Rheumatoid Arthritis Working Group

Presented at the Fourth Annual PRO Consortium Workshop – Silver Spring, MD – April 24 - 25, 2013

PRO CONSORTIUM CRITICAL PATH INSTITUTE

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 support 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

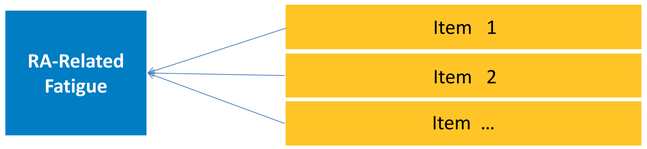
Milestone	Expected Date	Completed Date
Scoping Stage		09/30/2011
Content Validity Stage		
FDA confirmed willingness to participate in the project		12/07/2011
Consensus development workshop		08/28/2012
Agreement to conduct preliminary work with OMERACT	4 Q 2012	01/31/2013
Begin work with OMERACT after agreements are signed	2 Q 2013	
Submit briefing document to FDA with evidence to support fatigue as target concept	4 Q 2013	
Vendor selection and contracting for continuation of Content Validity Stage	1 Q 2014	
Completion of initial qualitative research and generate items (concept elicitation, selection and item generation – patients interviews & expert panels)	TBD once vendor is selected	
Refining initial instrument (cognitive interviewing, final expert panel, identification of ePRO platform, translatability assessment)		
Quantitative analysis of the Content Validity Stage		
Content Validity Summary document submitted to FDA for interim review		
Psychometric Analysis Stage	TBD	

Content of Interest

Proposed Endpoint Model for Treatment of RA

Endpoint Hierarchy	Concept(s)	Clinical Outcome Assessment (COA)/ Biomarker/Survival
Primary (Composite endpoint for indication [i.e., Treatment of RA])	**American College of Rheumatology (ACR) criteria** • Patient assessment of pain • Inflammation (CRP or ESR) • Signs (swollen joint count, tender joint count) • Disease activity • Patient assessment of physical function	• PRO • Biomarker • ClinRO • ClinRO & PRO • 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.**
- 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 will be kicked off once the five project agreements are signed. The objective of this collaboration is to develop a consensus definition of RA-related fatigue and a conceptual framework to be submitted to the FDA.
- Proposals were received from five contract research firms in response to RFP for the Content Validity Stage. This has been put on hold since the focus of the WG became more focused as a result of the Consensus Development Workshop. This work will be re-evaluated and potentially launched in 2014 after the preliminary step with OMERACT.

Topics for Discussion

Concern(s) 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

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

Working Group Participants

Company/Organization	Name
Boehringer Ingelheim Pharmaceuticals, Inc.	Mallik Angalakuditi
Eli Lilly & Company	April Naegeli (Co-Chair), Carol Lynn Gaich, Risa Hayes
GlaxoSmithKline	Boyka Stoykova, Maggie Tabberer
Johnson & Johnson	Fang Chiou, Chenglong Han
Novo Nordisk	Irene Schubert
Roche	Swati Tole, Alison Greene, Sarah Trease
UCB Pharma	Enkeleida Nikai (Co-Chair)
Nonmember Participants Affiliation	**Name**
OMERACT	Vibeke Strand, MD
OMERACT	Lee S. Simon, MD