Biomarkers: Project Update from the GRAPPA 2012 Annual Meeting

Oliver FitzGerald and Philip J. Mease

ABSTRACT. For members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), an important goal has been the identification of soluble biomarkers in psoriatic arthritis that might predict the development of radiographic progression. Work over the past year has resulted in approval of a draft protocol, and an announcement is forthcoming of the outcome of an assessment process for centers that applied to manage the project. GRAPPA is now ready to commence formal negotiations with potential funding partners and intends to initiate this project in the near future. (J Rheumatol 2013:40;1453–4; doi:10.3899/jrheum.130462)

Key Indexing Terms:
CASPAR PsA BioDam PSORIATIC ARTHRITIS
BIOMARKERS RADIOGRAPHIC PROGRESSION

In 2010, members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), together with the Outcome Measures in Rheumatology Clinical Trials (OMERACT) biomarker committee, agreed to support a study designed to validate soluble biomarkers as predictors of structural damage in psoriatic arthritis (PsA). The PsA BioDam study primary objective is to determine the independent predictive validity of several soluble biomarkers for predicting structural damage in PsA patients with active disease who are about to commence or change dose of standard disease-modifying antirheumatic drugs (DMARD) or initiate antitumour necrosis factor-α (TNF-α) therapy. The study will include assessment of biomarkers considered high priority candidates (e.g., high sensitivity C-reactive protein, matrix metalloproteinase-3, C-terminal propeptides of type II procollagen, or cleavage neoepitope of type II collagen) as well as a discovery arm for new candidate biomarkers. The primary radiographic outcome is increased number of erosions. Patients included will meet the ClASsification criteria for Psoriatic ARthritis (CASPAR)[1], will have been diagnosed for > 3 months and < 2 years (i.e., early disease), and will agree to participate for a minimum of 24 months following informed consent. Primary exclusion criteria are corticosteroid therapy within 4 weeks of enrollment, prior treatment with anti-TNF-α therapy or other biologic, and presence of spinal or entheseal disease as the only disease manifestation. Serum and urine samples will be collected under strict guidelines at 6 study intervals, and radiographs of hands and feet obtained yearly. The goal of the study is to enroll and longitudinally track 1000 patients; power calculations were developed by the study's statistician, Richard Cook. As evidenced by previous research efforts (e.g., CASPAR and GRAPPA Composite Exercise studies)[1,2], it is anticipated that these patients can be readily recruited from GRAPPA member investigative centers, representing a diverse global patient population.

At the 2012 annual meeting of GRAPPA, members were advised of the status of the PsA BioDam project. A draft protocol has been updated and approved by the study steering committee, and is now circulating to GRAPPA members and potential industry partners, who attended an information meeting immediately following the GRAPPA meeting. To date, a number of pharmaceutical companies have indicated interest and await elaboration regarding study management and budget before proceeding further.

Members also discussed a call for proposals from clinical research organizations and institutions to manage the PsA BioDam. The advantages and disadvantages of several models were considered, including management by a company external to an academic center [such as Canadian Research and Education (CaRE) Arthritis[3], which manages a similar BioDam study in rheumatoid arthritis]; and another model in which the study is conducted by an academic center with experience in conducting similar multicenter studies. Management applications have now been received and assessed by senior GRAPPA members, all of whom were independent of the organizations that responded. The applications were judged according to agreed criteria (Table 1), and the outcome from this process will be announced early in 2013.

From the Department of Rheumatology, St. Vincent's University Hospital and Conway Institute for Biomolecular Research, University College, Dublin, Ireland; and Seattle Rheumatology Associates, Department of Rheumatology Research, Swedish Medical Center, and Department of Medicine, University of Washington School of Medicine, Seattle, Washington, USA.

O. FitzGerald, MD, FRCPI, FRCP(UK), Department of Rheumatology, St. Vincent's University Hospital and Conway Institute for Biomolecular Research, University College; P.J. Mease, MD, Seattle Rheumatology Associates, Department of Rheumatology Research, Swedish Medical Center, Department of Medicine, University of Washington School of Medicine.

Address correspondence to Prof. O. FitzGerald, Bone and Joint Unit, St. Vincent's University Hospital, Elm Park, Dublin 4, Ireland. E-mail: oliver.fitzgerald@ucd.ie

Table 1. Criteria for assessment of applications to manage the PsA BioDam project.

1	Established record of interest in PsA clinical/translational research
2	Established research facility with record of organization of multi-site (international) projects including clinical, imaging, and bio-sample collection
3	Established project team with expertise to manage and deliver the study requirements
4	Demonstration of understanding of the key tasks associated with managing project (including regulatory issues, ethics applications, medical and safety monitoring, developing CRF, site training, etc)
5	Capacity to collect and store web-based clinical information
6	Capacity to log, aliquot, and store (longterm) large volume of patient samples
7	Capacity to store large number of radiographic and possibly other (e.g., MRI) images
8	Inclusion of initial candidate biomarker measurement and analysis in project proposal
9	Inclusion of proposal for assessing and scoring radiographic images initial project proposal
10	Agreement that intellectual property associated with project including all clinical, imaging, and bio-sample will be retained by GRAPPA
11	Budget tightly controlled with costing calculated to provide adequate support for all study activities
12	Support locally adequate in terms of study management, database support, statistical analysis, and maintenance of biorepository
13	Inclusion of SOP for collection, shipping, and storage of bio-samples
14	Staff requirements clearly outlined, including costs, salary management, and capacity
15	Proposal re funding mechanism/flow, assuming funding is from multiple pharmaceutical companies
16	Avoidance of institutional overheads
17	Commitment to communication strategy with other PsA BioDam steering group members, with GRAPPA membership, with pharmaceutical industry partners, and other potential future partners

CRF: case report form; MRI: magnetic resonance imaging; PsA: psoriatic arthritis; SOP: standard operating procedure.

Further, more structured engagement with potential industry partners will commence in early 2013. The PsA BioDam steering committee preference is that more than one pharmaceutical partner will be involved in supporting this project. It is also expected that the funding stream will be provided over ≥ 3-year time period. It is hoped that negotiations can be concluded by the end of second quarter 2013 and that the study can begin as soon as possible. Other issues that still need careful consideration include intellectual property, liability insurance, study management/flow, and institutional overheads. The steering group certainly prefers that GRAPPA retains all study intellectual property and that any risks and costs to GRAPPA are minimized.

REFERENCES

1. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H. Classification criteria for psoriatic arthritis: Development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.
2. Helliwell PS, Fitzgerald O, Fransen J, Gladman DD, Kreuger GG, Callis Duffin K, et al. The development of candidate composite disease activity and responder indices for psoriatic arthritis (GRACE project). Ann Rheum Dis 2013;72:986-91.
3. CaRE Arthritis — Arthritis Research and Education in Canada. Edmonton, Alberta. (Internet. Accessed May 9, 2013.) Available from: http://www.carearthritis.com