GUIDELINES FOR THE CONDUCT OF PHARMACOLOGICAL CLINICAL TRIALS IN HAND OSTEOARTHRITIS: CONSENSUS OF A WORKING GROUP OF THE ESCEO

J.-Y. Reginster[1] , N. K. Arden[2] , I. K. Haugen[3] , F. Rannou[4] , E. Cavalier[5] , O. Bruyère[1] , J. Branco[6] , R. Chapurlat[7] , S. C. Basset[8] , N. M. Al-Daghri[9] , E. M. Dennison[10], G. HerreroBeaumont[11], A. Laslop[12], B. F. Leeb[13], S. Maggi[14], O. Mkinsi[15], A. S. Povzun[16], D. Prieto-Alhambra[17], T. Thomas[18], D. Uebelhart[19], N. Veronese[14], C. Cooper[10]

1 Department of Public Health, Epidemiology and Health Economics, University of Liège, Liège, Belgium

2 Arthritis Research UK Centre for Sport, Exercise and Osteoarthritis, University of Oxford, Oxford, United Kingdom

3 Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

4 Division of Physical Medicine and Rehabilitation, Department of Rheumatology, AP-HP Cochin Hospital, Université Paris Descartes Sorbonne Paris Cité, Paris, France

5 Department of Clinical Chemistry, University of Liège, Liège, Belgium

6 CEDOC, NOVA Medical School, Universidade Nova de Lisboa, Department of Rheumatology, CHLO, Hospital Egas Moniz, Lisbon, Portugal

7 INSERM UMR 1033, Université de Lyon, Hôpital E Herriot, Lyon, France

8 TRB Chemedica International SA, Geneva, Switzerland

9 Biochemistry Department, College of Science, King Saud University, Riyadh, Saudi Arabia

10MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton General Hospital, Southamton, United Kingdom

11Department of Rheumatology, Bone and Joint Research Unit, Fundación Jiménez Diaz, Universidad Autonoma, Madrid, Spain

12Scientific Office, Austrian Medicines and Medical Devices Agency, AGES, Vienna, Austria

13Second Department of Medicine, Centre for Rheumatology Lower Austria, State Hospital Stockerau, Stockerau, Austria

14Aging program, National Research Council, Padova, Italy

15Rheumatology Department, IBN ROCHD University Hospital, Casablanca, Morocco

16Scientific Research Institute of Emergency Care n.a. l.l. Dzhanelidze, Saint-Petersburg, Russia

17NIHR Musculoskeletal Biomedical Research Unit, University of Oxford, Oxford, United Kingdom

18Department of Rheumatology, Hôpital Nord, CHU de St-Etienne & INSERM 1059, Université de Lyon, Saint-Etienne, France

19Division of Musculoskeletal, Internal Medicine and Oncological Rehabilitation, Department of Orthopedics and Traumatology, Hôpital du Valais (HVS), Centre Hospitalier du Valais Romand (CHVR), CVP, CransMontana, Switzerland

Objectives

To gather expert opinion on the conduct of clinical trials that will facilitate regulatory review and approval of appropriate efficacious pharmacological treatments for hand osteoarthritis (OA), which there is currently no approved medication in Europe.

Methods

The European Society on Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal diseases (ESCEO) organized a working group, which consisted of clinical scientists expert in the field of OA in academia and consulting for drug development within the pharmaceutical industry, and representatives of national or European licensing authorities. Members of the group prepared a full review of the literature on the design of studies in hand OA, which were presented to the group. After the presentations, a comprehensive discussion was held within the group and shared conclusions were reached.

Results

These recommendations provide guidance, not rigid rules, which should allow for better standardization of the conduct of clinical trials and facilitate registration and approval of new pharmacological treatments for hand OA. For inclusion in clinical trials, we recommend that patients fulfill the validated American College of Rheumatology criteria for the diagnosis of hand OA, which are currently the best available criteria. Trials of symptom modifying agents should assess effect on pain as the primary outcome, which could be measured either on a visual analogue scale or the Australian/ Canadian hand pain subscale. Secondary outcomes are multiple, and could include physical function, hand strength and health-related quality of life. The trial should be placebocontrolled and for a minimum duration of 3 months for a fast-acting drug, and not less than 6 months for a slowacting drug. For structure modifying agents, the optimal study duration is for 2 to 3 years to identify structural changes. The primary endpoint of structure modifying trials should measure effect on joint structure independent of any effect on symptoms, which can be included as secondary endpoints.

Conclusions

This consensus guideline is intended to provide a reference tool for practice, and should allow for better standardization of the conduct of clinical trials in hand OA. While the working group acknowledges that the methodology for performing clinical trials in hand OAwill evolve as knowledge of the disease increases, it is hoped that this guidance will support the development of new pharmacological treatments targeting hand OA.