

BIOBOS IBR MARKER VACCINE CHALLENGE TRIAL

Background

Biobos IBR Marker Vaccine provides active immunisation of cattle to reduce clinical symptoms caused by infection with bovine herpesvirus type 1, and to reduce excretion of the field virus.

Biobos is an inactivated vaccine that allows usage of the DIVA (Differentiating Infected from Vaccinated Animals) principle.

Study Objective

Demonstrate the efficacy of Biobos IBR Marker Vaccine in calves in a challenge trial.

Study Design

Seven 3 month old healthy Holstein calves without antibody to IBR were enrolled in the study. Five were vaccinated with 2 doses of Biobos IBR Marker Vaccine. Each dose of 2mL was delivered by intramuscular injection. The interval between the two doses of vaccine was 3 weeks.

Six months after vaccination calves were challenged with IBR virus delivered intranasally.

Local (injection site) reactions were evaluated on the days of vaccination and daily for 4 days. Clinical observations of animals after vaccination and revaccination were made daily for two weeks following each vaccination. Clinical observations of fever, apathy, nasal discharge, eye discharge and dyspnoea were made daily for three weeks following challenge with IBR virus and each observation was scored on a scale of 0 – 3.

Rectal temperatures were monitored daily for 4 days after each administration of the vaccine and daily for 21 days following challenge.

Blood samples were collected from animals to determine levels of antibodies against IBR virus by serum neutralisation test. Blood samples were taken before administration of the vaccine on days 0 and 21, prior to challenge on Day 211, and then 21 days later on Day 232 of the study.

Nasal swabs were collected daily to determine the virus excretion titre beginning on the day of challenge (Day 211) for 21 days.

Results

There were no local reactions in any of the calves after vaccination or after revaccination. There were no clinical observations reported in any of the calves after vaccination or revaccination. Rectal temperatures remained within physiological limits after vaccine administration.

Following challenge, daily clinical scores were much lower in the vaccinated calves compared to the unvaccinated controls. Clinical scores peaked in the unvaccinated control calves 5-7 days after challenge. Mean total clinical scores were significantly lower in the vaccinated animals (score 4.6) than unvaccinated calves (score 41.5).

Rectal temperatures after challenge were higher, and persisted high for longer in the unvaccinated controls, compared to the vaccinated calves. Rectal temperatures of vaccinated calves were slightly elevated from Day 6 to 7 after challenge, with maximum recorded temperature 39.7°C on Day 7 after challenge. Rectal temperatures in the unvaccinated control animals increased significantly between Day 5 and Day 10 after challenge. The maximum temperature was 41.1°C on Day 7 after challenge.

After the administration of one 2mL dose of Biobos IBR Marker Vaccine, the vaccinated animals showed seroconversion with titres 2-3 (\log_2) on Day 21 and with titres 5-6 (\log_2) after revaccination (Day 42). The serological profile of the unvaccinated control animals did not change during the observation period.

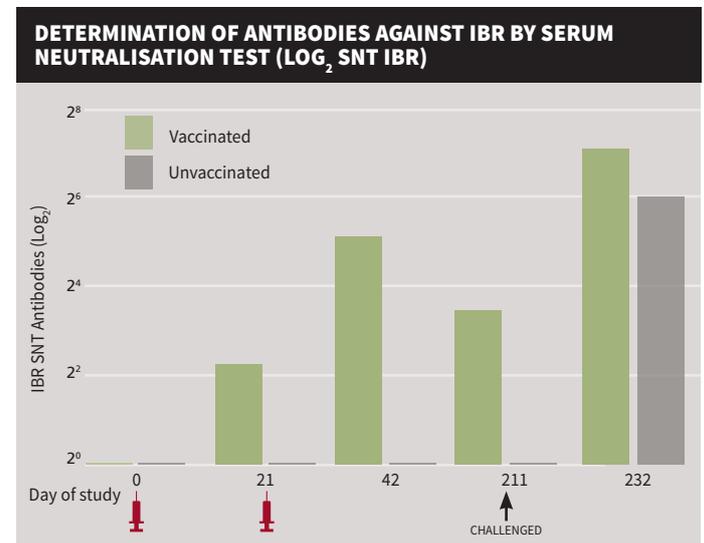


Figure 1. Determination of antibodies against IBR by serum neutralisation test

The vaccinated and control animals were challenged on Day 211 and were examined for antibodies against IBR 21 days later. All the monitored animals had high levels of specific neutralisation antibodies to IBR with titres 6-8 (\log_2) after challenge, refer Figure 1.

Virus titres in nasal swabs were lower and persisted for shorter duration in the vaccinated calves, compared to the unvaccinated controls, refer to Table 1 and Figure 2.

Day after challenge	Virus titre (log ₁₀) on days following challenge														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Mean of vaccinated calves	0	1.9	4.3	4.5	4.1	3.1	0.9	0	0	0	0	0	0	0	0
Mean of unvaccinated calves	0	5.2	7.7	8.5	7.9	7.5	7.3	7.0	5.6	4.9	3.9	2.6	1.2	0	0

Table 1. Isolation of IBR virus (log₁₀ TCID₅₀) after challenge

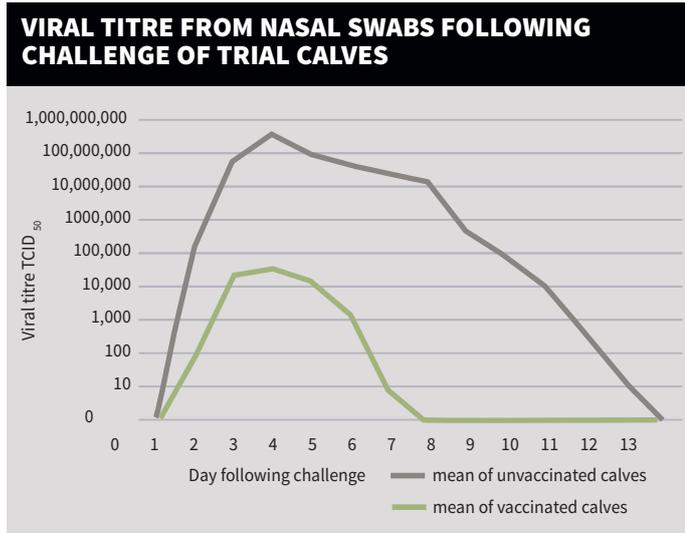


Figure 2. Viral titre TCID₅₀ from nasal swabs (log scale)

Virus excretion after the challenge (administered 190 days after revaccination with Biobos IBR Marker Vaccine) was measured by isolation of IBR virus from nasal swabs. In the vaccinated calves the virus was detected from Day 1 to Day 6 following the challenge. The maximum titre in all vaccinated calves ranged from 10^{4.3} TCID₅₀ to 10^{4.8} TCID₅₀ from Day 2 to Day 4 after challenge. The maximum average virus titre from nasal swabs of unvaccinated calves was 10^{8.5} TCID₅₀ on Day 3 after challenge.

Discussion

The level of IBR virus detected in nasal swabs was significantly (ie 10,000 times) lower in vaccinated animals compared with unvaccinated calves, at the peak of virus secretion. Viral shedding was also of shorter duration after challenge in the vaccinated calves. Overall IBR virus detected in nasal secretions of vaccinated calves was greatly reduced in vaccinated calves compared with the control animals, by almost 8,000 times. In a field situation, reducing the quantity of virus in the environment can play an important role in reducing spread of infection within groups of animals, and to neighbouring herds of animals.

The vaccine meets the European Pharmacopoeial test for efficacy of IBR vaccines, as

- Vaccinated calves showed only mild symptoms of IBR and unvaccinated controls showed typical symptoms of the disease
- The average number of days of virus excretion in vaccinated calves was least three days shorter than in the control group
- In at least 80% of vaccinated calves the maximum virus titre found in nasal swabs was at least 100 times lower than the average maximum titre found in control calves

Conclusion

Biobos IBR Marker Vaccine was shown to be efficacious in this challenge efficacy test performed according to the Pharmacopoeial monograph for IBR vaccines. Challenge occurred six months following administration of 2mL doses of vaccine, administered at 21 day intervals to three month old calves.

Vaccination with Biobos IBR Marker Vaccine reduces IBR virus in nasal secretions by almost 10,000 times, which impacts on viral secretion and disease spread.

Biobos IBR Marker Vaccine is a Restricted Veterinary Medicine registered pursuant ACVM ACT 1997, No. A11239

