

A new licensed quadrivalent antileptospiral canine vaccine prevents mortality, clinical signs, infection, bacterial excretion, renal carriage and renal lesions caused by *Leptospira Australis* experimental challenge

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OBJECTIVES

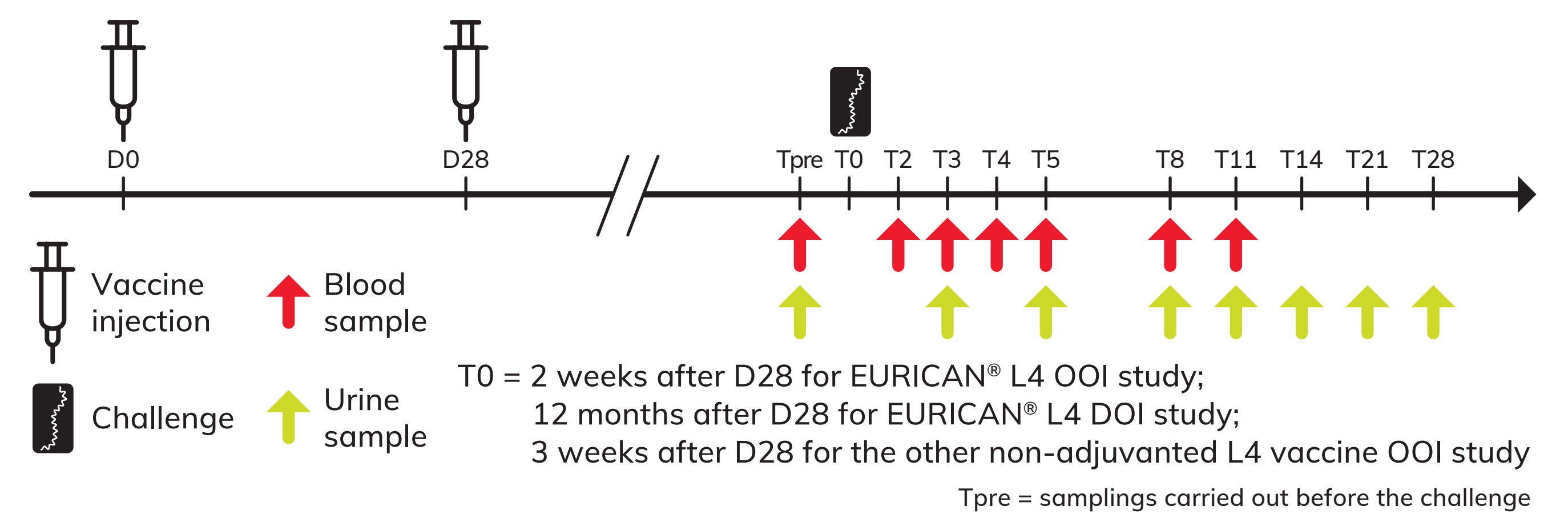
- Evaluate the onset and duration of immunity (OOI and DOI) induced by the newly licensed non-adjuvanted vaccine EURICAN® L4 (containing four *Leptospira* components: Canicola, Icterohaemorrhagiae, Grippityphosa, Australis) against a virulent canine strain of *L. Australis* recently isolated from the field.
- Evaluate the OOI induced by another licensed non-adjuvanted L4 vaccine tested with the same *L. Australis* challenge model developed to assess the efficacy of EURICAN® L4.

Materials & Methods

- Animals: puppies* aged between 7 and 10 weeks at the time of 1st vaccine injection (D0)
- Daily monitoring after challenge with scoring of clinical signs (general condition, dehydration, ocular signs, vomiting, diarrhoea and cutaneo-mucosal signs)
- Sampling (see schedule, as requested by European Pharmacopoeia monograph 0447) for:
 - hematology and blood chemistry (blood)
 - pathogenic *Leptospira* detection using a quantitative real-time PCR assay (blood, urine and kidney)
 - microscopic examination (kidney)

Monitoring of efficacy criteria

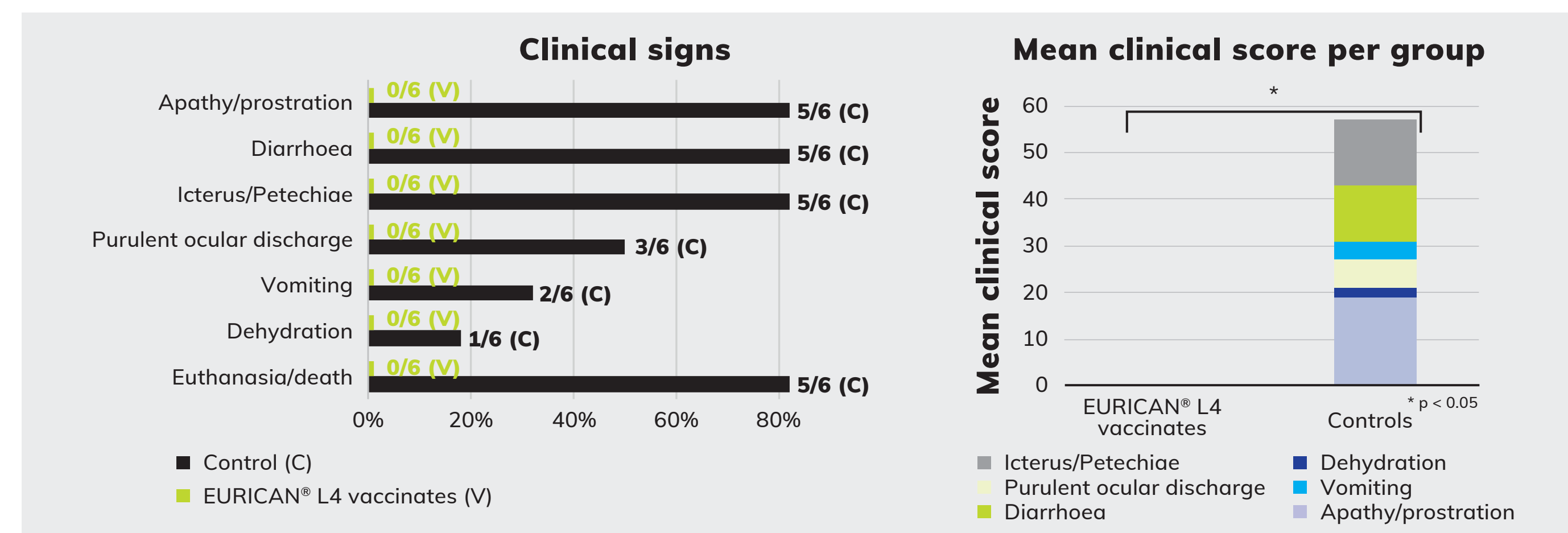
- Clinical signs & mortality**
- Infection:** qPCR on blood (detection of pathogenic *Leptospira*)
- Bacterial excretion:** qPCR on urine (detection of pathogenic *Leptospira*)
- Renal carriage:** qPCR on kidney (detection of pathogenic *Leptospira*)
- Renal lesions:** histological analysis on kidneys



Results for EURICAN® L4

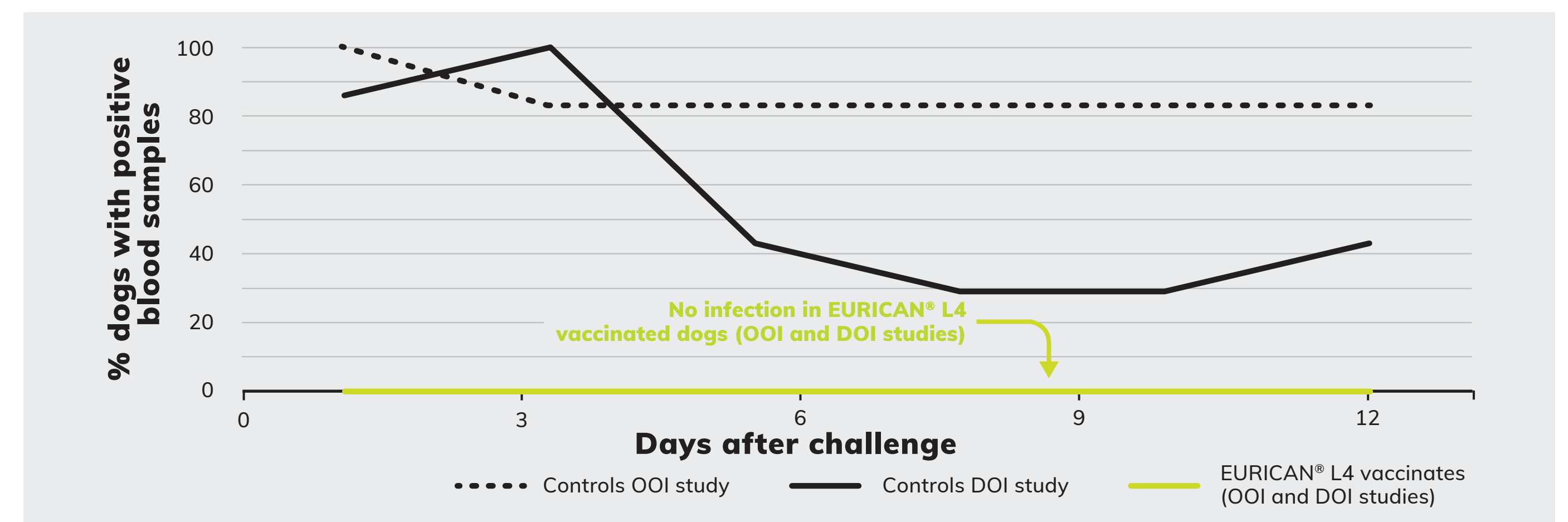
100% prevention of clinical signs and mortality demonstrated in a very severe challenge both in puppies and adult dogs

Onset of Immunity

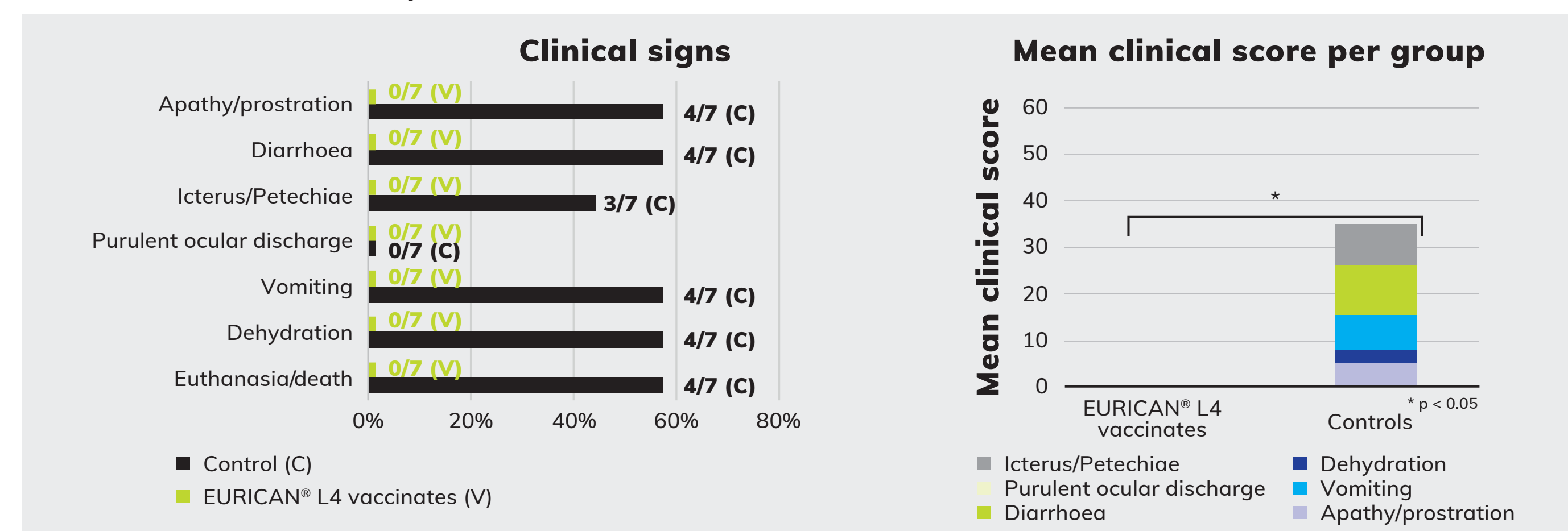


100% prevention of infection and 100% prevention of bacterial excretion demonstrated in a very severe challenge both in puppies and adult dogs

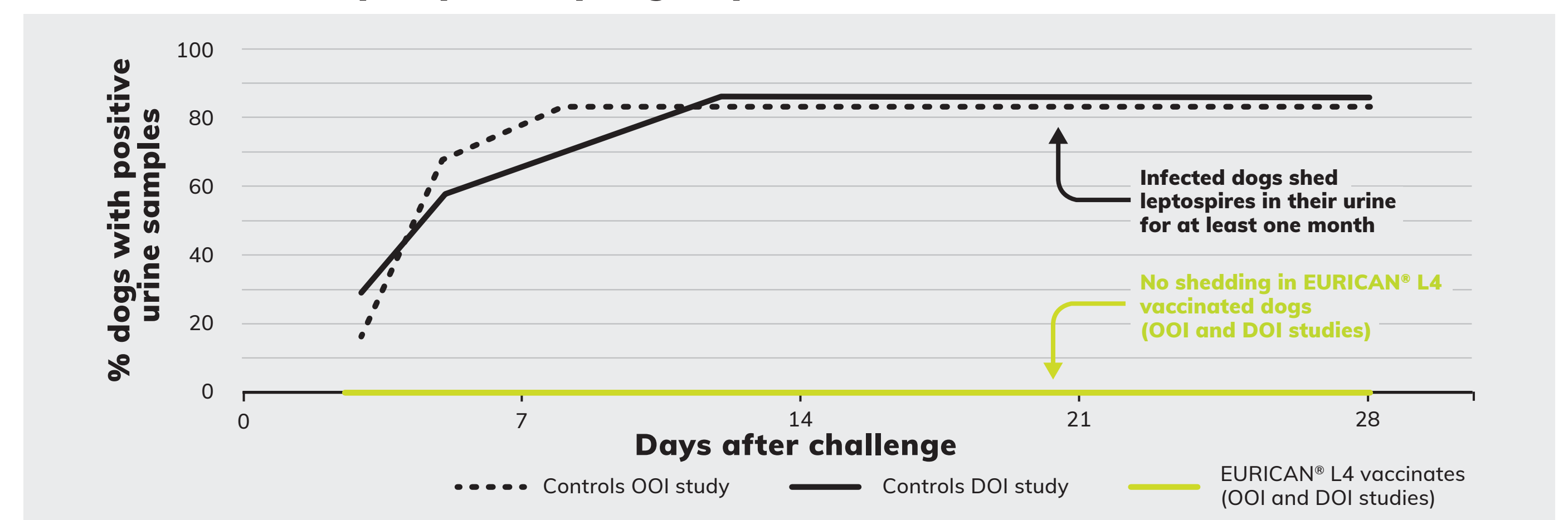
Evolution of the leptospiraemia per group



Duration of Immunity



Evolution of the leptospiruria per group



CONCLUSION FOR EURICAN® L4

Efficacy criteria	OOI study (puppies)				DOI study (adult dogs)				Claims
	Protected dogs	Affected dogs	Affected dogs	p value	Protected dogs	Affected dogs	Affected dogs	p value	
Mortality	100%	0%	83%	0.003	100%	0%	57%	0.012	prevent mortality
Clinical signs	100%	0%	83%	0.003	100%	0%	57%	0.012	prevent clinical signs
Infection	100%	0%	100%	<0.001	100%	0%	100%	<0.001	prevent infection
Bacterial excretion	100%	0%	83%	0.011	100%	0%	86%	<0.001	prevent bacterial excretion
Renal carriage	100%	0%	83%	0.003	100%	0%	71%	0.004	prevent renal carriage
Renal lesions	100%	0%	100%	<0.001	100%	0%	86%	<0.001	prevent renal lesions

p value in black indicates a significant difference between groups

- 100% prevention of mortality demonstrated in a very severe *Leptospira Australis* challenge both in puppies and adult dogs
- In face of a highly infectious challenge strain, EURICAN® L4 demonstrates full prevention
- Beneficial effect of vaccination against urinary tract infection
- Contributes to reduce the contamination of the environment
- No excretion in the environment

Results for the other licensed non-adjuvanted L4 vaccine

Efficacy criteria	OOI study (puppies)			
	Protected dogs	Affected dogs	Affected dogs	p value
Mortality	71%	29%	57%	0.212
Clinical signs	71%	29%	57%	0.212 / 0.429*
Infection	0%	100%	100%	NP
Bacterial excretion	43%	57%	71%	0.367 / 1.000*
Renal carriage	43%	57%	71%	0.367
Renal lesions	43%	57%	71%	0.367 / 0.505*

*p value for prevention/p value for reduction - NP: not performed

CONCLUSION

- In this immediate efficacy challenge model, the other licensed non-adjuvanted L4 vaccine neither prevented nor reduced any efficacy criteria against *L. Australis* circulating field isolate, despite a slightly lower severity of the challenge model.
- A contrario, EURICAN® L4 conferred 100% prevention of the 6 efficacy criteria as early as 2 weeks after a full primary vaccination.

*Studies were carried out in accordance with the EU Directive 2010/63/EU for animal experiments and the National Research Council's Guide for the Care and Use of Laboratory Animals. The Ethics Committee of Boehringer-Ingelheim Animal Health France, CE013, agreed by Research Ministry January 3, 2023, has approved the clinical studies which have been conducted in compliance with the project authorization 2019071817016518. Endpoints were defined to avoid unnecessary suffering of diseased dogs.

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