Infliximab for Rheumatoid Arthritis (RA)

- Risk of new or recurrent cancer during treatment with biologics in patients with immune-mediated inflammatory diseases and previous cancer: a meta-analysis
- Limited reduction of bone mineral density in patients with early rheumatoid arthritis receiving aggressive treatment: 10 year results of the NEO-RACo study
- Native structure of the monoclonal therapeutic CD20 antibody ocrelizumab
- Switching from intravenous to subcutaneous infliximab in patients with immune mediated diseases in clinical remission
- JAK-STAT inhibitors in noninfectious uveitis - A review
- Infliximab-Induced Vasculitis in a Rheumatoid Arthritis Patient: A Comprehensive Case Report
- Cardiovascular Outcomes of Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis: A Review of the Current Evidence
- Drug survival and predictor factors for discontinuation of first-line biologic therapy in rheumatoid arthritis: data from a real-world single-centre study

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Overview

Infliximab is a **tumor necrosis factor-alpha (TNFα) inhibitor** for rheumatoid arthritis treatment and other autoimmune diseases. It is a **chimeric monoclonal antibody** (human-mouse hybrid) that binds to TNF-α, preventing it from inducing inflammation and joint damage.

Mechanism of Action

- TNF-α is a pro-inflammatory cytokine that plays a key role in the **pathogenesis of RA**.
- Infliximab binds to both **soluble and membrane-bound TNF-α**, inhibiting its activity.
- This reduces inflammation, prevents further joint destruction, and improves symptoms.

Indications

Infliximab is indicated for **moderate to severe RA** in adults who:

- Have **failed to respond to conventional disease-modifying antirheumatic drugs (DMARDs)**, such as methotrexate.
- Require **biologic therapy** for better disease control.

It is used **in combination with methotrexate** to:

- Enhance efficacy.
- Reduce the risk of **antibody formation** against infliximab.

Dosage and Administration

- **Route: Intravenous (IV) infusion**.
- **Initial dose:** 3 mg/kg at **weeks 0, 2, and 6**.
- **Maintenance:** Every **8 weeks thereafter**.
- The dose can be increased to **10 mg/kg or shortened to every 4 weeks** if the response is inadequate.

Efficacy

- **Reduces symptoms** (pain, swelling, stiffness).
- **Slows disease progression** and prevents joint damage.
- Improves **physical function and quality of life**.
- Works **rapidly**, often showing improvement **within 2 weeks**.

Adverse Effects

- **Infusion reactions**: Fever, chills, pruritus, rash.
- **Infections**: Increased risk of **tuberculosis (TB), bacterial, viral, and fungal infections**.
- **Malignancy risk**: Small increased risk of **lymphoma**.
- **Autoimmune reactions**: Possible **lupus-like syndrome**.
- **Heart failure worsening**: Contraindicated in **moderate-severe heart failure**.
- **Demyelinating disease risk**: Avoid in patients with **multiple sclerosis** or other demyelinating disorders.

Precautions

- **Screen for tuberculosis (TB) and hepatitis B** before starting treatment.
- **Monitor for infections** throughout therapy.
- Use with **caution in elderly patients** due to a higher risk of infections.
- Not recommended in **pregnancy** unless benefits outweigh risks.

Comparison with Other Biologics

- Works **faster than some DMARDs** but requires IV infusions.
- Other TNF inhibitors (e.g., **adalimumab, etanercept**) are **self-injectable**.
- **Non-TNF biologics** (e.g., **rituximab, abatacept, tocilizumab**) may be used if infliximab fails.

Conclusion

Infliximab is a highly effective treatment for **rheumatoid arthritis**, particularly in **methotrexate-resistant cases**. While it provides significant relief and prevents joint destruction, careful **monitoring for infections and infusion reactions** is essential.

Duration of infliximab use during 10 years of follow-up was evaluated in patients with new-onset RA (case-control study using data from the BeSt Trial). Missing values on the exposure were imputed using the last observation carried forward. At 5-year and 10-year follow-ups, lateral X-rays were assessed for atlantoaxial subluxation (AAS) and subaxial subluxation (SAS). Multiple logistic regression models adjusted for age, gender, baseline Disease Activity Score (DAS44), ACPA-positivity, and rheumatoid factor-positivity were used to estimate ORs and their 95% CIs. Mediation analysis evaluated whether a potential association was mediated via mean DAS44.

Cervical deformity (AAS and/or SAS>2 mm) was observed in 108 (40%) of 272 patients. There was an 11% reduction in odds for cervical spine deformity (OR: 0.89, 95% CI: 0.81 to 0.98; p=0.02) for every 1-year increase in duration of infliximab use. Mediation analysis could not reveal an influence of DAS44 on the association between infliximab use and cervical spine outcomes.

There was evidence of a beneficial association between a longer duration of use of infliximab and cervical spine deformity after 10 years follow-up. Thus, it is important to balance the favorable effects of infliximab use for the joints and possibly the cervical spine with the potential adverse events of this medication when used continuously.

Trial registration number: Netherlands Trial Register Number: NTR262 [1)].

The study by Lebouille-Veldman et al. (2025) from Leiden University Medical Center, Brigham and Women's Hospital examines the long-term effects of infliximab use on cervical spine deformity in patients with new-onset rheumatoid arthritis (RA) over 10 years. This is a significant area of research, as RA is known to cause progressive joint damage, including cervical spine involvement, which can lead to severe disability. The study aims to determine whether infliximab, a TNF-α inhibitor, reduces the risk of atlantoaxial subluxation (AAS) and subaxial subluxation (SAS) over time.

Study Design and Methodology

The research employs a case-control study design within the BeSt Trial dataset, a well-established cohort in RA research. The exposure variable, duration of infliximab use, was analyzed with adjustments for confounders such as age, gender, baseline Disease Activity Score (DAS44), ACPA-positivity, and rheumatoid factor-positivity. Missing data were handled using the last observation carried forward (LOCF) method, a common but potentially biased imputation strategy.

While the use of multiple logistic regression models is appropriate for estimating odds ratios (ORs), the mediation analysis evaluating DAS44's role in the observed associations did not yield significant findings. This raises the question of whether other pathways, such as direct inhibition of inflammatory cytokines affecting cervical spine integrity, might be involved.

Key Findings and Interpretation

The study found that longer infliximab use was associated with a lower likelihood of cervical deformity. Specifically, there was an **11% reduction in odds per year of infliximab use** (OR: 0.89, 95% CI: 0.81 to 0.98; p=0.02). This suggests a potential protective effect against structural damage in the cervical spine.

However, it is notable that **40% of patients still developed cervical spine deformities** despite

treatment, indicating that infliximab may not completely prevent progression. Furthermore, the study does not differentiate between AAS and SAS in terms of response to infliximab, which could have provided more detailed insights.

Strengths of the Study

1. **Long Follow-up Period:** A 10-year follow-up provides robust data on the long-term effects of infliximab. 2. **Well-Defined Cohort:** The use of the BeSt Trial dataset ensures high-quality baseline data. 3. **Adjustment for Key Confounders:** The study controls for important clinical variables that could influence outcomes.

Limitations and Potential Biases

1. **Missing Data Handling:** The LOCF method assumes that missing values remain stable over time, which may not be appropriate for a chronic disease with fluctuating activity. 2. **Lack of Direct Causal Evidence:** While mediation analysis ruled out DAS44 as a mediator, the exact mechanism behind infliximab's protective effect remains unclear. 3. **Potential Selection Bias:** Patients who discontinued infliximab due to adverse effects or inefficacy were not explicitly accounted for, which might underestimate negative outcomes. 4. **No Consideration of Alternative Biologic Treatments:** The study does not compare infliximab with other biologic DMARDs (e.g., adalimumab, etanercept), limiting the generalizability of its findings.

Clinical Implications and Future Directions

The study reinforces the importance of early and sustained biologic therapy in RA to prevent long-term joint damage. However, the **risk-benefit ratio of prolonged infliximab use must be carefully weighed**, given its known risks, such as infections and malignancies. Future studies should: - Investigate whether **other TNF inhibitors** or different biologic classes provide similar protective effects. - Explore **radiographic and MRI markers** to better characterize cervical spine disease progression. - Assess whether **combination therapy with methotrexate** enhances or modifies the effect of infliximab.

Conclusion

Overall, this study provides valuable evidence that infliximab may help prevent cervical spine deformities in RA over a decade of follow-up. However, methodological limitations and the lack of mechanistic clarity warrant cautious interpretation. Further comparative studies are needed to establish whether infliximab is superior to other biologic agents in preserving cervical spine integrity.

1)
Lebouille-Veldman AB, Huizinga TWJ, Mekary RA, Vleggeert-Lankamp CLA. Infliximab use and cervical spine deformity in patients with rheumatoid arthritis. RMD Open. 2025 Mar 18;11(1):e005237. doi: 10.1136/rmdopen-2024-005237. PMID: 40102025.