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LETTER TO THE EDITOR

Response to letter regarding "Successful nutritional control of scratching and clinical signs associated with adverse food reaction: A randomized controlled COSCAD'18 adherent clinical trial in the United States" and "Successful nutritional control of scratching and clinical signs associated with adverse food reaction: A randomized controlled COSCAD'18 adherent clinical trial in the United Kingdom"

Dear Editors,

We thank Drs. Olivry, Saridomichelakis and Santoro for their insightful comments regarding our papers in which the recommended outcome measures portion of the COSCAD'18 and other criteria were used to evaluate the efficacy of dietary interventions for dogs with adverse reactions to food (AFR). It was our sincere intent to honor efforts of the International Committee for Allergic Diseases of Animals (ICADA) and the use of core outcome sets[1] to standardize evaluation of an intervention in canine dermatological disease and not to undermine it.

Our studies were controlled, double-masked, multicenter, prospective clinical studies to evaluate the effect of oral food challenge (dietary provocation) in patients with diagnosed AFR. We acknowledge COSCAD'18 was intended for therapeutic trials in moderate-to-severe atopic dermatitis (AD) and AFR studies could not fully fit within this expectation. Although not all dogs with AFR present with AD, dogs with AD and AFR are very similar in their classic clinical characteristics and these phenotypes overlap.[2,3] In a recent retrospective review, most dogs diagnosed with cutaneous AFR were pruritic, most often in a generalized pattern, with the ears, feet, and abdomen also being frequently affected.[4] The CADLI tool utilized in our studies and recommended by COSCAD'18 includes clinical assessment of these key body regions.[5] In our studies, sample size calculations were made assuming a 40% change from baseline for the response variables which is more conservative than the 50% assumption of change recommended in the COSCAD'18 guidelines and thus resulted in a sufficient number of patients being enrolled in our studies to detect a change of at least that size, if one was present. It is generally accepted that an oral food challenge will likely result in relapse of clinical signs within 14 days, thus we designed our studies for a 21-day observation period, instead of only 14 days after the oral food challenge. A recent publication confirms that an oral food challenge is likely to result in relapse of clinical signs of 50% of dogs by day 5, and by 90% or more of dogs by day 14, indicating that the 21-day observation period used in our studies was sufficient to allow for adequate time for clinical signs of relapse to occur.[6] The authors rechecked confidence interval (CI) calculations for CADLI and PVAS (95% CI are based on $\pm\ t[0.05] \times$ SE) and we confirm that these dogs were indeed stable based on CADLI and PVAS scores. In addition, our studies also provided data from a validated, objective measure of scratching behavior, from use of a wearable activity monitor and the results aligned well with results from CADLI and PVAS tools.[7]

These works conform to CONSORT reporting guidelines and contain extensive supporting data. Furthermore, all original manuscripts submitted to this Journal are subject to editorial and peer scientific review as well as consideration by both the editor and co-editor-in-chief assigned to the manuscript; acceptance for publication is dependent upon successful completion of that process.

In the absence of outcome criteria specifically for AFR, the COSCAD'18 criteria of CADLI and PVAS represent a set of well-recognized tools that serve to comprehensively assess clinical flares in dogs with AFR that were subjected to an intervention of dietary provocation in our studies. We would be happy to consider other tools that are appropriate for the clinical assessment of dogs with AFR for future studies and are open to future discussions.

Respectfully submitted,

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