Rheumatoid Arthritis Working Group

Presented at the Third Annual PRO Consortium Workshop, Silver Spring, MD – April 4, 2012

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 two PRO instruments that assess RA-related symptoms and RA-defining decrements in physical function, respectively, with the intention of supporting product labeling claims. These two instruments will support the evaluation of treatment benefit in medical product clinical trials for patients with moderate to severe RA.
- The WG seeks to collaborate with Outcome Measures in Rheumatology (OMERACT), American College of Rheumatology (ACR), and European League Against Rheumatism (EULAR) in the development of these new measures to facilitate the adoption of the measures by the scientific and clinical practice communities

Targeted Labeling Language

- Proposed labeling language for RA-related symptoms based on results from the PRO instrument: "*A higher percentage of patients treated with [X] achieved relief in RA-related symptoms (pain, stiffness, physical tiredness) than in the comparison group (placebo or alternative treatment)*"
- Proposed labeling language for RA-defining decrements in physical function based on results from the PRO instrument: *"A higher percentage of patients treated with [X] achieved improvement in RA-defining decrements in physical function than in the comparison group (placebo or alternative treatment)"*

Milestones

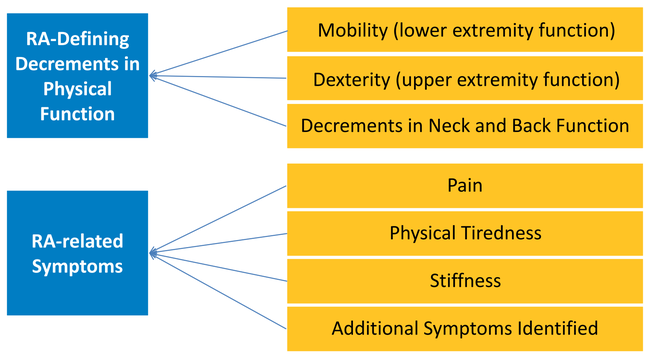
Milestone	Expected Date	Completed Date
Scoping Stage		09/30/2011
Content Validity Stage		
Confirmation of FDA willingness to participate in the project		12/07/2011
Vendor selection and contracting	06/30/2012	
Completion of background research (literature review and 1st expert panel)	TBD once vendor is selected	
Completion of initial qualitative research and generate items (concept elicitation, selection and item generation – patients interviews & expert panels)		
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 Testing Stage	TBD	

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
	Additional Concepts Proposed • RA-defining decrements in physical function not covered above • RA-related symptoms not covered above (e.g., stiffness, physical tiredness)	 • PRO • PRO
Secondary (Other treatment benefits)	• Improvement in RA-related symptoms • Improvement RA-defining decrements in physical function	• PRO • PRO

Target Population

- Adult patients aged 18 years and older, given that the largest proportion of patients are between 40 and 70 years of age
- A clinical diagnosis of definite RA based on ≥6/10 on the American College of Rheumatology Arthritis Classification Criteria
- Patients representative of the full spectrum of severity

Hypothesized Conceptual Framework



Updates

News of Interest

FDA agreed to participate in the qualification process for development of two PRO measures: 1) RA-related symptoms (e.g., pain, physical tiredness, and stiffness); and 2) RA-defining decrements in physical function (e.g., mobility, dexterity, decrement in neck and back function). The FDA recognizes the need for close collaboration between OMERACT and the WG.

- Informal discussions were held with key experts in RA during the EULAR and ACR meetings to raise awareness of the PRO Consortium instrument development effort in RA

Recent Accomplishments

- Finalized and disseminated the RFP for the Content Validity Stage
- OMERACT Executive Committee Representatives Dr. Vibeke Strand and Dr. Lee Simon have joined the RA WG as nonmember participants. Their participation will help ensure collaboration between the RA WG and OMERACT.

Topics for Discussion

Concern(s) Worth Noting

- Value in going through the EMA PRO Qualification process given the cost implications and logistical obstacles specific to interactions with EMA
- Opted for no requirement for ex-US data collection for the first phase of the PRO measure development due to lack of consensus on countries to include. This decision was deemed necessary to avoid inaccurate estimates of cost and timelines relating to the inclusion of ex-US populations

Unique Issues for the Working Group and the Resolution

- Value of proposed PRO instruments to the RA community and might they replace the current ACR criteria. The RA community views the ACR criteria as a favorable composite endpoint made up of ClinROs, PROs and Biomarkers, however, FDA would like to see improvements made. At this stage, the RA WG is not proposing a revision of the ACR criteria but only improvements (development of new or improvement of current measures) of two important concepts from the patient's point perspective namely the RA-related symptoms and RA-related decrements in physical function
  - FDA will participate in the qualification process for the 2 new proposed PRO instruments provided that instrument development includes involvement of representatives from the rheumatology academic community including OMERACT and ACR

Working Group Participants

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