Rabbit Haemorrhagic Disease (RHD) prevention program based on the use of a European RHDV-2 vaccine

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BACKGROUND AND OBJETIVES

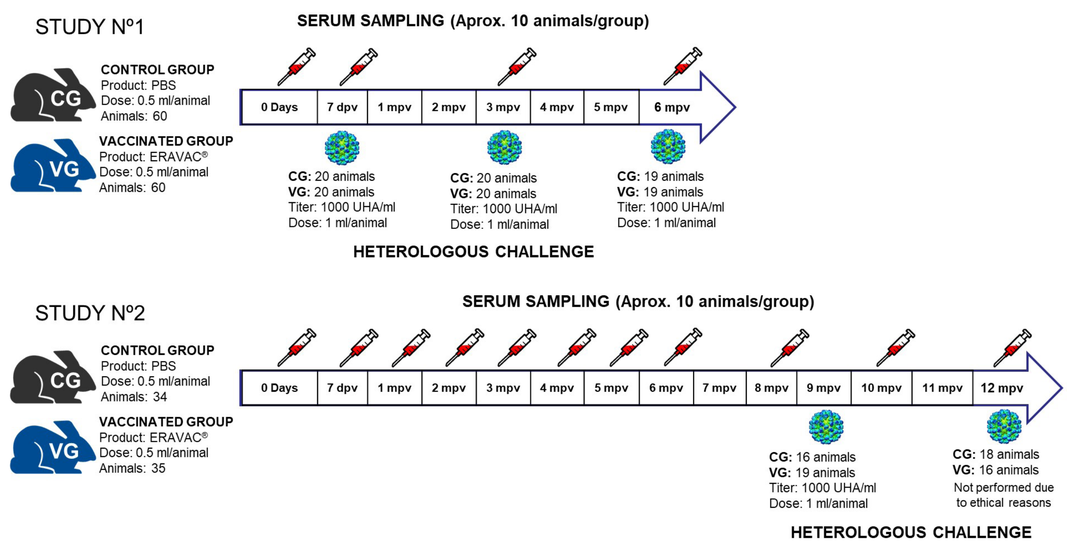
- Rabbit Haemorrhagic Disease (RHD) caused by RHD-2 virus (RHDV-2) is an emerging rabbit disease with high morbidity and mortality rates, resulting in economic losses for commercial rabbit farms[1].
- Vaccination is the main tool for RHD control and prevention[2].
- ERAVAC® is a RHDV-2 based vaccine authorized in the European Union by the European Medicines Agency[3].
- Currently, key information about RHDV-2 prevention schedule is scarce.

The two studies described here were aimed to evaluate the efficacy of ERAVAC® in naïve rabbits up to 6 months after immunization, although protection for a longer period of time (up to 12 month) as an aid to establish the most adequate prevention program for the disease was also explored.

MATERIAL AND METHODS

As shown in figure 1, two controlled, blind experimental trials (study 1 and 2) were conducted in 120 and 69 rabbits aged 35 days, who were randomized to receive the vaccine (vaccinated groups, VG) or a placebo (control group, CG). In the first study, vaccine efficacy was assessed based on cumulative survival rates after vaccination, by means of virulent heterologous challenges, and serological response prior to each challenge (Figure 1). The second study aimed to expand upon the previous work, looking for long term protection using the above mentioned efficacy indicators and sequential monitoring of serological response from 7 days post-vaccination (dpv) to 12 months post-vaccination (mpv) (Figure 1).

Figure 1: Experimental design of a 6- and a 12-month vaccination efficacy studies of a European RHDV-2 vaccine in rabbits.



** dpv (days post-vaccination); mpv (months post-vaccination)*

The serological response to vaccination was evaluated by assessing the presence of specific anti-RHDV-2 IgG in a competition ELISA[1]. The protection was assessed by the daily observation of clinical signs, and mortality was recorded up to 7 days post-challenge (dpc).

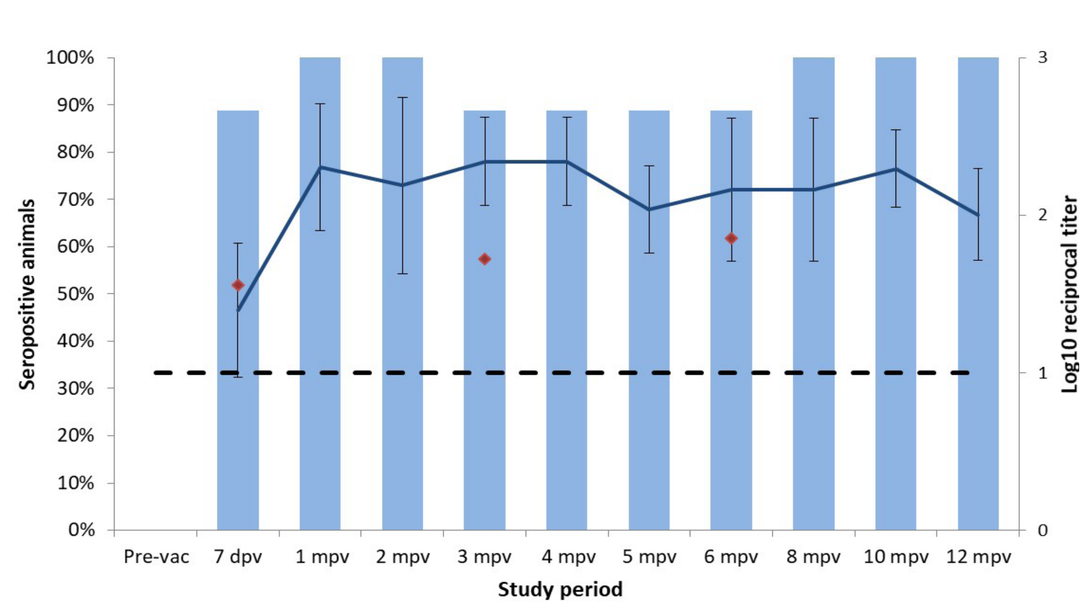
RESULTS

In both studies, all rabbits were antibody negative to RHDV-2 prior vaccination. In addition, animals in CG remained seronegative throughout the study, while rabbits in VG responded serologically to vaccination, and remained seropositive over the entire study period (Figure 2).

The sequential challenges in the CG induced cumulative mortality rates that ranged from 20.0 to 47.4% in both studies (Figure 3). In contrast, RHDV-2 vaccination provided a 100% survival rate in the VG in all challenges, as well as almost complete (95–100%) clinical protection.

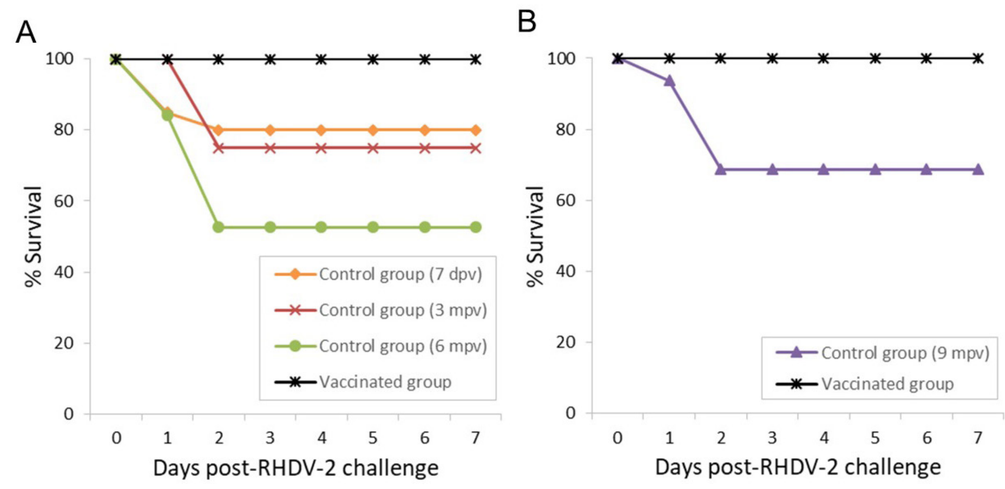
Although the challenge at 12 mpv could not be carried out due to ethical and welfare reasons, all vaccinated animals at that time point were seropositive. These animals showed average antibody titers similar to those between 1 to 10 mpv ($p<0.05$), and a significantly higher rate of antibody titers than those at 7 dpv ($p>0.05$). It is well known that humoral response is essential for protecting rabbits from RHDV-2[4]. All in all, antibody titers at 12 mpv allow predicting similar levels of clinical protection and survival in the face of a hypothetical challenge.

Figure 2: Percentage of seropositive rabbits (bars) and geometric mean of antibody titers of seropositive animals (line) following RHDV-2 vaccination in study 2, as well as, geometric mean of antibody titers of rabbits from study 1 (red diamond). Antibody titers are expressed as the reciprocal antibody titer, expressed as Log10. Sera with titers higher than 1/10 were considered positive (black dotted line).



** Pre-vac (prior to vaccination); dpv (days post-vaccination); mpv (months post-vaccination)*

Figure 3: Daily percentage of the survival rate of rabbits in the control and vaccinated groups challenged with heterologous RHDV-2 in study 1 (A) and study 2 (B). Survival rates were observed daily up to 7 days. Vaccinated groups are represented by the black line. The control groups are represented by the orange (7 dpv), red (3 mpv), green (6 mpv) and purple lines (9 mpv).



**dpv (days post-vaccination); mpv (months post-vaccination)*

The efficacy results of the RHDV-2 vaccine, by challenge and serological response, proved that establishing an annual revaccination program for the adequate protection of rabbits against RHDV-2 is possible. Moreover, the efficacy seen shortly after vaccination (7 dpv) would allow the use of this vaccine as an effective post-exposure treatment as suggested elsewhere[1]. This fact is corroborated in the clinical practice, since vaccination has allowed veterinarians to effectively control the disease since its re-emergence[2].

CONCLUSIONS

- RHDV-2 vaccine stimulates the humoral response at 7 dpv, inducing high and long lasting antibody titers up to 12 mpv.
- RHDV-2 vaccine confers protective immunity to virulent heterologous challenge.
- A RHDV-2 prevention program could be based on a vaccination interval of at least 12 months.

ACKNOWLEDGEMENTS

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