Early Aggressive Therapy in Polyarticular Juvenile Idiopathic Arthritis

Written by Maria Vinall

The Trial of Early Aggressive Treatment in Juvenile Idiopathic Arthritis [TREAT JIA; NCT00443430] addressed whether aggressive treatment, initiated early in the course of polyarticular juvenile idiopathic arthritis (JIA), can induce clinical inactive disease (CID) within 6 months. CID was defined as no active arthritis; no fever, rash, serosotis, splenomegaly, or generalized lymphadenopathy that was attributable to JIA; no active uveitis; normal erythrocyte sedimentation rate (ESR); and physician's global assessment of disease activity score of 0. Secondary objectives included the proportion of subjects who achieved clinical remission on medication (CRM) at 12 months (defined as CID for 6 continuous months on medication), serious adverse events, and change in ACR pediatric core set variables. Trial results were presented by the principal investigator of TREAT JIA, Carol Wallace, MD, Seattle Children's Hospital and University of Washington School of Medicine, Seattle, Washington, USA.

TREAT JIA was an NIH-NIAMS-funded, randomized, prospective, multicenter (15 sites), double-blind, placebo-controlled trial in children aged 2 to 16 years with rheumatoid factor (+) or (-) polyarticular JIA of <12 months duration. Subjects were randomized 1:1 to methotrexate (MTX) 0.5 mg/kg/week SQ (40 mg max)+etanercept (ETN) 0.8 mg/kg/week SQ (50 mg max)+prednisolone 0.5 mg/kg/day (60 mg max) tapered to 0 by 17 weeks (Arm 1; n=42) or methotrexate (same dose as Arm 1)+placebo etanercept and placebo prednisolone (Arm 2; n=43). All subjects also received daily NSAIDs and folate (1 mg). Participants were followed for 12 months. Subjects who failed to achieve at least an ACR pediatric 70 improvement after 4 months on therapy and those who did not achieve CID by 6 months received open-label treatment as in Arm 1. An intent-to-treat approach was used for efficacy analyses.

Eighty-five subjects were enrolled (median age 11.1 years; 75% female). Baseline characteristics showed that participants had an average of 5 months of symptoms before study entry with active disease, according to median values of ACR pediatric core variables (physician's global assessment of disease activity 7.5; parent global assessment of well-being 5.5; ESR 33; number of joints with arthritis 19; number of joints with limited motion 11.5, C-HAQ 1.1). Sixty-nine percent were ANA+ and 36% were RF+. Baseline characteristics did not differ between treatment groups, with the exception of a significantly higher number of active joints and ESR in Arm 2 (p=0.018 and 0.017, respectively), but they were not associated with response to treatment.

The trial did not meet its primary endpoint. At 6 months, CID was achieved in 40% of subjects in Arm 1 and 23% in arm 2 (p=0.088). Overall, however, CID was achieved by 32% of subjects—a high percentage, given the stringent CID definition that was considered. The only variable that was predictive of CID at 6 months was disease duration at baseline, with the odds of achieving CID increasing by 1.32 for each month earlier treatment was started after onset of symptoms (p=0.011).

At 4 months, 30 of 42 subjects (71%) in Arm 1, and 19 of 43 subjects (44%) in Arm 2 achieved an ACR pediatric 70 improvement (p=0.011). All six ACR pediatric core variables showed significant improvement by 6 months in both arms (all p values <0.001). By 12 months, 12 subjects (14%) achieved CRM (9 remained in Arm 1 and 3 remained in Arm 2 throughout the study; p=0.053). Safety did not differ between the two arms. There were three serious adverse events: pneumonia (Arm 1), psychosis (open-label), and septic joint (open-label). All events resolved.

Although this trial failed to achieve its primary endpoint, Dr. Wallace noted that the results demonstrate that it is possible to achieve CID by 6 months and CRM by 12 months in a meaningful proportion of patients with severe polyarticular JIA using early and aggressive treatment. These data suggest that there is indeed a "window of opportunity" to treat severe JIA early in the disease course. While MTX that was given subcutaneously was fully effective for some patients, the combination of MTX, prednisolone, and ETN showed a trend to provide a more complete and durable response without increased risk for serious adverse events.

Reduced CV Risk with Use of MTX and TNF-α Inhibitors in Patients with RA

Written by Debra Gordon, MS

Patients with rheumatoid arthritis (RA) who did not have preexisting coronary artery disease (CAD) and used methotrexate (MTX) for at least 24 months or a tumor necrosis factor (TNF) antagonist for at least 40 months were significantly less likely to develop cardiovascular disease (CVD) than those who did not use MTX or anti TNF therapy, according to researchers from Geisinger Medical Center in Danville, Pennsylvania, USA.

Lead researcher Rasa Bozaite-Gluosniene and her colleagues worked with electronic health records