S23

Multicentre follow-up field study of dogs vaccinated with LetiFend® (2017-2020)

Rubén Foj[1*], Susana Vivancos[1], Gloria Pol[1], Silvia Usero[1], Catia Morgado[1], Helena Arce[1], Pilar Brazis[1]

[1] *LETI PHARMA S.L.U., Barcelona, Spain*

*rfoj@leti.com

Background

LetiFend®, the first recombinant vaccine developed in Europe against canine leishmaniosis (CanL), obtained marketing authorisation in Europe in June 2016. Active immunisation of healthy non-infected dogs from 6 months of age by annual vaccination with LetiFend® reduces the risk of developing clinical leishmaniosis after natural exposure to *Leishmania infantum* with a proven efficacy of 72% [1]. Vaccination also plays a key role in the control of parasite burden and therefore reduce the size of the reservoir [1,2]. This, in turn, helps to reduce the risk of infection in humans (One Health strategy) [3].

The aim of the study was to assess the protective role of LetiFend® to prevent clinical CanL from *L. infantum* and its safety profile in the veterinary clinical practice after its launch in Iberia in 2017 (real-world evidence study).

Materials and methods

A prospective, multicentre, uncontrolled, observational field study was performed in endemic areas of Spain and Portugal, based on the three-year follow-up of the first dogs vaccinated with LetiFend®. 238 client-owned dogs from 26 veterinary clinics were vaccinated with LetiFend® between March and July 2017, in accordance with the summary of product characteristics [4].

After the primary vaccination, dogs were monitored annually prior to revaccination (days 365, 730 and 1095). The follow-up of vaccinated dogs consisted of a quantitative serological test for the detection of antibodies against *L. infantum* (IgG) by ELISA or indirect immunofluorescence (IFAT), and the evaluation of clinical

signs by the veterinarian physical examination. Laboratory confirmed cases of *Leishmania* infection and/or with clinical signs (related to CanL or unrelated) could not be revaccinated and were withdrawn from the study. However, healthy seropositive dogs with low IgG levels were retested after 6-8 weeks and revaccinated if they were finally seronegative.

Results

Dog population was heterogeneous, comprising 123 females and 115 males (51% vs 49%) aged between 6 months and 16 years old, with a wide range of pure breeds (73% vs 27% mixed-breed). Up to 91% were protected with external parasite repellents and 45% lived outdoors either some or all of the time (Figure 1).

Figure 1. Characterisation of the dogs included in the study.

After the three-year follow-up, 160 cases were monitored: 150/160 dogs (94%) showed no infection or clinical signs throughout the study and were revaccinated annually (healthy seronegative dogs) and the remaining cases (10/160 dogs; 6%) developed antibodies against *L. infantum* during the follow-up. Four of them (4/10 dogs) presented clinical signs attributable to CanL; three cases developed cutaneous leishmaniosis and only one case manifested the disease in its visceral form with weight loss, fever and anaemia. Sick dogs were reported to pharmacovigilance and withdrawn from the study, with the cumulative incidence of disease standing at 2.5% (4/160 dogs). By contrast, healthy seropositive dogs (6/10) were re-evaluated at 6-8 weeks: two of them were seronegative and they could be revaccinated; in all other cases, infection was confirmed, and they were removed from the study. Therefore, 152/238 dogs were revaccinated annually, with a cumulative revaccination rate of 64% (Figure 2).

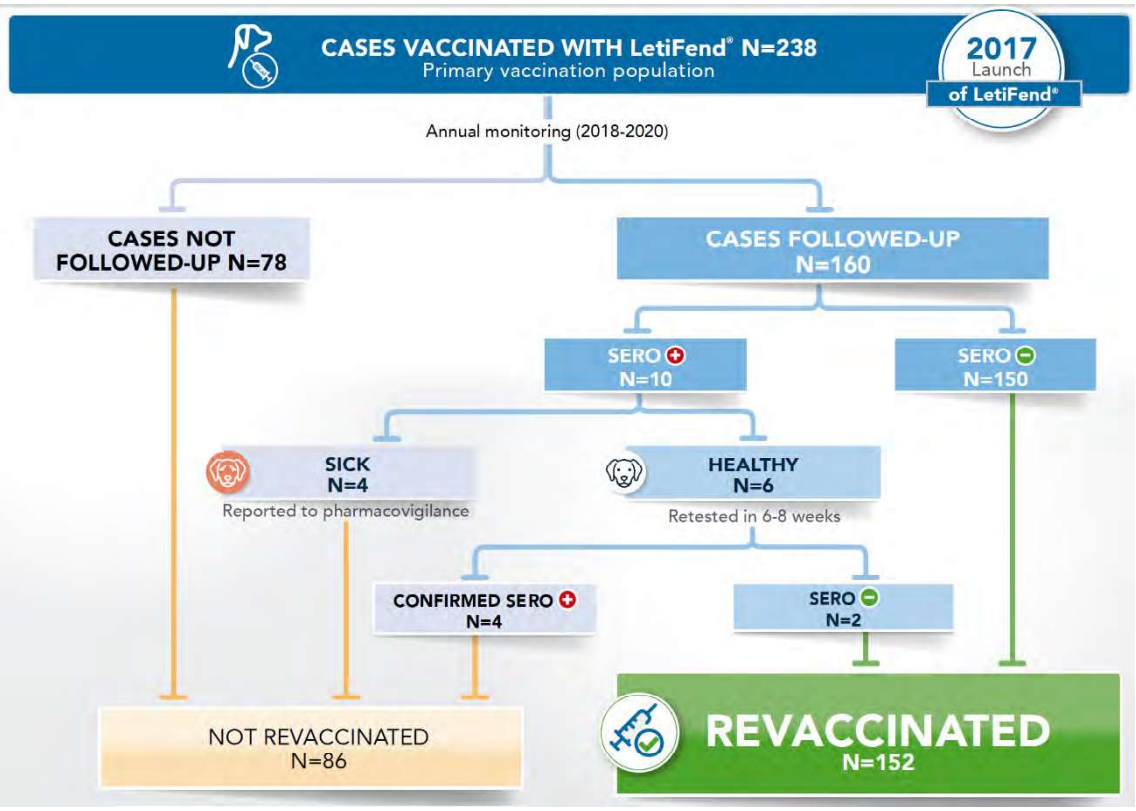

Figure 2. Clinical course of dogs vaccinated with LetiFend®.

No adverse events related to the administration of LetiFend® were reported. Besides, the vaccination did not interfere with the detection of anti-*L. infantum* antibodies by the serological techniques used.

Conclusions

This post-authorization study demonstrates that LetiFend® is a safe vaccine in non-infected dogs older than 6 months of age that has a real-world impact on the control of the disease incidence in endemic areas [1,5]. Only 2,5% of vaccinated dogs developed clinical leishmaniosis during the study and just one case manifested its visceral form. Overall, preventing measures against CanL (topical insecticides and vaccines) provide veterinarians with effective, safe and probably synergetic tools to prevent and control CanL in daily clinical practice.

References

1. Fernández Cotrina J., Iniesta V., Monroy I. *et al.* A large-scale field randomized trial demonstrates safety and efficacy of the vaccine LetiFend® against canine leishmaniosis. Vaccine. 2018; 36:1972-82.

2. Cacheiro-Llaguno C., Parody N., Renshaw-Calderon A. *et al.* Vaccination with LetiFend® reduces circulating immune complexes in dogs experimentally infected with *L. infantum*. Vaccine. 2020; 38:890–896.

3. Dantas-Torres F., Miró G., Baneth G. *et al.* Canine Leishmaniasis Control in the Context of One Health. Emerg Infect Dis. 2019; 25:1-4.

4. LetiFend®: EPAR - Product Information [Internet]. European Medicines Agency. Available at: https://www.ema.europa.eu/en/medicines/veterinary/EPAR/letifend.

5. Foj R., Pol G., Brazis P. *et al.* Leishmaniosis in vaccinated dogs: Clinical aspects. 27th Conference of the World Association for the Advancements of Veterinary Parasitology (WAAVP). 2019; Abstract Book: 92.