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The Modern State of Dry Eye: Part 2

Patient Selection, Innovative Approaches to Therapy, and the Latest Data

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Eye care professionals on the front lines of dry eye disease patient care review the challenges of treating a broad spectrum of dry eye patients, discuss different approaches to treatment, and review recent safety and efficacy data.

The various ages, ethnicities, and genders of adult patients with dry eye disease testify to the demographic diversity of this patient population; the various clinical presentations and underlying causes of disease demonstrate the pathophysiologic spectrum of dry eye disease patients, which may be of particular interest to clinicians tasked with treating this chronic disease.

Given the range of patients that clinicians treat, it should be unsurprising that a single solution to dry eye disease has not presented itself. As more options for dry eye disease treatment enter the discussion, the decision-making process becomes more complicated.

Eye care providers who rely on clinical trial data to assess the safety and efficacy of new treatments allow themselves to prescribe therapies armed with knowledge about the spectrum of performance they might expect from an intervention. A thorough review of safety and efficacy data is needed before including a new treatment option in a clinical algorithm.

These roundtables, which have been edited for brevity and clarity, have been published in two parts. In the first installment of this series, the real-world treatment dynamics that have led to undertreated and unsatisfied patients were reviewed. In this section, we'll discuss the challenges associated with treating this patient population, review Tyrvaya® (varenicline solution) nasal spray 0.03 mg (Oyster Point Pharma), as a therapeutic approach, and assess safety and efficacy data for Tyrvaya®.

Douglas K. Devries, OD: Patients arrive from any number of avenues to clinics specializing in dry eye disease. What are some common patterns you've noticed upon presentation?

Mitchell A. Jackson, MD: Many of the patients I see have already tried over-the-counter drops, and some have even been prescribed drops for dry eye disease. When they arrive in my clinic, they often tell me that the drops didn't work after a few rounds of administration—which means that it falls on us to educate them about treatment compliance and when it makes sense to try a different treatment.

Scott Hauswirth, OD: At my clinic, some patients present with dry eye disease flare-ups, others have low-intensity but consistent disease, and some fit elsewhere in the spectrum. Combine this variety of presentations with various lifestyle or demographic concerns—say, older patients who are already on drops, or younger adult patients with practical limitations that interfere with ideal compliance—and the task of finding an effective treatment for our patients' disease becomes more difficult.

Efficacy and Safety Data for Tyrvaya® (varenicline solution) Nasal Spray

In a separate roundtable, panelists discussed the latest data.

With Mitch Ibach, OD, FAAO; Cecelia Koetting, OD, FAAO; Marguerite B. McDonald, MD, FACS; and Inder Paul Singh, MD

To explore the results of the ONSET-1 and ONSET-2 studies,[1,2] which were a pair of pivotal clinical trials that evaluated the safety and efficacy of Tyrvaya (varenicline solution) for the treatment of the signs and symptoms of dry eye disease, a panel of leading eye care providers—two ophthalmologists and two optometrists—was convened. The exploration of the studies' results distills some of the finer points of the data, and arrives at the conclusion that the studies' authors made: that use of Tyrvaya nasal spray is an effective method for addressing dry eye disease.

Cecelia Koetting, OD, FAAO: In the ONSET-1 and ONSET-2 studies, 940 patients with mild, moderate, or severe dry eye disease were randomly assigned to vehicle or active drug.[1,2] These trials were randomized, vehicle-controlled, and double-masked, and enrolled patients with dry eye disease who were at least 22 years old (mean 61 years); 74% of those enrolled were female. Patients administered one spray of either active drug or vehicle in each nostril twice daily. The mean baseline anesthetized Schirmer's score was 5.1 mm, and the mean baseline eye dryness score (EDS) was 59.3.

The primary efficacy endpoint for ONSET-1 was mean change in Schirmer's Test Score (STS) from baseline at week 4. In ONSET-2, the primary efficacy endpoint was the percentage of patients achieving an improvement in STS of at least 10 mm from baseline at week 4.

RESULTS

Inder Paul Singh, MD: Tear film production was measured by anesthetized STS. Of the patients treated with Tyrvaya, 52% achieved at least a 10-mm increase in STS from baseline in the ONSET-1 study, and 47% achieved at least a 10-mm increase in STS from baseline in the ONSET-2 study, compared with 14% and 28% of vehicle-treated patients, respectively, at day 28.

Mitch Ibach, OD, FAAO: These data are informative, and their implications are clear to us clinicians who specialize in dry eye disease.

Marguerite B. McDonald, MD, FACS: In ONSET-1, Tyrvaya demonstrated a mean 11.7-mm improvement in STS from baseline to week 4 compared with a 3.2-mm improvement in STS in the vehicle arm. So far, we have talked about an increase in natural tear film, but reduction in symptoms was also measured as a secondary endpoint in these two pivotal trials. The investigators looked at symptoms in the clinic, which is likely most similar to how you treat patients.

At week 4 in ONSET-1, the Tyrvaya group had a mean 18.9-mm decrease in EDS compared with a 5.4-mm decrease in the vehicle group; the difference was statistically significant (Figure).[3] At 3 weeks in ONSET-1, the Tyrvaya group had a mean 16.0-mm decrease in EDS compared with a 6.3-mm decrease in the vehicle group.[3]

SAFETY

Dr. Singh: We should discuss the safety profile for Tyrvaya. In clinical trials, 82% of patients sneezed at least once.[3] The majority of patients who reported sneezing rated it as mild,[4] and in ONSET-2, 65% of patients reported that their sneezing resolved within 1 minute.[3]

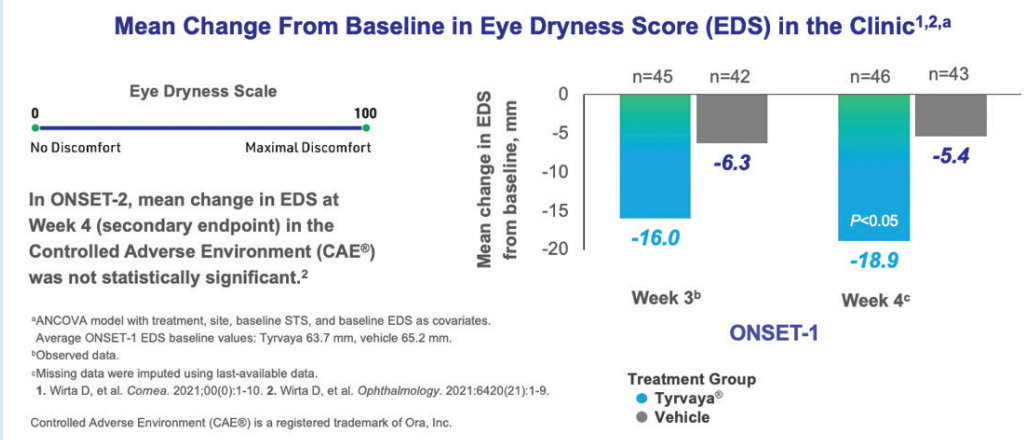

Figure. At week 4 in ONSET-1, the Tyrvaya group had a mean 18.9-mm decrease in EDS compared with a 5.4-mm decrease in the vehicle group. At 3 weeks, the Tyrvaya group had a mean 16.0-mm decrease in EDS compared with a 6.3-mm decrease in the vehicle group.

Dr. McDonald: In addition to sneezing, there are a few other common adverse reactions that patients may experience. In the clinical trials, 16% of patients coughed, 13% had throat irritation, and 8% had instillation-site (nose) irritation.[3-6] It is also worth noting that the discontinuation rate due to adverse reactions in the trials was almost identical between the Tyrvaya-treated patients and the vehicle-treated patients, at 2.0% and 2.1% respectively.[4-6]

When prescribing Tyrvaya®, I advise telling patients that sneezing is likely to occur after instillation, but that they do not need to readminister the nasal spray after this occurs. I also tell them that, although many patients reported sneezing in clinical trials, no patient discontinued Tyrvaya due to sneezing.

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3. Tyrvaya Prescribing Information. Princeton, NJ: Oyster Point Pharma; 2021.
4. Oyster Point Pharma. Data on file. OPP-101 (ONSET-2) Interim Clinical Study Report. October 13, 2020.
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Dr. Devries: It's easy to identify a successfully managed case of dry eye disease. The less successful cases frustrate us because the cause or causes are unclear: it could be a matter of patient compliance, lack of response to the treatment approach, or something else entirely.

Lisa M. Nijm, MD, JD: When patients have tried several drops and visited other providers before being referred to my clinic, oftentimes they are frustrated. Like most of us, these patients are looking for rapid relief, particularly if they have moderate or severe dry eye disease symptoms.

Dr. Jackson: Fortunately for our patients, another therapeutic option has entered the conversation, expanding the options eye care professionals can offer their patients. That option is Tyrvaya®.

TYRVAYA: A DIFFERENT APPROACH TO THERAPY

Dr. Nijm: Many of our patients do not know about Tyrvaya. What are some of the first details you tell patients when you think Tyrvaya may be a treatment option for their dry eye disease?

Marjan Farid, MD: It's important to lay out the top-line facts about Tyrvaya. I tell patients that Tyrvaya is a nasal spray approved for the treatment of the signs and symptoms of dry eye disease.[1] Further, articulating the approved administration and dosage of Tyrvaya is key. I tell patients that they will administer a single spray in each nostril twice a day, approximately 12 hours apart.[1] Patients should know that a Tyrvaya spray bottle must be primed with 7 actuations before initial use, and should be re-primed with 1 actuation if not used for more than 5 days. I tell them to review the Tyrvaya Instructions for Use before they initiate treatment. [Editors' note: For a discussion on safety and efficacy data relevant to Tyrvaya, see the sidebar.]

Dr. Hauswirth: We do not yet know the exact mechanism of action of Tyrvaya, but we do know that Tyrvaya is believed to activate the trigeminal parasympathetic pathway via the nose, which in turn results in increased basal tear film production.[1] The trigeminal parasympathetic pathway plays a role in tear film homeostasis,[2,3] and three structures key to the production of basal tear film—lacrimal glands, meibomian glands, and goblet cells—are innervated by the trigeminal parasympathetic pathway.[2,4]

Dr. Nijm: What are some of the potential advantages offered by Tyrvaya?

Dr. Devries: I think, first, we should consider that Tyrvaya's indication is for both signs and symptoms of dry eye disease. A treatment option that can be used for dual purposes is useful in our armamentarium.

Dr. Hauswirth: Patients who wear contact lenses daily may be candidates for Tyrvaya.* The importance of the ocular surface-sparing aspect of this approach cannot be emphasized

*Patients with contact lenses were excluded from the Tyrvaya clinical trials

enough. If you're the type of eye care provider who constantly stresses to patients the value of preservative-free drops, then the preservative-free nature of Tyrvaya should be appealing to you.

Dr. Devries: Knowing that Tyrvaya is Oyster Point Pharma's first product to market excited me. What did you think about Oyster Point Pharma being the company to launch Tyrvaya?

Dr. Jackson: Having a new company in the dry eye disease space is always welcome, because it means that fresh ideas will be a part of the conversation. As clinicians, we work to make sure that we are constantly learning and innovating. To see an industry partner have that same mindset is encouraging. ■

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TYRVAYA® IMPORTANT SAFETY INFORMATION

The most common adverse reaction reported in 82% of patients was sneezing. Events that were reported in 5-16% of patients were cough, throat irritation, and instillation-site (nose) irritation. Please see Brief Summary of Prescribing Information on the right side of this page and the full Prescribing Information at Tyrvaya-pro.com.

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tyrvaya®
(varenicline solution)
nasal spray 0.03 mg

BRIEF SUMMARY: Consult the full Prescribing Information for complete product information available at www.tyrvaya-pro.com.

INDICATIONS AND USAGE

TYRVAYA® (varenicline solution) nasal spray is a cholinergic agonist indicated for the treatment of the signs and symptoms of dry eye disease.

ADVERSE REACTIONS

Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In three clinical trials of dry eye disease conducted with varenicline solution nasal spray, 349 patients received at least 1 dose of TYRVAYA. The majority of patients had 31 days of treatment exposure, with a maximum exposure of 105 days.

The most common adverse reactions reported in 82% of TYRVAYA treated patients was sneezing. Other common adverse reactions that were reported in >5% of patients include cough (16%), throat irritation (13%), and instillation-site (nose) irritation (8%).

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary: There are no available data on TYRVAYA use in pregnant women to inform any drug associated risks. In animal reproduction studies, varenicline did not produce malformations at clinically relevant doses.

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data: *Animal Data*: Pregnant rats and rabbits received varenicline succinate during organogenesis at oral doses up to 15 and 30 mg/kg/day, respectively. While no fetal structural abnormalities occurred in either species, maternal toxicity, characterized by reduced body weight gain, and reduced fetal weights occurred in rabbits at the highest dose (4864 times the MRHD on a mg/m^2 basis).

In a pre- and postnatal development study, pregnant rats received up to 15 mg/kg/day of oral varenicline succinate from organogenesis through lactation. Maternal toxicity, characterized by a decrease in body weight gain, was observed at 15 mg/kg/day (1216 times the MRHD on a mg/m^2 basis). Decreased fertility and increased auditory startle response occurred in offspring at the highest maternal dose of 15 mg/kg/day.

Lactation: Risk summary: There are no data on the presence of varenicline in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies varenicline was present in milk of lactating rats. However, due to species-specific differences in lactation physiology, animal data may not reliably predict drug levels in human milk.

The lack of clinical data during lactation precludes a clear determination of the risk of TYRVAYA to an infant during lactation; however, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TYRVAYA and any potential adverse effects on the breastfed child from TYRVAYA.

Pediatric Use: Safety and efficacy of TYRVAYA in pediatric patients have not been established.

Geriatric Use: No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.

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Manufactured for: Oyster Point Pharma, Inc, 202 Carnegie Center, Suite 109, Princeton, NJ 08540
For more information visit www.tyrvaya-pro.com.
To report an adverse event, contact 1-877-EYE-0123.

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