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Fostera® PRRS Vaccine for One-Day-Old Piglets: Respiratory Efficacy, Duration of Immunity, and Safety Research

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Most every swine veterinarian and pork producer recognizes that porcine reproductive and respiratory syndrome virus (PRRSV) poses a major threat to profitable pork production. In fact, industry researchers have estimated that PRRS costs the US pork industry $664 million annually ($1.8 million/day) in production-related losses, and the cumulative impact of PRRSV totals more than $1 billion per year when other disease-control expenses are included.[1]

As the name implies, PRRS has two pathological presentations: causing *respiratory disease* in growing pigs (pneumonia, poor performance, immunosuppression), and causing *reproductive disease* in gestating gilts and sows (abortions and high rates of stillborns, mummies, and low-viability piglets). Direct economic damages caused by the respiratory form of PRRS are estimated at $362 million/year (equating to $62.52 per breeding female).[1]

This serious economic damage caused by PRRS in growing pigs has made use of modified-live PRRSV vaccines a seemingly necessary practice. However, available vaccines can widely differ in regard to ***when*** they can be administered and in the ***duration*** of immunological protection conferred. For instance, a vaccine that can be administered at 1 day of age may offer tangible benefits compared to a product that requires pigs to be at least 3 weeks of age. Moving PRRS vaccination early into the farrowing house (e.g., 1 day of age) can help provide earlier onset of disease protection, an important factor for operations where PRRS threatens pigs soon after weaning. In addition, the ability to administer a PRRS vaccine when newborn piglets are typically processed could enhance dosing convenience. Thus, when selecting a PRRSV vaccine to help prevent the detrimental respiratory impacts of PRRS in growing pigs, it is now appropriate to consider how early and conveniently a vaccine can be administered, and if disease protection can extend throughout the entire production cycle (through finishing).

PRRS vaccination at 1 day of age can help provide earlier onset of disease protection.

Fostera® PRRS

Fostera PRRS, from Zoetis, is the first and only PRRSV vaccine with a claim for administration as early as ***1 day of age*** to help ***prevent respiratory disease*** associated with PRRSV, with a ***duration of immunity of 26 weeks.*** Fostera PRRS helps support performance by

Fostera® PRRS can now be administered to pigs as early as 1 day of age, with a 26-week duration of immunity.

helping minimize the adverse affects of a subsequent PRRSV challenge, thereby allowing growing pigs to help maximize post-challenge weight gain.[2]

Fostera PRRS is licensed for the vaccination of healthy, susceptible swine in PRRS virus-positive herds as an ***aid in preventing reproductive and respiratory diseases*** caused by PRRS virus. A 19-week duration of immunity (DOI) against reproductive disease has been demonstrated in swine vaccinated prebreeding. A 26-week DOI has been demonstrated against respiratory disease. After aseptic rehydration of the freeze-dried vaccine with sterile diluent provided, Fostera PRRS is administered as a single 2-mL intramuscular (IM) dose to pigs 1 day of age or older.

Ongoing research has yielded additional enhancements (such as the reproductive claim) to the Fostera PRRS label since the vaccine was first licensed. This research and development process continues, as Fostera PRRS can now be administered to pigs as early as ***1 day of age***, with a DOI of 26 weeks (Fostera PRRS was previously approved for use only in pigs 3 weeks of age or older, with a DOI of 24 weeks). The demonstrated 26-week DOI for Fostera PRRS is at least 9 weeks longer than competitive vaccines. Thus, Fostera PRRS can help provide protection against PRRSV for the entire production cycle, leaving no gaps in respiratory protection from nursery through finishing.

The addition of this unique 1-day-old age claim to the Fostera PRRS label represents yet another attribute that further differentiates Fostera PRRS from other PRRSV vaccines. A summary of efficacy and safety research supporting the ability of Fostera PRRS to help prevent respiratory disease in pigs vaccinated at 1 day of age follows.

7-week Immunogenicity Study

Experiment Design —

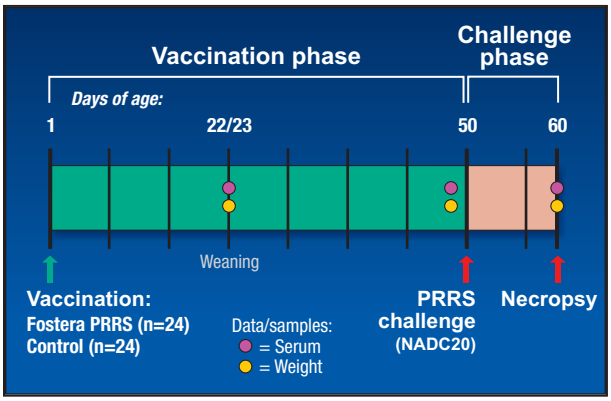
Three concurrent challenge studies conducted at a Nebraska research facility investigated the efficacy of Fostera PRRS in pigs vaccinated at 1 day of age. The first study (Figure 1) involved 48 healthy mixed-gender piglets that were farrowed from multiple sows negative for PRRSV (IDEXX ELISA S/P < 0.4).[3] Piglets were also confirmed to be PRRSV negative prior to vaccination. At 1 day of age (study day 1), piglets were randomly assigned to 2 treatment groups and received a single 2-mL IM injection in the neck with either:

- Fostera PRRS (n=24);
- Vaccine diluent (control, n=24).

Pigs in each treatment group were housed in separate BSL-2 rooms, with each treatment group occupying 3 pens (treatment groups were not commingled to avoid possible viral shedding from vaccinates to control pigs). Pigs were weaned at 22 or 23 days of age, and serological status for PRRSV was confirmed (IDEXX ELISA). Feed and water were provided ad libitum throughout the study, and pigs were monitored daily for general health status.

The 10-day challenge phase of the study involved administration of a virulent PRRSV respiratory challenge strain (NADC20) at 7 weeks of age. Animals were re-housed 3 to 4 days prior to challenge in a single room of 24 pens (2 pigs

Figure 1. 7-week study design and timeline.



Fostera® PRRS significantly reduced lung lesions by 98.4% compared to controls.

from the same treatment group per pen; randomized complete block design with pen location as the blocking factor). At 7 weeks of age (day 50/51), each pig received a PRRSV NADC20 isolate administered intranasally (1 mL/nostril) and IM (2 mL right neck).

Pigs were weighed before and after the 10-day challenge phase, and were observed daily post-challenge for signs of clinical PRRS (general condition, depression, sneezing, coughing, respiratory distress, etc.). All pigs were euthanized and necropsied 10 days post-challenge to allow scoring of lung lesions (percentage of consolidation for each lobe), the primary efficacy variable. Blood samples were collected from each pig at weaning (day 22), re-housing (day 47), and necropsy (day 60) for determination of PRRSV serology (ELISA).

Data were statistically analyzed by appropriate standard methods, with lung lesion percentages transformed for analysis and back-transformed least squares (LS) means reported. The pen was the experimental unit in the post-challenge phase, with animal as the sub-sample. Statistical significance was recognized at $P \leq 0.05$. All personnel performing clinical observations, laboratory assays, data collections, and necropsy evaluations were blinded to treatment group assignments. The study was conducted in accordance with the Zoetis Institutional Animal Care and Use Committee.

Results —

Lung lesion outcomes for the study (Figure 2) showed that a protective effect was conferred by Fostera PRRS vaccination. Mean lung consolidation was 43.9% in the control group compared to only 0.7% in Fostera PRRS vaccinates. Thus, Fostera PRRS significantly ($P \leq 0.0001$) reduced lung lesion severity by **98.4%** compared to controls.

Figure 2. Percent of lungs with lesions.

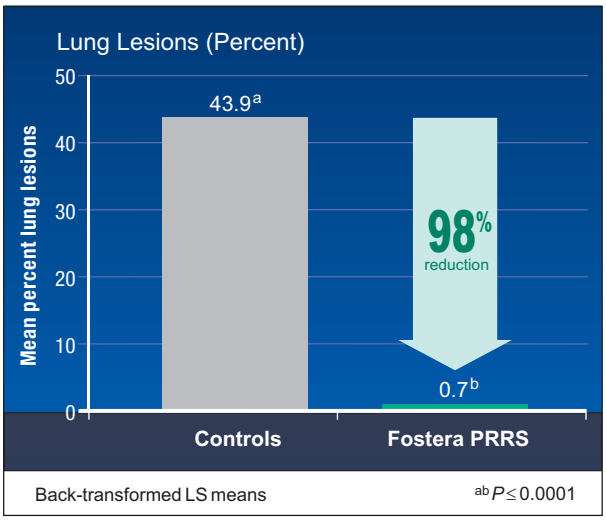


Table 1 – Percent of pigs ever exhibiting any clinical sign post-challenge.

Parameter	Control	Fostera PRRS
Poor condition (%)	100.0	27.3
Depression (%)	95.8	36.4
Respiratory distress (%)	95.8	40.9
Cough (%)	0.0	4.5
Other (%)*	8.3	4.5

*Carpus/hock swelling, leg paresis

Observations summarized in Table 1 document that disease signs were generally lower for Fostera PRRS vaccinates. Signs relating to poor general condition, depression, and respiratory distress were the most prevalent abnormal clinical conditions observed, but no PRRS-related mortalities occurred.

Fostera® PRRS

One-day-old pigs vaccinated with Fostera® PRRS had protective PRRSV antibodies by weaning.

Serology results (not shown) confirmed that all control pigs remained serologically negative (IDEXX ELISA S/P < 0.4) during the pre-challenge vaccination phase (days 22 and 47). In contrast, Fostera PRRS pigs seroconverted by day 22 (weaning, the first sample date) and continued to demonstrate positive antibody titers at subsequent sample dates (days 47 and 60). All control pigs seroconverted within 10 days following challenge (day 60).

Average body weights were significantly ($P \leq 0.05$) greater for Fostera PRRS vaccinates compared to controls both before and after challenge (at days 47 and 60, respectively), so no impacts of disease protection on body weight could be determined. Three animals died during the study (2 vaccinates pre-challenge, 1 control post-challenge), but necropsy results indicated causes unrelated to vaccination or PRRS virus. No other confounding disease factors were detected during the study.

18-Week Duration of Immunity Study

Experiment Design —

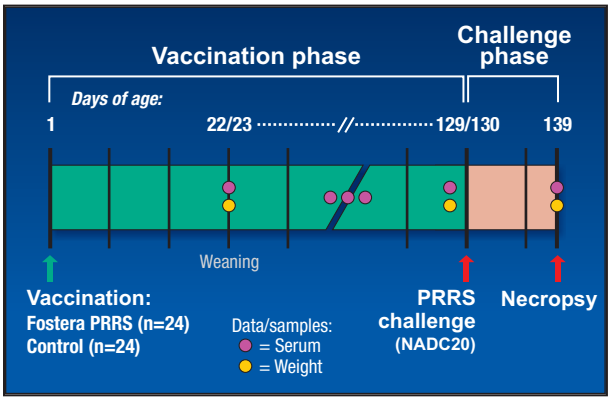
A second challenge study investigated the 18-week DOI provided by Fostera PRRS when administered to pigs at 1 day of age.[4] The protocol, timing, location, and conditions for this study were virtually identical to the 7-week study, but with the following exceptions (Figure 3):

- animals were re-housed at 127 days of age;
- virulent PRRSV challenge (NADC20) was administered at 129 or 130 days of age, over 18 weeks after day-1 vaccination;
- blood samples for serologic analysis were collected at weaning, re-housing, and necropsy as in the 7-week study, but 3 additional samples were collected on days 50, 78, and 106.

Results —

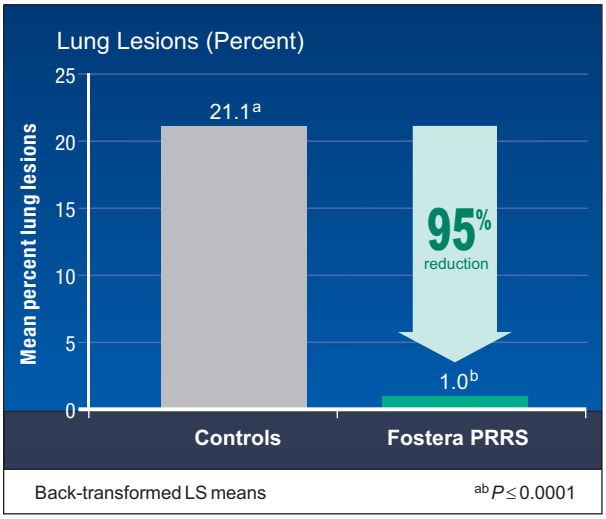
Lung lesion outcomes for the study (Figure 4) again demonstrated a protective effect provided by Fostera PRRS that extended to ***at least 18 weeks*** after day-1 vaccination. Mean lung consolidation was 21.1% in the control group compared to 1.0% for Fostera PRRS vaccinates. Thus, Fostera PRRS significantly ($P \leq 0.0001$) reduced lung lesion severity by **95.3%** compared to controls. As expected, lung damage was substantially less in the older control pigs in this study compared to the younger control pigs in the

Figure 3. 18-week study design and timeline.



Clinical signs of PRRS were generally lower for Fostera® PRRS vaccinates compared to controls.

Figure 4. Percent of lungs with lesions for the 18-week DOI study.



previous 7-week study, but a large reduction of lung lesion incidence and severity was achieved for Fostera PRRS vaccinates.

Clinical signs of PRRS were generally lower for Fostera PRRS vaccinates compared to controls (Table 2). Signs relating to poor general condition, depression, and respiratory distress were again the most prevalent abnormal clinical conditions observed, but no PRRS-related mortalities occurred.

Serology results (not shown) confirmed that all control pigs remained serologically negative (IDEXX ELISA S/P < 0.4) during the pre-challenge vaccination phase of this study. In contrast, Fostera PRRS pigs seroconverted by 22 days of age (weaning, the first sample date) and demonstrated positive antibody titers at all 5 subsequent sample dates. Following challenge, all control pigs seroconverted within 10 days.

Table 2 – Percent of pigs ever exhibiting any clinical sign post-challenge (18-wk DOI study).

Parameter	Control	Fostera PRRS
Poor condition (%)	21.7	15.0
Depression (%)	17.4	10.0
Respiratory distress (%)	13.0	5.0
Other (%)*	8.7	5.0

*Lame, unspecified

No differences ($P > 0.05$) in average body weights were detected between treatment groups before or after challenge. Four vaccinated pigs died or were euthanized pre-challenge, but necropsy results indicated causes unrelated to vaccination or PRRS virus. No other confounding disease factors were detected during the study.

Fostera® PRRS

Pigs vaccinated with Fostera® PRRS at 1 day of age experienced 93.2% less lung damage when challenged with PRRSV 26 weeks later.

26-Week Duration of Immunity Study

Experiment Design —

A third challenge study further investigated the DOI provided by Fostera PRRS, this time involving PRRSV challenge 26 weeks after vaccination at 1 day of age.[5] The protocol, timing, location, and conditions for this study were virtually identical to the initial 7-week study, but with the following exceptions (Figure 5):

- animals were re-housed at 181 days of age, 1 day before challenge;
- virulent PRRSV challenge (NADC20) was administered at 182 days of age, 26 weeks after vaccination at 1 day of age ;
- blood samples for serologic analysis were collected at weaning, re-housing, and necropsy as in the 7-week study, but 5 additional samples were collected on days 50, 78, 106, 134, and 161.

Results —

Lung lesion outcomes for the study (Figure 6) demonstrated that Fostera PRRS provided a protective effect that extended ***at least 26 weeks*** after day-1 vaccination. Mean lung consolidation was 17.7% in the control group compared to 1.2% for Fostera PRRS vaccinates. Thus, Fostera PRRS significantly ($P \leq 0.0001$) reduced lung lesion severity by **93.2%** compared to controls. Again, lesion severity was substantially less in the older (finishing) control pigs in this study compared to the young control pigs in the 7-week study, but a large reduction of lung lesion incidence and severity was still achieved for pigs vaccinated with Fostera PRRS at 1 day of age.

Figure 5. 26-week study design and timeline.

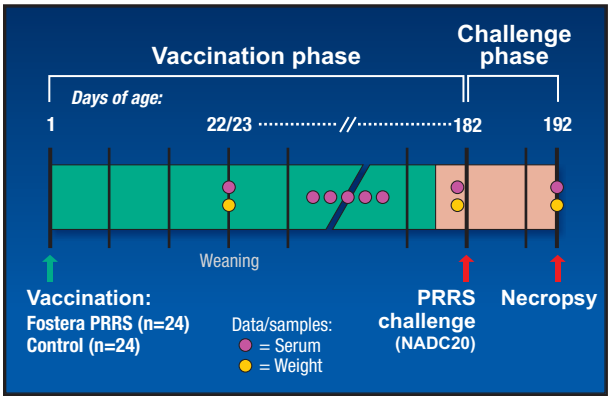
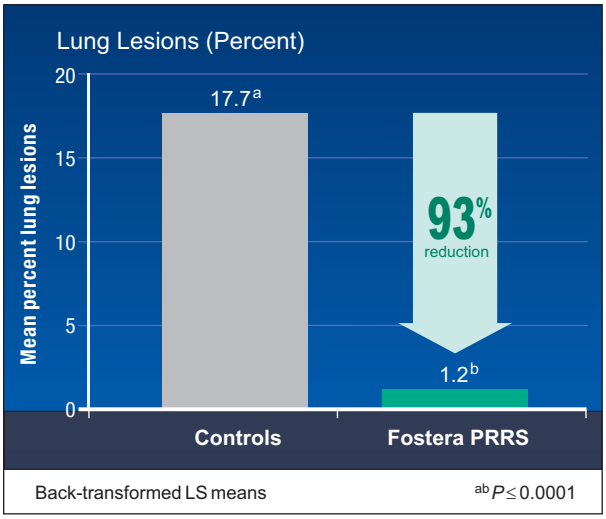


Figure 6. Percent of lungs with lesions for the 26-week DOI study.



Post-challenge clinical signs of PRRS were detected with less frequency in this study involving older pigs than in the other studies with younger pigs. No PRRS-related mortalities occurred.

As in the other studies, serology results (not shown) confirmed that all control pigs remained serologically negative (IDEXX ELISA S/P < 0.4) before challenge. In contrast, pigs vaccinated with Fostera PRRS seroconverted by 22 days of age (weaning, the first sample date) and demonstrated positive antibody titers at all 7 subsequent sample dates. Following challenge, all control pigs seroconverted within 10 days.

No differences ($P > 0.05$) in average body weights were detected between treatment groups before or after challenge. No pigs died and no other confounding disease factors were detected during the course of the study.

One-day-old piglets vaccinated with Fostera® PRRS had no injection site reactions or vaccine-related abnormal health events.

Safety Study

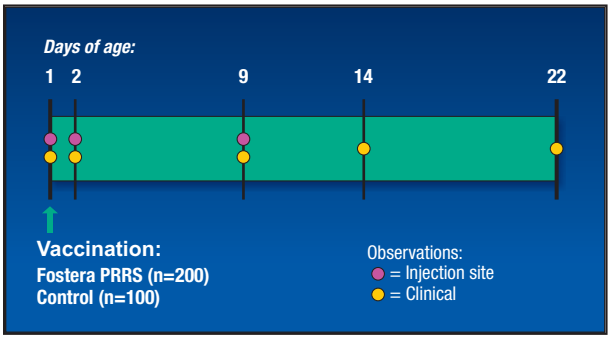
Experiment Design —

A clinical safety study involved 300 day-old piglets from 30 litters that were enrolled at a commercial production site in North Carolina.[6] The healthy piglets were derived from a breeding herd seropositive for PRRSV and received standard neonatal processing according to established site procedures. At 1 day of age, piglets were randomly assigned to 2 treatment groups (2:1 ratio) using a randomized complete block design with blocking based on crate location. Each piglet received a single 2-mL IM injection in the right neck with either:

- Fostera PRRS (n=200; 100 pigs for each of 2 different lots of Fostera PRRS).
- Sterile water (control, n=100).

Piglets were observed for adverse reactions within 5 hours and 1 day post-vaccination, and additional clinical observations were conducted at 9, 14, and 22 days of age (study conclusion). All injection sites were observed for adverse reactions and palpated at 1 and 8 days post-vaccination (2 and 9 days of age), with any reactions periodically reevaluated until resolution. Animals were also observed daily for any clinical disease or adverse events requiring treatment. All clinical disease cases were evaluated to determine if they were related to vaccine administration, and any pigs that died were necropsied and a diagnosis determined when possible. All personnel performing clinical observations, injection site reaction measurements, or data collections were blinded to treatment group assignments.

Figure 7. Safety study design and timeline.



The non-vaccinated control group provided baseline information regarding the current herd health conditions at the site. Conclusions regarding safety were based on the summary of the reported clinical observations, injection site reactions, and adverse events attributed to vaccination. Data were evaluated by appropriate methods using crate as the experimental unit. The protocol was reviewed and approved by the Zoetis Kalamazoo Ethical Review Board. A Zoetis Animal Welfare Risk Assessment was completed prior to initiation of the study.

Results —

No confounding disease factors were detected during the study which affected evaluation of vaccine safety. During the entire 21-day post-vaccination observation period, 25% of controls and 23.5% of vaccinates experienced some type of abnormal health observation, but none were were determined to be related to vaccination. Mortalities occurred for 11% of controls and 6.5% of vaccinates. Necropsies and submissions to a diagnostic laboratory indicated a variety of bacterial pneumonias for several pigs, all unrelated to vaccination or PRRS.

Within approximately 5 hours or 1 day after vaccination, 1.0% of control pigs and 3.0% of vaccinates demonstrated anorexia or diarrhea. Thus, the rate of abnormal post-vaccination observations was low for both treatment groups, suggesting no acute abnormalities were attributable to the use of Fostera PRRS in 1-day-old pigs.

No injection site reactions were detected in any animals at 1 day post-vaccination. At 9 days of age, 1 control piglet demonstrated a mild injection site reaction that resolved by 5 days later.

Fostera® PRRS

Fostera® PRRS helps provide early and long-lasting respiratory protection against PRRS virus for the entire production cycle.

Conclusions

Results of 3 challenge studies demonstrated that vaccination with Fostera PRRS at 1 day of age helped prevent respiratory disease caused by PRRSV. Lung lesion severity (percent of lung consolidation) in vaccinates was significantly ($P \leq 0.0001$) reduced by over 98%, 95%, and 93% compared to controls when pigs were challenged with virulent PRRSV at 7, 18, and 26 weeks after day-1 vaccination, respectively. In each study, all vaccinated pigs seroconverted by 3 weeks post-vaccination (the first sample date), indicating early development of immunological responses. Furthermore, the safety study confirmed that vaccination of 1-day-old piglets with Fostera PRRS is safe, evidenced by the complete absence of injection site reactions and any vaccine-related abnormal health events.

Convenient vaccination of 1-day-old piglets with Fostera PRRS offers swine veterinarians and pork producers the opportunity to help achieve early and long-lasting respiratory protection against PRRS virus for the entire production cycle, from nursery through finishing.

References

1. Holtkamp D, Kliebenstein J, Zimmerman J, Neumann E, Rotto H, Yoder T, Wang C, Yeske P, Mowrer C, Haley C. Assessment of the economic impact of porcine reproductive and respiratory syndrome virus on U.S. pork producer. *National Pork Board Research Report* 2011; NPB #10-158.
2. Data on file, Study Report No. 3127R-60-10-890, Zoetis Inc.
3. Data on file, Study Report No. 3127R-60-11-961, Zoetis Inc.
4. Data on file, Study Report No. 3121R-60-11-963, Zoetis Inc.
5. Data on file, Study Report No. 3121R-60-11-962, Zoetis Inc.
6. Data on file, Study Report No. B921R-US-13-142, Zoetis Inc.

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