Outcomes of Infectious Endophthalmitis in Patients With Systemic Antibiotic Allergies or Cross Reactions to Intravitreal Vancomycin or Ceftazidime

- Prethy Rao, MD, MPH
- Duncan E Berry, MD
- Benjamin I Meyer, BS

OBJECTIVE To review management, treatment outcomes and incidence of allergic reactions in a cohort of patients with antibiotic allergies to the standard intravitreal medications vancomycin and ceftazidime

PURPOSE The most widely used antibiotics for the treatment of infectious endophthalmitis are intravitreal vancomycin and ceftazidime. In the US, up to 10% of the general population has a reported penicillin (PCN) allergy. Despite good evidence that there is low cross-reactivity between penicillins and later-generation cephalosporins, many ophthalmologists still alter their approach in penicillin-allergic patients due to concern for allergic reaction.

METHODS This was a single-center, retrospective, longitudinal cohort study of endophthalmitis patients with a documented beta-lactam or cephalosporin allergy who received intravitreal antibiotics between 2005 - 2019. Patients were identified using ICD-9 and ICD-10 diagnosis codes for endophthalmitis along with the CPT code for intravitreal injection. Baseline findings, treatment strategy, complications and final outcomes were analyzed.

RESULTS Of 483 patients with endophthalmitis, 47 patients (9.7%) exhibited a documented beta-lactam and/or cephalosporin allergy. The most common causes of endophthalmitis were post cataract surgery (n=14; 30%) and post injection (n=10; 21%). Ninety-eight percent (46/47) received intravitreal vancomycin, 77% (36/47) ceftazidime, and 13% (6/47) amikacin. 78% (28/36) of patients who received ceftazidime had a documented penicillin allergy, and 14% (5/36) had a cephalosporin allergy. Of the 36 patients who received intravitreal ceftazidime, none experienced any allergic reaction. In those who did not receive ceftazidime, 30% (3/11) had a documented anaphylactic allergic reaction to penicillin but not to a cephalosporin. 55% (6/11) of these patients received intravitreal amikacin. 36% (4/11) of patients who did not receive intravitreal ceftazidime developed a retinal detachment, compared to 8% (3/36) of patients who were treated with intravitreal ceftazidime.

CONCLUSION In this preliminary study of a cohort of patients with documented allergies to beta-lactam and/or cephalosporin antibiotics, there were no documented allergic reactions after receiving standard intravitreal vancomycin or ceftazidime. Ophthalmologists should employ evidence-based practices when choosing antibiotics for the treatment of infectious endophthalmitis in antibiotic-allergic patients.

HUMAN RESEARCH Yes: Approved by institutional review board

Intraocular Pressure Following Administration of Suprachoroidal Triamcinolone Acetonide Suspension: Results From the Phase 3 PEACHTREE Clinical Trial

- Quan Dong Nguyen, MD, MSc
- Thomas A. Ciulla, MD, MBA

OBJECTIVE To evaluate the intraocular pressure (IOP) in patients with uveitic macular edema following suprachoroidal injection of CLS-TA (investigational suspension of triamcinolone acetonide).

PURPOSE To evaluate intraocular pressure (IOP) in patients with macular edema secondary to noninfectious uveitis (NIU) following suprachoroidal injection of CLS-TA (triamcinolone acetonide suspension), and to compare the IOP events in patients rescued during the PEACHTREE trial versus those who received only suprachoroidal CLS-TA treatment.

METHODS 160 subjects were randomized 3:2 to receive suprachoroidal injections of CLS-TA or sham at baseline and week 12, and rescue therapy if needed. Pre-defined criteria were established for the adminstraction of rescue therapy. The type of rescue therapy was at the investigators' discretion. Pre-injection IOP was assessed every 4 weeks through week 24. Endpoints included ≥ 30mmHg IOP as an IOP-related adverse event at any visit, IOP medication use, and surgical intervention for IOP. A post hoc analysis was conducted to compare IOP-related outcomes in patients who only received CLS-TA to patients who received rescue treatment in the control arm.

RESULTS In the analyses, 7.8% of subjects in the control arm experienced an IOP AE of IOP ≥30 mmHg at any post-baseline visit versus 5.2% in the CLS-TA arm; 9.4% of subjects in the control arm were given additional IOP lowering medication versus 7.3% in the in the CLS-TA arm. No surgical intervention was required for an elevated IOP AE in either group. By week 24, 13% of the subjects in the CLS-TA arm and 72% in the control arm required rescue therapy. Among subjects who received rescue therapy, intravitreal and periocular corticosteroids were most commonly prescribed. In the post hoc analysis, CLS-TA subjects who did not receive rescue treatment experienced lower rates of IOP ≥ 30mmHg at any

visit compared to control subjects who received rescue therapies (4.9% versus 10.9%). The use of IOP lowering medications in subjects who only received CLS-TA was lower than control subjects who received rescue therapy (7.2% versus 13.0%).

CONCLUSION Suprachoroidal injections of CLS-TA did not significantly increase IOP relative to sham control in the Phase 3 PEACHTREE trial. Study subjects who only received CLS-TA experienced lower rates of IOP events compared to subjects who also received rescue therapy, supporting a beneficial compartmentalization effect of a steroid delivered via the suprachoroidal space.

HUMAN RESEARCH Yes: Approved by institutional review board

Evaluating the True 3-Year Recurrence Rate in Non-infectious Posterior Segment Uveitis following an Injectable Fluocinolone Acetonide Insert

- Dilraj S Grewal, MD
- Dario A Paggiarino, MD

OBJECTIVE To review cases of non-infectious uveitis affecting the posterior segment that had recurrence imputed due to the use of prohibited anti-inflammatory medications in the phase 3 clinical trial.

PURPOSE Systemic anti-inflammatory treatment for non-ocular or fellow eye inflammation can confound study eye results in evaluation of the fluocinolone acetonide intravitreal (FAi) insert as conservative analyses categorize these as prohibited drugs and their use amounts to an imputed recurrence or treatment failure in the trial. We evaluated the reasons for use of such systemic medications during the trial to estimate the true recurrence rate.

METHODS Post hoc analysis of a prospective, randomized, double-masked, 36-month, phase 3 clinical trial, wherein subjects with a >1-year history of recurrent non-infectious posterior segment uveitis, who had experienced at least 2 separate recurrences requiring ≥3 months of systemic therapy or ≥2 intra-/periocular steroid injections, were randomized to treatment of their more severely affected eye with a 0.18mg FAi insert or sham injection. Recurrence was defined as 1) ≥ +2 increase in vitreous haze; or 2) ≥ 15-letter loss of VA; or was imputed in case of missing data or for use of prohibited anti-inflammatory medications (defined as oral corticosteroids or systemic immunosuppressants).

RESULTS Three-year recurrence rates of 56% (49/87) and 93% (39/42) were reported for FAi and sham eyes respectively ($p<0.001$). Twenty-seven (27) of the 49 recurrences in the FAi treatment group (55.1%) and 9 of the 39 recurrences in the sham group (23.1%) were

imputed as the result of prohibited systemic medication use. Each case was reviewed to determine the reason for the prohibited medication use, ie, non-ocular, fellow eye, and/or study eye inflammation, and to determine if there were other findings to indicate that the study eye did not respond to the FAi insert study treatment.

CONCLUSION Over 55% of the recurrences in the FAi group were due to the use of systemic anti-inflammatory medications over the 3-year trial. The conservative analysis considered those subjects treated with prohibited systemic medications as failures even when the medication was for a non-ocular or fellow-eye condition. Thus, the true 3-year recurrence rate in FAi-treated eyes may be less than 56%.

HUMAN RESEARCH Yes: Approved by institutional review board

Course of Macular Edema Through 36 Months With Fluocinolone Acetonide Intravitreal Insert for Non-infectious Uveitis Affecting the Posterior Segment

- Seenu M. Hariprasad, MD
- KEYUR PATEL, PHARMD

OBJECTIVE To report on the clinical course of macular edema through 36 months in eyes treated with a single sustained-release 0.18 mg FAi insert for NIU-PS.

PURPOSE Macular edema is an important cause of vision loss in non-infectious uveitis affecting the posterior segment (NIU-PS). In this study, the effect on macular edema through 36 months of a single sustained-release fluocinolone acetonide intravitreal (FAi) implant is compared with eyes receiving sham injection (and subsequently treated with standard local and systemic therapies as needed).

METHODS In this prospective, randomized, double-masked, 36-month, phase 3 clinical trial, subjects with a history of chronic NIU-PS (≥1 year), who had experienced at least two separate recurrences requiring ≥3 months of systemic therapy or ≥2 intra- or periocular steroid injections, were randomized to receive an FAi (n=87) or sham injection (n=42). At baseline and follow-up visits, central foveal thickness (CFT), central subfield thickness (CSFT), and total volume of central subfield were measured using OCT. The presence of macular edema was determined based on the investigator's clinical interpretation of all relevant findings.

RESULTS Macular edema was present in 51 (58.6%) FAi and 28 (66.7%) sham-treated eyes at baseline and in 9 (10.3%) and 9 (21.4%), respectively, at 36 months. Both groups showed a trend toward resolution of existing macular edema, and of the eyes with no macular edema at baseline, few in either group (≤3) developed macular edema at any post-baseline visit. At

baseline, a majority of eyes in each group had CSFT ≥300 µm (48 [55.2%] FAi and 27 [64.3%] sham). At 6 months, median decreases from baseline for CFT, CSFT, and total volume of central subfield were greater for the FAi than sham groups; changes in these parameters were similar at 36 months. Compared with the FAi group, more sham-treated patients received local (29 [69%] sham and 17 [19.5%] FAi) and systemic (21 [50%] sham and 30 [34.4%] FAi) adjunctive steroid or immunosuppressant medications throughout the 36-month study.

CONCLUSION In eyes with NIU-PS, the FAi insert had a beneficial effect on macular edema through 36 months. Macular edema decreased through the study period in sham-treated eyes as well, likely related to the adjunctive local and systemic anti-inflammatory/immunomodulatory medications these patients received.

HUMAN RESEARCH Yes: Approved by institutional review board

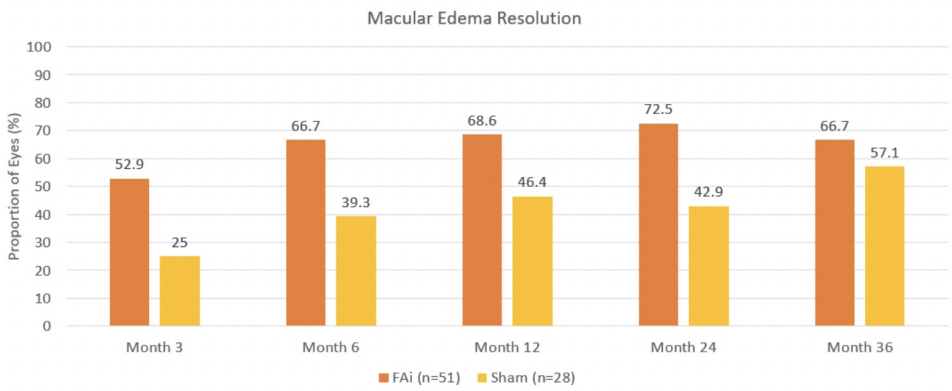

Figure 1. Among eyes with macular edema at baseline, the proportion in each treatment group without macular edema at subsequent study timepoints.

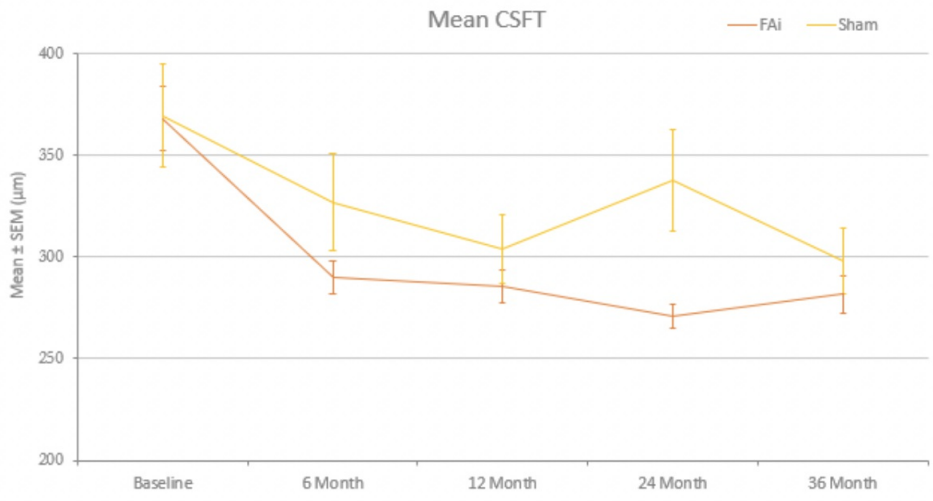

Figure 2. Mean CSFT from baseline through 36 months.