The topic, Disease-Modifying Antirheumatic Drugs (DMARDs) in Children with Juvenile Idiopathic Arthritis (JIA), is important, but other topics have higher priority for limited program resources. No further activity on this topic will be undertaken by the Effective Health Care (EHC) Program.


Key Questions:

Key Question 1. In children\textsuperscript{a} with JIA,\textsuperscript{b} does treatment with DMARDs,\textsuperscript{c} compared to conventional treatment (i.e., NSAIDs or corticosteroids) with or without methotrexate,\textsuperscript{d} improve laboratory measures of inflammation or radiological progression, symptoms (e.g., pain, symptom scores), or health status (e.g., functional ability, mortality)?

Key Question 2. In children with JIA, what are the comparative effects of DMARDs\textsuperscript{e} on laboratory markers of inflammation or radiological progression, symptoms (e.g., pain, symptom scores), or health status (e.g., functional ability, mortality)?

Key Question 3. In children with JIA, does the rate and type of adverse events\textsuperscript{f} differ between the various DMARDs or between DMARDs and conventional treatment with or without methotrexate?

\textsuperscript{a} “Children” are defined as individuals aged 18 years or younger.

\textsuperscript{b} “JIA” includes any category of any severity of the following:

- Juvenile rheumatoid arthritis (JRA) according to the American College of Rheumatology (ACR) definition;
- Juvenile chronic arthritis (JCA) according to the European League Against Rheumatism (EULAR) criteria;
- Juvenile idiopathic arthritis (JIA) according to the International League of Associations for Rheumatology (ILAR) criteria.

\textsuperscript{c} DMARDs evaluated are: abatacept, adalimumab, anakinra, canakinumab, etanercept, infliximab, intravenous immunoglobulin (IVIG), rituximab, rituximab, and tocilizumab (biologic DMARDs); and azathioprine, cyclosporine A, penicillamine, hydroxychloroquine, leflunomide, methotrexate, mycophenolate mofetil, sulfasalazine, tacrolimus (FK506), and thalidomide (non-biologic DMARDs).

\textsuperscript{d} Conventional treatments evaluated are: betamethasone, triamcinolone acetonide, triamcinolone hexacetonide, celecoxib, etodolac, ibuprofen, indomethacin, meloxicam, naproxen, oxaprozin, and tolfenamin.

\textsuperscript{e} This question is identical to Key Question 1, but focuses on comparisons of one DMARD versus another, rather than on comparisons of DMARDs versus conventional treatments.
without methotrexate?

Key Question 4. How do the efficacy, effectiveness, safety, and adverse effects of treatment with DMARDs differ among the various categories of JIA?

Key Question 5. What are the validity, reliability, responsiveness, and feasibility of the clinical outcomes measures for childhood JIA that are commonly used in clinical trials or within the clinical practice setting?

These instruments were assessed for test-retest reliability, inter- and intra-rater reliability, internal reliability, construct validity, responsiveness (standardized response mean and responsiveness index), and feasibility metrics such as time to administer.

Considerations

- The update surveillance of Comparative Effectiveness Review (CER) #28: Disease-Modifying Antirheumatic Drugs (DMARDs) in Children with Juvenile Idiopathic Arthritis (JIA) indicated there were new safety warnings and new trials since the publication of the 2011 CER. In addition, the three experts contacted as part of the surveillance assessment noted rapid changes in JIA treatment.

- However, in 2013, the American College of Rheumatology (ACR) updated their clinical guidelines on the treatment of JIA based on the new evidence. An update of the existing therefore CER would be duplicative as the target audience is likely already utilizing the ACR clinical guidelines.

Because of the known risks associated with DMARDs, we focused primarily on serious infections and the development of cancer when assessing adverse events. Other adverse events considered included mortality, hepatitis, bone marrow suppression, nausea or vomiting, and risks to fetus or pregnant mother.

Categories of JIA include:
- Systemic arthritis
- Oligoarthritis
- Rheumatoid-factor positive (RF+) polyarthritis
- Rheumatoid-factor negative (RF-) polyarthritis
- Enthesitis-related arthritis
- Psoriatic arthritis
- Other (arthritis of unknown cause with symptoms lasting more than 6 weeks).

The outcomes measures assessed were those most commonly used in clinical trials and practice, as well as newer instruments of particular interest that were selected in consultation with the project's technical expert panel (TEP). The outcome measures assessed were:

Measures of disease activity:
- Active joint count (AJC)
- Physician global assessment of disease activity (PGA)
- Parent/patient global assessment of well-being (PGW)

Measure of functional status/disability:
- Childhood Health Assessment Questionnaire (CHAQ)

Measures of health-related quality of life:
- Child Health Questionnaire (CHQ)
- Pediatric Quality of Life Inventory (PedsQL) 4.0
- Pediatric Quality of Life Inventory Rheumatology Module (PedsQL-RM)

Composite measures of response to therapy and developing definitions of disease status:
- American College of Rheumatology Pediatric Response Criteria (ACR Pediatric 30)
- Juvenile Arthritis Disease Activity Score (JADAS)
- A consensus-based definition of remission
- Flare
- Minimal disease activity (MDA)
http://www.rheumatology.org/Practice/Clinical/Guidelines/Juvenile_Idiopathic_Arthritis_(Members_Only)/

Surveillance of this topic will continue, but an update will not be initiated at this time.