Oclacitinib in feline nonflea-, nonfood-induced hypersensitivity dermatitis: results of a small prospective pilot study of client-owned cats

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Background – Oclacitinib is a Janus kinase inhibitor that decreases pruritus and lesions in allergic dogs. In cats, it is able to inhibit interleukin-31-induced pruritus; no information is available on its clinical effectiveness.

Hypothesis/Objectives – To evaluate the efficacy, ease of administration and tolerability of oclacitinib in feline nonflea-, nonfood-induced hypersensitivity dermatitis.

Methods – Cats >12 months of age and >3 kg body weight with a diagnosis of nonflea-, nonfood-induced hypersensitivity dermatitis were treated with oclacitinib, 0.4–0.6 mg/kg orally (p.o.) twice daily for 2 weeks, then once daily for an additional 14 days. Clinical lesions were evaluated with the Scoring Feline Allergic Dermatitis (SCORFAD) system and pruritus was evaluated with a 10-cm-long visual analog scale (VAS) before and at the end of the study. Owners assessed global efficacy, ease of administration and tolerability with a four-point scale.

Results – Twelve cats were treated with a mean initial oclacitinib dose of 0.47 mg/kg p.o. twice daily. There was good improvement in SCORFAD and VAS pruritus scores in five of 12 cases, while the other cats were unchanged, deteriorated or dropped out due to treatment failure. Owners scored global efficacy as good/excellent in four of 12 cases and ease of administration and tolerability as good/excellent in 10 of 12.

Conclusions and clinical importance – Oclacitinib at 0.4–0.6 mg/kg p.o. may be an effective and safe drug for some cats with nonflea-, nonfood-induced hypersensitivity dermatitis. Further studies are needed to identify the most effective dose range for this species.

Introduction

Feline allergic dermatitis is a common disease in veterinary dermatology and is the result of a cutaneous hypersensitivity reaction to environmental, food and/or flea allergens. Current therapies include allergen-specific immunotherapy, antihistamines, essential fatty acids, palmitoylethanolamide, glucocorticoids and ciclosporin.1,2 Oclacitinib (Apoquel; Zoetis, Rome, Italy) is a Janus kinase inhibitor which has been registered for the treatment of allergic pruritus and atopic dermatitis in the dog. When administered orally (p.o.) to cats at a dose of 0.4 mg/kg it was able to reduce pruritus induced by interleukin-31 significantly.3,4 There is scant information about the use of oclacitinib in cats and it is limited to experimentally induced asthma.5 Results of this preliminary trial demonstrated that a dose of 0.5–1.0 mg/kg p.o. twice daily for 28 days was safe and effective; serial clinical examinations and complete blood count, serum biochemical profile and urinalysis were performed; no adverse clinical signs or clinically relevant laboratory abnormalities were observed. The only report about the use of oclacitinib in a cat with a dermatological condition described a laboratory cat affected with mastocytosis that was successfully treated with oclacitinib at 1 mg/kg p.o. twice daily for 1 month.6

The aim of this small pilot study was to evaluate the response to and safety of oclacitinib in cats with nonflea-, nonfood-induced hypersensitivity dermatitis (NFnFID). Primary outcome measures were changes in pruritus and lesion scores. Secondary outcome measures were ease of administration, tolerability and development of adverse effects.

Materials and methods

This was an open multicentre study involving four clinics.

Animals

Cats >12 months of age and >3 kg body weight, diagnosed with NFnFID following the standard procedures and fulfilling Favrot’s feline allergy diagnostic criteria, were included in the study.7 Cats were not included if ectoparasitic infestations, bacterial or fungal infections, flea-allergy dermatitis or other diseases were diagnosed.
An adverse reaction to food was ruled out, when possible, with an 8 week home-cooked or commercial diet trial based on novel protein sources or hydrolysed food. Cats were tested for feline immunodeficiency virus and feline leukaemia virus before inclusion and positive cats were excluded. In some of the cases haematocrit and platelet counts and serology for toxoplasmosis (IgG and IgM) were evaluated before the trial. Cats were not allowed to eat raw meat during the whole treatment period and they were not allowed outdoors. Given that oclacitinib is not registered for cats, the owners were asked to sign an informed consent form.

Cats were not included if they had received long-acting injectable corticosteroids, ciclosporin or essential fatty acids 8 weeks or less before the trial and oral corticosteroids and antihistamines 2 weeks or less before inclusion. No dietary changes or any concomitant treatment was allowed during the trial with the exception of flea-control products. All cats had received regular ectoparasite control for at least 4 weeks before entering the study.

**Treatment**

Oclacitinib was administered at 0.4–0.6 mg/kg p.o. twice daily for 14 days, then once daily for 14 days. A recheck visit was arranged after 28 days of oclacitinib administration. Owners could choose to administer the drug with or without food, whatever was more convenient. Cats were weighed at visit 1 (V1) for correct dosing and visit 2 (V2) in order to record any change in weight. Ease of administration was rated by the owner at the recheck visit or at premature withdrawal on a four-point scale (0 = poor, 1 = fair, 2 = good and 3 = excellent). This scale and the scales assessing global efficacy and tolerability were designed by the authors and were not validated.

**Evaluation of clinical efficacy**

Investigators assessed the clinical lesions at the inclusion visit (V1) and at the recheck (V2) by means of the validated scale Scoring Feline Allergic Dermatitis (SCORFAD). On the same two occasions, owners scored the cat’s pruritus on a 10-cm-long visual analog scale (VAS), as validated for dogs. Global efficacy of oclacitinib was rated by the owner at the recheck visit or at premature withdrawal on a four-point scale (0 = poor, 1 = fair, 2 = good and 3 = excellent).

**Adverse events**

All adverse events, including weight loss of >10% of the initial weight, were recorded. Tolerability was rated by the owner at the recheck visit or at premature withdrawal on a four-point scale (0 = poor, 1 = fair, 2 = good and 3 = excellent).

**Results**

**Animals**

Twelve cats were included in the study; eleven had a diagnosis of NFNFIHD; one cat (cat 1) had a diagnosis of NFNFIHD although an adverse reaction to food was not excluded because the elimination diet could not be completed due to poor compliance. Breed, sex and age are summarized in Table 1. Median age was 4.7 years (range 2–11 years) and median weight 4.4 kg (range 3.3–5.7 kg). Previous treatments, duration of clinical signs and description of lesions are detailed in Table 1. Five cats were IgG and IgM negative for toxoplasmosis; one was tested only for IgG (test negative). Ten of the 12 cats had a complete blood count and biochemistry profile done before the therapy, all within normal limits.

**Treatment**

Oclacitinib was administered twice daily at a mean dose of 0.47 mg/kg (range 0.42–0.56 mg/kg) p.o. for 2 weeks and then once daily at the same dose for the next 4 weeks. Tolerability was rated by the owner at the recheck visit or at premature withdrawal on a four-point scale (0 = poor, 1 = fair, 2 = good and 3 = excellent).

**Table 1.** Signalment, previous treatments, lesion type, dose of oclacitinib and outcome of 12 cats with allergic skin disease treated with oclacitinib

| Case no. | Age (years) | Sex | Breed | Breed type | Lesion type | Duration of signs (months) | Lesion score V1 | Previous treatments | Dose (mg/kg) | V1 VAS | SCORFAD | V2 VAS | SCORFAD | Notes |
|----------|-------------|-----|-------|------------|-------------|--------------------------|----------------|---------------------|-------------|-------|---------|-------|---------|-------|-------|
| I        | 4           | 4   | MC    | MC         | M            | 13                        | 6              | None                | 0.45        | 5     | 6       | 6     | 4       | 2     | V2    |
| 2        | 2           | 5   | MC    | DSH       | P            | 6                        | 9              | None                | 0.54        | 6     | 3       | 3     | 0       | 0     | V1    |
| 3        | 3.8         | 3.8 | MC    | Exotic short hair | P | 2                        | 9              | None                | 0.45        | 6     | 3       | 3     | 0       | 0     | V1    |
| 4         | 4.3         | 4.3 | FS    | DSH       | P            | 3                        | 3              | None                | 0.42        | 2     | 2       | 2     | 0       | 0     | V1    |
| 5         | 5           | 5   | MC    | Ragdoll   | M            | 11                       | 11             | None                | 0.56        | 6     | 1       | 1     | 0       | 0     | V1    |
| 6         | 11          | 4.8 | FS    | Chartreux | P | 4                        | 15             | None                | 0.47        | 6     | 1       | 1     | 0       | 0     | V1    |
| 7         | 3           | 3   | MC    | Devon rex | M | 1                        | 5              | None                | 0.5         | 2     | 1       | 1     | 0       | 0     | V1    |
| 8         | 3           | 3   | MC    | Devon rex | N | 2                        | 5              | None                | 0.55        | 1     | 1       | 1     | 0       | 0     | V1    |
| 9         | 10           | 5   | MS    | DSH       | P            | 6                        | 6              | None                | 0.49        | 7     | 1       | 1     | 0       | 0     | V1    |
| 10        | 8           | 5   | FS    | DSH       | P            | 1                        | 5              | None                | 0.45        | 5     | 1       | 1     | 0       | 0     | V1    |
| 11        | 11          | 4   | MC    | DSH       | P            | 4                        | 7              | None                | 0.45        | 6     | 1       | 1     | 0       | 0     | V1    |
| 12        | 12          | 4.3 | MS    | Devon rex | P | 5                        | 3              | None                | 0.45        | 6     | 1       | 1     | 0       | 0     | V1    |

**Abbreviations:** A, self-induced alopecia; AMXC, amoxicillin-clavulanic acid; C, cefalexin; CSA, ciclosporin; DSH, domestic short hair; DSS, dexamethasone-sodium succinate; EG, eosinophilic granuloma; EP, eosinophilic plaque; F, female spayed; M, male castrated; MD, miliary dermatitis; MPA, methylprogesterone acetate; n.a., not applicable; P, prednisolone; SCORFAD, scoring feline allergic dermatitis lesional scoring system; VAS, visual analog scale; V1, visit 1 (day 1 of treatment); V2, visit 2.
2 weeks. Ease of administration was judged excellent by 11 owners and good by one.

Evaluation of clinical efficacy
The SCORFAD and VAS pruritus scores at V1 and V2 are reported in Table 1. Three cats did not complete the study after V1 (cats 2 and 10 due to poor response and cat 11 was lost, with the owner reporting no improvement), and their values were carried forward to V2.
Average SCORFAD scores (±SD) before and after treatment were 4.58 (±2.35) and 3.58 (±3.03), respectively. Average VAS pruritus scores (±SD) before and after treatment were 8.5 (±1.64) and 7.0 (±2.50), respectively. In four cats (numbers 1, 4, 9 and 12) there was an improvement of both SCORFAD and VAS pruritus scores; for cat 5 only pruritus improved, while for cat 6 only lesions improved. Cats 7 and 8 deteriorated, while cat 3 did not show any improvement.

Efficacy was judged as good to excellent by four of 12 owners, fair by three and poor by five. No apparent association was observed between successful outcome and lesion type or severity, oclacitinib dose administered or previous duration of the disease.

Adverse events
Tolerability was judged as excellent by 11 owners and fair by one. Adverse events were not recorded.

Discussion
The results of this study suggest that oclacitinib may suppress pruritus and clinical signs associated with allergy in some cats. The reasons why some cats responded and others did not are not clear, because no obvious correlation was found between the outcome and lesion type or severity, dose administered or any other variable. The number of cats included in the study was small, so the inclusion of a larger number of cases in a controlled study might identify clinical presentations for which oclacitinib is shown to be more effective. Owners of responsive cats (n = 5 of 12) were favourably impressed by the ease of administration and tolerability of oclacitinib.

The results of this study are less favourable than those obtained with ciclosporin or corticosteroids and are similar to those reported with essential fatty acids and antihistamines. Little is known about the pharmacokinetics and pharmacodynamics of oclacitinib in cats and it is possible that a higher dose or a different administration regimen might improve responsiveness; more studies are needed to assess this. The dosage chosen for this study (0.4–0.6 mg/kg p.o.) was based on that determined for dogs and used in experimental studies in cats. It was significantly lower than the dose used in a single case of feline mastocytosis (1 mg/kg), although that case report had not been published when the present trial started. In a study of feline asthma and in the cat with mastocytosis, oclacitinib was administered twice daily for 4 weeks, while in the present study it was given twice daily for 2 weeks, then once daily for another 14 days, as recommended for dogs. Unfortunately, no revisit was scheduled on day 14 in our trial, so we could not evaluate whether cats that were not responding well at V2 (once daily administration) might do better on twice daily dosing. As in dogs, concurrent food administration was not considered to influence the efficacy of oclacitinib, so owners were left free to give it with or without food. Retrospectively, the lack of standardization of administration procedures may have had an impact on clinical efficacy and further studies should be performed to clarify this point.

In the present study, no adverse effects were observed in any treated cat. Similarly to our study, no adverse effects were observed in a study of 24 cats treated with 0.5 or 1 mg/kg twice daily for 4 weeks; furthermore, complete blood count, serum biochemical profile and urinalysis did not show abnormalities after treatment. In our study we were unable to sample cats for biochemistry, haematology and urinalysis at the end of the trial because of financial constraints. In dogs, oclacitinib shows its main action on JAK-1 receptors and to a lesser degree on JAK-2; this could potentially cause problems of bone marrow suppression when used at high dosages and over a long period of time. Manufacturer information on the toxicity of the product in cats is needed prior to administration of high doses and it may be advisable to monitor blood cells counts on a regular basis during its administration, where dosages >1.0 mg/kg p.o., twice daily, are used.

Oclacitinib can have immunosuppressive effects in dogs and its use has been associated with demodicosis and (viral) papillomas in safety studies conducted by the manufacturer at higher dosages. Due to the lack of information on immunosuppressive effects of oclacitinib in cats, inclusion criteria previously used in a trial on the efficacy of ciclosporin in allergic cats were used. These criteria included negative feline immunodeficiency virus and feline leukaemia virus status and the absolute avoidance of raw meat to reduce the risk of toxoplasmosis. More studies are necessary to assess the immunosuppressive effects on cats and to determine which precautions are required in the feline species.

There are several weak points in this study. First of all, this was a small, noncontrolled pilot study and having a larger number of cases and a control group would have been desirable. The cats included, despite being selected for NFNFIHD, were not homogeneous regarding their clinical presentation and this could have influenced the final outcome. Furthermore, in the absence of data on the dosage of oclacitinib to be used in cats, the canine dose was used, and this may not be the optimal dose range for cats.

In conclusion, oclacitinib may represent an alternative treatment, particularly for cats in which corticosteroids are contraindicated or when oral administration of other drugs is difficult or causes adverse effects. More studies are required to determine the optimal dose and administration regimen and to assess its safety when administered long term, particularly if used at higher doses than those used in the present study. The authors would like to remind readers of the journal’s disclaimer, which is applicable to the use of oclacitinib in cats: “Authors may discuss products and formulations that are not available or licensed in the individual reader’s own country, or
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drugs that are licensed for human use and not for veterinary use. Readers need to bear this in mind and be aware of the prescribing laws pertaining to their own country."

References


Résumé

Contexte – L’oclacitinib est un inhibiteur Janus kinase qui diminue le prurit et les lésions chez les chiens allergiques. Chez le chat, il peut inhiber le prurit induit par l’interleukine-31; aucune information n’est disponible sur son efficacité clinique.

Hypothèses/Objectifs – Évaluer l’efficacité, la facilité d’administration et la tolérance de l’oclacitinib sur les dermatites par hypersensibilité non liées aux puces et non liées à l’alimentation.

Méthodes – Les chats de plus de 12 mois et de plus de 3 kg avec un diagnostic de dermatis par hypersensibilité non liée aux puces et non liée à l’alimentation ont été traités par l’oclacitinib per os à 0.4–0.6 mg/kg deux fois par jour pendant 2 semaines, puis une fois par jour 14 jours supplémentaires. Les lésions cliniques ont été évaluées par SCORFAD (Scoring Feline Allergic Dermatitis) et le prurit a été évalué par une échelle visuelle analogue (VAS) avant et à la fin de l’étude. Les propriétaires ont évalué l’efficacité globale, la facilité d’administration et la tolérance à l’aide d’une échelle à quatre points.

Résultats – Douze chats ont été traités avec une dose initiale moyenne d’oclacitinib de 0.47 mg/kg p.o deux fois par jour. Il y a eu une bonne amélioration du SCORFAD et des scores de prurit pour cinq des 12 cas alors que les autres chats restaient inchangés, s’aggravaient ou sortaient de l’étude à cause de l’échec du traitement. Les propriétaires ont noté l’efficacité globale comme bonne/excellente pour quatre des 12 cas et la facilité d’administration et la tolérance comme bonne à excellente pour 10 cas sur 12.

Conclusions et importance clinique – L’oclacitinib à 0.4–0.6 mg/kg p.o peut être efficace et sure pour des chats présentant une dermatis par hypersensibilité non liée aux puces ou à l’alimentation. D’autres études sont nécessaires pour identifier la dose la plus efficace dans cette espèce.

Resumen

Introducción – Occlacitinib es un inhibidor de la quinasa Janus que disminuye el prurito y las lesiones en perros alérgicos. En gatos es capaz de inhibir el prurito inducido por interleuquina 31; no hay información disponible de su efectividad clínica.

Hipopésis/Otjetivos – evaluar la eficacia, facilidad de administración y tolerabilidad de oclacitinib en dermatitis por hypersensibilidad felina no inducida por pulgas ni alimentaria.

Métodos – gatos mayores de 12 meses de edad y de más de tres kilos de peso con un diagnóstico de dermatitis de hipersensibilidad no inducida por pulgas ni por alergias alimentarias fueron tratados con occlacitinib, 0.4 a 0.6 mg/kg por vía oral (p.o.) dos veces al día durante dos semanas, y después una vez al día durante 14 días más. Las lesiones clínica se evaluaron mediante el sistema de evaluación de la dermatitis alérgica felina (SCORFAD) y el prurito se evaluó con una escala análoga visual de 10 cm de longitud (VAS) antes y al final del estudio. Los propietarios evaluaron la eficacia global, la facilidad de administración y tolerabilidad en una escala de cuatro puntos.
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Resultados – 12 gatos fueron tratados con una dosis inicial media de oclacitinib de 0,47 mg/kg por vía oral dos veces al día. Hubo mejora en SCORFAD y los valores de prurito VAS en cinco de los 12 casos, mientras que en los otros gatos no hubo cambios, deterioraron, o se sacaron del estudio debido a fallo en el tratamiento. Los propietarios valoraron la eficacia global como buena/excelente en cuatro de los 12 casos, y la facilidad de administración y tolerabilidad como buena/excelente en 10 de 12 casos.

Conclusiones e importancia clínica – oclacitinib de 0,4 a 0,6 mg/kg por vía oral puede ser efectivo y seguro como tratamiento en algunos gatos con dermatitis por hipersensibilidad no inducida por pulgas ni por alergia alimentaria. Se necesitan más estudios paréntesis para identificar el rango de dosis más efectivas en esta especie.

Zusammenfassung


Methoden – Katzen von > 12 Monaten Lebensalter und > 3kg Körpergewicht mit der Diagnose einer Hypersensibilitätsdermatitis, die nicht durch Floh oder Futter ausgelöst war, wurden mit Oclacitinib bei einer Dosis von 0,4-0,6mg/kg per os (p.o) zweimal täglich für 2 Wochen, dann einmal täglich für weitere 14 Tage behandelt. Die klinischen Läsionen wurden mittels Scoring Feline Allergic Dermatitis (SCORFAD) System, der Juckreiz mittels einer 10-cm-langen Visual Analogskala (VAS) vor und nach Ende der Studie beurteilt. Die Besitzer/innen beurteilten die allgemeine Wirksamkeit, die Leichtigkeit der Verabreichung und die Toleranz anhand einer vier-Punkte Skala.

Ergebnisse – Zwölf Katzen wurden mit einer durchschnittlichen Oclacitinib Dosis von 0,47 mg/kg p.o. zweimal täglich behandelt. Es bestand eine gute Verbesserung des SCORFAD und der VAS Juckreizwerte bei fünf der 12 Fälle, während die anderen Katzen unverändert blieben, sich verschlechterten oder aufgrund eines Therapieversagens aus der Studie ausfielen. Die Besitzer/innen bewerteten die allgemeine Wirksamkeit bei vier der 12 Fälle als gut/exzellent und die Einfachheit der Anwendung und die Toleranz als gut/exzellent bei 10 der 12 Katzen.

Schlussfolgerungen und klinische Bedeutung – Oclacitinib bei einer Dosierung von 0,4-0,6 mg/kg p.o. könnte ein effektives und sicheres Medikament sein für einige Katzen mit einer nicht durch Flohe und Futter ausgelösten Hypersensibilitätsdermatitis sein. Es sind weitere Studien nötig, um die wirksamste Dosisbreite für diese Spezies herauszufinden.

摘要

背景 — 奥拉替尼(Oclacitinib)是一种激酶抑制剂，可减轻犬瘙痒和过敏症状。可抑制猫的白介素31诱导性痒病，临床疗效显示对炎症无效。

假设/目的 — 评估奥拉替尼用于猫非跳蚤叮咬、非食物诱导的过敏性皮炎上的疗效，给药程度及耐受性。

方法 — 大于12月龄、体重大于3kg的猫，诊断为非跳蚤叮咬、非食物诱导的过敏性皮炎，使用奥拉替尼治疗。0.4-0.6mg/kg口服(p.o)，一日两次，连续两周，后改为一日一次，连续14天。在实验前后用猫过敏性皮炎评分体系(SCORFAD)评估临床症状，用1厘米长视觉模拟评分法(VAS)评估症状。动物主人用四分总体评估疗效，给药程度及耐受性。

结果 — 12只接受治疗的猫，奥拉替尼平均起效时间是0.47mg/kg口服，每日两次，12只其中的5只SCORFAD及VAS症状评分有明显改善，其余猫没有变化、恶化或放弃治疗。12只中的4只，主人总体评分好/极好，12只中10只给药程度和耐受性好/极好。

总结与临床意义 — 对于一些猫非跳蚤叮咬、非食物诱导的过敏性皮炎，奥拉替尼0.4-0.6mg/kg口服可能成为有效且安全的药物。鉴定猫的有效用量范围，还需进一步研究。

要約

背景 — オクラチンビニはアレルギーのイヌにおける搔痒と皮膚病変を減少させる酵素スイナーゼ阻害薬である。ネコにおいて、インフルエンザ31誘導性搔痒を抑制することがで、この臨床的な効果に対する有効な情報はない。

仮説/目的 — ネコの非ハ、非食物誘発性過敏性皮膚炎において、オクラチンビニの効果、投与しやすさならびに許容性を評価すること。

方法 — 非ハ、非食物誘発性過敏性皮膚炎と診断された12ヶ月齢以上のネコ12匹にオクラチンビニで0.4-0.6mg/kg・日2回経口投与で、2週間、その後1日1回で追加の2週間治療した。臨床症状を調査前後調査時、Oclacitinib in feline allergic dermatitis (SCORFAD)システムで評価し、搔痒を10cmの長さのvisual analog scale (VAS)で評価した。同様は全身的な効果、投与しやすさ、ならびに4点スケールで許容性を評価した。
結果   12頭のネコを初期オクラシチニブ用量を平均0.47mg/kg p.o.1日2回で治療した。12症例中5例でSCOR-FADおよびVAS挙触スコアで良好な改善を示し、一方、他のネコでは変化なし、悪化あるいは治療の失敗が原因でドロップアウトした。飼い主は12症例中4例で「全体的な効果を良好/非常によい」と評価し、投与のしやすさや許容性は12頭中10頭で「良好/非常によい」と評価した。

結論および臨床的な重要性   0.4–0.6mg/kg p.o.のオクラシチニブは非ノミ、非食物誘発性過敏性皮膚炎のネコに効果的で「安全な薬剤である可能性がある。さらに調査がこの動物種において、より効果的な用量の範囲を特定するために必要とされる。