Boehringer Ingelheim

TECHNICAL BULLETIN

REPROCYC PARVOFLEX® VACCINE DEMONSTRATES EFFICACY IN A REPRODUCTIVE HETEROLOGOUS PPV CHALLENGE IN GESTATING SOWS AND GILTS

Porcine parvovirus (PPV) is a significant swine pathogen that can cause reproductive failure in dams. Infection can cause fetal death and resorption, presentation of mummified fetuses at farrowing, and an irregular return to estrus. REPROCYC PARVOFLEX aids in the prevention of reproductive disease, and significantly reduces reproductive failure caused by PPV when administered to healthy sows and gilts 6 months of age or older prior to breeding.[1] The vaccine is safe to administer at any stage of gestation, protecting dams against reproductive failure caused by PPV.[2]

STUDY KEY FINDINGS

- In a challenge study, 96% of fetuses from gilts vaccinated with REPROCYC PARVOFLEX were in normal condition compared to only 38% of fetuses from non-vaccinated gilts.[1]
- In the study, 56% of fetuses from non-vaccinated gilts were born mummified, compared to 3% from vaccinated gilts.[1]
- A primary outcome parameter of the study was evidence of PPV in fetuses as determined by polymerase chain reaction (PCR) testing of fetal thoracic fluid. The mean number of affected fetuses in each litter was 1.41 among the vaccinated group, compared to 11.30 in the non-vaccinated group, a statistically significant difference.[1]
- REPROCYC PARVOFLEX includes the recent PPV strain 27a, which research has shown to be effective in establishing a broad spectrum of protection when incorporated into vaccines.[3]

STUDY OVERVIEW AND DESIGN

OVERVIEW

The study was conducted to determine the efficacy of REPROCYC PARVOFLEX in a reproductive challenge model with a heterologous PPV. The study used 40, 5- to 6-month-old pre-breeding gilts that had not been previously vaccinated against PPV and had no history of reproductive disease.[1]

STUDY DESIGN

The gilts were divided into three groups: Group 1 (N = 24) received REPROCYC PARVOFLEX, Group 2 (N = 12) received a placebo, and Group 3 included four gilts that served as the non-vaccinated, non-challenged controls. Treatments were randomly assigned, and gilts were commingled so that treatment was balanced across four pens.

On Day 0, Groups 1 and 2 each received a 2-mL dose of either REPROCYC PARVOFLEX or a product-matched placebo. On Day 21, the groups each received a 2-mL booster dose of their respective products. Gilts' estrous cycles were synchronized, and they were artificially inseminated between Days 37 and 50. On Day 74, pregnancy was confirmed in 22 gilts in Group 1, 10 gilts in Group 2 and four gilts in the control group.[1]

REFERENCES

[1] Data on file. Boehringer Ingelheim Animal Health USA Inc. Study #2013057.
[2] Data on file. Boehringer Ingelheim Animal Health USA Inc. Study #2016270.
[3] Zeeuw E, Leinecker N, Herwig V, et al. Study of the virulence and cross-neutralization capability of recent porcine parvovirus field isolates and vaccine viruses in experimentally infected pregnant gilts. *J Gen Virol* 2007;88:420–427.

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On Day 81 (approximately 40 days of gestation), the four control-group pigs were euthanized, and all fetuses tested negative for PPV infection via PCR. Gilts in the remaining groups were challenged with virulent PPV. All gilts were euthanized on Day 128 or 129 (90 days of gestation) for fetal evaluation and sample collection (Table 1). This included recording the position of each fetus in the uterus, as well as fetal condition, size and weight. Thoracic wash samples were collected from each fetus and tested for the presence of PPV by PCR.[1]

TABLE 1 – STUDY DESIGN[1]

TREATMENT	#V	1ST VACCINATION (D0)	2ND VACCINATION (D21)	BRED	PREGNANCY EVALUATION	#C	CHALLENGE (~40dG)	NECROPSY (~90dG)
Group 1 (REPROCYC PARVOFLEX)	24	REPROCYC PARVOFLEX 2 mL IM	REPROCYC PARVOFLEX 2 mL IM	D37–D50	D74	22	D81 2 mL IM & 4 mL IN PPV1	D128–129 Fetal evaluation & fetal thoracic fluid sampling
Group 2 (Placebo)	12	Placebo 2 mL IM	Placebo 2 mL IM			10		
Group 3 (Non-vaccinated, non-challenged control)	4	Not applicable				Not applicable		D81

#V = Number of animals vaccinated #C = Number of animals challenged dG = Days of gestation

STUDY RESULTS

RESULTS SUMMARY

The efficacy of the vaccine was confirmed by the clinical presentation of the fetuses at necropsy. A gilt was considered affected if one or more fetuses in a litter were not in normal condition (mummified/necrotic or stillborn). As shown in Table 2, the frequency of affected gilts in the vaccinated group was significantly less than the affected gilts in the placebo group; 5/22 affected versus 9/10 affected, respectively. Table 3 summarizes the fetus condition results. Only 38% of the fetuses from the placebo group were in normal condition compared to 96% of fetuses from the vaccinated group.[1]

TABLE 2 – GILT STATUS BASED ON CLINICAL CONDITION OF THE FETUSES[1]

Group	Frequency of Affected Gilts*	Mean Affected Fetuses	Percent of Affected Gilts*
Group 1 (REPROCYC PARVOFLEX)	5/22	0.55	23%
Group 2 (Placebo)	9/10	9.1	90%
Prevented Fraction Analysis, Group 1 vs. Group 2 (lower and upper 95% bound)			0.74 (0.38, 0.89)
P-value			<0.05

*A gilt with at least one abnormal fetus was considered affected.

TABLE 3 – SUMMARY OF FETUS CONDITION RESULTS[1]

Clinical Parameter	Groups	
	Group 1 (REPROCYC PARVOFLEX)	Group 2 (Placebo)
Number of gilts	22	10
Total number of fetuses	297	146
Mean litter size	13.5	14.6
Mean fetus size (cm)	19.3	14.4
Mean fetus weight (grams)	543.8	245.9
Number necrotic fetuses (%)	2 (1%)	9 (6%)
Number mummified fetuses (%)	10 (3%)	82 (56%)
Number normal fetuses (%)	**285 (96%)**	**55 (38%)**

Another primary outcome parameter was evidence of PPV in fetuses as determined by PCR of fetal thoracic fluid. A gilt was considered affected if one or more fetuses in a litter was PCR positive for PPV. The frequency of affected gilts in the vaccinated group was significantly less than affected gilts in the placebo group. The mean number of affected fetuses in each litter was 1.41 in the vaccinated group, compared to 11.30 in the placebo group.[1] Table 4 summarizes the gilt status based on PCR results from the fetal thoracic fluid samples.

TABLE 4 – GILT STATUS BASED ON PCR RESULT OF FETAL THORACIC FLUID SAMPLE[1]

Group	Frequency of Affected Gilts*	Mean Affected Fetuses	Percent of Affected Gilts*
Group 1 (REPROCYC PARVOFLEX)	10/22	1.41	45%
Group 2 (Placebo)	10/10	11.30	100%
Prevented Fraction Analysis, Group 1 vs. Group 2 (lower and upper 95% bound)			0.55 (0.29, 0.70)
P-value			<0.05

*A gilt with at least one abnormal fetus was considered affected.

CONCLUSION

This vaccination-challenge study demonstrates that two doses of REPROCYC PARVOFLEX given three weeks apart are efficacious in mitigating reproductive failure caused by virulent PPV when administered to healthy gilts prior to breeding.[1]

The efficacy is confirmed by the significant differences in the clinical condition of fetuses between vaccinated gilts (96% normal fetuses) and non-vaccinated gilts (38% normal fetuses) following the PPV challenge. Efficacy is also supported by the significant reduction in the frequency of PPV detection in the thoracic fluid of fetuses from vaccinated versus non-vaccinated gilts following the challenge.[1]

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