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ORIGINAL ARTICLE

# A placebo-controlled, double-blind study evaluating the effect of orally administered polyunsaturated fatty acids on the oclacitinib dose for atopic dogs

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**Abstract**

**Background:** Supplementation of polyunsaturated fatty acids (PUFA) enables dose reduction of prednisolone and ciclosporin in canine atopic dermatitis (cAD).

**Objective:** To determine if oral administration of PUFA reduces the dose of oclacitinib in cAD.

**Animals:** Twenty-two client-owned dogs with cAD receiving oclacitinib.

**Materials and Methods:** Dogs received a fish oil product (PUFA) or paraffin oil (placebo) for 16 weeks. Owners adjusted the oclacitinib dose according to daily pruritus assessments. On Day (D)0, D56 and D112, Canine Atopic Dermatitis Extent and Severity Index, fourth iteration (CADESI-04), pruritus Visual Analog Scale (PVAS), quality-of-life score (QoL), Global Assessment (GA), quality-of-coat (QoC) and adverse events were recorded.

**Results:** Mean daily oclacitinib dose was significantly reduced in the PUFA group from 0.51±0.20 mg/kg/24 h (D0) to 0.19±0.14 mg/kg/24 h (D85–112; $p<0.00001$) and not in the placebo group (D0: 0.70±0.33 mg/kg/24 h; D85–112: 0.53±0.35 mg/kg/24 h, $p=0.5422$). CADESI-04 did not change over time or differ between groups. PVAS was significantly lower in the PUFA group (2.8±1.5) compared to placebo (4.2±1.6) at D112 ($p=0.0375$). QoL and QoC improved only in the PUFA group (QoL: D0: 20±7, D112: 12±5, $p=0.0057$; QoC: D0: 0±0.5, D112: 1±0.5, $p=0.0410$). GA on D112 was higher in the PUFA group ($p=0.008$). No adverse events were observed.

**Conclusion:** Oral supplementation of PUFA allowed dose reduction of oclacitinib and improved PVAS, QoL, QoC and GA. The use of PUFA is recommended and was safe in the atopic study dogs receiving oclacitinib.

**KEYWORDS**
allergic dermatitis, dog, essential fatty acids, Janus kinase inhibitor, oil, omega 3

## INTRODUCTION

Canine atopic dermatitis (cAD) is a genetically predisposed, chronic recurrent inflammatory pruritic skin disease.[1] There are many similarities to human atopic dermatitis (AD).[2] In addition to the immune system itself, the skin barrier plays an important role in the pathogenesis of cAD, because skin barrier dysfunction increases the risk of allergic sensitisation.[3,4] Filaggrin mutations are known to predispose humans to AD and also might play a role in the impaired skin barrier of atopic dogs.[5,6] This protein is essential for the organisation of keratin filaments in keratinocytes during keratinisation. Equally important to keratinisation is the lipid barrier of the skin. It is composed of intercellular lipids in the stratum corneum (SC) such as ceramides, cholesterol and free fatty acids. The ultrastructure of the SC differs between atopic and healthy dogs.[7] An electron microscopic study has demonstrated that thickness and continuity of intercellular lipid lamellae are significantly reduced in atopic skin.[7] This disorganisation of lipid lamellae with excessively

large interlamellar spaces filled with abnormal lipids becomes even more severe after allergen exposure, as demonstrated in house dust mite-allergic dogs.[8] The skin barrier in dogs with cAD is leaky and allows environmental allergens to penetrate the skin, leading to sensitisation.[9] The clinical consequences are dry skin, pruritus and skin lesions, which significantly reduce the quality-of-life (QoL) of these patients and requires life-long therapy.[10,11] Omega-6 fatty acids, such as linoleic acid, can be used to modulate the conformation of lipid barriers, as it is a component of ceramide 1, which is decreased in human and canine AD.[12] It has particular significance for the organisation of lipid lamellae owing to its molecular structure.[13] Studies have shown that linoleate-enriched diets influence the skin barrier.[14,15] Omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), modulate eicosanoid synthesis, by decreasing pro-inflammatory and increasing anti-inflammatory eicosanoids.[16] In addition to the stabilisation of the epidermal lipid barrier, polyunsaturated fatty acids (PUFA) inhibit cellular activation and pro-inflammatory cytokine secretion.[17–19] Studies have demonstrated that oral supplementation with essential fatty acids can reduce the dose of various medications (prednisolone, ciclosporin and antihistamines) used for control of pruritus associated with AD.[20–24] As a result of the slow onset of action of PUFA, most of these studies evaluated the efficacy of the PUFA over 12 weeks.[25,26] Because dietary PUFA supplementation does not have an immediate effect, some researchers consider the relatively short duration of these trials as a limitation.[21]

A therapeutic agent for the pruritus associated with cAD is oclacitinib, a first-generation, nonselective, Janus kinase (JAK)1-predominant inhibitor with anti-inflammatory and anti-pruritic properties.[27] One clinical trial used marine oil in combination with standard dosing of oclacitinib. This study showed an improvement in Canine Atopic Dermatitis Extent and Severity Index, fourth iteration (CADESI-04) scores and improved pruritus control with once daily dosing.[28]

The primary objective of this study was to determine if supplementation with PUFA reduces the dose of oclacitinib needed to control pruritus in dogs with AD over 16 weeks. Secondary objectives were to evaluate the effect of oral administration of PUFA on pruritus, lesion scores, QoL and quality-of-coat (QoC) in dogs with cAD.

## MATERIALS AND METHODS

### Ethics

After consultation of the animal welfare department of Justus-Liebig-University Giessen (https://www.uni-giessen.de/de/fbz/fb10/institute_klinikum/klinikum/kramer) and the local responsible agency (Regierungspräsidium Giessen, study number V 54-19 c 20 15h 02 GI 18/17 kTV 5/2020), this study was not classified as an animal experiment according to the German law (https://www.gesetze-im-internet.de/tierschversv/BJNR312600013.html). Owner's written consent was obtained for all cases.

### Overview

This study was a 16-week, randomised, double-blinded and placebo-controlled trial. Client-owned dogs were randomised to PUFA group or placebo group by a third person not involved in any other aspect of this study.

### Dogs

Dogs with nonseasonal environmentally induced cAD were enrolled. Diagnosis was made by a compatible history, clinical examination and by exclusion of all other differential diagnoses. Food allergies were ruled out based on an incomplete or no response to an 8-week elimination diet (home-cooked or commercial hydrolysed dry food).[29,30] During this study, changes in feeding management were not allowed. Dogs with concurrent food-induced AD were included if they were receiving a stable diet for at least 3 months before inclusion and during the study. For at least 8 weeks before participation in the study, all dogs had to be receiving a consistent oclacitinib dose (Apoquel; Zoetis) with good pruritus control. Allergen-specific immunotherapy (ASIT) was allowed if it was started more than 12 months before enrolment and was continued during this study. Oral fatty acids were discontinued 12 weeks, and topical fatty acids 8 weeks, before the study respectively. Antimicrobial bathing and topical treatments were allowed at the same frequency as 3 months before inclusion. Ear medications were allowed as needed. Participating dogs received continuous flea and mite treatment. Dogs with skin infections were treated before inclusion.

### Study protocol

Dogs were examined three times during this study: On the day of enrolment, which was classified as Day (D)0, on D56 and on D112. At each of these appointments, the CADESI-04 was evaluated by the same first opinion veterinary surgeon.[31] Dogs were evaluated for secondary cutaneous infections by clinical examination at each visit. Cytological evaluation of impression smears was performed as needed. If skin infections occurred during the study, routine antimicrobial therapy was administered. The pruritus Visual Analog Scale (PVAS) and the QoL score were obtained from the owners.[10,11,32] For the Global Assessment (GA), owners rated their dog's overall condition compared to the previous visit. The score ranged from 'considerably worsened' (–2 points) to 'greatly improved' (+2 points).[20] Owners ranked QoC on a scale from dull (–1 points) to shiny (+1 points).[20] All

adverse events were recorded on D56 and D112. Body weight was recorded at each appointment.

## Oclacitinib dosage and dose adjustment scheme

The initial oclacitinib dose in mg/kg/24 h was assessed at the first appointment (D0). Owners were instructed to record the daily PVAS and oclacitinib dose in a diary (Appendix S1). Instructions on how to adjust the dose of oclacitinib were given (Figure 1). Individual variations from the dose adjustment scheme were allowed after consultation with the investigators.

## Randomisation, study product and placebo

The study product was a fish oil containing 180 mg/mL eicosapentaenoic acid (EPA) and 117 mg/mL docosahexaenoic acid (DHA; Omega-3 Support; WDT). The ratio of omega fatty acids was: omega-3:omega-6:omega-9 = 8.7:1.0:4.0. Paraffin oil for medical purposes served as placebo. Both oils were packaged in indistinguishable white bottles. A veterinary technician, not involved in any other aspects of the study, was responsible for labelling of the bottles and randomisation of the groups. Primary investigators were masked to the treatment groups for the duration of the study. The PUFA group received 3 mL/10 kg of

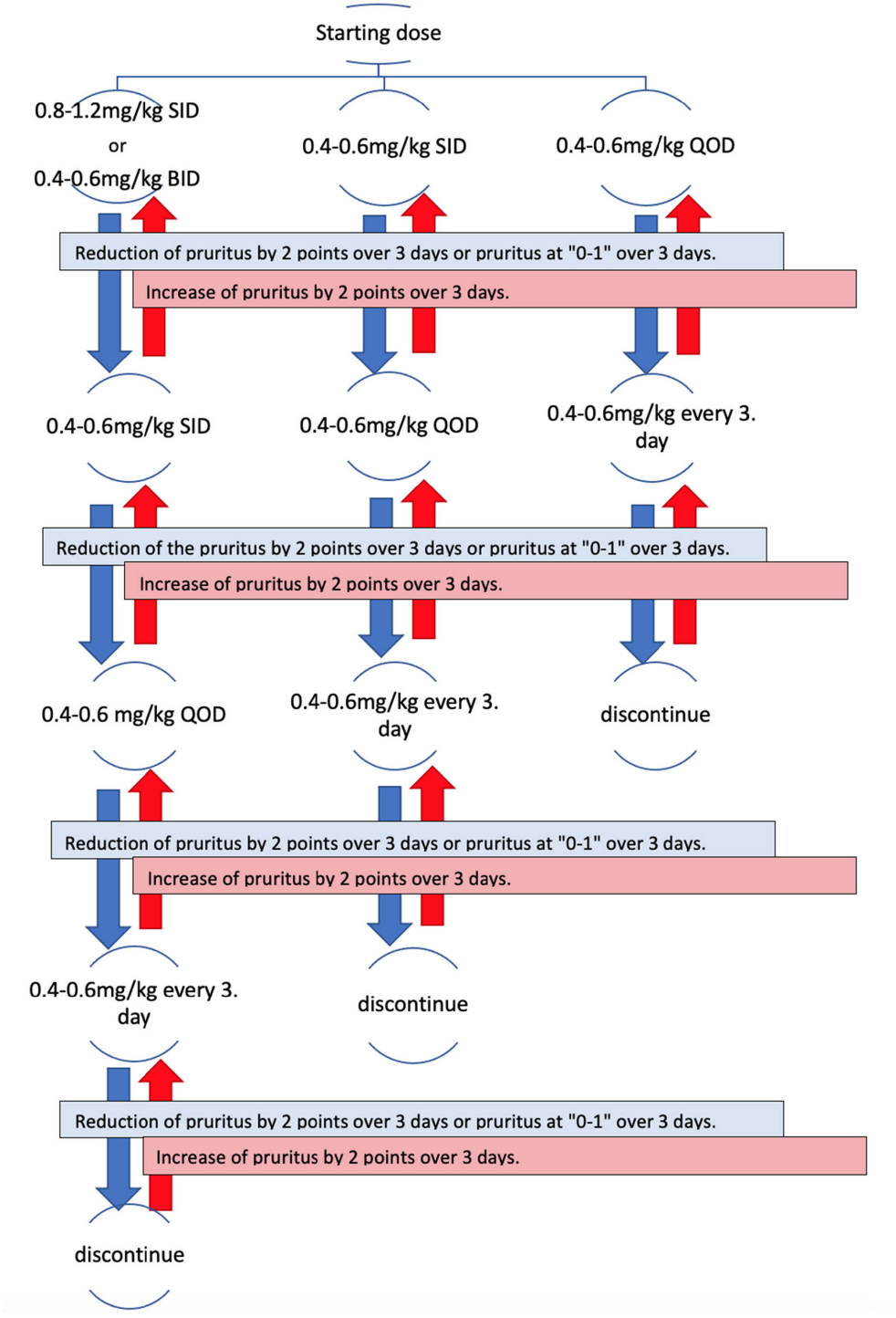


**FIGURE 1** Dosage adjustment scheme for oclacitinib dosage. BID, twice daily; QOD, every other day; SID, once daily.

fish oil and the placebo group received 3 mL/10 kg of paraffin oil once daily with a meal for the entire study period of 112 days.

## Assessment of efficacy and statistical methods

The average daily dose of oclacitinib reported in the diaries was calculated in 4 weeks intervals (D1–28, D29–56, D57–84 and D85–112). Dosages on D0 (representing the daily dose over 8 weeks before study inclusion) were compared with those in each interval. Statistical analyses and data graphing were performed using Excel (MS OFFICE; Microsoft). Continuous data (age, oclacitinib dosage, PVAS, QoL and CADESI-04) were tested for normality by performing the Shapiro–Wilk test. Normally distributed data were displayed as mean ± standard deviation (SD) and nonnormally distributed data were presented as median and range. For normally distributed data, two-tailed Student's *t*-tests were performed. If a subgroup was not normally distributed, the Wilcoxon–Mann–Whitney U-test was used. A $p < 0.05$ was defined as significant for all analyses. If a *p*-value of normally distributed data was significant, the effect size was calculated by using Cohen's *d*.[33] This helps to determine whether a significant result has practical relevance.[34] A Cohen's $d > 0.8$ is defined as a clinically relevant effect size.

For statistical analysis of the GA and the QoC, the *z*-score test on a single categorical value was performed to determine if the two populations differed significantly. A $p < 0.05$ was considered significant.

# RESULTS

## Dogs

Twenty-five dogs were included in the study. Three dogs dropped out and were excluded from further analysis: one placebo group dog developed acute diarrhoea in the first week, one placebo group dog was withdrawn on D96 because of worsening allergic clinical signs and one PUFA group dog was withdrawn after developing an unrelated cardiac arrhythmia after 22 days. Twenty-two dogs completed the trial—11 placebo and 11 PUFA—and were included in the statistical evaluation (Table S2). Mean age was 4.09 ± 1.92 years. Of the 22 dogs, nine were intact males, six were intact females, five were neutered males and two were spayed females (male: female ratio = 1.75). Two dogs of the placebo group developed secondary bacterial skin infections. Dog 6 developed superficial bacterial pyoderma on D56 and was treated with 20 mg/kg cefalexin (Cefalexin 600 mg; cp pharma) twice daily until D71. Dog 8 developed pyotraumatic dermatitis on D99 which was treated with antimicrobial and glucocorticoid ointment (Isaderm; Dechra).

## Concurrent diseases

Dog 21 had hypothyroidism treated with 8.2 μg/kg thyroxin (Wethyrox; WDT) once daily for more than 6 months before study entry. Dog 18 was diagnosed with primary epilepsy, and was treated with phenobarbital 6.3 mg/kg, potassium bromide 10.2 mg/kg and topiramate 9.4 mg/kg twice daily for more than 1 year before study entry. Both of these dogs were in the PUFA group.

## Diet

Twenty of the dogs received a commercial diet. Eight of them received a dry food with a high amount of PUFA (Anallergenic; Royal Canin or ZD; Hills). Four of these dogs were in the placebo group and four in the PUFA group (Table S2). Two dogs were fed with a home-cooked diet with horse meat. Both of them were in the PUFA group.

## Oclacitinib dose

Changes in oclacitinib doses over time are shown in Table 1. The mean initial dose (D0) of oclacitinib in the placebo group was 0.70 ± 0.33 mg/kg/24 h and 0.51 ± 0.20 mg/kg/24 h in the PUFA group. There was no significant difference between the initial doses ($p = 0.1303$). The mean doses were significantly different between the two groups ($p = 0.0168$) at the end of the study (D85–112). Cohen's *d* was 1.11, indicating a clinically relevant effect size. There was a significant difference between the mean initial dose (D0) and mean end dose (D85–112) in the PUFA group ($p < 0.00001$) and at all other time points.

## Other measures

Table 2 shows PVAS, CADESI and QOL scores.

### PVAS

There was a significant difference between the groups for PVAS score on D112. PVAS did not change over time in either group.

### CADESI

There was no significant difference in CADESI-04 between the groups, with no significant change over time.

### QoL

There was no significant difference for QoL scores between the two groups at any time point. There was no significant change over time for the placebo group;

**TABLE 1** Mean oclacitinib dose (mg/kg/24 h) and standard deviations (SD) of placebo and polyunsaturated fatty acids (PUFA) groups.

| | Mean oclacitinib dose ± SD (mg/kg/24 h) | | | | | Course of oclacitinib dose(*p*-value*) (Cohen's *d*[a]) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | D0 | D1–28 | D29–56 | D57–84 | D85–112 | D0 versus D1–28 | D0 versus D29–56 | D0 versus D57–84 | D0 versus D85–112 |
| Placebo group | 0.70±0.33 | 0.60±0.26 | 0.55±0.32 | 0.54±0.34 | 0.53±0.35 | 0.0454* (0.91[a]) | 0.2132 | 0.5124 | 0.5422 |
| PUFA group | 0.51±0.20 | 0.38±0.18 | 0.26±0.17 | 0.23±0.14 | 0.19±0.14 | 0.0004* (1.8[a]) | 0.0002* (1.98[a]) | 0.00004* (2.46[a]) | <0.00001* (3.45[a]) |
| Placebo group versus PUFA-group (*p*-value*) (Cohen's *d*[a]) | 0.1303 | 0.0510 | 0.0534 | 0.0500 | 0.0168* (1.11[a]) | | | | |

Abbreviations: D, day.
[a]Cohen's *d* only for normally distributed data with a significant *p*-value.
*$p<0.05$.

yet, the PUFA group did show improvement from D0 to D112 ($p=0.0057$). Cohen's *d* was 2.07 indicating a clinically relevant effect size.

### GA

The GA of dogs in the placebo group did not improve from D56 to D112 ($p=0.3898$) while the GA of the PUFA group did ($p=0.0024$; Table S1). GA was higher in the PUFA group compared to the placebo group on D112 ($p=0.0078$), and not on D56 ($p=0.1936$).

### QoC

The QoC of dogs in the placebo group did not improve from D0 to D112 ($p=1.000$), in contrast to the PUFA group ($p=0.0410$; Table S1).

## Adverse events

Adverse events were mild polyuria and polydipsia in one dog from the placebo group. This had been reported before the study in association with increased oclacitinib dose. One dog from the PUFA group developed increased flatulence for several days, which spontaneously resolved. No other gastrointestinal signs were observed.

# DISCUSSION

This study demonstrates that dogs with AD receiving oclacitinib can benefit from oral PUFA supplementation. Although no statistically significant differences between the treatment groups were evident until the last 4-week interval, a dose reduction of oclacitinib could be achieved after 4 weeks of PUFA administration. This was an unexpected finding because previous studies reported an effect only after 9–12 weeks.[20,21] The mean oclacitinib dose in the PUFA group decreased progressively at each of the 4-week intervals. This observation is attributed to the slow onset-of-action of PUFA.[20–26] Oclacitinib was completely discontinued in one dog in the PUFA group. This is in accordance with PUFA rarely being adequate as sole therapy for cAD.[25] Various studies have shown that PUFA supplementation has a drug-sparing effect.[20–24] In one study, the steroid-sparing effect of PUFA was reached after 64 days, and in another, the ciclosporin-sparing effect was evident at 12 weeks.[20,21]

In the placebo group, a significant dose reduction was observed when the starting dose (D0) was compared to the dose of the first 4-week interval (D0–28). One hypothesis to explain these results is the effect of the dose adjustment scheme on the owners. Owners were forced to critically assess the daily oclacitinib need of their dogs. Some dogs might have required a lower dose independent of other treatments, and

**TABLE 2** Pruritus Visual Analog Scale (PVAS), Canine Atopic Dermatitis Extent and Severity Index, fourth iteration (CADESI-04) and quality-of-life (QoL) of placebo and polyunsaturated fatty acids (PUFA) groups.

| | Placebo group | PUFA group | Placebo group versus PUFA group (*p*-value*) (Cohen's *d*[a]) |
|---|---|---|---|
| PVAS (mean±SD) | | | |
| D0 | 4.5±2.1 | 4.2±3.2 | 0.8152 |
| D56 | 4.1±2.1 | 3.3±1.8 | 0.3699 |
| D112 | 4.2±1.6 | 2.8±1.5 | 0.0375* (0.95[a]) |
| D0 versus D56 (*p*-value*) | 0.6889 | 0.4469 | |
| D0 versus D112 (*p*-value*) | 0.7754 | 0.2008 | |
| CADESI-04 (median, range) | | | |
| D0 | 16 (3–56) | 15 (5–24) | 0.7949 |
| D56 | 14 (3–80) | 12 (5–27) | 0.7642 |
| D112 | 12 (4–33) | 11 (5–27) | 0.5552 |
| D0 versus D56 (*p*-value*) | 0.5755 | 0.6419 | |
| D0 versus D112 (*p*-value*) | 0.6238 | 0.3576 | |
| QoL (mean±SD) | | | |
| D0 | 15±9 | 20±7 | 0.1841 |
| D56 | 11±6 | 14±6 | 0.2373 |
| D112 | 12±7 | 12±5 | 0.8945 |
| D0 versus D56 (*p*-value*) | 0.2495 | 0.0533 | |
| D0 versus D112 (*p*-value*) (Cohen's *d*[a]) | 0.3093 | 0.0057* (2.07[a]) | |

Abbreviations: D, day; SD, standard deviation.
[a]Cohen's *d* only for normally distributed data with a significant *p*-value.
*$p<0.05$.

their owners only realised this after critical evaluation. Another explanation for the dose reduction in these patients may be the placebo effect in general.

In the dose adjustment instructions, a reduction to every second or third day was recommended. This approach is not yet used in daily dermatological practice as a consequence of the pharmacokinetics of oclacitinib. PUFA supplementation enabled not only a decrease of the daily oclacitinib dose, but also a reduction in the dosing frequency.

There were no statistically significant PVAS changes in either group; yet, there was a significant difference in pruritus at the end of the study between the groups. No significant changes in CADESI-04 were found, probably because all the patients had good control of pruritus and lesions before participation. It is important to note that two dogs in the placebo group developed secondary bacterial skin infections while no dog in the PUFA group developed these. The QoC improved significantly and was described more often as shiny in comparison to the start of the trial. These findings were consistent with another study that reported PUFA supplementation improved skin and coat quality over 2 months.[35]

The overall improvement in patients of the PUFA group was confirmed by decrease in QoL score at the end of the study. Owners of dogs in the PUFA group noted a general improvement (GA) of their dogs during the study period, which was not noted by owners of dogs in the placebo group. The GA is measured by only one question and therefore is not as reliable as the QoL score validated for atopic dogs.[10,11,36] Adverse events were rarely reported and resolved without treatment.

A limitation of this study is subjective observations from owners that can be influenced by the placebo effect. Another limitation was the small number of patients and the lack of a standardised diet. This resulted in unequal supplementation of PUFA. The diverse diets reflect the common diets which dogs receive in routine veterinary practice. Because each dog served as its own control, diet should not have interfered with the results of the trial. Literature suggests that dogs that are fed a commercial dry food containing high-quality PUFA may not benefit from further supplementation of fatty acids.[25] All of these dogs in the PUFA group had an oclacitinib dose reduction suggesting that additional PUFA supplementation can be beneficial.

Administration of fish oil in combination with oclacitinib is safe for dogs with AD and decreases the daily maintenance dose of oclacitinib needed to control pruritus.

## AUTHOR CONTRIBUTIONS

**Laura Schäfer:** Conceptualization; methodology; investigation; writing – original draft. **Nina Thom:** Conceptualization; investigation; methodology; supervision; writing – review and editing.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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**Zusammenfassung**

**Hintergrund:** Die Supplementierung von vielfach-ungesättigten Fettsäuren (PUFA) ermöglicht eine Dosisreduktion von Prednisolon und Ciclosporin bei der atopischen Dermatitis (cAD) des Hundes.
**Ziel:** Das Ziel war es festzustellen, ob eine orale Verabreichung von PUFA die Dosis von Oclacitinib bei der cAD reduzieren kann.
**Tiere:** Zweiundzwanzig private Hunde mit cAD, welche Oclacitinib erhielten.
**Materialien und Methoden:** Die Hunde erhielten 16 Wochen lang ein Fischölprodukt (PUFA) oder Paraffinöl (Plazebo). Die BesitzerInnen passten die Oclacitinib Dosis entsprechend dem täglich erfassten Juckreiz an. Am Tag (D)0, D56 und D112 wurden der Canine Atopic Dermatitis Extent und Severity Index, 4th Auflage (CADESI-04), die Pruritus Visual Analog Scale (PVAS), Werte der Lebensqualität (QoL), eine Erfassung des Gesamtzustandes (GA), Fellqualität (QoC) und Nebenwirkungen festgehalten.
**Ergebnisse:** In der PUFA-Gruppe wurden durchschnittliche Oclacitinib Dosen von 0.51±0.20 mg/kg/24 h (D0) auf 0.10±0.14 mg/kg/24 h (D85-112) signifikant reduziert ($p<0.00001$), im Gegensatz zur Plazebo-Gruppe (D0: 0.70±0.33 mg/kg/24 h; D85-112: 0.53±0.35 mg/kg/24 h, $p=0.5422$). CADESI-04 änderte sich weder mit der Zeit noch zwischen den Gruppen. PVAS war in der PUFA-Gruppe (2.8±1.5) im Vergleich zur Plazebo-Gruppe (4.2±1.6) am D112 signifikant niedriger ($p=0.0375$). QoL und QoC verbesserte sich nur in der PUFA-Gruppe (QoL: D0: 20±7, D112: 12±5, $p=0.0057$; QoC: D0 0±0.5, D112: 1±0.5, $p=0.0410$). GA war am D112 in der PUFA-Gruppe höher ($p=0.008$). Es wurden keine Nebenwirkungen beobachtet.
**Schlussfolgerung:** Eine orale Supplementierung von PUFA ermöglichte eine Dosisreduktion von Oclacitinib und verbesserte PVAS, QoL, QoC und GA. Der Einsatz von PUFA wird empfohlen und zeigte sich in dieser Studie, bei der atopische Hunde Oclacitinib erhielten, als sicher.

**摘要**

**背景:** 在犬特应性皮炎(cAD)中,补充多不饱和脂肪酸(PUFA)可以减少泼尼松和环孢素的剂量。
**目的:** 确定口服PUFA是否能减少cAD的奥拉替尼剂量。
**动物:** 22只客户饲养的cAD患犬接受奥拉替尼治疗。
**材料和方法:** 犬接受鱼油产品(PUFA)或石蜡油(安慰剂)治疗16周。犬主根据每日瘙痒评估调整了奥拉替尼的剂量。在第(D)0天、第D56天和第D112天,记录犬特应性皮炎程度和严重程度指数、第4次迭代(CADESI-04)、瘙痒视觉模拟量表(PVAS)、生活质量评分(QoL)、总体评估(GA)、被毛质量(QoC)和不良反应。
**结果:** PUFA组的奥拉替尼日平均剂量从0.51±0.20mg/kg/24小时(D0)显著降低到0.19±0.14mg/kg/24 h (D85-112) ($p<0.00001$),而安慰剂组则没有(D0:0.70±0.33mg/kg/24;D85-112:0.53±0.35 mg/kg/24, $p=0.5422$)。CADESI-04没有随着时间的推移而变化,也没有在各组之间出现差异。在D112时,PUFA组的PVAS(2.8±1.5)显著低于安慰剂组(4.2±1.6) ($p=0.0375$)。仅PUFA组的生活质量和被毛质量有所改善(生活质量:D0:20±7, D112:12±5, $p=0.0057$;被毛质量:DO:0±0.5, D112:1±0.5, $p=0.0410$)。PUFA组D112的GA较高($p=0.008$)。未观察到不良反应。
**结论:** 口服补充PUFA可以减少奥拉替尼的剂量,改善PVAS、生活质量、被毛质量和GA。给接受奥拉替尼的特应性研究犬使用PUFA,值得推荐并且是安全的。

**Résumé**

**Contexte:** La supplémentation en acides gras polyinsaturés (AGPI) permet de réduire la dose de prednisolone et de ciclosporine dans la dermatite atopique canine (DAC).
**Objectif:** Déterminer si l'administration orale d'AGPI réduit la dose d'oclacitinib dans la DAC.
**Animaux:** Vingt-deux chiens de clients atteints de DAC et recevant de l'oclacitinib.
**Matériel et méthodes:** Les chiens reçoivent un produit à base d'huile de poisson (AGPI) ou d'huile de paraffine (placebo) pendant 16 semaines. Les propriétaires ajustent la dose d'oclacitinib selon les évaluations quotidiennes du prurit. Au jour (J)0, J56 et J112, le Canine Atopic Dermatitis Extent and Severity Index, 4th iteration (CADESI-04), le prurit Visual Analog Scale (PVAS), le score de qualité de vie (QoL), l'évaluation globale (GA), la qualité du pelage (QoC) et les effets indésirables sont enregistrés.
**Résultats:** La dose quotidienne moyenne d'oclacitinib est significativement réduite dans le groupe AGPI de 0.51±0.20 mg/kg/24 h (J0) à 0.19±0.14 mg/kg/24 h (J85-112) ($p<0.00001$) et non dans le groupe placebo (J0: 0.70±0.33 mg/kg/24 h; J85-112: 0.53±0.35 mg/kg/24 h, $p=0.5422$). Le CADESI-04 n'évolue pas dans le temps et

ne diffère pas d'un groupe à l'autre. Le PVAS est significativement plus bas dans le groupe AGPI (2.8±1.5) comparé au placebo (4.2±1.6) à J112 ($p$=0.0375). La QoL et la QoC s'améliorent uniquement dans le groupe AGPI (QoL: J0: 20±7, J112: 12±5, $p$=0.0057; QoC: J0: 0±0.5, J112: 1±0.5, $p$=0.0410). Le GA à J112 est plus élevé dans le groupe AGPI ($p$=0.008). Aucun événement indésirable n'est observé.
**Conclusion:** La supplémentation orale en AGPI permet de réduire la dose d'oclacitinib et d'améliorer le PVAS, la QoL, la QoC et l'GA. L'utilisation d'AGPI est recommandée et s'avère sûre chez les chiens atopiques de l'étude recevant de l'oclacitinib.

要約
背景: 犬アトピー性皮膚炎(cAD)において、多価不飽和脂肪酸(PUFA)を補充することにより、プレドニゾロンおよびシクロスポリンの減量が可能となる。
目的: 本研究の目的は、多価不飽和脂肪酸(PUFA)の経口投与により、犬アトピー性皮膚炎(cAD)におけるオクラシチニブの投与量が減少するかどうかを検討することであった。
対象動物: オクラシチニブを投与されているcADに罹患したオーナー所有犬22頭。
材料と方法: 犬には魚油製品(PUFA)またはパラフィン油(プラセボ)が16週間投与された。飼い主は毎日の掻痒の評価に従ってオクラシチニブの用量を調節した。Day(D)0、D56およびD112において、犬アトピー性皮膚炎重症度指数第4版(CADESI-04)、掻痒の視覚的アナログスケール(PVAS)、QOLスコア(QoL)、Global Assessment(GA)、Quality-of-coat(QoC)および有害事象を記録した。
結果: オクラシチニブの1日平均投与量は、PUFA群で0.51±0.20 mg/kg/24 h(D0)から0.19±0.14 mg/kg/24 h(D85-112)に有意に減少したが($p$<0.00001)、プラセボ群では減少しなかった(D0:0.70±0.33mg/kg/24 h、D85-112:0.53±0.35mg/kg/24 h、p=0.5422)。CADESI-04に経時的変化や群間差はみられなかった。PVASはD112でプラセボ群(4.2±1.6)に比べPUFA群(2.8±1.5)で有意に低かった($p$=0.0375)。QoLとQoCはPUFA群でのみ改善した(QoL:D0:20±7、D112:12±5、$p$=0.0057 ; QoC: QoL:D0:0±0.5、D112:1±0.5、$p$=0.0410)。D112でのGA値はPUFA群で高かった($p$=0.008)。有害事象は観察されなかった。
結論: PUFAの経口補充はオクラシチニブの減量を可能にし、PVAS、QoL、QoC、GAを改善した。PUFAの使用は推奨されるものであり、オクラシチニブ投与中のアトピー性疾患犬においても安全であった。

**Resumo**
**Resumo:** A suplementação de ácidos graxos poliinsaturados (PUFA) permite a redução da dose de prednisolona e ciclosporina na dermatite atópica canina (DAC).
**Objetivo:** Determinar se a administração oral de PUFA reduz a dose de oclacitinib na DAC.
**Animais:** Vinte e dois cães de propriedade de clientes com DAC recebendo oclacitinib.
**Materiais e Métodos:** Os cães receberam um produto de óleo de peixe (PUFA) ou óleo de parafina (placebo) durante 16 semanas. Os proprietários ajustaram a dose de oclacitinib de acordo com as avaliações diárias de prurido. No Dia (D)0, D56 e D112, Índice de Extensão e Gravidade da Dermatite Atópica Canina, 4ª iteração (CADESI-04), Escala Visual Analógica de prurido (PVAS), pontuação de qualidade de vida (QV), Avaliação Global (GA), qualidade da pelagem (QoC) e eventos adversos foram registrados.
**Resultados:** A dose média diária de oclacitinib foi significativamente reduzida no grupde 0.51±0.20 mg/kg/24 h (D0) para 0.19±0.14 mg/kg/24 h (D85-112) ($p$<0.00001) e não no grupo placebo (D0: 0.70±0.33 mg/kg/24 h; D85–112: 0.53±0.35mg/kg/24 h, $p$=0.5422). O CADESI-04 não mudou ao longo do tempo nem diferiu entre os grupos. O PVAS foi significativamente menor no grupo PUFA (2.8±1.5) em comparação ao placebo (4.2±1.6) no D112 ($p$=0.0375). A QV e QoC melhoraram apenas no grupo PUFA (QV: D0: 20±7, D112: 12±5, $p$=0.0057; QoC: D0: 0±0.5, D112: 1±0.5, $p$=0.0410). A IG no D112 foi maior no grupo PUFA ($p$=0.008). Nenhum evento adverso foi observado.
**Conclusão:** A suplementação oral com PUFA permitiu a redução da dose de oclacitinib, melhorou o PVAS, a QV, a QoC e a IG. O uso de PUFA é recomendado e foi seguro nos cães atópicos do estudo que receberam oclacitinib.

**Resumen**
**Introducción:** la suplementación con ácidos grasos poliinsaturados (PUFA) permite reducir la dosis de prednisolona y ciclosporina en la dermatitis atópica canina (cAD).
**Objetivo:** Determinar si la administración oral de PUFA reduce la dosis de oclacitinib en la cAD
**Animales:** Veintidós perros propiedad de clientes con AD que recibían oclacitinib.
**Materiales y métodos:** Los perros recibieron un producto de aceite de pescado (PUFA) o aceite de parafina (placebo) durante 16 semanas. Los propietarios ajustaron la dosis de oclacitinib según las evaluaciones diarias del prurito. En los días (D) 0, D56 y D112 se anotaron: índice de extensión y gravedad de la dermatitis atópica canina, cuarta revisión (CADESI-04), escala análoga visual de prurito (PVAS), puntuación de calidad de vida (QoL), evaluación global (GA), calidad del pelaje (QoC) y los eventos adversos.
**Resultados:** La dosis media diaria de oclacitinib se redujo significativamente en el grupo de PUFA de 0.51±0.20 mg/kg/24 h (D0) a 0.19±0.14 mg/kg/24 h (D85-112) ($p$<0.00001) y no en el grupo con placebo (D0: 0.70±0.33 mg/kg/24 h; D85-112: 0.53±0.35 mg/kg/24 h, $p$=0.5422). CADESI-04 no cambió con el tiempo ni difirió entre los grupos. PVAS fue significativamente menor en el grupo de PUFA (2.8±1.5) en comparación con el placebo (4.2±1.6) en el D112 ($p$=0.0375). La calidad de vida y la calidad del pelaje mejoraron solo en el grupo de PUFA (QoL: D0:

20±7, D112: 12±5, $p$=0.0057; QoC: D0: 0±0.5, D112: 1±0.5, $p$=0.0410). La GA en D112 fue mayor en el grupo de PUFA ($p$=0.008). No se observaron eventos adversos.
**Conclusión:** La suplementación oral con PUFA permitió reducir la dosis de oclacitinib y mejorar PVAS, QoL, QoC y GA. Se recomienda el uso de PUFA cuya administración fue segura en los perros del estudio atópicos que recibieron oclacitinib.