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Systemic JIA Guidelines Urged Early Treatment

BY AMY ROTMAN SCHONFELD
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NEW YORK – Early and aggressive therapy is warranted in the management of systemic juvenile idiopathic arthritis, which accounts for 10% of arthritis cases in children and which can be devastating, according to Dr. Randy Q. Cron.

Dr. Cron, director of pediatric rheumatology at the University of Alabama at Birmingham, is a coauthor of the fever 2011 ACR Recommendations for the Treatment of Juvenile Idiopathic Arthritis (JIA) that were published on April 1 (Arthritis Care Res. 2011;63:465-82) and which include guidelines for the treatment of systemic JIA.

According to the publication, “the JIA category of systemic arthritis proved to be especially challenging to evaluate. Attempts to exhaustively depict the myriad possible clinical presentations of systemic arthritis were impractical.”

The result was that systemic JIA guidelines include two treatment algorithms, one for the active systemic features (for example, fever) and one for the active arthritis. Patients who have both concurrent active systemic features and active arthritis can be treated according to suggestions from both algorithms.

For treating the systemic features of systemic JIA, three first-line options are available: nonsteroidal anti-inflammatory drugs (NSAIDs), systemic corticosteroids, and anakinra (Kineret). It should be noted that interleukin-1 inhibitors and interleukin-1 inhibitors other than anakinra were not considered when developing the recommendations, since they were not widely available commercially at the time. TNF-alpha inhibitors were not considered because of their relatively poor effectiveness for the systemic manifestations.

While NSAID monotherapy might also help some children, the recommendations say that its use is inappropriate for patients with active fever and physician global assessment of overall disease activity (MD global) score equal to 7 or 10. It should also not be used for more than 1 month in patients with active fever. Systemic glucocorticoids were recommended as initial therapy for patients with active fever and an MD global score of 7. Systemic glucocorticoids may also be added after 2 weeks of NSAID monotherapy in patients with active fever.

Anakinra was recommended for all patients with active fever who had poor prognostic features, no matter what they were currently taking. Anakinra was also recommended for patients who have or develop fever while on systemic glucocorticoids. Anakinra is a human recombinant interleukin-1 (IL-1) inhibitor that was approved to treat adults with moderate to severe arthritis who have not had an adequate response to conservative disease-modifying anti-rheumatic drug therapy. It is not currently approved for children with JIA.

Medications such as calcineurin inhibitors, intravenous immunoglobulin, methotrexate or thalidomide were not formally recommended but might have roles in the treatment of systemic JIA.

For the treatment of the arthritic features of systemic JIA, initiation of NSAID monotherapy (with or without glucocorticoid joint injections) was recommended for all patients, regardless of the level of disease activity or presence of poor prognostic features. It was assumed that most patients with newly diagnosed systemic arthritis would have been started with NSAIDs. The next step would be methotrexate for all patients with active arthritis who were taking NSAID monotherapy for less than one month. If escalation of therapy was needed, the next choices would be either addition of a TNF-alpha inhibitor or anakinra. The recommendations indicate that initiation of anakinra should take place early rather than later in the disease course. For patients with moderate or high disease activity, regardless of features of poor prognosis, it was suggested that patients be switched from anakinra to a TNF-alpha inhibitor.

The last option is abatacept, a costimulatory blocker, for those who fail to be controlled by methotrexate for 4 months of a TNF-alpha inhibitor and who have moderate to high disease activity.

During his presentation, Dr. Cron provided his perspective on the new systemic JIA recommendations. Most pediatricians have an interest in early treatment of juvenile idiopathic arthritis, and the recommendations call for early treatment of disease features and consideration of drug combination therapy. There is also a new emphasis on drug safety and monitoring in children, which is also of interest to pediatricians.

One of the key developments in systemic JIA recommendations is the statement that the level of disease activity should be considered when deciding whether to initiate a new drug. This is based on the fact that many drugs are effective for low or moderate disease activity, but not severe disease activity. The new recommendations also emphasize the importance of drug monitoring and adherence to treatment in children with systemic JIA.

The publication also includes two treatment algorithms, one for the active systemic features (for example, fever) and one for the active arthritis. Patients who have both concurrent active systemic features and active arthritis can be treated according to suggestions from both algorithms.
abatacept was associated with a greater proportion of serious infections than the use of a TNF-blocker alone; and the combination therapy, compared to the use of a TNF-blocker alone. Therefore, the combination of TNF-blockers including SIMPONI® and atacicept is not recommended (see Drug Interactions). Use with Anakinra Concurrent administration of adalimumab (or infliximab) and anakinra was associated with a greater proportion of serious infections and neutropenia and no additional benefits with the TNF-blocker alone. Therefore, the combination of anakinra with TNF-blockers, including SIMPONI®, is not recommended (see Drug Interactions).

Hematologic Cytoxenias There have been post-marketing reports of pancytopenia, thrombocytopenia, neutropenia, agranulocytosis, and thrombocytopenia in patients receiving SIMPONI®. Although, severe cytoxenias seen in the SIMPONI® clinical trials, caution should be exercised when using SIMPONI® in patients with a history of severe infections and neutropenia and liver enzyme elevation is not clear. SIMPONI® has not been studied in patients with severe renal, hepatic, or pulmonary disease. However, concomitant medications, including other TNF-α inhibitors, should also receive concomitant therapy. The safety data described below are based on 5 pooled, randomized, double-blind Phase 2 and 3 trials of SIMPONI® in patients with RA, PsA, and AS. These 5 trials included 639 control-treated patients and 1659 SIMPONI®-treated patients who received subsequent treatment with a TNF-blocker. There is insufficient information to determine if patients who received subsequent treatment with a TNF-blocker are at risk for infections. Therefore, the use of products for RA, PsA, or AS. Live Vaccines Live vaccines should not be given concurrently with SIMPONI® or abatacept as these products may lower the ability of their immune system to respond to infection. SIMPONI® should be used during pregnancy only if clearly needed. An embryotrophic developmental toxicity study was conducted in rats and rabbits. In this study, no adverse effects of SIMPONI® or abatacept on the male and female reproductive systems were observed. However, there was an increased incidence of fetal and postnatal deaths in the rabbits. Fewer joint counts, and significantly lowered levels, decreased the number of active joint counts, and significantly lowered levels, decreased the number of active joint counts, and significantly lowered levels. For the treatment of RA, SIMPONI® was associated with a greater proportion of serious infections and neutropenia and no additional benefits with the TNF-blocker alone. Therefore, the combination of anakinra with TNF-blockers, including SIMPONI®, is not recommended (see Drug Interactions). Use with Anakinra Concurrent administration of adalimumab (or infliximab) and anakinra was associated with a greater proportion of serious infections and neutropenia and no additional benefits with the TNF-blocker alone. Therefore, the combination of anakinra with TNF-blockers, including SIMPONI®, is not recommended (see Drug Interactions).

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