A masked, randomised clinical trial evaluating the efficacy and safety of lokivetmab compared to saline control in client-owned dogs with allergic dermatitis

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Background – Interleukin (IL)-31 is an important mediator in canine atopic dermatitis (cAD) and also may be dysregulated in other allergic diseases.

Hypothesis/Objectives – To demonstrate the efficacy and safety of lokivetmab (canine anti-IL-31 monoclonal antibody) for treatment of pruritus associated with allergic dermatitis in dogs.

Animals – Dogs that were at least moderately pruritic with a presumptive diagnosis of allergic dermatitis were enrolled in Portugal, Hungary, France and Germany by 12 primary care practitioners and two veterinary dermatology referral specialists.

Methods and materials – Dogs were randomised to receive either placebo (saline) or lokivetmab (1.0–3.3 mg/kg) by subcutaneous injection on Day (D)0. Owners evaluated pruritus using a validated Visual Analog Scale (pVAS) daily until D7 and then weekly until D28. The severity of dermatitis was assessed by the investigators using a modified VAS on D0, D7, D14 and D28.

Results – Beginning at D1, owner-assessed pVAS least square means were significantly reduced in the treatment group versus the placebo group (57.7% versus 21.8% reduction on D28). For all time points, investigator-assessed VAS means were significantly reduced in the lokivetmab group versus the placebo group (57.1% versus 20.5% reduction on D28). Overall, the occurrence of adverse health events during the evaluation period was comparable between the two groups.

Conclusions and clinical importance – Lokivetmab is a safe and efficacious treatment for dogs with allergic dermatitis.

Introduction

The pro-inflammatory cytokine interleukin (IL)-31 is produced by activated T lymphocytes in multiple species and its pruritogenic nature has been well-described. By binding to receptors on neurons (receptor complex consisting of IL-31 receptor A and oncostatin M receptor β), IL-31 triggers the activation of Janus kinases, which in turn signal to the brain, triggering an itch response and inducing scratching behaviour. In addition, IL-31 can stimulate the production of inflammatory mediators by promoting epithelial cell responses as demonstrated in transgenic mice overexpressing IL-31, a model in which severe pruritus as well as alopecia and skin lesions are induced. Anti-IL-31 antibodies have been demonstrated in NC/Nga mice (a mouse model for human atopic dermatitis) to reduce or eliminate the pruritic effects of IL-31. A comprehensive global programme has been conducted and reported to demonstrate both safety and efficacy of lokivetmab in dogs with atopic dermatitis (AD), which led to its registration for treatment of clinical manifestations of canine AD (cAD). The mode of action of lokivetmab combined with postmarketing studies on its use in pruritic skin diseases other than cAD, have suggested that it could be a valuable treatment alternative for dogs suffering from other allergic dermatoses. The objective of the study, therefore, was to demonstrate the efficacy and safety of lokivetmab for the treatment of pruritus associated with allergic dermatitis of various aetiologies in dogs.

Methods and materials

The main procedures for the study were similar to previous studies of oclacitinib and lokivetmab, and summarised below. All data were collected in compliance with the principles of the International Cooperation on Harmonisation for Veterinary Medicines (VICH) Good Clinical Practice (GCP) Guideline 9. The protocol was accepted 6 April 2021.

Sources of Funding: This study was initiated and funded by Zoetis Inc. (Parsippany, NJ, USA). The test article (lokivetmab or saline) was provided at no cost to the clinic and clinicians were compensated for the costs associated with each dog’s clinic visit.

Conflicts of Interest: All authors are employees of Zoetis Inc.
Animals were allocated randomly to one of two treatment groups in a priority field study with ciclosporin as the control product.6 With ≥45 lokivetmab-treated dogs and ≥45 controls, there was >80% power to show a 32.72% difference in means for the primary efficacy endpoint of percentage change from baseline owner-assessed pVAS at D28. This outcome assumed mean responses for percentage change from baseline of 16.81% and 49.53% for placebo and lokivetmab, respectively, using a two-sided 5% significance level for the comparison of treatment means at D28.6

### Treatment administration
Lokivetmab was provided as per commercial formulation in single-use vial containing 1 mL that contained no preservative. Vials provided contained solution in one of four concentrations (10, 20, 30 and 40 mg/mL). Based on the dosing chart, each dog was administered 1.0–3.3 mg/kg of lokivetmab depending upon the dog’s body weight.

### Prohibited and conditionally allowed medications and therapies
Withdrawal times for prohibited medications such as (and not limited to) oral and injectable corticosteroids, oclacitinib, ciclosporin and long-acting injectable antibacterials, were as described by Moyaert et al.8 (Table S1). Some treatments were allowed, under the condition that the owners, investigators and other study personnel adhered to minimal use and frequency of use guidelines for the concomitant medication (Table S1).

### Study schedule and variables measured
Baseline data (demographic, physical examination, initial assessment of pruritus and adherence to inclusion criteria) were collected at enrolment on D0. Owners performed an assessment of the severity of their dog’s iitch using the pVAS on D0 (before treatment and repeated approximately 4 h post-treatment), and D1–D7, D14, D21 and D28. This 10 cm long scale had descriptors along its side at 2 cm intervals to help the owners assess the severity of the dog’s pruritus during the past 24 h.12,13 The overall condition of the dog’s skin was evaluated by the investigator on a similar 10 cm VAS scale with descriptors at 2 cm increments adjusted to reflect different severities of skin condition: no (normal dog), very mild, mild, moderate, severe and extremely severe dermatitis (Figure S1).12 Combined with a general physical examination, these investigator-driven assessments were performed on D0, D7, D14 and D28. Dogs were observed for 30 min following administration for signs of immediate adverse reactions to treatment. Abnormal health events (AHE) and/or concomitant treatment reported by owners or identified on physical examination were recorded throughout the study.

On the final day of study (D28, or earlier for dogs withdrawn before D28), the dog’s overall response to treatment (RTT) was assessed by both the owner and the investigator by drawing a vertical line on a horizontal 10 cm scale ranging from “no improvement” to “excellent results”.

A physical examination including body weight was performed at each clinic visit. Any signs of ill health that were not pre-existing (or any change in severity) were reported on an AHE form. The condition of eyes and ears, and skin and appendages attributable to the pre-existing disease of allergic dermatitis was captured on the investigator severity of dermatitis VAS form and treatment differences between both groups reported as such. The investigators were instructed only to report a worsening of the associated clinical signs as an AHE.

Blood samples (haematological and serum chemical parameters) and urine samples (urinalysis and protein creatinine ratio) were collected at enrolment and study completion. Blood and urine were...
collected again at the discretion of the investigator if the dog presented for an AHE. All samples for haematological, serum chemical, urinalysis and urine protein creatinine ratio investigations were sent to the same laboratory.

In cases of suspected secondary bacterial infections, it was recommended to collect a swab sample for standard bacteriological investigation, including antibiogram, through standard veterinary procedures.

**Efficacy outcome measures**

The efficacy dataset excluded those dogs that were considered to have had a protocol deviation that affected the collection or integrity of their efficacy data, such as treatment with prohibited medications or visits performed outside the allowed visit windows. Dogs withdrawn from the study before D28 as a consequence of worsening signs of allergic dermatitis (lack of efficacy) were included in the analysis as failing to achieve 50% or 75% reduction from baseline for all subsequent time points after their withdrawal.

For the owner pVAS, data were summarised for D0, D0+4 h, D1–D7 (±1 day), D14 (±2 days), D21 (±2 days) and D28 (±3 days). For investigator VAS, data were summarised for D0, D7 (±1 day), D14 (±2 days) and D28 (±3 days).

The primary efficacy end-point was defined as the reduction from baseline of the owner-assessed pruritus as measured by pVAS, on D28.

Secondary efficacy end-points included percentage reduction from baseline of owner pVAS and investigator VAS at each time point, proportion of dogs achieving 50% and 75% decrease of owner-assessed pruritus compared at each time point compared to D0, percentage of dogs achieving a “normal range” on the pVAS on each of the study time points, and assessment of overall RTT from the owner and investigator at study completion or withdrawal. Using the pVAS, a score of 0–19 mm was assumed to be the best approximation of a “normal range”.

**Safety outcome measures**

Data from all animals were included in the dataset used for the assessment of safety, independent of the occurrence of protocol deviations. Similar to the study reported by Moyaert et al, frequencies of dogs reported to show at least one AHE were summarised by clinical signs, and frequencies of dogs receiving concomitant medication over the course of the study were summarised by an Anatomical Therapeutic Chemical classification system for veterinary medicinal products (ATC) functional use term.

Summary statistics (means with standard deviations or medians with ranges) were calculated by treatment and intended day of sampling for each haematological, serum chemical and quantitative urinalysis value, reporting the number of dogs that fell below, within or above the normal range (provided by the laboratory) at each day of sampling for haematological and serum chemical parameters specifically. In addition, shift tables provided the number of dogs that had an increased or decreased shift compared to baseline at each day of sampling.

**Data analysis**

Data analysis was performed using SAS v9.4 (SAS Institute; Cary, NC, USA) as described previously. Mixed linear models were fitted using PROC MIXED. Where appropriate, transformations were applied to end-points before statistical analysis as a remedial measure to address violations in the assumptions for the statistical models. The level of significance was set at \( p < 0.05 \) (two-sided).

**Results**

Sixty animals per treatment group were targeted for enrolment to allow for drop-outs and retention of 45 evaluable cases per treatment on D28. Withdrawals were allowed for missed assessments resulting from owner/investigator oversight and exclusions of data resulting from protocol deviations that could have biased the efficacy assessment.

**Aetiology**

The most common presumptive diagnosis was food allergy (41.5%), followed by AD (33.3%, in combination with other aetiologies) and contact allergy (33.3%). Flea allergy was least reported, with only 13.8% of the enrolled cases represented. Distribution of the different aetiologies was similar in both treatment groups (Table S2).

For 29.3% of the animals, an allergic component was identified that could not be assigned to any of the pre-defined categories with the information at hand at the time of enrolment; these were assigned as unspecified allergic dermatitis (in combination or not with any of the other causes).

**Treatment administration**

On D0, the lokivetmab dose ranged between 1.0 and 2.9 mg/kg. Nearly half of the dogs received a dose of 1–1.2 mg/kg (n = 30), 30% (n = 18) received a dose of 1.3–1.5 mg/kg, and only one animal received a dose >2 mg/kg.

**Assessment of effectiveness**

The primary effectiveness dataset at D28 comprised 99 dogs in the owner pVAS dataset (44 control, 55 lokivetmab-treated animals). Eighteen dogs were excluded/missing from the analysis of owner assessments in the control group, and six in the lokivetmab-treated group on D28. The datasets for owner pVAS and investigator VAS changed at each time point as a result of early withdrawals, missing assessments because of owner/investigator oversight (e.g. missed assessment at home or visit skipped) or data excluded from the analysis as a result of protocol deviations that could have biased the efficacy assessment (e.g. forbidden medications given or assessment performed outside the allowed window).

Four animals (one placebo, three lokivetmab-treated dogs) received forbidden medication during the study period and as a result their efficacy data were excluded from the D28 dataset. Data from one additional placebo-treated animal were excluded because the D28 assessment was performed outside of the allowed window (D28 ± 3 days). Data from 16 control animals and three...
lokivetmab-treated dogs were not available because they were withdrawn from the study before D28. All withdrawals were due to the result of worsening or lack of improvement of clinical signs of allergic dermatitis.

**Owner-assessed pVAS**

On D0, the pre-treatment mean pruritus score was 69 in the control group versus 70 in the lokivetmab-treated group. On D28, the least-square (LS) mean percentage reduction from baseline was significantly higher in the treatment group than the control group (57.7%) compared to the placebo group (21.8%; \( P < 0.0001 \)).

For all other time points (beginning with D1), the percentage reduction from baseline of owner-assessed pVAS LS means was significantly greater (\( P \leq 0.0109 \)) in the group of animals treated with lokivetmab versus the group of animals treated with saline, ranging from a 14.5% difference between treatment groups on D1 to a maximum of 37.2% on D14 (Figure 1).

At every study time point beyond D1 (for 50% reduction and/or D2 (for 75% reduction), the proportion of animals achieving \( \geq 50\% \) or 75% reduction in pVAS was significantly higher (\( P \leq 0.0013 \) for 50%; \( P \leq 0.0451 \) for 75%). Treatment success defined as \( \geq 50\% \) reduction in pVAS, achieved a maximum 26% on D6 in the control group, and decreased thereafter. In the lokivetmab-treated group, a maximum of 73% was reached on D14 and averaged between 66 and 70% during the last two weeks of the study period (Figure 2). In the control group, \( \leq 1\% \) of the dogs achieved 75% reduction at any of the time points, while in the lokivetmab-treated group, the percentage of dogs achieving 75% reduction varied between 2% on D0 (4 h post-dosing) to 32% of the animals on D21 (Figure 3).

At all time points after D0, the percentage of dogs achieving a “normal” VAS score was numerically higher in the lokivetmab-treated group compared to the control group. By D28, 45.5% of the lokivetmab-treated dogs were scored as “normal” in terms of level of pruritus versus 6.8% of the saline-treated dogs (Figure 4).

**Investigator severity of dermatitis VAS**

Similar to the pruritus assessment, a reduction in the VAS score reflected an improvement in the condition of the skin. For all time points, the percentage reduction from baseline of investigator-assessed condition VAS LS means was significantly higher (\( P < 0.0001 \)) in the lokivetmab-treated group compared to the control group. In the control group, dogs achieved 14.1, 20.6% and 20.5% reduction on D7, D14 and D28, respectively, compared to D0. In the lokivetmab-treated dogs, the corresponding reductions in percentages were 41.3%, 55.8% and 57.1%.

**Response to treatment (RTT)**

Owner and investigator RTT were significantly higher (\( P < 0.0001 \)) in the treatment group than the control group. Means were 67.8% and 70.1%, respectively, for treated dogs, and 33.1% and 29.9%, respectively, for controls.

**Adverse health events and concomitant medications:**

Overall, the occurrence of AHEs was comparable between both treatment groups: 14.5% in the control group (\( n = 9 \)) versus 11.5% in the lokivetmab-treated group (\( n = 7 \); Table S3).

Two dogs in each group were sampled for bacteriological culture owing to a suspected skin or ear infection, and one in each group subsequently was treated with systematic antimicrobials. For a control dog, a skin infection resulted in withdrawal before D28. Because this animal was withdrawn due to worsening signs of allergic dermatitis (lack of efficacy), it was treated as failing to achieve 50% and 75% reduction from baseline for all subsequent time points. One dog in the treatment group also received systemic antimicrobial therapy and was excluded from the efficacy analysis at all subsequent time points.

Overall, use of concomitant medication was comparable between both treatment groups. In the control group, 15 dogs were treated with oclacinib at the time of early withdrawal due to lack of efficacy. In the lokivetmab treatment group, three dogs received oclacinib as rescue treatment at the time of early withdrawal.

**Haematological and serum chemical investigation, and urinalysis**

For various serum chemical parameters, increasing and/or decreasing shifts were observed, yet these were not clinically significant and generally occurred in both groups. The mean serum chemical values remained within reference ranges at all study time points from D0 onwards.
Increasing and/or decreasing shifts were observed equally in both treatment groups for haematological parameters. Overall, mean values remained within reference range at all study time points from D0 onwards, except for MCHC (mean corpuscular haemoglobin concentration) where the mean value was below the
reference range (32.6–39.2 g/dL) for both control animals (32.3 g/dL) and lokivetmab-treated dogs (32.5 g/dL) on D0, and in the control group (32.5 g/dL) on D28. This was not considered clinically relevant.

Urinalysis did not reveal any concerns for potential treatment-related abnormalities.

Discussion

The objective of this study was to demonstrate the efficacy and safety of lokivetmab for the treatment of pruritus associated with an allergic dermatitis in dogs. The targeted population included dogs with presumptive...
diagnoses of food allergy, flea allergy, contact allergy and AD in any combination, or unspecified allergic pruritus. Diagnoses were established at the discretion of the investigators, who were mainly primary care veterinarians. This approach was deliberately selected to reflect field conditions in general practice, in which lokivetmab might be prescribed and administered. In a recent study following a similar design (with presumptive diagnoses), a comparable distribution of disease aetiology was reported, with approximately 45% of the dogs diagnosed as suffering from contact allergy.13 It is likely that more rigorous diagnostic criteria would have altered the distribution of the diagnoses,17,18 as the prevalence of allergic contact dermatitis is much lower when assessed exclusively by dermatology specialists.19

Results of this study showed significant reduction of owner-assessed pruritus after treatment with lokivetmab compared to placebo (saline) control. The results are comparable to a prior study which enrolled only dogs with a diagnosis of AD (Table 2).6

In this study, a 53% reduction in pruritus was observed 6 days after the start of lokivetmab treatment which is in line with what was previously reported for oclacitinib (55%).13 Equally, a peak in pruritus reduction was observed 14 days after injection of lokivetmab treatment. The antipruritic activity of lokivetmab remained unchanged after D14, and on D28 there was still a 58% reduction in pruritus in the treated animals. In a nine month field study in dogs with AD, the pruritus score decreased further with subsequent injections and reached a plateau after four consecutive monthly injections.6 A 50% reduction from baseline of mean pruritus score represents a clinically relevant threshold above which owners are satisfied with treatment.20 This percentage has been used subsequently as a standard for assessing the efficacy of treatments for pruritus.21–23 The proportion of animals exhibiting a 50% pruritus decrease on D14 (73%) in this study is nearly identical to the percentage reported for oclacitinib when treating a very similar population of animals diagnosed with allergic dermatitis.13

Another mechanism for determining efficacy is implementation of a threshold for what is considered to be a “normal” animal, where “normal” is defined as obtaining a pVAS score of <2 cm as proposed by Rybnicek et al.16 The percentage of dogs with pruritus scores in the “normal” range on D28 was 45.5% for lokivetmab-treated dogs compared with 6.8% for placebo-treated dogs. This is in line with what has been reported for atopic dogs treated with lokivetmab, where 39% of the animals was assessed as “normal” on D28.6 Therefore, it appears that neutralisation of IL-31 has an antipruritic effect in a broader population of pruritic dogs than just those with a confirmed diagnosis of AD. The data therefore suggest an association between allergic dermatoses in general and IL-31 dysregulation, as reported previously in humans.24,25

In addition to owner-assessed pruritus, the investigators assessed the severity of skin lesions using an unvalidated VAS, as has been described previously.12,13 Validated scales which have been developed for scoring cAD were not employed, because they are specific for cAD. The results of the investigator-assessed dermatitis VAS mirrored the findings of the owners’ pVAS scores, similar to what was observed with oclacitinib.13 This also is consistent with results obtained in dogs with cAD, where lokivetmab treatment had a positive effect on cutaneous inflammation as assessed by reduction of Canine Atopic Dermatitis Extent and Severity Index (CADESI)-03 scores.6,7

In total, 19 dogs were withdrawn from the study before D28: 16 in the control group and three in the treatment group. All were withdrawn owing to progressive or static clinical signs. Treatment failures are to be expected when managing dogs with allergic skin disease, and even drugs with broader modes of action – such as methylprednisolone and ciclosporin – failed to control clinical signs of some dogs with cAD in a trial reported previously.26

The occurrence of abnormal health events was low and comparable between the treatment and placebo groups, and the nonremarkable haematological and serum chemical data also support the safety of lokivetmab, even when used with a wide variety of medicines and vaccines commonly used in canine practice. It is acknowledged that the duration of this clinical trial was limited to 28 days. However, the long-term safety and efficacy of lokivetmab has been demonstrated previously in field trials where dogs with cAD were treated and evaluated for up to nine months.6

In conclusion, the results of this study demonstrate that neutralisation of IL-31 has an antipruritic effect in a broader population of dogs than just those with a confirmed diagnosis of cAD. In addition to alleviating pruritus, lokivetmab also reduces inflammatory skin lesions. It therefore is a safe and efficacious therapy for the treatment of dogs with various allergic dermatitides.

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Table 2. Summary of the different efficacy outcomes after treatment with lokivetmab in atopic and allergic animals for owner assessment of pruritus Visual Analog Scale (pVAS) on Day 28

| Efficacy outcome                              | Atopic dermatitis (Moyaert et al., 2017) | Allergic dermatitis |
|----------------------------------------------|------------------------------------------|---------------------|
| % reduction in pVAS compared to baseline LSM | 51.9                                     | 57.7                |
| 50% reduction in pVAS LSM proportion of dogs | 0.57                                     | 0.70                |
| 75% reduction in pVAS LSM proportion of dogs | 0.23                                     | 0.31                |
| % normal pVAS (0–19 mm)                      | 39.3                                     | 45.5                |

LSM least-square mean.
Résumé

Contexte – L’interleukine (IL)-31 est un médiateur important de la dermatite atopique canine (cAD) et peut aussi être déréglé dans d’autres dermatoses allergiques.

Hypothèses/Objectifs – Démontrer l’efficacité et l’innocuité du lokivetmab (anticorps monoclonal canin anti-IL-31) pour le traitement du prurit associé aux dermatites allergiques chez le chien.

Sujets – Les chiens qui étaient au moins modérément prurigineux avec un diagnostic présumé de dermatose allergique ont été enrôlés au Portugal, Hongrie, France, Allemagne par 13 praticiens généralistes et un vétérinaire spécialiste en dermatologie.

Matériaux et méthodes – Les chiens ont été randomisés pour recevoir soit le placebo (solution saline) soit du lokivetmab (1.0–3.3 mg/kg) par injection sous cutanée à Jour (D) 0. Les propriétaires ont évalué le prurit
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zu l’aide d’une échelle visuelle analogue (pVAS) validée une fois par jour jusqu’à D7 puis une fois par semaine jusqu’à D28. La sévérité de la dermatite a été évaluée par les investigateurs à l’aide d’une VAS modifiée à D0, D7, D14 et D28.

**Resultats** – Au départ à D1, la moyenne de pVAS des propriétaires étaient significativement diminuées dans le groupe traitement contre le groupe placebo (57.7% contre 21.8% de réduction à D28). À tous les moments, les moyennes de VAS par les investigateurs étaient significativement diminuées dans le groupe lokivetmab contre le groupe placebo (57.1% versus 20.5% de réduction à D28). En outre, les effets indésirables au cours de la période d’évaluation étaient comparables entre les deux groupes.

**Conclusions et importance clinique** – Le lokivetmab est un traitement sûr et efficace pour les chiens avec dermatite allergique.

**Zusammenfassung**

**Hintergrund** – Interleukin (IL)-31 ist ein wichtiger Mediator bei der atopischen Dermatitis des Hundes (cAD) und kann auch bei anderen allergischen Erkrankungen eine Dysregulation aufweisen.

**Hypothese/Ziele** – Es sollte die Wirksamkeit und die Sicherheit von Lokivetmab (caniner anti-IL-31 monoklonaler Antikörper) zur Behandlung von Juckreiz im Zusammenhang mit allergischer Dermatitis beim Hund gezeigt werden.

**Tiere** – Hunde mit zumindest moderatem Juckreiz und der vermeintlichen Diagnose einer allergischen Dermatose wurden in Portugal, Ungarn, Frankreich und Deutschland von 13 Haustierärzten und einem veterinärmedizinischen Überweisungstierarzt ausgewählt.

**Methoden und Materialien** – Die Hunde wurden zufällig ausgewählt, um entweder Plazebo (Kochsalzlösung) oder Lokivetmab (1.0-3.3 mg/kg) mittels subkutaner Injektion am Tag (D) 0 zu erhalten. Die BesitzerInnen evaluieren den Juckreiz mittels Visual Analog Scale (pVAS) bis zum D7 täglich und dann wöchentlich bis zum D28. Die Schwere der Dermatitis wurde von den UntersucherInnen mittels modifizierter VAS am D0, D7, D14 und D28 bestimmt.

**Ergebnisse** – Beginnend am D1 war das wenigste quadratische Mittel der durch BesitzerInnen erfassten pVAS in der Behandlungsgruppe im Gegensatz zur Plazebogruppe signifikant reduziert (57.7% versus 21.8% Reduktion am D28). Zu allen Zeitpunkten war der durch die UntersucherInnen erfasste VAS Durchschnitt in der Lokivetmab Gruppe im Vergleich zur Plazebogruppe signifikant reduziert (57.1% versus 20.5% Reduktion am D28). Insgesamt war das Auftreten von Nebenwirkungen auf die Gesundheit während der Untersuchungsphase in beiden Gruppen vergleichbar.

**Schlussfolgerungen und klinische Bedeutung** – Lokivetmab ist eine sichere und wirksame Behandlung bei Hunden mit einer allergischen Dermatitis.

**要約**

**背景** – インターロイキン (IL)-31は、犬アトピー性皮膚炎 (cAD) において重要なメディエーターであり、他のアレルギー疾患においても調節不能である可能性がある。

**仮説/目的** – 本研究の目的は、犬アレルギー性皮膚炎に伴う搔痒症の治療に対するlokivetmab (犬用抗IL-31モノクローン抗体) の有効性および安全性を実証することであった。
题目：Van Brussel et al.

背景 - ポルトガル、ハンガリー、フランス、ドイツにおいて、アレルギー性皮膚炎と推定診断された少なくとも中等度の瘙痒を伴う犬を、13人の獣医アレルギー診断専門医が登録した。

方法と材料 - 犬は、プラセボ（生理食塩水）またはlokivetmab（1.0〜3.3 mg/kg）のいずれかをD0日に皮下注射するように無作為に割り付けられた。臨床者は、有効なVisual Analog Scale（VAS）を用いて、D7までは毎日、その後D28までは週毎に、瘙痒を評価した。皮膚炎の重症度は、D0、D7、D14、D28に調査員が修正VASを用いて評価した。

結果 - D1以降、 indefiniteが評価したpVASの最小二乗平均値は、プラセボ群に対して治療群で有意に減少した（D28で57.7% vs 20.5%）。すべての時点での、治療責任獣医師が評価したVASの平均値は、lokivetmab群がプラセボ群に対して有意に減少した（D28で57.1%vs20.5%）。

結論 - lokivetmabはアレルギー性皮膚炎の犬に対する安全で効果的な治療法である。

Resumo

Contexto - A interleucina (IL)-31 é um importante mediador na dermatite atópica canina (DAC) e também pode estar desregulada em outras doenças alérgicas.

Hipótese.Objetivos - Demonstrar a eficácia e a segurança do lokivetmab (anticorpo monoclonal canino anti-IL-31) para o tratamento do prurido associado a dermatite alérgica em cães.

Animais - Cães com prurido ao menos moderado com diagnóstico presumitivo de dermatose alérgica foram inclusos em Portugal, Hungria, França e Alemanha por 13 veterinários clínicos gerais e um especialista em dermatologia veterinária.

Métodos e materiais - Os cães foram randomizados para receber placebo (solução salina) ou lokivetmab (1.0〜3.3 mg/kg) por via subcutânea no Dia (D)0. Os proprietários avaliaram o prurido diariamente usando uma escala visual analógica (pVAS) validada até o D7 e, a seguir, semanalmente até o D28. A gravidade da dermatite foi avaliada pelos investigadores nos D0, D7, D14 e D28 usando uma VAS modificada.

Resultados - Começando em D1, as médias dos mínimos quadrados de pVAS avaliadas pelos proprietários apresentaram redução significativa no grupo de tratamento versus o grupo placebo (57.7% versus 21.8% de redução no D28). Para todos os tempos experimentais, as VAS médias avaliadas pelos pesquisadores estavam significativamente reduzidas no grupo lokivetmab versus o grupo placebo (57.1% versus 20.5% de redução no D28). No geral, a ocorrência de eventos adversos durante o período de avaliação foi comparável entre os dois grupos.

Conclusões e importância clínica - Lokivetmab é um tratamento seguro e eficaz para cães com dermatite alérgica.