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LETTER TO THE EDITORS

Further research on Xyrem®/sodium oxybate treatment of patients with obstructive sleep apnea is needed

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To the editor:
We are happy to respond to Zvosec and colleagues about this paper as we have recently done for their concerns about our related paper [1].

The number of patients with adverse effects in the Phase 1 - single dose Xyrem® - study was listed in the original manuscript (last paragraph of Results). A tabular format was not used. Dr Zvosec and colleagues continue to raise concerns about the actual number of patients who withdrew due to adverse events (AEs). In the Phase 1 study " Nine patient withdrew due to adverse evenrts (AEs) and one for protocol violation." - (last sentence, 1st paragraph Results [1]). There was an error in numbers reported later in that paper as correctly noted by Zvosec and we addressed that in our reply to them previously.

Concerning the current paper, Figure 1 lists 10 patients excluded and suggests all were excluded due to AEs. In fact this should be 9AEs plus 1 protocol violation as noted (vide supra)

Adverse events were collected at each visit and coded using Medical Dictionary for Regulatory Activities dictionary (MedDRA version 8.0) (this was noted in the Legend of Table 3). As Zvosec will know, any and all adverse events, however trivial and even when not related to medications, are reported in any drug safety study. In this case, the event listed under the headings 1) "injury, poisoning, and procedural complication" and 2) "limb injury" are one in the same and was not related to Xyrem®

With respect to reporting of AHI and SaO2, we reported mean and standard deviations for these values. Given that the inclusion criteria already constrained the ranges for AHI and SaO2 and given that the mean and standard deviations were decreased for AHI (unchanged for SaO2) with treatment, we did not think that including ranges for these values would add substantially to the data.

We agree that not withstanding these results, physicians still need to exercise caution and be aware of potential respiratory depression when prescribing Xyrem® to patient with or at risk for sleep disordered breathing. We do not disagree, in fact have previously stated [2], that there may be a subset of patients that are more susceptible to Xyrem® and agree that a prospective study of extended use of doses of 9 g per night will go a long way to allay fears of respiratory depression.

CFP George, NT Feldman on behalf of the authors

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