Supplementary Material

Imepitoin effectively controls anxiety and fear associated with noise phobia in dogs.

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Results of Per Protocol Analysis

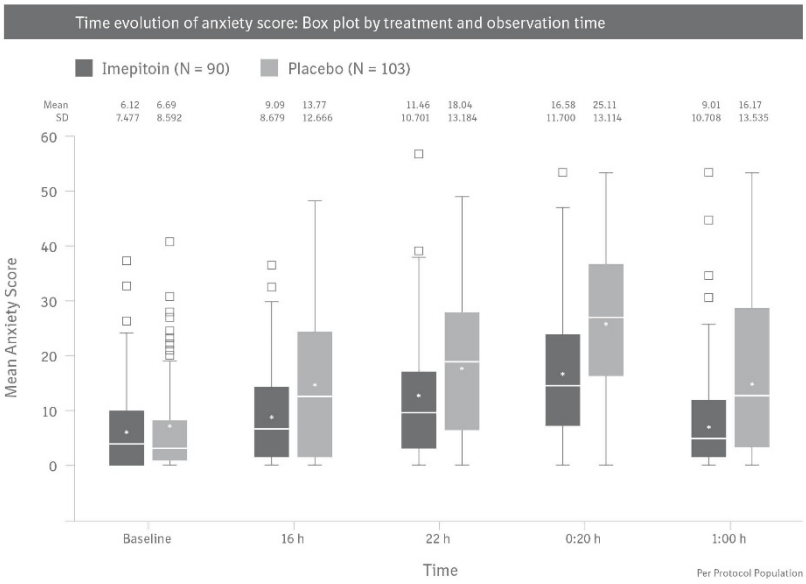
Per Protocol Populations were defined for sensitivity analyses and US-regulatory reasons, where patients with major protocol deviations were excluded. These protocol deviations included insufficient treatment compliance (9 in imepitoin and 9 in placebo group) and administration of other behaviour modifying drugs (1 case in placebo group). In addition, all patients from sites with less than 2 evaluable cases per group were excluded (in total 5 imepitoin and 9 placebo treated animals)

The 1st co-primary endpoint was owner-assessed overall treatment effect (Supplementary Figure 1). The analysis revealed an odds ratio of 4.477 (95%CI (2.34, 8.58), n = 193), which was substantially larger than 1, indicating superiority of imepitoin over placebo (p = 0.0002).

The 2nd co-primary endpoint was time evolution of the owner´s sum scoring indicative for the anxious response of their dogs (Supplementary Figure 2). The data were taken before treatment start (baseline) and post treatment at four consecutive time points during New Year´s Eve. The overall attenuated anxiety level in the imepitoin group was clearly detectable, and accompanied by a smaller data scatter. The negative estimate for the treatment difference of -6.4 (95%CI (-9.7, -3.1)) was significant (p = 0.0008).

The Per Protocol Analysis revealed similar results to the primary analysis, and accordingly substantiates its robustness.

Supplementary Figure 1: Histogram of owner's overall rating of treatment effect in Per Protocol Population.



Supplementary Figure 2: Evolution of anxiety score over time at baseline and on New Year's Eve in Per Protocol Population