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Efficacy and safety of a novel oral isoxazoline, sarolaner (Simparica™), for the treatment of sarcoptic mange in dogs

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ABSTRACT

The efficacy of the novel isoxazoline, sarolaner (Simparica™) was investigated in dogs with clinical signs consistent with sarcoptic mange and harbouring natural infestations of *Sarcoptes scabiei*. One placebo-controlled laboratory study and one multi-centred field study with a commercial comparator containing imidacloprid/moxidectin (Advocate® spot-on) were conducted. Oral or topical treatments were administered on Days 0 and 30. Up to 10 skin scrapings were taken for the assessment of *S. scabiei* infestations from each dog before treatment and on Days 14, 30, 44 and 60 in the laboratory study, and on Days 30 and 60 in the field study. In the laboratory study, efficacy was calculated based on the percent reduction of mean live mite counts compared to the placebo group. In the field study parasitological cure rate (% dogs free of mites) was determined and non-inferiority of sarolaner to the control product was assessed.

In the laboratory study 44 mixed breed dogs were enrolled in four batches. Due to decreasing mite counts in the placebo treated dogs, immunosuppression with dexamethasone (0.4 mg/kg three times per week for two weeks) was initiated in all dogs on study at that time (n = 6) and those subsequently enrolled (n = 14). In the field study, dogs were enrolled in a 2:1 ratio (sarolaner:comparator); 79 dogs were assessed for efficacy and safety, and an additional 45 dogs were assessed for safety only. There were no treatment related adverse events in either study.

In the laboratory study, no mites were found on any sarolaner-treated dogs 14 days after the first treatment except for one dog that had a single mite on Day 44. In the field study, the parasitological cure rate was 88.7% and 100% in the sarolaner group and 84.6% and 96.0% in the imidacloprid/moxidectin group, on Days 30 and 60, respectively. Statistical analysis showed that sarolaner was non-inferior to imidacloprid/moxidectin at both time points. The clinical signs of sarcoptic mange, including hair loss, papules, pruritus, erythema, and scaling/crusting improved throughout the study.

Sarolaner was safe, achieved 100% reduction in the numbers of *S. scabiei* detected and resulted in marked improvement of the clinical signs of sarcoptic mange in dogs following two monthly oral administrations.

1. Introduction

Sarcoptes scabiei var. *canis* is one of the mites most commonly infesting dogs worldwide and causes severe pruritus and may be associated with secondary bacterial pyoderma. Scabies is highly contagious and has zoonotic potential (Miller et al., 2013). Diagnosis is usually based on the presence of clinical signs and the detection of mites in skin scrapings. Infested dogs show severe pruritus, an erythematous rash and yellowish crusts on the skin (Arlian et al., 1995). The licenced treatment options for sarcoptic mange are limited mostly to topical products. Depending on the region, these may include selamectin and moxidectin/imidacloprid containing spot-on products, and in some countries amitraz dip. Shampooing or bathing with medicated or non-medicated products are generally part of the adjunctive therapy for clinical mange to rehydrate the skin and treat seborrhoea, but these procedures may also reduce the efficacy or shorten the residual activity of topical products. Extra-label use of macrocyclic lactones such as moxidectin and ivermectin have been reported to be effective via oral and injectable routes (Wagner and Wendleberger, 2000; Curtis, 2004) but to be

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effective these need to be given at high dose rates (0.2–0.5 mg/kg) and intervals of 1–2 weeks, risking potentially severe side effects. The only oral product approved in some countries for the treatment of sarcoptic mange is milbemycin oxime, however the need for every-other-day administration may not be an affordable or convenient option for most owners. Therefore a proven, convenient and safe, oral treatment option would provide a significant benefit for the care of sarcoptic mange patients.

Sarolaner (Simparica™ chewable tablets, Zoetis), the latest addition to the isoxazoline class of oral ectoparasiticides is a very potent insecticide and acaricide (McTier et al., 2016). With its monthly dosing schedule, sarolaner could provide a very convenient and effective treatment option for dogs suffering from mite infestations. A laboratory study was conducted to evaluate the efficacy of two monthly doses of sarolaner for the treatment of sarcoptic mange in dogs and a multi-centred field study in veterinary patients was conducted to confirm the efficacy and safety of this treatment and dosing regimen.

2. Materials and methods

The laboratory study was a masked, placebo controlled, randomized study conducted in South Africa. The field study was a masked, randomized trial that was conducted at veterinary practices in the UK, Spain, Italy, France, Belgium and Hungary and used a positive control containing imidacloprid and moxidectin (Advocate® Spot on, Bayer) that is approved for the treatment of sarcoptic mange in Europe. In both studies dogs received two monthly treatments. The studies were conducted in compliance with Good Clinical Practice, (VICH guideline GL9, EMEA, 2000). Masking was accomplished by separation of functions of study personnel. The person(s) who made clinical observations and conducted parasite counts was masked to experimental treatments. All treatments were dispensed by a dedicated dispenser, who was not involved in any other study activities. The protocol for the laboratory study was approved by the ClinVet Institutional Animal Care and Use Committee. Ethical approval for the field study was provided by the Zoetis Ethics Review Assessment team.

2.1. Laboratory study

2.1.1. Animals

Forty four mixed breed dogs of both sexes, ranging from seven months to 11 years of age and weighing 5.3–24.6 kg with natural *S. scabiei* infestations were enrolled. The dogs had clinical signs of sarcoptic mange and had live *S. scabiei* (adults, larvae or nymphs) confirmed in deep skin scrapings at enrolment. Dogs were housed in individual runs, so that no physical contact was possible between them. Dogs were fed an appropriate maintenance ration of a commercial dry canine feed for the duration of the study. Water was available *ad libitum*.

2.1.2. Experimental design and methods

Dogs were enrolled in four batches (minimum four dogs/batch) as adequate numbers of animals with clinical signs were confirmed positive for scabies mites in skin scrapings. Within batches, dogs were randomly allocated to treatment with sarolaner or placebo based on pre-treatment mite counts.

The severity of the clinical signs of *S. scabiei* infestation (erythema, scaling/crusting, papules, pustules, alopecia) were evaluated as follows: absent (no signs present); mild (intensity/density of the clinical sign is low and <25% of the animal's body is affected); moderate (clinical sign is of great intensity/density over <25% of the animal's body or is of lesser intensity/density but affects 25–50% of the body); severe (clinical sign is of great intensity/density and covers >50% of the animal's body).

To count mites, deep skin scrapings were taken from at least four separate sites on each dog. If no mites were detected in the first four scrapings, additional scrapings were made until live mites were found or the maximum of ten scrapings was reached. Selected scraping sites were those that had the most severe or most likely evidence of current mite infestation. Scrapings were conducted to an approximately constant depth (to capillary bleeding) over an area of approximately 2.5 cm^2. The collected material was transferred to mineral oil on a microscope slide and live *S. scabiei* mites (larvae, nymphs and adults) and eggs were counted using 20× magnification.

Day 0 for each batch of dogs was the day the first study treatment was given. Prior to treatment each dog was given a detailed physical exam to ensure suitability for inclusion and all dogs were observed for general health at least twice daily throughout the study. On Days 0 and 30, the 22 dogs allocated to treatment with sarolaner received tablets individually shaved and/or sanded to provide the target dose of 2 mg/kg. The 22 placebo-treated dogs received a single placebo tablet. Dogs were offered their normal ration of food approximately1 h prior to tablet administration. Dogs were hand pilled to ensure accurate and complete dosing and observed for general health and any reaction to treatment approximately 1, 3 and 6 h after treatment.

Deep skin scrapings and mite counts were performed on all dogs on Days 14, 30, 44 and 60. During the study it was noted that live mite counts were decreasing in the placebo-treated dogs. As this apparent self-clearing of mite infestations could interfere with the determination of efficacy, immunosuppression was initiated with intramuscular or subcutaneous dexamethasone (0.4 mg/kg three times per week for two weeks, Kortico®, Bayer) of all dogs on study at that time and for dogs subsequently enrolled. At this time, 12 dogs in each treatment group had already completed the study. Three dogs in each treatment group were on study having already received their first parasiticide treatment. Therefore these dogs received their immunosuppressive treatment between study days 0 and 30. Seven dogs in each group were enrolled after the decision was made and received immunosuppression before their first parasiticide treatment. Due to the initiation of immunsuppressive therapy, clinical signs of sarcoptic mange were not evaluated.

2.1.3. Data analysis

The primary variable for analysis was live mite count (adult, nymph and larvae combined). Assessment of efficacy was based on the percent reductions in mean live mite counts relative to placebo and pre-treatment counts calculated for each time point as follows:

$$\%\text{Efficacy} = \frac{(\text{Mean Placebo(Pretreatment)- Mean Treated})}{\text{Mean Placebo(Pretreatment)}} \times 100$$

The numbers and proportions of dogs that were mite free was calculated for each time point.

2.2. Field study

2.2.1. Animals

The patient population was recruited from veterinary practices located in various geographical and climatic locations in the EU. One dog in each household was allowed to be enrolled as the primary patient and only that dog received efficacy evaluations. Other dogs living in the same household as the primary dogs were enrolled as supplementary patients that were only evaluated for safety and palatability. The primary dog had to show clinical signs of sarcoptic mange and harbour live *S. scabiei* mites in deep skin scrapings. Dogs had to be at least 8 weeks of age and weigh at least 1.3 kg. There were no breed or gender restrictions, but dogs intended for breeding or that were pregnant or lactating were not eligible for

enrolment. Dogs with pre-existing conditions under stable veterinary management could be included. Dogs with clinical mange due to *Demodex* spp. mites or with existing uncontrolled medical conditions that might confound the study were excluded, as were dogs that had been treated with products with residual activity against *S. scabiei* within 30 days of the start of the study. Dogs came from single dog households and households with other dogs (up to a total of five dogs). The dogs were kept under their normal household conditions and thus, lived indoors only, outdoors only, or both indoors and outdoors. Each dog was enrolled with the written informed consent of the owner.

2.2.2. Experimental design and methods

On Day −1 or 0, primary dogs were examined to ensure suitability for enrolment (bodyweight, physical examination, skin scraping, and clinical sign assessment). Primary dogs were allocated in a ratio of 2:1 to one of two treatment groups to receive sarolaner or the commercial comparator, respectively, in a randomized block design with one-way treatment structure replicated in multiple clinics. Supplementary dogs received the same treatment as the primary dog.

All treatments were dispensed according to a randomization plan that was provided for each clinic before the start of the study. Treatment dispensing was based upon body weights recorded on Days 0 and 30, and treatments were administered by the Owner in the home environment on these Days. The Owners were not masked to treatment allocation. Animals were dosed with the appropriate strength sarolaner flavored, chewable tablet (Simparica™) to provide the recommended minimum dose of 2 mg/kg (range 2–4 mg/kg). The voluntary acceptance and consumption of sarolaner tablets within one minute after offering was evaluated by the Owner at each administration. The imidacloprid/moxidectin spot-on (Advocate®) was applied topically according to its label directions to deliver 10–25 mg/kg imidacloprid and 2.5–6.25 mg/kg moxidectin.

At clinic visits on Days 14, 30, and 60, primary dogs received a physical exam and were evaluated for the clinical signs of sarcoptic mange. Skin scrapings were conducted on Days 30 and 60. Supplementary dogs were given physical exams only at these clinic visits. The severity of clinical signs of sarcoptic mange (including pruritus, erythema, scaling/crusting, papules and hair loss) were evaluated on a four grade scale as absent, mild, moderate or severe. To assess presence/absence of mites, deep skin scrapings were conducted as described for the laboratory study. Skin scraping was repeated until a live mite was found or a maximum of 10 sites had been scraped. All dogs (primary and supplementary) that received at least one treatment were included in the safety assessment. All abnormal health events observed during the physical examinations by the veterinarian or observed by the owner between visits, were recorded.

2.2.3. Data analysis

Only primary dogs were included in the efficacy analysis. The animal (primary dog per household) was the experimental unit. The primary efficacy endpoint was the parasitological cure rate, which was defined as the percent of dogs for which no live mites were found in the skin scrapings. The secondary efficacy endpoint was the frequency distribution of the skin lesion severity grades at each post-treatment time point. Dogs that received concomitant medications that could have potentially affected the clinical signs of mite infestation were excluded from the analysis of skin lesion assessment. For the parasitological cure rate, non-inferiority of sarolaner to the positive control product was assessed at each time point using a margin of 15% at the one-sided $\alpha = 0.025$ significance level.

3. Results

3.1. Laboratory study

3.1.1. Efficacy

On Days 14, 30, 44, and 60, mite counts from 21, 20, 19, and 18 placebo-treated dogs, and from 22, 22, 20, and 20 sarolaner-treated dogs were included in the efficacy evaluation.

For all dogs (non-immunosuppressed and immunosuppressed), the efficacy based on arithmetic means for sarolaner-treated dogs compared to placebo-treated dogs or relative to the pre-treatment mean was >99% at all post treatment evaluations (Table 1). Arithmetic mean live mite counts were increased in the placebo group relative to pre-treatment at all post treatment evaluations except Day 60, when there was an 82.8% reduction.

Seventy seven percent (77%) of sarolaner-treated dogs were free of mites on Day 14, 100% were free of mites on Days 30 and 60, and only one live mite was found on a single sarolaner-treated dog on Day 44 (Table 2). The percentages of dogs with live mites in the placebo group on Days 14, 30, 44 and 60 were 52.4, 35.0%, 36.8 and 38.9%, respectively. Only two of 11 (18%) placebo-treated dogs that did not receive any immunosuppression harbored live mites on Day 60. In contrast, one of three dogs (33%) that were started on immunosuppression before Day 30, and all four dogs (100%) that were immunosuppressed for the entire study had live mites on Day 60.

3.1.2. Health observations

There were no adverse health events related to treatment with sarolaner noted in the study. In the placebo group, three dogs died during the study, two from canine ehrlichiosis and one due to glomerulonephritis. One additional, placebo dog was withdrawn due to a transmissible venereal tumour. Two dogs were removed from the sarolaner group when they were identified as pregnant during the study.

3.2. Field study

3.2.1. Animals

A total of 79 primary dogs (53 in the sarolaner group and 26 in the imidacloprid/moxidectin group) and 45 supplementary dogs (26 in the sarolaner group and 19 in the imidacloprid/moxidectin group) were enrolled and treated. All enrolled dogs completed the study. One dog in the imidacloprid/moxidectin group was inadvertently under-dosed at the second administration, therefore the Day 60 mite counts from this dog were excluded from the data analysis.

The mean age at enrolment was 4.2 years in the sarolaner group and 4.1 years in the imidacloprid/moxidectin group. In the sarolaner group, 48.1% of the dogs were purebreeds and 51.9% were mixed breeds, while in the imidacloprid/moxidectin group 31.1% were purebreeds and 68.9% were mixed breeds. In the sarolaner group, 57% of the dogs were females and 43% were males, while in the imidacloprid/moxidectin group 60% were females and 40% were males. At enrolment the mean body weight was 21.7 and 18.1 kg in the sarolaner and the imidacloprid/moxidectin treated groups, respectively.

3.2.2. Efficacy

Live mites were found in six sarolaner-treated dogs (11.3%) on Day 30, while on Day 60, no live mites were detected on any dog in the sarolaner group (Table 3). In the moxidectin/imidacloprid-treated group four dogs (15.4%) had live mites present in the skin scrapings on Day 30 and one dog (4.0%) on Day 60. Thus, the parasitological cure rate on Days 30 and 60 was 88.7% and 100% in the sarolaner group, and 84.6% and 96.0% in the moxidectin/imidacloprid group. The parasitological cure rate for

Table 1
Efficacy against *Sarcoptes scabiei* in the laboratory study: number of dogs, arithmetic mean live mite counts (nymphs, larvae and adults), ranges, percent reductions relative to pre-treatment count, and efficacy relative to placebo for dogs dosed with sarolaner chewable tablets administered orally once a month for two months.

Study day	Treatment group	Number of dogs[a]	Mite counts		Reduction/Efficacy[a] (%)	
			Arithmetic mean	Range	Versus pre-treatment	Versus placebo
0	Placebo	22	28.1	1–234	–	–
	Sarolaner	22	82.9	1–1577	–	–
14	Placebo	21	61.4	0–942	0.0	–
	Sarolaner	22	0.5	0–5	99.4	99.2
30	Placebo	20	28.6	0–463	0.0	–
	Sarolaner	22	0.0	0–0	100	100
44	Placebo	19	74.3	0–1263	0.0	–
	Sarolaner	20	0.1	0–1	99.9	99.9
60	Placebo	18	4.8	0–30	82.8	–
	Sarolaner	20	0.0	0–0	100	100

[a] 12 dogs in each treatment group never received immunosuppression; three dogs in each treatment group received immunosuppression between Day 0 and 30; in seven dogs in each group immunosuppression started before Day 0.

Table 2
Efficacy against *Sarcoptes scabiei* in the laboratory study: numbers and proportions of dogs with live mites or no live mites detected in skin scrapings for dogs dosed with placebo or sarolaner chewable tablets administered orally once a month for two months.

Study day	Treatment group	Number of dogs*	No live mites		Live mites	
			Number	%	Number	%
0	Placebo	22	0	0.0	22	100
	Sarolaner	22	0	0.0	22	100
14	Placebo	21	10	47.6	11	52.4
	Sarolaner	22	17	77.3	5	22.7
30	Placebo	20	13	65.0	7	35.0
	Sarolaner	22	22	100	0	0.0
44	Placebo	19	12	63.2	7	36.8
	Sarolaner	20	19	95.0	1	5.0
60	Placebo	18	11	61.1	7	38.9
	Sarolaner	20	20	100	0	0.0

* 12 dogs in each treatment group never received immunosuppression; three dogs in each treatment group received immunosuppression between Day 0 and 30; in seven dogs in each group immunosuppression started before Day 0.

Table 3
Efficacy against *Sarcoptes scabiei* in the field study: Number of dogs with no live mites, parasitological cure rates, confidence intervals and non-inferiority for dogs presented as veterinary patients and dosed with sarolaner chewable tablets administered orally or imidacloprid/moxidectin applied topically once a month for two months.

Study day	Treatment	Number of dogs		Parasitological cure rate[a]	Lower 97.5% CI	Non-inferior?[b]
		Total	No live mites			
30 ± 5	Sarolaner	53	47	88.7		
	Imidacloprid/moxidecin	26	22	84.6	−0.109	YES
60 ± 5	Sarolaner	53	53	100		
	Imidacloprid/moxidecin	25	24	96.0	−0.029	YES

[a] Parasitological cure rate defined as the percent of dogs in the given treatment group having no live mites in the skin scrapings on the respective study day.
[b] Parasitological cure rate of sarolaner determined to be non-inferior to imidicloprid/moxidectin if the one-sided exact lower 97.5% CI was greater than −0.15.

sarolaner was non-inferior to moxidectin/imidacloprid at both time points (Table 3).

At enrolment, the majority of the dogs in both groups had alopecia, papules, pruritus, erythema, and scaling/crusting (Table 4), and these signs were graded as moderate to severe in at least 50% of the dogs. These clinical signs of sarcoptic mange improved markedly throughout the study in both groups. At study completion only 25.5%, 2.0%, 2.0%, 5.9% and 11.8% of the dogs had hair loss, papules, pruritus, erythema, or scaling/crusting, respectively in the sarolaner group, while 16.7%, 0.0%, 12.5%, 8.3% and 12.5% of the dogs had these signs in the moxidectin/imidacloprid group (Table 4). Skin lesions that were present at study completion were mostly mild in nature. Skin lesions of moderate severity were only observed in five dogs at study completion of which moderate alopecia was reported in one dog in each group, moderate scaling/crusting in one dog in the sarolaner group, and moderate erythema and pruritus in one dog in each group at study completion. One dog in the moxidectin/imidacloprid group had severe pruritus at study completion and live mites were present on skin scraping.

3.3. Safety

There were no adverse reactions to treatment with sarolaner. Abnormal health events were reported in 10 dogs, seven in the sarolaner-treated group and three in the moxidectin/imidacloprid-treated group. In the sarolaner group, there were four dogs with various dermatologic abnormalities (bacterial cellulitis, bite wounds and pyotraumatic dermatitis), all of which resolved following treatment with an antimicrobial and/or anti-inflammatory

Table 4
Clinical signs of sarcoptic mange. Number (n) and percent (%) of dogs with clinical signs at enrolment and at study completion presented as veterinary patients and dosed with sarolaner tablets administered orally or imidacloprid/moxidectin applied topically once a month for two months.

Clinical sign	Sarolaner				Imidacloprid/moxidectin			
	Enrolment n = 53		Completion n = 51		Enrolment n = 26		Completion n = 24	
	n	%	n	%	n	%	n	%
Alopecia	53	100	13	25.5	26	100	4	16.7
Papules	50	94.3	1	2.0	26	100	0	0.0
Erythema	51	96.2	3	5.9	26	100	2	8.3
Pruritus	53	100	1	2.0	25	96.2	3	12.5
Scaling/Crusting	53	100	6	11.8	25	96.2	3	12.5

medication, one dog with pre-renal uraemia, one dog with a mammary mass and one dog with osteoarthrosis that received anti-inflammatory treatment. In the moxidectin/imidacloprid-treated group, there were two dogs with otitis and one dog with herniated spinal disc. None of these events were considered to be related to treatment with the test products.

3.4. Palatability

Sarolaner chewable tablets were voluntarily and fully consumed within one minute in 90.5% of all 158 occasions they were offered to primary and supplementary dogs.

4. Discussion

One placebo-controlled laboratory study and one multi-center clinical field study with a positive control was conducted to evaluate the efficacy of sarolaner against *S. scabiei*. Sarolaner achieved 100% parasitological cure in both studies following two monthly administrations and clinical signs of sarcoptic mange improved in treated dogs. The efficacy of sarolaner was non-inferior to the topically applied positive control in the field study; however parasitological cure was not achieved in one imidacloprid/moxidectin-treated dog after two monthly treatments whereas mites were eliminated from all sarolaner-treated dogs. Sarolaner tablets were also highly palatable with 90.5% acceptance by free choice within one minute of offering.

To the authors' knowledge this is the first report to document complete parasitological cure of sarcoptic mange in dogs following monthly treatment with an oral ectoparasiticide under both laboratory and field conditions. Previously, absence of mites in skin scrapings has been reported for topical products including selamectin (Shanks et al., 2000), imidacloprid/moxidectin (Fourie et al., 2006), and amitraz/fipronil/S-methoprene (Gaxiola et al., 2013) after two monthly administrations in laboratory studies. Parasitological cure was not achieved in all dogs after two monthly or four biweekly administrations of an amitraz/metaflumizone spot-on (Fourie et al., 2007) and after two monthly administration of pyriprole (Fourie et al., 2010). In dogs fitted with an imidacloprid/flumethrin collar, parasitological cure was reported after three months in a laboratory study (Stanneck et al., 2012). In a laboratory study with oral milbemycin, the presence of mites in skin scrapings was not evaluated, but only skin lesions were assessed (Miller et al., 1996), thus these results are difficult to compare with the current study.

Interestingly, in most of the above laboratory studies either no control group was included (Miller et al., 1996; Fourie et al., 2007; Stanneck et al., 2012) or a positive control product was used (Fourie et al., 2006, 2010). In the laboratory studies that used placebo-treated (Shanks et al., 2000) or untreated control animals (Gaxiola et al., 2013), a decrease in mite counts was reported in the control animals during the study period. These results are in line with the observations in the placebo-treated animals in the laboratory study reported here, in which at the end of the study, no mites were found in the skin scrapings of nine out of the 11 dogs that did not receive immunosuppression. In contrast, all placebo-treated dogs that received immunosuppressive treatment from the study start maintained the mite infestations throughout the study. These observations suggest that mite counts in laboratory studies may be biased by spontaneous cure and immunosuppressive treatment may be required to evaluate treatment success under laboratory conditions.

While *Sarcoptes* mites are notoriously difficult to find in skin scrapings (Miller et al., 2013), the dogs in both studies reported here were subjected to a high level of scrutiny to detect mites. Each dog was required to have 10 negative skin scrapings from different body areas to be declared parasitologically cured, providing a high level of confidence that these dogs were truly negative for mites. A similar high level of scrutiny was only reported in one previous laboratory study (Shanks et al., 2000) and in a multi-center field study (Six et al., 2000). In another field study eight skin scrapings were collected from each dog (Krieger et al., 2005), while in other studies only up to five skin scrapings were done (Fourie et al., 2006, 2007, 2010; Stanneck et al., 2012; Gaxiola et al., 2013).

Randomized, controlled multi-center field studies of similar scale and design have been reported for selamectin (Six et al., 2000) and for imidacloprid/moxidectin (Krieger et al., 2005). In both of these studies, complete parasitological cure was achieved following two monthly treatments in all dogs that was accompanied by an improvement in the pruritus and skin lesions characteristic of sarcoptic mange. In the field study reported here, pruritus, the most prominent clinical sign of sarcoptic mange, resolved in all but one sarolaner-treated dog (2%) and this dog had only mild pruritus at study completion. In contrast, in the imidacloprid/moxidectin-treated group, three dogs (12.5%) had varying degree of mild to severe pruritus following two monthly treatments. As pruritus in sarcoptic mange is thought to be a symptom of a hypersensitivity reaction to mite antigens, it may still be observed in dogs several weeks after parasitological cure because of the presence of the dead or decomposing mites in the skin following treatment. The day 14 mite count results in the laboratory study and the fact that pruritus resolved in all but one dog following two monthly treatments in the field study presented here indicates that sarolaner has rapid, miticidal activity.

The sarolaner tablets (Simparica™) were highly palatable in the target population with over 90% voluntary, full consumption. Owner non-compliance is reported as a frequent cause of mange treatment failures (Miller et al., 2013). The high palatability and ease of administration of these flavored, chewable tablets could reduce suboptimal efficacy results in dogs with sarcoptic mange due to non-compliance. This combined with excellent efficacy against *S. scabiei* following two monthly doses will make sarolaner a valuable tool for veterinarians and dog owners for the treatment of sarcoptic mange.

5. Conclusions

Sarolaner administered orally twice at monthly intervals at the minimum label dosage of 2 mg/kg was safe and achieved complete parasitological cure in dogs with natural infestations of *Sarcoptes scabiei*. In addition, the clinical signs of sarcoptic mange improved without topical or systemic concomitant treatment, and Simparica™ chewable tablets were highly palatable.

Conflict of interest

The studies reported here were funded by Zoetis, Florham Park, N.J. J.J.F. was an independent investigator contracted for the laboratory study. All other authors were employees of Zoetis and assisted with the design and conduct of the studies, interpretation of the data and manuscript review. There were no conflicting interests that could have influenced the conduct and reporting of these studies.

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