ABSTRACT

World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (WCO-IOF-ESCEO 2021): ESCEO Symposium Abstracts

ESCEO1
SIMILARITIES AND DIFFERENCES BETWEEN THE OARSI AND ESCEO GUIDELINES FOR THE MANAGEMENT OF KNEE OSTEOARTHRITIS

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Objectives: Knee osteoarthritis (OA) is a highly heterogeneous disease known to have significant impacts on quality of life. With newly published data and the identification of new OA phenotypes, the management of knee OA has become increasingly challenging. Two international organisations updated their treatment algorithms in 2019 for the non-surgical management of knee OA; (i) the Osteoarthritis Research Society International (OARSI) and (ii) the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Our aims were to examine the similarities and differences between these two guidelines and provide a narrative to help guide healthcare providers through the complexities of non-surgical management of knee OA.

Methods: A joint working group comprising selected authors of the 2019 OARSI and ESCEO guidelines as well as independent members convened for a 1-day meeting and jointly reviewed these guidelines (November 13, 2019). A comprehensive discussion was held among all members of the working group to discuss the treatment algorithms and the methodological approaches used to formulate recommendations in the OARSI and ESCEO guidelines. The working group was convened and funded by ESCEO.

Results: OARSI and ESCEO both recommend education, structured exercise and weight loss as core treatments, topical NSAIDs as first-line treatments and oral NSAIDs and intra-articular injections for persistent pain. Low-dose, short-term acetaminophen, pharmaceutical grade glucosamine and chondroitin sulfate are recommended by ESCEO. OARSI strongly recommends against the use of all glucosamine and chondroitin formulations and conditionally recommend against acetaminophen use. If symptoms persist, ESCEO recommended the short-term use of weak opioids (e.g. tramadol) whilst OARSI makes no such recommendation due to a poor safety profile and lack of treatment efficacy.

Conclusions: The guidelines agreed in the majority of their recommendations providing a framework of local guideline production. There were some differences that were thought to be predominantly the result of differences in guideline methodology. These algorithms provide a useful guide for patients and healthcare providers for the non-surgical management of knee OA.

ESCEO2
HOW CAN WE EXPLAIN THE DIFFERENCES BETWEEN THE OARSI AND ESCEO GUIDELINES FOR THE MANAGEMENT OF KNEE OSTEOARTHRITIS?

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Purpose: Knee osteoarthritis (OA) is a highly heterogeneous disease known to have significant impacts on quality of life. With newly published data and the identification of new OA phenotypes, the management of knee OA has become increasingly challenging. Two international organisations updated their treatment algorithms in 2019 for the non-surgical management of knee OA; (i) the Osteoarthritis Research Society International (OARSI) and (ii) the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Our aims were to examine the similarities and differences between these treatment algorithms for the non-surgical management of knee OA.

Methods: A joint working group comprising selected authors of the 2019 OARSI and ESCEO guidelines as well as independent members convened for a 1-day meeting and jointly reviewed these guidelines (November 13, 2019). The working group was selected for its experience across rheumatology and orthopaedics, knowledge of recommendations/guidelines for the management of OA, and was thought to be representative of the wider, international OA field. A comprehensive discussion was held among all members of the working group to discuss the treatment algorithms.

Results: Both the 2019 OARSI and ESCEO guidelines were constructed to provide a practical algorithm to help guide clinicians in their decision-making for the treatment management of knee OA. Both guidelines aimed to deliver patient-centred recommendations with both presenting personalised recommendations based upon a patients gastrointestinal and cardiovascular risk profile. OARSI further considered frailty and widespread pain/depression comorbidities whilst ESCEO also tailored treatments to participants aged over 75 years (this age group was not considered separately by OARSI). Both organizations used well-characterised procedures for the reporting of the treatment guidelines; however, some key differences were observed; these are summarised in Table 1. Specifically, there were differences in the constitution of the panel(s), literature search strategies used, voting procedures and scaling of the treatment recommendations.

In a stepwise manner, both OARSI and ESCEO recommended education, the provision of arthritis-related information, structured exercise and weight loss (if overweight) as core treatments (see Table 2). Both recommended topical non-steroidal anti-inflammatories (NSAIDs) as first-line treatments with non-selective NSAIDs and intra-articular injections recommended in those with persistent pain. OARSI, however, recommended topical NSAIDs as the first pharmacological treatment whilst ESCEO did not. Low-dose, short-term acetaminophen, pharmaceutical-grade glucosamine and chondroitin sulphate were recommended by ESCEO whilst OARSI strongly recommended against their use (all formulations). If symptoms persist, ESCEO recommended the short-term use of weak opioids (e.g. tramadol) whilst OARSI makes no such recommendation due to a poor safety profile and lack of treatment efficacy. OARSI does, however, recommend the use of duloxetine only for patients who have knee OA and widespread pain and/or depression.

Conclusion: The guidelines agreed in the majority of their recommendations providing a framework of local guideline production. There were some differences that were thought to be predominantly the result of differences in guideline methodology. These algorithms provide a useful guide for patients and healthcare providers for the non-surgical management of knee OA.

ESCEO3
PATIENTS TO BE INCLUDED IN CLINICAL TRIALS ASSESSING THE SAFETY AND EFFICACY OF NEW CHEMICAL ENTITIES AIMING AT THE TREATMENT OF SARCOPENIA

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Objective: Choosing the population to be enrolled in trials on sarcopenia

Material and methods: Clinical development of agents aiming at the treatment of sarcopenia has been facing several issues hampering the identification of valuable drugs to fight the disorder, thus delaying the requirements for marketing authorisation. Selection of the adequate population to study is challenging. The characteristics of the population vary depending on (a) the phase of the development plan (early proof of concept/dose finding or later confirmatory studies), (b) the expected mode of action/specific clinical setting, and (c) study duration. Patients with a "sarcopenic risk profile" are the starting requirement (choice of diagnostic criteria and diagnostic tools), followed by the disease stage where the intended intervention is likely to be effective (ambulant patients), and amenable for detection of efficacy (selection of efficacy tools and study duration). For the confirmatory phase 3 trials, characteristics that mimic the general sarcopenic population (including some frequent comorbidities) should also be present: the required external validity of these studies pays off the increased heterogeneity and resulting higher sample size.

Results: Diagnostic criteria are based on muscle strength and physical performance, rather than muscle mass; tools for each criterion (such as handheld dynamometer or gait speed) have been selected and their cutoffs proposed. Other characteristics include both genders, being above 70 years of age, ambulant, not recovering from acute disorders, with no mobility impairment due to other reasons than sarcopenia (e.g., osteoarthritis, Parkinson's disease), fair nutritional status and without near terminal disorders; these rely on the population risks that the drug is expected to mitigate, the impact that some disorders may have on the tools assessing efficacy and the fact that patients should be sufficiently fit so that they will reach the end of the study period.

The inclusion/exclusion criteria should convey robust samples with low dropouts, enhancing the effect of the intervention. In phase 3 trials, the population must also be sufficiently broad to allow extrapolation to the intended sarcopenic population.

References: Reginster JY, et al. https://doi.org/10.1007/s40520-020-01663-4.

Disclosures: Mário Miguel Rosa is a member of the Scientific Advice Working Party at the European Medicines Agency

ESCEO4

PRIMARY AND SECONDARY ENDPOINTS FOR CLINICAL TRIALS ASSESSING THE SAFETY AND EFFICACY OF NEW CHEMICAL ENTITIES AIMING AT THE TREATMENT OF SARCOPENIA

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Objectives: A working group under the auspices of the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) was convened to provide updated recommendations on the conduct of clinical trials investigating new treatments for sarcopenia.

Methods: Based on a comprehensive literature search of pharmacological interventions aimed at sarcopenia treatment the working group discussed and agreed on the most appropriate study design.

Results: Phase II trials provide proof of concept and identify the optimal dose for further investigation in phase III. A number of endpoints may be chosen to evaluate preliminary efficacy data, usually surrogate outcomes related to the drug's mode of action. Examples include measures of improvement of physical performance, muscle strength, mass or quality, and biomarkers of muscle metabolism and muscle-bone interaction.

The objective of phase III trials is to confirm evidence of efficacy and safety. Primary endpoints document clinically relevant outcomes tested for statistical significance in appropriately sized patient groups. We advise to use co-primary endpoints assessing both an objective amelioration of physical performance, which is a surrogate for hard clinical endpoints such as mortality, falls and fractures, as well as a subjective Patient Reported Outcome Measure (PROM). Physical performance may be captured by the 400-m walk test or by the Short Physical Performance Battery. For PROMs, we suggest two different sarcopenia-specific instruments, i.e. the Age-Related Muscle Loss questionnaire and the SarQoL questionnaire. Secondary endpoints can be based on efficacy variables employed in phase II.

Conclusions: Randomised double-blind placebo-controlled trials are expected to robustly establish efficacy as determined by co-primary endpoints of physical function and PROMs. Various secondary endpoints may deliver additional clinically relevant supportive information.

References: Update on the ESCEO recommendation for the conduct of clinical trials for drugs aiming at the treatment of sarcopenia in older adults. Reginster et al. Aging Clinical and Experimental Research, https://doi.org/10.1007/s40520-020-01663-4