Meeting Report

Report of the Sixth Joint WHO/ILAR Task Force Meeting on Rheumatic Diseases, January 16, 2000, Geneva, Switzerland

INTRODUCTION

The meeting was opened by Dr N.G. Khaltaev on behalf of the Director-General. Dr. Khaltaev welcomed the members of the task force to Geneva. He particularly stressed the importance of this meeting and its association with the Global Burden of Disease project and the Decade of Bone and Joint Disease. There are increasing data to demonstrate the importance of the contribution of musculoskeletal diseases to disability in both developed and developing countries.

Dr. Peter Brooks, Chairman of the ILAR Standing Committee on Clinical Studies, was elected Chair and Dr. Maarten Boers, Executive Committee Member of OMERACT, was elected Vice-Chair and both were also elected as Rapporteurs.

Dr. Brooks thanked Dr. Khaltaev and his staff for their hard work in helping to coordinate the meeting, and members of the task force for giving up their time to attend.

This meeting, the Sixth WHO/ILAR task force, extended the work of the fifth meeting, held in Geneva June 29 to July 2, 1993. At that meeting a new classification of antirheumatic drugs had been approved together with guidelines for the use of a variety of drugs in juvenile idiopathic arthritis and for the testing of antirheumatic drugs in both rheumatoid arthritis (RA) and osteoarthritis (OA). Also, the core set for outcome measures in rheumatoid arthritis was approved at this meeting (see below).

The meeting had been convened to review outcome criteria that had been developed by OMERACT (Outcome Measures in Arthritis Clinical Trials), to review criteria for the classification of rheumatic diseases that had been developed by a variety of national and international bodies, and to review the preliminary criteria for juvenile arthritis that had been developed by a standing committee of ILAR.

Dr. Maarten Boers outlined the development of OMERACT. This group had first come together in 1992 to review existing outcome measures in RA and attempt to come to some consensus on these. At that meeting a core set of outcome measures for RA clinical trials were developed, and these were subsequently approved by the last WHO/ILAR task force meeting in 1993. OMERACT 2, held in Ottawa in 1994, addressed issues of cost and cost effectiveness and of drug safety. OMERACT 3, held in Cairns, Australia in 1996, developed outcome measures in osteoarthritis and osteoporosis clinical trials and also discussed the issue of psychosocial function in musculoskeletal trials whilst OMERACT 4 developed outcome measures for ankylosing spondylitis (AS), systemic lupus erythematosus (SLE) and also continued to review response criteria in RA. Dr Boers outlined the important features of the OMERACT process in that it has an international chair of Dr. Maarten Boers, Dr. Peter Brooks, Dr. Lee Simon, Dr. Vibeke Strand, and Dr. Peter Tugwell, runs an internet distribution list, and organizes conferences on a biennial basis with ongoing working parties. It is constituted under the auspices of the International League of Associations for Rheumatology and has close collaboration with the Cochrane Initiative. The process brings together health professionals, methodologists, regulatory agencies, and the pharmaceutical industry to develop these outcome measures. Conferences are conducted with careful analysis of the literature and focus groups, where consensus can then be developed. All proceedings of OMERACT conferences have been published in the *Journal of Rheumatology*. Outcome measures developed by the OMERACT group must fulfil criteria of truthfulness — be free from bias, be relevant, be discriminative — distinguish between states that are of interest at one point in time and at different time points, and have reliability, reproducibility, and sensitivity to change. Finally, to fulfil OMERACT filter criteria the outcome measures must be feasible in terms of time, costs, and interpretability. Outcome measures developed by OMERACT must also address cross cultural issues.

OMERACT 5 was held in Toulouse, France, in May 2000 and addressed issues of drug safety, minimum clinically important differences in trials, economics, and imaging.

OUTCOME MEASURES FOR OSTEOARTHRITIS

These outcome measures for future phase 3 clinical studies in hip, knee, and hand OA have been developed at OMERACT 3 — Recommendations for a core set of outcome measures for future phase 3 clinical trials in knee, hip, and hand OA (Bellamy N, Kirwan J, Boers M, *et al*. Consensus development of OMERACT 3. J Rheumatol 1997;24:799-802).

The core set of outcome measures in OA should be: pain; physical function; patient global assessment; and for studies

of one year or longer, joint imaging (using standardized methods for taking and rating radiographs, or any demonstrably superior imaging technique).

Quality of life and/or utility measures are also strongly recommended, but further work should be carried out to assess the usefulness of biological markers, stiffness, measures of inflammation, and other assessments such as performance based measures, time to surgery, flares, or analgesic consumption before they are accepted as core measures.

OUTCOME MEASURES FOR ANKYLOSING SPONDYLITIS

This core set of endpoints in AS clinical trials was developed at OMERACT 4 (Van der Heijde DMFM, van der Linden SM, Dougados M, *et al*. Ankylosing spondylitis: plenary discussion and results of voting on selection of domains and some specific instruments. J Rheumatol 1999;26:1003-05).

Defined core sets have been developed for use in 4 settings — disease controlling antirheumatic therapy (DC-ART), symptom modifying antirheumatic drugs (SM-ARD) and physical therapy, and for clinical record keeping. These are as follows: (1) SM-ARD and physical therapy: physical function, spinal stiffness, patient global assessment, and spinal mobility and pain. (2) Clinical record keeping: add acute phase reactants and peripheral joints/entheses. (3) DC-ART: add fatigue, hip radiograph, spine radiograph.

OUTCOME MEASURES FOR SYSTEMIC LUPUS ERYTHEMATOSUS

A core set of outcome measures and response criteria were developed during OMERACT 4 (Strand V, Gladman D, Isenberg D, *et al*. Outcome measures to be used in clinical trials in systemic lupus erythematosus. J Rheumatol 1999;26:490-7; and Smolen JS, Strand V, Cardiel M, *et al*. Randomized clinical trials and longitudinal observational studies in systemic lupus erythematosus: consensus on primary core set of outcome domains. J Rheumatol 1999;26:504-07).

The core outcome domains to be measured in both randomized clinical trials and longitudinal observational studies in SLE are disease activity, health related quality of life, damage, and toxicity/adverse events.

OUTCOME MEASURES FOR OSTEOPOROSIS

The core endpoints for osteoporosis trials were discussed at OMERACT 3 (Sambrook PM, Cummings SR, Eisman JA, et al. Workshop report guidelines for osteoporosis trials. J Rheumatol 1997;24:1234-6).

Outcome measures for osteoporosis trials were discussed according to 2 broad groupings of trials — randomized trials where prevention of rapid bone loss was the primary aim, and randomized trials where prevention of fractures may be a feasible outcome because patients were already at high risk of osteoporotic fractures either on the basis of low bone mass or previous osteoporotic fracture.

Randomized trials where prevention of rapid bone loss was the primary aim. Two core outcome measures of clinical benefit were considered appropriate: (1) bone mineral density (BMD) — measured at 2 sites, the lumbar spine and proximal femur; (2) biochemical markers, which should include at least one resorption marker (which should be based on a urinary crosslink excretion) and at least one formation marker.

Non-core outcome measures of clinical benefit were considered to be: (1) fractures, (2) quality of life, (3) change in height (measured in a standardized fashion).

Randomized trials of fracture prevention in high risk population. Core outcome measures of benefit were: (1) fracture, (2) hip, knee and spine BMD, (3) biochemical markers, (4) change in height.

Non-core outcome measures of benefit in these studies would include: (1) quality of life instrument, (2) back pain measure, and (3) economic evaluation including health services utilization such as hospitalization, co-therapy, etc., and a measure of incident falls. It was recommended that these studies should be of 3–5 years' duration.

CRITERIA FOR CLASSIFICATION OF RHEUMATIC DISEASES

The following classification criteria for a variety of rheumatic diseases were presented. These had been developed over the years by committees representing national and international groups. It is recommended that WHO/ILAR adopt these well recognized classification criteria and encourage their use in clinical and epidemiological studies.

It should be noted that classification criteria should NOT be used as diagnostic criteria, but for the purpose of classifying patients in studies.

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Polyarteritis nodosa. Lightfoot RW Jr, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of polyarteritis nodosa. Arthritis Rheum 1990;33:1088-93.

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PRELIMINARY CRITERIA FOR CLASSIFICATION OF JUVENILE IDIOPATHIC ARTHRITIS

A proposal for the development of classification criteria for idiopathic arthritides in childhood had been drawn up by a standing committee of ILAR (J Rheumatol 1995;22:1566-9). These proposed classification criteria were then revised at a meeting in Durban in 1997 (J Rheumatol 1998;25:1991-3).

The classification of juvenile idiopathic arthritis:

- systemic
- oligoarthritis
  - persistent
  - extended
- polyarthritis (RF negative)
- polyarthritis (RF positive)
- psoriatic arthritis
- enthesitis related arthritis
- other arthritis
  - fits no other category
  - fits more than one category

RECOMMENDATIONS

1. That the outcome measures for osteoarthritis be approved

as WHO/ILAR core measures for trials in osteoarthritis.
2. That the outcome measures for ankylosing spondylitis be approved as WHO/ILAR outcome measures for clinical trials in ankylosing spondylitis.
3. That the outcome measures for SLE be adopted as the core outcome domains recommended by WHO/ILAR for clinical trials and longitudinal studies in systemic lupus erythematosus.
4. That the outcome measures for osteoporosis be adopted as WHO/ILAR outcome measures for osteoporosis clinical trials and referred to the WHO Task Force on osteoporosis for incorporation into their discussions and documentation.
5. That the criteria for classification of rheumatic diseases as presented be endorsed by WHO as the internationally recognized classification criteria for these diseases.
6. That the preliminary criteria for the classification of juvenile idiopathic arthritis be endorsed as WHO/ILAR classification criteria for juvenile arthritis.
7. That WHO/ILAR, the regional Leagues of Associations for Rheumatology, and OMERACT continue to work together to facilitate the development and distribution of classification and outcome criteria in the rheumatic diseases.

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