Baclofen, a French Exception, Seriously Harms Alcohol Use Disorder Patients Without Benefit

To the Editor: Dr Andrade's analysis of the Bacloville trial in a recent Clinical and Practical Psychopharmacology column, in which he concluded that "individualized treatment with high-dose baclofen (30–300 mg/d) may be a useful second-line approach in heavy drinkers" and that "baclofen may be particularly useful in patients with liver disease," deserves comment.[1]

First, Andrade failed to recall that the first pivotal trial of baclofen, ALPADIR (NCT01738282; 320 patients, as with Bacloville), was negative (see Braillon et al[2]).

Second, Dr Andrade should have warned readers that Bacloville's results are most questionable, lacking robustness. Although he cited us,[3] he overlooked the evidence we provided indicating that the Bacloville article[4] was published without acknowledging major changes to the initial protocol, affecting the primary outcome. Coincidentally (although as skeptics, we do not believe in coincidence), the initial statistical team was changed when data were sold to the French pharmaceutical company applying for the marketing authorization in France. As Ronald H. Coase warned, "If you torture the data long enough, it will confess."

Third, expecting that a reduction of, at best, a drink per day versus placebo, if confirmed and if possible in the long term in dependent users, could modify clinically relevant outcomes such as quality of life, morbidity, and mortality when there are already harms such as liver disease flies in the face of common sense.

Finally, the 2-fold increase in mortality with baclofen in Bacloville (highest dose allowed, 180 mg/d) was not significant, the series being short, but was in line with a large-scale pharmacoepidemiologic study in a real-life setting that suggested a dose-dependent increase in mortality with baclofen versus acamprosate and naltrexone.[5]

Individualizing treatment is the cornerstone of care, even more so for patients with substance use disorders, but it is about psychosocial care, to which access must be improved.[6] Promoting off-label use of high doses of baclofen worldwide in a core clinical journal is not serving patients' interests. In our humble opinion, France will remain the only country worldwide where baclofen has a marketing approval for the following reasons: (*a*) the French pharmaceutical company deliberately avoided the usual European marketing approval process and cannot expect an authorization by the US Food and Drug Administration, which relies on robust criteria (abstinence, no heavy drinking days, biochemical markers of alcohol use), and (*b*) the director of the French medicines agency granted a marketing approval despite the Special Scientific Committee's conclusion that the benefits/harms ratio was negative. The Chairman of the Committee commented that he "well understood that the benefit-risk assessment [of baclofen] was only one element, among others [behind the decision]."[2]

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