

9:00 AM

Adalimumab in Noninfectious Uveitis of Idiopathic Etiology – Efficacy Across Different Anatomical Locations the VISUAL I and VISUAL II Trials



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OBJECTIVE To evaluate adalimumab (ADA) efficacy in patients (pts) diagnosed with idiopathic uveitis and stratified by anatomical location of uveitis at study entry in VISUAL I and VISUAL II trials.

PURPOSE To assess ADA efficacy in active and inactive, non-infectious uveitis of idiopathic etiology across different anatomical locations of uveitis at study entry in pts recruited as part of the VISUAL program.

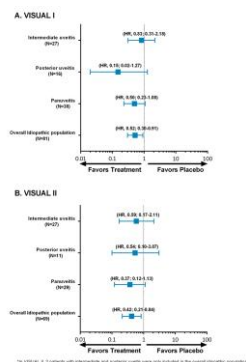
METHODS Exploratory data analyses from two global phase 3, double-masked trials: VISUAL I (active uveitis) and VISUAL II (inactive uveitis) were performed. Pts received placebo (PBO) or ADA subcutaneously (80 mg week (wk) 0, followed by 40 mg every other wk from wk 1 up to 80 wks). Oral prednisone was tapered according to a pre-specified schedule. The primary endpoint was time to treatment failure (TF) at or after wk 6 for VISUAL I; and at or after wk 2 for VISUAL II 1, 2. For this analysis, 'idiopathic'

uveitis diagnoses were stratified by location of uveitis at study entry (Intermediate, posterior, and panuveitis). Hazard ratios (HR) for time to TF were obtained for each anatomical location.

RESULTS The efficacy of ADA was significantly greater than PBO in pts with idiopathic uveitis overall (VISUAL I: 81 and VISUAL II: 69) in both VISUAL I and VISUAL II trials. After categorizing the idiopathic pts in both trials per anatomic location of uveitis at study entry, a trend in favor of ADA was observed in intermediate, posterior and panuveitis pts (Figure). Overall safety for both trials has been previously reported 1,2. References: 1) Jaffe GJ, Dick AD, Brezin AP, et al. N Engl J Med (2016); 375:932-43 2) Nguyen QD, Merrill PT, Jaffe GJ, et al. The Lancet (2016); 388(10050): 1183-92

CONCLUSION These exploratory analyses from the VISUAL I and VISUAL II trials show significantly higher efficacy in ADA-treated pts over PBO in pts with both active and inactive idiopathic uveitis. Furthermore, these analyses suggest that irrespective of the anatomical location of idiopathic uveitis at study entry, ADA-treated pts had a prolonged time to TF compared to PBO.

TAKE HOME MESSAGE Irrespective of the anatomical location of idiopathic uveitis at study entry in VISUAL I and VISUAL II trials, adalimumab-treated patients had a prolonged time to treatment failure compared to placebo



HUMAN RESEARCH This study involves human research.

IRB Approval Status: Approved by institutional review board

9:05 AM

The SAKURA Study: Corticosteroid Tapering Success With Every-Other-Month Intravitreal Sirolimus for Noninfectious Uveitis of the Posterior Segment



- Alay S. Banker, MD

OBJECTIVE To evaluate the role of intravitreal sirolimus in improving vitreous haze while reducing systemic corticosteroid needs in subjects with non-infectious uveitis of the posterior segment

PURPOSE The SAKURA program was comprised of two studies assessing the efficacy and safety of every-other-month intravitreal (IVT) sirolimus injections in subjects with active non-infectious uveitis of the posterior segment (NIU-PS). The proportion of subjects achieving systemic corticosteroid (CST) tapering success in conjunction with improvements in vitreous haze (VH) was examined.

METHODS The SAKURA program was two Phase III (one pivotal, one supportive) multinational, randomized, double-masked studies. SAKURA 1 included 347 subjects; SAKURA 2 included 245 subjects. Non-CST systemic immunosuppressants and topical CSTs were discontinued >30 days before baseline; subjects already receiving systemic CSTs at overall prednisone-equivalent dose >5 mg/d (Intent-to-Taper population) were

tapered off according to protocol schedule from baseline. Intent-to-Taper subjects achieving overall prednisone-equivalent dose ≤ 5 mg/d at Month 5 without rescue therapy were classified as CST tapering successes. VH=0 and CST tapering success with VH reduction (VH 0/0.5+) were assessed at Month 5.

RESULTS Subjects from both studies of the SAKURA program comprised the integrated Intent-to-Treat (ITT) population evaluating IVT sirolimus every other month 440 μ g vs 44 μ g active control, n=208 for each group. 46 (22.1%) subjects from the 440 μ g group and 32 (15.4%) subjects from the 44 μ g group in the integrated ITT population formed the Intent-to-Taper population. 21.2% vs 13.5% of subjects (440 vs 44 μ g, respectively) in the integrated ITT population achieved the primary endpoint of VH=0 at Month 5 (p=0.0381). In the integrated Intent-to-Taper population, tapering success at Month 5 was achieved in 69.6% (32/46) vs 68.8% (22/32) of subjects in the 440 μ g vs 44 μ g groups, respectively (p=0.9388). In addition, tapering success with VH reduction (VH 0/0.5+) at Month 5 was achieved in 43.5% (20/46) vs 28.1% (9/32) of subjects in the 440 μ g vs 44 μ g groups, respectively (p=0.1676).

CONCLUSION The integrated analysis of the SAKURA program demonstrated that the mTOR inhibitor IVT sirolimus 440 μ g achieved statistically significant improvements in VH in subjects with active NIU-PS. Subjects on oral CSTs at baseline achieved tapering success with VH reduction by Month 5 with numerically higher results observed with 440 μ g versus 44 μ g, confirming results seen in SAKURA 1.

TAKE HOME MESSAGE In the SAKURA Program, a greater proportion of subjects in the Integrated Intent-to-Taper population achieved CST tapering success with VH reduction with 440 μ g intravitreal sirolimus vs the 44 μ g dose.

HUMAN RESEARCH This study involves human research.

IRB Approval Status: Approved by institutional review board

9:15 AM

An Aseptic Protocol to Reduce the Risk of Endophthalmitis Following Intravitreal Injection



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- Michael Flory
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OBJECTIVE The aim of this study is to comparatively analyze the effect of different aseptic protocols on the incidence of endophthalmitis following intravitreal injection.

PURPOSE To identify risk factors for post-injection endophthalmitis by analyzing 37,646 intravitreal injections performed by 27 different retina specialists

METHODS A retrospective case-control series was performed. Multivariate analysis was utilized to identify risk factors for development of post-injection endophthalmitis. Prior to all injections, a technician applied 5% povidone-iodine (PI) to the eyelids and conjunctiva. There were four distinct aseptic protocols with regards to re-application of PI by physicians: physicians who did not re-apply PI, re-application of PI without the use of a lid speculum, re-application of PI prior to speculum placement and re-application of PI after speculum placement. Other analyzed variables included the use of gloves, a caliper to mark the injection site and the class of medication (steroid vs anti-VEGF).

RESULTS Thirty-three cases of presumed infectious endophthalmitis occurred after 37,646 injections (0.088%) performed by 27 physicians. The choice of aseptic protocol was found to be a statistically significant predictor of the incidence of endophthalmitis ($p=0.031$). When compared to the incidence of endophthalmitis for physicians who did not re-apply PI (0.124%, 20/16155), there was no statistical difference for re-application of PI without the use of a speculum (0.110%, 6/5472, $p=0.584$) or re-application prior to speculum insertion (0.122%, 5/4067, $p=0.863$). However, re-application of PI after insertion of the lid speculum was associated with a significantly decreased incidence of endophthalmitis (0.017%, 2/11952, $p=0.004$, Odds Ratio 0.113). Use of gloves ($p=0.119$), a caliper to mark the injection site ($p=0.496$) and the class of medication (0.740) were not found to be statistically significant risk factors for development of endophthalmitis.

CONCLUSION The application of povidone-iodine after placement of the lid speculum reduced the incidence of post-injection endophthalmitis approximately 7-fold compared to other aseptic protocols. Whether using a lid speculum or manual lid retraction, the eyelid should not be allowed to contact the injection site after the final application of povidone-iodine.

TAKE HOME MESSAGE To minimize the risk of post-injection endophthalmitis, the eyelids should not be allowed to contact the injection site following the final application of povidone-iodine.

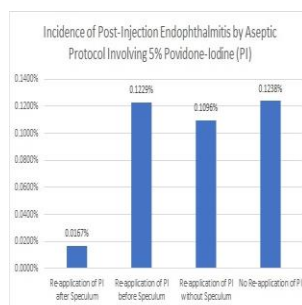


Table 1. Results of a Multivariate Logistical Regression Analysis of Potential Risk Factors for Post-Injection Endophthalmitis

Risk Factor	Number of injections (% of total)	Endophthalmitis (% of group)	P-value
Method of Re-application of Povidone-iodine by MD			
1) No Re-application	16,155 (42.9%)	20 (0.124%)	0.031*
2) Re-application without use of a speculum	5,472 (14.5%)	6 (0.110%)	
3) Re-application prior to speculum	4,067 (10.9%)	5 (0.123%)	0.863†
4) Re-application after speculum	11,952 (31.7%)	2 (0.017%)	0.004**
Use of Gloves			
1) No	25,798 (68.4%)	34 (0.093%)	0.119
2) Yes	11,910 (31.5%)	9 (0.076%)	
Use of Caliper			
1) No	24,588 (65.3%)	23 (0.094%)	0.496
2) Yes	13,060 (34.7%)	10 (0.077%)	
Drug Class			
1) Anti-VEGF	26,112 (69.4%)	21 (0.080%)	0.740
2) Steroid	1,534 (4.1%)	2 (0.130%)	

* $p < 0.05$

† Test for difference between group and injections without re-application of betadine by MD

HUMAN RESEARCH This study involves human research.

IRB Approval Status: Approved by institutional review board

9:20 AM

Clinical Course and One Year Outcome on Wide-Field Fluorescein Angiography Abnormalities in Susac's Syndrome

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- Sunil Srivastava, MD

OBJECTIVE Retrospectively review the one year outcomes on wide field fluorescein angiography abnormalities in Susac's Syndrome and how they respond to treatment.

PURPOSE Susac's syndrome is a rare condition characterized by the triad of encephalopathy, recurrent branch retinal artery occlusions (BRAO) and vestibuloauditory symptoms. We have previously shown novel changes in the wide field angiographic features in active Susac's syndrome. We will review our current understanding of these features and outline how these features respond to treatment.

METHODS This is a retrospective, observational, consecutive case series of patients at the Cleveland Clinic, Cole Eye Institute between September 2012 and January 2017. We evaluated the WFA at presentation, and after initiating systemic therapy. WFA studies were reviewed after 6 months and 1 year of treatment. We correlated these findings with disease activity as defined by MRI interpretation and clinical symptoms. We also reviewed the systemic treatment regimen and the number of flare ups seen during treatment.

RESULTS A total of 31 patients (25 female, 5 male) were included in this study and all had complete symptoms of Susac's syndrome. The average age at first presentation was 36.7 (range 21-76) and the average age of onset of symptoms of 33.6 (range 18-58). At presentation WFA displayed active vasculopathy in 25 out of 31 patients. Six different

types of features were identified on WFA: vascular wall hyperfluorescence, peripheral non-perfusion, peripheral capillary changes, peripheral active leakage, BRAO, diffuse background leakage. Systemic treatment was initiated with either IV methylprednisolone or oral prednisone in all patients. 26/31 patients started with IVIG, 25/31 patients started with mycophenolate mofetil, 11/31 patients started with rituximab and 5/31 patients were treated with cyclophosphamide. All patients with active vasculopathy responded to treatment with recurrence of retinal vascular disease in 4 patients and neurologic recurrence in 8 patients requiring a change in treatment.

CONCLUSION Though the exact pathogenesis of this disorder is unknown, it is thought to be a small vessel vasculopathy leading to micro infarction of cerebral, retinal and cochlear tissue. This study helps establish novel angiographic features of the disease within the retina. Over 1 year systemic immune suppression controls the retinal disease well. Further studies detailing the clinical course are underway.

TAKE HOME MESSAGE Susac's syndrome can present with a variety of findings on fluorescein angiogram. Early aggressive treatment is successful at treating the ocular, neurologic and vestibulochochlear symptoms.

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