



Multicenter randomized, and blinded European field study evaluating the efficacy and safety of Felpreva®, a novel spot-on formulation containing emodepside, praziquantel and tigelaner, in treating cats naturally infested with fleas and/or ticks



Dejan Cvejić^a, Klaus Hellmann^a, Gabriele Petry^b, Hannah Ringeisen^b, Hannah Hamburg^b, Róbert Farkas^c, Katrin Blazejak^d, Norbert Mencke^{d,*}

^a Klifovet GmbH, Geyerspergerstr. 27, 80689, München, Germany

^b Bayer Animal Health GmbH an Elanco Animal Health Company, Alfred Nobel Str. 50, 40789, Monheim, Germany

^c Department of Parasitology and Zoology, Faculty of Veterinary Medicine, Szent István University, István u. 2, Budapest, 1078, Hungary

^d Vetoquinol S.A., 37 rue de la Victoire, 75009, Paris, France

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ABSTRACT

The present field study evaluated the safety and 3-month preventive efficacy of a novel spot-on endectocide containing emodepside 2.04% w/v, praziquantel 8.14% w/v and tigelaner 9.79% w/v (Felpreva®, Vetoquinol) when administered at the intended commercial dose of 0.15 ml/kg body weight to privately owned cats infested by fleas (*Ctenocephalides felis*) and/or ticks (*Ixodes ricinus*, *Ixodes hexagonus*, *Rhipicephalus* spp.). The efficacy of Felpreva® to reduce the clinical signs associated with flea allergy dermatitis was also evaluated. A total of 326 cats, i.e. 120 and 206 infested by ticks and fleas respectively, from 16 different sites located in Hungary and Portugal were included on Day 0 and allocated in two Groups at a ratio of 2:1 (T1:T2). Cats of T1 were treated with Felpreva®, while cats of T2 were dosed with a commercial Control Product (Bravecto®, MSD Animal Health) licensed for the same indications. Of the 120 tick-infested cats, 79 and 41 were treated with Felpreva® and Bravecto® respectively, while of the 206 flea-infested cats, 139 were treated with Felpreva® and 67 with Bravecto®. Cats were physically examined on Days 7, 28, 56, 75 and 90; when present, fleas and ticks were counted and collected. Efficacy evaluation was based on the mean percent reduction of live parasite counts for each of five visits *versus* the pre-treatment count. Percent reductions of live flea and tick counts over all post-baseline periods were 99.74% (T1) *versus* 98.56% (T2) and 97.50% (T1) *versus* 98.65% (T2), respectively. Non-inferiority for the Felpreva® compared with the Bravecto® treated group was statistically demonstrated for both fleas and ticks. Three adverse events were observed and considered unlikely related to the treatment. These results show that the new topical combination product Felpreva® is safe and highly efficacious in treating flea and tick infections in cats for at least three months (90 days) with a single administration. In 16 cats that were identified with flea allergy dermatitis, the clinical signs of flea allergy dermatitis improved following treatment in both groups.

1. Introduction

Fleas and ticks are common ectoparasites of cats in many countries (Pennisi et al., 2015; Lefkaditis et al., 2016; Tulloch et al., 2017; Geurden et al., 2018; Abdullah et al., 2019). These arthropods cause direct damages (e.g. blood deprivation, skin lesions, tick paralysis, flea-allergic dermatitis) and transmit vector-borne diseases (VBDs) of veterinary and public health interest (Hill et al., 2006; Morelli, 2021).

Fleas are the predominant ectoparasites of domestic cats, which can be infested at high rates with the cat flea *Ctenocephalides felis*, followed by *Ctenocephalides canis* (the dog flea) and *Pulex irritans* (the human flea) (Farkas et al., 2009; Knaus et al., 2014; Persichetti et al., 2016). Flea allergy dermatitis is one of the most important dermatological conditions in small animal veterinary medicine. Fleas may transmit different pathogens, i.e. the zoonotic tapeworm *Dipylidium caninum*, and bacteria of the genera *Bartonella*, *Mycoplasma* and *Rickettsia* (Hill et al., 2006; Farkas

* Corresponding author.

E-mail address: norbert.mencke@vetoquinol.com (N. Mencke).

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et al., 2009). Ticks are usually considered less frequent in cats than fleas, though feline infestations are not uncommon and there is evidence of a global increased prevalence of tick infestations in cats (Tulloch et al., 2017; Little et al., 2018). Cats living in Europe may harbour several species of ticks, *Rhipicephalus sanguineus (sensu lato)*, *Ixodes ricinus*, *Ixodes hexagonus* and *Dermacentor reticulatus* being the most common (Ogden et al., 2000; Tulloch et al., 2017; Geurden et al., 2018). Ticks transmit relevant pathogens to cats, such as *Hepatozoon* spp., *Cytauxzoon* spp., *Ehrlichia* spp., *Anaplasma* spp. and *Borrelia* spp. (Little, 2010; Barker et al., 2019; Morelli et al., 2021). Many flea- and tick-borne pathogens have a recognized zoonotic potential (Kegler et al., 2018; Barker et al., 2019; Tørnqvist-Johnsen et al., 2020; Morelli et al., 2021).

The regular administration of appropriate ectoparasiticides is essential to control flea and tick infestation in cats and to reduce the risk of infection with the pathogens they may transmit. In recent years, different products containing isoxazolines have been licensed for use in cats infested with fleas and ticks (Geurden et al., 2017; Cavalleri et al., 2018a, b; Röhlich et al., 2018; Beugnet, 2021). Tigolaner is a newly developed molecule belonging to the chemical class of bispyrazoles and, though it is not an isoxazoline, it has the same efficacious mechanism of action against arthropods, i.e. it acts as antagonist of GABA-regulated chloride channels (International nonproprietary names for pharmaceutical substances: <http://www.who.int/publications/i/item/who-emp-rht-tsn-2018-1>).

The present study has investigated the efficacy and safety of a novel spot-on formulation containing tigolaner along with emodepside and praziquantel (Felpreva®, Vetoquinol) when administered to domestic cats naturally infested with ticks and/or fleas.

2. Materials and methods

2.1. Study design

This study was a controlled, randomized and blinded parallel group multicenter field study conducted in accordance with Veterinary International Conference on Harmonization Guidelines (VICH GL 9) (EMA, 2000) and to the EMEA/CVMP/EWP/005/2000-Rev.2 “Guidelines for the testing and evaluation of the efficacy of antiparasitic substances for the treatment and prevention of tick and flea infestations in dogs and cats” (EMEA, 2008).

The preventive efficacy and safety of a topical solution (Felpreva®) containing emodepside 2.04% w/v, praziquantel 8.14% w/v and tigolaner 9.79% w/v (Felpreva®, Vetoquinol) was evaluated in cats naturally infested with fleas and ticks, when administrated once at the intended commercial dose of 0.15 ml/kg body weight (BW), corresponding to a minimum of 3 mg/kg BW, 12 mg/kg BW and 14.4 mg/kg BW for emodepside, praziquantel and tigolaner respectively.

Felpreva® was evaluated for non-inferiority with a positive control product authorized for the target species in the EU market, i.e. a spot-on containing fluralaner (Bravecto®, MSD Animal Health).

2.2. Study sites, cat population and target parasites

As per guidelines two countries located in different geographical areas and with varying climatic conditions were selected. The study population consisted of client-owned cats presented at 16 veterinary practices equally located in Hungary and Portugal. The practices were selected in territories known for high prevalence of tick and/or flea infestation in companion animals. The target parasites were fleas (*C. felis*) and the common tick species (*I. ricinus*, *I. hexagonus*, *D. reticulatus* and *R. sanguineus (s.l.)*). Cat owners agreed to the participation of their animals in the study prior to enrolment and initiation of treatment, in terms of treatment, flea and/or tick count and collection procedures, and visits to veterinary practices at the required times.

2.3. Inclusion criteria

Cats were recruited before or at study Day 0 according to the following inclusion criteria: (i) cats living in households with a maximum of 3 cats and 2 dogs (maximum: 5 animals); (ii) cats with detected fleas and ticks (≥ 5 viable fleas and ≥ 3 attached and viable ticks); and (iii) adequate physical examination on Day 0.

Moreover, cats: (i) showing both (i.e. ≥ 5 viable fleas and ≥ 3 attached and viable ticks) were randomized according to the randomization list for tick households; (ii) with tick infestation (≥ 3 attached and viable ticks) but with less than 5 viable fleas (i.e. not meeting the inclusion criteria for flea infestation) were included and randomized as “tick patients”; (iii) with flea infestation (≥ 5 viable fleas) but with less than 3 attached and viable ticks (i.e. not meeting the inclusion criteria for tick infestation) were included and randomized as “flea patients”.

2.4. Exclusion criteria

The following animals were excluded from the study: (i) cats weighing less than 1.2 kg BW or less than 11 weeks-old on Day 0; (ii) females intended for breeding during the study until 4 months following the last dosing; (iii) queens known or suspected to be pregnant or lactating; (iv) cats with any history of apparent reactions to the Felpreva® and/or Bravecto® or any of their active compounds; (v) cats treated with an ectoparasiticide at a dosage and regimen known to provide efficacy against ticks and or fleas within the 12 weeks prior to Day 0; (vi) pre-existing medical and/or surgical condition except for routine surgical procedures.

2.5. Randomization

Cats were randomized per single household (flea or tick) according to a 2:1 ratio (Felpreva®: Bravecto®) in two groups, i.e. T1 (animals treated with Felpreva®) and T2 (animals treated with Bravecto®). All cats from the same household received the same treatment.

One cat per household was nominated as primary patient for efficacy and safety evaluations. In particular, if more than one cat in a household met the inclusion criteria, the cat with the highest number of fleas (≥ 5 viable fleas) or ticks (≥ 3 attached and viable ticks) was designated as the primary cat. All other cats in the same household were considered as supplementary patients and received safety evaluations.

Dogs living in the same household with cat(s) included into the study were treated with an adequate ectoparasiticide to eliminate flea infestation between animals.

2.6. Treatment

Cats infested with fleas and/or ticks were treated on Day 0 with Felpreva® (T1) or Bravecto® (T2) by the Dispenser in the clinic. Treatment dispensing was based on the body weights recorded on Day 0. Cats were dosed once with the appropriate pipette size of Felpreva® or Bravecto® to provide the recommended minimum dosage of 14.4 mg tigolaner + 3 mg emodepside + 12 mg praziquantel/kg body weight (Felpreva®) or following manufacturer’s recommendations to deliver 40 mg fluralaner/kg body weight (Bravecto®). Both products Felpreva® and Bravecto® were administered topically directly on the skin of the cats. Application was done with cat standing and application on the cat’s neck at the base of the skull, while the hair was divided with two fingers in this region until the skin was visible. The whole pipette volume was applied directly to the skin at one spot. Care was taken not to spill any product. The cat was restrained for about 1 min to allow the product to spread. No applied product got lost during administration.

2.7. Physical examinations and parasitological procedures

Cats enrolled in the study were subjected to a physical examination and body weighing on Day 0 (prior to inclusion), and post treatment at Day 7 (± 1), Day 28 (± 2), Day 56 (± 2), Day 75 (± 2) and Day 90 (± 2). The physical examination included an evaluation of clinical signs possibly related to flea allergy dermatitis and a visual inspection (thumb inspection and combing) for ectoparasites. The total body surface was combed with a flea comb provided. Each cat was combed for at least 10 min and the combing extended for at least another 5 min after the last flea was found. Tick assessment was carried out by thumb count, pushing the hair against its natural lap, thus skin and attached ticks are exposed, beginning at the head and systematically cover all areas of the animal.

A full body count was done for each study animal. Fleas and/or ticks eventually present on the animal were counted, categorized in viable/dead and attached/not attached (ticks), collected and appropriately stored.

A physical examination was performed on Day 0 (+ 2) and on Day 90 (± 2), and optionally on Day 7 (± 1), Day 28 (± 2), Day 56 (± 2) and Day 75 (± 2) for supplementary cats.

Adverse events (AEs) were evaluated at all physical examinations, and the application site was evaluated on Day 0 (prior to inclusion), and Day 7 (± 1) and Day 28 (± 2). Study completion was on Day 90 (± 2), or, in case of cat removal prior to Day 90 (± 2), on the day when the animal was removed from the study.

2.8. Efficacy assessment

The statistical unit was one cat per household nominated as primary patient for efficacy assessments. Efficacy criteria were separately assessed for non-inferiority by comparing post-baseline flea and tick counts with the control group.

Baseline comparability of treatment groups was assessed by means of descriptive tables on the following baseline information on Day 0: animal characteristics (breed, sex, age, hair type and body weight), animal husbandry, physical examinations for primary and supplementary cats separately and the parasite counts on Day 0 (live fleas and/or ticks) for primary cats only.

The primary efficacy criterion was the efficacy in terms of percent reduction for each visit (average of all visits) of the Felpreva®-treated group compared to the Bravecto®-treated group over the entire treatment period compared to baseline based on counts of live fleas and live and attached ticks. The secondary efficacy criterion was the efficacy of the Felpreva®-treated group compared to the Bravecto®-treated group for each separate visit compared to baseline, based on counts of live flea and live and attached ticks. This value was assessed as the percent reduction of flea and tick counts for each visit, separately.

As parasite counts in general show a strongly skewed distribution, a natural logarithmic transformation $\{\ln(\text{count} + 1)\}$ was applied to flea and tick counts and percentage reduction was calculated on transformed counts. Both, arithmetic and geometric mean of log-transformed counts were used for percentage reduction calculation.

Least squares means of percentage reduction over all post-baseline periods for the Felpreva®- and Bravecto®-treated groups were calculated from an analysis of variance with repeated measurements adjusted for baseline (main effect of treatment over all post-baseline periods). Considering the negative sign of reduction, non-inferiority was accepted, if the upper limit of the one-sided 97.5% confidence interval of the difference of $\mu_{IVP} - \mu_{CP}$ was smaller than $\Delta = 15\%$. The 5% level of significance ($P < 0.05$ for two-sided tests) was used to assess statistical differences (corresponding to a one-sided significance level of 2.5%).

3. Results

3.1. Study cats

In total 529 cats were considered suitable for enrolment in the study. The Intention-to-Treat (ITT) population consisted of primary flea-infested ($n = 206$) and tick-infested ($n = 120$) cats, and 139 and 79 of them were treated with Felpreva® (T1) and 67 and 41 with Bravecto® (T2), respectively.

Serious deviations from study protocol occurred for three and one primary flea-infested and tick-infested cats, respectively, thus leading to their exclusion from the Per-Protocol (PP) population, i.e. the total of cats with no major deviations from the protocol and included in the analysis of efficacy criteria. Thus, the PP population consisted of 203 (137 Felpreva®-treated, 66 Bravecto®-treated) and 119 (79 Felpreva®-treated, 40 Bravecto®-treated) cats, respectively, for flea and tick efficacy analysis. Regarding supplementary animals, i.e. 137 for fleas and 66 for ticks, 94 and 39 were treated with Felpreva® and 43 and 27 with Bravecto®, respectively.

3.2. Baseline infestations

On Day 0, the mean number of live fleas found in study cats was 10.6 (minimum–maximum: 5–47) and 12.4 (minimum–maximum: 5–150) in the Felpreva® and Bravecto® group, respectively. In tick-infested cats, the mean numbers of live ticks and fleas were 3.7 (minimum–maximum: 3–7 for Felpreva® group and 3–6 for Bravecto® group) and 0.8 (minimum–maximum: 0–14 for Felpreva® group and 0–8 for Bravecto® group) for the Felpreva® and Bravecto® group, respectively. All fleas were identified as *C. felis*, while the most common tick retrieved was *I. ricinus*, followed by *D. reticulatus*, *R. sanguineus* (s.l.) and *I. hexagonus* (Table 1).

3.3. Efficacy and safety evaluations

The analysis of efficacy was based on primary cats PP population. A supportive efficacy analysis was obtained based on primary cats of the ITT population. All animals which received at least one dose of Felpreva® or Bravecto® were included in the assessment of Safety Population (SP), which corresponded to the ITT population. The analysis of safety was performed for primary and supplementary cats.

3.3.1. Primary efficacy

Percentage reduction of live flea and tick counts over all post-baseline periods was 99.74% and 98.56% (fleas) and 97.50% and 98.65% (ticks) in the Felpreva® and Bravecto® treatment groups,

Table 1
Flea and tick species found at baseline: Per Protocol Population

	Total	Felpreva® group	Bravecto® group
Ticks (N) ^a	119	79	40
<i>Ixodes ricinus</i> (n, %)	80 (67.2)	55 (69.6)	25 (62.5)
<i>Ixodes hexagonus</i> (n, %)	5 (4.2)	2 (2.5)	3 (7.5)
<i>Rhipicephalus sanguineus</i> (s.l.) (n, %)	35 (29.4)	24 (30.4)	11 (27.5)
<i>Dermacentor reticulatus</i> (n, %)	36 (30.3)	23 (29.1)	13 (32.5)
Other species (n, %)	4 (3.4)	3 (3.8)	1 (2.5)
Not identified (n, %)	1 (0.8)	0 (0)	1 (2.5)
Fleas (N) ^a	203	137	66
<i>Ctenocephalides felis</i> (n, %)	199 (98.0)	135 (98.5)	64 (97.0)

Abbreviations: N, number of animals; n, number of ticks/fleas.

^a Some cats were infected by more than one tick species at baseline.

Table 2
Percentage reduction of flea and ticks counts over all post-baseline periods: Per Protocol Population

	Felpreva®	Bravecto®	Difference Bravecto® – Felpreva®	95% CI
Fleas				
No. of cats	137	66	–	–
Arithmetic mean ± SD	2.34 ± 0.46	2.34 ± 0.58	–	–
Geometric mean	9.39	9.40	–	–
Mean percent reduction over all post-baseline periods	–99.7387	–98.5651	–1.1736	–1.7558 to –0.5914
Ticks				
No. of cats	79	40	–	–
Arithmetic mean ± SD	1.52 ± 0.18	1.52 ± 0.20	–	–
Geometric mean	3.58	3.58	–	–
Mean percent reduction over all post-baseline periods	–97.5016	–98.6521	1.1505	0.2287–2.0724

Note: Data shown for Day 0 (+2).

Abbreviation: CI, confidence interval; SD, standard deviation.

respectively. Non-inferiority of Felpreva®-treated group compared to Bravecto®-treated group was shown by the 0.59% and 2.07% upper bound of the 95% confidence interval (CI) for fleas and ticks, respectively (Table 2).

3.3.2. Secondary efficacy

Percentage reduction of flea counts in the Felpreva® treatment group was 99.2% on Day 7, 99.8% on Day 28, 100% on Days 56 and 75, and 99.7% on Day 90. In the Bravecto® treatment group percentage reduction of flea counts was 99.0% on Day 7, 100% on Days 28 and 56, 99.2% on Day 75, and 98.5% on Day 90. Non-inferiority of the Felpreva® compared to the Bravecto® treatment group could be concluded for each study visit for the duration of 3 months (90 days) (data not shown).

Percentage reduction of tick counts in the Felpreva® group was 100% on Days 7, 28, 56 and 75, and 99.2% on Day 90. In the Bravecto® group, percentage reduction of tick counts was 100% on Days 7, 28 and 75, 99.1% on Day 56, and 98.1% on Day 90 (Table 3). Non-inferiority of the Felpreva® compared to the Bravecto® could be concluded for each study visit for the duration of 3 months (90 days). Flea allergy dermatitis (FAD) was assessed at study start in all cats ($n = 529$ primary as well as supplementary cats) based on pre-defined clinical signs (pruritus, crusts/scabs, papules, erythema, scaling and/or alopecia) all to be rated as being present (mild/moderate/severe) or absent.

Based on these criteria, overall 24 cats (4.5%) were diagnosed with FAD on day 0 (16 in the Felpreva® and 8 in the Bravecto® group). All these animals had no FAD sign at the study completion.

3.3.3. Efficacy versus single tick species

PP populations for each single tick species consisted of 23 and 13 (*D. reticulatus*), 55 and 25 (*I. ricinus*), and 24 and 11 (*R. sanguineus* (s.l.)) cats in the Felpreva® and Bravecto® group, respectively. The low number of cats infested with *I. hexagonus* ($n = 5$) prevented a statistical analysis.

Percentage reduction of *D. reticulatus* counts was 100% on all study days for the Felpreva® group and 97.3–100% from Day 7 (± 1) to Day 90 (± 2) for the Bravecto® group. Regarding *I. ricinus* counts, the percentage reduction in the Felpreva® group was constantly 100% on all study days except for Day 90 (± 2) (percentage reduction of 98.8%). The reduction in the Bravecto® group was 97–100% from Day 7 (± 1) to Day 90 (± 2).

Table 3

Mean percentage reduction of fleas and ticks counts in Felpreva® and Bravecto® groups

Day	7 (± 1)	28 (± 2)	56 (± 2)	75 (± 2)	90 (± 2)
Fleas					
Felpreva®	99.2	99.8	100	100	99.7
Bravecto®	99.0	100	100	99.2	98.5
Ticks					
Felpreva®	100	100	100	100	99.2
Bravecto®	100	100	99.1	100	98.1

The percentage reduction for *R. sanguineus* (s.l.) tick counts was 100% on all study days in the cats for both treatment groups (Table 4).

3.3.4. Safety

There was one serious adverse event (cat hit by car and died) observed in one of the Felpreva®-treated and three non-serious adverse events of the Bravecto®-treated cats. All four AEs were evaluated as unlikely related to the treatment.

4. Discussion

The present results show that the novel topical broad spectrum parasiticide containing emodepside 2.04% w/v, praziquantel 8.14% w/v and tigolaner 9.79% w/v (Felpreva®, Vetoquinol) is efficacious and safe when administered to cats infested with fleas or ticks at the minimum recommended dose. It could be confirmed that Felpreva® has a persistent efficacy over three months (90 days) after a single dose against live fleas and ticks, with a percent reduction of 99.7% and 99.2%, respectively. Non-inferiority with a commercial product already licensed for this indication was proven.

All fleas isolated from the study cats were identified as *C. felis*, i.e. the dominant flea species infesting cat populations in Europe (Gálvez et al., 2017). At the same time, efficacy data obtained for individual tick species regard the most important and spread species affecting felines in Europe (Claerebout et al., 2013; Geurden et al., 2017; Rohdich et al., 2018). In this view, the efficacy of Felpreva® against the three tick species (*I. ricinus*, *D. reticulatus* and *R. sanguineus* (s.l.)) affecting the vast majority of enrolled cats identified was remarkably high over a period of 90 days, i.e. constantly 100% with the sole exception of a percentage reduction of 98.8% for *I. ricinus* on Day 90 (± 2) (study completion).

The reliability of the present study was confirmed by data on infestation pressure for study cats. To assure that study cats were under infestation pressure during the whole study, the environmental challenge for ectoparasite infestations was descriptively evaluated based on other dogs and cats presented to the veterinary practices. These animals were

Table 4

Percentage reduction of different tick species counts in Felpreva® and Bravecto® groups

Day	7 (± 1)	28 (± 2)	56 (± 2)	75 (± 2)	90 (± 2)
Dermacentor reticulatus					
Felpreva®	100	100	100	100	100
Bravecto®	100	100	100	100	100
Ixodes ricinus					
Felpreva®	100	100	100	100	98.8
Bravecto®	100	100	98.6	100	97.0
Rhipicephalus sanguineus (s.l.)					
Felpreva®	100	100	100	100	100
Bravecto®	100	100	100	100	100

Note: Due to the low number of animals infested with *Ixodes hexagonus* (4.2%) no statistical evaluation was done.

infested with fleas and/or ticks, and/or required a control treatment for these ectoparasites.

Cats are constantly at risk to be (re-)infested with fleas and ticks from the environment. These pets thus require to be treated with medications which guarantee a persistent efficacy until the end of the treatment period, to control the direct clinical impact of these infestations and to minimize the clinical and epidemiological risk of vector-borne diseases. Fleas are traditionally considered as prevalent feline parasites whilst ticks in cats are erroneously of less concern. Nevertheless, recent data have proven that ticks are becoming a common pest of cat populations in Europe even where they are unexpected (Geurden et al., 2017; Rohdich et al., 2018; Wright, 2018; Buczek & Buczek, 2020). This recent information confirms a relatively new risk for cats represented by tick infestations and tick-borne pathogens. Thus, the high efficacy of Felpreva® against fleas and ticks is of importance not only for the direct pathogenic impact of these arthropods (e.g. anaemia, skin damages, allergic reactions) but also for the control of transmitted diseases. Although this was not investigated in the present study, it can be argued that Felpreva® has the potential to reduce the risk of pathogen transmission by fleas (e.g. *D. caninum*) to cats.

The use of broad-spectrum formulations containing an endo- and an ecto-parasiticide is particularly useful in cats living outdoors or allowed to free-roam, as they are at risk to acquire various internal and external parasites at the same time. In fact, large-scale studies have proven that cats of Europe are often simultaneously infected by internal cestodes and/or nematodes and/or external parasites (Beugnet et al., 2014; Giannelli et al., 2017; Genchi et al., 2021). Nonetheless, cats living indoors are also at risk of becoming infected by internal helminths via different routes (Morelli, 2021) and to be parasitized by arthropods. This is particularly true for fleas, which find in household indoor environments the best humidity and temperature parameters for their survival and reproduction (Dryden et al., 2011). Given that most pet cats are allowed to go outside (Foreman-Worsley et al., 2021) there is a frequent need to use broad spectrum parasitocides to control at the same time endo- and ecto-parasites affecting cats at risk of mixed infections and/or infestations. It is thus worthy of note that emodepside and praziquantel contained in the evaluated Felpreva® are efficacious against common intestinal nematodes and tapeworms, and lungworms (Altreuther et al., 2005; Reinemeyer et al., 2005; Di Cesare et al., 2015; Lee et al., 2019; Traversa et al., 2019; Crisi et al., 2020). The efficacy of Felpreva® against gastrointestinal nematodes and cestodes as well as lungworms was investigated, and efficacy shown by an equivalent multicenter field study (Cvejić et al., 2022).

The long efficacy duration against arthropods is an important feature of Felpreva®. Pets receiving a longer duration product are in general protected against fleas and ticks for more months per year compared to animals which receive formulations to be dosed monthly (Lavan et al., 2018, 2020, 2021). Possible gaps in terms of subsequent parasiticide administrations limit the time protection provided against ectoparasites, and the gap between administrations leaves the cat unprotected against fleas and ticks. This is of importance in terms of owner compliance as a recent survey has shown that cat owners have a common high level of preference of long-lasting formulations efficacious against fleas and ticks (Lavan et al., 2021). Such a high adherence to the use of long-lasting medications is probably due also to inferior number of administrations scheduled per year. As stress for pet cats (and probably for owners themselves) is a trigger for reducing the number of visits to the vets (Volk et al., 2011), a product assuring three months of protection against ticks and fleas after a single dose implies the advantage that owners are required to dose their cats once instead than three times in the same time interval.

5. Conclusion

The present results show that the new spot-on formulation Felpreva® containing tigolaner (plus emodepside and praziquantel) is efficacious and safe against natural flea and tick infestations in cats. A quick and

persistent efficacy of ectoparasiticides is of utmost relevance under those field circumstances where cats are at risk to be (re-)infested by arthropods and, at the same time, are exposed to vector-borne pathogens. The duration of Felpreva® was proven to provide up to three months protection following a single dose. Such an approach allows a safe, efficacious, and long-lasting fleas and ticks control for cats.

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Ethical approval and consent to participate

A clinical field study confirming the efficacy and safety of a veterinary medicinal product is required to obtain the marketing authorization according to Directive (2004)/28/EC and 2009/9/EC amending 2001/82/EC in Europe. Cat owners agreed to the participation of their animals in the study prior to enrolment and initiation of treatment, in terms of treatment, flea and/or tick count and collection procedures, and visits to veterinary practices at the required times.

CRediT author statement

Gabriele Petry, Hannah Ringeisen, and Hannah Hamburg have been involved in the design of the study, writing of study protocol, and monitoring of the study. Dejan Cvejić and Klaus Hellmann conducted the multicenter study with the veterinary clinics involved, evaluating and reporting the study results. Róbert Farkas conducted and reported the parasite diagnosis and Katrin Blazejak and Norbert Mencke wrote the manuscript in conjunction with Dejan Cvejić. All authors read and approved the final manuscript.

Declaration of competing interests

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Gabriele Petry, Hannah Ringeisen, and Hannah Hamburg have conducted and funded the study and are employees of Bayer Animal Health GmbH, an Elanco Animal Health company. Dejan Cvejić and Klaus Hellmann are employees of Klifovet GmbH Munich, Germany. Katrin Blazejak and Norbert Mencke are employees of Vetoquinol, Paris, France. Vetoquinol is the owner of the product Felpreva reported within this study. Róbert Farkas declares no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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