and more



Dr. Daluvoy discusses why she prefers separate procedures in Fuchs' dystrophy and cataract cases.

In the "Global Hot Topics" session of the 2017 Cornea Day at the ASCRS•ASOA Symposium & Congress, presenters discussed ocular surface reconstruction, Zika virus and the eye, the Asia Cornea Society Infectious Keratitis Study, management of bilateral limbal stem cell deficiency, addressing corneal blindness, global eye bank development, bioengineered corneas, transplantation of ex vivo expanded human corneal endothelial cells, producing corneal cells from induced pluripotent stem cells (iPS), and using long-term preserved corneas for DALK.

Maria Cortina, MD, Chicago, discussed why she thinks the Boston KPro is the treatment of choice in bilateral limbal stem cell deficiency (LSCD).

Surgical options for bilateral LSCD treatment fall into two categories: cell-based therapies and keratoprosthesis. Cell-based procedures can be broken down into allogeneic and autologous.

For keratoprosthesis, there are different devices for dry ocular surface and wet ocular surface. Dr. Cortina spoke about the Boston type 1 KPro for

wet ocular surface, which she said is the clear winner.

It avoids the need for immunosuppression, she said. There is also faster visual rehabilitation, and it's available worldwide. She did note that this type of KPro requires corneal tissue as a carrier, and there is a risk of sight-threatening complications. It's best approached by a multidisciplinary team.

Dr. Cortina said that the Boston type 1 KPro has good visual acuity results and long-term retention in patients with LSCD. It avoids the long-term risk of systemic immunosuppression needed for allogeneic transplantation. Patients should be followed closely and managed by an experienced team, since some sight-threatening complications can occur. Although there is limited evidence, Dr. Cortina said the evidence available suggests that long-term KPro outcomes are superior to cell-based therapies. However, she noted that more long-term studies and/or a randomized clinical trial would be helpful to further guide treatment choices in cases of bilateral LSCD.

Another session of Cornea Day featured point-counterpoint discussions on a variety of topics.

Keith Walter, MD, Winston-Salem, North Carolina, and **Melissa Daluvoy, MD**, Durham, North Carolina, spoke on either side of "Fuchs' Dystrophy and Cataract: Combined EK Triple vs. Staged Procedure."

Dr. Walter argued for a combined procedure, which he said makes life easier for everyone. Dr. Walter noted that when the cataract is done first, you make the patient's vision worse either immediately or in the near future. You could also cause the patient unnecessary pain or an infection from ruptured bullae.

When Descemet's stripping endothelial keratoplasty (DSEK) or Descemet's membrane endothelial keratoplasty (DMEK) is done first, Dr. Walter said you aren't doing the patient any favors either. This could still result in cataract formation and a risk for graft failure from the additional ultrasound trauma to the new graft.

Dr. Walter said there are many advantages of combined procedures. Combining can save the patient and family an extra trip to the OR, and there is faster visual recovery. Dr. Walter noted that you can use the same incision for both procedures, you just have to slightly enlarge it. It's easy to accomplish both procedures with minimal additional instrumentation or skill. It also saves OR time.

Dr. Walter shared considerations when combining procedures. First, he said it's important to know how the view will be during surgery. Severe edema may obscure the view. "You need to consider astigmatism management because the incision is a little larger," he added. Accurate Ks and IOL selection are



Cornea Society

Advancing the treatment of corneal disease

President's Message

Dear Cornea Society members,

Summer is here, and we are all busy enjoying the weather and time with our family. With the change of seasons everyone is outside and happy after a long winter. Change is everywhere you look, including the Cornea Society. We are looking to the future and trying to figure out how we can best position the Society to meet the changing dynamics of healthcare in our complicated world. There are so many challenges ahead, from MACRA to taxonomy codes. No one is sure how these will affect our subspecialty, but our goal is to position ourselves to withstand any change that comes our way. To that end, we have submitted an application for taxonomy codes in the future. ASCRS and AAO are helping us in this process. Our application is in, and we are hopeful we can prepare for what the future holds. We have been asked by the ABO to provide a liaison for the Cornea Society, and we have put two names forward.

This winter the Executive Committee met for a 1-day retreat in Chicago to identify the challenges we will face in the future. With the help of a facilitator, **John Riordan** and **Gail Albert**, we had a very productive meeting and laid out a plan for developing our strategic plan. We have identified three key areas we will work on. First of all, we will address our mission and vision. I will work with **Adam Moss**, **Deepinder Dhaliwal**, and **Preeya Gupta** to develop a vision statement for the future of our society. **Elmer Tu**, our president elect, will work with **Richard Davidson**, **Stephen Kaufman**, and **Jennifer Li** to evaluate our membership structure and leadership pipeline to ensure vibrancy in the future. **Bennie Jeng**, vice president of international relations, will work with **Mark Mannis**, **Shahzad Mian**, and **Julie Schallhorn** to analyze our organizational structure, including our board and committee structure.

Together this group of 12 of our members of different geographical, academic, and experiential backgrounds will begin to develop the future path for the Cornea Society. Do you have any ideas you want to share? We welcome your input and hope you will reach out to one of the 12 committee members or Gail Albert. Please make your voice heard. We are definitely stronger together.

Have you noticed that we do not have our own standalone meeting just for cornea? All the other specialties have a standalone meeting—retina, glaucoma, pediatrics, uveitis—but not cornea. We are busily working to start a new meeting just for our specialty. There will be more exciting news about this in the future. As soon as we secure the date, check the website for an announcement and make sure you can attend. I am certain it will be a great meeting, and you won't want to miss it.

Lastly, I want to give a big shout-out to **Jessica Ciralsky** who has been busy working with Gail Albert to make Cornea Society University a reality. During the ASCRS•ASOA Symposium & Congress, Jessica and Gail organized a dinner program just for our young physicians, "Getting to the Podium and What to Do Once I Get There." Attendees had the chance to practice and receive feedback from professionals about their speaking and content delivery. The future is bright and our young members are well-positioned to represent our society in the best possible light.

Enjoy the summer, kick back, take your issue of *Cornea* to the beach, browse the website, and know that we are working to make the Cornea Society strong. If you have ideas or want to chat, we welcome your input. Our strategic planning process is moving forward, and we hope you will let us know what you want to see our Society doing over the next 10 years.

Marian Macsai, MD
President, Cornea Society



Marian Macsai, MD

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Dr. Neff discusses new uses of CXL.

also important factors to consider. “You can keep the pupil dilated after phaco,” Dr. Walter said, adding that the surgeon can easily plan for topical anesthesia for a combined procedure.

Dr. Daluvoy argued that “less is more,” sharing her reasons for separate procedures. A staged procedure means less surgery time, less risk of IOL instability, less risk of DSEK/DMEK graft complications, less special positioning, and less risk of rejection.

Maybe you just need cataract surgery, Dr. Daluvoy said, adding that it’s possible to perform an “endothelial friendly” cataract surgery. With no EK needed, this would mean no risk of rebubbling and no risk of rejection.

When you perform cataract surgery first, she said there are a number of advantages. Intraoperatively, you can perform the cataract in a normal fashion. The CCC sizing and capsular tears are less of an issue, and the IOL complex/AC is more stable. Postoperatively, Dr. Daluvoy said that there is no special positioning required and no risk of graft detachment. The patient may be happy with the vision as well.

Some patients may only need an EK procedure. Intraoperatively, there is less pupil management required and less likelihood of leaky paracentesis incisions. Postoperatively, there is lower risk of graft dislocation and low risk for subsequent CE. A clear cornea and known refractive error can help ensure more accurate IOL choices. Accommodation can be preserved and there may be better quality of vision, Dr. Daluvoy said.

Corneal crosslinking (CXL) was the topic of another session at Cornea Day. The incorporation of CXL into a practice requires some careful consideration of several factors, including education, **Sam Garg, MD**, Tustin, California, told attendees. Surgeons should remind patients that CXL is not refractive surgery and that they will maintain their current visual status after the procedure. Patients should also know that there likely will be initial steepening followed by flattening and that 1% to 2% of those having CXL can experience complications.

The ideal CXL candidate is young, able to lay still, has a clear visual axis, and can see well in glasses, Dr. Garg said. Patients who are not good candidates usually are older and have scarring and very thin corneas.

There are also practice management concerns with CXL, according to **Nicole Fram, MD**, Los Angeles. For example, you’ll want to educate your staff about what CXL is, who is a candidate, and what financial considerations are involved. “The financial [aspect] is huge,” Dr. Fram said.

Consider where you will perform CXL; two typical locations would be a laser suite or a short procedure room. Make sure to train at least two technicians on how to work with CXL procedures, in case one technician is sick and unavailable. Block out 90 minutes for each CXL case, and always work with a sterile technique. This is important because there is a risk for bacterial keratitis, she said.

Some novel uses of CXL going forward include for infection, pellucid marginal degeneration, LASIK Xtra, and for pseudophakic bullous keratopathy, said **Kristiana Neff, MD**, Ladson, South Carolina. Other uses that researchers are beginning to explore include small incision lenticule extraction (SMILE, Carl Zeiss Meditec, Jena, Germany), leaking blebs, and scleral CXL for myopia. The use of CXL in these novel capacities requires more long-term study in larger cohorts, Dr. Neff said.

As part of a series of presentations focusing on dry eye disease, **Deborah Jacobs, MD**, Boston, addressed the pain syndrome that occurs in some patients, even if they have few clinical symptoms of dry eye. Dr. Jacobs discussed the difference between nociceptive and neuropathic pain, noting that patients with neuropathic pain and dry eye may be perceived as “crazy” because they have minimal symptoms. Research is ongoing for the best diagnostic criteria for dry eye as a pain syndrome, Dr. Jacobs said.

The use of biologicals to treat dry eye will continue to grow in the future, said **Bennie Jeng, MD**, Baltimore. He discussed autologous serum for dry eye and how far it has evolved in the past decade. However, “it’s not a magic bullet,” he said. Per the U.S. Food and Drug Administration’s definition of biologicals, there are other treatments that fall into this category, including allogeneic serum and amniotic membrane. **CN**

Editors’ note: Dr. Walter has financial interests with SightLife (Seattle). Dr. Fram has financial interests with Alcon (Fort Worth, Texas), Johnson + Johnson Vision (Santa Ana, California), and other ophthalmic companies. Dr. Garg has financial interests with Alcon, Allergan (Dublin, Ireland), and other ophthalmic companies. Dr. Jeng has financial interests with Alcon, Avedro (Waltham, Massachusetts), and other ophthalmic companies. Dr. Neff has financial interests with Sun Ophthalmics (Princeton, New Jersey). Drs. Jacobs, Cortina, and Daluvoy has no financial interests related to their comments.

Case-based presentations on decision-making in corneal transplantation



Dr. Talley Rostov presents a case she handled of Fuchs' dystrophy and cataract.

A symposium at the ASCRS•ASOA Symposium & Congress sponsored by the Cornea Society focused on decision-making in corneal transplantation, with case-based presentations. The session was moderated by **Anthony Aldave, MD**, and **Marian Macsai, MD**.

Francis Price, MD, Indianapolis, discussed managing corneal edema with moderate Fuchs' dystrophy in a 50-year-old. When making decisions, you have to consider patient symptoms, potential surgery, and objective findings on the exam, Dr. Price said.

The treatment choices have evolved over the years as to when to graft with Fuchs' dystrophy.

What you do depends on your options, Dr. Price said. Options will depend on the experience of the surgeon and the individual situation of the patient. For each option, Dr. Price said it's important to look at how reliable the visual recovery is and what the risks and complications are.

He said to choose the least invasive option, which for him is Descemet's membrane endothelial keratoplasty (DMEK), which is only Descemet's and endothelial cells. It offers the best visual recovery and least risk of rejection. "But we still have unpredictable refractive changes," Dr. Price said.

DMEK is becoming more like cataract surgery, Dr. Price said. Some patients are 20/20 or 20/40 by day 5, and DMEK accelerates cataract formation a little more than Descemet's stripping endothelial keratoplasty (DSEK) or penetrating keratoplasty (PK).

Dr. Price spoke about decision-making for cataract with corneal problems. Make sure the AC depth is deep enough for later phaco, he said, and if not, remove the lens during DMEK.

"In summary, it's all about decisions," he said, adding that the number one factor is patient symptoms.

Audrey Talley Rostov, MD, Seattle, presented a case of a 68-year-old woman with a history of Fuchs' dystrophy and cataract. She said to consider a number of factors, including what the BCVA is, if there is morning blur, how the patient's activities in daily life are affected, the grade of the cataract and the grade of the guttata, the pachymetry, and the endothelial cell density (ECD).

Dr. Talley Rostov's patient had a BCVA of 20/50, glare with headlights when driving at night but no morning blur, ECD of 870, and pachymetry of 589.

When considering treatment options, Dr. Talley Rostov said you need to decide when to do a combined procedure. With epithelial edema, a combined

procedure would be indicated. It would also be indicated for stromal edema with morning blur, pachymetry generally greater than 620 microns (which depends on the baseline), and ECD of less than 800.

Rajesh Fogla, MD, Hyderabad, India, described corneal ectasia in an atopic patient with prior hydrops. His case involved a 14-year-old male with a history of vernal conjunctivitis for the past 5 years. The patient had a history of eye rubbing and presented with a sudden decrease in vision in the right eye for the past week. Dr. Fogla noticed diffuse corneal edema involving the inferior half of the ectatic cornea and acute hydrops.

To treat the patient, he used an inferior peripheral iridectomy and C3F8 (13%) gas injected into the AC. There was good resolution of the edema 1 month later.

Dr. Fogla said that hydrops can be managed using non-expansile gas injection into the anterior chamber. If the scar does not involve the visual axis, consider deep anterior lamellar keratoplasty (DALK) surgery. Preoperative evaluation and surgical planning are essential, Dr. Fogla added, and intraoperative microperforation can be managed effectively. Postoperatively, Dr. Fogla said to manage the ocular surface judiciously.

The final section of the symposium looked at management of corneal opacification and graft failure, and presentations focused on corneal scarring in a younger patient with reduced endothelial cell density, visually significant recurrent corneal stromal dystrophy following PTK, Descemet's stripping automated endothelial keratoplasty (DSAEK) failure, and PK failure. **CN**

Editors' note: Dr. Price has financial interests with Haag-Streit (Koniz, Switzerland). Dr. Talley Rostov has financial interests with Allergan (Dublin, Ireland), Bausch + Lomb (Bridgewater, New Jersey), Ocular Therapeutix (Bedford, Massachusetts), and Shire (Lexington, Massachusetts). Dr. Fogla has no financial interests related to his comments.



The 6th Biennial Scientific Meeting
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In conjunction with
the 17th National Congress of Cornea & Ocular Surface
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May 17 (Thu) - 20 (Sun) , 2018
Shangri-La Hotel ·Qingdao, China



www.acs2018qingdao.com

CSU at ASCRS

We had a very successful Cornea Society University (CSU) presence at the 2017 ASCRS•ASOA Symposium & Congress in Los Angeles. Many programs geared toward the CSU community were highlighted on our Facebook and Twitter accounts and were well received. During Cornea Day on May 5, we had a booth with information about upcoming CSU programs and networking opportunities. A survey was conducted at the booth targeting residents, fellows, and cornea specialists in their first 5 years of practice. We received great feedback on future CSU activities, including future column topics, features for the CSU interactive website, and goals for live events. We also held our first live event, the inaugural CSU Dinner Series on Friday night immediately following the Cornea Day program. We had a great turnout. The dinner program focused on “Getting to the Podium and What to Do Once I Get There.” Fellows and young cornea specialists had the opportunity to interact and network with colleagues as well as practice a podium presentation and receive real-time feedback in a fun environment, complete with dinner, drinks, stress balls, and Slinkys. **CN**

—Jessica Ciralsky, MD, CSU editor



Look for more events at AAO 2017! Be sure to visit our booth at AAO and watch your inbox for monthly CSU newsletters.

30th Biennial Cornea Conference

The conference will be held October 12–14, 2017, in Boston



30th Biennial
Cornea Conference

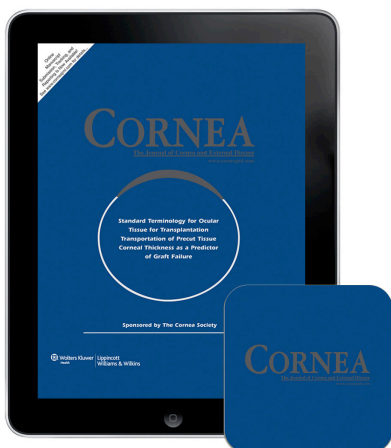
The Biennial Cornea Conference is the premier global cornea and ocular surface academic research conference, bringing together more than 200 leaders and trainees from academia and industry to explore current basic, clinical, and translational research developments. This year the conference will consist of a dedicated evening of scientific posters (October 12) and 2 days of lectures (October 13–14).

To commemorate the 30th year of the conference, a portion of the program is dedicated to **Claes Dohlman, MD**, honoring his 60 years of contributions to corneal science and education.

This conference is co-hosted by Massachusetts Eye and Ear, a Harvard Medical School teaching hospital, and Boston University School of Medicine with support from Tufts University School of Medicine. Topics will include Ocular Surface, Immunology and Microbiology, Endothelial Cell Biology, and Innovation and New Techniques.

To learn more and register, visit eye.hms.harvard.edu/cornea/conference. The deadline for early registration is September 15. **CN**

Cornea journal report



In 2016, the journal received 1,129 new submissions. Of these, 30.5% were accepted for publication. In 2017, the submission rate has increased slightly. With this volume we are able to publish papers online in 6 to 8 weeks and in print 4 to 5 months after acceptance. The quality of submissions appears to be increasing as well. The vast majority of published papers are from outside of the U.S. and represent all parts of the world.

Esen Akpek, MD, Johns Hopkins University, and **Bennie Jeng, MD**, University of Maryland, have increased their commitment to the journal as newly appointed assistant editors. We welcome their help and expertise in managing the growing number of papers.

The journal continues to encourage the submission of new and interesting material relevant to the cornea and external eye disease. **CN**

—Alan Sugar, MD, editor-in-chief



Expert Insights You Can Apply to Your Practice

Cornea 2017

Keeping the Old, or
Breaking the Mold?

New Orleans | Nov. 11

Program Directors:
Bennie H. Jeng, MD
Carol L. Karp, MD
Jennifer Y. Li, MD

Your registration for Cornea Subspecialty Day includes:

- Flexibility to float among all Subspecialty Day meetings on Saturday.
- Access to the AAO 2017 exhibit hall on Saturday.

Member Registration Opens: June 28

Nonmember Registration Opens: July 12



Cornea Society

Advancing the treatment of corneal disease

In conjunction with the Cornea Society

aao.org/2017

Subspecialty Day AAO 2017

AAO Mid-Year Forum: Young physicians' impressions



Dr. Rao and her colleagues visit Capitol Hill during the AAO Mid-Year Forum.

The Cornea Society gave two young physicians the opportunity to attend the AAO Mid-Year Forum in April in Washington, D.C. as participants in the Advocacy Ambassador Program. Below are their impressions of the program and a recap of their experiences.

Rohini Rao, MD

My background in advocacy for medicine and problems facing healthcare at large was limited to a summer experience at the American Medical Students Association during college. So, needless to say, I was very excited about visiting

Capitol Hill and talking with my state representatives about the issues that face ophthalmology. My experience was incredibly eye-opening. During the first evening debrief of the weekend, I began to understand some of the issues, and I was able to get behind the importance of increased access to and lower pricing of compounded drugs, as well as funding for the National Institutes of Health (NIH) and vision research. The morning before our visit to Capitol Hill was when I learned how to present. I was in a group of five residents, two fellows, an oculoplastic surgeon in private practice,

and a pediatric ophthalmologist at an academic center. With our distinct backgrounds and career aspirations, it was incredible to join together to promote the issues that face our field.

When meeting with our senators and representatives or their staff, we shared stories about our patients—the ones who need intravitreal antibiotics in the middle of the night for endophthalmitis, the ones who are sent in from 3 hours away by their community ophthalmologists to receive fortified topical antibiotics for severe corneal ulcers, the ones who cannot afford prednisolone after routine cataract surgery, or the ones we treat at the VA who benefit from developments in eye safety research. Sharing our experiences bonded us and made our message stronger.

I was particularly impressed by the discussions we had with our state representatives. Each staffer, though young, was well informed about the relevant healthcare issues and was eager to learn about the issues facing ophthalmology. I left each meeting feeling like I imparted a meaningful message. I was so excited to learn that Congress voted to boost NIH funding. I have no doubt that our hard work during Advocacy Day played a role in this.

Advocacy Day also opened my eyes to all the issues that loom on the horizon for the healthcare system. This experience has encouraged me to keep my eyes open and continue to look for ways to advocate for our patients and for our specialty. Thank you for allowing me to participate in this meaningful experience.

Daniel Terveen, MD

I arrived in Washington, D.C. several hours before the start of the Mid-Year Forum, hoping to spend some time exploring our nation's capital. I made my way down to the National Mall and wandered through the monuments immortalizing the incredible individuals who sacrificed so much for the rights and freedoms of our country. As the sun started to set, I walked through the Mountain of Despair framing the statue of Martin Luther King Jr., and stood

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CORNEA and EYE BANKING FORUM 2017

NEW ORLEANS
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Cornea Society
Advancing the treatment of corneal disease.



**Register
Today!**

Join us for a one-day educational program featuring the latest scientific developments in corneal surgery, eye banking, and more. Over 25 scientific free-papers will be presented in addition to two 30-minute symposia covering:

- **Keratoconus:** The Forum will be held on World Keratoconus Day so the Cornea Society and EBAA are partnering with the National Keratoconus Foundation to invite speakers to discuss topics related to this disease.
- **Corneal Preservation Time Study (CPTS):** Speakers will provide an overview of the CPTS, highlighting findings regarding the impact of preservation time as well operative factors on graft success and cell loss following DSEK.

For more information, to register, or to submit an abstract, visit forum.corneasociety.org.

Abstract submissions due August 14

Early-bird registration ends September 15

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University of Iowa ophthalmology residents Lindsay McConnell, MD, Daniel Terveen, MD, Tyler Risma, MD, and Steven Christiansen, MD, with Cynthia Bradford, MD (center), president of the American Academy of Ophthalmology, advocate on Capitol Hill.

beside his likeness, looking out toward the Jefferson Memorial. Standing there, I thought of all that was in store for me over the next couple of days and remembered a paraphrased quote from MLK Jr.: “Our lives begin to end the day we become silent about things that matter.” This sentiment embodies the essence of advocacy: fighting for the causes we believe in, the people we care about, and the future that we want for our profession and our country. Physicians advocate everyday. We advocate for our patients and their families, for our employees, and for our colleagues.

I first became interested in political advocacy working with my local legislators. During that time, I saw the powerful way in which advocacy could shape policy. Advocates speaking with conviction and passion on topics in which they were familiar had a profound impact on the decisions legislators made. By helping guide legislation, physicians are able to ensure that the needs of patients are being addressed while protecting and safeguarding our profession.

In Washington, we advocated in order to protect access to valuable medications for patients through compounding and competitive pricing, to ease

regulatory burdens on providers, and to ensure continued financial support for the National Eye Institute through the NIH. The legislators and staffers were attentive and genuinely interested in our concerns, recognizing our expertise when it comes to patient care. Our efforts were rewarded with some early returns including the recent Omnibus budget from Congress, which expands funding for the NIH. In addition, several legislators signed on to letters ensuring access to compounded medications and urging CMS to remove penalties from PQRS during the transition to MACRA. Perhaps one of the most valuable aspects of being an Advocacy Ambassador is the mentorship from leaders in my state and in our profession. As a young ophthalmologist, the advice and guidance on how to develop one’s career is invaluable. Advocating with legislators drew

many parallels to first surgeries in residency. We watched leaders in our field interact with legislators, focusing on intricacies such as word choice and body language. In the next meeting we took the lead in the discussion, with mentoring ophthalmologists jumping in when we got in trouble. In both early surgery and early advocacy, a little timolol under the tongue does wonders.

The second day of the Mid-Year Forum consists of a program called L.E.A.P., which functions to give young ophthalmologist the tools they need to become a leader and advocate in their community. There were many incredible talks and teaching points from leading ophthalmologists on topics ranging from Twitter to mission work, and everything in between. The talk that struck me as most profound came from **Keith Carter, MD**. In his comments he described how ophthalmology had left the house of medicine and that this was the root of the biggest challenges facing our profession. Through his talk, I realized ophthalmologists need to take an active role in state and national medical societies. We need to focus on educating medical students and other medical providers on the value we provide and our shared common interests. We need to continue to support local and rural hospitals and emergency rooms with expert opinion and service when asked. We need to integrate with other primary care doctors as the primary eyecare providers in this country. We need to work with other surgical specialties to promote patient safety by ensuring that surgery is performed safely. In short, we need to reenter the house of medicine. I am so grateful and honored that the Cornea Society gave me the opportunity to attend the Mid-Year Forum. Through the experience, I learned many valuable skills to share with my co-residents and will continue to advocate for our profession in my community and state. **CN**

Business meeting announcement

The Cornea Society business meeting will take place on Friday, November 10, during the Cornea and Eye Banking Forum at the Astor Crowne Plaza in New Orleans. All members are invited to attend. Check the Society website for updates: www.CorneaSociety.org. **CN**

TRAVATAN Z[®]

(travoprost ophthalmic solution) 0.004%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE

TRAVATAN Z[®] (travoprost ophthalmic solution) 0.004% is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION

The recommended dosage is one drop in the affected eye(s) once daily in the evening. TRAVATAN Z[®] (travoprost ophthalmic solution) should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the intraocular pressure lowering effect.

Reduction of the intraocular pressure starts approximately 2 hours after the first administration with maximum effect reached after 12 hours.

TRAVATAN Z[®] Solution may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Pigmentation

Travoprost ophthalmic solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. Pigmentation is expected to increase as long as travoprost is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of travoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with TRAVATAN Z[®] (travoprost ophthalmic solution) 0.004% can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes

TRAVATAN Z[®] Solution may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation

TRAVATAN Z[®] Solution should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Macular Edema

Macular edema, including cystoid macular edema, has been reported during treatment with travoprost ophthalmic solution. TRAVATAN Z[®] Solution should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Angle-closure, Inflammatory or Neovascular Glaucoma

TRAVATAN Z[®] Solution has not been evaluated for the treatment of angle-closure, inflammatory or neovascular glaucoma.

Bacterial Keratitis

There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Use with Contact Lenses

Contact lenses should be removed prior to instillation of TRAVATAN Z[®] Solution and may be reinserted 15 minutes following its administration.

ADVERSE REACTIONS

Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. The most common adverse reaction observed in controlled clinical studies with TRAVATAN[®] (travoprost ophthalmic solution) 0.004% and TRAVATAN Z[®] (travoprost ophthalmic solution) 0.004% was ocular hyperemia which was reported in 30 to 50% of patients. Up to 3% of patients discontinued therapy due to conjunctival hyperemia. Ocular adverse reactions reported at an incidence of 5 to 10% in these clinical studies included decreased visual acuity, eye discomfort, foreign body sensation, pain and pruritus. Ocular adverse reactions reported at an incidence of 1 to 4% in clinical studies with TRAVATAN[®] or TRAVATAN Z[®] Solutions included abnormal vision, blepharitis, blurred vision, cataract, conjunctivitis, corneal staining, dry eye, iris discoloration, keratitis, lid margin crusting, ocular inflammation, photophobia, subconjunctival hemorrhage and tearing.

Nonocular adverse reactions reported at an incidence of 1 to 5% in these clinical studies were allergy, angina pectoris, anxiety, arthritis, back pain, bradycardia, bronchitis, chest pain, cold/flu syndrome, depression, dyspepsia, gastrointestinal disorder, headache, hypercholesterolemia, hypertension, hypotension, infection, pain, prostate disorder, sinusitis, urinary incontinence and urinary tract infections.

In postmarketing use with prostaglandin analogs, periorbital and lid changes including deepening of the eyelid sulcus have been observed.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C

Teratogenic effects: Travoprost was teratogenic in rats, at an intravenous (IV) dose up to 10 mcg/kg/day (250 times the maximal recommended human ocular dose (MRHD)), evidenced by an increase in the incidence of skeletal malformations as well as external and visceral malformations, such as fused sternebrae, domed head and hydrocephaly. Travoprost was not teratogenic in rats at IV doses up to 3 mcg/kg/day (75 times the MRHD), or in mice at subcutaneous doses up to 1 mcg/kg/day (25 times the MRHD). Travoprost produced an increase in post-implantation losses and a decrease in fetal viability in rats at IV doses > 3 mcg/kg/day (75 times the MRHD) and in mice at subcutaneous doses > 0.3 mcg/kg/day (7.5 times the MRHD).

In the offspring of female rats that received travoprost subcutaneously from Day 7 of pregnancy to lactation Day 21 at doses of \geq 0.12 mcg/kg/day (3 times the MRHD), the incidence of postnatal mortality was increased, and neonatal body weight gain was decreased. Neonatal development was also affected, evidenced by delayed eye opening, pinna detachment and preputial separation, and by decreased motor activity.

There are no adequate and well-controlled studies of TRAVATAN Z[®] (travoprost ophthalmic solution) 0.004% administration in pregnant women. Because animal reproductive studies are not always predictive of human response, TRAVATAN Z[®] Solution should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

A study in lactating rats demonstrated that radiolabeled travoprost and/or its metabolites were excreted in milk. It is not known whether this drug or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when TRAVATAN Z[®] Solution is administered to a nursing woman.

Pediatric Use

Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

Geriatric Use

No overall clinical differences in safety or effectiveness have been observed between elderly and other adult patients.

Hepatic and Renal Impairment

Travoprost ophthalmic solution 0.004% has been studied in patients with hepatic impairment and also in patients with renal impairment. No clinically relevant changes in hematology, blood chemistry, or urinalysis laboratory data were observed in these patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Two-year carcinogenicity studies in mice and rats at subcutaneous doses of 10, 30, or 100 mcg/kg/day did not show any evidence of carcinogenic potential. However, at 100 mcg/kg/day, male rats were only treated for 82 weeks, and the maximum tolerated dose (MTD) was not reached in the mouse study. The high dose (100 mcg/kg) corresponds to exposure levels over 400 times the human exposure at the maximum recommended human ocular dose (MRHD) of 0.04 mcg/kg, based on plasma active drug levels. Travoprost was not mutagenic in the Ames test, mouse micronucleus test or rat chromosome aberration assay. A slight increase in the mutant frequency was observed in one of two mouse lymphoma assays in the presence of rat S-9 activation enzymes.

Travoprost did not affect mating or fertility indices in male or female rats at subcutaneous doses up to 10 mcg/kg/day [250 times the maximum recommended human ocular dose of 0.04 mcg/kg/day on a mcg/kg basis (MRHD)]. At 10 mcg/kg/day, the mean number of corpora lutea was reduced, and the post-implantation losses were increased. These effects were not observed at 3 mcg/kg/day (75 times the MRHD).

PATIENT COUNSELING INFORMATION

Potential for Pigmentation

Patients should be advised about the potential for increased brown pigmentation of the iris, which may be permanent. Patients should also be informed about the possibility of eyelid skin darkening, which may be reversible after discontinuation of TRAVATAN Z[®] (travoprost ophthalmic solution) 0.004%.

Potential for Eyelash Changes

Patients should also be informed of the possibility of eyelash and vellus hair changes in the treated eye during treatment with TRAVATAN Z[®] Solution. These changes may result in a disparity between eyes in length, thickness, pigmentation, number of eyelashes or vellus hairs, and/or direction of eyelash growth. Eyelash changes are usually reversible upon discontinuation of treatment.

Handling the Container

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

When to Seek Physician Advice

Patients should also be advised that if they develop an intercurrent ocular condition (e.g., trauma or infection), have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice concerning the continued use of TRAVATAN Z[®] Solution.

Use with Contact Lenses

Contact lenses should be removed prior to instillation of TRAVATAN Z[®] Solution and may be reinserted 15 minutes following its administration.

Use with Other Ophthalmic Drugs

If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes between applications.

Rx Only

U.S. Patent Nos. 5,631,287; 5,889,052, 6,011,062; 6,235,781; 6,503,497; and 6,849,253

Alcon[®]

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For newly diagnosed patients with elevated IOP

Power from the start. Foundation for the journey.

Sustained 30% IOP lowering at 12, 14, and 20 hours postdose in a 3-month study^{1*}

TRAVATAN Z[®]
(travoprost ophthalmic
solution) 0.004%

TRAVATAN Z[®] Solution has no FDA-approved therapeutic equivalent available

INDICATIONS AND USAGE

TRAVATAN Z[®] (travoprost ophthalmic solution) 0.004% is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

Dosage and Administration

The recommended dosage is one drop in the affected eye(s) once daily in the evening. TRAVATAN Z[®] Solution should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the IOP lowering effect.

TRAVATAN Z[®] Solution may be used concomitantly with other topical ophthalmic drug products to lower IOP. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Pigmentation—Travoprost ophthalmic solution has been reported to increase the pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as travoprost is administered. After discontinuation of travoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. The long-term effects of increased pigmentation are not known. While treatment with TRAVATAN Z[®] Solution can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes—TRAVATAN Z[®] Solution may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation—TRAVATAN Z[®] Solution should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Macular Edema—Macular edema, including cystoid macular edema, has been reported during treatment with travoprost ophthalmic solution. TRAVATAN Z[®] Solution should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Angle-closure, Inflammatory, or Neovascular Glaucoma—TRAVATAN Z[®] Solution has not been evaluated for the treatment of angle-closure, inflammatory, or neovascular glaucoma.

Bacterial Keratitis—There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Use With Contact Lenses—Contact lenses should be removed prior to instillation of TRAVATAN Z[®] Solution and may be reinserted 15 minutes following its administration.

Adverse Reactions

The most common adverse reaction observed in controlled clinical studies with TRAVATAN Z[®] Solution was ocular hyperemia, which was reported in 30 to 50% of patients. Up to 3% of patients discontinued therapy due to conjunctival hyperemia. Ocular adverse reactions reported at an incidence of 5 to 10% in these clinical studies included decreased visual acuity, eye discomfort, foreign body sensation, pain, and pruritus. In postmarketing use with prostaglandin analogs, periorbital and lid changes including deepening of the eyelid sulcus have been observed.

Use in Specific Populations

Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

For additional information on TRAVATAN Z[®] Solution, please refer to the Brief Summary of Prescribing Information on the following page.

***Study Design:** Double-masked, randomized, parallel-group, multicenter noninferiority comparison of the efficacy and safety of travoprost 0.004% preserved with benzalkonium chloride (BAK) and TRAVATAN Z[®] Solution after 3 months of treatment in patients with open-angle glaucoma or ocular hypertension. Baseline IOPs were 27.0 mm Hg (n=322), 25.5 mm Hg (n=322), and 24.8 mm Hg (n=322) at 8 AM, 10 AM, and 4 PM for TRAVATAN Z[®] Solution. At the end of month 3, the TRAVATAN Z[®] Solution group had mean IOPs (95% CI for the treatment differences) of 18.7 mm Hg (-0.4, 0.5), 17.7 mm Hg (-0.4, 0.6), and 17.4 mm Hg (-0.2, 0.8) at 8 AM, 10 AM, and 4 PM, respectively. Statistically equivalent reductions in IOP (95% CI about the treatment differences were entirely within ± 1.5 mm Hg) were demonstrated between the treatments at all study visits during the 3 months of treatment.¹

Reference: 1. Lewis RA, Katz GJ, Weiss MJ, et al; for Travoprost BAC-free Study Group. Travoprost 0.004% with and without benzalkonium chloride: a comparison of safety and efficacy. *J Glaucoma*. 2007;16(1):98-103.

Start strong with BAK-free TRAVATAN Z[®] Solution