Review of Circumvent® Efficacy[1]

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Introduction

Through its line of Circumvent® vaccines, Merck Animal Health has a strong track record of providing effective products to protect swine against the ubiquitous porcine circovirus type 2 (PCV2). Joining the lineup with Circumvent PCV and Circumvent PCV M is the new Circumvent PCV G2. As the next generation of circovirus protection, it is the **only** PCV2 vaccine that is approved for use in pigs as early as 3 days of age. Replacing the monovalent vaccine, Circumvent PCV, it provides two convenient dosing options – one dose or two lower-volume doses – and offers industry-leading 5-month duration of immunity (DOI). Choose between a single, 2-mL injection given to pigs 3 weeks of age or older, or two lower-volume doses, with the initial injection given to pigs as early as 3 days of age and the second dose given approximately 3 weeks later.

In adding this new product to the lineup, Merck Animal Health's goal is to provide customers with the same level of efficacy and protection against PCV2 that the other Circumvent products offer, but now with even more convenient options and the longest DOI on the market.

Merck Animal Health reviewed all of its Circumvent products to assure customers that the numerous options available are equally effective in aiding in the prevention and control of PCV2, particularly as it relates to viremia – the presence of PCV2 virus in the blood. All are licensed using the co-infection challenge of PCV2 and porcine reproductive and respiratory syndrome virus (PRRSv) to measure vaccine efficacy under experimental conditions that mimic the real world of present-day pig production.

Materials and Methods Overview

Circumvent comparison study design:

Merck Animal Health used different study designs over time. The common feature of all studies was our PCV2/PRRSv co-infection challenge model, which enables Merck Animal Health to apply the licensure study data to a wide population of pigs and production scenarios. In all studies following challenge, PCV2 infection was monitored by a minimum of weekly blood collection for PCV2 viremia, and nasal and fecal swabs for the presence of PCV2. Tissues were collected at necropsy. There are several study design features that have changed over time. For example, in our most recent Circumvent PCV M and Circumvent PCV G2 efficacy studies, both vaccinated and control pigs were co-mingled to provide a more stringent continual challenge as non-vaccinated control pigs started shedding PCV2 at high levels by 2 weeks post-exposure. In prior studies, vaccinated and control pigs were housed in separate rooms. Studies also varied by how long the pigs were monitored after challenge. In the conditional license and Circumvent PCV studies, the pigs were monitored for 42 days post-challenge; for Circumvent PCV M, 24 days; and for the current Circumvent PCV G2 studies, 35 days.

Laboratory testing protocols and procedures:

Laboratory testing has also changed over time. All studies used the immunofluorescence assy (IFA) test to measure PCV2 serum antibody levels. Polymerase chain reaction (PCR) was used in all studies to detect or measure PCV2 in serum and swab samples. However, the conditional license, Circumvent PCV and Circumvent PCV M used a standard procedure that produces a "yes" or "no" result. In the current Circumvent PCV G2 studies, a quantitative test format (qPCR) was used. With regard to tissue infection, early studies used PCR to detect PCV2, while the Circumvent PCV M and Circumvent PCV G2 studies used immunohistochemistry. Lymphoid lesions evaluation was done only in the Circumvent PCV G2 studies. No label claims are made for lesion reduction.

Summary

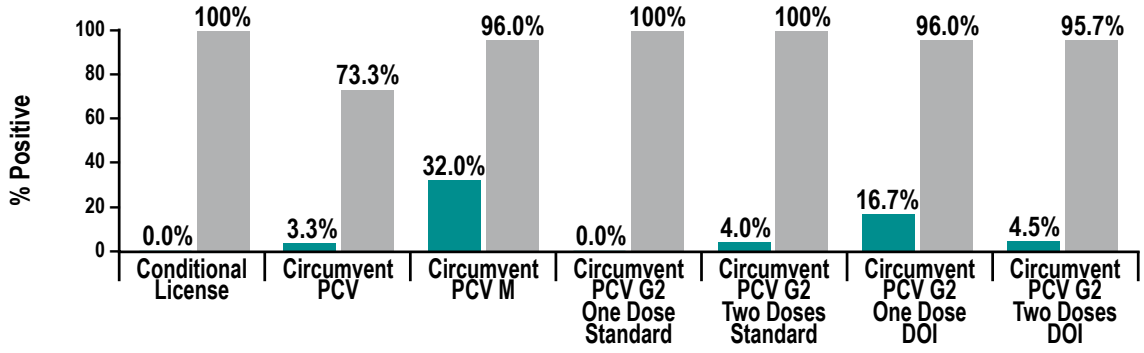
In total, these changes reflect advancements in technology, what Merck Animal Health has learned by working with PCV2 in the laboratory and customer feedback over the past 10 years. The main parameter or efficacy target for evaluating our PCV2 vaccines is viremia. That said, the overarching strategy for our PCV2 vaccine development efforts is to produce products that prevent viremia in the laboratory. This target has served Merck Animal Health and our customers well. In field studies and diagnostic investigations, a common finding is the absence of viremia in Circumvent-vaccinated pigs, regardless of which product. Accordingly, viremia provides the best and most consistent measure of how our different Circumvent products have performed over time in the laboratory.

Results Overview

Effective against viremia:

Chart 1 presents viremia data, showing the percentage of pigs found to be viremic during the post-challenge period. For all Circumvent product options, vaccinated pigs exhibited no viremia or very minimal viremia compared to controls. Utilizing vaccines that are labeled to help prevent viremia is highly effective because the disease cycle is broken early and damage caused by infection is limited or virtually eliminated. Plus, more viremia-free days means less shedding to other pigs in the group.

Chart 1: Percentage of Viremic Pigs



Discussion

With the objective of providing more options, Merck Animal Health reviewed all of its Circumvent products to assure customers that the numerous choices are equally effective to aid in the prevention of PCV2 viremia. To test its Circumvent vaccines, Merck Animal Health is the only company that uses a PCV2/PRRSv co-infection challenge. The researchers use a natural promoter, PRRSv, to stimulate the immune system, which mimics field conditions to ensure that the pigs being tested are susceptible to PCV2. We are the only company that uses a natural promoter to test our PCV2 vaccines. Other companies typically use "artificial" chemical promoters to stimulate the immune system. The difference is important because while PCV2 is a hardy and durable virus that is commonly found with pork operations worldwide and is widely viewed as a devastating disease and a strong promoter of other pathogens, it is not readily infectious or virulent in laboratory challenge models, because PCV2 requires actively dividing, stimulated immune cells to cause infection.

1. Data on file.

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