Uveitis refers to a heterogeneous group of intraocular inflammatory diseases that can lead to visual impairment and blindness if left untreated.1–3 Uveitis is classified based on the anatomic location (anterior, intermediate, posterior, or panuveitis) or etiology of inflammation (e.g., infectious or noninfectious).2,4 Noninfectious uveitis is often associated with systemic disease, such as sarcoidosis, Behçet’s disease, or ankylosing spondylitis.2,3,5 Idiopathic (undifferentiated) uveitis, which has no identifiable specific autoimmune or inflammatory association, represents approximately 30% of noninfectious uveitis cases.1,6–8

Treatment of noninfectious immune-mediated uveitis may vary based on the anatomic location and severity of inflammation and includes corticosteroids, immunosuppressive agents, and biologics, such as tumor necrosis factor (TNF) inhibitors.2 The TNF inhibitor adalimumab (AbbVie Inc., North Chicago, IL) lowers the risk of treatment failure and visual acuity loss in patients with active or inactive disease, as reported in the VISUAL randomized controlled trials.9–11

The response of noninfectious uveitis to therapy may vary by etiology.7,12,13 To date, no prospective analysis has been conducted to determine the efficacy of adalimumab among patients with noninfectious uveitis of different etiologies. The objective of this post hoc analysis of the VISUAL I and VISUAL II trials was to assess the efficacy of adalimumab in patients with active or inactive (corticosteroid-dependent), noninfectious uveitis across different etiologies.
certain immunosuppressants concomitantly; 31% of patients received treatment with either azathioprine, cyclosporine, methotrexate, or mycophenolate mofetil.

**VISUAL II** enrolled adult patients ≥ 18 years old with inactive noninfectious intermediate, posterior, or panuveitis who were dependent on oral prednisone 10 to 35 mg/day for ≥ 28 days before baseline visit to maintain inactivity. Key exclusion criteria were receipt of ≥ 1 immunosuppressive drug (not including corticosteroids) within 28 days of the baseline visit, isolated anterior or infectious uveitis, and corneal or lens opacity that would preclude visualization of the fundus or that would likely require cataract surgery during the trial. Patients were randomized 1:1 to subcutaneous adalimumab 80 mg followed by 40 mg EOW or matching placebo. Prednisone was tapered for all patients starting from week 2 and reached 0 mg by week 19 at the latest, depending on their dose at baseline. Patients could receive stable doses of one immunosuppressant; at baseline, 48% of the placebo group and 47% of the adalimumab group were receiving concomitant immunomodulators.

The study complied with the ethical principles of the Declaration of Helsinki. Institutional review board or independent ethics committee approval was obtained for each trial, and all patients signed a statement of informed consent before enrollment.

**Efficacy and Safety Analyses**

For this post hoc analysis, patients were categorized into different uveitis etiologies, which they presented at study entry, as predefined in the VISUAL studies. Patients with idiopathic uveitis diagnoses were further stratified by location of uveitis at study entry (intermediate, posterior, or panuveitis). Efficacy was assessed by time to treatment failure, defined as the time from randomization to occurrence of one or more of the following four criteria affecting at least one eye: (1) new, active, inflammatory chorioretinal or vascular lesions; (2) inability to achieve ≤ 0.5+ anterior chamber (AC) cell grade at week 6 or a 2-step increase in AC cell grade relative to best state achieved after week 6 (VISUAL I), or a 2-step increase in AC cell grade relative to baseline at or after week 2 (VISUAL II); (3) inability to achieve ≤ 0.5+ vitreous haze (VH) grade at week 6 or a 2-step increase relative to best state achieved after week 6 (VISUAL I), or a 2-step increase in VH grade relative to baseline at or after week 2 (VISUAL II); and (4) worsening of best corrected visual acuity by ≥ 15 letters relative to best state achieved at any other visit (VISUAL I) or relative to baseline at or after week 2 (VISUAL II; Table 1). Time to treatment failure was analyzed using time to event analysis, in which the probability of an event was calculated over time. The hazard ratio was calculated to compare the risk of an event between treatment groups. Safety was monitored by frequency and severity of adverse events (AEs) and reported for patients who received at least 1 dose of study drug.

**Statistical Analyses**

Baseline characteristics were compared between treatment groups using chi-square test for categorical data and t test for quantitative data. Efficacy analyses were performed using the intent-to-treat (ITT) data set, excluding patients from non-compliant sites. Patients without treatment failure through week 80 and those prematurely discontinuing without treatment failure were counted as censored observations. A subgroup analysis was done by etiology and among patients with idiopathic uveitis stratified by location of uveitis at study entry (intermediate, posterior, or panuveitis). Time to treatment failure was analyzed using the Kaplan–Meier method and a log-rank test at a 2-sided significance level of 5%, if in a subgroup at least 20 patients per treatment group were available. Hazard ratios (HR) for time to treatment failure with 95% CI were calculated with Cox proportional hazards regression with treatment as factor. Safety was assessed in all patients who received ≥ 1 dose of study drug. All statistical tests were exploratory in nature.

**Results**

A total of 217 patients from VISUAL I (adalimumab, n = 110, 54% female, mean age 42.7 y; placebo, n = 107, 61% female, 42.6 y) and 226 patients from VISUAL II (adalimumab, n = 115, 57% female, 42.9 y; placebo, n = 107, 61% female, 42.2 y) were included in the ITT set in this analysis; 6 patients (VISUAL I) and 3 patients (VISUAL II) were excluded from the ITT set because of compliance issues at the study sites.

| Table 1. Criteria for treatment failurea for VISUAL I and VISUAL II clinical trials. |
|----------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **VISUAL I**                     | **VISUAL II**                   |
| Week 6 visit                     | At or after week 2 visit        |
| New, active, inflammatory lesions relative to baseline | New, active, inflammatory lesions relative to baseline |
| Anterior chamber cell gradeb     | -2-step increase relative to best state achievedd |
| Vitreous haze gradec             | -2-step increase relative to best state achievedd |
| Visual acuityd                   | Worsening of BCVA by ≥15 letters relative to best state achieved |

BCVA = best corrected visual acuity.

aTreatment failure defined as ≥ 1 of the 4 criteria in ≥ 1 eye.
bStandardization of Uveitis Nomenclature criteria.
cNational Eye Institute/Standardization of Uveitis Nomenclature criteria.
dEarly Treatment Diabetic Retinopathy Study.

A 2-step increase was represented by a change of grade 0 to grade 2+; or grade 0.5+ to grade 3+. 
Baseline characteristics were broadly similar between adalimumab and placebo groups in both studies (Table 2). By etiology, the largest subgroup comprised patients with undifferentiated or idiopathic uveitis (including pars planitis) in both studies (Table 2). As the subgroup of patients with pars planitis was small (VISUAL I, n = 7; VISUAL II, n = 5), these data were pooled with the idiopathic uveitis group. The second largest subgroups were birdshot chorioretinopathy (BCR) in VISUAL I and Vogt-Koyanagi-Harada syndrome in VISUAL II. Slight differences in etiology were observed between treatment groups; a greater proportion of patients in the placebo group had intermediate uveitis, whereas Behçet’s disease was more common in the adalimumab group in both VISUAL I and VISUAL II. Additionally, in VISUAL II, a greater proportion of patients in the placebo group had intermediate uveitis, whereas panuveitis was more common in the adalimumab group; none of these differences were statistically significant (Table 2).

**Time to Treatment Failure**

The risk of treatment failure was significantly lower in the adalimumab group compared with the placebo group in the idiopathic uveitis subgroup in both trials (VISUAL I: HR, 0.50 [95% CI, 0.30–0.84]; P = .006; VISUAL II: HR, 0.43 [95% CI, 0.22–0.83]; P = .010). All other subgroups showed a trend in favor of adalimumab, except for the sarcoidosis subgroup in the VISUAL II trial (Figure 1a,b).

After categorizing the patients with idiopathic uveitis by anatomic location, a risk of treatment failure trend favoring adalimumab was observed in patients with intermediate, posterior, or panuveitis (Figure 2a,b). Treatment failure occurred earlier for patients with idiopathic uveitis receiving placebo than for those receiving adalimumab in both VISUAL I and II.

**Safety**

The rates of overall and serious AEs were comparable in the adalimumab and placebo groups in VISUAL II (Table 3). The rates of overall and serious AEs were higher in the adalimumab group than the placebo group in VISUAL I. Analysis of AEs by etiology subgroups is not presented here because of the low number of events in most categories.

**Discussion**

One of the challenges in conducting randomized clinical trials in uveitis stems from the necessity to pool patients with different inherent underlying etiologies in order to recruit numbers of patients sufficient to attain adequate overall power. There is a paucity of prospective, randomized, controlled clinical trials that inform us on the efficacy of therapeutic agents regarding specific uveitis etiologies.

TNF inhibitors have been reported in case series to successfully control uveitis secondary to Behçet’s disease, BCR, sarcoidosis, juvenile idiopathic arthritis (JIA), ankylosing spondylitis, and Crohn’s disease. However, less is known about whether treatment success is affected by the underlying cause of uveitis. In a previous prospective study of 31 patients with refractory noninfectious uveitis, 68% demonstrated clinical response to adalimumab after 10 weeks of treatment, with 39% maintaining response through 1 year. Although no significant differences in treatment response based on anatomic location of uveitis were observed, the patient groups were not large enough to

**Table 2. Demographics and baseline characteristics of patients (intent-to-treat population).**

|                          | VISUAL I (n = 110) | Placebo (n = 107) | P value | VISUAL II (n = 115) | Placebo (n = 111) | P value |
|-------------------------|-------------------|-------------------|---------|-------------------|-------------------|---------|
| Female, n (%)           | 59 (54)           | 65 (61)           | 0.29c   | 66 (57)           | 72 (65)           | 0.25b   |
| White, n (%)            | 88 (80)           | 86 (80)           | 0.95c   | 96 (83)           | 93 (84)           | 0.95b   |
| Age, y, mean ± SD       | 42.7 ± 15.6       | 42.6 ± 14.2       | 0.97    | 42.9 ± 12.9       | 42.2 ± 14.0       | 0.72c   |
| Duration of uveitis, mo, mean ± SD | 40.2 ± 51.2 | 51.0 ± 72.2 | 0.22   | 59.5 ± 64.5       | 62.9 ± 67.7       | 0.70c   |
| Duration of treatment, d, median (IQR) | 133 (63–315) | 91 (62–155) | 0.96c  | 245 (119–564)     | 155 (77–357)     | 0.12d   |
| Type of uveitis, n (%)  |                   |                   |         |                   |                   |         |
| Intermediate            | 24 (22)           | 23 (21)           |         | 17 (15)           | 30 (27)           |         |
| Posterior               | 36 (33)           | 37 (35)           |         | 39 (34)           | 34 (31)           |         |
| Panuveitis              | 50 (45)           | 47 (44)           |         | 57 (50)           | 46 (41)           |         |
| Intermediate/posterior  | 0                 | 0                 |         | 2 (2)             | 1 (1)             |         |
| Diagnosis, n (%)        |                   |                   |         |                   |                   |         |
| Idiopathic (including pars planitis) | 42 (38) | 50 (47) |         | 31 (27)           | 43 (39)           |         |
| Birdshot chorioretinopathy | 24 (22)   | 20 (19)           |         | 15 (13)           | 15 (14)           |         |
| Multifocal choroiditis and panuveitis | 8 (7)    | 3 (3)             |         | 5 (4)             | 2 (2)             |         |
| Vogt-Koyanagi-Harada disease | 11 (10) | 14 (13)          |         | 26 (23)           | 25 (23)           |         |
| Sarcoidosis             | 10 (9)            | 8 (7)             |         | 18 (16)           | 14 (13)           |         |
| Behçet’s disease        | 12 (11)           | 4 (4)             |         | 10 (9)            | 6 (5)             |         |
| Other*                  | 3 (3)             | 8 (7)             |         | 10 (9)            | 6 (5)             |         |
| Concomitant immunomodulators, n (%) |             |                   |         |                   |                   |         |
| Azathioprine            | 4 (4)             | 4 (4)             |         | 3 (3)             | 11 (10)           |         |
| Cyclosporine            | 10 (9)            | 3 (3)             |         | 15 (13)           | 11 (10)           |         |
| Methotrexate            | 9 (8)             | 12 (11)           |         | 19 (17)           | 14 (13)           |         |
| Mycophenolate mofetil or equivalent | 11 (10) | 14 (13)         |         | 17 (15)           | 17 (15)           |         |

*Any diagnosis of uveitis other than those listed.

bP value was calculated using the chi-square test.

cP value was calculated using the two-sample t test.

IQR = interquartile range; six patients (VISUAL I) and three patients (VISUAL II) were excluded from the intent-to-treat set for compliance issues at the study sites.
evaluate differences based on etiology. A retrospective study of 88 patients with refractory uveitis receiving infliximab demonstrated that patients with BCR or JIA had a higher rate of remission compared with patients without BCR or JIA; patients without idiopathic uveitis had a higher rate of remission compared with patients with idiopathic uveitis. Another small study of infliximab across various etiologies showed that Behçet’s disease was one of the disease entities associated with complete remission in patients receiving TNF inhibitor therapy based on logistic regression analyses. An expert panel of the American Uveitis Society reviewed the available data and recommended TNF inhibitors as primary treatment for patients with Behçet’s disease in 2014.

Although the present studies had a small number of patients with Behçet’s disease, the results may provide further support for the efficacy of TNF inhibitors in patients with Behçet’s, as a small trend toward a lower risk of treatment failure was observed in VISUAL I, and no treatment failures were reported in the subgroup of patients with Behçet’s disease who received adalimumab in VISUAL II. To our knowledge, this is the largest analysis to date to assess TNF inhibitor efficacy across different uveitis etiologies. Overall, the study showed significantly lower risk of treatment failure with adalimumab compared with placebo in patients with idiopathic uveitis (including pars planitis) irrespective of anatomic location of inflammation. Furthermore, all other patient groups showed a numeric trend favoring adalimumab, except the subgroup of patients with sarcoidosis in the

Figure 1. Risk of treatment failure by uveitis etiologies. (a) VISUAL I and (b) VISUAL II; in VISUAL II, HR for Behçet’s uveitis (n = 16) was not estimable because there were 0 events in the adalimumab group. "Idiopathic VISUAL I: P = .006; VISUAL II: P = .010; Birdshot choroidopathy VISUAL I: P = .089; Vogt–Koyanagi–Harada syndrome VISUAL II: P = .279; overall VISUAL I: P < .001, VISUAL II: P = .004; subgroups with n < 20 per treatment group were not compared with log-rank test. HR = hazard ratio.

| Etiology                                      | Overall Population (n=217) |
|-----------------------------------------------|----------------------------|
| Idiopathic (including pars planitis) (n=92)   | 0.50 (0.30–0.84)           |
| Birdshot choroidopathy (n=44)                 | 0.49 (0.21–1.14)           |
| Sarcoidosis (n=18)                            | 0.47 (0.13–1.67)           |
| Multifocal choroiditis & panuveitis (n=11)    | 0.60 (0.11–3.35)           |
| Vogt-Koyanagi-Harada syndrome (n=25)          | 0.72 (0.30–3.35)           |
| Behçet’s (n=16)                               | 0.68 (0.12–3.71)           |
| Other (n=11)                                  | 0.73 (0.15–3.63)           |
| **Multifocal choroiditis & panuveitis (n=7)** | **0.57 (0.39–0.84)**       |
| Vogt-Koyanagi-Harada syndrome (n=51)          | 0.67 (0.33–1.38)           |
| Overall Population (n=226)                    | 0.57 (0.39–0.84)           |

| HR (95% CI) | Favors Treatment | Favors Placebo |
|-------------|------------------|----------------|
| 0.01        | 0.1              | 0.1            |
| 0.1         | 1                | 1              |
| 1           | 10               | 100            |
| 10          | 100              | 1000           |
| 100         | 1000             | 10000          |
| 1000        | 10000            | 100000         |
| 10000       | 100000           | 1000000        |
| 100000      | 1000000          | 10000000       |
| 1000000     | 10000000         | 100000000      |
| 10000000    | 100000000        | 1000000000     |
| 100000000   | 1000000000       | 10000000000    |
| 1000000000  | 10000000000      | 100000000000   |
| 10000000000 | 100000000000     | 1000000000000  |

**Figure 1.** Risk of treatment failure by uveitis etiologies. (a) VISUAL I and (b) VISUAL II; in VISUAL II, HR for Behçet’s uveitis (n = 16) was not estimable because there were 0 events in the adalimumab group. "Idiopathic VISUAL I: P = .006; VISUAL II: P = .010; Birdshot choroidopathy VISUAL I: P = .089; Vogt–Koyanagi–Harada syndrome VISUAL II: P = .279; overall VISUAL I: P < .001, VISUAL II: P = .004; subgroups with n < 20 per treatment group were not compared with log-rank test. HR = hazard ratio.
VISUAL II trial. Other prospective randomized trials have looked specifically at the efficacy of TNF inhibitor therapy in sarcoidosis affecting the lungs or other organs. Nonrandomized trials have also reported positive effects of adalimumab or TNF inhibitors in uveitis secondary to sarcoidosis, including improvement of the intraocular inflammatory signs such as vasculitis, macular edema, papillitis, choroidal involvement, or corpus vitreous cells in 85% of patients. In this setting, the finding of a trend against the efficacy of adalimumab in sarcoidosis-related uveitis in only 1 of the 2 VISUAL trials is most likely due to the relatively low patient numbers with this diagnosis. Although a numeric trend in favor of adalimumab efficacy was observed in the other patient groups, the number of patients in each subgroup was small. Further inference may be gleaned from the VISUAL III trial, which addressed long-term efficacy and safety of adalimumab in patients with non-infectious uveitis, and reported a positive effect of long-term adalimumab treatment on quiescence across etiologies, including the 14% of patients with sarcoidosis. For patients who entered with active uveitis, there was an increase in the proportion of quiescence at week 78 compared with baseline (60% vs 7%); for those who entered with inactive uveitis, the proportion of quiescence at week 78 was 74%.

Therapy with TNF inhibitors may increase the risk of infections. In VISUAL I and VISUAL II, the rate of serious infections with adalimumab treatment was low (3.2–8.0 per 100 patient-years) and consistent with the overall safety profile of adalimumab. Neurologic AEs including demyelination have been reported in some studies of TNF inhibitors, suggesting a causal association. In VISUAL I, one subject with intermediate idiopathic uveitis receiving adalimumab was reported to have demyelinating disease. The mechanism of action of how TNF inhibitors may be associated with demyelination has yet to be established. It has been noted that there is a higher prevalence (~1%) of multiple sclerosis (MS) in patients with uveitis than in the general population, and increased prevalence of MS has been reported within subgroups of uveitis, specifically intermediate uveitis. Therefore, patients with intermediate uveitis may need to consider neurologic screening to exclude the presence of brain lesions before beginning TNF inhibitor therapy. Further analysis of VISUAL III data stratified by diagnosis is needed to understand the long-term safety of adalimumab in specific etiologies.

Limitations of this study include the fact that the data may not reflect real-world clinical practice, as patients were required to discontinue steroids per trial design. Artificial prednisone taper in VISUAL I and VISUAL II could trigger treatment failure; in clinical practice, prednisone tapering would be performed at a slower rate. Although the studies were appropriately powered to show efficacy of the primary endpoint, the power is limited for the individual etiologies. Another limitation of this study was the small number of patients in some of the subgroups; however, small subgroups were anticipated

| Events (E/100 PY) | VISUAL I | VISUAL II |
|------------------|----------|-----------|
|                  | Adalimumab | Placebo  | Adalimumab | Placebo  |
|                  | n = 111 (62.4 PY) | n = 112 (44.3 PY) | n = 115 (94.5 PY) | n = 114 (71.0 PY) |
| Any AE           | 657 (1052) | 430 (972) | 831 (879) | 642 (905) |
| SAE              | 18 (28.8) | 6 (13.6) | 13 (13.8) | 10 (14.1) |
| AE leading to discontinuation of study drug | 13 (20.8) | 5 (11.3) | 11 (11.6) | 7 (9.9) |
| Serious infection | 5 (8) | 3 (6.8) | 3 (3.2) | 2 (2.8) |
| Malignancy       | 2 (3.2) | 0 | 1 (1.1) | 0 |
| AE leading to death | 1 (1.6) | 0 | 2 (2.1) | 0 |
| Any active TB    | 1 (1.6) | 0 | 0 | 0 |
| Any latent TB    | 1 (1.6) | 0 | 3 (3.2) | 1 (1.4) |
| Any demyelinating disease | 1 (1.6) | 0 | 0 | 0 |
| Injection site reaction | 28 (44.9) | 7 (15.8) | 36 (38.1) | 16 (22.6) |

AE = adverse event; SAE = serious adverse event; PY = patient-year; TB = tuberculosis.

VISUAL II trial. Other prospective randomized trials have looked specifically at the efficacy of TNF inhibitor therapy in sarcoidosis affecting the lungs or other organs. Monoclonal antibodies against TNF (adalimumab and infliximab) are considered effective in treating refractory sarcoidosis and at the present time are considered as third-line therapy for this disease after glucocorticoids and antimetabolites (e.g., methotrexate, azathioprine). Nonrandomized trials have also reported positive effects of adalimumab or TNF inhibitors in uveitis secondary to sarcoidosis, including improvement of the intraocular inflammatory signs such as vasculitis, macular edema, papillitis, choroidal involvement, or corpus vitreous cells in 85% of patients. In this setting, the finding of a trend against the efficacy of adalimumab in sarcoidosis-related uveitis in only 1 of the 2 VISUAL trials is most likely due to the relatively low patient numbers with this diagnosis. Although a numeric trend in favor of adalimumab efficacy was observed in the other patient groups, the number of patients in each subgroup was small. Further inference may be gleaned from the VISUAL III trial, which addressed long-term efficacy and safety of adalimumab in patients with non-infectious uveitis, and reported a positive effect of long-term adalimumab treatment on quiescence across etiologies, including the 14% of patients with sarcoidosis. For patients who entered with active uveitis, there was an increase in the proportion of quiescence at week 78 compared with baseline (60% vs 7%); for those who entered with inactive uveitis, the proportion of quiescence at week 78 was 74%.

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because all forms of uveitis are rare diseases. The strengths of the study include the representative etiology distribution and the stringent definition of the primary endpoint.

**Conclusions**

This post hoc analysis from the VISUAL I and II trials showed that patients with an idiopathic diagnosis of either active or inactive noninfectious uveitis had a lower risk of treatment failure if they received adalimumab versus placebo. Furthermore, all other subgroups showed a trend in favor of adalimumab, with the exception of sarcoidosis in VISUAL II. Patients with idiopathic uveitis who received adalimumab, regardless of anatomic location, had a lower risk of treatment failure compared with those who received placebo. If there is a differential effect of adalimumab relative to different etiologies, it was not large enough to become significant with the limited power in these studies. The study did not identify one etiology as being non-responsive to adalimumab. This suggests that there is not a large differential response among different etiologies.

**Acknowledgments**

This study was supported by AbbVie Inc. (North Chicago, IL). The sponsor contributed to study design and was involved in the collection, analysis, and interpretation of the data, and in the writing, review, and approval of the manuscript. Medical writing support was provided by Maria Hovenden, PhD, Complete Publication Solutions, LLC (North Wales, PA) and was funded by AbbVie. P. Merrill had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Disclosures of interest**

P. T. Merrill has served on the steering committee for the VISUAL studies and has served as a consultant and on advisory boards for Santen, Allergan, Alimera, and Eyepoint. A. Vitale has served as a consultant for ACIONT. M. Zierhut has served on advisory boards as a consultant for AbbVie. E. Fortin has served on advisory boards and as a consultant for AbbVie, Alcon and Allergan. H. Goto has served on advisory boards for AbbVie. M. Kron and A. P. Song are AbbVie employees and may hold AbbVie stock or options. S. Pathai was an AbbVie employee at the time of the study.

**Funding**

This work was supported by the AbbVie [N/A].

**Data sharing**

AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymized, individual, and trial-level data (analysis data sets), as well as other information (e.g., protocols and Clinical Study Reports), as long as the trials are not part of an ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications.

These clinical trial data can be requested by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). Data requests can be submitted at any time and the data will be accessible for 12 months, with possible extensions considered. For more information on the process, or to submit a request, visit the following link: https://www.abbvie.com/our-science/clinical-trials/clinical-trials-data-and-information-sharing/data-and-information-sharing-with-qualified-researchers.html.

**Meeting presentation**

This study was presented, in part, at the May 2017 Annual Meeting for the Association for Research in Vision and Ophthalmology in Baltimore, MD, and at the August 2017 Annual Meeting of the American Society of Retina Specialists in Boston, MA.

**Trial registration**

ClinicalTrials.gov numbers, NCT01138657 (VISUAL I; https://clinicaltrials.gov/ct2/show/NCT01138657), NCT01124838 (VISUAL II; https://clinicaltrials.gov/ct2/show/NCT01124838).

**References**

1. Suttorp-Schulten MS, Rothova A. The possible impact of uveitis in blindness: a literature survey. Br J Ophthalmol. 1996;80(9):844–848. doi:10.1136/bjo.80.9.844.
2. Pan J, Kapur M, McCallum R. Noninfectious immune-mediated uveitis and ocular inflammation. Curr Allergy Asthma Rep. 2013;14(1):1–8. doi:10.1007/s11882-013-0409-1.
3. Tomkins-Netzer O, Talat L, Bar A, et al. Long-term clinical outcome and causes of vision loss in patients with uveitis. Ophthalmology. 2014;121(12):2387–2392. doi:10.1016/j.ophtha.2014.07.007.
4. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of Uveitis Nomenclature Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop. Am J Ophthalmol. 2005;140:509–516. doi:10.1016/j.ajo.2005.03.057.
5. Barry RJ, Nguyen QD, Lee RW, Murray PI, Denniston AK. Pharmacotherapy for uveitis: current management and emerging therapy. Clin Ophthalmol. 2014;8:1891–1911. doi:10.2147/OPTH.S7778.
6. Wakefield D, Chang JH. Epidemiology of uveitis. Int Ophthalmol Clin. 2005;45(2):1–13. doi:10.1097/01.IOC.0000155938.83083.94.
7. Jabs DA. Immunosuppression for the uveitides. Ophthalmology. 2018;125(2):193–202. doi:10.1016/j.ophtha.2017.08.007.
8. Rodriguez A, Calonge M, Pedroza-Seres M, et al. Referral patterns of uveitis in a tertiary eye care center. Arch Ophthalmol. 1996;114(5):593–599. doi:10.1001/archophthalmol.1996.01100130585016.
9. Jaffe GI, Dick AD, Brezin AP, et al. Adalimumab in patients with active noninfectious uveitis. N Engl J Med. 2016;375(10):932–943. doi:10.1056/NEJMoa1509852.
10. Nguyen QD, Merrill PT, Jaffe GI, et al. Adalimumab for prevention of uveitic flare in patients with inactive non-infectious uveitis controlled by corticosteroids (VISUAL II): a multicentre, double-masked, randomised, placebo-controlled phase 3 trial. Lancet. 2016;388(10050):1183–1192. doi:10.1016/S0140-6736(16)31339-3.
11. HUMIRA® (adalimumab). Full Prescribing Information. North Chicago, IL, USA: AbbVie Inc.; 2016.
12. Kruh JN, Yang P, Suelves AM, Foster CS. Infliximab for the treatment of refractory noninfectious uveitis: a study of 88 patients with long-term follow-up. Ophthalmology. 2014;121(1):358–364. doi:10.1016/j.ophtha.2013.07.019.
13. Vallet H, Sepe P, Biard L, et al. Infliximab versus adalimumab in the treatment of refractory inflammatory uveitis: a multicenter study from the French Uveitis Network. Arthritis Rheumatol. 2016;68(6):1522–1530. doi:10.1002/art.39667.
14. Tynjala P, Kotaniemi K, Lindahl P, et al. Adalimumab in juvenile idiopathic arthritis-associated chronic anterior uveitis. Rheumatology (Oxford). 2008;47(3):339–344. doi:10.1093/rheumatology/kem356.
15. Niccoli L, Nannini C, Benucci M, et al. Long-term efficacy of infliximab in refractory posterior uveitis of Behcet’s disease: a 24-
16. Rudwaleit M, Rodevant E, Holck P, et al. Adalimumab effectively reduces the rate of anterior uveitis flares in patients with active ankylosing spondylitis: results of a prospective open-label study. *Ann Rheum Dis.* 2009;68(5):696–701. doi:10.1136/ard.2008.092585.

17. Artoonsombudh P, Gevorgyan O, Payal A, Siddique SS, Foster CS. Infliximab treatment of patients with birdshot retinochoroidopathy. *Ophthalmology.* 2013;120(3):588–592. doi:10.1016/j.ophtha.2012.05.048.

18. Baughman RP, Bradley DA, Lower EE. Infliximab in chronic ocular inflammation. *Int J Clin Pharmacol Ther.* 2005;43(1):7–11. doi:10.5414/CPP43007.

19. Suhler EB, Lowder CY, Goldstein DA, et al. Adalimumab therapy for refractory uveitis: results of a multicentre, open-label, prospective trial. *Br J Ophthalmol.* 2013;97(4):481–486. doi:10.1136/bjophthalmol-2012-302292.

20. Levy-Clarke G, Jabs DA, Read RW, Rosenbaum JT, Vitale A, Van Gelder RN. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. *Ophthalmology.* 2014;121(3):785–796 e783. doi:10.1016/j.ophtha.2013.09.048.

21. Riancho-Zarrabeitia L, Calvo-Rio V, Blanco R, et al. Anti-TNF-alpha therapy in refractory uveitis associated with sarcoidosis: multicenter study of 17 patients. *Semin Arthritis Rheum.* 2015;45(3):361–368. doi:10.1016/j.semarthritis.2015.05.010.

22. Brito-Zeron P, Perez-Alvarez R, Pallares L, et al. Sarcoidosis: an update on current pharmacotherapy options and future directions. *Expert Opin Pharmacother.* 2016;17(18):2431–2448. doi:10.1080/14656566.2016.1258061.