

A double-blinded, randomized, methylprednisolone-controlled study on the efficacy of oclacitinib in the management of pruritus in cats with nonflea nonfood-induced hypersensitivity dermatitis

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Background – Oclacitinib is a Janus-kinase inhibitor that decreases interleukin-31-induced pruritus in cats. At 0.4–0.6 mg/kg/day orally, it decreased pruritus and skin lesions in <50% of allergic cats.

Hypothesis/Objectives – To evaluate efficacy and safety of oclacitinib in feline nonflea nonfood-induced hypersensitivity dermatitis (NFNFIHD).

Animals – Forty cats with NFNFIHD.

Methods and materials – Cats were randomly assigned to receive oclacitinib (group A, 20 cats, 0.7–1.2 mg/kg) or methylprednisolone (group B, 20 cats, 0.5–1 mg/kg) orally twice daily for 28 days. On day (D)1 and D28, lesions were evaluated using the Scoring Feline Allergic Dermatitis (SCORFAD) scale and owners assessed pruritus using a Visual Analog Scale (VAS) and quality of life (QoL) questionnaire. Results were analysed by General Linear Mixed Model ($P < 0.05$). Haematochemical analyses were performed on D1 and D28.

Results – In both groups all parameters improved significantly, with no difference at either time point. Group A had a 61% mean SCORFAD and 54% pruritus VAS improvement, compared with 69% and 67% in group B; 70% of cats in group A and 75% in group B achieved a $\geq 50\%$ reduction of pruritus VAS scores; with 60% and 80% of SCORFAD. There were five non-responders in group A and three in group B. The QoL score improved in both groups (25 and 21%). Four of 14 cats had mild increases in kidney function tests (oclacitinib group) and three of 12 cats had elevated alanine transferase (methylprednisolone group).

Conclusions and clinical importance – Oclacitinib appears to be effective for treating pruritus and lesions in cats with NFNFIHD, albeit methylprednisolone seemed to perform better.

Introduction

Allergic dermatitis due to environmental, food or flea hypersensitivities is commonly encountered in cats. Cases of allergic dermatitis that are not responsive to flea control and to elimination food trials have been called “nonflea, nonfood-induced hypersensitivity dermatitis” (NFNFIHD).¹ Pharmacological treatments for NFNFIHD are variable with the most widely used drugs being glucocorticoids and ciclosporin.² Other therapies that have less consistent efficacy include allergen-specific immunotherapy, fatty acids, palmitoylethanolamide and antihistamines.^{2,3} Among these, glucocorticoids and ciclosporin offer the best results: the former is rapidly effective,

although associated with potentially severe adverse effects when used long term, whereas the latter needs two to three weeks to reach its maximum efficacy and in its liquid form is not always easy to administer.²

In dogs, oclacitinib (Apoquel, Zoetis Italia; Rome, Italy), a Janus-kinase inhibitor which blocks pro-inflammatory, pro-allergic and pruritogenic cytokines such as interleukin (IL)-31, decreases allergic pruritus and improves lesions of allergic dermatitis.⁴ In dogs, oclacitinib has an efficacy comparable to that of prednisone, albeit with fewer adverse effects.^{5,6}

In cats oclacitinib is not licensed (i.e. approved for use) but could provide a treatment alternative for cases in which the few registered drugs do not work, or are difficult to administer or cause unacceptable adverse effects. Oclacitinib per os (p.o.) in cats at 0.4 mg/kg was reported to significantly reduce IL31-induced pruritus.⁷ A preliminary open pilot study assessed the efficacy of oclacitinib in cats with allergic dermatitis: cats >12 months of age and 3 kg body weight were treated with oclacitinib, 0.4–0.6 mg/kg (mean dose 0.47 mg/kg) p.o. twice daily for two weeks, then once daily for another two weeks.⁸ Oclacitinib was reported to suppress pruritus and clinical

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signs associated with skin allergy in < 50% of the cats. Higher dosages have been used in other preliminary studies. A dosage of 1 mg/kg p.o. twice daily for one month was effective in a laboratory cat affected with mastocytosis, whereas a trial with 0.5–1.0 mg/kg p.o. twice daily for 28 days was safe and effective for feline experimentally induced asthma.^{9,10}

The aim of this randomized, double-blinded, methylprednisolone-controlled study was to evaluate the effectiveness and safety of oclacitinib, given at 1 mg/kg p.o. twice daily for four weeks, in cats affected with NFNFIHD. The hypothesis was that oclacitinib at a higher dose than previously reported would be as effective as oral methylprednisolone in decreasing pruritus and skin lesions in cats with skin allergy.⁸

Methods and materials

Animals

Cats >12 months of age and weighing >3 kg, diagnosed with NFNFIHD following procedures and fulfilling published diagnostic criteria for feline allergy were included in the study.¹¹

Cats were not included if they had ectoparasitic diseases, bacterial or fungal infections or if flea-allergy dermatitis was diagnosed. All cats received regular ectoparasite control for at least four weeks before entering the study and tested negative for feline immunodeficiency virus (FIV) and feline leukaemia virus (FeLV). Adverse food reaction was ruled out by means of an eight-week home-cooked or commercial diet trial based on novel protein sources or hydrolysed food. Neither dietary changes nor concurrent treatments were allowed during the trial, with the exception of flea-control products. Cats were not included if they had received long-acting injectable glucocorticoids, ciclosporin or essential fatty acids eight weeks or less before entering the trial and short-acting oral glucocorticoids and antihistamines two weeks or less before inclusion. In addition, pregnant or lactating cats, breeding animals and cats with presence or history of malignant neoplasia were excluded. Cats were not allowed to eat raw meat during the whole treatment period and were not allowed outdoors. Given that oclacitinib is not registered for cats, owners were asked to sign an informed consent form.

Randomization, blinding and treatment procedures

Cats were allocated to group A or group B following a computer-generated randomization sequence of blocks of four cats each. Oclacitinib (Apoquel®, Zoetis Italia) or methylprednisolone tablets (Medrol vet®, Zoetis Italia) were dispensed to the owner in white plastic bottles with identical appearance and labelled (respectively) with an A or a B. Cats in group A weighing ≤4 kg were administered half a 5.4 mg oclacitinib tablet twice daily for 28 days, whereas cats weighing >4 kg received one tablet. Cats in group B weighing ≤4 kg were administered half a 4 mg methylprednisolone tablet twice daily for 28 days, whereas cats weighing >4 kg received one tablet. Veterinarians responsible for the clinical evaluation were masked to the group assignment of the cats.

Evaluation of clinical efficacy

Clinical lesions were assessed by means of the validated scale Scoring Feline Allergic Dermatitis (SCORFAD).¹² Pruritus was scored by the owner by means of a 10 cm-long Visual Analog Scale (VAS) validated for dogs and with descriptors adapted to the cat.^{13,14} Quality of life (QoL) of cats and owners was evaluated by means of a questionnaire validated for cats with skin diseases.¹⁵ All parameters were assessed at the time of inclusion (D0) and at the end of the trial, after 28 days of treatment (D28).

Adverse events and safety assessment

All adverse events including weight loss > 10% of the initial body weight were recorded on the clinical report form and investigated.

Eventual dropouts due to adverse events also were registered. Every cat underwent a complete general and dermatological examination at the beginning and at the end of the study (after D28) and, if permitted by the owner, a haematological and biochemical screening was performed at these timepoints, including complete blood count (CBC), serum glucose (GLU), urea (BUN), creatinine (CREA), total protein (TP), albumin (ALB) and liver transaminases (ALT and ALP) parameters.

Primary and secondary outcomes and statistical evaluation

The primary outcome was the improvement of pruritus VAS scores. Secondary outcomes were improvements of SCORFAD and QoL scores, as well as the number of animals achieving a decrease of pruritus VAS >50%, a pruritus VAS <2, a decrease of SCORFAD <50% or a decrease of QoL scores >5 points. The number of non-responders also was compared between groups.

Using data from a noncontrolled pilot study with a pruritus VAS basal value of 8.5 (± 1.64 SD) and a 95% confidence interval, and considering as a significant result a difference of ≥20% between the two treatments, it was decided to include 20 cats per group for a total of 40 cats. Statistical evaluation of efficacy was performed by means of a General Mixed Linear Model using an Intention-To-Treat Analysis with the last reported value carried forward. Data were analysed using SAS v9.2 (SAS Institute; Cary, NC, USA). The level of significance was set at $P < 0.05$.

Results

Animals, treatment and evaluation of clinical efficacy

Forty cats were enrolled in the study, 20 in group A and 20 in group B. Group assignment, breed, sex, age, weight and duration of clinical signs for each cat are summarized in Table S1. There was no difference in parameters between groups at D0.

Treatments were administered for four weeks: oclacitinib was administered twice daily at a mean total daily dose of 0.9 mg/kg p.o. (range 0.7–1.2 mg/kg) and methylprednisolone at a mean total daily dose of 0.77 mg/kg p.o. (range 0.5–1 mg/kg).

Pruritus VAS, SCORFAD and QoL scores at D0 and D28 for each cat are reported in Table S1. Clinical parameters improved significantly in both groups, with no difference between groups at any time point for any parameter. Mean scores, standard deviation and percent improvement for each parameter and each group are described in Table 1. Score improvement for each SCORFAD reaction pattern is presented in Table 2. A higher number of cats treated with methylprednisolone achieved an improvement of pVAS by ≥50%, a pVAS score ≤2, an improvement of SCORFAD by ≥50%, a SCORFAD score ≤2 or a ≥5-point decrease of QoL score compared to cats treated with oclacitinib (Figure 1). There were five non-responders in group A and three in group B, in which minimal or no improvement was observed.

Assessment of safety

Thirty cats had a complete blood count and biochemistry profile evaluated before therapy; three cats had only a biochemistry profile. Cats that had pre- and post-treatment evaluation for each parameter and cats presenting post-therapy abnormalities beyond reference ranges are presented in Table S2. All changes were considered mild, with the exception of ALT increment in group B. The ALT value was twice the higher reference value in one case

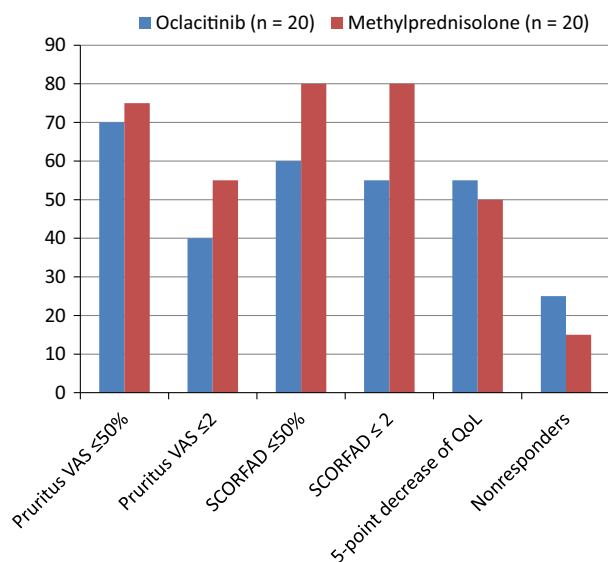
Table 1. Mean pruritus Visual Analog Scores (VAS), lesional scores (Scoring Feline Allergic Dermatitis, SCORFAD) and quality of life (QoL) scores before (D0) and one month after (D28) treatment with oclacitinib or methylprednisolone in cats with allergic dermatitis

Treatment	D0	D28	P	% Improvement
Pruritus VAS (no difference between groups $P = 0.337$)				
Oclacitinib	7.5 (1.5)	3.4 (3)	0.0001	54%
Methylprednisolone	7.3 (1.2)	2.4 (2.7)	0.0001	67%
SCORFAD (no difference between groups $P = 0.154$)				
Oclacitinib	6.2 (2.3)	2.4 (2)	0.0001	61%
Methylprednisolone	4.9 (2.1)	1.5 (1.8)	0.0001	69%
QoL (no difference between groups $P = 0.976$)				
Oclacitinib	21.0 (5.3)	15.8 (7.3)	0.0002	25%
Methylprednisolone	19.6 (7.4)	15.6 (8.5)	0.0002	21%

Standard deviation is shown in brackets.

Table 2. Number of cats presenting a particular SCORFAD reaction pattern, percentage score improvement for each SCORFAD reaction pattern in cats with cutaneous allergy treated with oclacitinib or methylprednisolone for 28 days

SCORFAD reaction pattern	Group A—oclacitinib		Group B—methylprednisolone	
	Number of cats	% Score improvement	Number of cats	% Score improvement
Alopecia	20	57	16	60
Miliary dermatitis	8	71	9	100
Excoriations	14	58	12	80
Eosinophilic plaque	4	78	3	100

**Figure 1.** Percentage of cats in each group showing a decrease of pruritus Visual Analog Score (VAS) or of Scoring Feline Allergic Dermatitis (SCORFAD) by $\geq 50\%$ or to a score ≤ 2 , or showing a decrease of quality of life (QoL) scores of ≥ 5 points, and percentage of non-responders.

and thrice in two cases. There was no significant weight change in any cat.

Adverse events

Adverse events are listed in Table S1. Two methylprednisolone-treated cats were withdrawn prior to D28 for worsening of clinical signs. Their D0 values were carried forward to D28 for evaluation of clinical efficacy. All oclacitinib-treated cats completed the study. Other adverse events that did not cause drop-outs from the study were vomiting (one cat) and lethargy (one cat), both in the methylprednisolone group.

Discussion

To the best of the authors' knowledge, this is the first study assessing the efficacy of oclacitinib given twice daily for one month at 1 mg/kg to treat skin allergy in cats. It should be reminded that oclacitinib is not registered for use in cats and veterinarians need to remember prescribing laws in their country regarding the administration of nonlicensed products.

A previous open study conducted with the canine protocol (0.4–0.6 mg/kg twice daily for two weeks, then once daily) reported a relatively low success rate.⁸ In that study the average SCORFAD improvement was 22% and the average pruritus VAS improvement was 18%, much lower than 61% and 54%, respectively, as observed in this study. The reasons could be two-fold: first, the mean dose in our study (0.9 mg/kg/day) was higher than that used in a previous study (0.47 mg/kg/day).⁸ Second, in the present study this dose was given twice daily until the end of the four-week period. In the other study,⁸ final clinical evaluations were made at a timepoint at which animals had been treated once daily for two weeks.⁸ It could well be that improvement could have been greater, even at a lower dose, if given twice daily. The results of the present study suggest that the canine dose and protocol is insufficient to keep lesions and pruritus under control in allergic cats, and a higher dose and/or frequency of administration are needed. Our results also are in line with another open study conducted with a similar dose (0.5–0.8 mg/kg), albeit with the canine protocol.¹⁶ In that study 66.6% of cats (10 of 15) showed improvement of SCORFAD and pruritus VAS, compared to 60% and 70%, respectively, in our study.¹⁶ As in the previous pilot study, no clinical presentation pattern of allergic dermatitis (miliary dermatitis, head and neck pruritus, eosinophilic plaque or granuloma, self-induced alopecia) seems to be associated with a higher or lower success rate of the treatment.⁸

Oclacitinib and methylprednisolone at the dosages used in this study were both efficacious. There was no statistical difference in lesions, pruritus VAS or QoL at any timepoint between the two groups, possibly due to a low of power of this study. As methylprednisolone seemed to perform better than oclacitinib for every parameter analysed, we can conclude that for short-lasting treatments oclacitinib does not offer any advantage over corticosteroids. Methylprednisolone was chosen as the control drug in accordance with a previous study, which indicated a total daily dose of 1.4 mg/kg required to control signs of feline allergy.¹⁷ The administration of methylprednisolone was split into two daily doses in order to maintain the blinding, as oclacitinib also was given twice daily. Even if not statistically significant, methylprednisolone treatment yielded better clinical results than oclacitinib and a lower number of non-responders. Interestingly, cats treated with oclacitinib showed a slightly higher improvement of QoL compared to those treated with methylprednisolone. This could be due to cases which presented deterioration of clinical signs, vomiting and lethargy, observed in the methylprednisolone group only.

As in previous canine and feline studies, QoL improved less than the clinical parameters (21–25% compared to 54–69%), suggesting that twice daily administration of tablets represents a relevant disturbing factor for the cat and its owner, in spite of improvement of pruritus and skin lesions.¹⁸ This could be confirmed by the observation that twice weekly administration of ciclosporin (as opposed to twice daily) was associated with a 50% improvement of QoL, albeit with similar clinical results.¹⁹ The impact of drug administration on the QoL should always be taken into consideration besides clinical improvement. This is particularly relevant when planning life-long treatment protocols, such as in cases of allergic dermatitis.

Besides the evaluation of clinical benefit and QoL improvement, safety is another factor to be considered when treating allergic animals for a long period of time. Unfortunately, no data on pharmacokinetics, pharmacodynamics or safety are known for oclacitinib in cats; the information collected in this study after one month of treatment, cannot be representative of a long lasting use in allergic cats. In the present study, after one month of drug administration, mild changes of biochemical parameters were observed in both groups, with the exception of ALT increase in the methylprednisolone group. Four of 14 cats treated with oclacitinib had a mild increase in renal values. Of these, only one had pretreatment values at the upper reference range, whereas the others had values within the normal range. It is not possible to know if these cats had an undiagnosed, subclinical renal disease, as urinalysis and symmetrical dimethylarginine (SDMA) test – an early marker of kidney disease – were not performed prior to drug administration. It would be advisable to assess renal function before oclacitinib administration to cats, until further information becomes available. Furthermore, as there are no data on the potential immunosuppressive effects of oclacitinib in cats, screening for FeLV and FIV before treatment should be performed, in order to avoid administration to positive cats. Again, as the

safety of oclacitinib has not been assessed in cats, it is advised to monitor the cat on a regular basis for adverse effects.

In conclusion, oclacitinib appears to be effective in treating pruritus and clinical signs of allergic dermatitis in cats. Oclacitinib may be a useful alternative treatment when glucocorticoids are contraindicated and a rapid relief of pruritus is required.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Table S1. Treatment group (A oclacitinib, B methylprednisolone), signalment, drug dose (per kg body weight), duration of clinical signs, Scoring Feline Allergic Dermatitis scores (SCORFAD), pruritus Visual Analog Scale (VAS) scores and Quality of Life (QoL) scores at Day 0 (D0) and after 28 days (D28) and adverse events reported for each cat.

Table S2. Haematology and biochemical parameters recorded outside the normal range on D28 for cats receiving oclacitinib or methylprednisolone.

Résumé

Contexte – L'occlacitinib est un inhibiteur de Janus kinase qui diminue le prurit induit par l'interleukine-31 chez le chat. A 0.4-0.6 mg/kg/jour per os, il diminue le prurit et les lésions cutanées pour <50% des chats allergiques.

Hypothèses/Objectifs – Evaluer l'efficacité et l'innocuité de l'occlacitinib chez les chats atteints de dermatite par hypersensibilité non liée aux puces et non liée à l'alimentation (NFNFIHD).

Sujets – Quarante chats NFNFIHD.

Méthodes – Les chats ont été répartis au hasard pour recevoir soit de l'occlacitinib (groupe A, 20 chats, 0.7–1.2 mg/kg) ou de la méthylprednisolone (groupe B, 20 chats, 0.5–1 mg/kg) oralement deux fois par jour pendant 28 jours. Aux jours (D)1 et D28, les lésions ont été évaluées par SCORFAD (Scoring Feline Allergic Dermatitis) et les propriétaires ont évalués le prurit à l'aide d'une échelle visuelle analogue (VAS) et un questionnaire de qualité de vie (QoL). Les résultats ont été analysés par General Linear Mixed Model ($P < 0.05$). Les analyses hémo-biochimiques ont été réalisées à D1 et D28.

Résultats – Dans les deux groupes, tous les paramètres se sont significativement améliorés sans différence quelque soit le moment. Le groupe A a fait un score de 61% de SCORAD et une amélioration de 54% de VAS en comparaison avec 69% et 67% pour le groupe B; 70% des chats du groupe A et 75% des chats du groupe B ont montré une diminution $\geq 50\%$ des scores de VAS de prurit; avec 60% et 80% de SCORFAD. Il y avait 5 non répondant dans le groupe A et trois dans le groupe B. Le score de QoL s'est amélioré dans les deux groupes (25 et 21%). Quatre des 14 chats avaient une augmentation modérée des valeurs rénales (groupe oclacitinib) et trois des 12 chats avaient une transférase alanine élevée (group méthylprednisolone).

Conclusion et importance clinique – L'occlacitinib semble efficace pour le traitement du prurit et des lésions chez les chats avec NFNFIHD bien que la méthylprednisolone semble être plus efficace.

Resumen

Introducción – el oclacitinib es un inhibidor de la Janus-quinasa que disminuye el prurito inducido por interleuquina 31 en los gatos. A una dosis de 0,4 a 0,6 mg/kg/día por vía oral, disminuyó el prurito y las lesiones cutáneas en <50% de gatos alérgicos.

Hipótesis/Objetivos – evaluar la eficacia y la seguridad del oclacitinib en dermatitis felina por hipersensibilidad no inducida por pulgas ni alimentos (NFNFIHD).

Animales – Cuarenta gatos con NFNFIHD.

Métodos – los gatos fueron asignados al azar para recibir oclacitinib (grupo A, 20 gatos, 0,7–1,2 mg/kg) o metilprednisolona (grupo B, 20 gatos, 0,5–1 mg/kg) por vía oral dos veces al día durante 28 días. En el día (D) 1 y D28, las lesiones se evaluaron utilizando la escala de Dermatitis alérgica felina (SCORFAD) y los propietarios evaluaron el prurito utilizando un cuestionario de Escala análoga visual (VAS) y calidad de vida (QoL). Los resultados se analizaron mediante un modelo general lineal mixto ($P < 0,05$). Se realizaron análisis de química sanguínea en D1 y D28.

Resultados – en ambos grupos, todos los parámetros mejoraron significativamente, sin diferencia en ninguno de los puntos de tiempo. El grupo A tuvo una mejoría promedio de 61% en el SCORFAD y 54% en el VAS de prurito, en comparación con el 69% y el 67% en el grupo B; el 70% de los gatos en el grupo A y el 75% en el grupo B lograron una reducción de $\geq 50\%$ de los valores VAS de prurito; con 60% y 80% de SCORFAD. Hubo cinco animales que no respondieron en el grupo A y tres en el grupo B. Los valores de la calidad de vida mejoraron en ambos grupos (25 y 21%). Cuatro de 14 gatos tuvieron aumentos leves en los valores clínicos de la de función renal (grupo de oclacitinib) y tres de 12 gatos tuvieron alanina transferasa

elevada (grupo de metilprednisolona).

Conclusiones e importancia clínica – el oclacitinib parece ser eficaz para tratar el prurito y las lesiones en gatos con NFNFIHD, aunque la metilprednisolona parece tener mejores resultados.

Zusammenfassung

Hintergrund – Oclacitinib ist ein Janus-Kinase Inhibitor, der Interleukin-31-induzierten Juckreiz bei Katzen vermindert. Bei einer Dosis von 0,4-0,6 mg/kg/Tag *per os* verminderte es den Juckreiz und die Hautveränderungen bei <50% der allergischen Katzen.

Hypothese/Ziele – Eine Evaluierung der Wirksamkeit und der Sicherheit von Oclacitinib bei Katzen mit Nonflea-Nonfood (Nicht durch Flöhe-nicht durch Futter)-induzierter Hypersensibilitätsdermatitis (NFNFIHD).

Tiere – Vierzig Katzen mit NFNFIHD.

Methoden – Die Katzen wurden zufällig eingeteilt, um Oclacitinib (Gruppe A, 20 Katzen; 0,7-1,2 mg/kg) oder Methylprednisolon (Gruppe B, 20 Katzen; 0,5-1 mg/kg) *per os* zweimal täglich 28 Tage lang zu erhalten. Am Tag (D) 1 und am D28 wurden die Veränderungen mittels Scoring Feline Allergic Dermatitis (SCORFAD) Skala evaluiert und die BesitzerInnen beurteilten den Juckreiz mittels Visual Analog Scale (VAS) und einem Quality of Life (Lebensqualität; QoL) Fragebogen. Die Ergebnisse wurden mit einem General Linear Mixed Model analysiert ($P < 0,05$). Eine hämatochemische Analyse wurde am Tag1 und Tag28 durchgeführt.

Ergebnisse – In beiden Gruppen verbesserten sich alle Parameter signifikant, ohne Unterschiede zu den jeweiligen Zeitpunkten. Gruppe A hatte einen 61%igen durchschnittlichen SCORFAD und 54% VAS Verbesserung des Juckreizes im Vergleich zu 69% bzw 67% in Gruppe B; 70% der Katzen in Gruppe A und 75% in Gruppe B erzielten eine $\geq 50\%$ ige Reduktion des VAS Juckreiz Wertes; mit 60% bzw 80% SCORFAD. Es gab fünf Tiere in Gruppe A, die keine Verbesserung zeigten und drei in Gruppe B. Der QoL Wert verbesserte sich in beiden Gruppen (25 und 21%). Vier von 14 Katzen zeigten eine milde Zunahme bei einem Nierenfunktionstest (Oclacitinibgruppe) und drei von 12 Katzen zeigten eine erhöhte Alanintransferase (Methylprednisolongruppe).

Schlussfolgerungen und klinische Bedeutung – Oclacitinib scheint zur Behandlung des Pruritus und der Hautveränderungen bei Katzen mit NFNFIHD wirksam zu sein, wobei allerdings Methylprednisolon eine etwas bessere Wirkung zeigte.

要約

背景 – オクラチニブは、猫のインターロイキン31誘発性掻痒を軽減するヤヌスキナーゼ阻害剤である。0.4~0.6 mg / kg /日の経口投与によって、アレルギー猫の50%未満で掻痒および皮膚病変が減少した。

仮説/目的 – 本研究の目的は、猫の非ノミ非食物誘発性過敏性皮膚炎(NFNFIHD)におけるオクラチニブの有効性及び安全性を評価することである。

被験動物 – NFNFIHDを有する40頭の猫。

方法 – 1日2回、28日間オクラチニブ(A群、20頭の猫、0.7~1.2mg / kg)またはメチルプレドニゾロン(B群、20頭の猫、0.5~1mg / kg)を経口投与するように猫をランダムに割り当てた。1日目(D1)およびD28に、Scoring Feline Allergic Dermatitis (SCORFAD)尺度を使用して病変を評価し、オーナーは、Visual Analog Scale (VAS) を使用して掻痒を評価し、質問票によって生活の質(QoL)を評価した。結果は一般線形混合モデル($P < 0.05$)により解析した。血液生化学解析はD1およびD28に実施した。

結果 – 両群において、全パラメータが有意に改善し、どちらの時点においても差を認めなかった。B群では69%の平均SCORFADおよび67%の掻痒VASの改善と比較し、A群では61%の平均SCORFADおよび54%の掻痒VASの改善を示した。A群猫の70%、B群猫の75%が掻痒VASスコアの50%以上の減少を達成した。また、SCORFADにおいては60%および80%であった。治療に無反応な症例がA群に5頭、B群に3頭いた。両群においてQoLスコアに改善を認めた(25および21%)。14頭中4頭の猫が腎機能検査において緩徐な上昇を示し(オクラチニブ群)、12頭中3頭の猫がアラニントランスフェラーゼに上昇を示した(メチルプレドニゾロン群)。

結論と臨床的重要性 – オクラチニブは、メチルプレドニゾロンほどではないが、NFNFIHD猫の掻痒および病変部の治療に有効であるように思われる。

摘要

背景 – 奥拉克替尼是一种Janus激酶抑制剂,可降低白介素-31诱导的猫瘙痒。每日口服0.4-0.6mg/kg,它可以减少<50%的猫过敏性瘙痒和皮肤病变。

假设/目的 – 评估奥拉克替尼治疗猫非跳蚤、非食物过敏性皮炎(NFNFIHD)的疗效和安全性。

动物 – 四十只NFNFIHD患猫。

方法 – 将猫随机分配接受奥拉克替尼(A组、20只猫、0.7-1.2mg/kg)或甲基强的松龙(B组、20只猫、0.5-1mg / kg),每日口服两次,疗程28天。在第1天和第28天,使用猫过敏性皮炎(SCORFAD)评分表评估病变,并且让主人填写瘙痒评分表(VAS)和生活质量(QoL)问卷评价瘙痒,结果采用一般线性混合模型进行分析($P < 0.05$)。同时,在第1天和第28天进行血液化学分析。

结果 — 两组的各项指标均有明显改善,并且在任一时间点均无差异。A组的平均SCORFAD为61%,VAS改善为54%,而B组分别为69%和67%。70%A组的猫和75%B组的猫瘙痒VAS评分降低 $\geq 50\%$;以及60%和80%的SCORFAD。A组有5只无反应,B组有3只无反应。两组的QoL评分均有所提高(25%和21%)。奥克拉克替尼组中,14只猫中有4只肾功能指标轻度增加;而甲基强的松龙组中,12只猫中有3只丙氨酸转移酶升高。

结论和临床意义 — 奥克拉克替尼对治疗NFNFIHD猫的瘙痒和病变似乎有效,但甲基强的松龙表现更好。

Resumo

Contexto — O oclacitinib é um inibidor de janus-kinase que reduz o prurido induzido por interleucina-31 em gatos. Em uma dose de 0,4-0,6 mg/kg por via oral, ele foi capaz de reduzir o prurido e as lesões cutâneas em <50% dos gatos alérgicos.

Hipótese/Objetivos — Avaliar a eficácia e a segurança do oclacitinib no tratamento da dermatite por hipersensibilidade não induzida por pulgas ou alimentos (NFNFIHD).

Animais — Quarenta gatos com NFNFIHD.

Métodos — Os gatos foram randomizados para receber oclacitinib (grupo A, 20 gatos, 0,7-1,2 mg/kg) ou metilprednisolona (grupo B, 20 gatos, 0,5-1,0 mg/kg) por via oral, duas vezes ao dia por 28 dias. No dia (D) 1 e D28, as lesões foram avaliadas utilizando a escala do Escore de Dermatite Alérgica Felina (*Scoring Feline Allergic Dermatitis*, SCORFAD) e a escala analógica visual de prurido para avaliação por proprietários (VAS, *visual analogue scale*) e o questionário de qualidade de vida (QoL). Os resultados foram analisados pelo Modelo Linear Misto ($P < 0.05$). Análises hematológicas foram realizadas no D1 e D28.

Resultados — Em ambos os grupos, todos os parâmetros melhoraram significativamente, sem diferenças significativas entre os tempos experimentais. O grupo A apresentou em média 61% de melhora no SCORFAD e 54% no prurido VAS, comparado com 69% e 67% no grupo B; 70% dos gatos do grupo A e 75% do grupo B alcançaram uma redução $\geq 50\%$ nos escores de prurido VAS; com 60% e 80% do SCORFAD. No grupo A houve um total de cinco animais refratários e no grupo B, três. O escore QoL melhorou em ambos os grupos (25 e 21%). Quatro dos 14 gatos apresentaram aumentos discretos nos testes de função renal (grupo oclacitinib) e três de 12 gatos apresentaram aumento na alanina transferase (grupo metilprednisolona).

Conclusões e importância clínica — O oclacitinib parece ser eficaz no tratamento do prurido e lesões em gatos com NFNFIHD, apesar de aparentemente a metilprednisolona ter apresentado um melhor desempenho.

Supporting Information

Table S1. Treatment group (A, oclacitinib; B methylprednisolone), signalment, drug dose (per kg body weight), duration of clinical signs, Scoring Feline Allergic Dermatitis scores (SCORFAD), pruritus Visual Analog Scale (VAS) scores and Quality of Life (QoL) scores at Day 0 (D0) and after 28 days (D28) and adverse events are reported for each cat.

Case	Group	Age (Months)	Weight kg	Dose mg/kg	Sex	Breed	Duration of signs	SCORFAD D0	SCORFAD D28	VAS D0	VAS D28	QoL D0	QoL D28	Adverse events
1	A	108	6	0.9	Mc	Dsh	72	6	0	7	1	16	10	Intense urine odour
2	A	18	3.3	0.8	Mc	Dsh	7	8	5	8	9	18	32	None
3	A	24	4	0.7	Fs	Dsh	12	4	0	7	3	10	9	None
4	A	96	5.4	1	Mc	Dsh	18	5	1	4.5	1	24	14	None
5	A	72	3.7	0.7	Fs	Dsh	12	3	2	7.5	3	25	23	None
6	A	18	5	1	Mc	Dsh	10	5	4	7	7	20	20	None
7	A	144	3.8	0.7	Mc	Chartreux	120	5	5	7.5	3	26	16	None
8	A	84	6	0.9	Mc	Dsh	75	3	1	7	0	30	7	None
9	A	120	6	0.9	Mc	Dsh	72	7	3	9	2.5	22	15	None
10	A	84	5	1	Fs	Dsh	10	7	0	7	0	26	7	None
11	A	156	6	0.9	Fs	Dsh	72	7	7	8	8	27	24	None
12	A	96	4.8	1.1	Fs	Birman	60	5	2	7	7.5	12	10	None
13	A	48	3.5	0.75	Fs	Dsh	2	7	2	5	2.5	20	20	None
14	A	168	6.7	0.8	Mc	Siamese	24	11	1	9	4.5	25	16	None
15	A	96	6.5	0.83	Mc	Persian	96	8	5	9	7	25	29	None
16	A	42	5	1	Fs	Siberian	18	3	3	6.5	7	16	15	None
17	A	18	3.6	0.75	Fs	Abyssinian	32	6	0	9	0.5	19	20	None
18	A	105	5.5	0.98	Fs	Dsh	72	10	1	9	0	15	7	None
19	A	108	4.2	1.2	Fs	Dsh	15	9	3	10	0	22	14	None
20	A	120	3	0.9	Fs	Dsh	12	4	3	5	2	21	8	None
Mean		86.25	4.85	0.89			40.55	6.15	2.40	7.45	3.43	20.95	15.80	
SD		46.01	1.15	0.14			35.43	2.30	2.01	1.49	3.07	5.28	7.34	
Case	Group	Age	Weight	Dose	Sex	Breed	Duration of signs	SCORFAD	SCORFAD	VAS	VAS	QoL	QoL	Adverse events

		(Months)	kg	mg/kg				D0	D28	D0	D28	D0	D28	
21	B	72	5	1	Fs	Dsh	7	5	2	5.5	0	10	9	None
22	B	36	4.2	0.95	Fs	Dsh	10	3	0	7	0.5	21	13	None
23	B	46	4.3	0.93	Fs	Dsh	14	7	0	7	2.8	31	19	None
24	B	108	3.6	0.55	Fs	Dsh	6	4	2	5	3.5	11	14	None
25	B	36	4.2	0.95	Fs	Dsh	24	1	0	6.8	1.8	20	16	None
26	B	72	5	0.8	Mc	Dsh	60	5	0	6	0	19	9	None
27	B	24	3.6	0.55	Fs	Dsh	12	4	2	7	0	24	21	Lethargy
28	B	120	5.5	0.72	Mc	Dsh	n.d.	7	2	8.5	4.5	26	28	Vomit
29	B	36	4	1	Fs	Dsh	3	5	0	6.8	0.3	22	14	None
30	B	64	4.7	0.85	Fs	Dsh	36	9	0	6	2.5	25	28	None
31	B	32	3.9	0.5	Fs	Dsh	n.d.	8	1	7.5	1	12	1	None
32	B	48	4.1	1	Mc	Dsh	6	4	0	7.5	0.5	13	5	None
33	B	18	6.4	0.62	Mc	Dsh	6	3	2	8	0.5	17	12	None
34	B	30	4.6	0.86	Mc	Abyssinian	12	5	5	7.5	7.5	18	18	Drop out for worsening
35	B	156	8	0.5	Mc	Dsh	60	4	1	9	0	16	11	None
36	B	24	6	0.66	Mc	Dsh	13	3	0	6	2.5	4	7	None
37	B	84	5.3	0.75	Mc	Dsh	72	6	6	8.5	8.5	30	30	Drop out for worsening
38	B	24	5.5	0.72	Mc	Dsh	12	4	4	8	8	24	30	None
39	B	96	4.5	0.9	Fs	Dsh	24	8	3	10	2.5	32	18	None
40	B	13	6	0.7	Mc	Dsh	6	3	0	7.5	1	17	8	None
Mean		57.0	4.9	0.8			21.3	4.9	1.5	7.3	2.4	19.6	15.6	
SD		38.9	1.1	0.2			24.9	1.7	2.3	1.1	3.5	8.6	9.4	

n.d. not determined; SD standard deviation; Dsh domestic short haired.

Table S2. Haematology and biochemical parameters recorded outside the normal range on D28 for cats receiving oclacitinib or methylprednisolone

Case	Group	Parameter	Pre value	Post value	Reference range
1	A	Neutrophils	4.43	2.11	2.5-12.50 x 10 ⁹ /L
2	A	Urea*	16.3	28	6-15 mg/dL
2	A	Creatinine	1.4	1.7	0.6-1.6 mg/dL
4	A	Urea *	34.6	42.5	17.6-32.8 mg/dL
6	A	Alanine-amino transferase	61	95	20-85 U/L
7	A	Creatinine	1.5	1.87	0.6-1.6 mg/dL
9	A	Platelets	362	42	150-600 x 10 ⁹ /L
10	A	Urea *	28.04	30.84	6-15 mg/dL
11	A	Neutrophils	4.80	1.65	2.5-12.5 x 10 ⁹ /L
11	A	Urea	32	33.64	6-15 mg/dL
11	A	Creatinine	1.6	1.98	0.6-1.6 mg/dL
13	A	Creatinine	Normal**	2.57	0.65-2 mg/dL
13	A	Albumin	Normal**	4.4	3-4 g/dL
13	A	Alanine-amino transferase	Normal**	134	32-87 U/L
17	A	Lymphocytes	3.4	8.48	0.9-6.88 x 10 ⁹ /L
20	A	Alanine-amino transferase	61	189	12-130 U/L

25	B	White blood cells*	4.5	3.4	5.5-19.5 x 10 ⁹ /L
25	B	Lymphocytes	1.6	0.6	0.8-7 x 10 ⁹ /L
25	B	Glucose	156	180	74-159 mg/dL
25	B	Alanine-amino transferase	100	274	12-130 U/L
27	B	Alanine-amino transferase	85	153	20-85 U/L
30	B	Lymphocytes	3.92	8.48	0.4-6.8 x 10 ⁹ /L
33	B	Albumin	3.7	4.3	3-4.2 g/dL
35	B	Platelets*	53	48	151-600 x 10 ⁹ /L
35	B	Glucose*	353	414	74-159 mg/dL
35	B	Alanine-amino transferase	29	237	12-130 U/L
36	B	Neutrophils	5.7	1.6	3-12 x 10 ⁹ /L
36	B	Glucose	156	169	74-159 mg/dL
39	B	Alkaline phosphatase	49.9	187	10-160 U/L

Pre-and post-treatment values and relative reference range are reported. Reference ranges for the same parameter may be different due to different laboratories used. Cats with mildly elevated urea values were included if creatinine was well within the normal range and if they did not have a history of kidney disease.

* parameters that were altered before entering the study and that worsened thereafter; **parameters which were declared to be within normal range by the referring veterinarian, but which were not available.