Pharmacokinetic profiles of 5 mg/kg ibudilast, a phosphodiesterase inhibitor, orally administered to dogs in fasted and non-fasted states. A preliminary study.

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Abstract

Ibudilast (AV-411) is a non-selective inhibitor of cyclic nucleotide phosphodiesterase (PDE). It is currently marketed for human use in Asian countries for the treatment of asthma, cerebrovascular disorders and ocular allergies. Ibudilast has also been found to have an analgesic action for neuropathic pain at doses 5-10 times higher than those used in asthma therapy. Six healthy Labrador dogs were randomly assigned to two treatment groups using an open, single-dose, two-treatment, two-phase, cross-over design (2x2 Latin-square). Dogs in group 1 (n=3) were fasted for at least 10 hours overnight before the beginning of the experiment and 4 h following dosing while dogs in group 2 (n=3) received food ad libitum. During the first phase, each dog in group 1 and 2 received a single dose of 5 mg/kg ibudilast administered orally. After 1-week washout period the groups were rotated and the experiment was repeated. The analytical method, validated for dog plasma, was shown to be linear in the range 0.10–20 µg/mL. The limit of detection (LOD) and quantification (LOQ) were 0.03 and 0.1 µg/mL, respectively. No behavioural or health alterations were observed in the animals during or after the study. Ibudilast was detectable in plasma for up to 24 h showing a wide variability between animals. Although no statistically significant differences were observed in the present study between the fed and fasted states, examination of the raw data suggests that an effect may be present. The wide degree of variation observed in area under the curve (AUC) suggests that the investigation of population pharmacokinetic modelling is warranted.

Keywords: pharmacokinetics; ibudilast; dog; non-selective cyclic nucleotide phosphodiesterase inhibitor

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