Author's response to reviews

Title: Dose patterns in subjects chronically exposed to opioids: a large cohort study in the United States

Authors:

M Soledad Cepeda (scepeda@its.jnj.com)
Mila Etropolski (metropol@its.jnj.com)
Rachel Weinstein (rweinst1@its.jnj.com)
Daniel Fife (dfife@its.jnj.com)
Raymond Boston (drrayboston@yahoo.com)
Amy Matcho (amatcho@its.jnj.com)

Version: 2 Date: 17 September 2009

Author's response to reviews:

September 17, 2009

Doctor
Melissa Norton
Editor-in-Chief
BMC Palliative Care

Doctor Norton,

Dr. Robin Cassady-Cain the In House Editor of BMC Medicine stated in his response to our previous submission to BMC Medicine that he had copied over the details of our manuscript to BMC Palliative Care. We would like to proceed with the review process in BMC Palliative Care.

Little data exist on how stable opioid dose is with chronic exposure. Studies that have evaluated opioids for the treatment of chronic pain usually have limited follow-up periods (weeks) and in the trials with longer follow-up periods, lack of generalizability has been identified as a substantial limitation. This manuscript helps fill this gap in knowledge. We characterized opioid dose in patients chronically exposed using the PharMetrics database, the largest health care claims database in United States. We evaluated more than fifty thousand subjects who received at least 2 strong opioid prescriptions in 2000 and we examined their opioid dispensings for up to 8 years of follow-up.

The Editorial Board members comment was “Dose escalation cannot be well demonstrated when patients are only assessed every 6 months since cancer patients usually die within this interval and therefore a considerable number of patients considered "intermittent" in their study may in fact be "continuous" undetected due to time between assessments".
We indeed have continuous prescription information while the patient is enrolled. We chose to do the analysis in 6-month periods due to the lengthy follow-up observed in most patients. We fully agree with the need to assess whether the loss of subjects who for any reason did not continue to the next 6-month period could impact the results. This is why we examined separately the dose of opioids for subjects who remained in the cohort during all or part of the next 6-month period from subjects who, for any reason, did not continue to the next 6-month period. We found that the opioid dose among subjects whose exposure ended in a given 6-month time period was similar to the opioid dose among subjects who remained exposed in the next 6-month time period. We did not modify the manuscript as this analysis was already included.

We hope that you find our response to the concern appropriate. We look forward to your response,

M. Soledad Cepeda, M.D., Ph.D
Associate Director Epidemiology
Johnson & Johnson Pharmaceutical Research and Development
1125 Trenton Harbounrton Rd, Titusville, NJ 08560
Office: E30001
Tel: 609 730 2413
Fax: 609 730 7927
E-mail: scepeda@its.jnj.com