GUIDELINES FOR JUVENILE IDIOPATHIC ARTHRITIS MANAGEMENT: IS THERE A ROOM FOR COMBINED METHOTREXATE AND LЕFLUNOMIDE TREATMENT IN THE TREATMENT RECOMMENDATIONS

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Objectives: To set recommendations for the management of children and adolescents living with JIA and assess whether there is a room for combined methotrexate and leflunomide therapy, adopting treat to target approach.

Methods: The treatment guidelines were developed based on systematic review, local studies, formal consensus and feedback. Initiation of methotrexate or leflunomide was recommended for polyarticular JIA children who, after 3 month of treatment, did not respond to methotrexate or leflunomide monotherapy, or those whose DMARD dose could not be optimised; a new management step was introduced where a combination of both medications was administered. This was a multicentre study including 76 JIA patients who had been treated with the combination of methotrexate plus leflunomide. All patients were classified according to the International League of Associations for Rheumatology (ILAR) criteria. Recorded data included: demographics, JIA subtype, reason for starting combined treatment, treatment duration, withdrawals, causes of discontinuation, efficacy and safety. Patients were classified as “responders” or “non-responders”. Responders were those patients with articular improvement >ACR-Paediatric 30 and/or ocular improvement according to the Standardisation of Uveitis Nomenclature Working Group (SUN) definitions. Efficacy was assessed at 3, 6- and 12 month outcomes.

Results: Out of the 76 children there were, oligoarthritis (34%), polyarthritis (31%), systemic JIA with synovitis (4 joints) (20%), and psoriatic arthritis (15%). Mean age at initiation of combined therapy 10.2±3.4 years, mean disease duration is 9.4±4.8 months. The combined therapy was superior to methotrexate alone and did not significantly increase the rate of adverse events. ACR-Ped 30 was achieved in 64% at 3 months, 75% at 6 months. This was superior to methotrexate alone (37.3% and 53.8%; p<0.01 at 3- and 6-months respectively). At 1 year, 81% reached Ped 30, 74.5% reached ACR-Ped 50, 64% achieved ACR-Ped 70 whereas 51% met ACR-Ped 90 criteria. There were no serious adverse events. One of the two DMARDS was stopped in 51% of the children; of them: 25% were due to adverse events, clinical remission in 25% whereas 21% were switched to ant-TNF therapy according to guidelines due to ineffectiveness of MTX. All patients who had had uveitis responded well and achieved clinical remission. Some of the patients who had had uveitis responded well and achieved clinical remission. Some of the patients who had had uveitis responded well and achieved clinical remission. Some of the patients who had had uveitis responded well and achieved clinical remission.

Conclusions: The children with polyarticular JIA who did not respond to methotrexate or leflunomide, combination of methotrexate and leflunomide treatment appeared to be efficacious and maintain a durable response. The current recommendation would be to use combined methotrexate and leflunomide treatment in children with polyarticular JIA who are either intolerant to higher methotrexate doses or who did not have a satisfactory response to methotrexate. The combination should be considered prior to the use of a biologic agent.