Author's response to reviews

Title: Transdermal fentanyl for the treatment of pain caused by osteoarthritis of the knee or hip, an open, multicentre study

Authors:

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Author's response to reviews: see over
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Response to reviewers’ comments

Reviewer: Tuan V Nguyen

1. A CONSORT diagram has been included and, as far as possible, we have abided by the CONSORT guidelines.

2. This was an open study -- the rationale for this, and citations to previous studies, have been added in the 1st paragraph of the discussion.

3. Variation by centre/investigator was checked using ANCOVA and found not to be significant. A note has been added in the statistical methods section.

4. A table has been added (new table 2) as requested. Details of AEs have been added to the abstract.

5. The column headings on Table 2 have been clarified -- the second column is not the endpoint score but the change from baseline to endpoint. Confidence intervals have been added.

6. Confidence intervals have been added to Table 3 (now table 4).

Reviewer: Robert Theiller

1. WOMAC sub-item scores are now shown in Table 4.

2. Since this was an uncontrolled study, it is not possible to calculate relative effect size, however the absolute effect size has been given (p. 12) and more detail about the proportion of patients who improved by at least one pain category have also been provided.

3. Cognitive effects and dizziness are relatively common when starting strong opioids. We have added information that there were no falls or fractures which might be a concern with dizziness.

We have made all the minor revisions requested

Reviewer: Serge Perrot

1. Previous treatment was at the investigators’ discretion. Some patients may have received higher doses of weak opioids at an earlier stage but lowered the dose because of side-effects. Furthermore, the starting dose of 25mcg/h fentanyl corresponds with a maximum dose of weak opioid, so it would not really make sense to titrate up and convert on the basis of equianalgesic dose. Also, there is no evidence that high doses of weak opioids cause less side-effects or are more efficacious than low dose strong opioids.

The rationale to switch to fentanyl was inadequate pain control despite current analgesia. Since this was a naturalistic study, participants were not forced to use the
maximum dose of weak opioids before switching to fentanyl.

We agree that the benefits of metoclopramide are unclear.

The initial run-in period allowed treatment optimization and reduced the possibility that improvements were due to improved pain management rather than the new treatment.