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Infliximab for refractory non-infectious uveitis: 10-year safety and steroid-sparing outcomes from an ophthalmology-led service

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Tables 1 and 2 are available in the Supplementary Files section.

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What was known before

- Adalimumab is the only UK licensed biologic for non-infectious uveitis. When adalimumab fails, alternatives are unlicensed and access to funding is inconsistent.
- Infliximab is an established treatment with a well-characterised safety profile, used by rheumatology, gastroenterology and dermatology. In ophthalmology it is used off-label in refractory uveitis, but is usually delivered by other specialties; there is little guidance on how ophthalmologists should recognise and manage its complications.

What this study adds

- Most patients in this 10-year cohort had already failed adalimumab. On infliximab, most reduced prednisolone to ≤5 mg/day without increasing other immunosuppression.
- Adverse events were common but usually manageable. Serious adverse events occurred in 2/44 (5%) and adverse events led to discontinuation in 8/44 (18%). We give case-based guidance for several potential adverse events (Boxes 1 to 4).
- An ophthalmology-led infusion service is feasible with rapid access to other specialties and resuscitation support.

Abstract

Background:

To describe the real-world safety, steroid-sparing effect, treatment duration, infusion interval, and operational features of a medical ophthalmology-led biologic service managing non-infectious uveitis(NIU) patients with infliximab(IFX).

Methods:

Retrospective cohort review of patients receiving IFX for NIU at a tertiary NHS centre from March 2016 to March 2026. Primary outcomes were adverse events(AEs), serious adverse events(SAEs) and discontinuations; secondary outcomes were oral corticosteroid requirement and visual acuity.

Results:

44 patients contributed 1208 months of IFX exposure (100.7 patient-years), with a median of 21.5 months(IQR 9.5–32.0). 37/44 (84%) had previously received adalimumab. AEs were reported by 20/44 (45%), including

infections in 10/44 (23%) and rash in 9/44 (20%). SAEs occurred in 2/44 (5%): incident heart failure and anaphylaxis, each in 1/44 (2%). AEs led to discontinuation in 8/44 (18%). By 12 months, 10/44 (23%) had stopped IFX, most commonly due to ineffectiveness. Worse eye visual acuity changed by <15 ETDRS letters from baseline in 29/33 (88%), improved by ≥15 letters in 3/33 (9%), and worsened by ≥15 in 1/33 (3%). Among those using prednisolone at baseline, the median daily dose fell from 15 mg to 5.5 mg by month 12; at latest review (median 27 months) the median was 4.0 mg/day, with 18/21 (86%) taking ≤5 mg/day and 5/21 (24%) steroid-free.

Conclusions:

IFX was generally well tolerated and was associated with lower corticosteroid requirements in NIU. A medical ophthalmology-led biologic infusion service is feasible and safe but close collaboration with other medical specialties is critical for safe governance and delivery.

Introduction

The precisely organised tissues supporting phototransduction in the eye can be rapidly and irreversibly disrupted by inflammation. Non-infectious uveitis (NIU) is a major cause of visual morbidity and impaired quality of life, and timely treatment is particularly important for long-term vision outcomes(2). Where corticosteroids and steroid-sparing immunosuppressive therapies fail to achieve disease control and quiescence in sight-threatening disease, systemic biologics are considered. Internationally, subcutaneous adalimumab is the only licensed biologic therapy for NIU in adults (3), with efficacy and safety having been established by the VISUAL 1 and 2 trials (4,5). When adalimumab is ineffective, poorly tolerated, or when anti-drug antibodies develop, clinicians require an alternative escalation biologic or small molecule therapy.

Infliximab (IFX), a chimeric monoclonal antibody targeting TNF-alpha, has emerging evidence base supporting its use for refractory NIU. This evidence base is informed by trials in Behçet's disease (6–10), and numerous case series in NIU (11–16). However, these ophthalmology series offered limited information on service delivery models, including which specialty delivered treatment or how the adverse events were assessed and managed. IFX has recently been removed from the National Health Service 'high cost drugs' list in the United Kingdom, potentially increasing access but raising questions about how services can be delivered and demand met.

In the UK, a small number of NHS-commissioned pathways provide funding for select indications, including treatment-refractory sarcoidosis and Behçet's disease (17,18). Access for off-label, uncommissioned indications depends upon local exceptional funding arrangements, with a 'postcode lottery' potentially driving inequity. Many ophthalmic units rely on non-ophthalmic infusion services (e.g. rheumatology) to prescribe and monitor treatment, where service pressures and waiting times may delay or fragment clinical care. We report a decade's experience delivering IFX infusions as a medical ophthalmology-led service, highlighting safe use and our practical delivery arrangement. We present real-world cases alongside practical guidance on managing IFX-related adverse events.

Methods

Study setting

Guy's and St Thomas' Hospital NHS Foundation Trust is a tertiary referral centre in central London which supports patients across South England, including those under Moorfields Eye Hospital who require biologic infusions. An on-site infusion unit, shared by medical and neuro-ophthalmology and neurology, provides access to therapies including IFX, rituximab, tocilizumab, and abatacept. The unit is supported by a general emergency department and medical emergency 'crash' team.

Study population, design and analysis

This retrospective cohort analysis included all consecutive patients newly prescribed IFX for NIU between March 2016 and March 2026. Patients were identified from pharmacy records of infusions prescribed under medical ophthalmology. We extracted baseline patient and treatment characteristics from the electronic medical record. The primary outcomes were adverse events, serious adverse events, and IFX discontinuation, with reasons. Adverse events were untoward clinical events that had a reasonable probability of causal relationship, as determined by retrospective review. Adverse events were categorised as serious if they fulfilled ICH E2A criteria i.e. resulting in death; life-threatening; requiring hospitalisation or prolonging an existing admission; causing persistent disability, leading to a congenital anomaly or requiring urgent intervention to prevent a serious outcome (19). Discontinuations were classified according to the primary reason, as either due an adverse event, ineffectiveness or elective withdrawal following sustained disease quiescence. Temporary treatment holds which were then followed by resumption of the same treatment course were not counted as discontinuations. Discontinuation followed by later reintroduction was counted as discontinuation of the original treatment course. A change in route of administration was not counted as discontinuation. Secondary outcomes were oral corticosteroid requirement and worse eye visual acuity outcomes over time, reported using the logMAR scale. Worse eye was selected at baseline and the same eye assessed during subsequent time points. We present categorical data as n/N (%), where n is the number of patients with the characteristic or outcome and N is the relevant cohort or subgroup denominator, continuous data as median (IQR), and AE incidence per 100 patient-

years. Retention on therapy is summarised using a Kaplan-Meier curve, where retention is presented to 36 months following initiation. We obtained approval from the Guy's and St Thomas' Clinical Governance Committee (Service Evaluation ID 15584).

Dosing protocols

IFX was administered by intravenous infusion, including biosimilar preparations. Induction was 5 mg/kg at week zero, followed by 5 mg/kg at weeks 2 and 6, with occasional variation at the treating clinician's discretion. Thereafter, patients were maintained on IFX 8-weekly (per NHS commissioning guidance for use in refractory sarcoidosis or Behçet's disease) or via an individualised dosing frequency, most typically 6-weekly, with interval shortening or extension informed by severity of threat to sight, disease activity status, safety and patient tolerability.

Service processes

Assessment of IFX therapy eligibility, medical history, medication and allergy history was overseen by a consultant, with review in a multidisciplinary team meeting (MDT). Approval to commence therapy followed individual Drug and Therapeutics Committee application, or discussion in a sarcoidosis multidisciplinary team meeting, or external multidisciplinary team review by a UK Behcet's Centre of Excellence, to secure commissioned funding. Pre-treatment investigations and basic clinical assessment (weight, height, blood pressure, blood sugar, chest auscultation and counselling) were overseen by a clinical nurse specialist or resident doctor. Screening investigations included full blood count, renal profile, liver function tests, C reactive protein, infection screening for viral hepatitis (B, C), human immunodeficiency virus, tuberculosis (via an interferon-gamma release assay) and chest radiograph. All patients received vaccination advice including Pneumovax and seasonal flu. Recommendation for COVID-19 vaccination was added from 2021. Testing of varicella zoster IgG and recommendation for Shingrix vaccination was added from 2025 following updated NHS Green Book guidance (20).

IFX was administered in an on-site four bed infusion suite shared with the neurology service, with approximately half the patients under the care of ophthalmology. Two nurses oversaw four infusions at a time. Pre-medication (hydrocortisone 200 mg IV and chlorphenamine 10 mg IV) was given to those who had experienced a previous infusion reaction, or who had >16 week interval between infusions. Nurses delivered

infusions with ophthalmology consultant oversight and an escalation pathway in place in the event of infusion reactions.

Blood monitoring and biologic prescribing took place at weekly MDT meetings involving specialist pharmacists, medical and neuro-ophthalmology consultants, resident doctors, a service administrator, and a clinical nurse specialist. In the event of a complication or serious adverse event, the clinical team liaised with specialists in rheumatology, dermatology, cardiology, immunology/allergy, neurology, gastroenterology, respiratory medicine and infectious diseases, as required.

Therapeutic drug monitoring was performed routinely 6–12 weeks after initiation. The timing of subsequent drug levels was variable and was performed in response to a change in clinical circumstance, such as loss of clinical control or worsening side effects. Anti-drug antibodies were tested for using a chemiluminescence immunoassay (CLIA). This test was performed sequentially by our laboratory only when a trough IFX level of <2.5 µg/mL was detected via an enzyme-linked immunosorbent assay. We did not test anti-infliximab antibody levels independently of IFX levels.

Results

Baseline characteristics

We identified and included 44 patients with NIU receiving IFX (Table 1). Birdshot chorioretinopathy was the most common diagnosis and 37/44 (84%) had previously been treated with adalimumab. A subsequent diagnosis of chronic intraocular leptospirosis was made in one patient, initially classified as idiopathic NIU following metagenomic deep sequencing on an aqueous sample.

Treatment exposure and dosing

Over the 10-year period, 1045 infusions were delivered for NIU. The median time from the decision to treat to the first infusion was 50 days (IQR 31–70). In total, the 44 patients received IFX for 1208 months (100.7 patient-years). The median IFX exposure to the cut-off date or discontinuation was 21.5 months (IQR 9.5–32.0).

Treatment duration was at least 12 months in 31/44 (70%), at least 24 months in 20/44 (45%), at least 36 months in 10/44 (23%), and at least 60 months in 5/44 (11%). After the loading period, the planned initial maintenance interval was 6 weekly in 31/44 (70%), 8-weekly in 12/44 (27%) and 4-weekly in 1/44 (2%). The maintenance interval was changed at least once in 26/44 (59%) patients: it was shortened at some point in 21/44 (48%) and extended in 21/44 (48%), with 16/44 (36%) both shortened and extended (Fig. 1).

Discontinuation

Over the whole study period, 21/44 (48%) discontinued an IFX treatment course (Fig 2.) Discontinuation was due to adverse events in 8/44 (18%) (Table 2), ineffectiveness in 9/44 (20%) (Supplementary Table 1), elective withdrawal after prolonged disease quiescence in 2/44 (5%), and other reasons in 2/44 (5%): revised diagnosis and pregnancy, each in 1/44 (2%). Among patients who stopped due to ineffectiveness, 2/9 (22%) were found to have developed anti-IFX antibodies (Box 4). Elective withdrawals occurred late, at 23 and 66 months. Within the first 12 months, 10/44 (23%) stopped IFX: 6/44 (14%) for ineffectiveness, 3/44 (7%) for adverse events and 1/44 (2%) due to pregnancy (IFX may be continued during pregnancy (1)). No patients died or were lost to follow up.

Adverse events

At least one adverse event or side-effect was documented in 20/44 (45%). This broad category included patient-reported symptoms and laboratory abnormalities and does not imply definite causal attribution to IFX. Reported infections occurred in 10/44 (23%). These were generally mild, with no cases of infection related hospitalisation. Rash or other dermatologic events occurred in 9/44 (20%), with no cases of severe cutaneous reactions such as Stevens-Johnson syndrome. Serious adverse events included anaphylaxis in 1/44 (2%) (See Box 1) and incident heart failure in 1/44 (2%) (see Box 2). No cases of active tuberculosis occurred during follow-up.

Adverse events led to infliximab interruption or discontinuation in 9/44 (20%) patients (Table 2): 8/44 (18%) discontinued treatment, while 1/44 (2%) temporarily interrupted treatment during investigation of suspected drug-induced lupus and subsequently resumed infliximab. The rate of adverse-event-related discontinuation was 7.9 per 100 patient-years. Interruptions or discontinuations were attributed to infusion reactions in 3/44 (7%), 2/44 (5%) early and 1/44 (2%) at month 42; infection and lupus-like dermatologic changes each in 2/44 (5%) (See Box

3); and cardiac and systemic AEs each in 1/44 (2%). Most patients were able to continue systemic immunomodulation after switching.

Therapeutic Drug Monitoring and Anti-drug antibodies

Where early levels (6-12 weeks post initiation) were available, IFX concentrations were generally high, with most above the upper limit of quantification (>20 µg/mL). Across the whole study period, anti-IFX antibodies were detected in 3/44 (7%) patients, all with an undetectable or near undetectable IFX concentration (<0.3 µg/mL). Because antibody testing was conditional on a low drug level (<2.5 µg/mL), we could not determine the antibody status in those with IFX concentrations above this threshold.

Steroid exposure

28/44 (64%) were taking prednisolone at IFX initiation, with a median daily dose of 15 mg/day (IQR 6.9–30.0). Among these baseline prednisolone users, the median dose fell to 5.5 mg/day (IQR 3.1–10.0) at month 12. Among baseline steroid users, 6/28 (21%) had no 12-month data because they had discontinued before month 12 or not yet reached month 12 at the time of study closure. At the point of latest review beyond 1 year (median 27.0 months, IQR 23.0–42.0), the median prednisolone dose among baseline prednisolone users was 4.0 mg/day (IQR 0.0–5.0); 18/21 (86%) were taking ≤5 mg/day and 20/21 (95%) were taking ≤10 mg/day (Fig. 3). 5/21 (24%) were steroid-free at latest evaluable follow-up; a further 4/28 (14%) baseline steroid users reached 0 mg at some point during follow-up but subsequently restarted prednisolone. Among baseline steroid users, a reduction in their dose was not accompanied by widespread intensification of other immunomodulatory therapy. In the first 12 months, 3/21 (14%) underwent intensification, with 2/21 (10%) commencing azathioprine and 1/21 (5%) increasing methotrexate dose. 6/21 (29%) patients reduced or stopped concomitant immunomodulatory therapy.

Visual acuity

Visual acuity at 12 months was available for 33/44 (75%) patients - the remainder had discontinued before month 12 or had not yet reached that point at study close. Visual acuity was stable in most patients: 29/33 (88%) changed by less than 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters of baseline, 3/33 (9%) gained ≥15 letters, and 1/33 (3%) lost ≥15 letters following choroidal neovascularisation reactivation. Median

logMAR acuity in the worse-seeing eye was 0.18 (IQR 0.10–0.80) at baseline and 0.20 (IQR 0.02–0.47) at month 12.

Discussion

To our knowledge, this represents the largest UK ophthalmology-led infliximab infusion cohort reported to date. The removal of infliximab from the NHS high-cost drugs framework may permit wider uptake across the UK, but will require infrastructure capable of delivering biologic infusions, and clinical teams comfortable managing and investigating adverse events. In this 10-year retrospective cohort of 44 NIU patients, IFX demonstrated an acceptable safety profile. Whilst adverse events were reported in 20/44 (45%), these were largely non-serious and led to discontinuation in 8/44 (18%) patients. Our data also suggest that IFX may provide a feasible option for patients who fail adalimumab. The strongest clinical signal in this cohort was steroid sparing. Among baseline prednisolone users, 18/21 (86%) had reached ≤5 mg/day by final review, 20/21 (95%) had reached ≤10 mg/day, and 5/21 (24%) were steroid-free. This wasn't accompanied by widespread escalation of concomitant oral immunomodulatory therapy, although changes in background treatment may have contributed to steroid tapering in individual patients.

Head-to-head randomised trials comparing adalimumab with IFX in non-infectious uveitis (NIU) are lacking. Observational case series are mixed, for example in their 2016 series of 160 patients, Vallet et al. reported broadly comparable efficacy and safety between the two agents (15), whereas another large study of 330 patients by Maalouf et al. found a significantly lower relapse rate with IFX compared to adalimumab (16). One practical advantage of IFX over adalimumab is the capacity for weight-based dosing and for flexible adjustment of the dosing frequency. The dosing frequency has direct implications for service capacity planning: for example, a 4-weekly schedule requires approximately six to seven additional infusion visits per year versus 8-weekly dosing. This equates to roughly 20 extra hours of hospital time with each visit taking 3 hours. There is variation in practice internationally, from 8-weekly maintenance in Japanese centres (21–23) to 4–6 weekly in the French Uveitis Network (16), while Kruh et al. describe 4-weekly dosing until remission followed by incremental extension to 10–12 weeks(12). An important consideration beyond service capacity is the burden placed upon patients with higher frequency dosing, and potential impact on quality of life, about which little is currently known.

Adverse events were recorded in 20/44 (45%) patients, higher than the 28% reported in a comparable real-world anti-TNF treated cohort (15), possibly reflecting our inclusion of minor and self-reported events. Serious events were rare however. Infection-related hospitalisation, tuberculosis and severe cutaneous reactions each occurred in 0/44 (0%) over 100.7 patient-years, compared to a pooled serious-infection rate of 2% in a meta-analysis of infliximab-treated non-infectious uveitis observational series (24). In the wider literature, anti-TNFs have been associated with an approximately twice the odds of serious infections compared to placebo (25). Cases of new-onset heart failure are a rare but recognised risk of IFX (26)(27). Whether our patient's cardiac function (Box 2) normalised due to IFX discontinuation or heart failure medication is unclear. In two patients, IFX was successfully reintroduced after the adverse event had been investigated and managed, demonstrating that adverse events should not necessarily preclude continued use, especially given limited alternatives.

This was a retrospective study without a comparator group. Retrospective assessment of adverse events from clinical notes limits certainty regarding their attribution to IFX. The cohort was also heterogeneous in terms of diagnosis, prior therapy, dosing interval and concomitant immunosuppression – as such disease-specific interpretation is not possible. The corticosteroid and visual acuity outcomes were assessed for those patients remaining on IFX and therefore describe those continuing treatment rather than the cohort as a whole. In this study retention should not necessarily be interpreted as a proxy for effectiveness, given treatment may have continued due to relative tolerability of the drug, or the limited alternatives available in refractory NIU. Likewise, preserved central acuity does not necessarily equate to inflammatory control in conditions where the peripheral retina may be disproportionately affected. Nevertheless, the visual acuity outcomes in this infliximab-treated NIU cohort were good.

Conclusion

Overall, IFX was well tolerated in this cohort of predominantly adalimumab-refractory patients. A significant number experienced a clinically meaningful steroid-sparing effect, alongside preserved visual acuity. This series also demonstrates the feasibility of an ophthalmology-led biologic infusion service operating within a large NHS Trust. By retaining prescribing and infusion delivery within the medical ophthalmology team, we offer a

model for service delivery able to respond to sight-threatening clinical presentations promptly. Nevertheless, we highlight that the range of adverse events observed during treatment – allergic, infectious, cardiac, dermatologic, and autoimmune – means that safe delivery of these drugs requires close collaboration with other medical specialties alongside robust escalation pathways.

References

1. Rothova A, Suttorp-van Schulten MS, Frits Treffers W, Kijlstra A. Causes and frequency of blindness in patients with intraocular inflammatory disease. Br J Ophthalmol. 1996 Apr;80(4):332–6. doi:10.1136/bjo.80.4.332 PubMed PMID: 8703885.
2. National Institute for Health and Care Excellence. Adalimumab and dexamethasone for treating non-infectious uveitis [NICE Technology Appraisal Guidance TA460]. 2017. Available from: https://www.nice.org.uk/guidance/ta460.
3. Jaffe GJ, Dick AD, Brézin AP, Nguyen QD, Thorne JE, Kestelyn P, et al. Adalimumab in Patients with Active Noninfectious Uveitis. N Engl J Med. 2016 Sep 8;375(10):932–43. doi:10.1056/NEJMoa1509852 PubMed PMID: 27602665.
4. Nguyen QD, Merrill PT, Jaffe GJ, Dick AD, Kurup SK, Sheppard J, 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 Sep 17;388(10050):1183–92. doi:10.1016/S0140-6736(16)31339-3 PubMed PMID: 27542302.
5. Tugal-Tutkun I, Mudun A, Urgancioglu M, Kamali S, Kasapoglu E, Inanc M, et al. Efficacy of infliximab in the treatment of uveitis that is resistant to treatment with the combination of azathioprine, cyclosporine, and corticosteroids in Behçet's disease: an open-label trial. Arthritis Rheum. 2005 Aug;52(8):2478–84. doi:10.1002/art.21231 PubMed PMID: 16052571.
6. Ohno S, Nakamura S, Hori S, Shimakawa M, Kawashima H, Mochizuki M, et al. Efficacy, safety, and pharmacokinetics of multiple administration of infliximab in Behçet's disease with refractory uveoretinitis. J Rheumatol. 2004 Jul;31(7):1362–8. PubMed PMID: 15229958.
7. Sfikakis PP, Theodossiadis PG, Katsiari CG, Kaklamanis P, Markomichelakis NN. Effect of infliximab on sight-threatening panuveitis in Behçet's disease. Lancet. 2001 Jul 28;358(9278):295–6. doi:10.1016/s0140-6736(01)05497-6 PubMed PMID: 11498218.
8. Niccoli L, Nannini C, Benucci M, Chindamo D, Cassarà E, Salvarani C, et al. Long-term efficacy of infliximab in refractory posterior uveitis of Behcet's disease: a 24-month follow-up study. Rheumatology (Oxford). 2007 Jul;46(7):1161–4. doi:10.1093/rheumatology/kem101 PubMed PMID: 17478466.
9. Calvo-Río V, Blanco R, Beltrán E, Sánchez-Bursón J, Mesquida M, Adán A, et al. Anti-TNF-α therapy in patients with refractory uveitis due to Behçet's disease: a 1-year follow-up study of 124 patients. Rheumatology (Oxford). 2014 Dec;53(12):2223–31. doi:10.1093/rheumatology/keu266 PubMed PMID: 24996907.
10. Martel JN, Esterberg E, Nagpal A, Acharya NR. Infliximab and adalimumab for uveitis. Ocul Immunol Inflamm. 2012 Feb;20(1):18–26. doi:10.3109/09273948.2011.633205 PubMed PMID: 22324897.
11. 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 Jan;121(1):358–64. doi:10.1016/j.ophtha.2013.07.019 PubMed PMID: 24011995.
12. Suhler EB, Smith JR, Giles TR, Lauer AK, Wertheim MS, Kurz DE, et al. Infliximab therapy for refractory uveitis: 2-year results of a prospective trial. Arch Ophthalmol. 2009 Jun;127(6):819–22. doi:10.1001/archophthalmol.2009.141 PubMed PMID: 19506209.

13. Suhler EB, Smith JR, Wertheim MS, Lauer AK, Kurz DE, Pickard TD, et al. A prospective trial of infliximab therapy for refractory uveitis: preliminary safety and efficacy outcomes. Arch Ophthalmol. 2005 Jul;123(7):903–12. doi:10.1001/archopht.123.7.903 PubMed PMID: 16009830.
14. Vallet H, Seve P, Biard L, Baptiste Fraison J, Bielefeld P, Perard L, et al. Infliximab Versus Adalimumab in the Treatment of Refractory Inflammatory Uveitis: A Multicenter Study From the French Uveitis Network. Arthritis Rheumatol. 2016 Jun;68(6):1522–30. doi:10.1002/art.39667 PubMed PMID: 27015607.
15. Maalouf G, Andrillon A, Leclercq M, Sève P, Bielefeld P, Gueudry J, et al. Lower Relapses Rate With Infliximab Versus Adalimumab in Sight-Threatening Uveitis: A Multicenter Study of 330 Patients. Am J Ophthalmol. 2022 Jun;238:173–80. doi:10.1016/j.ajo.2022.02.002 PubMed PMID: 35172172.
16. NHS England. Clinical Commissioning Policy: Infliximab for refractory sarcoidosis (excluding neurosarcoidosis) (adults) [2204].London: NHS England; 2023. Available from:https://www.england.nhs.uk/wp-content/uploads/2023/11/clinical-commissioning-policy-infliximab-for-refractory-sarcoidosis-excluding-neurosarcoidosis-adults.pdf.
17. Moots RJ, Fortune F, Jackson R, Thornburn T, Morgan A, Carr DF, et al. Infliximab vs interferon-α in the treatment of Behçet's syndrome: clinical data from the BIO-BEHÇET'S randomized controlled trial. Rheumatology (Oxford). 2025 May 1;64(5):2882–91. doi:10.1093/rheumatology/keae585 PubMed PMID: 39432564.
18. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (E2A). ICH Harmonised Guideline. 1994.
19. UK Health Security Agency. Shingles (herpes zoster). In: Immunisation against infectious disease (The Green Book). London: UKHSA; 2025 [updated 12 August 2025]. Available from: https://assets.publishing.service.gov.uk/media/689cba1b1c63de6de5bb12a9/Green-book-chapter-Shingles_12_8_24.pdf.
20. Russell MD, Dey M, Flint J, Davie P, Allen A, Crossley A, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: immunomodulatory anti-rheumatic drugs and corticosteroids. Rheumatology (Oxford). 2023 Apr 3;62(4):e48–88. doi:10.1093/rheumatology/keac551 PubMed PMID: 36318966.
21. Horiguchi N, Kamoi K, Horie S, Iwasaki Y, Kurozumi-Karube H, Takase H, et al. A 10-year follow-up of infliximab monotherapy for refractory uveitis in Behçet's syndrome. Sci Rep. 2020 Dec 17;10(1):22227. doi:10.1038/s41598-020-78718-z PubMed PMID: 33335139.
22. Yamada Y, Sugita S, Tanaka H, Kamoi K, Kawaguchi T, Mochizuki M. Comparison of infliximab versus ciclosporin during the initial 6-month treatment period in Behçet disease. Br J Ophthalmol. 2010 Mar;94(3):284–8. doi:10.1136/bjo.2009.158840 PubMed PMID: 19692382.
23. Ohno S, Umebayashi I, Matsukawa M, Goto T, Yano T. Safety and efficacy of infliximab in the treatment of refractory uveoretinitis in Behçet's disease: a large-scale, long-term postmarketing surveillance in Japan. Arthritis Res Ther. 2019 Jan 5;21(1):2. doi:10.1186/s13075-018-1793-7 PubMed PMID: 30611312.
24. Xiong A, Liu D, Chen H, Yang G, Xiong C, Shuai Y, et al. The Efficacy and Safety of Infliximab in Refractory Noninfectious Uveitis: A Meta-Analysis of Observational Studies. Frontiers in Pharmacology. Frontiers Media S.A.; 2021. doi:10.3389/fphar.2021.620340

25. Bongartz T, Sutton AJ, Sweeting MJ, Buchan I, Matteson EL, Montori V. Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: Systematic review and meta-analysis of rare harmful effects in randomized controlled trials. Journal of the American Medical Association. 2006. doi:10.1001/jama.295.19.2275
26. Kwon HJ, Coté TR, Cuffe MS, Kramer JM, Braun MM. Case reports of heart failure after therapy with a tumor necrosis factor antagonist. Ann Intern Med. 2003 May 20;138(10):807–11. doi:10.7326/0003-4819-138-10-200305200-00008 PubMed PMID: 12755552.
27. Page RL, O'Bryant CL, Cheng D, Dow TJ, Ky B, Stein CM, et al. Drugs That May Cause or Exacerbate Heart Failure: A Scientific Statement From the American Heart Association. Circulation. 2016 Aug 9;134(6):e32-69. doi:10.1161/CIR.0000000000000426 PubMed PMID: 27400984.
28. Vultaggio A, Matucci A, Nencini F, Pratesi S, Parronchi P, Rossi O, et al. Anti-infliximab IgE and non-IgE antibodies and induction of infusion-related severe anaphylactic reactions. Allergy. 2010 May;65(5):657–61. doi:10.1111/j.1398-9995.2009.02280.x PubMed PMID: 19951375.
29. Janssen-Cilag Ltd. Electronic Medicines Compendium (emc). 2025. Remicade 100 mg powder for concentrate for solution for infusion – Summary of Product Characteristics (SmPC).
30. Celltrion Healthcare United Kingdom Limited. Electronic Medicines Compendium (emc). 2026. Remsima 120 mg solution for injection in pre-filled pen – Summary of Product Characteristics (SmPC).
31. U.S. Food and Drug Administration. REMICADE (infliximab) prescribing information. Silver Spring, MD: FDA; 2013. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/103772s5359lbl.pdf.
32. Arnaud L, Mertz P, Gavand PE, Martin T, Chasset F, Tebacher-Alt M, et al. Drug-induced systemic lupus: revisiting the ever-changing spectrum of the disease using the WHO pharmacovigilance database. Ann Rheum Dis. 2019 Apr;78(4):504–8. doi:10.1136/annrheumdis-2018-214598 PubMed PMID: 30793701.
33. Araújo-Fernández S, Ahijón-Lana M, Isenberg DA. Drug-induced lupus: Including anti-tumour necrosis factor and interferon induced. Lupus. 2014 May;23(6):545–53. doi:10.1177/0961203314523871 PubMed PMID: 24557776.
34. Ishikawa Y, Fujii T, Ishikawa SK, Yukawa N, Hashimoto M, Furu M, et al. Immunogenicity and Lupus-Like Autoantibody Production Can Be Linked to Each Other along With Type I Interferon Production in Patients with Rheumatoid Arthritis Treated With Infliximab: A Retrospective Study of a Single Center Cohort. PLoS One. 2016;11(9):e0162896. doi:10.1371/journal.pone.0162896 PubMed PMID: 27643491.
35. He M, Yang J, Yan S, Shu Q, Liu PC. Conducting a real-world study of Tumor Necrosis factor-alpha inhibitors-induced Systemic Lupus Erythematosus based on the FAERS database. Sci Rep. 2025 Feb 26;15(1):6838. doi:10.1038/s41598-025-90566-3 PubMed PMID: 40000785.
36. Brun MK, Goll GL, Jørgensen KK, Sexton J, Gehin JE, Sandanger Ø, et al. Risk factors for anti-drug antibody formation to infliximab: Secondary analyses of a randomised controlled trial. J Intern Med. 2022 Sep;292(3):477–91. doi:10.1111/joim.13495 PubMed PMID: 35411981.

Box 1. Anaphylaxis

A woman with birdshot chorioretinopathy on IFX developed chest tightness and hypotension at her 4th infusion. She had previously discontinued adalimumab after developing allergic symptoms alongside anti-adalimumab antibodies.

Management
Stop infusion and treat per anaphylaxis protocol. Send tryptase level during episode and at 1–2 hours post reaction. Refer to Allergy/Immunology. Formal skin testing for excipients and intravenous allergen challenge may be considered in specialist centres.

Risk factors
Anti-drug antibodies (ADAs) increase the risk of hypersensitivity reactions and their appearance may precede clinical events. Factors such as intermittent dosing and absence of concomitant immunosuppressive therapy have been associated with higher risk of developing ADAs (28).

Outcome
In this case allergy testing confirmed a severe polysorbate 80 excipient allergy. Polysorbate 80 is found in all IV and SC infliximab formulations.(29,30)

Can IFX be restarted?
Further IFX is contraindicated if proven anaphylaxis or IgE-mediated reaction. In the event of an excipient reaction, a switch to an alternative biologic without that excipient may be considered. Abatacept was chosen as it does not contain Polysorbate 80.

Box 2. Heart failure

A young woman with panuveitis and diffuse anterior scleritis developed new-onset heart failure after receiving >30 months of IFX 5 mg/kg every 4 weeks. Echocardiography showed mild biventricular dysfunction.

Management
Stop IFX and refer urgently to cardiology. Send NT-proBNP and perform ECG and echocardiography. Cardiac MRI may be useful in equivocal cases and when a patient has another systemic disease, such as sarcoidosis, which may cause cardiac involvement.

Risk factors
Pre-existing moderate or severe heart failure (New York Heart Association [NYHA] Class III/IV), age >65 years (27).

Outcome
In this case cardiac function normalised following cessation of IFX and introduction of long term heart failure medication.

Can IFX be restarted?
Re-challenge is contraindicated. A non-TNF biologic should be used instead, with cardiology follow-up and repeat echocardiography to confirm recovery.

Box 3. Rash and arthralgia

A man with Vogt–Koyanagi–Harada disease on IFX 5 mg/kg every 6 weeks developed large-joint arthralgia and a macular rash over the shins and forearms at month 20. He had had a previous similar rash with adalimumab. ANA titre was 1:1280 and dsDNA Crithidia positive but ELISA negative. C3/C4 and dsDNA levels were normal. They had trace blood and protein in their urine with normal renal function.

Management
Pause IFX and refer to rheumatology and dermatology. Evaluation should include testing for antinuclear antibodies (ANA), anti-double stranded DNA (dsDNA), anti-histone antibodies, complement levels (C3, C4) and urinalysis. ANA and anti-dsDNA positivity are common in IFX-treated patients. Approximately half of initially ANA-negative patients develop a positive ANA and around one-fifth develop anti-dsDNA (31), however clinical lupus is much less common. Drug induced lupus is suggested by a temporal association with IFX exposure, absence of pre-existing systemic lupus erythematosus and resolution after drug withdrawal (32,33).

Risk factors for Drug Induced Lupus
Female sex, underlying autoimmune conditions and the presence of anti-IFX antibodies(34). The median time to development is 7 months (35).

Outcome
Specialty opinion was that our patient's rash and inflammatory arthralgia were unlikely to represent true drug induced SLE. His infusion intervals were increased to 8 weekly and his arthralgia and rash resolved.

Can infliximab be restarted?
Re-challenge is not recommended if drug induced lupus is confirmed.

Box 4. Development of anti-drug antibodies (ADAs)

A young woman with panuveitis secondary to sarcoidosis restarted IFX. She had experienced two prolonged treatment interruptions: first due to pregnancy (patient's choice to pause therapy) and later following a mild drug reaction. Trough IFX levels three months after restarting IFX were <0.3 µg/mL with anti-IFX levels of 1280 ng/mL (our assay's reported normal range is 0-9ng/ml).

Management
Low antibody titres may be overcome by increasing the IFX dose, reducing the infusion interval or adding an immunomodulator. In the NOR-DRUM randomised trial protocol, which featured a range of non-ophthalmic autoimmune disorders, patients with initially low anti-IFX concentrations (defined as <50 ng/mL using an in-house assay) underwent dose escalation (36). In contrast, high antibody concentrations, as encountered here, typically necessitate switching to another biologic.

Risk factors for anti-IFX development
Absence of baseline use of concomitant immunosuppressants and prolonged drug holidays (especially >11 weeks) have been associated with ADA development (36)

Outcome
This patient was managed with intravitreal dexamethasone implants.

Figures

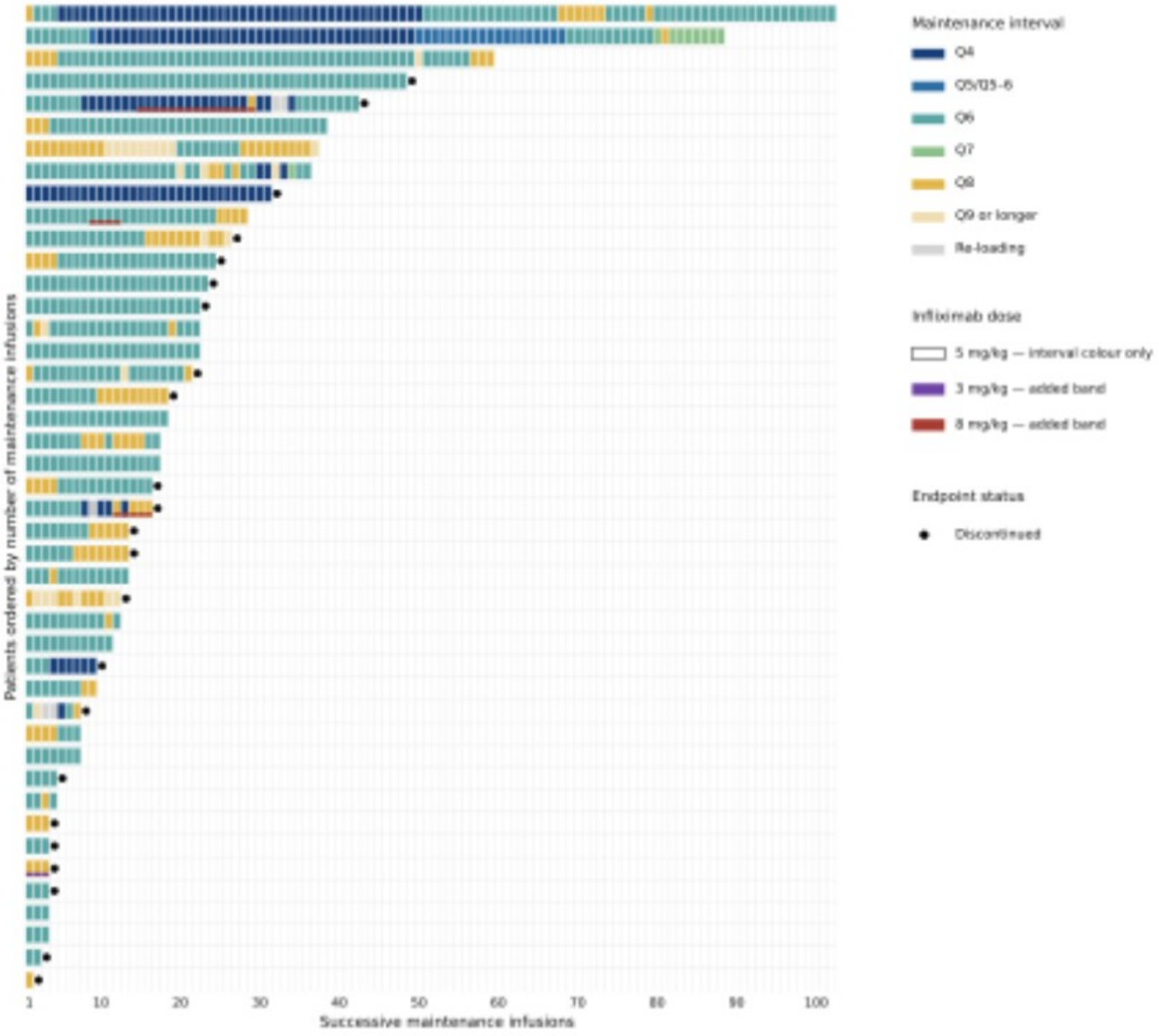


Figure 1

Dose and interval frequency

Maintenance interval and dose for each patient over successive infusions. Each cell represents one infusion.

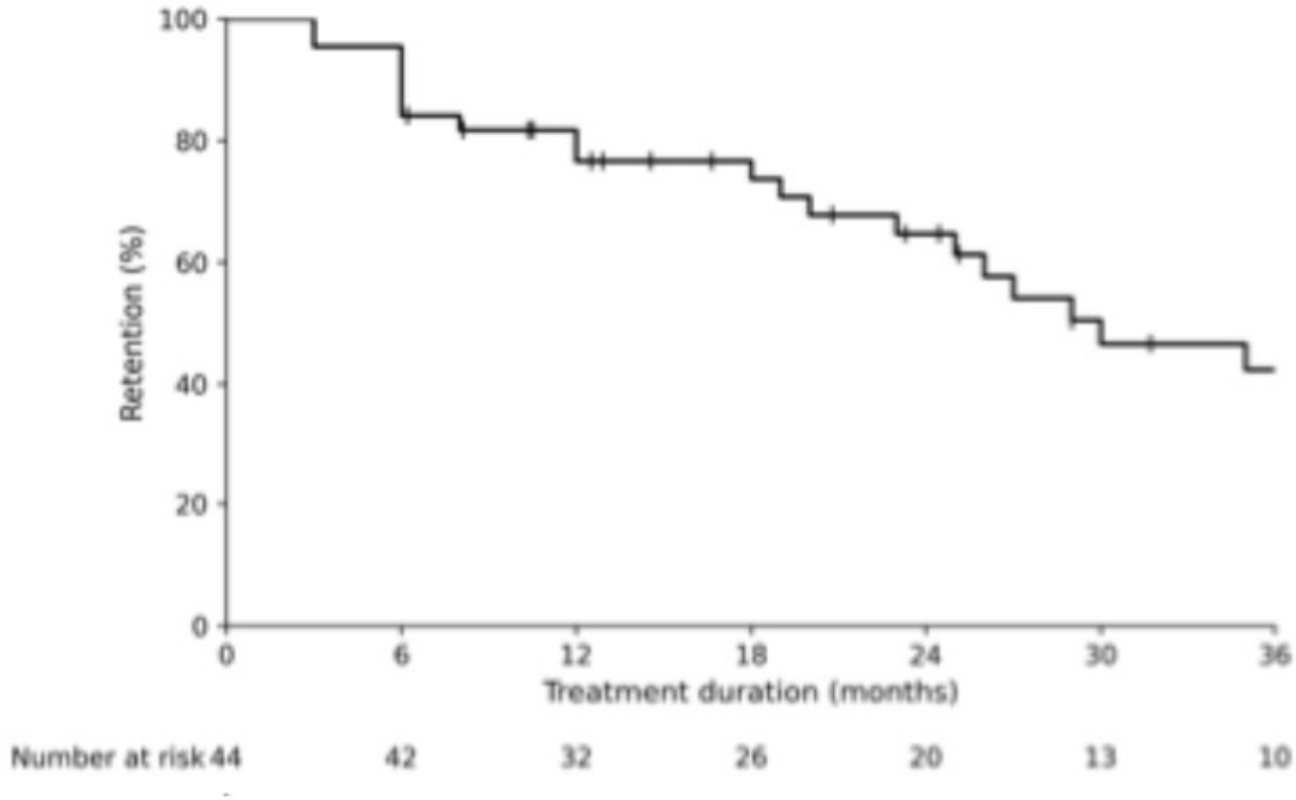


Figure 2

Kaplan-Meier plot showing infliximab retention up to 36 months

Events are discontinuations for any reason; patients still receiving IFX at study close were censored. Numbers at risk are shown below the axis.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.docx
- Table21.docx
- Supplementarytable1.docx