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Attached is an Abstract of a Zoetis Presentation at the

NORTH AMERICAN VETERINARY DERMATOLOGY FORUM (NAVDF), 2013

TITLE: EFFICACY AND SAFETY OF OCLACITINIB (ZOETIS INC, MADISON, NEW JERSEY, USA) COMPARED TO PLACEBO FOR THE CONTROL OF ATOPIC DERMATITIS IN CLIENT-OWNED DOGS

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EFFICACY AND SAFETY OF OCLACITINIB (ZOETIS INC, MADISON, NEW JERSEY, USA) COMPARED TO PLACEBO FOR THE CONTROL OF ATOPIC DERMATITIS IN CLIENT-OWNED DOGS

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ABSTRACT: Janus kinase (JAK) enzymes play central roles in cytokine signaling and in the signal transduction of many pro-inflammatory and pruritogenic cytokines. Oclacitinib, a targeted JAK inhibitor, selectively inhibits the function of a variety of cytokines dependent on JAK1 enzyme activity. This study evaluated the efficacy and safety of oclacitinib for the control of atopic dermatitis (AD). Eighteen veterinary dermatology specialists enrolled 299 dogs with a documented history of chronic, non-seasonal AD. Minimum enrollment criteria included "moderate itching/dermatitis" as identified by the owner and a dermatologist's score of ≥25 using the Canine AD Extent and Severity Index (CADESI-02). Dogs were randomized to treatment with either oclacitinib (0.4-0.6mg/kg twice-daily for 14 days and then once-daily for maintenance therapy for up to 112 days) or placebo. Success at Day 28 was a ≥2 cm (10cm Visual Analog Scale (VAS) reduction from baseline in Owner Pruritus VAS assessment and a ≥50% reduction from baseline in CADESI-02 assessment. Sixty-six percent (VAS) and 49% (CADESI-02) of oclacitinib-treated dogs were considered a success compared to 4% for both variables in the placebo-treated dogs. Success in oclacitinib-treated dogs was similar to Day 28 for all subsequent time points (Days 56, 84, 112) while assessments for placebo-treated dogs fell to <2.5%. Owners observed significantly better ($p<0.0001$) VAS scores compared to placebo at all time points assessed. The dermatologists' CADESI-02 scores mirrored these findings. Diarrhea and/or emesis were reported infrequently; with similar frequency between groups. In this study, oclacitinib was effective in controlling AD, decreasing pruritus and improving skin condition.

This study was self funded by Pfizer Animal Health, now known as Zoetis Inc.

All authors are current or former employees of Zoetis Inc. There are no conflicts of interest declared.

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TITLE: EFFICACY AND SPEED OF ONSET OF OCLACITINIB (ZOETIS INC, MADISON, NEW JERSEY, USA) FOR THE CONTROL OF PRURITUS AND ASSOCIATED SKIN LESIONS IN DOGS WITH CANINE ALLERGIC DERMATITIS

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ABSTRACT: Oclacitinib, a targeted janus kinase (JAK) inhibitor, selectively inhibits the function of a variety of cytokines dependent on JAK1 enzyme activity. This study evaluated the efficacy and speed of onset of oclacitinib for the control of pruritus associated with allergic dermatitis. A total of 436 client-owned dogs with moderate to severe pruritus (owner-assessed) and a presumptive diagnosis of allergic dermatitis were enrolled. Dogs were randomized to receive either oclacitinib at 0.4-0.6mg/kg orally twice-daily or placebo. An enhanced Visual Analog Scale (VAS) was used by owners to assess pruritus severity from Days 0-7 and by veterinarians to assess dermatitis severity on Days 0 and 7. Pre-treatment owner and veterinarian VAS scores were similar for both groups. Oclacitinib produced rapid relief from pruritus; by 24 hours a 28.6% reduction in the mean owner VAS scores was observed for oclacitinib-compared to a 13.9% reduction with placebo-treated dogs. Oclacitinib pruritus scores were significantly better than placebo ($p<0.0001$) on each assessment day. At Day 7, the reduction in owner VAS score in oclacitinib-treated dogs was 65.0% indicating a change from “severe” to “very mild” itching. By comparison, placebo-treated dogs continued to experience ‘severe” itching and a VAS reduction of 26.9%. The 28.6% reduction in the owner VAS scores for oclacitinib-treated dogs observed in the first 24 hours exceeded the total reduction (26.9%) in pruritus scores for placebo treated dogs after 7 full days of therapy. The Day 7 reduction in veterinarian VAS scores was 64.2% for oclacitinib- and 20.9% for placebo-treated dogs.

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TITLE: COMPARISON OF THE ONSET AND ANTI-PRURITIC ACTIVITY OF THE JAK INHIBITOR OCLACITINIB TO PREDNISOLONE AND DEXAMETHASONE IN AN IL-31 CANINE MODEL OF PRURITUS

COMPARISON OF THE ONSET AND ANTI-PRURITIC ACTIVITY OF THE JAK INHIBITOR OCLACITINIB TO PREDNISOLONE AND DEXAMETHASONE IN AN IL-31 CANINE MODEL OF PRURITUS

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ABSTRACT: Interleukin (IL)-31 is a cytokine that has been shown to induce pruritic behaviors in dogs. IL-31 has been detected in the serum of dogs with naturally-occurring atopic dermatitis. Based on these findings, we have developed a canine model of pruritus using recombinant canine IL-31 (cIL-31), providing a way to evaluate antipruritic activity of potential therapeutic compounds. The objective of the current studies was to compare the onset and efficacy of anti-pruritic action of the novel Janus kinase (JAK) inhibitor, oclacitinib, with prednisolone and dexamethasone in this IL-31 itch model. Pruritic behaviors (e.g. licking, scratching, head-shaking and body rubbing) displayed by Beagle dogs were observed by video surveillance and scored over a two hour period following intravenous injection of cIL-31. A single clinically relevant oral dose of oclacitinib (0.4 mg/kg) significantly reduced pruritus (-80%) 1 to 3 hours post dose compared to placebo controls. In contrast, a single dose of prednisolone (0.25 mg/kg, p.o.) did not significantly reduce pruritus at two hours while a 0.5 mg/kg dose of prednisolone only significantly reduced pruritus by 37% 10 to 12 hours after dosing. When a similar comparison was made between an oral dose of oclacitinib (0.4 mg/kg) and injectable dexamethasone (0.2 mg/kg, IM), oclacitinib but not dexamethasone, significantly reduced pruritus 1 to 3 hours post dose. These data indicate that the JAK inhibitor, oclacitinib, has a faster onset of action than prednisolone and dexamethasone in the IL-31 canine model of pruritus and a greater inhibition of pruritus in the first 12 hours.

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EFFECTS OF OCLACITINIB AND PREDNISOLONE ON SKIN TEST SENSITIVITY

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ABSTRACT: Allergic dermatitis associated with environmental allergens is a frequent diagnosis in pruritic dogs. Selection of allergens for immunotherapy can be done with intradermal testing (IDT) or allergen specific IgE (ASIgE) serology. Frequently this testing is recommended after therapy is initiated and the pruritus is partially controlled. Removing treatment can be a hurdle to obtaining owner consent for diagnostic testing. The study objective was to determine if the Janus kinase inhibitor, oclacitinib at the intended label dose, or prednisolone interfere with IDT or ASIgE serology testing. Twenty-four dogs were sensitized to house dust mites (HDM) and had at least a 2-fold increase in circulating HDM-specific IgE for 7 weeks post-sensitization. Dogs were given oral treatment with placebo, oclacitinib (0.4 mg/kg) or prednisolone (0.5 mg/kg) BID for 14 days. Skin testing for HDM sensitivity was performed one week predosing and 12 hours following the last dose. IDT was quantitatively scored by a blinded investigator. All prednisolone dogs experienced dramatic decreases or complete loss in sensitivity to intradermal dust mite injection while oclacitinib or placebo dogs experienced no significant decrease. Neither prednisolone nor oclacitinib significantly impacted HDM-specific IgE levels. Thus short term oclacitinib treatment does not significantly interfere with IDT allowing dogs whose pruritus is controlled with oclacitinib to continue treatment while on-going identification of allergens is evaluated. In contrast, prednisolone dogs require a washout period before IDT. Further, short term treatment with oclacitinib or prednisolone does not significantly change dust mite IgE titers and will not interfere with ASIgE serology testing.

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Conflicts of interest: All authors are current employees of Zoetis Inc.