Dr Andrade Replies

To the Editor: I appreciate the thoughtful comments on my appraisal of baclofen,[1] offered by Drs Braillon and Naudet. With regard to their first point, the ALPADIR study[2] was admittedly as large as the Bacloville study[3] and did study high dose baclofen but was dissimilar to the Bacloville study in many other regards. For example, the ALPADIR study recruited abstinent alcoholics rather than current drinkers, did not limit recruitment to high-risk alcohol consumption, used a lower target dose of baclofen, and was shorter in duration. In any case, the ALPADIR study was included in the meta-analyses that were discussed in my article, including meta-analyses that examined benefits with high dose baclofen. There was therefore no call to draw especial attention to the ALPADIR study.

With regard to the second point, my article did cite the detailed critique of the Bacloville study[4] as well as the careful, point-by-point response of the authors.[5] Given that the responses appeared reasonable, there did not seem to be a need to repeat the criticisms and the refutations in my article; interested readers could visit the references and judge for themselves. That the data were "tortured" is a presumption, and, in any case, as I showed in my strong criticisms of the primary and secondary analyses, even if the data were improperly analyzed, the statistical analysis presented by the Bacloville authors was actually disadvantageous to their objectives. As a further note, my discussion on and interpretation of the analyses differed from what was presented by the Bacloville authors.

With regard to the third point, the advantage over placebo by, for example, a drink a day in the baclofen arm must be viewed from the perspective of the considerable number of placebo patients who switched to open-label baclofen while continuing to be analyzed as placebo patients. This is another example of the plan of analysis being disadvantageous to the study authors; a larger advantage for baclofen may have been identified had the data from switchers been differently analyzed.

With regard to the fourth point, in both abstract and text I drew readers' attention to the elevated risk of serious adverse events, including death, with high dose baclofen. There were too few deaths in the Bacloville study for meaningful conclusions to be drawn. With regard to the cohort study by Chaignot et al,[6] greater mortality with baclofen could have been due to confounding by indication, something that the authors themselves acknowledged; for example, they could not adjust their analyses for indications for drug prescription, for indices of heavy drinking, or for indices of elevated baseline risk. Nevertheless, this subject is definitely a matter of potential concern.

I strongly refute that my commentary promotes off-label use of high dose baclofen. The abstract positioned baclofen as only a possible second-line intervention in only a subset of alcoholics and for only a specific treatment objective; risks were emphasized. The detailed guidance provided in the text was even more heavily nuanced. Finally, the guidance was not stated in a vacuum, it was in line with the Cagliari Statement.[7]

As a final note, the Bacloville study design and analysis were admittedly messy, which was actually the reason for my commentary and take on the study findings (see the Afternotes section in the commentary). There are many lessons to be learnt for investigators who wish to research the subject further, and, yes, I agree that the last word on the subject remains to be said.

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