2:45 PM

Baseline Deep Capillary Plexus Loss Is Associated With the Long-Term Recovery of Photoreceptor Integrity After Treatment of Diabetic Macular Edema

- Young Hee Yoon, MD
- Byung Gil Moon, MD
- Junyeop Lee, MD, PhD
- Taewoong Um

OBJECTIVE We investigated if the degree of deep capillary plexus (DCP) loss may predict the long-term recovery of photoreceptor integrity and visual acuity in patients with diabetic macular edema (DME).

PURPOSE To determine the correlation between the baseline DCP integrity and long-term photoreceptor recovery as well as visual outcome after treatment in patients with DME.

METHODS We retrospectively analysed 67 DME eyes which resolved macular edema after consecutive anti-VEGFs or additional dexamethasone implant and followed up for 12 months after initial DME resolution. Data of best corrected visual acuity (BCVA), spectral domain-optical coherence tomography (SD-OCT) and OCT angiography (OCTA) were collected at baseline, 6 and 12 months. Correlation analysis was performed between parameters of DCP integrity; vascular flow density (VD) and area of foveal

avascular zone (FAZ) - and parameters of photoreceptor integrity; ellipsoid zone (EZ) and external limiting membrane (ELM) integrity.

RESULTS During 12 months, macular edema remained resolved with additional treatment on as needed basis. At baseline, DCP-VD and DCP-FAZ were poorly correlated with the degree of EZ or ELM integrities (all $p>0.05$). The degree of EZ or ELM integrities recovered significantly from baseline at 12 months ($p<0.001$ and $p<0.001$). The degree of EZ and ELM recovery was well correlated with baseline DCP-VD ($p=0.004$, $p=0.009$) and DCP-FAZ ($p=0.007$, $p=0.009$). And DCP-VD and DCP-FAZ were significantly correlated with change in BCVA from baseline at 12 months ($p=0.003$, $p=0.042$). In anti-VEGF nonresponders, baseline DCP integrity was worse than in anti-VEGF responders, and the degree of photoreceptor recovery at 12 months was also poorer in each parameters (EZ recovery of 2.0 vs. 26.1%, and ELM recovery of 0.3 vs 13.9%, $p<0.001$ and $p<0.001$, respectively).

CONCLUSION The degree of DCP loss at the time of effective treatment was closely correlated with the long-term recovery of photoreceptor integrity and visual outcome in patients with treated DME.

TAKE HOME MESSAGE The degree of deep capillary plexus (DCP) loss can predict the long-term recovery of photoreceptor integrity and visual outcome in patients with diabetic macular edema (DME).

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

2:53 PM

Prevention of Macular Edema in Patients With Diabetic Retinopathy Undergoing Cataract Surgery With Intravitreal Aflibercept Injection – PROMISE Study

- Rishi P. Singh, MD
- Fabiana Q. Silva, MD
- Felipe Ferreira Conti, MD
- Richard E. Gans, MD

OBJECTIVE To determine the safety and efficacy of intravitreal aflibercept injection (IAI) in patients with diabetic retinopathy (DR) in the prevention of macular edema (ME) following cataract surgery.

PURPOSE Macular edema following cataract surgery is more likely to occur in patients with pre-existing conditions such as diabetic retinopathy. The purpose of this pilot study was to evaluate whether anti-VEGF therapy given at the time of surgery might be safe and effective in reducing the risk of macular edema in these patients.

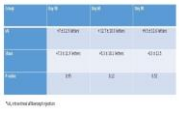
METHODS A prospective randomized trial was conducted in patients undergoing cataract surgery with a history of DR at baseline. Patients were randomized to IAI or sham injection at the time of surgery. The primary objective of the study was the incidence and severity of ocular and non-ocular adverse events (AEs) through 90 days. Secondary objectives included the percentage of patients who develop ME within 90 days following cataract surgery defined as any of the following: i) ≥30% increase from pre-operative baseline in central subfield thickness (CST), ii) best-corrected visual acuity (BCVA)

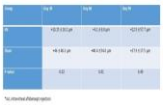
decrease of >5 ETDRS letters from the Day 7, and visual acuity loss due to retinal thickening. Mean changes from baseline in ETDRS BCVA score and in CST were also evaluated.

RESULTS A total of 26 eyes of 21 patients were included in the study (13 eyes in each group). There were no statistically significant differences in age (IAI group: 66.5 ±10.3 years, Sham group: 66.7 ± 10.9 years), baseline ETDRS BCVA (IAI group: 69.4 ±10.7 letters, Sham group: 68.7 ± 11.8 letters) and baseline CST (IAI group: 259.1±32.0 µm, Sham group: 251.9 ± 24.5 µm) between groups (P>0.05). No serious AEs were observed during the study. The sham group demonstrated a higher percentage of patients with ME versus those treated with IAI (44.45% of eyes in the Sham group versus 23.1% of eyes in the IAI group) within 90 days following surgery. There were no differences between the changes from baseline in BCVA (IAI group: +9.5 ±12.6 letters, Sham group: +13 ±12.5 letters, p=0.52; Table 1) and CST (IAI group: +22.5 ±57.7 µm, Sham group: +37.9 ±37.5 letters, p=0.49; Table 2) at day 90 between groups. However there were statistically significant differences in CST between the groups at day 30 and 60.

CONCLUSION The use of IAI in patients with DR for the prevention of ME following cataract surgery showed no significant adverse events. While there were statistically significant differences in retinal thickness at day 30 and 60, there were not meaningful differences in mean gain of visual acuity or CST at 90 days. Additional larger prospective studies are needed to further validate these findings.

TAKE HOME MESSAGE Patients with diabetic retinopathy have a higher risk of developing macular edema following cataract surgery.





HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

3:01 PM

A Novel Injection Technique for Dexamethasone Intravitreal Implant: (An Unfunded Investigator Sponsored Trial)

- Michael A. Singer, MD
- Stan Conston, BS Physics
- Matthew A Reilly, PhD
- Ron Yamamoto

OBJECTIVE To demonstrate a new way to inject dexamethasone intravitreal implant in order to minimize possible vitreous hemorrhage and retinal trauma.

PURPOSE Dexamethasone intravitreal implant (Ozurdex) injections, while generally safe and efficacious, have been shown to cause vitreous hemorrhage and retinal injury during injection. Dexamethasone implants were tested in vivo to quanitfy the force of injection of standerd injection technique in order to devolpoment of a new safer technique.

METHODS 6 Dex implants were injected into a calibrated water bath. 3 implants were injected using rapid compression (within 1 second) of the actuator button, (Fast Injection group). 3 Dex implants were injected under the same conditions using a 3 second technique to depress the actuator, (Slow Injection group). Average velocity was measured using high speed photography (240 frames per second). Impact velocity was measured 16 mm from the injector tip, representing the distance to the retina in a standard eye. Average acceleration was calculated using the difference between initial velocity and impact velocity. Impact force was calculated from the average pellet mass times the average acceleration.

RESULTS The average pellet mass of the implant was 1.179 mg. In the Fast Injection group, the mean impact velocity of the pellet was 273.3 +/- 20.8 cm/sec and the mean impact force was 0.74 +/- 0.08 mN. In the Slow Injection group, the mean impact velocity was 21.7 +/- 3.6 cm/sec and the mean impact force was 0.04 +/- 0.027 mN. There was a significant reduction in velocity ($p<0.0001$) and impact force ($p<0.0002$) in the Slow Injection group compared to the Fast Injection group. By placing the thumb at the front of the actuator button and rolling it in a backward motion, a slower injection technique was reproducibly demonstrated. This action was reinforced by hearing two or three click sounds as opposed to one sound using the fast depression technique.

CONCLUSION By depressing the Dexamethasone intravitreal implant injector over a longer time interval, the impact velocity and impact force of the Dex implant pellet were reduced by >90%. This injection time was reliably controlled by using a novel injection method. This technique should reduce future instances of retinal damage from Dexamethasone intravitreal implant injections.

TAKE HOME MESSAGE By modifying the dexamethasone intravitreal implant injection technique, the implact force can be reduced by afactor of 10. This may results in less vitreous hemmorhage and retinal damage.

3:15 PM

Factors Associated with Worsening Proliferative Diabetic Retinopathy in Eyes Treated with Panretinal Photocoagulation or Ranibizumab

- Carl W. Baker, MD

OBJECTIVE Compare rates and identify predictive factors for events that represent worsening of proliferative diabetic retinopathy (PDR) in eyes treated with panretinal photocoagulation (PRP) or ranibizumab

PURPOSE To compare the development, timing, and severity of events that may represent worsening of PDR. Including vitreous hemorrhage, retinal detachment, anterior segment neovascularization (neovascularization of the iris/neovascularization of the angle [NVI/NVA]), neovascular glaucoma (NVG), vitrectomy, and administration of PRP in the ranibizumab group or supplemental PRP in the PRP group.

METHODS In a randomized clinical trial (55 United States sites) 394 study eyes from 305 adults with PDR, visual acuity 20/320 or better, no history of PRP were randomized to either PRP or intravitreous ranibizumab injections (0.5-mg/0.05mL) for PDR and were followed for 2 years. Eyes in both groups received ranibizumab injections for diabetic macular edema, including 53% of eyes in the PRP group. Main outcome measure was time from randomization to a composite PDR-worsening outcome defined as the first

occurrence of vitreous hemorrhage, retinal detachment, anterior segment neovascularization, or neovascular glaucoma.

RESULTS Cumulative probability of PDR-worsening through 2 years was 42% (PRP) vs 34% (ranibizumab) (hazard ratio [HR] = 1.33, 99% CI= 0.90-1.98; *P* = 0.063). Worse baseline levels of diabetic retinopathy severity were associated with increased risk of PDR-worsening regardless of treatment group (64% high-risk PDR or worse vs. 23% moderate PDR or better, *P* < 0.001). In the PRP group, eyes receiving pattern scan vs. conventional single-spot were at higher risk for PDR-worsening (60% vs. 39%, HR = 2.04, 1.02-4.08; *P* = 0.008), irrespective of the number of spots placed or of sittings to complete the initial PRP. Eyes in both groups with vision-impairing (visual acuity 20/32 or worse) center-involved DME (CI-DME) at baseline were required to receive ranibizumab. Therefore the composite outcome was compared in the subgroup of eyes that did not have vision-impairing CI-DME at baseline. For these eyes, the rate of PDR-worsening was greater with PRP than ranibizumab (45% vs. 31%, *P* = 0.008).

CONCLUSION In eyes with PDR, ranibizumab resulted in less PDR-worsening compared to PRP, especially in eyes not required to receive ranibizumab for CI-DME. Although anti-VEGF therapy requires compliance to a more frequent visit schedule than PRP, these findings provide additional evidence supporting use of ranibizumab as an alternative therapy to PRP for PDR, at least through 2 years of follow-up.

TAKE HOME MESSAGE Ranibizumab resulted in less worsening of proliferative diabetic retinopathy compared to panretinal photocoagulation, especially in eyes not required to receive ranibizumab for diabetic macular edema.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

3:23 PM

Incremental Cost-Effectiveness of Intravitreous Ranibizumab Compared With Panretinal Photocoagulation For Proliferative Diabetic Retinopathy

- Neil M. Bressler, MD

OBJECTIVE Evaluate incremental cost-effectiveness ratios (ICERs) of 0.5-mg ranibizumab therapy compared with panretinal photocoagulation for proliferative diabetic retinopathy.

PURPOSE Randomized clinical trial results suggest that ranibizumab is an alternative treatment to panretinal photocoagulation (PRP) when managing proliferative diabetic retinopathy (PDR), with or without concomitant diabetic macular edema. However, ranibizumab injections are costly. Thus, it would be useful to examine the relative cost-effectiveness of these two treatment modalities.

METHODS In a pre-planned secondary analysis of the Diabetic Retinopathy Clinical Research Network Protocol S, efficacy, safety, and resource utilization data through 2 years of follow-up for 213 adults with PDR were analyzed. Subjects received intravitreous 0.5-mg ranibizumab at baseline and as often as every 4 weeks based on a structured re-treatment protocol or PRP at baseline for PDR; eyes in both groups could receive ranibizumab for concomitant DME. Main outcome measures are incremental cost-effectiveness ratios evaluated within two pre-specified subgroups for the study eye: eyes with baseline vision-impairing (Snellen equivalent 20/32 or worse) DME and without baseline vision-impairing DME.

RESULTS Of the 46 participants with PDR and vision-impairing DME at baseline, 21 were assigned to the ranibizumab group and 25 to the PRP group (plus ranibizumab for DME). Among the remaining participants without baseline vision-impairing DME, 80 and 87 were in the ranibizumab and PRP groups, respectively. For participants with and without baseline vision-impairing DME, the ICERs of ranibizumab therapy compared with PRP were $55,568/quality-adjusted life-year and $662,978/QALY, respectively, over 2 years. Thus, over 2 years, compared with PRP, 0.5-mg ranibizumab as given in this trial is within the $50,000/QALY-$150,000/QALY range frequently cited as cost-effective in the United States for eyes presenting with PDR and vision-impairing DME, but not for those with PDR without vision-impairing DME.

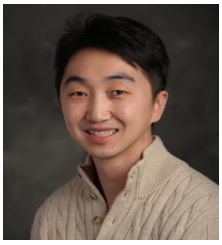
CONCLUSION In developed countries such as the United States, ranibizumab through 2 years as an alternative therapy to PRP for PDR with vision-impairing DME at baseline provides clinically relevant benefits, and also is cost effective. However, for the more common presentation in this trial of PDR without vision-impairing DME, through 2-years, PRP is a more cost-effective treatment option.

TAKE HOME MESSAGE In developed countries such as the U.S., ranibizumab through 2 years as an alternative therapy to PRP for PDR with vision-impairing DME at baseline, but not without such DME, is cost effective.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

3:31 PM

Postoperative Vitreous Hemorrhage After Diabetic Vitrectomy: Case-Control Analysis



- Samuel C. Kim, MD
- Alexander Melamud, MD, MA
- David J. Warrow, MD
- Ferdinand Rodriguez Agramonte, MD
- Devon T. Collins, MPH, CPH, CHES

OBJECTIVE To evaluate the role of hypotony as a cause of VH in the early post-operative period following small gauge vitrectomy surgery, and to review the visual outcomes in patients with this complication.

PURPOSE Postoperative Vitreous hemorrhage (PVH) occurring soon after small gauge pars plana vitrectomy (PPV) is a common complication in diabetics with proliferative diabetic retinopathy. Postoperative hypotony is common in small gauge vitrectomy and possibly a risk factors associated with VH. This study set out to investigate whether post-operative hypotony is related to early PVH in diabetics after PPV.

METHODS A retrospective case-control analysis was performed comparing eyes that developed PVH with those who did not. PVH was defined as VH occurring on postop day 1 (POD1) after PPV. Inclusion criteria included all eyes that underwent PPV for complications of PDR between January 2010 to July 2015. Exclusion criteria were as follows: less than 3 months of postop follow-up, use of silicone oil, and prior PPV. Data was collected on IOP on POD1, use of tamponade, pre-op anti-VEGF, pre-op PRP, and suturing of sclerotomies. Patients with PPV in both eyes were randomly selected to have only one eye included. Descriptive statistics, bivariate and multivariate regression models were used.

RESULTS The sample yielded 535 eyes, 260 (48.6%) cases with postoperative hemorrhage and 275 (51.4%) controls without PVH. Eyes with PVH were more likely to be male (41.2% female vs. 49.1% male) and younger (median age 55.5 vs. 63.0 in controls), with type I diabetes (12.3% cases vs. 4% control). VH was more likely in phakic patients (70.0% cases vs 59.6% control) and those who had membrane peeling during surgery (41.5% cases vs. 25.8% controls). A significant difference ($p=0.003$) was shown in postop IOP (mmHg) for both a difference in means (16.2 in cases, 18.1 in controls) and bivariate logistic regression. Bivariate logistic regression was significant for both the continuous and categorical forms of postop IOP. There is 1.89 greater odds of having 'low postop day 1 IOP (6-10mmHg)' for those with postop VH. A multivariate logistics regression model found age and post-operative IOP to demonstrate statistical significance in association with postoperative vitreous hemorrhage.

CONCLUSION Eyes with lower day one postoperative IOP and younger patients were significantly more likely to suffer early post-operative vitreous hemorrhage. Careful attention to surgical techniques that help to avoid postoperative hypotony may reduce the incidence of vitreous hemorrhage in the early recovery period in diabetic patients undergoing vitrectomy surgery.

TAKE HOME MESSAGE Postoperative hypotony after PPV for diabetic complications increase the risk for postoperative vitreous hemorrhage.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

3:39 PM

Endolaserless Vitrectomy With Intravitreal Aflibercept For Proliferative Diabetic Retinopathy (PDR)-Related Vitreous Hemorrhage (Laser Less Trial)

- Dennis M. Marcus, MD
- Harinderjit Singh, MD
- Amina Farooq, MD
- Davis C. Starnes, BS
- Harveen Walia, BS, MS
- Heather Frazier

OBJECTIVE To determine the safety, visual, and anatomic outcomes when intravitreal aflibercept injection (IAI) is used in the setting of PDR-related vitreous hemorrhage undergoing endolaserless vitrectomy.

PURPOSE For PDR eyes not requiring vitrectomy, DRCR Protocol S demonstrated better visual acuity outcomes, decreased visual field loss, need for vitrectomy, and DME development in the ranibizumab group compared to the PRP group. IAI may treat neovascularization and unrecognized DME in the setting of vitreous hemorrhage and may be a viable alternative to intraoperative endolaser during vitrectomy.

METHODS Phase I/II open label, randomized, prospective, interventional study of endolaserless vitrectomy and 2mg IAI for PDR-related vitreous hemorrhage. Eyes receive one preoperative and intraoperative IAI. Eyes are randomized to a q8 week group receiving 4 postoperative q4week IAI followed by q8 week IAI or to a q16week group receiving 2 postoperative q4week IAI followed by q16week IAI for 52 weeks. Additional IAI for PDR progression or DME may be used. The following are performed

monthly: Adverse event monitoring, ETDRS BCVA, IOP measurement, slit lamp biomicroscopy, indirect ophthalmoscopy, and SD-OCT. Quarterly wide-field fluorescein angiography and fundus photography are performed.

RESULTS Twenty-three patients (6 females,17 males;20 Type II,3 Type I diabetic;average age 54 (range:26-77 years);7 Caucasian, 15 African American, 1 Asian;5 pseudophakic and 18 phakic) have been enrolled. Nineteen eyes underwent endolaserless vitrectomy with IAI and were randomized. Preoperative average BCVA was 35 (range 0-84) letters (snellen 20/200). For 14 eyes with 1 month postoperative follow-up, average visual acuity was 70 letters (snellen 20/40) with average letter gain of 37 (range:-4 loss to+84 gain). For 10 eyes with 2 months postoperative follow-up, average letter gain was 44 (range:-1 loss to+82 gain). At 1 month postoperatively, 7 of 14 eyes demonstrated DME with OCT CST >300 um. For 10 eyes, average OCT CST was 296um at 2 months followup (31 um thinning from 1 month postoperative visit). Two eyes demonstrated intraoperative peripheral tears and received local cryotherapy. No other short term ocular or any systemic adverse events were observed by 2 months postoperatively.

CONCLUSION Endolaserless vitrectomy with IAI for PDR-related vitreous hemorrhage demonstrates short-term safety with significant improvement in visual acuity.

TAKE HOME MESSAGE For proliferative diabetic retinopathy-related vitreous hemorrhage requiring surgery, aflibercept with endolaserless vitrectomy may be a safe and viable treatment.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

3:55 PM

Topline Results From Prospective, Double-Masked Phase 2b Clinical Trial Evaluating ALG-1001 (Luminate®) Compared to Bevacizumab in Patients With DME

- David S. Boyer, MD
- Peter K. Kaiser, MD
- Baruch D. Kuppermann, MD, PhD
- Jeffrey S. Heier, MD
- Hugo Quiroz-Mercado, MD
- Peter A. Campochiaro, MD
- Vicken Karageozian
- Hampar L. Karageozian, Parm.D, MSC, MBA
- Lisa Karageozian, MBA
- John Park, PhD
- Julia Kornfield, PhD
- Linda Kutscher

OBJECTIVE To report the Phase 2b, 6-month topline results of DEL MAR clinical trial using ALG-1001 1.0mg, 2.0mg and 3.0mg in treating patients with centrally-involved diabetic macular edema (DME).

PURPOSE To investigate the safety and efficacy of ALG-1001, a synthetic RGD-class oligopeptide, as compared to bevacizumab in patients with DME. Studies have shown that ALG-1001 inhibits integrin receptors in vitro and arrests aberrant blood vessel growth in vivo meditated by αvβ3, αvβ5 as well as α2β1 and α5β1—integrin sites expressed in neovascular ocular tissue from patients with diabetic retinopathy.

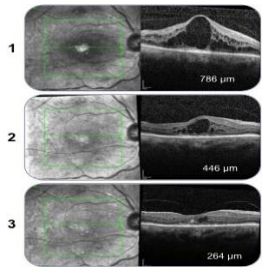
METHODS 136 patients with DME involving the fovea, visual acuity of 20/40 to 20/320 (Snellen equivalent), and central 1-mm macular subfield thickness of ≥ 350 μm on spectral-domain optical coherence tomography (SD-OCT) from 32 U.S. sites were

randomly assigned to four groups. Groups received 1.0, 2.0, or 3.0mg of ALG-1001, or 1.25mg of bevacizumab. The ALG-1001 groups received 3 monthly intravitreal injections (week 0, 4, and 8) while the bevacizumab group received up to 6 monthly injections (week 0, 4, 8, 12, 16, 20). The efficacy outcomes were change (from baseline) in BCVA and central macular thickness (CMT) at week 20. The safety outcomes were adverse events.

RESULTS At study week 20, continuous monthly bevacizumab was compared to 12 weeks post loading with ALG-1001. The mean (SD) change in BCVA were 5.2(6.86), 2.7(7.31), -1.5(9.97) and 7.0(8.21) letters gained in 1.0, 2.0 and 3.0mg ALG-1001 versus 1.25mg bevacizumab, respectively. The mean (SD) change in CMT were -77(141), -16(110), -1(152) and -104(107)mm, respectively. There were no drug related serious adverse events in the ALG-1001 groups. The primary endpoint of non-inferiority in BCVA at week 20 was met with 5.2 letters vs 7.0 letters gains in the 1.0mg ALG-1001 vs 1.25mg bevacizumab. The secondary endpoint of non-inferiority in OCT CMT at week 20 was met with -77mm vs -104mm in the 1.0mg ALG-1001 vs 1.25mg bevacizumab.

CONCLUSION ALG-1001 met its primary and secondary endpoints of BCVA and CMT change at week 20. Three doses of ALG-1001 demonstrated non-inferiority to 6 doses of bevacizumab (≤3 letters difference in BCVA and ≤30mm difference in CMT) at week 20. ALG-1001 showed 12 week durability from the last dose in monotherapy use and appears to have a U-shaped dose response curve with peak efficacy at 1.0mg.

TAKE HOME MESSAGE Three doses of anti-integrin ALG-1001 monotherapy demonstrated non-inferiority to 6 doses of bevacizumab (≤3 letters difference in BCVA and ≤30µm difference in CMT) in patients with DME at week 20.



HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

4:03 PM

Predictability of IOP Response in Patients Receiving Prior Steroid and Subsequent 0.2 ug/day Fluocinolone Acetonide Intravitreal Implant Therapy

- Seenu M. Hariprasad, MD
- Clare Bailey, BM, BCh, MD, FRCP, FRCOphth

OBJECTIVE One can utilize data from a UK EMR audit to investigate the predictability of IOP response in patients receiving a prior steroid to IOP response associated with subsequent Fluocinolone Implant therapy.

PURPOSE The Fluocinolone Acetonide Implant has been available in Europe for 3 years longer than in the US. Data from a UK EMR audit is available allowing for validation of predictability of IOP response with a prior steroid to IOP response associated with Fluocinolone Implant therapy. IOP outcomes following Fluocinolone Implant therapy in eyes treated with a prior intravitreal steroid will be assessed.

METHODS The Medisoft™ audit tool of the UK EMR systems was used to search electronic medical records across 14 UK sites (performed in September 2016). This process identified 345 eyes (from 305 patients) with DME that received the Fluocinolone Implant. Mean follow-up was 428 days. Of these eyes, 113 underwent previous therapy with an intravitreal steroid. IOP measurements from these eyes were collected and analyzed.

RESULTS In patients with a history of receiving a prior ocular steroid, two groups were created: (a) no significant IOP elevation and (b) significant IOP elevation requiring treatment. After treatment with the Fluocinolone Implant, for those patients with no prior IOP-related event after receiving a prior steroid, there were no cases of IOP > 30 mmHg or initiation of IOP lowering medication. After treatment with the Fluocinolone Implant, for those patients where a significant IOP elevation was observed after receiving a prior steroid, there was a significantly greater incidence of IOP response and use of IOP lowering medication. The differences between groups were assessed by a variety of IOP measures including IOP > 30 mmHg (0% versus 14.5%, p<0.008) and initiation of IOP lowering medication (0% versus 26.1%, p<0.001).

CONCLUSION This real-world safety data shows that IOP increases > 30 mmHg and IOP lowering medication use associated with the Fluocinolone Implant can be predicted by whether a steroid response occurred with prior intravitreal steroid use. This predictability provides an important clinical tool to mitigate the most significant side effect associated with Fluocinolone Implant therapy in the treatment of DME.

TAKE HOME MESSAGE IOP increases > 30 mmHg and IOP lowering medication use associated with the Fluocinolone Implant can be predicted by whether a steroid response occurred with prior intravitreal steroid use.

	History of IOP-Related Events		
IOP-Related Events s/p Fluocinolone Acetonide implant administration	No n (eyes)=44	Yes n (eyes)=69	P-value
Glaucoma surgery	0 (0.0%)	1 (1.4%)	0.422
Trabeculectomy	0 (0.0%)	0 (0.0%)	
IOP increase of 10 mmHg or more	3 (6.8%)	19 (27.5%)	0.007
IOP elevation to over 21 mmHg	5 (11.4%)	33 (47.8%)	<0.001
IOP elevation to over 25 mmHg	3 (6.8%)	22 (31.9%)	0.002
IOP elevation to over 30 mmHg	0 (0.0%)	10 (14.5%)	0.008
Any treatment-emergent IOP-lowering medication	0 (0.0%)	18 (26.1%)	<0.001

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Exempt from approval

4:08 PM

Initial Efficacy, Anatomic and Safety Outcomes After Fluocinolone Acetonide 0.2 µg/Day Implant in DME: The PALADIN Real-World Observational Study

- Jay G. Prensky, MD, FACS

OBJECTIVE To evaluate the efficacy, anatomic and safety outcomes after fluocinolone acetonide 0.2 µg/day implant in patients with DME: 6 month data analysis

PURPOSE To determine real-world visual and anatomic outcomes following treatment with fluocinolone acetonide 0.2 µg/day (FAc; ILUVIEN®) in patients with diabetic macular edema (DME), previously treated with corticosteroids without a clinically significant rise in IOP, and to evaluate outcomes by baseline vision and additional post-implant treatment.

METHODS Prospective non-randomized, open-label Phase 4 study, aiming to enroll ~150 patients at 60 US study centers. Patients were eligible for FAc treatment based on the Prescribing Information. Baseline characteristics, including DME duration, best corrected visual acuity (BCVA), central subfield thickness (CST), intraocular pressure (IOP) and lens status were evaluated in 91 eyes with 6 month completed data. Total patient enrollment is 174 eyes. Changes from baseline BCVA (n=91) and CST (n=87) after 6 months were assessed and analyzed by baseline vision; additional therapies following FAc implant were reported.

RESULTS At Month 6, significant improvements compared with baseline were observed in overall mean BCVA and CST (+3.7 ETDRS letters, P=0.002; -36.0 microns, P=0.001) in FAc implant-treated patients. Changes from baseline in mean BCVA and CST were

numerically greatest in patients with baseline vision worse than 20/100 (Table 1). Among the 91 eyes assessed at Month 6, 65.9% received no additional DME treatments. For those receiving adjunctive therapy, anti-VEGF was administered in 26 eyes (28%) with an average of 2.4 injections over 6 months. During the 6-month period, the mean number of additional DME injections was similar in patients with better vision and those with 20/100 or worse. Mean IOP at 6 months compared with baseline was 15 mmHg and 17 mmHg, respectively. IOP increased in 6 eyes (6.4%) but none required IOP-lowering surgery. Cataract developed in 1 patient (6.3%); 4 out of 16 phakic eyes required surgery (25%).

CONCLUSION Initial 6-month outcomes show anatomic and visual improvements following FAc implant use. Patients with the worst vision at baseline achieved the most improvement in visual and anatomic outcomes. Data up to 6 months suggests decline in additional DME therapies post FAc regardless of vision status. Further analyses will examine treatment burden prior to and post FAc; longer-term data is required.

TAKE HOME MESSAGE The fluocinolone acetonide 0.2ug/day implant offers an additional option for treatment of DME that reduces the need for subsequent Anti-VEGF or steroid.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board