Title

Comment on: CONVENTIONAL AND BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS FOR OSTEOARTHRITIS: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS: Reply

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Disclosure statement – MD reports a grant from AstraZeneca funding a non-drug PI-led study in Nottingham (Sons of Gout study) and honoraria for Advisory boards on osteoarthritis and gout for AstraZeneca, Grunenthal, Mallinckrodt, and Roche, outside the submitted work. WZ reports honoraria for Grunenthal and speaker fees for Bioiberica and Hisun, outside the submitted work. All other authors have declared no conflicts of interest.

SIR,

We are grateful to Drs Tecer and Kucuk for their interest and comment on our recent publication on disease-modifying anti-rheumatic drugs (DMARDs) for osteoarthritis (OA).(1)

We agree with the current view that identifying distinct phenotypes in OA, which have different responses to mechanistically diverse treatments, is an important aim in optimising the management of people with OA. In relation to DMARDs, the major endo-phenotypic variable of interest is the presence of joint inflammation.(2) The epitome of OA driven by inflammation is erosive hand OA. We therefore conducted a subgroup analysis of individuals with erosive hand OA and did not find a difference between DMARDs and placebo for this phenotype. Although limited by a small sample size (n=193), the findings were markedly homogenous (I^2 = 0.0%, p value 0.846). This suggests that inflammation in OA is different from that in RA.

Certainly, it is widely accepted that some individuals with OA report neuropathic-like pain. Its prevalence in people with knee OA varies by population, but generally affects a minority of individuals.(3) In our location in the East Midlands, United Kingdom, the prevalence of neuropathic-like pain in community-derived people with chronic knee pain is 14%.(4) Unfortunately, we were unable to examine people with neuropathic-like pain separately in our meta-analysis as this was not measured or reported for the trials. However, it is unlikely that the presence of this type of pain, estimated to affect 23% of study populations,(3) would explain the lack of efficacy of DMARDs for pain relief in OA. In fact, similar rates of neuropathic-like pain have been reported in rheumatoid arthritis (RA) and other inflammatory arthritides (5) for which DMARDs are commonly used. Therefore the reasons why DMARDs are effective for RA, but not OA, cannot be fully explained by the presence of neuropathic-like pain in OA.

Nevertheless, better characterisation of pain phenotypes in OA patients is important and we suggest that clinical trials should assess important baseline characteristics that may serve as subgroup factors, such as the presence of neuropathic-like pain, synovitis, and pain elsewhere. Such information may not be of primary interest for individual trials, however, its assessment would provide an excellent opportunity for future individual patient data meta-analyses to identify predictors of treatment response.

In conclusion, further research on predictors of response to treatments is important and should be facilitated by the assessment of potential predictors in all clinical trials in OA, irrespective of whether these baseline measures are useful for the individual trials.

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