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Evaluation of the speed of kill of sarolaner (Simparica™) against induced infestations of three species of ticks (*Amblyomma maculatum, Ixodes scapularis, Ixodes ricinus*) on dogs

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ABSTRACT

The rapid speed of kill of sarolaner (Simparica™, Zoetis), a novel isoxazoline compound, was demonstrated against three tick species known to infest dogs in Europe or the United States. Efficacy was measured against an existing infestation and against subsequent weekly re-infestations for 35 days after treatment.

Dogs were randomly allocated to treatment with a single oral dose of either placebo or sarolaner (2 mg/kg) based on pre-treatment host-suitability tick counts. Dogs were infested with approximately 50 unfed adult *Ixodes scapularis*, *Ixodes ricinus* or *Amblyomma maculatum* ticks on Days−2, 7, 14, 21, 28 and 35. Tick counts were conducted at 4 (*I. scapularis* only), 8, 12 and 24 h after treatment on Day 0 and after each subsequent re-infestation.

No treatment-related adverse reactions occurred during any of these studies. Dogs in the placebo-treated groups maintained adequate tick infestations (recovery of 20–70% of applied ticks) throughout the duration of the studies. Following treatment, live tick counts were significantly reduced relative to placebo at the 8 h post treatment counts indicating that sarolaner started killing existing infestations of ticks rapidly after treatment. Efficacy was 90.1% against *I. ricinus*, 98.8% against *I. scapularis*, and 99.2% against *A. maculatum* within 12 h, and 100% efficacy was achieved at 24 h after treatment against all three tick species. This speed of kill was maintained throughout the month with ≥95.7%, ≥98.7% and ≥89.6% efficacy against *I. scapularis, I. ricinus*, and *A. maculatum*, respectively, at 24 h after re-infestation at least through Day 28.

1. Introduction

Amyblyomma maculatum (Gulf Coast tick) and *Ixodes scapularis* (black legged or deer tick) are tick species that infest dogs in the United States. *Ixodes ricinus* (castor bean or sheep tick) is an important species infesting dogs in Europe (Chomel, 2011). Most ticks that infest dogs and cats, including the genera *Amblyomma* and *Ixodes*, use an ambush technique called questing to locate the host; the ticks crawl onto weeds, grasses, bushes or other leafy vegetation, extend their forelegs, which contain a sensory apparatus called a Haller organ, and wait for the host to brush against the vegetation. When this occurs, the tick releases from the vegetation and crawls onto the host (Dryden and Payne, 2004). The ticks use their chelicerae to cut the dermis and insert their hypostome containing backward directed spikes. Many ticks reinforce this attachment by secreting a cement-like substance from the salivary glands. Once the attachment is secure, the tick begins its slow blood-feeding phase which may last for several days. The slow feeding phase is followed by the rapid feeding phase. During the rapid feeding phase, which occurs 12–36 h before the tick detaches from the host, the mated female may increase dramatically in size often reaching up to one hundred times her unfed body weight (Blagburn and Dryden, 2009).

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Blood feeding by ticks can cause irritation, debilitation through blood loss, and paralysis or death from the section of salivary toxins. In addition, ticks are vectors for a number of serious pathogens affecting dogs, man and other animals. In the United States, *A. maculatum* is known to transmit *Rickettsia parkeri,* a spotted fever group rickettsia recently found to be pathogenic to humans, resulting in an eschar-producing febrile illness (Jiang et al., 2012; Chomel, 2011). This tick also transmits *Hepatozoon americanum*, which causes American canine hepatozoonosis, though the dog must ingest the tick to become infected (Ewing and Panciera, 2003; Blagburn and Dryden, 2009). *Ixodes scapularis* is the main vector of *Borrelia burgdorferi* sensu lato (Lyme disease) in the United States and is also the vector of *Anaplasma phagocytophilum* (causes anaplasmosis in humans and canines) and *Babesia microtis* (causes human babesiosis). Both *A. maculatum* and *I. scapularis* may also cause tick paralysis (Blagburn and Dryden, 2009) which can affect birds, reptiles, humans, dogs, and a wide variety of other mammals. In Europe, *Ixodes ricinus* is the main vector of *B. burgdorferi* sensu lato and is also the vector of the tick borne encephalitis virus as well as a number of other pathogens of humans and domestic animals (Jaenson et al., 2012). Reports from Asia, Europe, and the United States have documented *Bartonell henselae* DNA in *Ixodes* spp. and while pathogen transfer has not been confirmed in dogs, a recent study showed *I. ricinus* to be a competent vector of *Bartonella birtlesii* in a murine model (Reis et al., 2011).

In the past two decades, throughout the United States and Europe, the tick population in established regions has become more abundant and the geographical distribution has continued to expand (Jaenson et al., 2012; Leighton et al., 2012). This change can be explained by two main factors: first, the high availability of large numbers of important tick maintenance hosts, second, a warmer climate with milder winters and a prolonged growing season that permits greater survival and proliferation over a larger geographical area of both the tick itself and its hosts (Blagburn and Dryden, 2009; Jaenson et al., 2012; Lindgren et al., 2000). The increase in the tick population means that humans and their pets are encountering more ticks and are exposed to more ticks per encounter and that pet owners are seeing more ticks on their pets than in the past. Numerous studies support the efficacy of host targeted tick control products (Dryden, 2009). The successful transmission of tick borne diseases to the host may require a prolonged period of attachment usually 24–48 h or longer (Little, 2007), though for some rickettsial pathogens transmission may possibly occur within as little as 4 h (Nicholson et al., 2010). Thus a product's speed of kill, defined as the time required to kill ticks that are already attached or to kill ticks after re-infestation, is key in the selection of an acaricide to reduce a dog's potential risk of contracting tick-borne diseases. Additionally, products with rapid efficacy are more effective in ameliorating the irritation and debilitating effects due to blood loss or tick toxicosis.

A new class of ectoparasitics, the isoxazolines, have shown excellent efficacy against fleas and ticks following oral administration (Rohdich et al., 2014; Shoop et al., 2014). Sarolaner is a new, potent isoxazoline that provides treatment and month long control of ticks and fleas on dogs following a single oral dose (McTier et al., 2016). Laboratory studies confirmed the excellent efficacy of sarolaner for the entire month against the major species of ticks infesting dogs in the EU and US (Geurden et al., 2016; Six et al., 2016). As the speed of kill and consequent interruption of feeding is critical for acaricides to reduce the chances of transmission of tick-borne diseases, laboratory studies were conducted to evaluate the speed of kill of sarolaner against three tick species (*I. scapularis*, *I. ricinus* and *A. maculatum*) for a period of five weeks after treatment.

2. Materials and methods

Three laboratory studies were conducted in purpose bred dogs to evaluate the speed of kill of the minimum single oral dose of 2 mg/kg bodyweight sarolaner against induced tick infestations and weekly challenges up to 35 days post treatment. Efficacy against *I. scapularis* was evaluated at a research facility in Sugar Land, Texas. The *I. ricinius* study was carried out in Glenamoy, Ireland and the study with *A. maculatum* was conducted in Greenbrier, Arkansas. All studies were conducted in accordance with the World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines for evaluating the efficacy of parasiticides for the treatment, prevention and control of flea and tick infestation on dogs and cats (Marchiondo et al., 2013) and complied with Good Clinical Practice, (EMEA, 2000). Protocols were reviewed and approved by the local and or Zoetis Institutional Animal Care and Use Committee. Masking of all studies was assured through the separation of functions with all personnel conducting observations or animal care or performing infestations and counts masked to treatment allocation.

2.1. Animals

Purpose bred Beagle and mongrel dogs of both sexes, aged 6 months to 7.5 years and weighing 6.0–26.0 kg were used. All dogs had not been treated with an ectoparasiticide for at least 60 days or demonstrated good tick retention (recovery of at least 25% of the applied ticks at 48 h after infestation) prior to treatment and were in good health at enrolment. Each dog was individually identified by a unique microchip or ear tattoo. Dogs were individually housed in indoor pens such that no physical contact was possible between dogs from Day 0 to the end of the study. Dogs were fed an appropriate maintenance ration of a commercial dry canine feed for the duration of the study. Water was available ad libitum.

2.2. Experimental design

Day 0 for each study was the day dogs were administered the study treatment. A physical exam was performed on each dog by a veterinarian to determine health and suitability prior to inclusion in the study. Dogs were acclimatized for a minimum of 12 days before treatment and general health observations were performed twice daily from the start of the acclimation period to the end of the study. All dogs were examined to ensure they were free of ticks and were then infested between Day −9 and Day −6 to determine host suitability. The number of live attached ticks present on each dog was counted 48 (±2) hours after this infestation.

The studies followed a randomized, complete block design and block was based on the pre-treatment host-suitability tick counts and pen location. For the *I. scapularis* and *I. ricinus* studies, there were eight dogs per group. For *A. maculatum*, seven dogs were allocated per group. Dogs were ranked according to decreasing host suitability tick counts and randomly allocated within blocks. In the *I. scapularis* study, 64 dogs were ranked in blocks of eight and assigned to one of four placebo or one of four sarolaner groups with one group of each treatment assigned for tick counts at 4, 8, 12 or 24 h after treatment and subsequent tick infestations on Days 7, 14, 21, 28 and 35. In the *I. ricinus* study, 48 dogs were ranked in blocks of six and assigned to one of three placebo or one of three sarolaner groups with one group of each treatment assigned for tick counts at 8, 12 or 24 h after treatment or subsequent tick infestations on Days 7, 14, 21, 28 and 35. In the *A. maculatum* study, 42 dogs were assigned to one of one of three placebo or one of three sarolaner groups with one group of each treatment assigned for tick counts at 8, 12 or 24 h after treatment or subsequent tick infestations on Days 7, 14, 21, 28 and 35.

For tick infestations (Days −2, 7, 14, 21, 28 and 35), dogs were manually held or sedated (*I. ricinus*) and a pre-counted aliquot of approximately 50 (1:1 sex ratio, 3:2 female:male was used for *I. ricinus* to increase the chances of >25% retention rate in untreated dogs) adult unfed ticks were placed onto the hair coat and allowed to disperse on the dog. The dogs infested with *A. maculatum* were placed in travel crates for 2–4 h after infestation to restrict the dogs' movement and facilitate tick attachment.

Tick counts were performed by personnel trained in the standard procedures in use at the test facility. Protective gloves and clothing were changed between dogs to prevent cross-contamination. Personnel conducting parasite or other observations were unaware of treatment assignments, and dogs were examined in a non-systematic order. Initially, the dog's entire body was examined, pushing the hair against its natural nap, exposing, counting and removing the ticks. After the manual inspection, an extra-fine tooth comb was used to comb the animal to remove any otherwise missed ticks. Each dog was examined for at least 10 min. If ticks were encountered in the last minute, combing was continued in one minute increments until no ticks were encountered. The ticks were examined to assess viability and the numbers of live ticks were quantified.

2.3. Treatment administration

Dose selection was made based on bodyweights measured on Day−2. Dogs were dosed with from one to three tablets (placebo or sarolaner (Simparica™ chewable tablets, Zoetis) strengths of 5, 10, 20, or 40 mg) such that the sarolaner dose was as close as possible to the minimum label dosage of 2 mg/kg without under-dosing. Dogs were hand-pilled to ensure accurate dose delivery. Food was offered prior to and after dosing. Dogs were observed for general health and any reaction to treatment approximately 1, 3 and 6 h after treatment.

2.4. Ticks

Ticks were considered pathogen free, as the unfed adult ticks used in the studies had been maintained for at least one generation in the colonies on pathogen-free hosts. The *I. scapularis* ticks were from a colony initiated with wild caught ticks from Oklahoma and locally collected ticks are introduced into the colony at least once every two years. *Ixodes ricinus* were from a European colony that has annual introductions of wild caught ticks. The *A. maculatum* were pooled from colonies in Oklahoma and Texas that both periodically introduce new wild caught ticks.

2.5. Data analysis

The individual dog was the experimental unit and the primary endpoint was live tick counts. Tick counts were transformed by the $\log_e(\text{count} + 1)$ transformation prior to analysis in order to stabilize the variance and normalize the data. Using the PROC MIXED procedure (SAS 9.2, Cary NC), transformed counts were analyzed using a mixed linear model. The fixed effect was treatment group and the random effects were room and block within room at each timepoint [in the *I. ricinus* study, the random effect was block at each timepoint]. Testing was two-sided at the significance level α=0.05. Percent efficacy was calculated using Abbott's formula:

$$\%\text{reduction} = 100 \times \frac{\text{mean count (placebo)} - \text{mean count (treated)}}{\text{mean count (placebo)}}$$

3. Results

3.1. Efficacy

Placebo-treated dogs maintained *I. scapularis* tick infestations throughout the study (Table 1) with approximately 25–50% of the applied infestation recovered at each time-point. The 4-hour timepoint was assessed for *I. scapularis* as it was expected to be the species most rapidly affected by sarolaner treatment, since it tends to attach and initiate feeding faster than the other species. However, at 4 h there was no significant reduction in live tick counts compared with placebo ($P > 0.05$, Table 1), therefore this timepoint was not evaluated for the other two species. Geometric mean live tick counts for sarolaner-treated dogs were significantly lower than placebo within 8 h after treatment on Day 0 ($P = 0.0002$), and within 12 h after re-infestations on Days 7–28 ($P \leq 0.0019$). Following the Day 35 infestation, counts were significantly lower by 24 h ($P \leq 0.0001$). Efficacy for sarolaner-treated dogs was 98.8% and 100% at 12 and 24 h respectively after treatment, and ≥95.7% by 24 h after infestation on Days 7, 14, 21 and 28, and 74.9% on Day 35.

Placebo-treated dogs maintained *I. ricinus* infestations throughout the study (Table 2) with approximately 35–50% of the applied infestation recovered at each time-point. Geometric mean live tick counts for sarolaner-treated dogs were significantly lower than placebo within 8 h after treatment on Day 0 ($P = 0.0003$) and after re-infestations on Days 7–28 ($P \leq 0.0409$). Following the Day 35 infestation, counts were significantly lower by 12 h ($P = 0.0022$). Efficacy for sarolaner-treated dogs was 90.1% and 100% at 12 and 24 h respectively after treatment, ≥94.9% by 12 h after infestation on Days 7, 14, 21 and 28, and 95.2% at 24 h on Day 35.

Placebo-treated dogs maintained *A. maculatum* tick infestations throughout the study (Table 3) with approximately 20–70% of the applied infestation recovered at each time-point. Geometric mean live tick counts for sarolaner-treated dogs were significantly lower than placebo within 8 h after treatment on Day 0 ($P \leq 0.0001$) and at 12 h after re-infestations on Days 7and 35 ($P \leq 0.0028$), and within 24 h after re-infestations on Days 14, 21 and 28 ($P \leq 0.0001$). Efficacy for sarolaner-treated dogs was 99.2% and 100% at 12 and 24 h respectively after treatment, and ≥94.1% by 24 h after infestation on Days 7, 14, 21 and 35, and 89.6% on Day 28.

3.2. Safety

There were no adverse events observed in any of the studies that were considered related to sarolaner treatment.

4. Discussion

In these studies, sarolaner demonstrated a rapid speed of kill against existing and subsequent re-infestations of ticks. This consistent and rapid persistent speed of kill against new infestations is notable when the biology of the ticks is considered, as counts were conducted soon after infestation and during this period the ticks had to disperse, penetrate the haircoat, attach, and begin feeding in order to ingest an effective dose.

The sustained efficacy against these tick species for up to 35 days is consistent with the results of dose confirmation studies which reported ongoing effectiveness through Day 35 when assessed at 48 h after treatment or re-infestation (Geurden et al., 2016; Six et al., 2016). The speed of kill and persistent efficacy of sarolaner is also comparable to those reported for some common marketed spot-on formulations (Baker et al., 2011; Endris et al., 2003; Bonneau et al., 2010; Baggott et al., 2011).

In these studies, live tick counts were significantly reduced relative to placebo at the 8 h counts, indicating that sarolaner quickly

Table 1
Geometric and (arithmetic) mean *Ixodes scapularis* (black legged tick) counts and ranges for placebo control and treated dogs and percent efficacy relative to controls at various times after treatment and re-infestation for dogs treated once orally with sarolaner at 2 mg/kg.

		Placebo		Sarolaner			
Day[a]	Hour[b]	Mean	Range	Mean	Range	Efficacy[c] (%)	P value[*]
0	4	18.2 (18.8)	11–25	21.4 (23.6)	8–36	0.0	0.4174
	8	17.4 (19.9)	6–34	7.6 (8.8)	2–17	56.5 (56.0)	0.0002
	12	24.1 (25.0)	16–40	0.3 (0.4)	0–1	98.8 (98.5)	<0.0001
	24	17.2 (17.4)	14–21	0.0 (0.0)	0–0	100	<0.0001
7	4	20.0 (20.9)	11–28	17.0 (18.0)	10–29	15.0 (13.8)	0.5060
	8	11.0 (13.3)	5–28	11.8 (14.3)	5–24	0.0	0.7795
	12	20.6 (22.4)	7–32	1.7 (1.9)	1–4	91.7 (91.6)	<0.0001
	24	13.3 (14.6)	5–24	0.0 (0.0)	0–0	100	<0.0001
14	4	21.5 (23.3)	11–36	17.1 (19.3)	6–36	20.7 (17.1)	0.4649
	8	12.4 (16.4)	2–33	13.6 (16.6)	4–30	0.0	0.7891
	12	9.8 (10.9)	4–19	3.0 (4.3)	0–11	68.8 (60.9)	0.0019
	24	11.1 (12.1)	5–19	0.1 (0.3)	0–2	98.7 (97.9)	<0.0001
21	4	19.1 (20.1)	12–31	23.7 (25.4)	9–36	0.0	0.3734
	8	12.7 (13.9)	5–24	18.1 (20.9)	7–34	0.0	0.1511
	12	19.5 (19.9)	14–27	5.1 (6.1)	2–14	74.0 (69.2)	<0.0001
	24	11.4 (13.9)	4–28	0.5 (0.6)	0–2	95.7 (95.5)	<0.0001
28	4	21.0 (23.9)	4–34	19.0 (20.4)	8–29	9.5 (14.7)	0.7129
	8	18.2 (20.9)	5–37	16.5 (18.0)	8–36	9.6 (13.8)	0.7121
	12	27.3 (29.3)	11–44	10.4 (11.3)	6–19	62.0 (61.5)	0.0008
	24	16.5 (17.5)	8–25	0.5 (1.0)	0–6	97.2 (94.3)	<0.0001
35	4	16.2 (18.0)	8–38	21.2 (21.9)	12–28	0.0	0.3357
	8	14.0 (16.8)	5–31	16.8 (18.1)	8–33	0.0	0.5232
	12	15.5 (16.8)	7–24	12.8 (14.8)	3–25	17.6 (11.9)	0.4966
	24	13.1 (14.4)	4–24	3.3 (4.6)	0–13	74.9 (67.8)	<0.0001

[a] Day of treatment (0) and subsequent weekly tick infestations.
[b] Time after treatment or subsequent weekly tick infestations.
[c] Efficacy relative to placebo based on geometric means; efficacy based on arithmetic means is given in parentheses if different.
[*] *P* value for comparison of geometric mean tick counts within a row, $P \leq 0.05$ indicates significant difference.

Table 2
Geometric and arithmetic mean *Ixodes ricinus* (castor bean tick) counts and ranges for placebo control and treated dogs and percent efficacy relative to controls at various times after treatment and re-infestation for dogs treated once orally with sarolaner at 2 mg/kg.

		Placebo		Sarolaner			
Day[a]	Hour[b]	Mean	Range	Mean	Range	Efficacy[c] (%)	*P* value[*]
0	8	22.9 (23.1)	19–30	5.3 (7.6)	1–23	76.7 (67.0)	0.0003
	12	19.8 (20.9)	8–28	2.0 (4.4)	0–14	90.1 (79.0)	<0.0001
	24	17.7 (20.4)	5–31	0.0 (0.0)	0–0	100	<0.0001
7	8	18.7 (19.3)	14–29	7.3 (9.0)	2–18	61.2 (53.2)	0.0001
	12	17.9 (18.0)	15–21	0.5 (0.8)	0–4	97.5 (95.8)	<0.0001
	24	18.3 (19.0)	11–24	0.0 (0.0)	0–0	100	<0.0001
14	8	25.6 (26.0)	20–35	8.0(11.1)	1–27	65.5 (57.2)	0.0004
	12	22.1 (22.3)	18–25	0.9 (2.0)	0–8	96.1 (91.0)	<0.0001
	24	21.0 (21.3)	17–28	0.0 (0.0)	0–0	100	<0.0001
21	8	23.0 (23.4)	17–31	13.5 (15.4)	4–31	41.4 (34.2)	0.0409
	12	23.3 (23.9)	17–32	0.8 (1.9)	0–10	96.6 (92.1)	0.0001
	24	20.0 (20.9)	12–30	0.3 (0.4)	0–2	98.7 (98.2)	<0.0001
28	8	24.8 (25.1)	17–31	19.0 (19.4)	4–31	23.2 (22.9)	0.0170
	12	23.4 (23.6)	17–32	1.2 (1.8)	0–10	94.9 (92.6)	<0.0001
	24	18.1 (19.8)	12–30	0.2 (0.4)	0–2	99.0 (98.1)	<0.0001
35	8	24.2 (24.8)	19–33	15.7 (17.8)	4–26	35.1 (28.3)	0.0922
	12	23.1 (23.8)	13–30	7.4 (9.3)	2–26	67.9 (61.1)	0.0022
	24	17.0 (18.1)	8–24	0.8 (1.6)	0–9	95.2 (91.0)	<0.0001

[a] Day of treatment (0) and subsequent weekly tick infestations.
[b] Time after treatment or subsequent weekly tick infestations.
[c] Efficacy relative to placebo based on geometric means; efficacy based on arithmetic means is given in parentheses if different.
[*] *P* value for comparison of geometric mean tick counts within a row, $P \leq 0.05$ indicates significant difference.

started killing existing infestations of ticks resulting in rapid, effective control with efficacy of 90.1% against *I. ricinus*, 98.8% against *I. scapularis* and 99.2% against *A. maculatum* within 12 h post-treatment, and 100% efficacy within 24 h post-treatment against all three tick species. This rapid speed of kill was maintained throughout the month with ≥95.7%, ≥98.7% and ≥89.6% efficacy against *I. scapularis, I. ricinus,* and *A. maculatum*, respectively, at 24 h after re-infestation at least through Day 28.

The increasing emergence of infection by zoonotic pathogens transmitted through tick bites to dogs and humans has triggered a

Table 3
Geometric and arithmetic mean *Amblyomma maculatum* (Gulf Coast tick) counts and ranges for placebo control and treated dogs and percent efficacy relative to controls at various times after treatment and re-infestation for dogs treated once orally with sarolaner at 2 mg/kg.

		Placebo		Sarolaner			
Day[a]	Hour[b]	Mean	Range	Mean	Range	Efficacy[c] (%)	*P* value[*]
0	8	31.1 (33.1)	21–50	3.0 (6.6)	0–19	90.3 (80.2)	<0.0001
	12	27.1 (29.0)	13–44	0.2 (0.3)	0–1	99.2 (99.0)	<0.0001
	24	30.1 (32.1)	17–50	0.0 (0.0)	0–0	100	<0.0001
7	8	36.0 (36.9)	27–48	32.1 (33.3)	17–42	10.9 (9.7)	0.5895
	12	30.5 (31.3)	22–45	15.1 (18.9)	5–43	50.3 (39.7)	0.0028
	24	23.5 (25.6)	13–45	1.1 (1.4)	0–3	95.2 (94.4)	<0.0001
14	8	37.6 (38.1)	29–50	28.5 (29.0)	20–39	24.3 (24.0)	0.0234
	12	25.0 (26.4)	11–39	13.1 (16.9)	4–50	47.6 (36.2)	0.0768
	24	9.7 (10.1)	6–14	0.2 (0.4)	0–3	97.8 (95.8)	<0.0001
21	8	26.8 (28.4)	14–42	29.7 (31.1)	18–43	0.0	0.7902
	12	10.5 (13.0)	1–25	16.6 (22.0)	4–47	0.0	0.2573
	24	18.4 (20.9)	9–45	1.1 (2.4)	0–13	94.1 (88.4)	<0.0001
28	8	29.9 (33.7)	10–50	22.5 (23.1)	16–32	24.9 (31.4)	0.2655
	12	16.1 (17.3)	7–27	15.4 (17.9)	7–40	4.4 (0.0)	0.8638
	24	17.0 (18.1)	10–29	1.8 (2.6)	0–7	89.6 (85.8)	<0.0001
35	8	28.6 (32.1)	7–50	17.4 (19.1)	3–32	39.3 (39.6)	0.0837
	12	29.8 (31.0)	13–50	10.2 (11.6)	2–20	65.9 (62.7)	0.0006
	24	17.2 (17.0)	10–25	0.6 (0.7)	0–3	96.7 (95.8)	<0.0001

[a] Day of treatment (0) and subsequent weekly tick infestations.
[b] Time after treatment or subsequent weekly tick infestations.
[c] Efficacy relative to placebo based on geometric means; efficacy based on arithmetic means is given in parentheses if different.
[*] *P* value for comparison of geometric mean tick counts within a row, $P \leq 0.05$ indicates significant difference.

renewed interest in comparative medicine and the concept of 'one medicine/one health' that unites human and veterinary sciences when addressing the epidemiology, treatment and prevention of tick borne infections (Otranto et al., 2009a,b; Dantas-Torres et al., 2012). The use of an ectoparasiticide such as sarolaner, which has a rapid speed of kill that persists for one month or longer after treatment, will be an important tool in the prevention and control of tick borne disease. An initial attachment and feeding of at least 24–48 h is required before transmission of many tick-borne pathogens can occur (Little, 2007; Salinas et al., 2010). If the infected ticks are killed within that time period, the transmission may be prevented (Wengenmayer et al., 2014). With its rapid speed of kill and sustained high efficacy within 24 h for a full month after a single dose, sarolaner is likely to effectively reduce the chances of ticks surviving and/or feeding for this critical time period. Thus, the use of sarolaner in a tick-control program should also reduce the chances of dogs becoming infected with tick-borne diseases, being affected by tick paralysis, and minimize deleterious health effects associated with tick infestation. Confirmatory studies using disease transmission models will be needed to definitively evaluate efficacy against the transmission of tick-borne pathogens.

5. Conclusions

Sarolaner has a quick onset of action against *A. maculatum*, *I. scapularis* and *I. ricinus*, resulting in the rapid kill of existing and subsequent re-infestations of ticks for a month after a single oral dose of 2 mg/kg. This rapid speed of kill and consistent and persistent efficacy against ticks following oral administration makes sarolaner a convenient and effective treatment for tick control. Used in a control program, sarolaner will reduce the impact of tick infestation and has the potential to reduce the risk of dogs contracting tick-borne diseases or tick paralysis.

Conflict of interest

The studies reported here were funded by Zoetis, Florham Park, NJ. RHS, TG, SPM, MRM, and NS are current employees of Zoetis. LC, WRE and AM were investigators contracted for these studies. All authors 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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