8:50 AM

Confirmatory 1-Year Study Results of an Injectable Fluocinolone Acetonide Intravitreal Insert to Treat Noninfectious Posterior Segment Uveitis

- Glenn J. Jaffe, MD
- Jyotirmay Biswas, MD

OBJECTIVE To evaluate the one year efficacy and safety of an injectable fluocinolone acetonide intravitreal insert for treating non-infectious posterior segment uveitis (NIPU).

PURPOSE Uveitis treatment includes local and/or systemic corticosteroids or immunosuppression. This study tested the hypothesis that a single administration of an injectable fluocinolone acetonide intravitreal insert (FAI) delivering daily microdoses for 36 months can reduce the proportion of subjects who have a uveitis recurrence.

METHODS This trial was the second of two prospective, multi-center, randomized, double masked, safety and efficacy studies of an FAI. Patients with a > 1yr history of recurrent NIPU, who had experienced at least 2 separate recurrences requiring ≥ 3m systemic therapy or ≥ 2 intra- or periocular steroid injections, were randomized to treatment with FAi (N=101) or sham (N=52) injection. The primary efficacy endpoint was NIPU recurrence. Visual acuity (VA) and macular thickness/edema were secondary efficacy

outcomes. Safety results included rates of adverse events including, but not limited to, cataract and elevated IOP.

RESULTS A total of 153 subjects were enrolled in 15 centers in India. Uveitic recurrences affecting the posterior segment, or requiring rescue with peri- or intraocular steroids and/or systemic treatment, were reported for 32.7% of FAI treated eyes and 59.6% of sham eyes, p=0.002. Both groups had small improvements in mean VA at 1 yr and macular edema was resolved in 67.7% (21/31) and 57.1% (8/14) of FAI and sham eyes that had edema at baseline. Through 1 yr, 23.8% and 7.7% of FAi and sham subjects had an IOP increase ≥12 mm Hg in the study eye, 1 of the FAi study eyes required IOP lowering surgery. Cataract surgery was performed on 18.0% and 8.6% of phakic study eyes in the FAi and sham groups respectively.

CONCLUSION The results of this study confirm 1 yr findings from a previous multinational study. The FA intravitreal insert is effective to treat and prevent recurrent uveitis, and side effects are transient and/or manageable. Patients will continue in the study for 2 more yrs.

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

8:58 AM

Controlling Uveitic Recurrences: Results From a Phase 3 Study of 0.18 mg Fluocinolone Acetonide Insert (FAi) in Noninfectious Posterior Uveitis

- Quan Dong Nguyen, MD, MSc
- Keyur Patel
- Dario A Paggiarino, MD

OBJECTIVE To evaluate role of fluocinolone acetonide insert in decreasing rate of recurrences of inflammation as well as number of recurrent episodes in patients with intermedaite, posterior and pan-uveitis

PURPOSE Cumulative damage from repeated inflammatory episodes has been associated with significant visual morbidity in patients with non-infectious posterior uveitis (NIPU). The number of recurrences of uveitis over 1 year was compared among eyes treated with the FAi and those treated with a sham injection in a prospective, randomized, double-masked phase 3 clinical trial.

METHODS Subjects with a > 1-year history of recurrent NIPU, who had experienced at least 2 separate recurrences requiring ≥ 3 months of systemic therapy or ≥ 2 intra- or periocular steroid injections, were randomized to treatment with FAi or sham. Cumulative recurrence of uveitis, defined as 1) ≥ +2 increase in anterior chamber cells; or 2) ≥ +2 increase in vitreous haze; or 3) ≥ 15-letter loss of VA; or imputed in case of missing data or rescue treatment for ocular inflammation, was compared through 1 year of the on-going 3-year clinical trial.

RESULTS 129 subjects (87 FAi, 42 sham) with NIPU were enrolled. During the first year of the study, the recurrence rate in FAi randomized eyes (33/87, 37.9%) was significantly lower than in sham eyes (41/42, 97.6%), $p<0.001$. A total of 63 recurrences were reported in FAi treated eyes (0.7±1.22/eye) versus 105 recurrences in sham treated eyes (2.5±1.67/eye). Multiple (>1) recurrences were observed in 18.4% (16/87) of the FAi treated eyes and 67% (28/42) of the sham treated eyes. Adverse events included ocular hypertension and cataract. IOP increased 1.3±3.57 and 0.2±4.17 mmHg on average in FAi and sham injection eyes, respectively.

CONCLUSION Treatment with the FAi resulted in a reduced 1-year rate of uveitic recurrences as well as cumulative total recurrent episodes. Other studies are being conducted to illustrate and confirm the benefit-to-risk profile of FAi in the management of patients with NIPU.

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

9:06 AM

Injectable Fluocinolone Acetonide Intravitreal Insert Reduces the Need for Adjunctive Treatment in Noninfectious Posterior Segment Uveitis

- Sunil Srivastava, MD

OBJECTIVE To evaluate the use of adjunctive medications in a clinical trial of non-infectious posterior segment uveitis (NIU-PS) patients treated with an injectable fluocinolone acetonide intravitreal insert.

PURPOSE Long-term and repeated combinations of systemic and local medical therapy are often required to treat NIPU. This study tested the hypothesis that one fluocinolone acetonide intravitreal insert (FAi) delivering microdoses for 36 months can effectively control the disease and reduce the need for additional anti-inflammatory therapies.

METHODS This was a controlled, prospective, double masked multi-center trial using a 2:1 blocked randomization based on therapy at study entry. Subjects who had experienced at least 2 separate recurrences of NIPU requiring ≥ 3 months of systemic therapy or ≥ 2 intra- or periocular steroid injections and with a > 1-year history of the disease, were randomized to treatment in one study eye with FAi (N=87) or sham (N=42) injection. Treatment of a recurrence was at each investigator's discretion. When possible, systemic therapy was used only if local therapy failed.

RESULTS One year follow-up visits were completed by 86 FAi and 40 sham subjects. Analysis of the full intent-to-treat cohort (N=129) indicated a reduced reliance on adjunctive medications to control intraocular inflammation in the FAi treated patients. Six (6.9%) FAi eyes, versus 26 (61.9%) sham eyes received at least one intra/peri-ocular steroid injection. Four out of the 6 FAi eyes required a single injection while one-half of the 26 sham eyes required multiple injections up to maximum of 5. Systemic treatment was used in 17/87 (19.5%) and 17/42 (40.5%) of FAi and sham patients respectively. Topical steroids for the control of uveitic inflammation were prescribed to 18/87 (20.7%) and 20/42 (47.6%) of FAi and sham eyes.

CONCLUSION Treatment with a single intravitreal injection of the FAi provided effective anti-inflammatory treatment for one year and significantly reduced the need for adjunctive therapies in this group of patients vs sham patients.

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

9:15 AM

Antimicrobial Injection Frequency in the Management of Presumed Bacterial Endophthalmitis: An International Survey of Retina Specialists

- Colin A. McCannel, MD
- David Xu, BS
- Aaron Nagiel, MD, PhD
- Ehsan Rahimy, MD

OBJECTIVE To determine the preferred frequency of antimicrobial injection in the management of presumed bacterial endophthalmitis.

PURPOSE To determine retina specialists' practice patterns in the management of presumed bacterial endophthalmitis, in particular the use of repeated injection of antimicrobials.

METHODS A 17 question web based survey was sent electronically to an international group of 2,978 retina physicians from the American Society of Retina Specialists membership database. Questions addressed the respondent's management of bacterial endophthalmitis, including the frequency of intravitreal antimicrobial injection, concurrent use of intraocular steroid injection, and vitreous and anterior chamber sampling for culture.

RESULTS 787 retina specialists responded to the survery (26.4% response rate) by answering all questions. 69% of respondents never or rarely performed repeat

intravitreal antimicrobial injections. Among those performing repeat injections, 92% reported performing 2 sets of injections, at an interval of every other day or twice weekly (83%). Concurrent adjunctive steroid injection was perfomred "routinely" or "frequently" by 34% of respondents. Vitreous sampling is performed "routinely" or "frequently" by 87% of respondents. Physicians in an academic practice ($p=0.002$) and early career physicians within the first 5 years of practice ($p<0.001$) were more likely to perform repeat intravitreal injections.

CONCLUSION There is substantial variability in physician practice patterns in the management of presumed bacterial endophthalmitis. There does not appear to be a clear consensus regarding antimicrobial administration frequency. Single intravitreal antimicrobial injection is more common than repeat injections. Additional studies are needed to establish the optimal antimicrobial administration frequency.

9:20 AM

Endophthalmitis After Intravitreal Injection of Vascular Endothelial Growth Factor (VEGF) Inhibitors: Management and Visual Outcomes

- Kunyong Xu, MD, MHSc
- Eric K. Chin, MD
- David RP Almeida, MD, MBA, PhD

OBJECTIVE To assess the presentation, management, and visual outcomes for patients with endophthalmitis after intravitreal injection of VEGF inhibitors

PURPOSE We describe the presentation of patients developing endophthalmitis following intravitreal injection with VEGF inhibitors. Moreover, we evaluate the management by comparing the outcomes of immediate tap-and-injection of antibiotics versus initial surgical pars plana vitrectomy (PPV). Finally, we analyze the predictive factors of final visual outcomes.

METHODS This is a retrospective single-center non-randomized interventional study. Only cases with presumptive endophthalmitis following anti-VEGF injections between 2006 and 2016 were included and the endophthalmitis had to have occurred within three weeks of intravitreal injection. All patients received a vitreous biopsy sent for cultures prior to the initiation of treatment [tap and injection of antibiotics only (TAI group) versus PPV with intravitreal antibiotics (PPV group)].

RESULTS A total of 258,357 intravitreal injections occurred over the 10-year period, of which 40 patients (0.016%) had endophthalmitis within 3 weeks after injection. In total, 34 (85.0%) patients had pain and 25 (62.5%) cases had hypopyon on initial examination. The BCVA (LogMAR) on final visit was significantly worse for patients

who had a positive culture for *Stretococcus* species (4.3, SD = 1.0) (approximately LP to NLP) compared to those who had a positive culture for *coagulase-negative Staphylococcus* (0.6, SD = 0.3) (approximately 20/80) ($p < 0.001$). There was no statistically significant difference in final BCVA between TAI and PPV groups. Younger age (<85 years old) and lower intraocular pressure (IOP) at presentation were predictive of achieving a final BCVA of 20/400 or better after treatment. Initial management (TAI vs PPV), duration of symptoms, presence of pain, presence of hypopyon, presenting BCVA, and culture status were not found to be predictive of final visual outcomes.

CONCLUSION No significant difference in final BCVA was detected between TAI and PPV groups. Younger age and lower IOP at presentation were associated with better long-term visual outcomes.

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

9:25 AM

Endophthalmitis Rates of Prefilled Ranibizumab Syringes Compared to Conventional Ranibizumab Vials: An International Multicenter Study

- Yoshihiro Yonekawa, MD
- Philip Storey, MD, MPH
- Zujaja Tauqeer, DPhil, MSc
- Jeremy D. Wolfe, MD, MS
- Sumit P. Shah, MD, FACS
- Ankoor R Shah, MD
- Takashi Koto, MD, PhD
- Ashkan M. Abbey, MD
- Yuki Morizane, MD, PhD
- Edward H Wood, MD
- Priya Sharma, MD
- Mio Morizane Hosokawaka, MD
- Karen W Jeng, MPH
- Anthony Obeid, Medical Doctorate
- Durga Borkar, MD
- Eric Chen, MD
- Patrick Dewey Williams, MD
- Makoto Inoue, MD
- Fumio Shiraga, MD
- Akito Hirakata, MD
- Annabelle A Okada
- Chirag P. Shah, MD, MPH
- Jonathan L. Prenner, MD
- Bozho Todorich, MD, PhD
- Sunir J. Garg, MD

OBJECTIVE To determine if there is a difference in the rates of endophthalmitis between prefilled syringes vs conventional vials of ranibizumab.

PURPOSE Pre-filled syringes are emerging as an alternative to the vial-and-syringe method used for administration of intravitreal biologics. By eliminating several steps in the administration of intravitreal injections, pre-filled syringes hold the potential to decrease risk of infectious endophthalmitis.

METHODS We conducted a multicenter retrospective cohort study of intravitreal injections with pre-filled syringe and single-vial formulations of 0.5 mg ranibizumab. Billing records and endophthalmitis logs were used to identify the total number of injections as well as patients who developed endophthalmitis following injection. Chart reviews were subsequently performed for these patients to confirm the endophthalmitis diagnosis. The primary outcome of the study was to compare the incidence of post-injection endophthalmitis between pre-filled and single-vial ranibizumab.

RESULTS A total of 186,393 ranibizumab injections were performed: 54,585 using pre-filled syringes, and 131,808 using vials. We identified 54 cases of acute bacterial post-injection endophthalmitis in the total cohort (0.03% [1 in 3,452]). The rate of endophthalmitis for pre-filled ranibizumab was 0.02% (12/54,585 [1 in 4,549]), compared to 0.03% (42/131,808 [1 in 3,138]; p = 0.254) after ranibizumab in vials. The odds ratio for developing endophthalmitis following vial versus pre-filled ranibizumab was 1.45 (95% CI: 0.76 to 2.75; p = 0.257).

CONCLUSION The rate of endophthalmitis following intravitreal ranibizumab injection was low. Pre-filled syringes resulted in a lower rate of endophthalmitis, but the difference was not statistically significant.

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

9:30 AM

Long-term Anti-VEGF Treatment Following Vitrectomy for Endophthalmitis in Patients With Neovascular AMD

- Zofia Michalewska, MD, PhD
- Karolina Boninska, MD
- Jerzy Nawrocki, MD, PhD

OBJECTIVE The main outcome measures was visual acuity and central retinal thickness at least once yearly after vitrectomy in endophthalmitis.

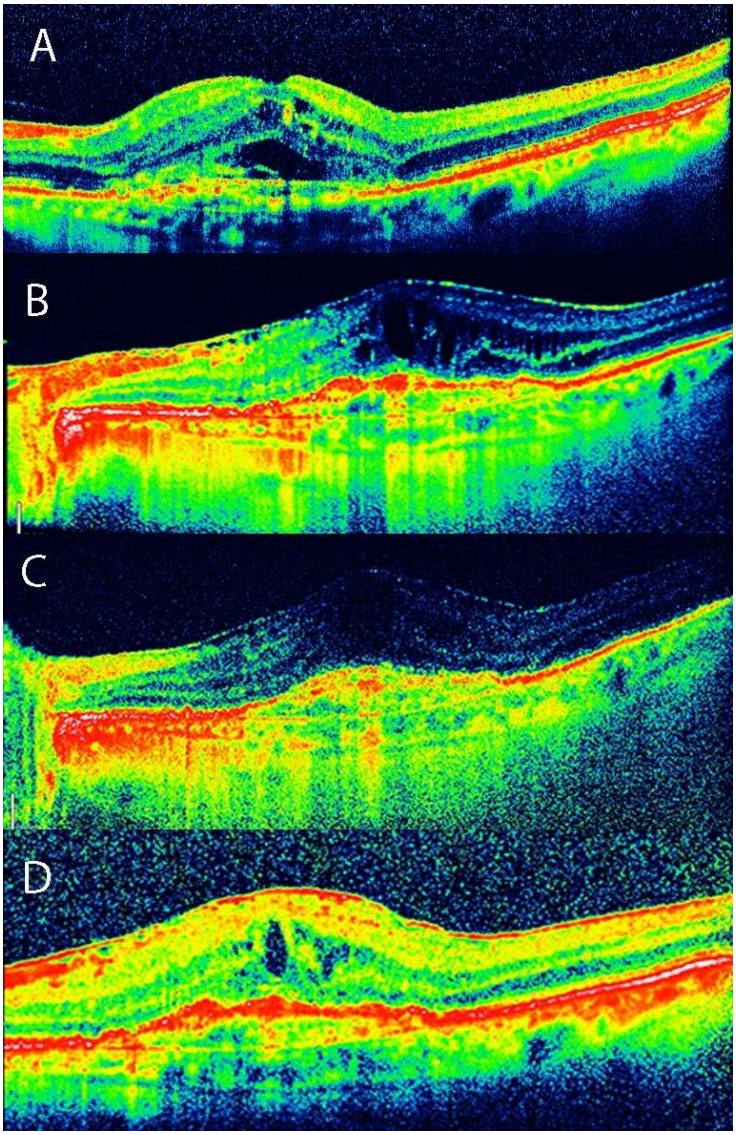
PURPOSE To present effects of long-term anti- vascular endothelial growth factor (VEGF) treatment in eyes after vitrectomy for endophthalmitis in neovascular age related macular degeneration (nAMD).

METHODS

We retrospectively assembled patients after vitrectomy for endophthalmitis, in the course of nAMD. Core vitrectomy, with intravitreal vancomycin in the infusion line was performed. Taps were always taken from the vitreous. Spectral domain optical coherence tomography was performed monthly both before and after surgery. Each month a single 7 mm scan and 6x6mm 3-dimensional scan were taken. The follow-up mode was used. In addition to monthly SD-OCT, a visual acuity was checked with early treatment diabetic retinopathy study (ETDRS) charts and intraocular pressure was also measured monthly. Anti-VEGF injections were performed on an “as needed” basis.

RESULTS Eight eyes of six patients (mean age 72 years) were included in this study. Mean visual acuity at the diagnosis of choroidal neovascularization (CNV) was 0.58 (20/32 Snellen). Mean visual acuity changed to 0.43 (20/44 Snellen) after a mean of 19 intravitreal anti- VEGF injections (p=0.45). At the first diagnosis of endophthalmitis, mean visual acuity was 0.01 (20/2000 Snellen). The mean time from first symptoms to surgery was twelve hours (2.5-26 hours). Final mean visual acuity was 0.31 (20/63 Snellen) one year after vitrectomy and 0.4 (20/50 Snellen) at the end of follow up (12-84 months), which was statistically indifferent from visual acuity at the visit just before endophthalmitis (p=0.69). The mean frequency of injections after surgery did not significantly differ from the presurgical scheme of treatment (p=0.97).

CONCLUSION Early vitrectomy for endophthalmitis is safe and might be recommended even for patients with visual acuity better than light perception. Early intervention enables continuation of anti-VEGF injections and does not influence the frequency of injections. This treatment results in satisfactory visual acuity in the long term.



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

9:35 AM

Clinical Course and Outcomes at 3 Years After Severe Fungal Endophthalmitis in 14 Eyes Following Contaminated Bevacizumab Intravitreal Injection

- Mallika Goyal, MD
- Sreekumar Reddy, MD
- Sridhar Annam

OBJECTIVE Late complications & subsequent surgical procedures over 3 years in 14 eyes that underwent intensive primary treatment for 12 months following post injection severe aspergillus endophthalmitis

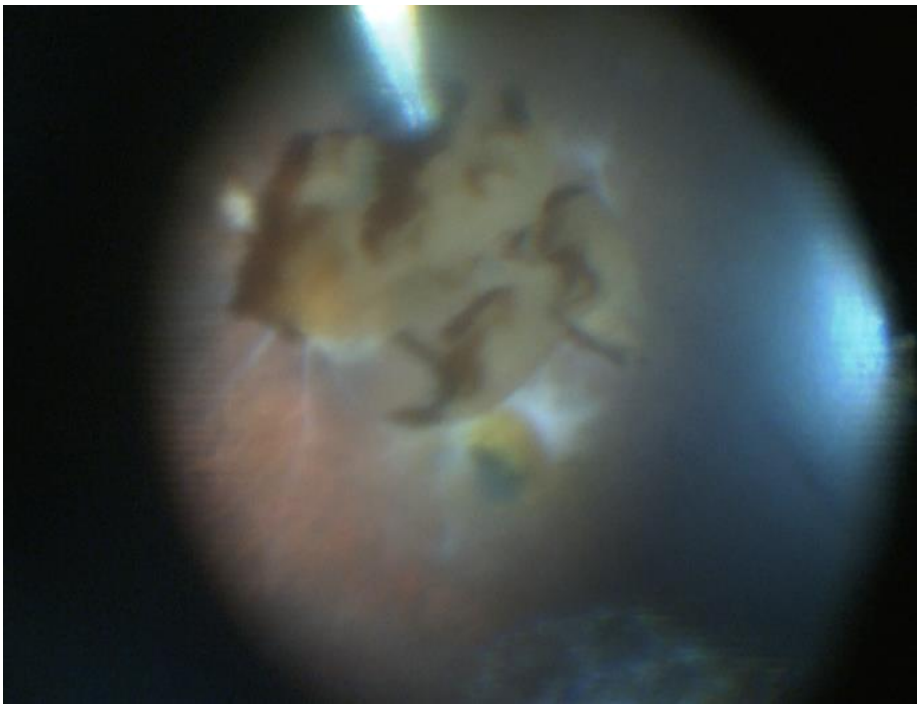
PURPOSE The purpose of this paper is to alert clinicians to the possibility of unanticipated complications & surgical situations that continue to manifest long after the primary problem of severe fungal infection & inflammation has resolved. This information would enable the physician to be vigilant & prevent these complications where possible and/ or manage these optimally in time.

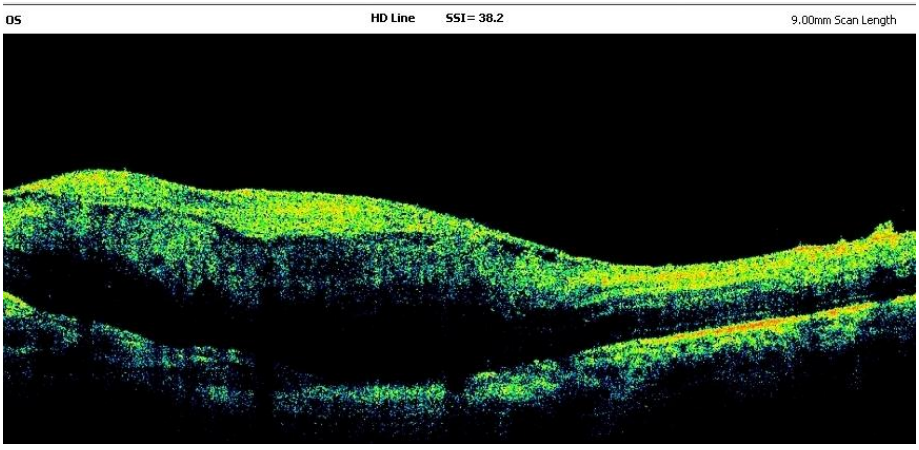
METHODS Retrospective chart review of 14 consecutive eyes with severe endophthalmitis caused by aspergillus fumigatus & aspergillus terreus 2-12 weeks following injection of contaminated bevacizumab. Clinical features, response to initial management, role of mycology drug sensitivity test, need for multiple vitreous procedures including complete vitrectomy & periodic intravitreal injection of antifungal drugs for 12 months was

documented. This 1-year data was presented at the ASRS annual meeting in 2016. Subsequent unanticipated complications during year 2 & 3 requiring specific management, including additional surgical procedures, surgical complications & final outcomes are detailed in this paper.

RESULTS Mean visual acuity at 3 years is 20/400. 12 of 14 eyes have hypotony (2-6 mm Hg); 14/14 eyes have large elevated macular scars with epimacular membranes. 13 of 14 eyes were phakic & developed significant cataract with posterior synechiae; all underwent phacoemulsification (single surgeon) in year 2 & 3. Two patients (diabetics) developed neovascular glaucoma 3 months after phacoemulsification & were treated with ranibizumab, panretinal laser & glaucoma shunt surgery with stable outcome; 1 eye had posterior dislocation of IOL requiring vitreous surgery for IOL removal; 1 eye had severe postoperative inflammation from unrecognised nuclear fragment drop requiring vitrectomy & phacofragmentation; 8 eyes had severe PC opacification requiring YAG laser; 3 eyes had rhegmatogenous retinal detachment (RD) with choroidal detachment & underwent vitreous surgery with 5000 cs silicon oil injection; oil has been retained for over 18 months now.

CONCLUSION Post injection Aspergillus endophthalmitis causes long term sequlae after the infection has resolved. These include hypotony, large macular scars, epimacular membranes, rhegmatogenous RD, cataract, posterior synechiae. Cataract surgery has higher risk of dropped nucleus & posterior IOL dislocation due to the prior multiple vitreous procedures, & of postoperative neovascular glaucoma in diabetics.





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