Response to Letter to the Editor: “Transdermal buprenorphine plus oral paracetamol vs an oral codeine–paracetamol combination for osteoarthritis of hip and/or knee: a randomised trial. Comments on the article by Conaghan et al.”

We thank Endenburg and colleagues for their interest in our trial and they raise a number of important issues. A question was raised on how optimal pain control with minimal side effects was defined within the study. This was a collaborative judgement between the Investigators and patients. Investigators would up or down titrate the subjects’ dose at the end of each titration week based on escape medication use, pain scores and reported adverse events. If either the investigator or the subject were unsure as to whether optimum pain control had been achieved, the patient would remain on the same dose for a further week. Clearly this dialogue included individual patient acceptance of a given level of side effects.

In order to address the question regarding the (expectedly large) number of patients who were lost to follow up, the full analysis population was also presented in the original publication for the primary endpoint. The missing box-scale (BS)-11 pain scores and escape medication use from the subject diary cards were replaced by the last observation carried forward (LOCF). Missing observations due to discontinuation were extrapolated to study completion (Day 84, Week 12).

We can provide further information on the baseline patient characteristics. There were no data collected on the patient’s level of education, duration or severity of osteoarthritis (OA). Patients were eligible for entry into the study if they had a clinical diagnosis of OA. The severity of OA was not recorded, as a pain score of ≥5 on the BS-11 pain scale at study entry was used as one of the entry criteria for assessing eligibility for inclusion within the study. The primary pain site for patients entering the study was OA of the hip(s) and/or knees. Body mass index was similar between groups with a mean weight at baseline of 81.35 kg in the 7-day buprenorphine patch plus oral paracetamol group and 83.54 kg in the co-codamol group. The WOMAC questionnaire was an exploratory analyses and the mean scores for all components of the WOMAC questionnaire showed that subjects in both treatment groups had a decrease between baseline and the end of the observation period. At baseline mean (SD – standard deviation) scores were 174.2 (52.71) in the 7-day buprenorphine patch plus oral paracetamol group and 184.1 (50.31) in the co-codamol group. By the end of the titration period, these had decreased to 85.5 (53.81) and 104.8 (50.31), respectively. At the end of the assessment period, the scores were 130.9 (73.91) in the 7-day buprenorphine patch plus oral paracetamol group and 141.2 (71.05) in the co-codamol tablets group. Compliance was not a formal endpoint of the study. However compliance was shown to be poor for anti-emetic use. Patient diaries and returned clinical supplies indicated that many patients did not take these as advised.

With respect to the total number of patients that were screened, the protocol didn’t stipulate the collection of numbers screened or reasons for screening ‘failure’. Patients were informally screened by a general practitioner going through the entry criteria with the patient. All patients were enrolled at formal screening, so we have no data on screening ‘failures’.

Author contributions

All authors contributed to the drafting and content of this letter and gave final approval for the manuscript.

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The original clinical study was designed and funded by Napp Pharmaceuticals.

Conflict of interest

PG Conaghan has participated in osteoarthritis advisory boards and/or speaker meetings for Amgen, AstraZeneca, Bioiberica, Mundipharma and Servier.

CM O'Brien received payment from Napp Pharmaceuticals Limited for her role as Study Statistician. M Wilson is Executive Director of European Medical Operations at Mundipharma Research Limited. JP Schofield is Medical Director at Napp Pharmaceuticals Limited. Mundipharma Research Limited and Napp Pharmaceuticals Limited are independent associated companies.

Reference


PG Conaghan*, C.M. O’Brien, M. Wilson, J.P. Schofield
University of Leeds, Section of Musculoskeletal Disease, Chapel Allerton Hospital, Leeds, West Yorkshire LS7 4SA, United Kingdom

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