PROACTIVE
Pre-Competitive Consortium for Osteoarthritis
Clinical Trial Outcomes Improvement

MARCH 17, 2023
DENVER, COLORADO

A meeting of the PROACTIVE Consortium, chaired by Dr. Lee Simon was held in Denver prior to the OARSI annual Congress.

AGENDA

- Introductions
- Review of Methodology Committee discussions
- Next steps

PARTICIPANTS

INDUSTRY	REPRESENTATIVE
Ampio Pharmaceuticals	Howard Levy, MBBCh, PhD (Zoom)
Biosplice Therapeutics	Yusuf Yazici, MD Sarah Kennedy, PhD Christopher Swearingen, PhD (Zoom)
Eupraxia Pharmaceuticals	Vik Peck, BSc/BJourn, PMP
Nordic Bioscience Clinical Development	Asger Reinstrup Bihlet, PhD
Novartis	Vineeth Varanasi, MBBS, PhD Peter Mesenbrink, PhD (Zoom)
Rottapharm Biotech	Lucio Rovati, MD Claudio Giuliano, MS, MBA
TrialSpark	Niti Goel, MD Christopher Knight, MS
Xalud Therapeutics	Howard Rutman, MD Morgan Stokes
ORGANIZATIONS	
Arthritis Foundation	Jason Kim, PhD Maria Vassileva, PhD Michelle McLeod, PhD
GOVERNMENT	
FDA	Raj Nair, MD (Zoom) Yura Kim, PhD (Zoom)
INDIVIDUALS	
Francis Berenbaum, MD, PhD	Jean Liew, MD (Zoom)
Alan Brett, PhD	Elena Losina, PhD
Jennifer Gewandter, PhD, MPH (Zoom)	Ali Mobasheri, MSc, DPhil
Michael LaValley, PhD (Zoom)	Lee Simon, MD

The Methodology Committee met virtually on March 7, 2023. Several key issues were discussed, including:

1. What does disease progression mean? What does structural change mean? There is no regulatory definition of disease modification.

2. Presently, joint failure is the end game; is there the potential to identify an earlier indicator of structural change?
3. What should be measured?
4. Understanding the clinical benefit of what is being measured. What are the changes and what is the meaningfulness of these changes?
5. Increasing focus on a therapy's MOA; targeting specific pathways and identifying phenotypes.
6. Consideration of patient reported outcomes – i.e., illness assessment vs. disease assessment (clinician).

As a result of the meeting, the following next steps were confirmed:

1. A Symptom outcome measures (pain, function, PRO) sub-group and a Structural outcomes sub-group were identified; each subgroup will compile a list of outcome measures used in clinical trials to identify how symptoms and structure are currently measured.
    a. Report to be circulated to all Consortium members for review and input.
2. The PROACTIVE co-chairs will take the lead on the identification and acquisition of potential datasets (i.e., observational; clinical trials – positive negative, inconclusive); and FDA.

PROPOSED SUB-GROUP COMMITTEE MEMBERS

Symptoms (pain, function)	Structural
Robin Christensen, PhD	Alan Brett, PhD
Jen Gewandter, PhD, MPH	Jamie Collins, PhD
Francis Guillemin, MD, PhD	Philip Conaghan, MBBS, PhD
Michael LaValley, PhD	David Felson, MD, MPH
Jean Liew, MD	Chris Ladel, PhD
Elena Losina, PhD	Peter Mesenbrink, PhD
	Chris Swearington, PhD

INVITED SUB-GROUP COMMITTEE PARTICIPATION BY FDA

Yura Kim, PhD
Nikolay Nikolov, MD

DISCUSSION

1. Creation of a roadmap on measuring outcomes (i.e., means vs thresholds; composite outcomes)
2. Patient participation in PROACTIVE
    a. Understanding MCID from patient perspective
3. Patient reported outcomes (symptoms/function)
    a. Long-term recall follow-up is difficult
    b. Validation of the "period of recall"
4. Patient global impression of change vs. clinicians' impression
5. Possible inclusion of individuals from FDA Device division

NEXT STEPS

1. Methodology sub-groups to meet virtually to identify a current list of outcome measures used in clinical trials (Symptoms; Structure)
2. List of outcome measures to be circulated to members of PROACTIVE for input
3. Identification of datasets by PROACTIVE co-chairs; submission of data requests
4. Identification of individuals to serve on the Executive and Steering Committees.

Following the submission of outcome measure reports and the identification/acquisition of datasets, an analytic strategy for evaluating the performance of different outcome measure definitions will be developed by the Methodology Committee and subsequently reviewed by members of PROACTIVE.