

# Assessing Single Joints in Arthritis Clinical Trials

JON T. GILES, PHILIP MEASE, MAARTEN BOERS, BARRY BRESNIHAN, PHILIP G. CONAGHAN, ALISON HEALD, WALTER P. MAKSYMOWYCH, JEAN-FRANCIS MAILLEFERT, LEE SIMON, WAYNE TSUJI, RICHARD WAKEFIELD, THASIA WOODWORTH, H. RALPH SCHUMACHER, and CLIFTON O. BINGHAM III

**ABSTRACT.** Endpoints and outcome measurements to detect changes in joint structure for the assessment of single joints are needed to enable rheumatology clinical trials of therapies targeting preservation of joint structure, especially via locally applied therapies. While the assessment of certain aspects of single joint inflammation and function is accepted in the evaluation of osteoarthritis (OA) using the WOMAC, it tends to be limited to the knee and hip. The advent of therapies that are directed toward a single joint in inflammatory arthritis, including intraarticular cytokine antagonists and gene therapeutics, requires reliable measures to assess change over time in single joints and the clinical meaningfulness of such change. Traditionally, clinical trials for inflammatory arthritis have used composite response indices such as American College of Rheumatology response or improvement in Disease Activity Score as outcomes based on multiple joint clinical measures, acute phase reactants, and functional status. However, it is not known whether these will appropriately detect changes referable to single joint intervention. This Special Interest Group was developed to bring together interested individuals to identify and evaluate outcome measurements for single joints. The knee was the initial focus, as clinical, radiographic, and functional assessments have been well developed for knee OA. A PubMed English language review was conducted before OMERACT 8, evaluating existing clinical instruments in the context of the OMERACT filter. At OMERACT 8, the group developed a research agenda to perform additional validation studies of clinical and functional indices, imaging, synovial histopathology, and soluble biomarkers. (J Rheumatology 2007;34:641–7)

*Key Indexing Terms:*

OUTCOME ASSESSMENT  
RELIABILITY

ARTHRITIS  
RESPONSIVENESS

VALIDITY  
JOINT EXAMINATION

Pharmacotherapies for inflammatory arthritis have traditionally been delivered systemically, either as oral small molecules or parenteral biologics, administered to patients with multiple affected joints. Composite assessment criteria used in clinical trials of these agents [e.g., American College of Rheumatology (ACR) responder criteria, or EULAR response measured by Disease Activity Score for rheumatoid arthritis (RA) or psoriatic arthritis (PsA), or PsARC for PsA] are

weighted heavily according to standardized assessment of tender and/or swollen joint counts as well as global assessments. The ability of composite measurements to assess interventions directed toward a single joint has not been studied, but it is likely that some validity and discriminative ability would be lost if utilized outside of their intended polyarticular framework.

The need for therapies that are directed toward “refracto-

*From the Division of Rheumatology, Johns Hopkins University, Baltimore, Maryland, USA; Division of Rheumatology Research, University of Washington, Seattle, Washington, USA; VU University Medical Center, Amsterdam, The Netherlands; Department of Rheumatology, St. Vincent's University Hospital, and The Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Dublin, Ireland; University of Leeds, Leeds UK; Targeted Genetics Corporation, Seattle, Washington, USA; Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA; Department of Medicine, University of Alberta, Edmonton, Alberta, Canada; Dijon University Hospital, INSERM-ERM 0207, University of Burgundy, Dijon, France; Amgen, Seattle, Washington, USA; Academic Unit of Musculoskeletal Disease, University of Leeds, Leeds UK; Roche Pharmaceuticals, Welwyn Garden City, UK; Veterans Affairs Medical Center, Philadelphia, Pennsylvania, USA; and Divisions of Rheumatology and Allergy and Clinical Immunology, Johns Hopkins University, Baltimore, Maryland, USA.*

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*J.T. Giles, MD, Division of Rheumatology, Johns Hopkins University; P.J. Mease, MD, Seattle Rheumatology Associates, Chief, Division of Rheumatology Research, Swedish Medical Center, Clinical Professor;*

*University of Washington; M. Boers, MD, PhD, VU University Medical Center, Amsterdam; B. Bresnihan, MD, FRCP, Professor of Rheumatology, Department of Rheumatology, St. Vincent's University Hospital, and The Conway Institute of Biomolecular and Biomedical Research, University College Dublin; P.G. Conaghan, MBBS, PhD, FRACP, FRCP, Professor of Musculoskeletal Medicine, University of Leeds; A. Heald, MD, Senior Director, Clinical Affairs, Targeted Genetics Corporation; L. Simon, MD, Associate Clinical Professor of Medicine, Harvard Medical School, Beth Israel Deaconess Medical Center; W. Maksymowych, FRCP, Professor, Department of Medicine, University of Alberta; J.F. Maillefert, MD, PhD, Associate Professor of Rheumatology, Dijon University Hospital, INSERM-ERM 0207, University of Burgundy; W. Tsuji, MD, Clinical Development, Amgen Inc.; R. Wakefield, BM, MRCP, Senior Lecturer, Consultant in Rheumatology, Academic Unit of Musculoskeletal Disease, University of Leeds; T. Woodworth, MD, Senior Director, Arthritis/Bone Clinical Research, Roche Pharmaceuticals, UK; H.R. Schumacher, MD, Professor of Medicine, University of Pennsylvania; C.O. Bingham III, MD, Divisions of Rheumatology and Allergy and Clinical Immunology, Johns Hopkins University.*

*Address reprint requests to Dr. J.T. Giles, Division of Rheumatology, Johns Hopkins University, 5501 Hopkins Bayview Circle, Suite 1B.1, Baltimore, MD 21224, USA. E-mail: gilesjoint@jhmi.edu*

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ry" inflamed joints that may fail to respond to systemically delivered therapy is being addressed by several groups, who have stimulated the need for this Special Interest Group (SIG). Further, in disorders such as gout and osteoarthritis (OA) that may be characterized by aggressive mono- or pauciarticular involvement, a similar approach may be useful. Already, intraarticular corticosteroids are commonly used in these conditions, as well as hyaluronate derivatives. Preliminary evidence has suggested that approaches such as intraarticular injections of tumor necrosis factor inhibitors<sup>1</sup> and other cytokine antagonists, gene transfer agents that express cytokine antagonists<sup>2,3</sup>, growth factors or their antagonists, or other antiinflammatory approaches are feasible. However, the lack of validated assessment criteria may hinder development of these agents in the treatment of single joints.

Single joint assessments have been developed for OA of the knee and hip. Past and present efforts by OMERACT and OARSI have developed clinical trial outcomes for OA<sup>4</sup>, with most work focusing on relief of signs and symptoms measured by the Western Ontario and McMaster University Osteoarthritis Index (WOMAC) and its component domains (patient and physician global assessments, and patient assessment of pain), but with limited attention to changes in clinical examination (swelling/tenderness). Intraarticular delivery of hyaluronic acid derivatives has been approved for the treatment of OA; however, the requirements for approval for these "devices" have sometimes differed from the criteria for "drugs," with different standards and benchmarks used. These standards, which include the demonstration of safety and "substantial equivalence" to a previously marketed device, do not typically require the preclinical and extensive clinical testing required for investigations drugs and biologics<sup>5</sup>. The development of structure-modifying therapies for OA requires additional exploration of the role of advanced imaging techniques, as well as the validation of biochemical and imaging biomarkers that may reflect disease activity, changes in joint structure, and outcomes. Additional correlations between novel assessment methods and clinical assessment and functional evaluation are needed. Further, short-term measurements to provide preliminary evidence of efficacy in proof of concept and short-term clinical studies may not necessarily equate with longterm assessments of clinically relevant benefit and outcomes. The relationships between changes in single joint status and various measurements of disease state and function have largely been unexplored.

While the assessment of therapeutic response has been developed for clinical trials of OA (primarily for the knee only), these methods of single joint assessment may not be valid in RA or other forms of inflammatory arthritis. The established Minimal Clinical Importance Difference (MCID) for OA assessments are also likely to differ in inflammatory arthritis. The responsiveness of these OA measurements in response to therapeutic intervention in inflammatory disease is unknown, and whether outcomes such as OMERACT-

OARSI responses in OA are applicable to inflammatory diseases also has not been explored.

### Objectives of the Special Interest Group

The primary objective of this SIG was to develop a core set of domains to assess therapeutic responses in single joints. An initial focus of this SIG was to determine whether clinical and functional assessments of the knee joint used in OA studies can be used for inflammatory arthritis, or if new assessments will be required. This SIG was intended to cover in more depth the specific areas of interest regarding single joint assessment that will be integrated with other OMERACT groups. The longterm goals of the group also complement the early assessment of the joint Superworkshop by examining single joints in this framework, and to ultimately determine applicability across a range of disease states and other joints, and longer term outcomes. The participation of OMERACT members from other groups including OA, ultrasound, magnetic resonance imaging (MRI), and histopathology/synovitis will be helpful in guiding the discussions and directions of this SIG to take advantage of the collective experience and previously conducted evaluations.

*Longterm objectives.* The longterm objectives of this SIG were:

1. To establish key domains needed for single joint assessment;
2. To review currently used assessments of single joints and determine if these have been validated in inflammatory arthritis as well as OA, specifically in the setting of therapeutic delivery of agents designed to act on single joints;
3. To determine which domains have validated assessment instruments;
4. To evaluate the need for developing instruments to assess other joints for which methods may not currently exist;
5. To develop a research plan to ensure all such measures fulfill the requirements of the OMERACT filter.

The short-term focus of the group was the knee joint, with an initial evaluation of clinical and functional assessments of this joint in RA and OA, which will serve as a model for later expansion to other joints and disease states.

### Methods

A group of interested individuals was assembled in the Spring of 2005, under the co-chairmanship of C. Bingham and P. Mease. Monthly teleconferences were held over the year to discuss the preliminary goals of the SIG and to develop a preliminary agenda. A fellow (J. Giles) was chosen to participate in the SIG. The Chairs of the SIG met with members of the OMERACT Executive Board and the other representatives of the Superworkshop at EULAR 2005 in Vienna. In line with the ongoing work of the surrogate measures ("Superworkshop") group, the decision was made to focus first on the knee joint in RA.

Pre-conference literature reviews were conducted to evalu-

ate the performance characteristics (using the OMERACT filter) of the clinical examination, patient-derived functional assessments, and imaging modalities in OA and RA of the knee. A summary of the results of the literature review was presented, the details of which are to follow in a separate publication. Integration of the Single Joint SIG within the context of the larger Superworkshop on Surrogate Measures was also discussed. Additional participants (e.g., physiotherapy, orthopedics, outcome researchers) will be sought through the course of review of existing data to expand the SIG to reflect these important domains of inquiry.

*Clinical examination.* A comprehensive literature review eval-

uated clinical domains of inquiry for the assessment of the knee in arthritis clinical trials. A search was conducted in PubMed for English language publications using individual or linked search terms including osteoarthritis, rheumatoid arthritis, knee, examination, assessment, validity, reliability, responsiveness, change, outcome, and the individual components of the knee examination from 1966 to 2005. Additional pertinent references were identified from the bibliographies of these sources and included for review. Data were synthesized for the individual components of the clinical knee examination in OA and RA regarding validity (truth), reliability/responsiveness to change (discrimination), and feasibility.

Table 1. Characteristics of published evaluations of clinical knee examination in OA and RA.

|  | Cibere <sup>6</sup> | Theiler <sup>7</sup> | Jones <sup>8</sup> | Bellamy <sup>9</sup> | Hart <sup>10</sup> | Cushnaghan <sup>11</sup> | Claessens <sup>12</sup> | Altman <sup>13</sup> | Marks <sup>14</sup> | Hauzeur <sup>15</sup> | Karim <sup>16</sup> | Kraus <sup>17</sup> | Ike <sup>18</sup> |
|--|---------------------|----------------------|--------------------|----------------------|--------------------|--------------------------|-------------------------|----------------------|---------------------|-----------------------|---------------------|---------------------|-------------------|
| Multicomponent assessment <sup>†</sup>   | ✓                   | ✓                    | ✓                  | ✓                    | ✓                  | ✓                        | ✓                       | ✓                    | ✓                   |                       |                     |                     |                   |
| Single component assessment <sup>†</sup> |                     |                      |                    |                      |                    |                          |                         |                      |                     | ✓                     | ✓                   | ✓                   | ✓                 |
| Evaluated in OA                          | ✓                   | ✓                    | ✓                  | ✓                    | ✓                  | ✓                        | ✓                       | ✓                    |                     | ✓                     | ✓                   | ✓                   | ✓                 |
| Evaluated in RA                          |                     |                      |                    |                      |                    |                          |                         |                      | ✓                   | ✓                     | ✓                   | ✓                   | ✓                 |
| Examination components assessed          |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Bony swelling                            |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Qualitative                              |                     |                      |                    | ✓                    | ✓                  | ✓                        | ✓                       | ✓                    |                     |                       |                     |                     |                   |
| Semiquantitative                         | ✓                   |                      |                    |                      |                    |                          |                         |                      | ✓                   |                       |                     |                     |                   |
| Effusion                                 |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Qualitative                              | ✓                   | ✓                    | ✓                  |                      |                    |                          | ✓                       |                      | ✓                   |                       | ✓                   |                     |                   |
| Semiquantitative                         |                     |                      |                    |                      |                    |                          |                         | ✓                    | ✓                   |                       |                     |                     |                   |
| Synovitis/soft tissue swelling           |                     | ✓                    | ✓                  |                      | ✓                  | ✓                        | ✓                       |                      | ✓                   |                       |                     |                     |                   |
| Circumference                            |                     | ✓                    |                    |                      |                    |                          |                         |                      | ✓                   |                       |                     |                     |                   |
| Tenderness/pain                          |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Qualitative                              |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Global                                   |                     |                      | ✓                  |                      | ✓                  |                          | ✓                       |                      |                     |                       |                     |                     |                   |
| Location-specific                        | ✓                   |                      | ✓                  |                      | ✓                  | ✓                        |                         | ✓                    |                     |                       |                     |                     |                   |
| Pain on movement                         | ✓                   |                      |                    |                      | ✓                  | ✓                        |                         |                      |                     |                       |                     |                     |                   |
| Quantitative                             |                     | ✓                    |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Range of motion                          | ✓                   |                      |                    | ✓                    |                    | ✓                        |                         | ✓                    | ✓                   |                       |                     |                     |                   |
| Alignment                                |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Qualitative*                             | ✓                   |                      |                    |                      |                    |                          |                         | ✓                    |                     |                       |                     |                     |                   |
| Quantitative*                            |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     | ✓                   |                   |
| Active crepitus                          |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Global qualitative                       | ✓                   |                      |                    |                      | ✓                  |                          |                         | ✓                    |                     |                       |                     |                     |                   |
| Location-specific                        | ✓                   |                      | ✓                  |                      |                    | ✓                        |                         |                      |                     |                       |                     |                     | ✓                 |
| Warmth                                   | ✓                   | ✓                    | ✓                  |                      |                    | ✓                        |                         | ✓                    | ✓                   |                       |                     |                     |                   |
| Erythema                                 |                     |                      |                    |                      |                    |                          |                         | ✓                    | ✓                   |                       |                     |                     |                   |
| Instability                              |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Mediolateral                             | ✓                   | ✓                    |                    |                      |                    | ✓                        |                         | ✓                    | ✓                   |                       |                     |                     |                   |
| Anteroposterior                          | ✓                   | ✓                    |                    |                      |                    | ✓                        |                         | ✓                    | ✓                   |                       |                     |                     |                   |
| Domains Assessed                         |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Validity (diagnostic)                    |                     | ✓                    |                    |                      | ✓                  |                          | ✓                       | ✓                    |                     | ✓                     | ✓                   | ✓                   | ✓                 |
| Reliability                              |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Intraobserver                            |                     |                      | ✓                  |                      |                    | ✓                        |                         |                      | ✓                   | ✓                     |                     | ✓                   |                   |
| Interobserver                            | ✓                   | ✓                    |                    | ✓                    | ✓                  | ✓                        |                         |                      | ✓                   | ✓                     |                     |                     |                   |
| Standardization used                     | ✓                   |                      |                    | ✓                    |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Responsiveness to change                 |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |
| Feasibility                              |                     |                      |                    |                      |                    |                          |                         |                      |                     |                       |                     |                     |                   |

<sup>†</sup> Denotes number of examination components studied in the publication. \* i.e., normal/varus/valgus. \*\* Assessed with goniometer.

Thirteen studies of oral therapies, physical therapy, surgical interventions, and intraarticular therapy that evaluated at least one quantitative, semiquantitative, or qualitatively assessed component of the clinical knee examination were first reviewed (Table 1), including bony enlargement, effusion, synovitis, tenderness, range of motion, and alignment<sup>6-18</sup>. The sensitivities and specificities of each measurement were tabulated and compared to other variables regarding responsiveness to change, reliability, feasibility, and whether assessed in clinical trials in RA or other inflammatory arthritis. Data were synthesized for individual components of the clinical knee examination in OA and RA regarding validity (truth), reliability, responsiveness to change (discrimination), and feasibility. In general, the reported methods for clinical evaluation of the knee joint in arthritis have been validated only for diagnostic validity and primarily in the context of OA. Intraobserver reliability is generally good, particularly for experienced examiners<sup>8,11,14,15,17</sup>. Interobserver reliability is best for quantitative assessments, and standardization/training improved interobserver reliability for some but not all qualitative or semiquantitative assessments<sup>6,9</sup>. We found no data available on responsiveness to change in response to therapeutic intervention.

*Patient-derived assessments of joint function.* We also reviewed the literature focusing on the most commonly used knee-specific and generic patient-derived assessments used in OA and RA of the knee. The instruments included WOMAC, the Knee Injury and Osteoarthritis Outcome Score (KOOS), Rheumatoid Arthritis Outcome Score (RAOS), Lequesne Index, SF-36, and the Stanford Health Assessment Questionnaire (HAQ) (Table 2). Individual features of each question-

naire were tabulated, and data regarding validity, reliability, and responsiveness to change in RA compared to OA are summarized. Few studies have evaluated the performance of patient-derived assessments developed for knee OA<sup>19-29</sup> in the context of inflammatory arthritis<sup>27,28,30</sup>. The RAOS for inflammatory arthritis is a modification of the KOOS for OA and includes all WOMAC domains, but responsiveness to change over time with pharmacologic intervention is not known<sup>31</sup>. While several studies have utilized active functional assessments in OA including walk time, stair climbing, and distance traveled, these have not been widely used in RA or other inflammatory arthritides<sup>32,33</sup>.

It is important to note that while many of the domains assessed with these instruments are common to most joints (i.e., pain, function), the items within the domain will vary depending on the joint or joint group of interest. This will present some difficulty in comparison in trials in which the single joint of interest may vary across subjects. Additional research will be needed to determine if it is possible to establish a basic instrument of joint function that retains the core items required to assess the domain, while at the same time retaining its performance characteristics across various joints or joint groups.

*Imaging.* Results of a literature review comparing imaging modalities in the assessment of OA and RA of the knee were presented (Tables 3 and 4 summarize the findings for RA). In general, performance characteristics of both MRI and ultrasound for validity, reliability, and responsiveness to change have been superior to clinical examination or plain radiography for the assessment of inflammation (synovitis or effusion) in OA and RA of the knee<sup>34,35</sup>. Unlike clinical examination

Table 2. Characteristics and evaluation of commonly used knee-specific and generic patient-derived assessment instruments in OA and RA of the knee.

|                            | WOMAC  | Lequesne ISK                                   | KOOS               | RAOS                    | SF-36  | HAQ                      |
|----------------------------|--|--|--------------------|-------------------------|--|--------------------------|
| Knee-specific instrument   | ✓  | ✓  | ✓                  | ✓                       |  |                          |
| Generic instrument         |  |  |                    |                         | ✓  | ✓                        |
| Domains                    |  |  |                    |                         |  |                          |
| Pain                       | ✓  | ✓  | ✓                  | ✓                       | ✓  | ✓                        |
| Stiffness/symptoms         | ✓  |  | ✓                  | ✓                       |  |                          |
| General function           | ✓  | ✓  | ✓                  | ✓                       | ✓  | ✓                        |
| Activities of daily living | ✓  | ✓  | ✓                  | ✓                       | ✓  | ✓                        |
| Leisure activities         |  |  | ✓                  | ✓                       | ✓  |                          |
| Quality of life            |  |  | ✓                  | ✓                       | ✓  |                          |
| Evaluation in knee OA      |  |  |                    |                         |  |                          |
| Validity                   | Bellamy <sup>19</sup>                          | Lequesne <sup>21</sup>                         | Roos <sup>25</sup> | —                       | Brazier <sup>26</sup>                            |                          |
| Reliability                | Bellamy <sup>19</sup><br>Bellamy <sup>19</sup> | Faucher <sup>22</sup><br>Faucher <sup>22</sup> | Roos <sup>24</sup> | —                       | Ware <sup>27</sup><br>—<br>Brazier <sup>26</sup> | Bruce <sup>29</sup><br>— |
| Responsiveness to change   | Angst <sup>20</sup>                            | Theiler <sup>23</sup>                          | Roos <sup>24</sup> | —                       | Keller <sup>28</sup>                             | Bruce <sup>29</sup>      |
| Evaluation in knee RA      |  |  |                    |                         |  |                          |
| Validity                   | Wolfe <sup>30</sup>                            | —  | —                  | Bremander <sup>31</sup> | Ware <sup>27</sup>                               | —                        |
| Reliability                | —  | —  | —                  | Bremander <sup>31</sup> | —  | —                        |
| Responsiveness to change   | —  | —  | —                  | Bremander <sup>31</sup> | Keller <sup>28</sup>                             | —                        |

Table 3. Summary of literature for magnetic resonance imaging in evaluating RA knees.

| Evaluation            | Gd  | DCMRI |
|-----------------------|-----|-------|
| Synovial hypertrophy  |     |       |
| Validity              | +++ | +++   |
| Reliability           | ++  | ++    |
| Sensitivity to change | ++  | ++    |
| Erosions              |     |       |
| Validity              | ?   |       |
| Reliability           | ?/+ |       |
| Sensitivity to change | ?   |       |
| Bone edema            |     |       |
| Validity              | ?   |       |
| Reliability           | ?   |       |
| Sensitivity to change | ?   |       |

“+ or ?” refer to the relative quantity of literature on a given area. Gd: gadolinium MRI; DCMRI: dynamic contrast-enhanced MRI.

and plain radiography, relevant pathologic structures (i.e., synovial hypertrophy in RA) can be directly visualized with MRI and ultrasound. For the assessment of articular damage, MRI has distinct advantages over ultrasound, plain radiography, and the clinical examination in both knee RA and OA because it can tomographically assess cartilage and bone<sup>36</sup>. Although rapidly expanding, little work outside the hand/wrist and knee has been conducted for MRI in the context of RA. Feasibility issues for MRI include expense and patient tolerability, while operator training and experience may limit multi-center applications utilizing ultrasound.

**Synovial histology and biomarkers.** It is recognized that the integration of synovial histology/biomarkers will provide important comparisons with observed changes in imaging and serum biomarkers. Representatives from this SIG participated in discussions with the synovial histopathology and soluble biomarkers group at OMERACT 8 in further developing a research agenda to cross-validate various modalities in the assessment of the single joint.

#### Preliminary application of clinical and functional assessments in a clinical trial of single joints

Prior to the conference, based largely on the results of the literature reviews (discussed above) showing limited published data for the performance characteristics of clinical and functional assessments of the knee in inflammatory arthritis, a small pilot study was initiated within a human Phase IA trial of a novel intraarticular gene transfer agent by members of the SIG affiliated with the Phase IA trial. The goal of the pilot study was to examine the responsiveness to change of 2 clinical examination findings, joint tenderness and swelling, each semiquantitatively graded on a zero to 3 scale (none, mild, moderate, severe/large; at the discretion of the examiner). This study included patients with RA, psoriatic arthritis, or ankylosing spondylitis with peripheral joint involvement<sup>3</sup>. Semiquantitative, graded clinical assessments of joint tender-

Table 4. Summary of literature for ultrasonography in evaluating RA knees.

| Evaluation                      | GS | PD |
|---------------------------------|----|----|
| Synovial hypertrophy, effusions |    |    |
| Validity                        | ++ | +  |
| Reliability                     | +  | ?  |
| Sensitivity to change           | +  | +  |
| Erosions                        |    |    |
| Validity                        |    | ?  |
| Reliability                     |    | ?  |
| Sensitivity to change           |    | ?  |

“+ or ?” refer to the relative quantity of literature on a given area. GS: grey-scale ultrasonography; PD: power Doppler ultrasonography.

ness and swelling were performed at baseline and at each study visit out to 24 weeks after delivery of the experimental agent. Within the context of this small trial, neither serial assessments of joint tenderness, nor swelling, nor the combination were adequate measures to definitively distinguish active therapy from placebo. This may be because the study was not adequately powered for efficacy, the measures have not been validated or the nature of the particular measurement scales used, or the therapy was not effective. Efficacy and safety outcomes of the study and the results of the pilot sub-study will be reported in separate publications. Further investigations using these clinical examination measures, a patient-derived functional assessment, and a radiographic assessment have been incorporated into the next Phase I/II trial to assess which of these measures individually or in combination should be developed and validated to detect a therapeutic effect.

#### Discussion points from OMERACT 8

The work performed by the SIG thus far highlights the limited information available to guide selection of appropriate domains for single joint assessment in inflammatory arthritis. Even for the knee, a large and accessible joint for which the most information is available, validation of the clinical examination and its sensitivity to change over time, and for functional indices and their sensitivity to change over time, are poorly studied in inflammatory arthritis. Recent data presented at ACR 2005<sup>37</sup> suggest that clinical examination for swelling in inflammatory arthritis is poorly correlated with the more sensitive imaging modalities of ultrasound and MRI in detecting synovitis, confirming the importance of additional correlative studies.

OMERACT 8 group interaction prompted consensus on key issues concerning further direction for research initiatives. The group felt that a focus on inflammatory arthritis was vital for a number of scientific and practical reasons:

1. The potential that a true therapeutic effect will be detected is greater in interventional trials of inflammatory arthritis compared to OA. The ability to discern a therapeutic effect

will allow greater certainty in the determination of performance characteristics for assessment measures.

2. A focus on inflammatory arthritis will provide integration into other studies that are under way.

### Research agenda

Several research opportunities were proposed to allow further evaluation of key domains for assessing therapeutic response in single joints:

1. A clinical trial integrating clinical examination, functional assessments, imaging, histopathology, and soluble biomarkers with intraarticular corticosteroids in patients with active RA of the knee.
2. Continuing to investigate responsiveness to change of clinical and patient-derived functional assessments in a Phase II trial of a novel intraarticularly delivered gene-transfer cytokine antagonist (discussed above). Various assessments will be investigated in this study, including interobserver variability in tenderness and swelling scores and correlation between tenderness and swelling assessments with subjective patient responses on the RAOS questionnaire, with a feasibility study to determine if the number of items can be reduced. Because the study involves joints outside the knee, a comparison of the knee-specific assessments to other joints will be performed. The correlation between MRI findings, clinical assessments of swelling and tenderness, and patient-derived functional assessments will be determined in a subset of patients.
3. Opportunities to mine existing longitudinal clinical trials data to compare the performance characteristics of therapeutic responses in single joints within the context of aggregate measures using multiple joint assessments will be further explored.

### Outstanding issues

Despite the extensive research agenda proposed at the SIG meeting, several questions originally posed by the SIG will require additional further study, as follows.

Can we use the method ultimately derived for knee assessment to inform investigations of other joints, for which there may be fewer existing assessment instruments?

How do clinically measurable changes in a single joint translate into functional improvement that is meaningful to the individual patient and feasible to demonstrate and describe in a large cohort of patients? For example, improvement of a single metacarpophalangeal joint may be highly significant for a pianist in a study, but this significance may be diluted by the aggregate experience in which such improvement may not be as important.

How do short-term changes in single joints correlate with longterm outcomes such as joint survival?

Can studies from physical therapy, orthopedic, crystalline arthritis literature help to further define the research agenda?

Additional interested individuals were identified at OMERACT 8 to participate in the ongoing activities of the Single Joint SIG. Working subgroups were established to address specific research tasks and to develop more formal working groups.

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