# Rheumatoid Arthritis Working Group

## Presented at the Fifth Annual PRO Consortium Workshop – Silver Spring, MD – April 29-30, 2014

## Background

### Rationale for Rheumatoid Arthritis (RA) Working Group (WG)

- PRO Consortium member representatives and FDA advisors identified RA as a priority area with an unmet need for a 'fit-for purpose' PRO measure, as defined by the FDA, for use in evaluating treatment benefit in RA clinical trials

### Goal of the RA WG

- To develop and qualify a PRO instrument that assesses RA-related fatigue and supports product labeling claims of treatment benefit.

In the Scoping Stage Summary Document submitted to the FDA in September 2011, the RA WG proposed that the most important unmet measurement needs in RA trials were standardized PRO instruments assessing RA-related symptoms and RA-defining decrements in physical function. The FDA, in its response in December 2011, acknowledged that "the PRO measures currently used in RA patients could be improved to meet current standards for measurement. We agree to participate in the qualification process for both PRO instruments you have proposed provided that instrument development includes involvement of representatives from the rheumatology academic community including OMERACT and ACR."

In May 2012, a few members of the RA WG met with RA patients and clinical experts to assess interest in a joint development activity. Experts and patients were eager to participate in an activity, which would include representatives from FDA, clinical societies, and other key stakeholders. Subsequently, PRO Consortium leadership, supported by the RA WG, organized a consensus development workshop to identify a path forward (see Updates).

## Milestones

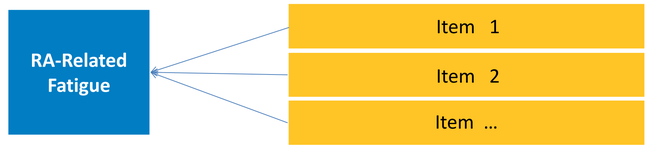
| Milestone | Expected Date | Completed Date |
|---|---|---|
| Scoping Stage | | 09/30/2011 |
| Content Validity Stage | | |
| FDA confirmed willingness to participate in the project | | 12/07/2011 |
| Consensus development workshop | | 08/28/2012 |
| Agreement to conduct preliminary work with OMERACT | 4 Q 2012 | 01/31/2013 |
| Begin work with OMERACT after agreements are signed | 2 Q 2013 | January 2014 |
| Submit briefing document to FDA with evidence to support fatigue as target concept | 3 Q 2014 | |
| Vendor selection and contracting for continuation of Content Validity Stage | 4 Q 2014 | |
| Completion of initial qualitative research and generation of draft items and instrument (concept elicitation, concept selection, and item generation through patient interviews and expert panel input) | TBD once vendor is selected | |
| Refining initial instrument (cognitive interviewing, expert panel meeting, identification of ePRO platform, translatability assessment) | | |
| Quantitative component of the Content Validity Stage | | |
| Submit exploratory endpoint qualification briefing document to FDA | TBD | |

## Content of Interest

### Proposed Endpoint Model for Treatment of RA

| Endpoint Hierarchy | Concept(s) | Endpoint Type |
|---|---|---|
| **Primary** (Composite endpoint for indication [i.e., Treatment of RA]) | **American College of Rheumatology (ACR) criteria**<br>• Patient assessment of pain<br>• Inflammation (CRP or ESR)<br>• Signs (swollen joint count, tender joint count)<br>• Disease activity<br>• Patient assessment of physical function | • PRO<br>• Biomarker<br>• ClinRO<br>• ClinRO and PRO<br>• PRO |
| **Secondary** (Other treatment benefits) | • Improvement in RA-related fatigue | • PRO |

### Hypothesized Conceptual Framework




## Updates

### News of Interest

- As stated above, the FDA requested that the RA WG involve outside stakeholders in the PRO instrument development process. The PRO Consortium was uniquely positioned to initiate, organize, and convene a diverse group of key stakeholders for a face-to-face workshop.
- The RA WG held the workshop, titled "Toward Consensus Development: Qualifying Endpoint Measures for Rheumatoid Arthritis Clinical Trials," on August 28, 2012, in Silver Spring, MD.
- Along with RA WG members and C-Path personnel, participants included RA patients and representatives from the FDA, American College of Rheumatology (ACR), Outcome Measures in Rheumatology (OMERACT), European League Against Rheumatism, and the National Institute of Arthritis and Musculoskeletal and Skin Diseases.
  - Objective: To identify RA-related symptoms and RA-defining decrements in physical functioning that could be investigated by the RA WG for use as PRO endpoints in clinical trials to support label claims.
  - Outcome: WG to focus on FDA qualification of a measure to support a secondary endpoint of fatigue to document treatment benefit.
  - Workshop overview presented as a poster during 2013 ISPOR European Congress
- Following the stakeholder workshop, the WG released an RFP to OMERACT to conduct a review of the literature and to gather clinical experts' input to define the concept of fatigue and explore its measurement in patients with mild to severe RA
  - Funding committed by five member firms with the execution of Project Agreements currently underway

## Updates - continued

### Recent Accomplishments

- The preliminary project with OMERACT was officially started in January 2014.
  - The objectives are to (1) generate a consensus definition of RA-related fatigue, (2) develop a conceptual framework, and (3) document the added value of measuring fatigue in the assessment of RA treatment benefit. A briefing package will be prepared and submitted to the FDA for review prior to moving forward with the development/qualification of an instrument to measure RA-related fatigue.
  - Based on encouragement from the FDA, the RA WG will collaborate with the PROMIS team to leverage work done regarding literature review to document gaps in the measurement of fatigue in rheumatoid arthritis.
- PROMIS representatives, Drs. San Keller and Jim Witter, joined the RA WG as Nonmember Participants.

## Topics for Discussion

### Concerns Worth Noting

- Due to the delays in progression of milestone achievements, several sponsoring firms have had to drop out of the RA WG as a result of lack of funding from their respective organizations. Any of those firms can rejoin the RA WG at a future date if funding circumstances change.

### Unique Issues for the Working Group and the Resolution of those Issues

- RA Consensus Development Workshop
  - Bringing stakeholders together
  - FDA engagement
  - Requirement to work with OMERACT

## Working Group Participants

| Company/Organization | Name |
|---|---|
| Boehringer Ingelheim Pharmaceuticals, Inc. | Kate Burslem, Jeramiah Trudeau |
| Eli Lilly & Company | April Naegeli (Co-Chair), Enkeleida Nikai (Co-Chair) Carol Lynn Gaich, Risa Hayes |
| GlaxoSmithKline | Boyka Stoykova, Maggie Tabberer |
| Novo Nordisk | Claire Sampson, Lise Højbjerre, Anne Kirstine Busk, Irene Schubert |
| Takeda | Ghaith Mitri |
| UCB Pharma | Simon Borghs |
| **Nonmember Participants' Affiliation** | **Name** |
| OMERACT | Vibeke Strand, MD; Lee S. Simon, MD |
| PROMIS | James Witter, MD, PhD; San Keller, PhD |