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Efficacy of a novel topical fipronil, (S)-methoprene, eprinomectin and praziquantel combination against naturally acquired intestinal nematode and cestode infections in cats

Martin Knaus[a,*], Marawan A. Abu-Madi[b], Froylán Ibarra-Velarde[c], Dawie J. Kok[d], Ilir Kusi[e], Rezart Postoli[e], S. Theodore Chester[f], Joseph Rosentel[f], Roberto Alva[g], Jennifer Irwin[g], Martin Visser[a], Renate Winter[a], Steffen Rehbein[a]

[a] Merial GmbH, Kathrinenhof Research Center, 83101 Rohrdorf, Germany
[b] Qatar University, Department of Health Sciences, College of Arts and Sciences, Doha, Qatar
[c] Universidad Nacional Autónoma de México, Coyoacán CP 04510, México D.F., Mexico
[d] ClinVet International (Pty) Ltd., 9321 Bloemfontein, South Africa
[e] Universiteti Bujqësor, Fakulteti i Mjeksise Veterinare, Kodër Kamëz, Tirana, Albania
[f] Merial Limited, Duluth, GA 30096, USA
[g] Merial Limited, Athens, GA 30601, USA

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ABSTRACT

The efficacy of a novel topical combination formulation of fipronil, (S)-methoprene, eprinomectin and praziquantel against naturally acquired intestinal nematode and cestode infections in cats was evaluated in seven negative control, blinded studies. Cats were selected based on a pre-treatment faecal examination indicating a patent infection with at least hookworms (two studies), *Toxocara* ascarids (one study), taeniid cestodes (two studies) or *Dipylidium* cestodes (two studies). In each study, cats were assigned randomly to blocks of two animals each, based on decreasing pre-treatment body weight and were randomly allocated to one of two groups of six to 12 cats: untreated (control) or treated with topical fipronil (8.3%, w/v), (S)-methoprene (10%, w/v), eprinomectin (0.4%, w/v) and praziquantel (8.3%, w/v) (BROADLINE®, Merial) at 0.12 mL/kg body weight (providing a minimum of 10 mg fipronil + 12 mg S-methoprene + 0.5 mg eprinomectin + 10 mg praziquantel per kg body weight). The topical treatment was administered directly on the skin in the midline of the neck in a single spot once on Day 0. For parasite recovery and count, cats were euthanized humanely and necropsied seven or ten days after treatment. A single treatment with the novel topical combination product provided 91% efficacy against *Ancylostoma braziliense*, ≥99% efficacy against *Ancylostoma tubaeforme*, and >97% efficacy against *Toxocara cati*. Similarly, excellent efficacy was established against *Taenia taeniaeformis*, *Dipylidium caninum* and *Diplopylidium* spp. as demonstrated by >97% and up to 100% reductions of cestode counts in the treated cats when compared to the untreated controls ($P < 0.01$). All cats accepted the treatment well based on health observations post-treatment and daily health observations. No adverse experiences or other health problems were observed throughout the studies. The results of this series of controlled studies demonstrated high efficacy and excellent acceptability of the novel topical combination formulation of fipronil, (S)-methoprene, eprinomectin and praziquantel against a broad range of feline intestinal nematode and cestode infections.

* Corresponding author. Tel.: +49 8032 70750; fax: +49 8032 707525.
E-mail address: martin.knaus@merial.com (M. Knaus).

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1. Introduction

Cats can harbour a wide variety of internal parasites. Despite an increase in prophylactic use of anthelmintics and increasing awareness of protozoan parasites in the last two decades, helminths still are recognized as being widespread and important parasites of cats. This prevalence is true not only for cats of high risk populations, such as stray feral cats or cats from rescue shelters (e.g., Miró et al., 2004; Robben et al., 2004; Ingstrup, 2008; Palmer et al., 2008; Gracenea et al., 2009; Duarte et al., 2010; Ładczuk and Balicka-Ramisz, 2010; Claerebout et al., 2011; Joffe et al., 2011; Lucio-Forster and Bowman, 2011; Becker et al., 2012; Blagburn et al., 2012), but also for pets (e.g., Coati et al., 2003; Palmer et al., 2008; Gates and Nolan, 2009; Ładczuk and Balicka-Ramisz, 2010; Barutzki and Schaper, 2011; Claerebout et al., 2011; Joffe et al., 2011; Itoh et al., 2012; Mugnaini et al., 2012; Näreaho et al., 2012). Because of access to the outdoors, even pet cats are at risk of being infected with gastrointestinal helminths, which may be diagnosed more often in cats from rural areas than in those from urban environments (Coati et al., 2003; Miró et al., 2004; Mircean et al., 2010; Capári et al., 2013).

The most prevalent helminth parasites of domestic cats are ascarid and ancylostomatid nematodes and taeniid and dipylidiid tapeworms. *Toxocara cati* is the most common nematode parasite of the gastrointestinal tract of cats throughout the world. *Ancylostoma* hookworms are the second most common nematodes of cats with two main species. While *Ancylostoma tubaeforme* is a cosmopolitan parasite of cats, *Ancylostoma braziliense* has a more restricted distribution and occurs in both cats and dogs in Africa and North and South America. *Taenia taeniaeformis* and *Dipylidium caninum* are by far the most prevalent tapeworms found in cats and have a worldwide distribution. Other species of cestodes which parasitize cats have a more restricted geographic distribution, such as *Echinococcus multilocularis* or *Diplopylidium* and *Joyeuxiella* species, or have been recorded incidentally only, e.g., *T. crassiceps*, *T. hydatigena* or *T. pisiformis* (Stoichev et al., 1982; Wilson-Hanson and Prescott, 1982; Bowman et al., 2002; Takács and Takács, 2002; Schuster et al., 2009).

The novel topical formulation Broadline®[1] (Merial) is a broad spectrum product combining the acaricide/insecticide fipronil and the insect growth regulator (S)-methoprene with two well-known anthelmintics, the macrocyclic lactone, eprinomectin, and praziquantel, a quinoline derivative. While topical fipronil and (S)-methoprene combinations or topical formulations containing praziquantel have been available for several years for the treatment of feline parasites, the anthelmintic properties of eprinomectin in cats are described for the first time in these studies. The studies reported here were designed to evaluate the efficacy and acceptability of the novel topical combination when administered to cats harbouring naturally acquired intestinal nematode and/or cestode infections.

[1] Broadline® is a trademark of Merial; all other marks are the property of their respective owners.

2. Materials and methods

The design of the studies was in accordance with the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) – GL7, "Efficacy of Anthelmintics: General Requirements" (Vercruysse et al., 2001), VICH GL20 "Efficacy of Anthelmintics: Specific Recommendations for Felines" (Vercruysse et al., 2002), and the "World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines for evaluating the efficacy of anthelmintics for dogs and cats" (Jacobs et al., 1994). All studies were conducted in compliance with VICH GL9, entitled *Good Clinical Practice* and in compliance with local animal welfare legislation and were approved by an Independent Animal Care and Use Committee. All personnel involved in collecting efficacy data were blinded to the treatment assignment of the animals.

2.1. Experimental animals

The seven studies were conducted in the Republic of South Africa (Studies 1 and 4), Albania (Studies 2, 3 and 6), Qatar (Study 5), and Mexico (Study 7). A total of 138 (71 male, 67 female) domestic short-haired cats, owned by the respective contract research organization, weighing between 0.7 and 4.56 kg prior to treatment, and aged approximately three months to seven years at the time of treatment, were included (details are presented in Table 1). The animals were housed individually during the entire studies and acclimated to the study facilities for at least seven days prior to treatment. The environmental conditions were identical for all animals within a study.

2.2. Selection of animals based on pre-treatment faecal examination

The selection criterion for inclusion of cats was the documented presence of a patent infection with specific target parasites, i.e., hookworms (two studies), *Toxocara* ascarids (one study), taeniid cestodes (two studies), or *Dipylidium* cestodes (two studies), as confirmed by examination of faecal samples collected during the acclimation period.

Faecal samples collected during the acclimation period were processed similarly in all studies. First, faeces were examined visually and macroscopically for the presence of cestode proglottids. Samples were then tested for nematode and cestode eggs using modified McMaster techniques to establish faecal nematode egg counts (Studies 1–6) or a double centrifugation/sucrose floatation technique (Study 7). Solutions used for floatation (zinc sulphate solution adjusted to a specific gravity of 1.3, four studies; Sheater's sucrose solution, three studies), amount of faeces processed (1 g or 4 g of faeces, one study each; 2 g of faeces, five studies) and the sensitivity of counting techniques (1 egg ≡ 25 eggs per g [EPG], three studies; 1 egg ≡ 50 EPG, one study; 1 egg ≡ 67 EPG, two studies) varied between sites. Parasites were identified based on the distinct morphology of their faecal forms, and results were reported as eggs

Table 1
Characteristics of experimental animals and results of pre-treatment faecal examination.

Study/group	Sex[a]	Approximate age (range)	Pre-treatment[b] body weight (kg)	Pre-treatment[c] faecal examination			
				Dipylidiid (evidence[d])	Taeniid (evidence)	Hookworm (EPG[e], range)	*Toxocara* (EPG, range)
Study 1 – target parasite: *Ancylostoma braziliense*							
Untreated	6 M, 4 F	4 months–adult	1.4–3.3	4/10	3/10	800–3600	0
Treated[f]	7 M, 3 F	5 months–adult	1.4–3.0	1/10	5/10	933–4867	0
Study 2 – target parasite: *Ancylostoma tubaeforme*							
Untreated	5 M, 5 F	4 months–7 years	0.9–3.3	4/10	0/10	100–800	0–1000
Treated[f]	5 M, 5 F	5 months–7 years	0.9–3.3	3/10	0/10	50–700	0–20,050
Study 3 – target parasite: *Toxocara cati*							
Untreated	4 M, 6 F	3 months–4 years	0.9–2.6	6/10	0/10	0–8250	50–4750
Treated[f]	2 M, 8 F	3 months–4 years	0.7–3.6	6/10	0/10	0–1000	100–2050
Study 4 – target parasite: *Taenia taeniaeformis*							
Untreated	6 M, 5 F	4 months–3 years	1.3–3.2	0/11	11/11	0–667	0–1200
Treated[f]	3 M, 8 F	5 months–2 years	1.1–3.0	0/11	11/11	0–2600	0
Study 5 – target parasite: *Taenia taeniaeformis*							
Untreated	8 M, 4 F	7 months–3 years	1.2–4.6	5/12	12/12	0–100	0
Treated[f]	11 M, 1 F	8 months–3 years	1.5–4.5	3/12	12/12	0–500	0–100
Study 6 – target parasite: *Dipylidium caninum*							
Untreated	5 M, 5 F	7 months–4 years	1.2–3.6	10/10	0/10	0–18,600	0–1150
Treated[f]	6 M, 4 F	8 months–3 years	1.5–3.1	10/10	0/10	0–1250	0–8450
Study 7 – target parasite: *Dipylidium caninum*							
Untreated	2 M, 4 F	1.5 years–4 years	2.3–3.9	6/6	0/6	2/6[d]	1/6[d]
Treated[f]	1 M, 5 F	8 months–4 years	2.2–3.6	6/6	0/6	0/6[d]	1/6[d]

[a] M, male; F, female.
[b] Day-3, Day-2 or Day-1 prior to treatment (=Day 0).
[c] Day-6 or Day-5 prior to treatment (=Day 0).
[d] Number of positive cats/number of cats in group.
[e] EPG, eggs per gram of faeces.
[f] Broadline® = fipronil (8.3%, w/v), (S)-methoprene (10%, w/v), eprinomectin (0.4%, w/v) and praziquantel (8.3%, w/v) at 0.12 mL/kg body weight.

per gram for each nematode and presence/absence of cestode proglottids/eggs (Studies 1–6) or presence/absence of nematode eggs and cestode proglottids/eggs (Study 7). All cats included were shown to harbour at least hookworm (Studies 1 and 2), *Toxocara* (Study 3), taeniid cestode (Studies 4 and 5) or dipylidiid cestode (Studies 6 and 7) infections (Table 1). Apart from the target parasite for each study, faecal examinations also showed evidence of co-infections with various other gastrointestinal helminths in many cats, as shown in Table 1.

2.3. Experimental design

The studies were conducted under a similar protocol utilizing a randomized block design. Replicates of two cats each were formed sequentially, based on decreasing pre-treatment body weights. Within replicates, animals were allocated randomly to one of two groups: untreated control group or treated group.

The treatment (fipronil (8.3%, w/v), (S)-methoprene (10%, w/v), eprinomectin (0.4%, w/v) and praziquantel (8.3%, w/v)) was administered topically at the minimum therapeutic dose of 0.12 mL/kg body weight (providing a minimum of 10 mg fipronil + 12 mg (S)-methoprene + 0.5 mg eprinomectin + 10 mg praziquantel per kg body weight) directly on the skin in the midline of the neck, between the base of the skull and the shoulder blades, in a single spot once on Day 0. All cats were observed for health problems and adverse events hourly for four hours post-treatment and thereafter once daily until the end of the study.

All study animals were euthanized humanely and necropsied to obtain a total gastrointestinal helminth count seven days (Studies 1, 2, 3, 6, 7) or ten days (Studies 4 and 5) after treatment.

2.4. Parasite recovery and count

The contents of the whole gastrointestinal tract (stomach, small and large intestines) were collected. To facilitate the isolation and counting of helminths, organ contents were washed through appropriately sized sieves to remove debris. Counts of parasites were made on total gastrointestinal contents. Helminths were identified to species/genus, if possible, according to their morphology.

2.5. Data analysis

Parasite counts for the target parasite in each individual study were transformed to the natural logarithm of (count + 1) for calculation of geometric means for each treatment group. Efficacy for the topically treated group was calculated as the percent efficacy using the formula $100 \times [(C - T)/C]$, were C is the geometric mean among untreated controls and T is the geometric mean among the treated animals. The log-counts of the treated group were compared to the log-counts of the untreated control group using a F-test adjusted for the allocation blocks. The Mixed procedure in SAS® Version 9.1.3 was used for this analysis with group as the fixed effect and allocation blocks as the random effect. Testing was two-sided at the significance level $\alpha = 0.05$.

In addition to the analysis of target parasite counts, counts of helminth species which occurred as co-infections with target parasites in one study only (*A. braziliense* and *Diplopylidium* spp. in Studies 4 or 5, respectively) were analyzed as described before. Species which occurred as co-infection with target parasites in more than one study were included in a combined analysis per parasite as follows: *A. tubaeforme*, Studies 1, 3, 4, 5, 6 and 7; *T. cati*, Studies 2, 4, 6 and 7; *T. taeniaeformis*, Studies 1, 3 and 7; *D. caninum*, Studies 1, 2, 3 and 4. Overall efficacy was calculated as percent reduction in worm counts as $100[(C - T)/C]$, were C is the geometric mean among untreated controls and T is the geometric mean among the treated animals treated. Helminth counts were analyzed using the Van Elteren rank test with individual studies considered to be blocks for this combined analysis. The PROC MIXED procedure in SAS, version 9.1.3 was used with group as a fixed effect and individual study as the random effect. A two-tailed significance level of 0.05 was used for all tests.

3. Results

No adverse events or other health problems were observed throughout the studies, indicating that the topical treatment was well accepted. No medications other than the investigational product were administered.

Identification of helminth parasites recovered from the gastrointestinal tract of the cats revealed the presence of nematodes (*A. braziliense*, Studies 1 and 4; *A. tubaeforme*, Studies 1–7; *T. cati*, Studies 2, 3, 4, 6, 7), cestodes (*D. caninum*, Studies 1, 2, 3, 4, 6, 7; *Diplopylidium* spp., Study 5, Figs. 1 and 2; *T. taeniaeformis*, Studies 1, 3, 4, 5, 7) and one trematode (*Echinoparyphium* spp., Study 1) (Table 2).

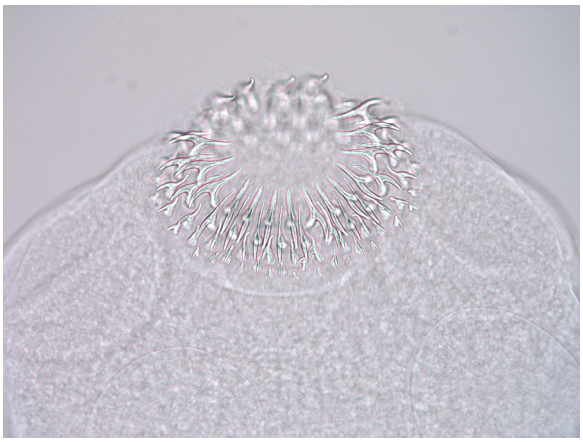

Fig. 1. Scolex of *Diplopylidium* spp. (© Merial).

The studies met the recommendations as to adequacy-of-infection as specified by VICH GL7 and VICH GL20, because at least six cats in each untreated (control) group harboured the minimum number of parasites of the target species accepted as adequate, i.e. 10 *A. braziliense*, 20 *A. tubaeforme*, 5 *T. cati*, 4 *T. taeniaeformis*, and 2 *D. caninum*.

The results of the seven studies as regards the target parasites are summarized in Table 3. Cats treated with the combination product had significantly ($P < 0.01$) fewer adult *A. braziliense*, *A. tubaeforme*, *T. cati*, *T. taeniaeformis* and *D. caninum* than the untreated controls with a reduction of the worm burden ranging from ≥91% to 100%.

Analysis of data of the nematode and cestode parasites occurring as co-infection with the target parasites revealed efficacies of 90.7% and 100% against *A. braziliense* and *Diplopylidium* spp., respectively, and overall efficacies of >97% for all other species in the analysis of pooled data across studies (Table 4).

In Study 5, 100% efficacy was demonstrated against the cestode *Diplopylidium* spp. Based on the minimum number

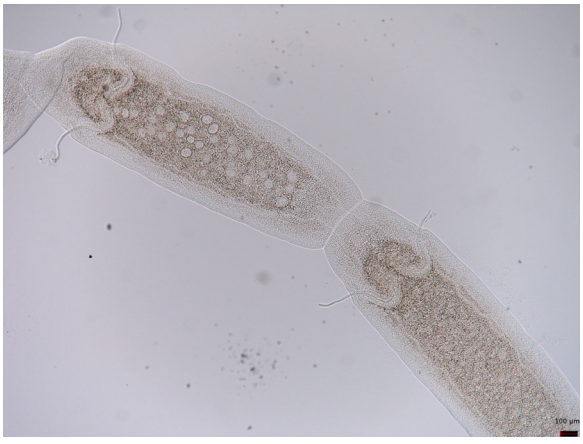

Fig. 2. Mature proglottid of *Diplopylidium* spp. (© Merial).

Table 2
Parasites recovered from the gastrointestinal tract of the study animals following necropsy seven (Studies 1, 2, 3, 6 and 7) or ten days (Studies 4 and 5) after treatment.

Study/group	Number of cats infected/number of cats in group (range of counts)						
	Ancylostoma braziliense	*Ancylostoma tubaeforme*	*Toxocara cati*	*Dipylidium caninum*	*Diplopylidium* spp.	*Taenia taeniaeformis*	*Echinoparyphium* spp.
Study 1 – target parasite: *Ancylostoma braziliense*							
Untreated	10/10 (10–114)	5/10 (0–27)	0/10	4/10 (0–63)	0/10	7/10 (0–19)	1/10 (1)
Treated[a]	6/10 (0–25)	0/10	0/10	0/10	0/10	0/10	1/10 (123)
Study 2 – target parasite: *Ancylostoma tubaeforme*							
Untreated	0/10	10/10 (2–71)	5/10 (0–37)	8/10 (0–75)	0/10	0/10	0/10
Treated[a]	0/10	2/10 (0–2)	1/10 (0–1)	2/10 (0–1)	0/10	0/10	0/10
Study 3 – target parasite: *Toxocara cati*							
Untreated	0/10	5/10 (0–34)	10/10 (1–16)	8/10 (0–140)	0/10	1/10 (0–1)	0/10
Treated[a]	0/10	0/10	1/10 (0–1)	1/10 (0–2)	0/10	0/10	0/10
Study 4 – target parasite: *Taenia taeniaeformis*							
Untreated	8/11 (0–53)	5/11 (0–1)	3/11 (0–11)	5/11 (0–21)	0/11	11/11 (1–26)	0/11
Treated[a]	3/11 (0–2)	1/11 (1)	0/11	0/11	0/11	0/11	0/11
Study 5 – target parasite: *Taenia taeniaeformis*							
Untreated	0/12	7/12 (0–56)	0/12	0/12	8/12 (0–130)	10/12 (0–44)	0/12
Treated[a]	0/12	0/12	0/12	0/12	0/12	2/12 (0–1)	0/12
Study 6 – target parasite: *Dipylidium caninum*							
Untreated	0/10	7/10 (0–33)	3/10 (0–5)	8/10 (0–181)	0/10	0/10	0/10
Treated[a]	0/10	0/10	0/10	1/10 (0–2)	0/10	0/10	0/10
Study 7 – target parasite: *Dipylidium caninum*							
Untreated	0/6	1/6 (1)	2/6 (0–2)	6/6 (10–279)	0/6	3/6 (0–6)	0/6
Treated[a]	0/6	0/6	0/6	1/6 (0–142)	0/6	0/6	0/6

[a] Treated = Broadline® spot on for cat applied at minimum therapeutic dose [fipronil (8.3%, w/v), (S)-methoprene (10%, w/v), eprinomectin (0.4%, w/v) and praziquantel (8.3%, w/v) at 0.12 mL/kg body weight].

of two parasites accepted as an adequate infection for the other dipylidiid cestode, eight of the 12 untreated control animals were adequately infected with cestodes in Study 5. Thus, this study was considered to meet the sense of adequacy-of-infection as specified by VICH GL7 and VICH GL20 for *Diplopylidium* spp.

4. Discussion

Apart from the echinostome trematodes found in two cats from South Africa, the helminths recovered from the gastrointestinal tract of the untreated control animals are common parasites of cats, and the occurrence of all parasites has been documented previously in the countries where the studies were conducted (Flores-Barroeta, 1955; Baker et al., 1989; King et al., 2006; Abu-Madi et al., 2007, 2010; Knaus et al., 2011, 2012).

Results of the current series of studies which targeted three nematodes and two cestodes of cats demonstrate that Broadline® is highly effective against naturally acquired infections of those feline parasites. Although partly based on relatively low levels of infection, analyses of the data for parasites occurring in co-infection with the target parasites demonstrated statistically significant difference between the counts of treated and untreated control animals. The analysis of the overall observations of effects of topical fipronil, (S)-methoprene, eprinomectin and praziquantel against these parasites is therefore considered conclusive

Table 3
Parasite counts and therapeutic efficacy in cats of Broadline® against naturally acquired intestinal nematode and cestode parasites – target parasites.

Parasite	Study	Untreated		Treated[a]		Efficacy (%)[b]	*P*-value[c]
		NI/NG[d]	GM[e] (range)	NI/NG	GM (Range)		
Ancylostoma braziliense	1	10/10	31.30 (10–114)	6/10	2.80 (0–25)	91.0	0.002
Ancylostoma tubaeforme	2	10/10	19.01 (2–71)	2/10	0.20 (0–2)	99.0	<0.001
Toxocara cati	3	10/10	5.14 (1–16)	1/10	0.07 (0–1)	98.6	<0.001
Taenia taeniaeformis	4	11/11	6.40 (1–26)	0/11	0	100	<0.001
	5	10/12	8.30 (0–44)	2/10	0.10 (0–1)	98.5	<0.001
Dipylidium caninum	6	8/10	13.68 (0–181)	1/10	0.12 (0–2)	99.2	0.001
	7	6/6	54.90 (10–279)	1/6	1.30 (0–142)	97.7	0.008

[a] Treated = Broadline® spot on for cat applied at minimum therapeutic dose [fipronil (8.3%, w/v), (S)-methoprene (10%, w/v), eprinomectin (0.4%, w/v) and praziquantel (8.3%, w/v) at 0.12 mL/kg body weight].
[b] Efficacy = 100 [(geometric mean untreated (control) – geometric mean Topical FMEP)/geometric mean untreated (control)].
[c] Two-sided *P*-value comparing the worm burden of the Topical FMEP group with the untreated (control) group.
[d] NI/NG: Number of cats Infected/Number of cats in Group.
[e] Geometric mean parasite count (based on transformation to ln [count + 1]).

Table 4
Parasite counts and therapeutic efficacy in cats of Broadline® against naturally acquired intestinal nematode and cestode parasites – analysis of species which occurred as co-infection with the target parasite.

Parasite	Occurring in study/studies	Untreated		Treated[a]		Efficacy (%)[d]	*P*-value
		NI/TN[b]	GM[c] (range)	NI/TN	GM (range)		
Ancylostoma braziliense	4	8/11	3.22 (0–53)	3/11	0.30 (0–2)	90.7	0.014[e]
Ancylostoma tubaeforme	1, 3, 4, 5, 6, 7	30/59	1.31 (0–56)	1/59	0.01 (0–1)	99.1	<0.001[f]
Toxocara cati	2, 4, 6, 7	13/37	0.64 (0–37)	1/37	0.02 (0–1)	97.1	<0.001[f]
Taenia taeniaeformis	1, 3, 7	11/26	0.91 (0–19)	0/26	0	100	<0.001[f]
Dipylidium caninum	1, 2, 3, 4	25/41	3.78 (0–140)	3/41	0.08 (0–2)	97.9	<0.001[f]
Diplopylidium spp.	5	8/12	6.00 (0–130)	0/12	0	100	0.0039[e]

[a] Treated = Broadline® spot on for cat applied at minimum therapeutic dose [fipronil (8.3%, w/v), (S)-methoprene (10%, w/v), eprinomectin (0.4%, w/v) and praziquantel (8.3%, w/v) at 0.12 mL/kg body weight].
[b] NI/NG: number of cats infected/total number of cats.
[c] Geometric mean parasite count (based on transformation to ln [count + 1]).
[d] Efficacy = 100 [(geometric mean untreated (control) – geometric mean Topical FMEP)/geometric mean untreated (control)].
[e] Two-sided *P*-value comparing the worm burden of the Topical FMEP group with the untreated (control) group.
[f] Probability from Van Elteren rank test.

and provides additional evidence of the efficacy of the new combination product against *A. braziliense*, *A. tubaeforme*, *T. cati*, *D. caninum* and *T. taeniaeformis*.

The macrocyclic lactone eprinomectin was developed and registered originally as a topical formulation for use in cattle at a dosage of 0.5 mg per kg body weight with indications against a broad range of both external and internal parasites, including common nematodes of the gastrointestinal tract and lungworms (Shoop and Soll, 2002). The bioavailability of eprinomectin following the topical administration of the novel fipronil, (S)-methoprene, eprinomectin and praziquantel combination to cats as spot-on is similar to that following the pour-on administration of the 0.5% (w/v) eprinomectin solution (EPRINEX® Pour-On, Merial) to cattle (Kvaternik et al., 2014). The efficacy of eprinomectin at 0.5 mg per kg body weight administered as a single spot directly onto the skin of cats in the novel topical fipronil, (S)-methoprene, eprinomectin and praziquantel combination against feline hookworm and ascarid infections demonstrated in the present studies is comparable to results noted in studies which assessed the efficacy of eprinomectin administered topically at the same dosage to cattle infected with bovine hookworms and ascarids (Avcioglu and Balkaya, 2011; Rehbein et al., 2012).

Praziquantel has been used for the treatment of feline tapeworm infections for many years with oral, injectable and spot-on formulations available for use in cats against infections with *T. taeniaeformis*, *E. multilocularis* and *D. caninum* (Dey-Hazra, 1976; Gürlap et al., 1976; Rommel et al., 1976; Bauditz and Sachs, 1979; Oakley, 1991; Jenkins and Romig, 2000). Beside the worldwide distributed *D. caninum*, cestodes of the other two genera belonging to the same family of tapeworms (Dipylidiidae), *Diplopylidium* and *Joyeuxiella*, have a more restricted distribution (mainly Mediterranean basin, Middle East, Middle Asia) and their heteroxenous life-cycle with domestic and wild canids and felids serving as definitive hosts is partly unknown (Schuster et al., 2009). In Europe, *Diplopylidium* and/or *Joyeuxiella* species are observed in cats in Albania, Bulgaria, France, Greece, Italy, Portugal and Spain (e.g., Haralampides, 1978; Stoichev et al., 1982; Dorchies et al., 1990; Calvete et al., 1998; Porqueddu et al., 2004; Knaus et al., 2011, 2012; Waap et al., 2013). Apart from providing consistently high efficacy against *D. caninum*, praziquantel administered at 5 mg per kg body weight was reported to be highly effective against another dipylidiid tapeworm in cats, *J. pasqualei* (Gürlap et al., 1976; Dorchies et al., 1990). However, there is also one case report describing the successful removal of a *Joyeuxiella* infection from a cat following subcutaneous injection of praziquantel at 25 mg per kg body weight only while the administration of injectable praziquantel at 5 mg per kg body weight did not remove all parasites (Schuster and Montag, 2000). In one study of the current series presented here, for the first time, praziquantel was demonstrated to provide excellent efficacy against *Diplopylidium*. Since *D. caninum*, *Diplopylidium* and *Joyeuxiella* species are closely related, praziquantel may thus be the compound of choice for the treatment of the structurally similar dipylidiid cestodes in cats.

Results of the current series of studies, as well as other controlled laboratory studies including cats with induced nematode (Knaus et al., 2014; Prullage et al., 2014) and *E. multilocularis* infections (Tielemans et al., 2014) demonstrate that Broadline® (fipronil, (S)-methoprene, eprinomectin and praziquantel) is highly effective in cats against naturally acquired and induced infections of adult gastrointestinal nematodes and cestodes. In addition, results of this series of controlled studies have been confirmed in a multicenter field study conducted in seven countries of Europe where cats treated with the novel spot-on combination showed >99.9% and 100% faecal egg count reductions for *Toxocara* and hookworms, respectively, and had no evidence of taeniid and *Dipylidium* infections after treatment (Rehbein et al., 2014).

Conflict of interest

The work reported herein was funded by Merial Limited, GA, USA. All authors are current employees or contractors of Merial.

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