Trials in Vaccinology 5 (2016) 24–31

Contents lists available at ScienceDirect

Trials in Vaccinology

journal homepage: www.elsevier.com/locate/trivac

Efficacy and safety of a new intradermal PCV2 vaccine in pigs

M. Sno *, E. Cox, H. Holtslag, T. Nell, S. Pel, R. Segers, V. Fachinger, M. Witvliet

MSD Animal Health, PO Box 31, 5830 AA Boxmeer, The Netherlands

ARTICLE INFO

Article history:
Received 16 September 2015
Revised 7 January 2016
Accepted 11 January 2016
Available online 21 January 2016

Keywords:
Porcine Circovirus
PCV2
Intradermal vaccination
Mycoplasma hyopneumoniae

ABSTRACT

The safety and efficacy of a new intradermal one dose vaccine containing Porcine Circovirus type 2 (PCV2) antigen – Porcilis® PCV ID – was evaluated in laboratory studies and under field conditions. In addition, the concurrent use with an intradermal *Mycoplasma hyopneumoniae* vaccine – Porcilis® M Hyo ID ONCE – was evaluated.

Vaccination with Porcilis® PCV ID resulted in small transient local reactions in a high percentage of the vaccinated animals with no temperature increase. In both the onset of immunity and duration of immunity challenge studies with PCV2 or *M. hyopneumoniae*, significant reduction of the PCV2 load in lymphoid tissue, lungs, serum and fecal swabs and *M. hyopneumoniae*-induced lung lesions were observed. In two field trials on two different farms where both PCV2 and *M. hyopneumoniae* were present, vaccination with Porcilis® PCV ID and/or Porcilis® M Hyo ID ONCE of 3 week old piglets resulted in a significant reduction of PCV2 viraemia, mortality and lung lesion scores at slaughter. In addition, a significant positive effect on average daily weight gain (between 44 and 59 g/day) in the finishing phase was observed. The results support that this new intradermal vaccine is safe and efficacious against PCV2 and may be used concurrently with Porcilis® M Hyo ID ONCE.

1. Introduction

Porcine Circovirus type 2 (PCV2) is the causative agent of the "Post-weaning Multisystemic Wasting Syndrome", but is also involved in a number of other disease syndromes which have been collectively named Porcine Circovirus Diseases (PCVD) [1,2]. The most pronounced PCVDs are Porcine Respiratory Disease Complex (PRDC), Porcine Dermatitis and Nephropathy Syndrome (PDNS), enteritis, reproductive failure, granulomatous enteritis, congenital tremors and exudative epidermitis. Subclinical PCV2 infections are characterized by poor growth performance [3–6].

Although intramuscular vaccines against PCV2 [7,8] are routinely used in the pig industry, no intradermal vaccines have been available until now. Intradermal (ID) vaccination has the advantage of targeting antigen presenting cells in the epidermis in close proximity to skin-draining lymph nodes [9,10]. Combined with needle free administration, ID vaccination is also more animal friendly and prevents accidental transmission of pathogens caused by reusing needles as well as broken needles in the muscle. The objective of the present studies was to evaluate the safety and efficacy under laboratory and field conditions of a new intradermal vaccine that is based on Porcilis® PCV and is named Porcilis® PCV ID (MSD Animal Health). In addition, concurrent use (at the same time, but different vaccination sites) with Porcilis® M Hyo ID ONCE (MSD Animal Health) was also investigated.

2. Materials and methods

2.1. Vaccines

A vaccine containing inactivated, baculovirus-expressed ORF2 antigen of PCV2 and a vaccine containing *Mycoplasma hyopneumoniae* cells, both adjuvanted with an oil-in-water emulsion, Xsolve® (Porcilis® PCV ID and Porcilis® M Hyo ID ONCE, MSD Animal Health) were tested. The vaccines were administered with the IDAL® (IntraDermal Administration of Liquids, MSD Animal Health) injector either alone or concurrently as a single 0.2 ml dose to 3 week old piglets according to the manufacturer's instructions.

2.2. Quality

All laboratory studies and sample testing were conducted in compliance with GLP, while all field studies were conducted in compliance with GCP. All laboratory studies were performed after the approval of the Ethical Committee for Animal Experiments of MSD Animal Health.

* Corresponding author.
E-mail address: Melanie.sno@merck.com (M. Sno).

http://dx.doi.org/10.1016/j.trivac.2016.01.002
1879-4378/

2.3. Safety trials

2.3.1. Laboratory trial

Two groups of healthy SPF pigs were either vaccinated with Porcilis® PCV ID at 19–21 days of age (vaccinated group, $N = 20$) or injected with phosphate buffered saline (control group, $N = 10$). The piglets were monitored daily for abnormal systemic and local (by palpating) reactions until 42 days after vaccination. Body weight was recorded on the day of vaccination, and at 21 and 42 days post vaccination. Rectal temperature was recorded one day before vaccination, just before vaccination, 4 h after vaccination and daily for four days. Both at 14 and 28 days post-vaccination, 5 animals from the vaccinated group were sacrificed for examination of the injection site. The remaining animals were subjected to the above described procedure at 42 days post-vaccination.

2.3.2. Field trial

A GCP field safety study was performed according to a controlled, randomized and blinded design in three commercial pig farms in The Netherlands. In each farm, approximately 90 healthy 18–24 days old piglets were allocated randomly to one of three groups. The pigs in group 1 (PCV) were vaccinated with Porcilis® PCV ID, the pigs in group 2 (PM) with Porcilis® PCV ID and Porcilis® M Hyo ID ONCE concurrently (Porcilis® PCV ID in one side of the neck and Porcilis® M Hyo ID ONCE in the other side), the piglets in group 3 (Control) remained untreated. The piglets were observed for immediate reactions during or immediately after vaccination and general health one day before vaccination, at vaccination, 1 and 4 h after vaccination and daily for 28 days. The injection site was examined by palpating for local reactions at 1 and 4 h after vaccination and daily for 28 days. Rectal temperature was measured one day before vaccination, just before vaccination, 4 h after vaccination and daily for 4 days. All study piglets were weighed individually at admission (day −1) and on day 21.

2.4. Efficacy trials

2.4.1. Vaccination-challenge experiments

The onset of immunity (OOI) and duration of immunity (DOI) for Porcilis® PCV ID (PCV group) alone or Porcilis® M Hyo ID ONCE (M group) alone, and for concurrent use of Porcilis® PCV ID and Porcilis® M Hyo ID ONCE (PM group) were evaluated in experimental PCV2 or *M. hyopneumoniae* challenge studies; the experimental design of these studies is summarized in Table 1. In each experiment, 3 week old pigs, maternally-derived antibody positive for PCV2 and free of *M. hyopneumoniae*, were randomly divided into groups (PCV, PM, M or control) at the time of vaccination. Blood samples were taken just before vaccination, between vaccination and challenge (DOI only), at the time of challenge and 1, 2 (PCV2 challenge studies only) and 3 weeks after challenge. Fecal swabs (PCV2 challenge studies only) were collected at the time of challenge and 1, 2 and 3 weeks after challenge.

At 5 (for OOI) or 26 weeks of age (for DOI), pigs were challenged intranasally (3 ml per nostril, $\pm 10^6$ $TCID_{50}$) with a recent Dutch PCV2 field isolate. Three weeks after PCV2 challenge, all pigs were necropsied and the inguinal lymph nodes, tonsil and lung were collected. Blood samples, fecal swabs and tissue samples were tested for quantification of the PCV2 viral load by qPCR. In addition the blood samples were also tested for the presence of PCV2 and M hyo antibodies.

M. hyopneumoniae challenge was performed at 6 (for OOI) or 25 weeks of age (for DOI) intratracheally on two consecutive days with 10 ml of a culture of a Danish field isolate (provided by Dr. N. Friis, National Veterinary Laboratory, Copenhagen) containing $\pm 10^7$ CCU/ml. Three weeks after challenge, the pigs were necropsied to evaluate lung lesions which were scored according to Goodwin & Whittlestone as previously described [11]; the maximum score is 55.

During the studies, pigs were observed daily for general clinical abnormalities.

2.4.2. Field trials

Two combined GCP field efficacy and safety studies (studies A and B) were performed according to a controlled, randomized and blinded design in two Hungarian pig herds with both an *M. hyopneumoniae* and PCV2 infection. Healthy three week old suckling piglets were allocated randomly, within litters, to treatment groups of approximately 600 (study A) or 330 (study B) piglets each. The pigs in group one (PCV) were vaccinated intradermally with Porcilis® PCV ID, the piglets in group two (PM) were vaccinated intradermally with Porcilis® PCV ID and Porcilis® M Hyo ID ONCE concurrently, the piglets in group three (M) were vaccinated intradermally with Porcilis® M Hyo ID ONCE (study B only) and the piglets in group four (control) remained untreated. The primary efficacy parameters were mortality (study A only), *M. hyopneumoniae*-like lung lesions at slaughter (study B only), PCV2 viraemia and the average daily weight gain (ADWG) during finishing (i.e. between 9–10 and 21–23 weeks post vaccination (wpv). Also, serological response following vaccination or field infection was measured. The pigs were weighed individually at time of vaccination, transfer to the finishing unit and just prior to slaughter. Medication was recorded and pigs that died during the studies were examined post-mortem to establish the cause of death. Forty (study A) to 60

Table 1
Experimental design challenge experiments.

Study type	Group	*n*	Challenge material	Age at vaccination	Challenge at … wpv	Samples taken at … wpv	
						Blood samples	Fecal swabs
OOI	Porcilis® PCV ID	15	PCV2 field isolate	3 weeks	2	0, 2, 3, 4, 5	2, 3, 4, 5
	Porcilis® PCV ID + Porcilis® M Hyo ID ONCE	15					
	Unvaccinated control	15					
DOI	Porcilis® PCV ID	20	PCV2 field isolate	3 weeks	23	0, 7, 17, 21, 22, 23, 24, 25, 26	23, 24, 25, 26
	Unvaccinated control	20					
OOI	Porcilis® PCV ID + Porcilis® M Hyo ID ONCE	20	*M. hyopneumoniae* field isolate	3 weeks	3	0, 2, 6	
	Porcilis® M Hyo ID ONCE	20					
	Unvaccinated control	20					
DOI	Porcilis® PCV ID + Porcilis® M Hyo ID ONCE	40	*M. hyopneumoniae* field isolate	3 weeks	22	0, 11, 22, 25	
	Porcilis® PCV ID	40					