040. LEFLUNOMIDE AS A DMARD IN JIA: EFFICACY AND TOLERABILITY BASED ON A MINIMUM OF THREE YEAR FOLLOW UP DATA

Sarah Sacks1, Ruth Finch2, Elaine Parsons3, Joel David2, Akhila Kavirayani and Oxford University Hospitals NHS Foundation Trust.

1Rheumatology, Wexham Park Hospital, Slough, 2Children’s Outpatient Department, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, 3Oxford Paediatric and Adolescent Rheumatology Centre, Oxford University Hospitals NHS Trust, 4Rheumatology Department, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust and 5Paediatric Rheumatology, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, Oxford, UK

Background: Leflunomide is a widely used oral DMARD in the treatment of adults with inflammatory arthritis. It reversibly inhibits dihydroorotate dehydrogenase, the rate limiting step in pyrimidine synthesis, thus interfering with DNA synthesis, repair & cellular replication. Although previously described in literature to be a safe/ effective alternative to Methotrexate in JIA, it is not commonly used in Paediatric Rheumatology, due to a combination of factors which may include lack of familiarity with the drug leading to reluctance to prescribe, paucity of clear dosing guidelines and uncertainty regarding tolerability. Methotrexate intolerance often necessitates escalation of treatment to biologic therapy (estimated £9000 per year), which is significantly more expensive than Leflunomide (estimated approx. £200 per year).

Aims: We present 3 year or longer follow up data for children with JIA treated with Leflunomide at our institution.

Methods: 33 children/young people with JIA who had initiated treatment with Leflunomide between 2010 and 2014 were identified from our Paediatric Rheumatology Database. Information was collected on demography, indication for starting Leflunomide and adverse effects over a 3-7 year follow up period. Efficacy was evaluated by documenting additional treatments required after commencing Leflunomide.

Results: Age at commencement of Leflunomide ranged from 6 to 18 years (mean age 12.6). 9 were male, 24 female. See Table 1 for subtypes of JIA. Initial dose was titrated by the prescribing physician according to body weight and increased in increments as tolerated. Eventual dose ranged from 5 to 20mg. Dosage regimens included daily, alternate day or weekday dosing. The main indication for starting Leflunomide was Methotrexate intolerance in 24/33 (73%) patients. It was started as an adjunct to biologic therapy in 10/33 (30%) cases. Overall, Leflunomide was well tolerated (Table 2 - reported side effects). 5/33 (15%) patients were intolerant leading to discontinuation (excluding 2 who had ongoing symptoms despite cessation). 2/33 (6%) patients developed uveitis whilst on Leflunomide. 9/33 (27%) patients required either no additional treatment or infrequent steroid joint injections. 8/9 (89%) of these patients had either persistent/extended oligo-JIA or RF negative poly-JIA. 2 patients previously intolerant to Methotrexate were able to successfully restart Methotrexate after stopping Leflunomide.

Conclusions: Based on this retrospective analysis, we propose the potential use of Leflunomide as a highly cost-effective, safe, alternative oral DMARD which merits consideration in the following situations: Children with JIA (especially oligoarticular and RF negative polyarticular JIA) in whom Methotrexate intolerance is a profound problem (either Methotrexate-associated nausea or recurrent transaminitis) where escalation to biologic therapy is not justified. As an adjunct DMARD to anti-TNF therapy in children who are Methotrexate intolerant. Where Methotrexate needs to be given a drug-holiday i.e. Methotrexate intolerance might possibly abate at a later stage, thereby allowing a successful re-trial of Methotrexate in line with published data, we would not recommend the use of Leflunomide as a DMARD for children with JIA-associated uveitis. We intend to extend this study to include our entire cohort of patients on Leflunomide.