Golimumab in juvenile idiopathic arthritis (JIA) - associated uveitis unresponsive to adalimumab

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Index

1 Background

Uveitis is a potentially blinding complication of juvenile idiopathic arthritis (JIA) [1–3]. Early and complete control of ocular inflammation in JIA is important. Treatment moves step-by step, starting with topical and/or systemic steroids and followed by conventional disease-modifying anti-rheumatic drugs (cDMARDs), usually methotrexate (MTX). In refractory cases treatment with anti-tumor necrosis factor (TNF)-α agents is recommended [4, 5]. Among these adalimumab (ADA), a fully humanised antibody against TNF-α and the only TNF-α inhibitor approved for uveitis as of 2021, has become the drug of choice. ADA shows efficacy in around 75% of patients in the first 18 months of treatment [6, 7]. In case of no response or loss of response to ADA, a switch to another biological agent is recommended [5, 8, 9]. However, the choice of biological drug *i*s not clearly defined. The question remains: Is persistence in an attack on the TNF- α pathway promising in these patients? In this regard data from small numbers of patients provide evidence that switching to a second anti-TNF agent may be beneficial [8, 10]. As such golimumab (GLM), another fully humanised anti-TNF-α monoclonal antibody approved for the treatment of polyarticular JIA, has shown promising results in small heterogeneous case series [11–13].

Abbreviations:

- *JIA Juvenile idiopathic arthritis*
- *Anti-TNF anti- tumor necrosis factor*
- *ADA Adalimumab*
- *GLM Golimumab*
- *SUN Standardization of Uveitis Nomenclature*

2 Aim

The aim oft he study ist o evaluate the effectiveness of golimumab in patients with JIA associated Uveitis that experienced a treatment failure to ADA

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3 Patients

Patients that suffered a loss of response to ADA and were subsequently switched to GLM from November 2012 to February 2019 will be included. Patients diagnosed and treated in the department of pediatric rheumatology and the uveitis clinic of the Medical University of Graz are eligible. Due to the retrospective nature and the classification as orphan disease no sample size calculation is feasible; a sample size of around 10 patients is to be expected.

Inclusion Criteria:

- Patients diagnosed with JIA according tot he ILAR-criteria and associated Uveitis
- Golimumab treatment following treatment with
- Age between 1 and 25 years

Exclusion Criteria:

- Patient not fulfilling diagnostic criteria of a JIA associated
- Patients that were not previously treated with ADA

4 Outcome measures

4.1 Main outcome measures

The main outcome measures are assessed at predefined time points month 1, month 3 and every 3 months thereafter) including intraocular inflammation as determined by anterior chamber cell count, best-corrected visual acuity (BCVA), corticosteroid-sparing potential, and ocular complications. Results of slit-lamp examination, applanation tonometry, ophthalmoscopy, fluorescein angiography, and spectral-domain optical coherence tomography were evaluated. Anterior chamber

(AC) cells and vitreous haze (VH) are graded by SUN criteria [16]. BCVA is determined using a Snellen chart.

4.2 Secondary Outcomes

- Demographic data of patients
- JIA-subtype
- anatomically localization of uveitis
- Uveitis complication
- medication
- opthalmological investigations, including visual acuity, intraocular pressure, fundoscopic findings
- Laboratory parameters under treatment (whole blood count, lever and kidney enzymes, CRP, autoimmune lab (ANA, ds-DNA, anti-drug-Ab, RF, HLA-B27.

5 Methods

A single-centre, retrospective study in patients with JIA-associated uveitis who were treated with GLM for active uveitis that had proved refractory to at least one cDMARD and to ADA.

6 Statistics

6.1 Scheduled Evaluations

Descriptive statistics will be used. Continuous data will be evaluated via median and quartiles or mean and standard deviation, with respect to the data distribiution. Categorical data will be given as absolute and relative proportions. Differences between groups will be evaluated with chi-square or fisher exact test. Time to treatment failure will be evaluated via Kaplan-Meier plots.

6.1 Sample size

Due to scarce data (JIA associated uveitis is an orphan disease) no sample size calculation is feasible. A number of 10 patients ist o be expected. The nature oft he study is explorative.

7 Data protection

All patients will be given a numerical code. The data files will be saved in a secure computer at the department of pediatrics and analyzed pseudo-anonymously.

8 Benefit-Risk ratio

Therapeutic options after treatment failure of ADA for JIA associated uveitis are limited and the risk of ocular complications is high. Thus, these patients are in high need for effective treatment options. The data of the present study can help guide physicians in their choice of treatment in such cases.
A better informed treatment might reduce the burden of systemic steroids and reduce uveitis complications with their associated vision loss. In addition, data form this study might serve as a pilot for further studies.
As this is a retrospective study no risk of harm to the study population is to be expected. All data have been collected in advance and patients have been treated according to international guidelines. Thus the risk-benefit ratio is to be judged favourably.

9 References

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