

## Use of an injectable, sustained-release formulation of moxidectin to prevent canine subcutaneous dirofilariosis

L. Rossi, E. Ferroglio, A. Agostini

*Dirofilaria (Nochtiella) repens* is the agent of canine subcutaneous dirofilariosis, a mosquito-transmitted nematodiasis endemic to several countries in southern Europe, Africa and Asia (Pampiglione and others 1995). Prepatency lasts for six to nine months (Cancrini and others 1989). Mild clinical signs such as pruritus, dermal swelling and subcutaneous nodules have been reported in infected dogs (Baneth and others 2002), but of greater concern are zoonotic human cases caused by ocular and pulmonary migration of immature nematodes. There is evidence from adequate reporting systems that human cases are a relatively frequent event wherever a canine reservoir exists (Pampiglione and others 1995).

Since no adulticide treatment for dirofilariosis is registered, and off-label use of melarsomine has only recently been suggested on the basis of a single case report (Baneth and others 2002), prevention remains the best available option to protect dogs and, consequently, to prevent exposure of human beings. In Europe, three macrocyclic lactones are now used successfully, in monthly dosing regimens, against *D repens* infection in dogs: two by oral administration, ivermectin (Marconcini and others 1993) and moxidectin (Rossi and others 2002), and selamectin, by pour-on application (Genchi and others 2002). However, lack of owner compliance, by delayed initiation of preventive treatment or missed monthly doses, has occasionally allowed dogs to become infected. This short communication describes a field trial to test the prophylactic activity against *D repens* of a new injectable, sustained-release formulation of moxidectin, which has been shown to confer complete protection against the related nematode *Dirofilaria immitis* following a single injection (Lok and others 2001).

The animals studied were all client-owned dogs living within an area of 350 km<sup>2</sup> near Turin, in the north west of Italy. In this area, circulating microfilariae of *D repens* have been found in 40 to 50 per cent of unprotected adult dogs (Rossi and others 1996) and clinical cases have been reported in human beings (Pampiglione and others 1991). Dogs to be treated were selected if they lived permanently outdoors, were over 12 months old, and had a negative heartworm antigen test (Solo Step CH Test; Heska) and the absence of circulating microfilariae, based on a modified Knott's test (Balbo and Panichi 1968).

A total of 141 dogs from the clientele of three participating veterinary clinics were enrolled in the trial. Eightyfive dogs (42 males and 43 females comprising 18 breeds, age range one to 16 years old, bodyweight ranging from 3 to 50 kg) (group A) were injected subcutaneously with moxidectin SR (Guardian-SR; Fort Dodge) at a dose of 0.17 mg moxidectin/kg bodyweight between May 31 and June 16, 1999. Another 32 dogs (18 males and 14 females comprising eight breeds, age range two to 10 years old, bodyweight ranging from 4 to 60 kg) (group B) served as positive controls and were treated with moxidectin tablets (Guardian; Fort Dodge) at a dose of 3 µg/kg bodyweight, five times at monthly intervals, between June and October 1999. Finally, a negative control group was created at the end of the study, in June 2000, by enrolment of the first 24 dogs (14 males and 10 females comprising five breeds, aged from one to 10 years old, bodyweight ranging from 4 to 45 kg) presented to the participating veterinary clinics that had not received any antifilarial prophylactic treatment during 1999. This option was chosen for ethical reasons, since harmful *D immitis* is present in the study area. The test dogs remained resident with their owners and allowed to be naturally exposed to mosquitoes, which are the intermediate hosts of *D repens*.

The treated dogs were examined clinically on four occasions during the trial, on study days 0, 90, 180 and 365. The efficacy

of the treatments against *D repens* was assessed on the same dates by using a modified Knott's test for microfilariae, and circulating microfilariae were identified to the species level based on their size and morphological features (Balbo and Panichi 1968). No microfilaria antigen test is currently available for the diagnosis of *D repens* infection.

The treatments were well tolerated and no sign suggestive of an adverse reaction to either formulation of moxidectina was recorded. The trial was completed by 106 of the 117 treated dogs (76 in group A and 30 in group B); 11 dogs could not complete the trial for causes unrelated to the treatment (five changes of residence, two heart failures, one trauma and one malignant neoplasia in group A; one case of aggressive behaviour and an undetermined cause, three months after administration of the fifth moxidectin tablet, in group B).

None of the treated dogs had developed a patent infection with *D repens* by study day 365 but seven of the 24 dogs (29 per cent) selected for the negative control group had a patent *D repens* infection, confirming that dogs living in the study area were naturally exposed to infection with this agent.

**These results show that administration of an injectable, sustained-release formulation of moxidectin, carried out in June 1999 to provide 0.17 mg active ingredient per kg bodyweight, was safe and 100 per cent effective as a preventive treatment for dogs naturally exposed to infection with *D repens* in an enzootic area in southern Europe.**

### References

- BALBO, T. & PANICHI, M. (1968) La filariosi del cane. Epizootologia e diagnosi di laboratorio. *La Nuova Veterinaria* **44**, 18-32
- BANETH, G., VOLANSKY, Z., ANUG, Y., FAVIA, G., BAIN, O., GOLSTEIN, R. E. & HARRUS, S. (2002) *Dirofilaria repens* infection in a dog: diagnosis and treatment with melarsomine and doramectin. *Veterinary Parasitology* **105**, 173-178
- CANCRINI, G., TASSI, P. & COLUZZI, M. (1989) Ivermectin against larval stages of *Dirofilaria repens* in dogs. *Parassitologia* **31**, 177-182
- CANCRINI, G., YANCHANG, S. & COLUZZI, M. (1988) Influenza della temperatura sullo sviluppo larvale di *Dirofilaria repens* in cane. *Parassitologia* **30** (Suppl 1), 38
- GENCHI, C., SOLARI BASANO, F., MARRONE, R. V. & PETRUSCHKE, G. (1998) Canine and feline heartworm in Europe with special emphasis in Italy. In *Recent Advances in Heartworm Disease: Symposium '98*. Ed R. L. Seward. Batavia, American Heartworm Society, pp 75-82
- GENCHI, C., POGLAYEN, G. & KRAMER, L. (2002) Efficacia di selamectin nella profilassi delle infestazioni da *Dirofilaria repens* nel cane. *Veterinaria* **16**, 69-71
- LOK, J. B., KNIGHT, D. H., WANG, G. T., DOSCHER, M. E., NOLAN, T. J., HENDRICK, M. J., STEBER, W. & HEANEY, K. (2001) Activity of an injectable, sustained-release formulation of moxidectin administered prophylactically to mixed-breed dogs to prevent infection with *Dirofilaria immitis*. *American Journal of Veterinary Research* **62**, 1721-1726
- MARCONCINI, G., MAGI, M. & HECHT CONTIN, B. (1993) Sulla validità dell'ivermectina nella profilassi dell'infestazione con *Dirofilaria repens* in cani naturalmente esposti al contagio. *Parassitologia* **35**, 67-71
- PAMPIGLIONE, S., CANESTRI TROTTI, G. & RIVASI, F. (1991) La dirofilariosi humaine en Italie. *Annales de Parasitologie Humaine et Comparée* **66**, 195-203
- PAMPIGLIONE, S., CANESTRI TROTTI, G. & RIVASI, F. (1995) Human dirofilariosis due to *Dirofilaria (Nochtiella) repens*: a review of world literature. *Parassitologia* **37**, 149-193
- ROSSI, L., MENEGUZZI, P. G., GRIBAUDO, L. & BALBO, T. (1996) An epidemiological study of canine filariosis in north west Italy: what has changed in 25 years? *Veterinary Research Communications* **20**, 308-315
- ROSSI, L., FERROGLIO, E. & AGOSTINI, A. (2002) Use of moxidectin tablets in the control of canine subcutaneous dirofilariosis. *Veterinary Record* **150**, 383