Clin Drug Investig (2018) 38:385–386
https://doi.org/10.1007/s40261-018-0628-2

LETTER TO THE EDITOR

Nalmefene Phase IV Study: A Seeding Flying in the Face of Evidence?

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Published online: 23 February 2018

Barrio et al. [1] concluded "data provided by this phase IV study (110 patients included, 88 reporting data at the 1-month visit) suggest nalmefene is an effective, well-tolerated treatment for alcohol dependence in real-world, clinical settings". This deserves robust comment.

First, psychological interventions (delivered by appropriately trained and competent staff, based on a relevant evidence-based treatment manual) are the recommended treatment [2].

Second, flawed marketing claims about the effectiveness of nalmefene were seen as early as 2014 and the ineffectiveness of nalmefene has been confirmed by two meta-analyses showing evidence that the reduction in drinking with nalmefene is not different from placebo [3–10]. Pharmacologically assisted treatment for alcohol use disorder is only evidence based for acamprosate, naltrexone and disulfiram, for the maintenance of abstinence. However, long-term multi-factorial life-style interventions, the cornerstone for treatment, are effective [2, 11]. The paradigm of a reduction in drinking, assuming that vulnerable and dependent individuals could reduce their consumption over the long term, is not logical because the duration of the intoxication is a critical issue and alcohol is a human carcinogen (Class 1) with dose-related increases in cancer prevalence being either exponential (e.g. oral cavity, pharynx) or linear (e.g. oesophagus, breast) beginning at one to two drinks per day [12]. This alternative to abstinence, based on an old short-term study with surrogate endpoints, was rapidly dismissed when considering data 1 year after discharge from the study [13]. Long-term phase III studies must use relevant health outcomes (quality of life, accidents/injuries, morbidity), not declarative subjective surrogates. Abstinence remains the appropriate goal for people with alcohol dependence or with psychiatric/physical co-morbidity. Nevertheless, when a patient prefers another approach, he/she should be advised strongly that abstinence is most appropriate, but should not be refused access to care.

Third, Barrio et al. stated "satisfaction was globally high for both professionals and patients, and overall nalmefene was well tolerated, with no serious adverse events reported". However, the lack of detailed information on adverse event screening and monitoring suggest a poor method that may explain the discrepancy with a meta-analysis reporting the threefold increased risk of withdrawal from treatment on nalmefene and an elevated (Peto odds ratio = 1.32) risk of psychiatric serious adverse events, albeit not statistically significant [14].

Four, psychoactive substances are usually used in conjunction, in this instance especially tobacco, the first avoidable cause of premature death. Tobacco cessation treatment improves other substance use, predicting more favourable long-term outcomes [15]. The lack of data about this issue is a major limitation.

This comment refers to the article available at https://doi.org/10.1007/s40261-017-0590-4.

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Administration of a costly placebo must not be an alternative to demanding evidence-based care. Patients with alcohol-use disorders are vulnerable people deserving of psychological interventions. This is possible. The Improving Access to Psychological Therapies (IAPT) programme launched in 2008 in England to offer psychotherapies—largely cognitive-behavioural treatment—is a beacon. It inspired health authorities in Quebec, who recently invested US$35 million to launch its first public psychotherapy program [16]. Spain, as in France, must offer adequate access to psychotherapy.

Funding No source of funding was used to prepare this letter.

Compliance with Ethical Standards

Conflict of interest All authors have no conflicts of interest to declare.

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