

Re-evaluation of the current guidelines for the registration of structure-modifying drugs in osteoarthritis

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Recent innovations in the pharmaceutical drug discovery environment have generated new chemical entities with the potential to become disease-modifying drugs for osteoarthritis (DMOAD). Regulatory agencies acknowledge that such compounds may be granted a DMOAD indication, providing they demonstrate that they can slow down disease progression. Progression would be calibrated by a surrogate for structural change, by measuring joint space narrowing on plain X-rays, with the caveat that this effect on JSN translates into a clinical benefit for the patient. The Group for the Respect of Ethics and Excellence in Science (GREES) suggested that Magnetic Resonance Imaging (MRI) may be used as an outcome in phase II studies but that further data is needed before accepting MRI as a primary end-point in phase III clinical trials. The GREES emphasises the importance of acquiring additional information on biochemical markers in order to help better understanding of the mode of action of drugs to be used in OA. The GREES do not recommend time to joint surgery as a primary endpoint of failure for DMOAD in hip or knee OA, as the parameter has sensitivity but lacks specificity. In contrast, a lack of progression of joint space narrowing has a predictive value above 90 % for not having surgery. The primary endpoint should remain the demonstration of a significant difference compared to placebo, in the mean JSN, over a period of 2-3 years.

