

## Summary of Studies Related to OMIDRIA

***Published and presented clinical data and manuscripts in preparation report that in post-launch (i.e., not included in current labeling), prospective and retrospective, double-masked and open-label, cohort and case-controlled, single- and multi-center, adult and pediatric studies, the use of OMIDRIA statistically significantly:***

- Prevents IFIS
- Prevents iris prolapse
- Compared to steroids:
  - Reduces CME
  - Decreases breakthrough iritis
  - Reduces pain
- Compared to epinephrine:
  - Decreases complication rates
  - Decreases use of pupil-expanding devices
  - Enables performance of surgery and postoperative care without the use of steroids
  - Shortens surgical time
  - Reduces need for opioids (i.e., fentanyl) during surgery while decreasing VAS pain scores
  - Prevents miosis during femtosecond laser-assisted surgery
  - Improves uncorrected visual acuity on day after surgery

This collection of studies is summarized below.

### Published Articles in Peer-Reviewed Journals

1. **Lindstrom RL, et al. Intracameral phenylephrine and ketorolac injection (OMS302) for maintenance of intraoperative pupil diameter and reduction of postoperative pain in intraocular lens replacement with phacoemulsification. *Clin Ophthalmol.* 2014; 8: 1735-1744**

*Overview:* This article describes the results of one of the two pivotal Phase 3 studies that supported the approval of OMIDRIA by FDA. This double-masked, placebo-controlled, multicenter study enrolled over 400 patients randomized 1:1 to either OMIDRIA or placebo.

*Highlights:* OMIDRIA was clinically meaningfully superior to placebo in maintaining intraoperative mydriasis and preventing miosis ( $p < 0.0001$ ) and in reducing postoperative pain ( $p = 0.0002$ ). All secondary efficacy results favored OMIDRIA, including analyses supporting prevention of miosis (patients with  $< 6$  mm pupil diameter at completion of cortical clean-up and those with  $< 6$  mm diameter at any time during surgery), which were significant for OMIDRIA (95.9% versus 77.0% and 9.2% versus 38.0%, respectively;  $p < 0.0001$  for each endpoint). OMIDRIA was well tolerated and had a safety profile similar to placebo.

2. **Grob SR, et al. Management of mydriasis and pain in cataract and intraocular lens surgery: review of current medications and future directions. *Clin Ophthalmol.* 2014; 8: 1281-1289**

*Overview:* This article, published around the time that OMIDRIA was approved by FDA, reviews medications commonly used with cataract surgery for intraoperative mydriasis as well as for

pain and inflammation control, outlining limitations with currently available treatments.

*Highlights:* It describes OMIDRIA as a new product to address these issues and summarizes the clinical trials supporting approval of OMIDRIA, noting that OMIDRIA demonstrates statistically significant and clinically meaningful differences when compared to placebo in maintaining intraoperative mydriasis ( $p < 0.00001$ ) and in reducing pain in the early postoperative period ( $p = 0.0002$ ).

**3. Osher RH, et al. Management of mydriasis and pain in cataract and intraocular lens surgery: review of current medications and future directions. *Expert Rev. Ophthalmol.* 2015; 10(2): 91–10**

*Overview:* This article, published shortly after OMIDRIA was approved by FDA, describes various pharmacologic agents administered before, during, and/or after, cataract surgery to achieve mydriasis and to treat postoperative pain and inflammation.

*Highlights:* It underscores the important efficacy and safety advantages of OMIDRIA as the only FDA-approved drug that is indicated both to prevent miosis and to reduce postoperative pain associated with cataract surgery.

**4. Hovanesian J, et al. Intracameral phenylephrine and ketorolac during cataract surgery to maintain intraoperative mydriasis and reduce postoperative ocular pain: Integrated results from 2 pivotal phase 3 studies. *J Cataract Refract Surg.* 2015; 41: 2060-2068**

*Overview:* This article describes the pooled results of the two pivotal Phase 3 studies that supported the approval of OMIDRIA by FDA. Both were double-masked, placebo-controlled, multicenter studies, each enrolling over 400 patients randomized 1:1 to either OMIDRIA or placebo.

*Highlights:* Across the pooled data, OMIDRIA was clinically meaningfully superior to placebo in both maintenance of pupil diameter ( $p < 0.0001$ ) and reduction of postoperative pain ( $p < 0.001$ ). OMIDRIA also reduced by half the number of patients experiencing moderate-to-severe (Visual Analog Scale [VAS] pain score of  $\geq 40$ ) pain and increased by 53% the number of patients who were entirely pain-free (VAS = 0), with p-values of 0.0014 and 0.0027, respectively. OMIDRIA not only reduced pain, it reduced the use of pain medications, with 43% more placebo-treated patients requiring pain medications on the day of surgery. One of the most commonly used pain medications used was fentanyl, an opioid.

**5. Lawuyi LE, Gurbaxani A. The clinical utility of new combination phenylephrine/ketorolac injection in cataract surgery. *Clin Ophthalmol.* 2015; 9: 1249-1254**

*Overview:* This article, published shortly after FDA approval of OMIDRIA, examines the literature to date on the current treatments used to manage mydriasis, pain, and inflammation in cataract extraction surgery.

*Highlights:* It emphasizes that maintenance of mydriasis and control of ocular inflammation throughout cataract surgery are crucial for successful surgical outcomes, stating that intraoperative miosis compromises visualization of the surgical field and can lead to complications (e.g., posterior capsular tears, vitreous loss, increased surgical times) while postoperative inflammation often compromises the best-uncorrected vision following surgery, often leading to multiple clinic visits. The article highlights the efficacy and safety advantages of OMIDRIA over other pharmacologic and mechanical options available to cataract surgeons and their patients.

**6. Gonzalez-Salinas R, et al. Patient considerations in cataract surgery – the role of combined therapy using phenylephrine and ketorolac. *Patient Prefer Adherence* 2016; 10: 1795-1801**

*Overview:* This article is written with an emphasis on patient outcomes, including patient comfort, associated with cataract surgery and describes the role played by OMIDRIA as an innovative treatment that contributes to improved patient outcomes.

*Highlights:* It emphasizes the importance of sufficient mydriasis for successful surgical outcome in cataract surgery noting that poor pupil dilation can lead to serious sight-threatening complications that significantly increase the cost of surgery and decrease patient comfort. The article highlights the important roles played by phenylephrine and ketorolac in cataract surgery (i.e., pupil dilation, prevention of miosis, pain and inflammation control, and reduction of cystoid macular edema following surgery). The article then notes that OMIDRIA, which is a combination of phenylephrine and ketorolac delivered directly to the eye tissues during surgery, has been shown in clinical trials to be effective, combining the positive effects of both drugs with a good safety profile and patient tolerability.

**7. Bucci F et al. Comparison of the frequency of use of a pupil expansion device with and without an intracameral phenylephrine and ketorolac injection 1%/0.3% at the time of routine cataract surgery. *Clin Ophthalmol.* 2017; 11: 1039-1043**

*Overview:* This article, conducted by a physician who started using OMIDRIA following its FDA approval, evaluates whether OMIDRIA decreases the need for the Malyugin Ring®, a pupil-expanding device, to manage small pupils relative to the physician's usual standard of care (i.e., epinephrine) during cataract surgery. It compares the use of the Malyugin Ring in 1004 consecutive cataract surgery cases prior to availability of OMIDRIA (Dec 2013-Feb 2015) to 915 consecutive cases in which OMIDRIA was used (June 2015 to April 2016). In the control group only, epinephrine injections were used as per surgeon judgment, and the number of patients with a history of alpha-1 blocker use and physician's use of the femtosecond laser were recorded for both groups.

*Highlights:* In the 1,004 cases performed in the historical control group, the Malyugin Ring was needed nearly 79 times (7.87%). In the 915 cases performed in the treatment group, the surgeon chose to use the Malyugin Ring only 27 times (2.95%;  $p < 0.001$ ). There was no significant difference in the number of femtosecond laser cases between the two groups, yet 4 (2.65%) femtosecond patients in the control group required a Malyugin Ring, while none needed the ring in the femtosecond group that received OMIDRIA. Furthermore, Malyugin Ring use in alpha-1 blocker patients was 12/49 (24.49%) in the control group and 6/49 (12.74%;  $p = 0.05$ ) in the OMIDRIA group. The authors conclude that the antimiotic/anti-inflammatory effects of OMIDRIA reduced facility costs, surgical time, and other complexities related to use of the Malyugin Ring during cataract surgery.

**8. Donnenfeld E, et al. Intracameral ketorolac and phenylephrine effect on intraoperative pupil diameter and postoperative pain in cataract surgery. *J Cataract Refract Surg.* 2017; 43: 597-605**

*Overview:* This article describes the results of the full-factorial study that supported the approval of OMIDRIA by FDA. The randomized, double-masked, multicenter study evaluated OMIDRIA compared with a balanced salt solution (vehicle), ketorolac, and phenylephrine on pupil diameter during cataract surgery and on early postoperative ocular pain.

*Highlights:* OMIDRIA was significantly better than the vehicle and ketorolac in maintaining mydriasis ( $p < 0.0001$  each). Ocular pain assessed using the Visual Analog Scale was significantly

reduced for the study drug compared with the vehicle or phenylephrine ( $p < 0.042$  and  $p < 0.009$ , respectively). Significantly fewer patients treated with OMIDRIA (3 [6.1%]) had an intraoperative pupil diameter smaller than 6 mm compared with those treated with the vehicle (25 [47.2%];  $p < 0.0001$ ), ketorolac (18 [34.6%];  $p < 0.0004$ ), or phenylephrine (11 [22.4%];  $p < 0.0216$ ). The authors conclude that both ketorolac and phenylephrine contributed to the therapeutic effects of maintenance of pupil size and reduction in postoperative pain, with the combination showing superiority to either agent alone in maintaining an intraoperative pupil diameter of 6 mm or larger.

**9. Mamalis N. Importance of pupil dilation for cataract surgery. *J Cataract Refract Surg Editorial*. 2017; 43(5): 583-584**

*Overview:* This is an editorial accompanying the Donnenfeld article published in JCRS described above. It was written by the Editor of JCRS who is also the 2015 recipient of the Life Achievement Honor Award from the American Academy of Ophthalmology (AAO).

*Highlights:* Dr. Mamalis first describes the increased risk for complications associated with inadequate initial mydriasis or intraoperative miosis during cataract surgeries, including: posterior capsule tear, vitreous loss, zonular fiber breaks, possible iris damage and iris chafing, retained lens cortical material, corneal edema and cystoid macular edema. The editorial addresses the OMIDRIA results published by Donnenfeld *et al* and notes the safety advantages of the drug. He points out that, in addition, to its beneficial effects on the pupil, OMIDRIA decreases postoperative pain in cataract patients. Dr. Mamalis concludes that “A well-dilated pupil during cataract surgery can decrease the incidence of posterior capsule tears as well as vitreous loss, zonular fiber disruption, and remnant lens material. This can help provide better outcomes after cataract surgery and could be especially important in the era of premium intraocular lenses and more demanding patients and cataract surgeons” and suggests that OMIDRIA could be helpful in patients with intraoperative floppy iris syndrome (IFIS) and calls for a study to examine this (see Silverstein *et al.* below).

**10. Katsev DA, et al. Intracameral ketorolac concentration at the beginning and end of cataract surgery following preoperative topical ketorolac administration. *Clin Ophthalmol*. 2017; 11: 1897–190**

*Overview:* The purpose of this study was to evaluate the intracameral concentration of ketorolac at the beginning and end of cataract surgery following its preoperative topical administration. Study patients received topical ketorolac eye drops in the standard recommended dosage both one day before surgery and on the day of surgery prior to operation.

*Highlights:* Despite documented good compliance with topical medication use, 8 of 12 patients (66.67%) had unmeasurable (i.e., below the level of quantification or  $<1$  ng/mL) intracameral ketorolac levels at the end of surgery. The remaining 4 patients had levels ( $\leq 6.3$  ng/mL) that were clinically irrelevant. This study demonstrates the clear advantage of the delivery method for OMIDRIA – directly intracamerally during the cataract surgery procedure (see Waterbury below.)

**11. Rosenberg ED, et al. Visual outcomes, efficacy, and surgical complications associated with intracameral phenylephrine 1.0%/ketorolac 0.3% administered during cataract surgery. *Clin Ophthalmol*. 2018; 12: 21-28**

*Overview:* This study compared visual outcomes, surgical time, and perioperative surgical complications after cataract surgery with intracameral use of either OMIDRIA or epinephrine

during cataract surgery. It consisted of a single-center retrospective review of 641 eyes (389 patients) undergoing cataract surgery, 260 eyes receiving OMIDRIA and 381 receiving epinephrine in the irrigation solution. All patients received a 3-day standard preoperative regimen of topical NSAIDs and a standard regimen of topical mydriatics preoperatively on the day of surgery.

*Highlights:* Intracameral use of OMIDRIA during cataract surgery demonstrated statistical superiority to intracameral epinephrine at reducing complications, need for pupillary dilating devices, and surgical time.

**12. Visco D. Effect of phenylephrine/ketorolac on iris fixation ring use and surgical times in patients at risk of intraoperative miosis. *Clin Ophthalmol.* 2018; 12: 301-305**

*Overview:* This retrospective study analyzed 46 “high-risk” patients who underwent cataract surgery at a single site using either OMIDRIA or epinephrine in the irrigation solution. The qualifying factors for “high-risk” were poor pupil dilation ( $\leq 5.0$  mm) at the presurgical examination after a standardized topical regimen of mydriatic agents and/or a history of intraoperative floppy iris syndrome (IFIS) in the fellow eye. The endpoints were use of pupil expanding devices and surgical time.

*Highlights:* Eighteen (50%) of the patients in the epinephrine group and no patients in the OMIDRIA group required iris fixation ring insertion to maintain pupil dilation or to control IFIS ( $p = 0.0034$ ). Mean surgical time was significantly clinically meaningfully shorter in the group of patients who received OMIDRIA ( $p = 0.0068$ ).

**13. Waterbury LD. Alternative drug delivery for patients undergoing cataract surgery as demonstrated in a canine model. *J Ocul Pharmacol Ther.* 2018; 34: 154-160**

*Overview:* The purpose of this study was: (1) to determine ketorolac concentrations in selected ocular tissues following the intracameral administration of OMIDRIA delivered in irrigation solution during lens replacement surgery in beagle dogs; and (2) to compare the ketorolac initial dose and resultant concentrations from the animal study to those achieved in aqueous and vitreous by topical administration in patients undergoing cataract surgery or vitrectomy, respectively.

*Highlights:* Concentrations of ketorolac when administered by the intracameral route in the dosing solution in dogs were found to be considerably higher in both aqueous and vitreous compared to what is achieved with topical dosing in patients. In addition, adequate therapeutic concentrations of ketorolac in aqueous and vitreous humor were achieved even at 10 hours post-dose. Critical concentrations (i.e., necessary to inhibit adequately the levels of the inflammatory mediators COX-1 and COX-2) in the aqueous that envelopes the iris/ciliary body, which are sites of prostaglandin E2 synthesis, and the vitreous are not achieved by topical dosing in clinical studies after cataract surgery but are by direct intracameral dosing as determined in this study. Based on these studies and clinical data, OMIDRIA delivered during surgery as an irrigation solution may preclude the need for topically administered pre- and postoperative NSAIDs.

**14. Silverstein SM, et al. Effect of phenylephrine 1.0%-ketorolac 0.3% injection on tamsulosin-associated intraoperative floppy-iris syndrome. *J Cataract Refract Surg.* 2018; 44(9): 1103-1108**

*Overview:* The purpose of this randomized, double-masked, prospective study was to determine the effect of OMIDRIA on different components of intraoperative floppy-iris syndrome (IFIS).

Fifty men with a history of being treated with tamsulosin (an alpha-1 adrenergic blocker) and having standard cataract extraction surgery were randomized 1:1 to a treatment group that received OMIDRIA in the irrigation solution or to a control group that received basic saline solution. Pupil dilation, iris billowing, and iris prolapse were measured using standardized recording and measurement methods.

*Highlights:* Iris prolapse occurred in three patients (12.0%) in the OMIDRIA group and in 14 patients (56.0%) in the control group ( $p < 0.001$ ). Stage 3 (severe) pupil billowing occurred in one eye (4.0%) in the OMIDRIA group and in ten eyes (40.0%) in the control group ( $p < 0.001$ ). The author concludes that the use of OMIDRIA in patients at risk for IFIS led to significantly better prevention of miosis, less pupil billowing, and a reduced incidence of iris prolapse – in other words, OMIDRIA prevents IFIS. This randomized study and publication addresses the comment in the Mamalis editorial (see Mamalis above).

**15. Al-Hashimi S, et al. Medical and surgical management of the small pupil during cataract surgery. *J Cataract Refract Surg.* 2018; 44: 1032-1041**

*Overview:* In this review article by the ASCRS Refractive Cataract Surgery Subcommittee, complications associated with small pupils in cataract surgery are discussed as are risk factors for intraoperative miosis. The paper discusses options that can make surgery technically easier and safer in patients who are at risk for interoperative miosis, thus maximizing the postoperative outcomes and patient satisfaction.

*Highlights:* OMIDRIA is highlighted as an option that can be used during surgery to manage intraoperative miosis in order to maximize postoperative outcomes and patient satisfaction. Specifically, the data describing the advantages of OMIDRIA are summarized, including the favorable impact of OMIDRIA on mydriasis, miosis, postoperative pain, complication rates, use of pupil-expanding devices, IFIS, and surgical time.

**16. Walter K, et al. Continuous intracameral phenylephrine- ketorolac irrigation for miosis prevention in femtosecond laser-assisted cataract surgery: reduction in surgical time and iris manipulation. *J Cataract Refract Surg.* 2019 Apr; 45(4): 465-469**

*Overview:* This retrospective cohort study was conducted at an academic medical center and analyzed femtosecond laser-assisted cataract procedures performed in 200 consecutive patients, 100 of whom had epinephrine added to irrigation solution and 100 of whom had OMIDRIA added to irrigation solution. All patients received a standardized regimen of pre-operative topical bromfenac for two days before surgery. All procedures were performed by the same surgeon using the same laser (Catalys®) and operative conditions. Endpoints were surgical time and the use of pupil-expansion devices.

*Highlights:* Patient demographics were similar between the groups, including mean baseline pupil size of 7.1 mm. Surgical times were significantly reduced in the OMIDRIA group vs. epinephrine, at 8.1 vs. 9.4 minutes, respectively ( $p = 0.007$ ). When eliminating the eyes that required a pupil expansion device, a significant reduction in surgical time remained for OMIDRIA vs. epinephrine (8.1 vs. 9.0 minutes, respectively;  $p = 0.018$ ). In the OMIDRIA group, only two eyes (2%) required a pupil expansion device vs. the epinephrine group with 12 (12%) ( $p = 0.009$ ). These data demonstrate that OMIDRIA reduces femtosecond laser-assisted cataract surgery time and reduces the need for pupil expansion devices.

**17. Donnenfeld, E, et al. Effect of intracameral phenylephrine and ketorolac 1%/0.3% on intraoperative pain and opioid use during cataract surgery. *Clin Ophthalmol.* 2019; 13: 2143-50**

*Overview:* This prospective, masked, 2-cohort study of 60 patients, undergoing cataract surgery by the same surgeon, compared the effect of OMIDRIA (phenylephrine and ketorolac 1.0%/0.3%, N=41) vs epinephrine (N=19) on pain reduction and opioid usage during cataract surgery. All patients received routine preoperative and postoperative topical medications. Outcome measures included the need for IV fentanyl for ocular discomfort during surgery and pain as measured by mean visual analog scale (VAS) pain scores on a scale from 0 (no pain) to 10 (extreme pain) measured 10 minutes postoperatively in the recovery room. A composite endpoint identified 'responders' as being patients who (1) did not require fentanyl and (2) experienced no to minimal pain (VAS score  $\leq 3$ ). Patients were masked to their respective treatment groups.

*Highlights:* A smaller proportion of patients required intraoperative fentanyl in the OMIDRIA group compared to the control group (9.8% vs 42.1%;  $P = 0.006$ ). Mean VAS pain scores were significantly (48.9%) lower in the OMIDRIA group than in the control group (2.3 vs 4.5;  $P < 0.0001$ ). The proportion of patients with VAS scores  $\leq 3$  was significantly greater in the OMIDRIA group (85.0%) than in the control group (31.6%) ( $P < 0.0001$ ). For the composite endpoint, patients receiving OMIDRIA were 94% less likely to require fentanyl or to have moderate-to-severe pain (pain VAS  $\geq 4$ ; odds ratio 0.06; 95% confidence interval 0.02–0.24) than patients receiving epinephrine. Study results suggest that the routine use of intracameral OMIDRIA during cataract surgery can significantly reduce patient pain as well as the need for opioids.

**18. Walter K, et al. Rate of pseudophakic cystoid macular edema using intraoperative and topical nonsteroidal anti-inflammatory drugs alone without steroids. *J Cataract Refract Surg.* 2020; 46: 350-354**

*Overview:* This is a retrospective single academic center chart review to determine the rate of postoperative cystoid macular edema (CME) in patients undergoing cataract surgery treated with intraoperative intracameral and postoperative topical NSAIDs without steroids. Patients were identified through a medical record search tool using criteria and code for a pre-specified period of time. Patients with a history of uveitis, diabetic macular edema, retinal vein occlusions, epiretinal membranes, vitreomacular traction or any prior history of macular edema were excluded. Additionally, any patients with less than 6 weeks of postoperative follow-up were excluded.

*Highlights:* Overall, 824 patient records were reviewed, and the analysis included 504 eyes. Two eyes developed postoperative CME (rate = 0.40%, 95% confidence interval 0.0005 to 0.0143). The rate of CME (0.40%) in patients treated with OMIDRIA and postoperative topical NSAIDs without steroids was well below historical published rates derived from a literature review of CME development in patients using traditional topical corticosteroid with or without topical NSAIDs. The dual NSAID combination of intraoperative OMIDRIA administered intracamerally and perioperative topical bromfenac was effective in limiting the rate of clinically significant pseudophakic CME.

**19. Visco D, et al. Effect of intracameral phenylephrine/ketorolac 1.0%/0.3% on postoperative cystoid macular edema, iritis, pain and photophobia following cataract surgery. [Article in Press] *J Cataract Refract Surg.* April 2020**

*Overview:* The purpose of this study was to assess the efficacy of intracameral OMIDRIA (phenylephrine and ketorolac intraocular solution) 1%/0.3% during cataract surgery in reducing the risk of postoperative cystoid macular edema (CME), rebound iritis and ocular pain. In 2,218

eyes undergoing cataract surgery, the study compared intraoperative intracameral OMIDRIA (1,334 eyes) versus 10 weeks of postoperative topical loteprednol etabonate 0.5%, a corticosteroid (control group, 884 eyes) on the incidence of postoperative CME, iritis and patient pain/photophobia. All eyes received bromfenac (Bromsite/Prolensa), an NSAID, 2 days preoperatively and 10 weeks postoperatively.

*Highlights:* Compared with the control group, the OMIDRIA group had less postoperative CME (0.52% vs 0.47%,  $P=0.021$ ), breakthrough iritis (1.72% vs 4.86%,  $P<0.001$ ), and pain (1.27% vs 4.19%,  $P<0.001$ ). The incidence of photophobia trended lower in the OMIDRIA group vs. the control group but was not statistically significant (0.90% vs 1.13%,  $P=0.590$ ). Use of intracameral OMIDRIA resulted postoperatively in a 3-fold reduction in CME, a more than 3-fold decrease in ocular pain, and a reduction in rebound iritis by more than half.

**20. Wilson, ME, et al. Safety and Efficacy Data Supporting FDA Approval of Intracameral Phenylephrine and Ketorolac 1.0%/0.3% for Pediatric Cataract Surgery: Clinical Safety and Pupil and Pain Management. [Article in Press] *J Cataract Refract Surg.* April 2020**

*Overview:* This multicenter, double-masked, Phase 3 registration study was conducted at 17 U.S. sites and powered to assess the safety of phenylephrine and ketorolac (PE/K) 1.0%/0.3% compared to phenylephrine (PE) 1.0% in children ages birth through 3 years undergoing cataract surgery. Intraoperative pupil diameter and postoperative pain were also assessed. Safety endpoints were assessed up to 90 days postoperatively. From surgical videos, a masked central reader measured change in pupil diameter from immediately prior to incision to wound closure. Postoperative pain was measured using Alder Hey Triage Pain Score at 3, 6, 9, and 24 hours following wound closure and recorded by parent/caregiver. This study was powered to assess safety only since the FDA indicated that efficacy could be extrapolated from the adult population.

*Highlights:* Seventy-two patients received masked intervention. There were no notable changes in vital signs or ophthalmological complications in either group. Mean change in pupil diameter was similar between PE/K 1.0%/0.3% and PE 1.0% (mean difference in AUC -0.071;  $P = 0.599$ ). Postoperative ocular pain scores and overall mean scores were lower in the PE/K group at all individual time points, and differences in overall mean scores were statistically significant at 6 and 24 hours ( $P=0.029$  and  $0.021$ , respectively). The study demonstrated that phenylephrine and ketorolac 1.0%/0.3% was safe for use in children and maintained mydriasis during cataract surgery. Postoperative pain levels were lower in the PE/K 1.0%/0.3% group.

**Manuscripts Submitted to and Under Review by Peer-Reviewed Journals**

**1. Matossian C, et al. Teves N. Clinical outcomes of phenylephrine/ketorolac intraocular solution versus epinephrine in cataract surgery in a real-world setting. Manuscript submitted to *Clinical Ophthalmology.* 2019**

*Overview:* This study, conducted by a physician who started using OMIDRIA following its FDA approval, compares the clinical outcomes in cataract patients treated with either OMIDRIA or epinephrine in the standard irrigation solution. This was a retrospective chart review of cataract surgery patients who received treatment between March 1, 2015 and December 31, 2016 at one of two clinics by a single surgeon practicing at both locations. Endpoints were need for pupil-expansion devices and surgical times.

*Highlights:* A total of 635 eyes in 375 patients underwent cataract surgery with either OMIDRIA (n=275) or epinephrine (n=360) in the irrigation solution. Only 6 (2.2%) pupil-expansion devices were required in the OMIDRIA group compared with 24 (6.7%) in the epinephrine group (p = 0.0080). Mean surgical time was significantly shorter with OMIDRIA (16.5 min) compared with epinephrine (17.8 min; p = 0.0056). This study demonstrates that, relative to epinephrine, OMIDRIA decreases the need for pupil-expansion devices and leads to shorter surgical times for cataract surgery, likely leading to better surgical and safety outcomes for cataract surgery patients and reduced costs.

#### **Abstracts Presented at International Academic Conferences**

1. **Gayton JL. Effect of early phenylephrine and ketorolac injection 1% / 0.3% on pupil diameter in traditional and femtosecond-assisted cataract surgery. Podium presentation at ASCRS-ASOA Symposium and Congress; April 13-17, 2018; Washington, DC**

*Overview:* The purpose of this study was to determine the effect of early usage of OMIDRIA on pupil dilation in patients undergoing cataract surgery with femtosecond-assisted or traditional phacoemulsification approach. Data were collected for 57 patients who underwent cataract surgery with traditional phacoemulsification approach and 20 patients with femto-assisted procedures. All patients received a standard regimen of preoperative topical mydriatic agents.

*Highlights:* For traditional phacoemulsification, the mean pupil diameter was 6.65 mm at baseline and 7.42 mm intraoperatively before IOL insertion. For femtosecond-assisted surgery, the mean pupil diameter was 6.69 mm at baseline and 7.65 mm prior to IOL insertion. OMIDRIA maintained or increased pupil size when used in both traditional phacoemulsification or femtosecond laser-assisted cataract procedures even though femtosecond laser-assisted cataract surgery typically results in increased miosis.

2. **Waterbury LD. Alternative method of providing effective drug concentrations in the posterior segment as demonstrated in a canine pharmacokinetic model. Poster presentation at ARVO; April 30, 2018; Honolulu, HI**

*Overview:* This article uses a canine pharmacokinetic model to determine whether effective drug concentrations of ketorolac in the posterior segment can be obtained by direct infusion of OMIDRIA into the aqueous humor during cataract surgery and determines a calculated duration of activity based on the model. OMIDRIA diluted in irrigation solution was administered to 20 canines during lens replacement surgery. Ketorolac concentrations were determined by LC/MS in aqueous, cornea, conjunctiva, iris-ciliary body, vitreous, retina, choroid, retinal pigment epithelium, sclera, and lens capsule from 4 dogs per time point (0, 2, 6, 8 and 10 hours post-surgery). Concentration levels for tissues and time points were converted to log<sub>10</sub> values, and linear coefficient values were determined along with 'best fit' equations for each tissue.

*Highlights:* Use of OMIDRIA provided therapeutic concentrations of ketorolac not only in the anterior but also in the posterior segment. Using the best fit linear regression analysis, levels of ketorolac in posterior tissues were sufficient to inhibit cyclooxygenase I (COX-1) up to 24 hours after administration, with directly determined 10-hour values and calculated values at 20 hours post dose, for the retina, vitreous, and posterior sclera. Even at 20 hours post dose, all values were in excess of what is required for 50% inhibition of COX-1 obtained from human recombinant COX-1. Use of OMIDRIA, unlike topical dosing, provides therapeutic concentrations to both anterior and posterior ocular tissues. Furthermore, use of OMIDRIA ensures adequate

therapeutic concentrations in both the anterior and posterior segments for up to 20 hours after the procedure.