TITLE: Long-Term Sustained Clinical Remission after Stopping First-Line Anti-TNF Agents in Patients with Rheumatoid Arthritis, Psoriatic Arthritis, or Ankylosing Spondylitis: Clinical Effectiveness

DATE: 7 November 2014

RESEARCH QUESTION

What is the long-term clinical effectiveness (ability to maintain sustained clinical remission) in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), or ankylosing spondylitis (AS) who remain on methotrexate (MTX) after using an anti-TNF agent plus MTX as first-line treatment?

KEY FINDINGS

Two randomized controlled trials (RCTs) and one non-randomized study were identified regarding the long-term clinical effectiveness (not necessarily clinical remission) in patients with RA who remain on MTX after using an anti-TNF agent plus MTX as first-line treatment.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 10), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, RCTs, and non-randomized studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1 2010 and 28 October, 2014. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

<table>
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<th>Table 1: Selection Criteria</th>
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<td>Population</td>
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<td>Intervention</td>
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<td>Comparator</td>
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<td>Outcomes</td>
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<td>Study Designs</td>
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RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by RCTs and non-randomized studies.

Two RCTs and one non-randomized study were identified regarding the long-term clinical effectiveness (not necessarily clinical remission) in patients with RA who remain on MTX after using an anti-TNF agent plus MTX as first-line treatment. No relevant health technology assessment reports, systematic reviews, or meta-analyses were identified. In addition, no relevant literature including patients with PsA or AS was identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Two RCTs and one non-randomized study were identified regarding the long-term clinical effectiveness in patients with RA who remain on MTX after using an anti-TNF agent plus MTX as first-line treatment. Results specifically related to clinical remission were not presented in any of the abstracts; however, the full text of the articles may contain this information.

The OPTIMA¹ and the HIT HARD² RCTs reported: maintenance of good clinical responses,¹ no difference in rates of adverse events,¹ no difference in clinical outcomes,² and reduced radiographic progression¹,² in patients with early RA who remained on MTX after using adalimumab plus MTX as first-line therapy compared with placebo plus MTX. Patients with RA in the BeSt study³ who remained on MTX after using infliximab plus MTX as first-line therapy had no change in the rate of radiographic progression within the year after cessation of infliximab. A detailed summary of findings can be found in Table 2.

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¹ OPTIMA ² HIT HARD ³ BeSt

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Table 2: Summary of Findings

<table>
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<tr>
<th>Lead Author, Year</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcomes</th>
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<tr>
<td><strong>Randomized Controlled Trials</strong></td>
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<tr>
<td>Smolen, 20141</td>
<td>Patients with early RA (less than one year)</td>
<td>ADA + MTX 26 wks, followed by MTX monotherapy 52 wks</td>
<td>• Placebo + MTX 26 weeks, followed by MTX monotherapy 52 wks OR ADA + MTX 52 wks • ADA + MTX 78 wks</td>
<td>• Intervention group achieved and “mostly maintained” a higher proportion of good responses (low disease activity [DAS28 &lt; 3.2] and radiographic non-progression) at week 78 • No difference in adverse events between groups</td>
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<td>Detert, 20132</td>
<td>DMARD naive Patients with early RA (less than one year)</td>
<td>ADA + MTX 24 wks followed by MTX monotherapy up to 48 wks</td>
<td>Placebo + MTX 24 weeks followed by MTX monotherapy up to 48 weeks</td>
<td>• No difference in DAS28, ACR, or HAQ scores between groups • Greater reduction in radiographic progression in intervention group</td>
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<td>van den Broek, 20113</td>
<td>Patients with RA</td>
<td>Infliximab + MTX until DAS ≤ 2.4 for 6 months followed by MTX monotherapy</td>
<td>None</td>
<td>• No change in rate of radiographic progression one year post MTX monotherapy • Reintroduction of infliximab in 48% of patients</td>
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ACR = American College of Rheumatology; ADA = adalimumab; DAS28 = 28 joint disease activity score with C-reactive protein; DMARD = disease modifying antirheumatic drug; HAQ = Health Assessment Questionnaire; MTX = methotrexate; RA = rheumatoid arthritis; wks = weeks

No relevant literature including patients with PsA or AS was identified, therefore no summary can be provided.
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses
No literature identified.

Randomized Controlled Trials


Non-Randomized Studies


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APPENDIX – FURTHER INFORMATION:

Systematic Reviews and Meta-analyses - Anti-TNF Agent Dose Reduction


Randomized Controlled Trials - Unclear Crossover Therapy


Non-Randomized Studies - Anti-TNF Agent Dose Reduction


Review Articles