Clinical Effectiveness and Safety of Leflunomide in Rheumatoid Arthritis

Morgan Schultz¹, Stephanie Keeling², Steven Katz², Walter Maksymowych², Dean Eurich³, Jill Hall¹

¹Faculty of Pharmacy and Pharmaceutical Sciences, ²Faculty of Medicine and Dentistry, ³School of Public Health, University of Alberta

Presented by:
Morgan Schultz
BSc(Pharm), PharmD Student
University of Alberta
September 12th, 2015
Presenter Disclosure

- Presenter’s Name: Morgan Schultz

- I have no current or past relationships with commercial entities

- Speaking Fees for current program:
  - I have received no speaker’s fee for this learning activity
Commercial Support Disclosure

- This program has received no financial or in-kind support from any commercial or other organization.
Objectives

- To inform pharmacists of a research project being completed in the area of rheumatology at the University of Alberta
- To describe the proportion of patients self-reporting achievement of a clinically meaningful response with leflunomide therapy
- To inform pharmacists of reported side effects and discontinuation rates with leflunomide in patients with rheumatoid arthritis
Background

- Leflunomide is a disease modifying anti-rheumatic drug (DMARD)
  - Indicated for treatment of rheumatoid arthritis
Canadian Rheumatology Association Recommendations

In certain situations:
1. DMARD contraindication
2. High disease activity with poor prognostic factors (particularly early disease)

DMARD monotherapy: MTX unless contraindicated

Inadequate response

DMARD combination therapy: with MTX unless contraindicated

Switch DMARD

Inadequate response

1st Anti-TNF: with MTX unless CI

Inadequate response
Problem

- In 7 of 10 provinces, including Alberta, patients must fail leflunomide therapy prior to receiving provincial drug coverage of biologic DMARDs
- However, no guidelines (Canadian, American, European) specifically recommend that leflunomide should be trialled before initiating biologic therapy
- Risks of leflunomide therapy:
  - Hepatic toxicity
    - Led to FDA Black Box warning in 2010
Research Objectives

- To assess the proportion of patients achieving a clinically meaningful response with leflunomide at 3 months
  - Defined as remission or low disease activity

- To assess the proportion of patients experiencing adverse effects (AEs) including:
  - Those requiring therapy discontinuation
  - Description of adverse effects
    - Infections
    - Liver toxicities
Methods

Development of self-reported, standardized questionnaire

Selection of population-based cohort from RAPPORT database

Distribution to $n = 1,956$ recipients during February & March 2015

RAPPORT: Rheumatoid Arthritis Pharmacovigilance Program
Results

- N = 714 completed the survey
  - 36.5% response rate
- Of those who provided information regarding type of inflammatory arthritis:
  - 82.6% had Rheumatoid Arthritis
  - 15.7% had Psoriatic Arthritis
- The majority (72.4%) reported an initial dose of 20mg daily
- The majority (97.4%) reported previously taking methotrexate
- Of the 392 respondents who disclosed their insurance coverage:
  - 22% reported having Alberta Blue Cross coverage
Clinical Response

- Of the 395 respondents who reported taking leflunomide for at least 3 months:
  - 38% reported a clinical response
    - Defined as remission or low disease activity
Of the 407 respondents, 236 (58%) discontinued therapy.

Of those who reported rationale for discontinuation (n=230):
- 36.1% discontinued due to AEs
- 28.7% discontinued due to lack of efficacy
- 24.8% discontinued due to both AEs and lack of efficacy
- Other 10.4%
Of the 226 respondents that described their adverse effects:
- 52.2% reported nuisance side effects (hair loss, nausea, stomach pain)
- 38.5% reported diarrhea
- 7.1% reported liver toxicity
- 5.8% reported a serious infection
Discussion & Conclusion

- Achievement of a clinically meaningful response with leflunomide was self-reported by a minority of survey respondents, with a greater proportion reporting AEs.
- Serious AEs were rare, however a substantial number of patients discontinued leflunomide due to AEs.
- Current policies requiring failure of leflunomide therapy prior to coverage of biologic DMARDs should be reassessed.
References


