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## Post-Injection Endophthalmitis in the Comparison of AMD Treatments Trials (CATT)

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### Abstract

**Objective**—To describe the incidence and outcomes of endophthalmitis after intravitreal injections of anti-VEGF agents in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT) and to assess the effect of use of prophylactic topical antimicrobials on incidence.

**Design**—Cohort study within a randomized clinical trial.

**Participants**—Patients enrolled in CATT.

**Methods**—Patients with neovascular age-related macular degeneration received intravitreal injections of ranibizumab or bevacizumab under one of three dosing regimens. The study protocol specified pre-injection preparation to include use of a sterile lid speculum and povidone iodine (5%). Use of pre-and post-injection antibiotics was at the discretion of the treating ophthalmologist. Patients were followed monthly for two years.

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<sup>‡</sup>A listing of the CATT Research Group is in the Appendix

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**Main Outcome Measures**—Development of endophthalmitis and visual acuity.

**Results**—Endophthalmitis developed after 11 of 18,509 injections (1 per 1,700; 0.06%; 95% Confidence Interval (0.03%, 0.11%)), and among 11 of 1185 patients (0.93%; 95% Confidence Interval (0.52, 1.66)). Incidence of endophthalmitis was 0.15% among injections with no antibiotic use, 0.08% among injections with pre-injection antibiotics only, 0.06% among injections with post-injection antibiotics only, and 0.04% among injections with pre-and post-injection antibiotics ( $p=0.20$ ). All eyes were treated with intravitreal antibiotics and 4 had vitrectomy. Among the 11 affected eyes, the final study visual acuity was 20/40 or better in 4 (36%) eyes, 20/50-20/80 in 2 (18%) eyes, 20/100-20/160 in 3 (27%) , and <20/800 in 2 (18%) eyes. The final visual acuity was within 2 lines of the visual acuity before endophthalmitis in 5 (45%) eyes.

**Conclusion**—Rates of endophthalmitis were low and similar to those in other large scale studies. Use of topical antibiotics either before or after injection does not appear to reduce the risk for endophthalmitis.

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Intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) drugs have become one of the most commonly performed procedures in ophthalmology, with an estimate of more than 3 million per year for the Medicare population.<sup>1</sup> Although infrequent, endophthalmitis is the complication of greatest concern due to poor functional outcomes in some patients even with prompt treatment.

The rate of endophthalmitis following intravitreal injections varies in the literature. In large prospective randomized trials, the endophthalmitis rate ranges from six in an estimated 26,300 injections (0.02%) to three in 3125 (0.10%).<sup>2-4</sup> In retrospective case series, in which generally one or a small number of institutions or practices report their findings, the rates vary more widely<sup>3,4</sup>. The largest meta-analysis performed to date analyzed 43 published articles and found an endophthalmitis incidence of 197 in 350,535 injections (0.056%)<sup>4</sup>

The few generally agreed upon preventive strategies include the use of povidone iodine on the ocular surface immediately before the injection and the use of a lid speculum.<sup>5</sup> Other precautions, such as use of gloves<sup>5</sup>, and strategies to minimize droplet contamination such as use of a mask or minimizing talking during injection remain controversial.<sup>6-8</sup>

The administration of prophylactic pre- or post-injection topical antibiotics has been required in many clinical trials and is routinely practiced by many ophthalmologists. Recommendations for antibiotic use have been recently called into question by reports of lower endophthalmitis rates among those patients who did not receive pre- or post-injection antibiotics in some DRCR.net studies<sup>6</sup>. Additionally, the use of prophylactic topical antibiotics has been demonstrated to cause rapid development of antibiotic resistant virulent bacteria on the ocular surface and displacement of commensal flora with more virulent species.<sup>9-11</sup>

We report the rate of endophthalmitis in the Comparison of Age-related Macular Degeneration Treatments Trials (CATT), a multicenter randomized clinical trial, and describe the impact of endophthalmitis on visual acuity. We also examine the effect of pre- or post-injection use on the endophthalmitis rates in this large cohort.

## Methods

A detailed discussion of the methodology for the CATT has been published previously<sup>12-14</sup>. From February 2008 through December 2009, 1185 patients from 43 clinical centers in the United States were enrolled into the trial. Eyes were eligible for the study if they had active choroidal neovascularization secondary to age-related macular degeneration (AMD), no previous treatment, and visual acuity between 20/25 and 20/320. Patients were randomized to intravitreal injections of either ranibizumab or bevacizumab administered monthly, or pro re nata (PRN) for two years, or monthly for one year followed by PRN for one year. Bevacizumab was prepared centrally by an aseptic filling facility and distributed in small glass vials. Ranibizumab was obtained by each clinic through their normal commercial sources. Ophthalmologists were masked to the identity of the drug at the time of treatment and throughout follow-up. The study was approved by an institutional review board associated with each center. All patients provided written informed consent.

Patients were evaluated every 28 days and treated with intravitreal injections according to their assigned treatment. The CATT protocol for intravitreal injection required application of 5% povidone iodine and use of a sterile eyelid speculum. Use of topical antibiotic medications either before or after the injection was at the discretion of the treating ophthalmologist.

Study ophthalmologists examined patients as soon as possible after a report of symptoms of endophthalmitis. The diagnosis of presumed endophthalmitis was made by the examining ophthalmologist on the basis of clinical examination. Signs of endophthalmitis included the presence of pain, decreased visual acuity, conjunctival injection, corneal edema, anterior chamber cell and flare, hypopyon, vitritis, and intraretinal hemorrhage. Study ophthalmologists initiated treatment with intravitreal antimicrobial medications and, in some instances, vitrectomy upon making the diagnosis of presumed endophthalmitis.

All reported cases of presumed endophthalmitis; i.e., treated with intravitreal antibiotics, in CATT were identified and reviewed in detail. Cases with positive cultures were classified as endophthalmitis. Cases with negative or no cultures and no later episodes of inflammation after additional anti-VEGF treatment were also classified as endophthalmitis. However, cases with negative cultures that had a subsequent episode of severe inflammation following intravitreal injection of the assigned study drug that completely resolved with topical steroids only were classified as severe non-infectious inflammation, and not as endophthalmitis.

Incidence rates and associated 95% confidence intervals were calculated on a per injection basis and a per patient basis.<sup>15</sup> Comparisons of rates were evaluated by chi-square tests with exact calculations of p-values.

## Results

Eleven eyes developed endophthalmitis after 18,509 injections in 1185 patients (Table 1). The incidence rate per injection was 0.06% (95% Confidence Interval (0.03%, 0.11%) or 1 per 1,700 injections. The incidence rate per patient was 0.93% (95% Confidence Interval

(0.52%, 1.66%). Of the eleven eyes with endophthalmitis, four were treated with ranibizumab and seven with bevacizumab.

Incidence rates of endophthalmitis for four groups defined by use of topical antibiotics before and after injection are displayed in Table 1. Antibiotics were used both before and after injection for 9961 (54%) injections and were not used at either time for 2000 (11%) injections. The rate of endophthalmitis was highest in the group with no antibiotic use (0.15%) and lowest in the group with antibiotics administered both before and after (0.04%); however, the differences in incidence rates among the four groups were not statistically significant ( $p=0.20$ ). Povidone iodine was used per protocol for 18,332 (99.04%) of the 18,509 injections. Among the 11 injections resulting in endophthalmitis, povidone iodine was used for 10 and not used for one (Table 2, Week 56) because the patient had an allergy to shellfish.

Of the 11 endophthalmitis patients, one patient had no culture, one had a specimen obtained at primary vitrectomy, two had anterior chamber tap alone and seven had vitreous tap. Of the ten cultures, three were negative, three were positive for staphylococcus epidermidis, one was positive for staphylococcus aureus, and three were positive for streptococcal species (Table 2). Three patients had a vitrectomy between 5 days and 2 months after the initial treatment for endophthalmitis.

Among 11 affected eyes, the final study visual acuity was 20/40 or better in 4 (36%) eyes, 20/50-20/80 in 2 (18%) eyes, 20/100-20/160 in 3 (27%) , and <20/800 in 2 (18%) eyes (Table 2). The final visual acuity was within 2 lines of the visual acuity before endophthalmitis in 5 (45%) of eyes.

In addition to the 11 eyes that developed endophthalmitis, three (0.25%; 95% Confidence Interval (0.08%, 0.74%)) of the 1185 eyes developed severe non-infectious inflammation. For two of the patients, the post-injection inflammation initially was presumed to be due to endophthalmitis and treated with intravitreal antibiotics. Vitreous samples were negative for bacteria or fungus. Each patient subsequently developed severe inflammation similar to the original episode immediately after the next challenge with the same drug (ranibizumab in one case and bevacizumab in one case) and in each case, the inflammation resolved with topical steroids only and no antibiotics. One additional patient, treated with ranibizumab, developed severe post-injection inflammation considered by the treating ophthalmologist to be an immune phenomenon, and the episode resolved promptly with topical steroid therapy.

## Discussion

The rates of endophthalmitis in CATT (0.06% per injection, 0.93% per patient) are consistent with the results of other large clinical trials of intraocular injections of anti-VEGF agents.<sup>16-21</sup> The ratio of culture negative to culture positive cases was similar to post-operative endophthalmitis after cataract surgery, and visual acuity outcomes after treatment were consistent with large series of post cataract surgery endophthalmitis.<sup>22-24</sup>

The rate of infection did not appear to be influenced by the use of topical antibiotic medication before or after the injection. While most practitioners agree on the use of topical

povidone iodine and a lid speculum for intravitreal injections, the use of antibiotics in conjunction with intravitreal injections has changed substantially over the last 10 years. Since anti-VEGF injection became common clinical practice in 2005, pre- or post- injection topical antibiotics have been used in the vast majority of cases. In CATT, investigators elected to use pre- or post- injection antibiotics in 90% of the intravitreal injections given during the period of study between February 2008 and December 2011. The practice was supported by clinical conjunctival culture data demonstrating significant reduction in positive conjunctival cultures following antibiotic instillation.<sup>25, 26</sup>

More recently, several studies demonstrating increased antibiotic resistance in conjunctival bacteria due to repeated topical antibiotic exposure and an apparent lack of efficacy in preventing endophthalmitis, have resulted in a dramatic decline of topical antibiotic use.<sup>9-11,27,28</sup> Bhavsar and colleagues reported the rate of endophthalmitis in four DRCRnet studies among patients using and not using topical prophylactic antibiotics.<sup>6,29</sup> The endophthalmitis rate was higher among those using prophylactic topical antibiotics than those not using antibiotics (0.13% versus 0.03%;  $p=0.25$ ). Similarly, Bhatt and colleagues found no difference in endophthalmitis rates between 2,287 patients who received topical antibiotics and 2,480 patients who did not.<sup>16</sup> Cheung and colleagues found the lowest rate of endophthalmitis among more than 15,000 injections in eyes that did not receive any prophylactic antibiotics.<sup>30</sup>

Following the reports of emerging resistance and limited effectiveness, there has been a dramatic shift away from using topical antibiotics in the peri-injection setting. In annual surveys by the American Society of Retina Specialists, the proportion of members reporting use of topical antibiotics decreased from approximately 90% in 2008 to 20% in 2013.<sup>31,32</sup> The totality of the published evidence at this point, combined with the findings in CATT, do not support a clinically important benefit of prophylactic topical antibiotics in reducing the risk of endophthalmitis following intravitreal injections.

Among the CATT culture positive endophthalmitis cases, three of seven (42%) were a *Streptococcus* species. Higher rates of *Streptococcus* species following intravitreal injections than after intraocular surgery have been previously reported.<sup>33,34</sup> McCannel and Wen have suggested that oropharyngeal droplet contamination may be responsible.<sup>35</sup> Although still controversial, recommendations for reducing risk of Streptococcal endophthalmitis include controlling droplet contamination with such measures as minimizing speaking during the injection, or wearing a facemask.

There were three cases of severe non-infectious inflammation after injection in CATT that were of particular interest. In each case, there was convincing evidence that the inflammation was not due to infection. All cultures were negative, but negative cultures have been reported in several studies of endophthalmitis when it was highly likely that an infectious organism was present.<sup>21,36</sup> Instead, what was unique in these three cases was that the inflammation either completely resolved with topical steroids alone and no antibiotic (one case following a ranibizumab injection), or the patient developed a recurrent episode of severe inflammation similar to the original event with subsequent injection of the same anti-VEGF injection (one case with ranibizumab and one with bevacizumab), and the

inflammation resolved with topical steroids and no antibiotics. These cases highlight the fact that not all cases of severe inflammation after injection are infectious and that there is a clinical distinction between severe non-infectious inflammation and infectious endophthalmitis. Severe non-infectious inflammation is used to denote a transient, self-limited inflammatory reaction that occurs after intravitreal injection. This is distinguished from infectious endophthalmitis where the source of inflammation is an intraocular microbe.<sup>4</sup>

Eyes with severe non-infectious inflammation, also referred to in the literature as non-infectious endophthalmitis, have a typical clinical presentation. Patients usually have symptoms of decreased vision and minimal pain soon after the intravitreal injection (i.e. day 0-day 2). Patients develop marked anterior chamber reaction with cell and flare but often will not have hypopyon or fibrin. Posteriorly, patients develop a “pseudogranulomatous” appearance, with large cellular aggregates and moderate vitreous haze.<sup>37</sup> This contrasts with the presentation of infectious endophthalmitis, where findings of pain, decreased visual acuity, conjunctival injection, corneal edema, anterior chamber cell and flare, hypopyon, fibrin, vitritis, and intraretinal hemorrhage typically occur two or more days after injection, when the micro-inoculum of bacteria has had time to cause a consequential cellular reaction.

In summary, the rate (0.06%, or 1 per 1,700) of endophthalmitis in CATT per injection was similar to rates in other large clinical trials evaluating anti-VEGF drugs for neovascular AMD. Topical antibiotics used before or after injection did not result in a statistically or clinically significant reduction in the risk for endophthalmitis ( $p=0.20$ ). Patients who developed endophthalmitis were treated with intravitreal antibiotics and in 4 cases (36%), vitrectomy. The final study visual acuity was within 2 lines of the visual acuity before endophthalmitis in 5 (45%) of 11 eyes. Three patients developed severe non-infectious inflammation that resolved with topical steroids.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## REFERENCES

1. Williams, GA. [August 10, 2014] IVT injections: Health policy implications.. Review of Ophthalmology. 2014. [http://www.revophth.com/content/d/retinal\\_insider/c/48732/](http://www.revophth.com/content/d/retinal_insider/c/48732/).
2. Brown DM, Kaiser PK, Michels M, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med. 2006; 355:1432–44. [PubMed: 17021319]
3. Heier JS, Brown DM, Chong V, et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology. 2012; 119:2537–48. Epub 2012 Oct 17. [PubMed: 23084240]
4. Fileta JB, Scott IU, Flynn HW Jr. Meta-analysis of infectious endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents. Ophthalmic Surg Lasers Imaging Retina. 2014; 45:143–9. [PubMed: 24635156]



5. Jager RD1, Aiello LP, Patel SC, Cunningham ET Jr. Risks of intravitreal injection: a comprehensive review. *Retina*. 2004; 24:676–98. [PubMed: 15492621]
6. Bhavsar AR, Googe JM Jr, Stockdale CR, et al. Risk of endophthalmitis after intravitreal drug injection when topical antibiotics are not required: the diabetic retinopathy clinical research network laser-ranibizumab-triamcinolone clinical trials. *Arch Ophthalmol*. 2009; 127:1581–3. [PubMed: 20008710]
7. Wen JC, McCannel CA, Mochon AB, Garner OB. Bacterial dispersal associated with speech in the setting of intravitreal injections. *Arch Ophthalmol*. 2011; 129:1551–4. [PubMed: 21825179]
8. Doshi RR, Leng T, Fung AE. Reducing oral flora contamination of intravitreal injections with face mask or silence. *Retina*. 2012; 32:473–6. [PubMed: 22374155]
9. Kim SJ, Toma HS. Antimicrobial resistance and ophthalmic antibiotics: 1-year results of a longitudinal controlled study of patients undergoing intravitreal injections. *Arch Ophthalmol*. 2011; 129:1180–8. [PubMed: 21911665]
10. Milder E, Vander J, Shah C, Garg S. Changes in antibiotic resistance patterns of conjunctival flora due to repeated use of topical antibiotics after intravitreal injection. *Ophthalmology*. 2012; 119:1420–4. [PubMed: 22420958]
11. Dave SB, Toma HS, Kim SJ. Changes in ocular flora in eyes exposed to ophthalmic antibiotics. *Ophthalmology*. 2013; 120:937–41. [PubMed: 23415422]
12. The Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group. Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *Engl J Med*. 2011; 364:1897–908. Epub 2011 Apr 28.
13. The Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. *Ophthalmology*. 2012; 119:1388–98. [PubMed: 22555112]
14. DeCroos FC, Toth CA, Stinnett SS, et al. Optical coherence tomography grading reproducibility during the Comparison of Age-related Macular Degeneration Treatments Trials. *Ophthalmology*. 2012; 119:2549–57. [PubMed: 22939114]
15. Newcombe RG. Two-sided confidence intervals for the single proportion: Comparison of seven methods. *Statistics in Medicine*. 1998; 17:857–72. [PubMed: 9595616]
16. Bhatt SS, Stepien KE, Joshi K. Prophylactic antibiotic use after intravitreal injection: effect on endophthalmitis rate. *Retina*. 2011; 31:2032–6. [PubMed: 21659941]
17. Mason JO 3rd, White MF, Feist RM, et al. Incidence of acute onset endophthalmitis following intravitreal bevacizumab (Avastin) injection. *Retina*. 2008; 28:564–7. [PubMed: 18398358]
18. Scott IU, Edwards AR, Beck RW, et al. A phase II randomized clinical trial of intravitreal bevacizumab for diabetic macular edema. *Ophthalmology*. 2007; 114:1860–7. [PubMed: 17698196]
19. Aggio FB, Farah ME, de Melo GB, et al. Acute endophthalmitis following intravitreal bevacizumab (Avastin) injection. *Eye (Lond)*. 2007; 21:408–9. [PubMed: 17277758]
20. Artunay O, Yuzbasioglu E, Rasier R, et al. Incidence and management of acute endophthalmitis after intravitreal bevacizumab (Avastin) injection. *Eye (Lond)*. 2009; 23:2187–93. [PubMed: 19218994]
21. Wu L, Martinez-Castellanos MA, Quiroz-Mercado H, et al. Twelve-month safety of intravitreal injections of bevacizumab (Avastin): results of the Pan-American Collaborative Retina Study Group (PACORES). *Graefes Arch Clin Exp Ophthalmol*. 2008; 246:81–7. [PubMed: 17674014]
22. Endophthalmitis Vitrectomy Study Group. Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. *Arch Ophthalmol*. 1995; 113:1479–96. [PubMed: 7487614]
23. Eifrig CW, Flynn HW Jr, Scott IU, et al. Acute-onset postoperative endophthalmitis: review of incidence and visual outcomes (1995–2001). *Ophthalmic Surg Lasers*. 2002; 33:373–8. [PubMed: 12358290]
24. Busbee BG, Recchia FM, Kaiser R, et al. Bleb-associated endophthalmitis: clinical characteristics and visual outcomes. *Ophthalmology*. 2004; 111:1495–503. discussion 1503. [PubMed: 15288977]



25. Isenberg, s; Apt, L.; Yoshimori, R., et al. Chemical preparation of the eye in ophthalmic surgery IV: a comparison of povidone-iodine in conjunction with prophylactic antibiotic. *Arch Ophthalmol.* 1985; 103:1340–2. [PubMed: 2994609]
26. de Caro JJ, Ta CN, Ho HK, et al. Bacterial contamination of ocular surface and needles in patients undergoing intravitreal injections. *Retina.* 2008; 28:877–83. [PubMed: 18536606]
27. Moss JM, Sanislo SR, Ta CN. A prospective randomized evaluation of topical gatifloxacin on conjunctival flora in patients undergoing intravitreal injections. *Ophthalmology.* 2009; 116:1498–501. [PubMed: 19501409]
28. Yin VT 1, Weisbrod DJ, Eng KT, et al. Antibiotic resistance of ocular surface flora with repeated use of a topical antibiotic after intravitreal injection. *JAMA Ophthalmol.* 2013; 131:456–61. [PubMed: 23430175]
29. Bhavsar AR, Stockdale CR, Ferris FL 3rd, et al. Update on risk of endophthalmitis after intravitreal drug injections and potential impact of elimination of topical antibiotics. *Arch Ophthalmol.* 2012; 130:809–10. [PubMed: 22801859]
30. Cheung CS, Wong AW, Lui A, et al. Incidence of endophthalmitis and use of antibiotic prophylaxis after intravitreal injections. *Ophthalmology.* 2012; 119:1609–14. [PubMed: 22480743]
31. ASRS. Preferences and Trends Membership Survey. Mitra, RA.; Pollack, JS., editors. American Society of Retina Specialists; Chico, CA.: 2008. 2008
32. ASRS. Preferences and Trends Membership Survey. Stone, TW.; Mitra, RA., editors. American Society of Retina Specialists; Chicago, IL.: 2013. 2013
33. Simunovic MP, Rush RB, Hunyor AP, Chang AA. Endophthalmitis following intravitreal injection versus endophthalmitis following cataract surgery: clinical features, causative organisms and post-treatment outcomes. *Br J Ophthalmol.* 2012; 96:862–6. Epub 2012 Mar 24. [PubMed: 22446145]
34. McCannel CA. Meta-analysis of endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents: causative organisms and possible prevention strategies. *Retina.* 2011; 31:654–61. [PubMed: 21330939]
35. Wen JC, McCannel CA, Mochon AB, Garner OB. Bacterial dispersal associated with speech in the setting of intravitreal injections. *Arch Ophthalmol.* 2011; 129:1551–4. Epub 2011 Aug 8. [PubMed: 21825179]
36. Shane TS, Martin DF, for the Endophthalmitis-Ganciclovir Implant Study Group. Endophthalmitis after ganciclovir implant in patients with AIDS and cytomegalovirus retinitis. *Am J Ophthalmol.* 2003; 136:649–54. [PubMed: 14516804]
37. Georgopoulos MK, Polak KF, Prager F, et al. Characteristics of severe intraocular inflammation following intravitreal injection of bevacizumab (Avastin). *Br J Ophthalmol.* 2009; 93:457–62. [PubMed: 19033289]

**Table 1**

## Incidence of Endophthalmitis by Use of Antibiotics

<b>Antibiotic Use</b>	<b>Injections</b>	<b>Cases</b>	<b>Rate</b>	<b>95% Confidence Interval</b>
None	2000	3	0.15%	(0.05%, 0.44%)
Pre-injection only	1301	1	0.08%	(0.01%, 0.43%)
Post-injection only	5247	3	0.06%	(0.05%, 0.25%)
Pre- and post-injection	9961	4	0.04%	(0.02%, 0.10%)
Total	18509	11	0.06%	(0.03%, 0.11%)

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**Table 2**  
Summary of Eyes with Endophthalmitis or Severe Non-infectious Inflammation

Injection Week	Previous Injections	Topical Antibiotics		Days to Presentation	Intravitreal Antibiotics	Vitrectomy	Culture Result	Visual Acuity	
		Before	After					Before	Final
<b>Endophthalmitis</b>									
0	0	No	Yes	2	Yes	Yes	Streptococcus	20/32	20/25
4	1	No	Yes	3	Yes	Yes	Negative	20/32	20/63
8	2	Yes	Yes	1	Yes	No	Staphylococcus	20/40	20/63
24	5	No	No	1	Yes	No	Streptococcus	20/40	<20/800*
48	10	No	No	11	Yes	No	Negative	20/25	20/32
52	12	Yes	Yes	2	Yes	Yes	Streptococcus	20/32	20/160
56	14	Yes	Yes	2	Yes	No	Staphylococcus	20/32	20/32
60	14	Yes	Yes	1	Yes	No	Not done	20/63	<20/800**
76	13	No	Yes	4	Yes	No	Staphylococcus	20/32	20/32
84	21	Yes	No	1	Yes	Yes	Staphylococcus	20/32	20/100
100	21	No	No	2	Yes	No	Negative	20/25	20/160
<b>Severe Non-infectious Inflammation</b>									
12	3	Yes	Yes	4	No	No	Not done	20/40	20/40
72	12	Yes	Yes	17	Yes	No	Negative	20/40	20/160
76	18	Yes	Yes	2	Yes	No	Negative	20/16	20/16

\* Last study visit at week 32

\*\* Visual acuity returned to 20/63 before a retinal hemorrhage and choroidal detachment at week 80