

Effects of intranasal or parenteral respiratory vaccination administered on-arrival or delayed in auction-derived feedlot heifers

Hudson R. McAllister,¹ MS; Sherri A. Powledge,¹ MS; Timothy R. Parks,² DVM; Marshall N. Streeter,² PhD; John P. Hutcheson,² PhD; Audie Waite,³ BS; *John T. Richeson,¹ PhD

¹Department of Agricultural Sciences, West Texas A&M University, Canyon, TX 79016

²Merck Animal Health, Lenexa, KS 66219

³Agri-Research, Canyon, TX 79015

*Corresponding author: Dr. John T. Richeson, jrcheson@wtamu.edu

Abstract

The objective was to evaluate health, performance and serum antibody responses of auction-derived heifers to an intranasal or parenteral MLV administered on d 0 or 28. Three arrival blocks of heifers, initial BW = 459 lb ± 1.7 lb (208 kg ± 27kg; n = 600), were randomly assigned to treatments in a 2 × 2 factorial arrangement. The generalized complete block design consisted of 15 pens/treatment with pen as the experimental unit and 10 heifers/pen. Treatments were: 1) Bovilis® Nasalgen® 3 and Bovilis® Vista® BVD on d 0 (NAS0); 2) Bovilis® Vista® 5 SQ on d 0 (VIS0); 3) Bovilis® Nasalgen® 3 and Bovilis® Vista® BVD on d 28 (NAS28); 4) Bovilis® Vista® 5 SQ on d 28 (VIS28). Body weight and blood samples were collected on d 0, 28 and 56. Activity (351.4 vs 354.3 min/d) and rumination time (282.6 vs 285.4 min/d) was less ($P < 0.01$) for delayed vs arrival vaccinated heifers. A timing × vaccine × day interaction existed ($P < 0.01$) for BRSV- and IBRV-specific antibody titers; VIS28 had the greatest ($P < 0.01$) BRSV antibody titer on d 56. For IBRV antibody titer on d 28, VIS0 was greatest, NAS0 was intermediate, and VIS28 and NAS28 were least ($P < 0.01$). Percentage of chronically ill heifers were reduced for arrival vs delayed (1.3 vs 4.7%; $P = 0.02$) and arrival vaccinated heifers had a reduction in antimicrobial treatment cost (\$4.63 vs \$7.31; $P = 0.02$). These data indicate improvement in some health outcomes for the parenteral route and arrival timing of MLV, but performance was not affected.

Key words: beef heifers, intranasal, parenteral, vaccine

Introduction

Bovine respiratory disease (BRD) is the most prevalent and expensive health challenge for U.S. feedlots.^{1,2} Most viral and bacterial pathogens associated with BRD enter through the mucosal surfaces of the nose and mouth, and use of intranasal vaccines is increasing in both the cow calf and feedlot segments of the beef industry because they stimulate mucosal immunity.³ Intranasal respiratory vaccines may contain modified-live virus (MLV) antigens, or attenuated versions of infectious bovine rhinotracheitis (IBRV), bovine respiratory syncytial virus (BRSV), and parainfluenza-3 virus (PI3V). Due to the exclusion of bovine viral diarrhoea virus (BVDV) antigens from commercial intranasal vaccines because of safety concerns, BVDV prevention also requires administration of a bivalent, parenteral vaccine containing BVDV type 1 and 2. Therefore, it may be more appealing to some producers to use a pentavalent parenteral vaccine but research is needed to understand differences in the safety, efficacy and efficiency of the different vaccine types used in newly received, auction-derived feedlot cattle.

More than 90% of U.S. feedlots vaccinate against respiratory disease.⁴ The timing of respiratory vaccination may be as important as vaccine selection itself. Most feedlots vaccinate on arrival; however, improved health and performance outcomes may exist for high-risk cattle that receive delayed vaccine administration.^{5,6} Delayed vaccination allows for the stress of transportation and relocation to be mitigated before vaccine antigen stimulation, which may improve vaccine safety, but the expected timing of natural virus challenge is also important regarding when a vaccine should be administered.⁷ The objective of this study was to evaluate the safety and efficacy of a parenteral or intranasal MLV vaccine administered on d 0 or 28 in auction-derived feedlot heifers on feed 56 days.

Materials and methods

This experiment was conducted from March 2020 to May 2020 at the Agri-Research Center located 10.9 km northwest of Canyon, Texas. Animal methods and procedures were approved by the IACUC committee at West Texas A&M University (protocol# 2020.04.001) before study initiation.

Arrival procedures

A total of 600 crossbred beef heifers, initial BW = 459 lb ± 1.7 lb (208 kg ± 27 kg), obtained from auction markets in Alabama, Kentucky and Texas were shipped to the Agri-Research Center on March 26, 2020 (Block 1), March 27, 2020 (Block 2), and April 2, 2020 (Block 3). An a priori power calculation was not conducted. The number of animals used was determined by research budget constraints and pen availability and the appropriate stocking rate at the research site. A total of 60 pens with 10 animals per pen allowed appropriate bunk space and pen area for 600 cattle. Upon arrival, initial BW was recorded, and each heifer received duplicate color-coded ear tags and a 3-axis accelerometer ear-tag^a. Heifers also received a multivalent clostridial vaccine^b, oral fenbendazole suspension^c, parenteral anthelmintic^d, metaphylactic administration of tildipirosin^e and a growth promoting implant^f. Randomization and allocation occurred according to chute order and a predetermined randomization table. Pens contained 10 head and there was a total of 60 pens (n = 15/treatment). Treatment pens were equally represented in each block. Heifers were also tested for persistent infection with bovine viral diarrhoea virus at arrival processing and if positive were removed from the study within 72 hours of arrival at study location (n = 1). Individual body weights were recorded on d 0, 28 and 56. Blood was collected from a randomly selected subset of 3 heifers per pen for BRSV, BVDV- and IBRV-specific antibody titer analysis on d 0, 28 and 56.

Treatments

The generalized complete block design consisted of 15 pens per treatment with pen as the experimental unit and 10 heifers per pen. Treatments were: 1) intranasal MLV and subcutaneous MLV on d 0 (NAS0); 2) subcutaneous MLV on d 0 (VIS0); 3) intranasal MLV and subcutaneous MLV on d28 (NAS28); 4) subcutaneous MLV on d 28 (VIS28). NAS0 and NAS 28 calves received intranasal administration of trivalent MLV^g containing live attenuated strains of infectious bovine rhinotracheitis, bovine respiratory syncytial virus, and parainfluenza 3 virus and subcutaneous administration of a monovalent MLV vaccine^h containing live attenuated strains of bovine virus diarrhea virus types 1 and 2. VIS0 and VIS28 calves received pentavalent MLV vaccineⁱ containing live attenuated strains of bovine rhinotracheitis virus, bovine virus diarrhea virus types 1 and 2, parainfluenza 3 and bovine respiratory syncytial virus. Cattle assigned to NAS28 and VIS28 did not receive their initial MLV vaccine until d 28 of the study period. From this 2 × 2 factorial arrangement of treatments, main effects of vaccine type (intranasal^g vs. parenteralⁱ) and vaccination timing (d 0 vs. 28) were evaluated if an interaction was not evident ($P > 0.05$) for a dependent variable. Because treatment pens were assigned randomly to avoid pen effect bias, heifers from different vaccine treatments may have had nose-to-nose contact, a potential limitation of the current study.

BRD case definition

Heifers were evaluated daily by a trained observer at approximately 1000 h and the BRD case definition followed standard procedure of the research facility. Heifers received a clinical illness score (CIS, 0 to 3 severity scale).⁸ Morbidity investigators were blinded to experimental treatment and recorded identification numbers of heifers with a CIS of 1, 2 or 3. Heifers were pulled as a suspect clinical BRD case if they were assigned a CIS of 1, 2 or 3. Cattle with a CIS of 1 required a rectal temperature $\geq 40^\circ\text{C}$ to be classified as a BRD case and possessed mild depression including but not limited to isolation with head down, ears drooping but responsive to stimulation and or displaying mild dyspnea with gauntness and nasal or ocular discharges. A CIS of 2 or 3 were treated for BRD regardless of rectal temperature. A CIS of 2 exhibited moderate depression including recumbency or standing isolated with head down and obvious depression, may have stumbled if forced to trot, and noticeable dyspnea with gauntness and nasal/ocular discharges. A CIS of 3 was an animal that exhibited severe depression or moribund status. Animals with CIS 3 would have exhibited signs such as recumbency or when walking, ataxia, knuckling, or swaying, inability to stand, excess salivation/lacrimation, pronounced dyspnea and gauntness, and near death. Heifers that qualified for BRD retreatment were weighed for calculation of antibiotic dose. Following a 7-day post metaphylactic interval (PMI) and meeting the BRD case definition after expiration of the PMI, cattle were treated with a combination of florfenicol and flunixin meglumine^j and considered BRD1.

If a post-treatment interval (PTI) of 3 days expired and BRD was diagnosed for a second time, then cattle received enrofloxacin^k and were classified as BRD2. The same PTI of 3 days was implemented prior to the third treatment. If cattle were treated a third time oxytetracycline^l was administered and cattle were classified as BRD3. Cattle that received a CIS of 3 were eligible to be retreated prior to completion of PMI or PTI without meeting rectal temperature criteria at the discretion of the morbidity investigator. If cattle required a fourth

treatment the animal was moved to another pen and considered a chronic removal. Chronic removal, treatment and euthanasia were determined according to the BRD case definition. Post treatment intervals for the different antimicrobials used were determined according to manufacturer recommendations and industry accepted standards. It is important to note that a shorter PTI could result in greater relapse with less time for convalescence, but the 3-day duration of PTI in this study is typical among industry and research for the drugs used.

Housing and management

Heifers were housed in soil surfaced pens that were approximately 150ft² (13.94 m²) with 9 inches (22.86 cm) of bunk space per animal. Throughout the study heifers had ad libitum access to water via automatic watering units and slick bunk feed management was used. Feed delivery and removals were recorded daily and recorded on a pen basis. Nutrient and dry matter analyses of the diet were conducted weekly and retained to ensure uniform feed quality and composition throughout the study (Table 3).

Statistical analysis

All data were analyzed in SAS^m. This experiment was a generalized complete block design with a 2 × 2 factorial arrangement of treatments. Interactions were tested first, then main effects of route of vaccination (VAC) and timing of vaccination (TIME). Pen was defined as experimental unit with 15 pens per treatment and 10 heifers per pen. Performance, activity, and health data were analyzed using the MIXED procedure and a subset of 3 heifers per pen were selected for antibody titers that were log₂ transformed and analyzed as repeated measures. The error term of pen (ID*block) was considered as the random effect in the model. Activity and rumination data were averaged by pen and day prior to statistical analysis in PROC MIXED with repeated measures. For all dependent variables, statistical significance was declared at $P \leq 0.05$ and tendencies were noted at $0.05 < P \leq 0.10$.

Results and discussion

Performance outcomes

Performance outcomes are displayed in Table 1 as least squared means. There were no significant interactions or main effects for any performance variables ($P \geq 0.19$). The NAS0 and VIS0 treatments received a MLV on arrival containing antigens that stimulate an inflammatory response.⁹ Cytokines associated with inflammation promote anorexia and tissue catabolism that can affect DMI and ADG.¹⁰ Due to the inflammatory response from vaccination on d 0, a transient decrease in performance in the arrival group is plausible from d 0 to 28; whereas, delayed vaccinated groups were expected to have decreased performance following MLV administration on d 28.¹¹ Conversely, immunological protection afforded by vaccination should positively impact performance if health is improved. Nevertheless, neither scenario clearly influenced performance outcomes in this study, as no statistical differences were detected, yet these opposing factors may have confounded the performance outcomes in this study. Richeson et al. reported that ADG was increased from d 14 to 28 for cattle administered a 14-d delayed MLV compared to those administered an arrival MLV, 1.43 and 1.03 lb/day; (0.65 vs. 0.47 kg/day, respectively).¹² In a similar study, Richeson et

Table 1: Effects of parenteral or intranasal vaccination on day 0 or 28 on performance of heifers at high risk of

Item	Arrival ¹		Displayed ²		SEM ⁴	P - value		
	Vista 5	N3 + V-BVD ³	Vista 5	N3 + V-BVD		VAC	Time	V × T
Body weight, lb								
d 0	454	459	462	458	8.70	0.96	0.67	0.62
d 28	559	568	572	563	10.4	0.99	0.71	0.40
d 586	640	648	651	642	12.4	0.94	0.85	0.47
Average daily gain, lb/d								
d 0 to 28	3.74	3.90	3.91	3.74	0.14	0.96	0.95	0.26
d 28 to 56	2.88	2.85	2.84	2.79	0.13	0.76	0.66	0.98
d 0 to 56	3.30	3.38	3.31	3.28	0.11	0.84	0.98	0.39
Dry matter intake, lb/d								
d 0 to 28	11.22	11.18	11.64	11.59	0.31	0.92	0.19	0.97
d 28 to 56	17.34	17.14	16.76	16.72	0.46	0.80	0.30	0.87
d 0 to 56	14.26	14.12	14.17	13.93	0.34	0.64	0.70	0.88
Feed efficiency, F:G								
d 0 to 28	3.04	2.90	2.99	3.66	0.31	0.31	0.25	0.19
d 28 to 56	5.98	5.92	5.83	5.87	0.20	0.93	0.64	0.82
d 0 to 56	4.28	4.16	4.15	4.11	0.09	0.10	0.36	0.65

¹ Arrival treatment cattle received Nasalgen 3 and Vista BVD and CFP or Vista 5 on d 0.

² Delayed treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 28.

³ BOVILIS Nasalgen 3 and BOVILIS Vista BVD CFP.

al., compared on arrival MLV to a 14-d delayed MLV and reported that daily BW gains in the delayed cattle were greater for the duration of the study 1.65 vs. 1.43 lb/d (0.75 vs. 0.65 kg/d).⁵ However, Richeson et al. reported that ADG was not affected throughout the duration of a 56-d receiving trial comparing on arrival vs. 14-d delayed respiratory and clostridial vaccination.¹³ Similarly, Poe et al. found no difference in ADG between arrival or 14-d delayed vaccination. The effect of MLV vaccination on animal performance is complicated by the negative growth effects that MLV vaccination can cause, yet health improvement afforded by immunological protection can have a positive impact on growth.¹⁴

Clinical health outcomes

Clinical health outcomes are reported in Table 2 and Figure 1. There were no interactions observed ($P \geq 0.09$), but a main effect of vaccine timing existed for the percentage of cattle requiring a third BRD treatment (BRD3; $P = 0.03$). The arrival vaccinated cattle had fewer percentage of BRD3 treatments than delayed (3.67 vs. 8.00%; $P = 0.03$). There was also a tendency for arrival vaccinated treatments to have fewer BRD1 than delayed (17.67 vs. 25.00%; $P = 0.07$). Percentage of chronically ill cattle was reduced for arrival vs. delayed (1.3 vs. 4.7%; $P = 0.02$) and tended to be less for VIS vs. NAS (1.7 vs. 4.3%; $P = 0.06$). Arrival vaccinated heifers had a reduction in antimicrobial treatment cost (4.63 vs. \$7.31; $P = 0.02$). Days to third treatment tended ($P = 0.06$) to have an interaction of VAC ×

TIME where VIS0 was the least compared to NAS0, VIS28 and NAS28 (24.0 vs 35.6, 35.5 and 34.8 d). Most BRD outbreaks begin within the first 14 days of feedlot arrival.^{15,16} In this population of heifers, the average time of initial BRD treatment occurred later than typical for most high-risk cattle populations with the average days to first treatment being d 21 across treatments (Figure 1). All heifers received tildiprosin^e on arrival to the study location which has been shown to decrease BRD incidence in newly received beef cattle and probably increases the number of days to initial BRD treatment.¹ The timing of BRD outbreak is important when evaluating vaccine timing and morbidity findings attributed to vaccine timing in the current study may be explained 3-fold. First, the delayed groups (VIS28 and NAS28) had an average days to first treatment of 22.0, and they received the MLV on day 28 which may have influenced their clinical presentation and/or convalescence as MLV can cause inflammation, fever and depression analogous to natural BRD.¹⁷ Second, the arrival groups had an average days to first treatment of 19.2, and most of these cattle probably had adequate time to respond immunologically to the MLV administered on d 0 resulting in improved immunological protection against natural virus challenge compared to the 28-d delayed procedure. Third, if natural virus and bacterial challenge peaked near d 28, the delayed MLV administration concurrent with peak wild-type virus infection could have altered the virulence of the naturally acquired pathogens and overall clinical presentation.⁷ Vaccination with

Table 2: Effects of parenteral or intranasal vaccination on day 0 or 28 on morbidity, mortality, chronicity and antibiotic treatment cost of heifers at high risk of developing BRD.

Item	Arrival ¹		Delayed ²		SEM ⁴	P - value		
	Vista 5	N3+V-BVD ³	Vista 5	N3+V-BVD		VAC	Time	V × T
BRD incidence ⁵ , % of enrolled								
First, %	14.7	20.7	28.0	22.0	0.04	1.00	0.07	0.14
Second, %	6.0	10.7	11.3	14.0	0.03	0.20	0.13	0.72
Third, %	2.0	5.3	7.3	8.7	0.02	0.23	0.03	0.60
Days to treatment								
First	19.0	19.4	23.9	20.0	2.19	0.39	0.24	0.22
Second	28.6	30.1	31.4	32.1	3.43	0.55	0.19	0.99
Third	24.0	35.6	35.5	34.8	4.44	0.09	0.10	0.06
Chronically ill, %	0.0	2.7	3.3	6.0	0.01	0.06	0.02	1.00
Mortality, %	1.3	0.0	0.0	0.6	0.01	0.57	0.57	0.09
Antibiotic treatment cost, \$/hd	3.61	5.65	7.63	7.00	1.13	0.54	0.02	0.24

¹ Arrival treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 0.

² Delayed treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 28.

³ BOVILIS Nasalgen 3 and BOVILIS Vista BVD CFP.

⁴ Standard error of the mean.

⁵ Percentage of enrolled cattle treated for BRD.

Table 3: Composition of the common receiving diet fed to heifers.

Item	Inclusion (% dry matter basis)
Flaked corn	40.0
Alfalfa hay	38.5
Dried distillers grains	6.0
Molasses blend	10.0
Micro ingredient	1.0
Supplement	4.5
Nutrient composition	
DM, %	80.2
CP, DM%	16.1
NEm, kcal/100lb	80.9
NEg, kcal/100lb	50.0

live-attenuated antigen in the face of natural virus challenge could result in negative health outcomes but a negative control treatment is required to elucidate safety of MLV vaccination. The morbidity results in the current study conflict with some of the previous research on MLV vaccination timing in high-risk cattle. Rogers et al. reported that when heifers were vaccinated parenterally with an MLV 30 days post-arrival at the feedlot, the percentage of heifers that required a second BRD treatment was less for delayed than arrival vaccinated cattle.⁶ However, other research resulted in no effect of vaccination timing on BRD morbidity.^{13,14} The inconsistent findings of vaccine timing on health outcomes in the literature are attributable to differences in pathogen dynamics, stress-induced immunosuppression, and other factors between different study populations. Overall, the current data indicate improvement in some health outcomes for the parenteral route and arrival timing of MLV respiratory vaccination.

Serum antibody titers

Antibody titer results are displayed in Figures 4 to 8. A timing × vaccine × day interaction existed ($P < 0.01$) for BRSV- and IBRV-specific antibody titers. The VIS28 group had the greatest ($P < 0.01$) BRSV antibody titer on d 56. For IBRV antibody titer on d 28, VIS0 was greatest, NAS0 was intermediate, and VIS28 and NAS28 were least ($P < 0.01$). This observation was expected because the delayed treatments, NAS28 and VIS28, did not receive MLV vaccination until d 28. The BVDV titers were analyzed as change in BVDV because baseline (d 0) treatment means differed. It is also important to note that a BVDV PI was present in block 3, which probably confounded the BVDV antibody response attributable to vaccination on d 0

or 28. A day \times vaccine interaction was observed ($P = 0.03$) for change in BVDV-specific antibody titers on d 28, such that NAS tended to be greater than VIS (6.41 vs 5.30; $P = 0.08$), but the biological relevance of this finding is not clear. For BVDV-specific antibody titers, a main effect of time existed such that arrival was greater than delayed throughout the course of the 56-d study ($P < 0.01$).

Heifers received the same BVDV antigens and parenteral route of administration due to the lack of BVDV antigens in the intranasal vaccine and the requirement for parenteral vaccination of BVDV in the NAS groups. Arrival treatment groups had greater percentage of cattle that were seropositive for BVDV at 74.1 vs. 43.3% of delayed vaccinated cattle at day 56. This may be due to the extended length of time the arrival treatment groups possessed for seroconversion but also suggests adequate antibody response to BVDV occurred when the vaccine was administered on arrival immediately after marketing stress. The delayed treatment groups were inoculated for 28 days fewer than the arrival treatment groups which could be responsible for the difference in antibody concentration at the end of the study (d 56). It was reported that vaccines may continually increasing antibody titer response for up to 3 months post-vaccination against BVDV also that stress-induced immunosuppression can enhance the antibody titer responses to MLV vaccination.^{18,19} For IBRV titers, there was a timing effect ($P = 0.002$) and a tendency for a timing \times vaccine interaction ($P = 0.06$). The VIS0 treatment had the greatest percentage seropositive against IBRV, VIS28 was the least, and NAS0 and NAS28 were intermediate (60.7, 34.1, 37.0, and 43.7%, respectively). Immunosuppression is a complicated concept regarding how it effects the replication of MLV antigens. Immunosuppression causes an increase in the replication of the MLV vaccine antigen which ultimately leads to a higher antibody titer response; however, it also increases the risk of morbidity in the animal. In the present study, titer levels increased with time in both arrival and delayed vaccination groups indicating that a detectable immune response occurred to both vaccine timing and vaccine types evaluated presently.

Activity and rumination behavior

Activity and rumination results are reported in Figures 2 and 3, respectively. There was a day \times timing interaction ($P < 0.01$) observed for activity; delayed vaccinated heifers had less daily activity than arrival vaccinated heifers (351.4 vs. 354.3 min/d; $P < 0.01$). An interaction of day \times timing on rumination minutes per day was observed, resulting in reduced rumination time for delayed vs. arrival heifers (282.6 vs. 285.4 min/d; $P < 0.01$). Previous research has demonstrated that animals clinically diagnosed with BRD spent more time lying down than healthy counterparts.²⁰ In a study by Pillen et al., the number of steps taken by cattle diagnosed with BRD was decreased compared to healthy controls from d -6 to d -1 of BRD diagnosis (843 and 1,472 steps, respectively). The BRD cases also exhibited an overall decrease in motion index from d -6 to BRD diagnosis on d 0.²¹ These data support the idea that accelerometer tags that continuously monitor animal activity and rumination may aid in the early detection of BRD but may also provide corroboration of clinical health findings between experimental treatments evaluated in research settings. The reduced activity and rumination time observed for the delayed groups in the present study may be explained by the interaction of MLV vaccination during the late BRD outbreak

in this study population, or lack of immune protection prior to natural virus challenge in the delayed vaccinated resulting in greater morbidity. Delayed vaccinated heifers were beginning to break with clinical BRD immediately before their initial MLV was administered on d 28, increasing the chances of the MLV reverting to virulence or causing other negative health effects and thereby decreasing overall activity.²² In the present study, delayed heifers exhibited decreased duration of rumination and activity compared to arrival vaccinated heifers which corroborates the clinical health impacts observed from the timing of BRD outbreak and concurrent administration of a MLV in the delayed groups.

Conclusion

There was no difference between intranasal and parenteral vaccination, or the timing of vaccination, on performance outcomes evaluated in this study. The parenteral groups tended to have fewer chronic heifers compared to intranasal. The BRSV- and IBRV-specific antibody titer response was greater for the parenteral treatments, which supports the paradigm that circulating IgG is more strongly stimulated by parenteral vaccination against these 2 antigens. Arrival MLV vaccination decreased the percentage of chronically ill heifers and antibiotic treatment cost compared to 28-d delayed vaccination. Furthermore, heifers that were vaccinated on arrival had greater activity and rumination minutes. The current data suggests that on arrival vaccination with a parenteral MLV was the most advantageous vaccination strategy in this population of auction-derived heifers. A negative control group is needed in future BRD vaccination studies to determine if differences between arrival and delayed vaccination are attributable to improved vaccine safety, enhanced vaccine efficacy, or both.

Endnotes

- a Allflex® Livestock Intelligence™, Merck Animal Health, Madison, NJ
- b Bovilis® Vision® 7 Somnus with Spur®, Merck Animal Health, Madison, NJ
- c Safe-Guard®, Merck Animal Health, Madison, NJ
- d Ivomec®, Boehringer Ingelheim Animal Health, Duluth, GA
- e Zuprevo®, Merck Animal Health, Madison, NJ
- f Revalor®-IH, Merck Animal Health, Madison, NJ
- g Bovilis® Nasalgen® 3 Merck Animal Health, Madison, NJ
- h Bovilis® Vista® BVD CFP, Merck Animal Health, Madison, NJ
- i Bovilis® Vista® 5 SQ, Merck Animal Health, Madison, NJ
- j Resflor Gold, Merck Animal Health, Madison, NJ
- k Baytril® 100, Elanco Animal Health, Greenfield, IN
- l Biomycin® 200, Boehringer Ingelheim Animal Health, Duluth, GA
- m SAS version 9.4, SAS Inst. Inc., Cary, NC

Funding

This research study was funded by Merck Animal Health.

Conflict of interest

T. R. Parks, M. N. Streeter, and J. P. Hutcheson are employed by Merck Animal Health, the company that provided funding and product for testing in this research study.

Author contributions

All authors provided substantial contribution to the experimental design, data acquisition, and analysis and interpretation of data. Drafting and revision was provided by all authors and their approval of the final version to be published was granted.

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Figure 1: Cumulative percentage of BRD incidence of heifers receiving an on arrival or delayed intranasal or parenteral respiratory vaccine.

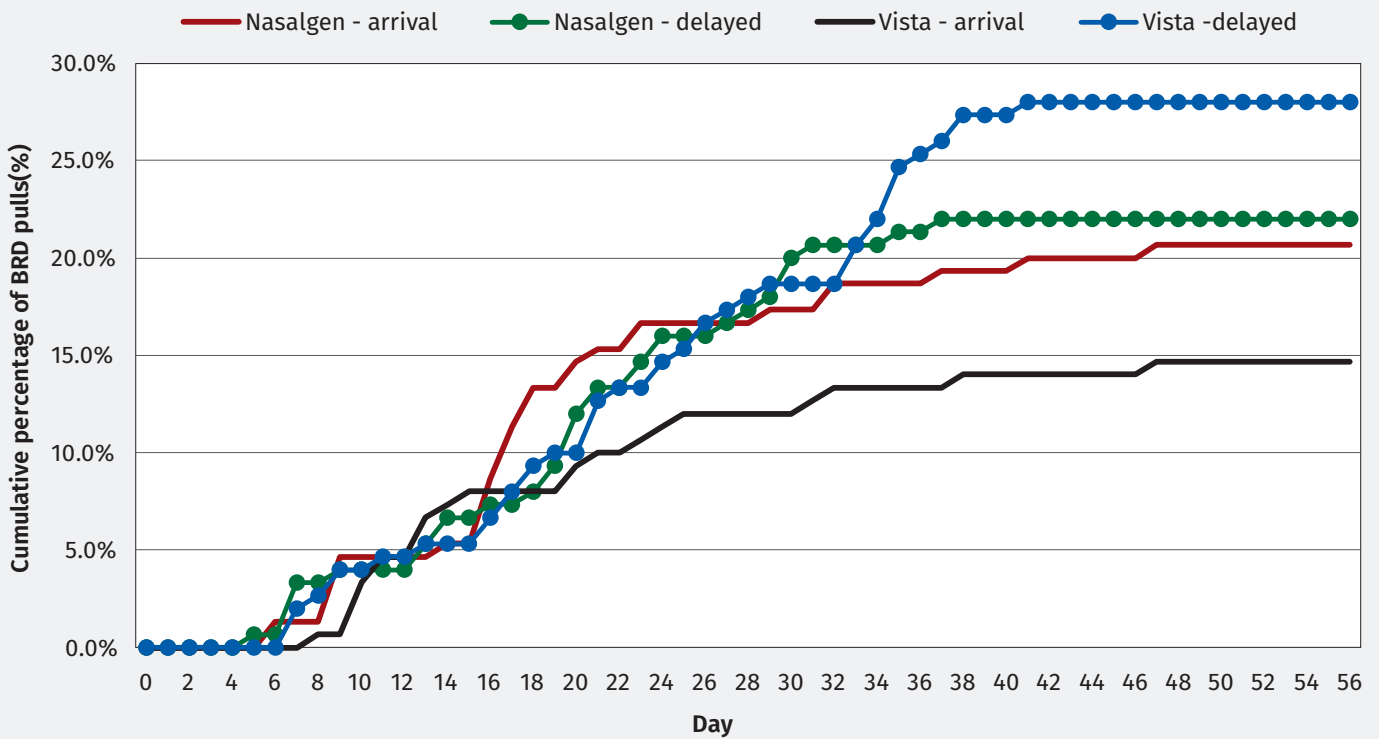
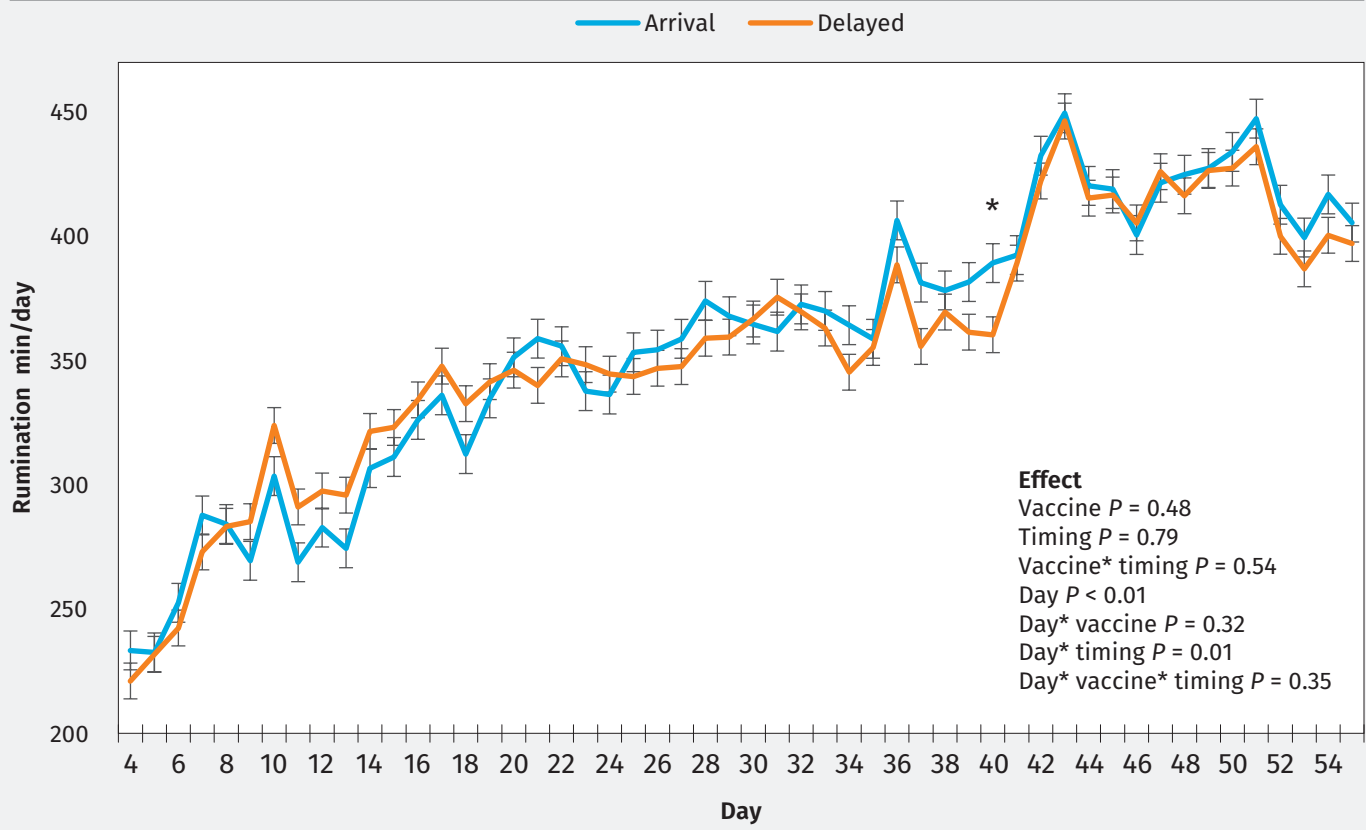


Figure 2: Effect of vaccination timing (d 0 or 28) on activity of heifers at risk of developing BRD. Arrival treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 0. Delayed treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 28.



* Arrival differs from delay $P \leq 0.05$

Figure 3: Effect of vaccination timing (d 0 or 28) on rumination of heifers at risk of developing BRD. Arrival treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 0. Delayed treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 28.



* Arrival differs from delay $P \leq 0.05$

Figure 4: Effect of parenteral or intranasal vaccination on day 0 or 28 on BRSV- specific antibody titers at risk of developing BRD.

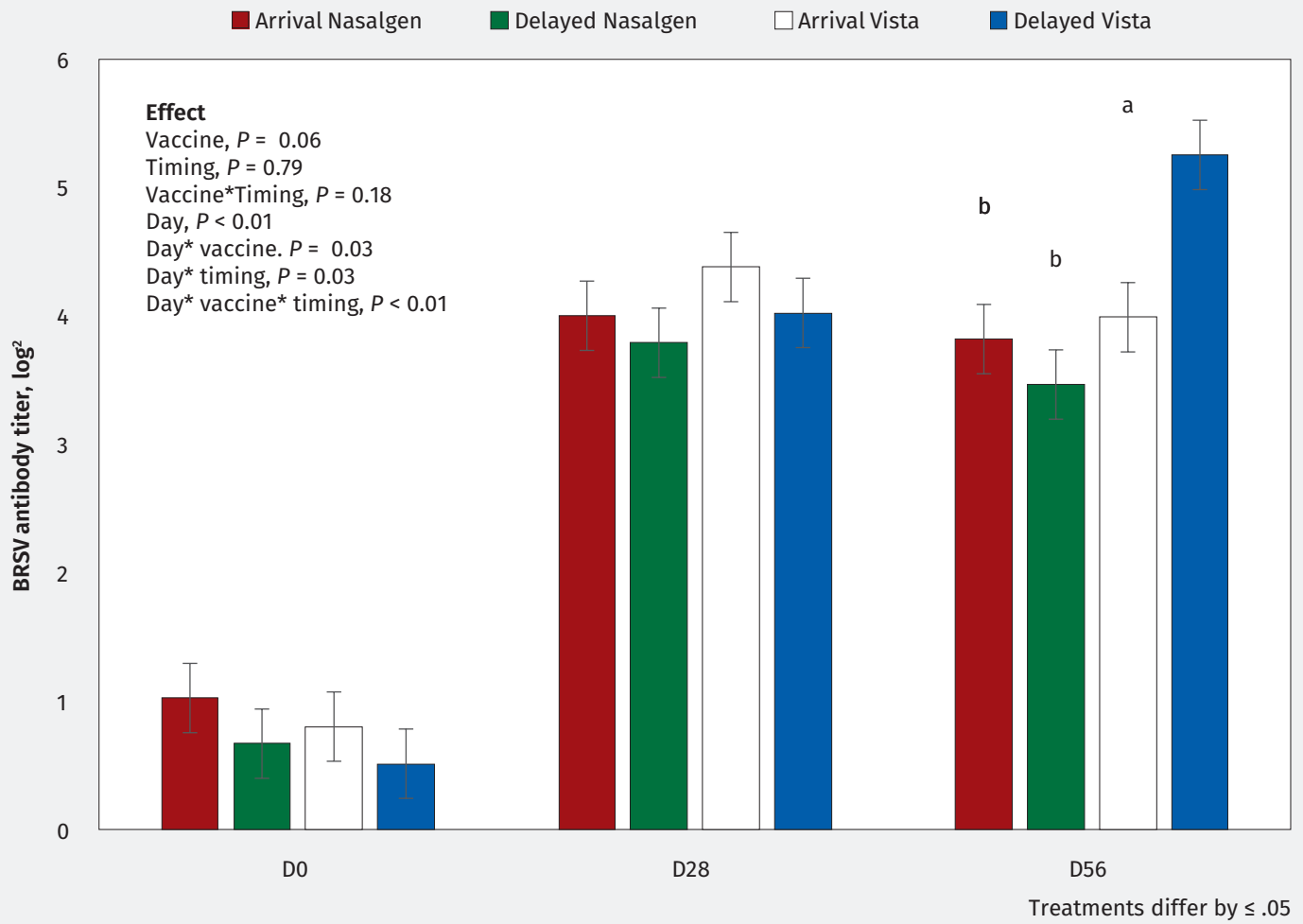


Figure 5: Effect of parenteral or intranasal vaccination on day 0 or 28 on IBRV-specific antibody titers at risk of developing BRD.

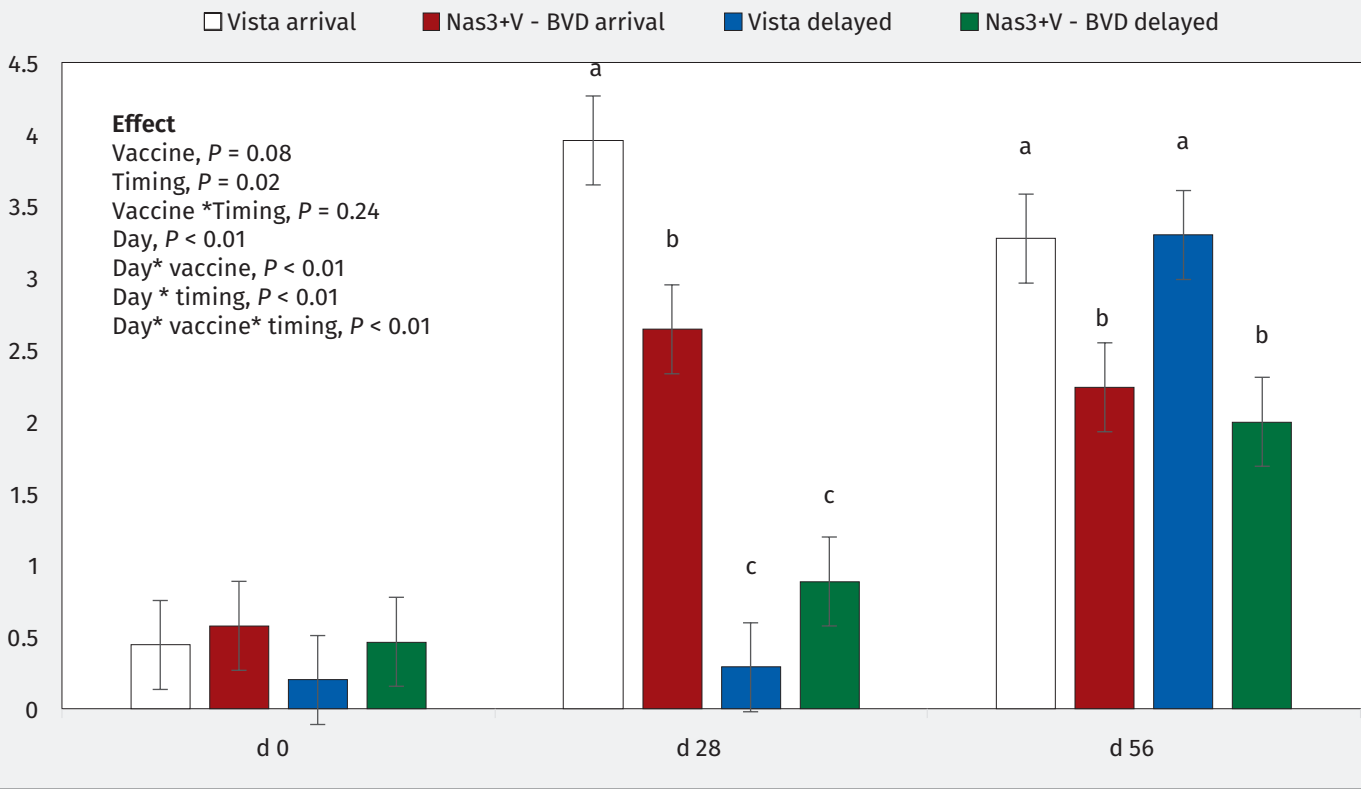


Figure 6: Effect of vaccination type (Nasalgen or Vista) on BVDV-specific antibody titer of heifers at risk of developing BRD. Nasalgen treatments Nasalgen 3 and Vista BVD CFP on d 0 or d 28. Vista treatments received Vista 5 on d 0 or 28.

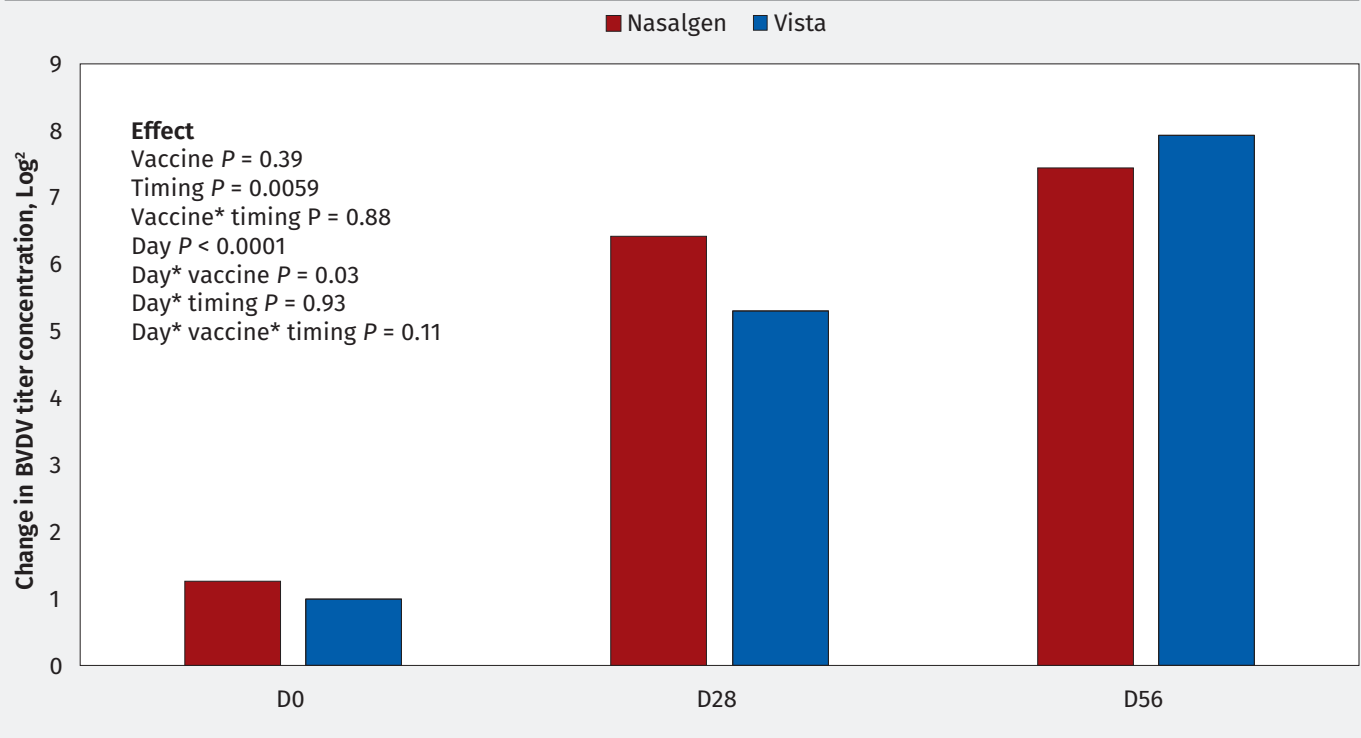


Figure 7: The effect of vaccination timing (d 0 or 28) on percentage BVDV seroconversion in sampled cattle. Arrival treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 0. Delayed treatment cattle received Nasalgen 3 and Vista BVD CFP or Vista 5 on d 28.

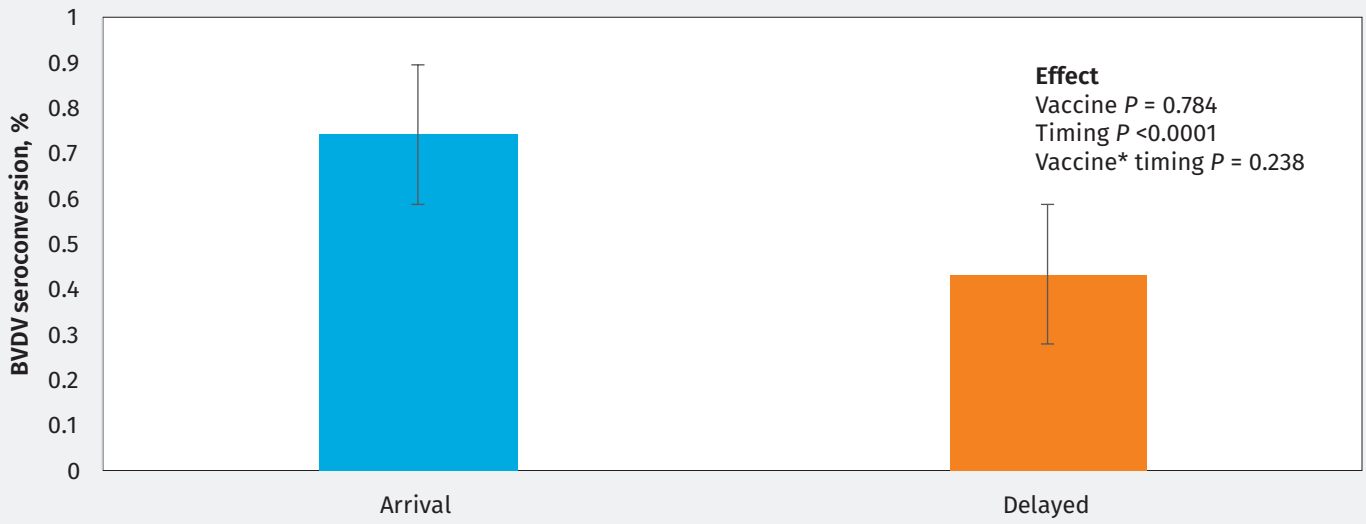


Figure 8: The effect of % IBRV seroconversion in sampled cattle that received an intranasal or parenteral respiratory vaccination on arrival or delayed.

