PEER REVIEWED

Efficacy of a combination modified-live IBR-BVD-PI3-BRSV vaccine + *Mannheimia haemolytica* toxoid against challenge with virulent bovine respiratory syncytial virus (BRSV) in young calves 60 days of age

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Abstract

Efficacy of attenuated (*att*) bovine respiratory syncytial virus (*att*BRSV) as an antigen fraction in a multivalent 6-way vaccine containing modified-live virus and an inactivated *Mannheimia haemolytica* bacterin-toxoid was given as a single subcutaneous injection, and evaluated by an aerosol challenge by nebulization in young calves with virulent BRSV strain 21 d after vaccination. A total of 32 Holstein calves, seronegative to BRSV and 60 days-of-age at the time of vaccination, were used in the study. Calves were allocated to 2 treatment groups with 16 animals per group, and received either a single dose of a modified-live bovine herpes virus-1, bovine viral diarrhea virus, parainfluenza 3 virus, bovine respiratory syncytial virus vaccine + *M. haemolytica* bacterin-toxoid, or corresponding placebo formulation without targeted BRSV antigen. Administration of the 6-way vaccine containing BRSV fraction induced significantly higher virus-neutralizing antibody ($p=0.0003$) and anti-BRSV IgG titers ($p=0.0006$) in vaccinated animals compared to the placebo group. Consequently, BRSV-vaccinated calves had significantly ($p<0.0001$) higher arterial partial pressures of oxygen (PaO2), significantly ($p<0.0001$) lower percentage of lung lesions, and significantly reduced mortality rate ($p<0.0001$) than did placebo vaccinated calves subsequent to BRSV challenge. Furthermore, there was a 61.2% reduction in virus shedding and duration of shedding ($p<0.0001$), indicating strong vaccine efficacy.

Key words: BRSV, lung lesions, mortality, toxoid, 5-way vaccine

Introduction

Bovine respiratory disease (BRD) is the most common disease in beef and dairy cattle and a major cause of morbidity, mortality, and economic losses in the cattle industry worldwide.[9] BRD costs are estimated by the beef producer by identifying the direct and indirect costs associated with disease.[10] It has been estimated that BRD in feedlots results in losses from $23.23 to $151.18 per animal compared with those that remain healthy.[16] Approximately 32 million head of cattle are slaughtered in the United States each year, equating to more than a billion dollars in losses because of BRD.[1] Multiple viral pathogens have been implicated in BRD, including bovine viral diarrhea virus (BVDV), bovine herpesvirus type-1 (BHV-1), bovine respiratory syncytial virus (BRSV), bovine parainfluenza type-3 (PI3), and more recently bovine coronavirus (BCoV).[7,11,13] BRSV is a pneumovirus, classified in the family Paramyxoviridae that infects the upper and lower respiratory tract with viral shedding from nasal secretions. BRSV is endemically present in cattle populations worldwide and clinically affects primarily young calves in recurrent seasonal outbreaks.[19] Clinical disease in young calves often occurs when passive immunity has waned and is characterized by pyrexia, coughing, and tachypnea, often progressing rapidly to dyspnea.[19] In addition to management practices, vaccination remains one of the key factors in controlling the spread of BRSV and the associated morbidity and mortality in beef and dairy cattle worldwide. Unvaccinated calves are highly susceptible to BRSV infection, and are at high risk of developing BRD with potential lethal consequences. Early attempts to prevent BRSV infections using formalin-inactivated virus as a vaccine resulted in enhanced disease following inoculation with virulent BRSV.[8] The efficacy of several commercially available modified-live BRSV vaccines administered parenterally has been demonstrated in a BRSV-challenge model that produces typical lung lesions and acute clinical signs of BRSV.[3,6,19]

Timing of vaccine administration against BRD antigens is key for vaccine efficacy and BRD prevention.[14] In North America, key animal handling time periods, such as shortly

after birth (neonatal calves), during branding (60 to 120 d of age), at weaning (~205 d of age), and on arrival at production sectors such as stocker, backgrounder, and/or feedlot facilities are most commonly used to vaccinate cattle.[14] In the present report we share the results of a study where the aim was to evaluate the efficacy of *att*BRSV fraction from a multivalent, modified-live virus (MLV) vaccine plus a *Mannheimia haemolytica* bacterin-toxoid in calves ~60 d of age following single SC administration and challenge with virulent BRSV strain at 21 d post-vaccination.

Materials and Methods

Animals and Husbandry

Thirty-two (32) BRSV seronegative (<1:8) Holstein calves were sourced from a commercial dairy for the study. The age of the animals at the time of study start and vaccination (day 0) was 7 to 9 weeks (Table 1). Neonatal Holstein calves were removed from their dams at birth and fed 1.5 L of pooled frozen bovine colostrum that was previously screened by ELISA for lack of antibodies against BRSV. Calves were further fed with 2 L of milk replacer twice daily and, depending on their age, with ad libitum water, grass-legume hay, and commercial pelleted calf ration that met or exceeded nutritional requirements. At birth, animals were vaccinated against enteric rotavirus and coronavirus[a] and no other treatments were administered prior to study start. During the vaccination phase, animals were housed in individual hutches. At the time of challenge, calves were group housed in a single covered pen in a BSL-2 facility at University of Saskatchewan. All study procedures were in accordance with established guidelines within the Canadian Council on Animal Care, and study protocols were reviewed and approved by the Committee on Animal Care and Supply at the University of Saskatchewan.

Experimental Design and Randomization

This was a randomized, controlled study with 32 calves enrolled in order to evaluate the efficacy of the *att*BRSV fraction in a combination MLV-toxoid vaccine administered as a single SC dose for protection of young calves ~ 60 d of age against virulent BRSV challenge. There were 2 treatment groups (vaccinated and placebo), each utilizing 16 calves. The study design was completely randomized. During the vaccination phase, calves were housed in individual pens such that each animal was not in contact with any other animal. During the challenge phase, animals from both treatment groups were commingled in a single pen. Animal was the experimental unit for both vaccination and challenge phases. Calves were allocated to treatment and vaccination pens, per the randomization plan generated by a Zoetis biometrics representative. The random treatment allocation plan was created using a SAS statistical program[b] that utilized a random number generator function. Study inclusion criteria required that all calves be clinically healthy, not persistently infected with BVDV, and seronegative for antibodies against BRSV (serum VN antibody titer < 1:8 on day of vaccination).

Vaccination and Challenge

Calves in the vaccine treatment group were administered a combination multivalent, BHV-1, BVDV, PI3V, BRSV MLV vaccine + a *Mannheimia haemolytica* bacterin-toxoid vaccine,[c] while the animals in the control group received placebo formulated in the same way as the study vaccine, but without the *att*BRSV fraction. A single 2-mL (vaccine or placebo) dose was administered SC in the neck region to animals at ~60 d of age (Table 1). On d 21 post-vaccination, individual calves were challenged by the aerosol route with virulent BRSV, Asquith strain (2.3×10^3 $TCID_{50}$/mL dose) as previously described.[4,5] At the end of the study all remaining animals were humanely euthanized in compliance with Canadian Council of Animal Care guidelines for humane euthanasia and disposed by secure burial.

Clinical Assessment

Post-vaccination, all animals were observed by trained personnel for undesirable systemic reactions associated with vaccination (depression, trembling and/or tachypnea) within 4 hours after vaccine administration. On d –1 and 0 prior to challenge and on d 1 through 8 post-challenge with the BRSV inoculum, calves were observed and scored for presence of respiratory clinical signs (depression, respiratory rate,

Table 1. Summary of study design in calves experimentally challenged with BRSV after vaccination with a combination BHV-1, BVDV (types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* toxoid.[c]

		Route of challenge	Number of calves per treatment group		Dose of challenge ($TCID_{50}$) and volume	Age at Vaccination (days)	Study day of	
Virus	Strain		Placebo†	Vaccinates†			Aerosol Challenge	Completion
BRSV	Asquith	Intranasal	16	16	2.3×10^3 $TCID_{50}$/mL	2 months	21	29

†Vaccinates administered a modified-live BHV-1, BVDV (types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* (Bovi-Shield Gold One Shot, Zoetis, Parsippany, NJ). In the placebo vaccine, test antigen fraction *att*BRSV was removed.

dyspnea, and cough) and the rectal temperature of each calf was recorded. Clinical assessments were made at the same time each morning by a veterinarian unaware of treatment status of the calves. Calves were humanely euthanized by barbiturate overdose 8 d after challenge if not found dead or euthanized earlier for humane reasons due to advanced BRSV-induced respiratory disease. Calves euthanized prior to d 8 after challenge exposure were euthanized according to criteria previously described.[4] These criteria were consistent with the Canadian Council of Animal Care guidelines and were approved by the Committee on Animal Care and Supply at the University of Saskatchewan.

Sample Collection

Deep nasal swab specimens were collected for virus isolation from both nares prior to challenge with virulent BRSV, and on d 2 through 8 after challenge. Swabs were processed as previously described.[4] Serum samples were collected obtained by jugular venipuncture from each animal on study days -5 (pre-vaccination), 20 (pre-challenge), and 29 (or day of euthanasia). Samples were processed as previously described[12] and stored frozen until tested. Arterial blood samples were collected from the caudal thoracic aorta on day 27[4] and tested for arterial oxygen partial pressure (PaO2) by use of a gas analyzer,[d] previously corrected for rectal temperature.

Laboratory Analysis

Serum samples were assayed for presence of BRSV neutralizing (VN) antibodies and for specific anti-BRSV IgG levels by ELISA as previously described.[4,5] In addition, colostrum used to feed calves was assessed for presence of anti-BRSV IgG levels by the same ELISA.

Quantitative virus isolation-virus shedding was determined by use of a microisolation plaque assay with bovine embryonic lung fibroblasts as previously described.[12,18] This assay has a maximum calculated sensitivity of 10 pfu/mL.

Postmortem Analysis

At necropsy, lungs of each calf were removed *in toto* and analyzed for the percentage of pneumonic tissue as previously described.[4,5] Animals that died or were euthanized for humane reasons post-challenge, but prior to last day of challenge, were necropsied and scored as described.

Statistical Analysis

A designated Veterinary Medicine Research and Development biometrician was responsible for data summaries and analyses of data entered into the centralized data management system.[b] Prevalence of clinical disease in each of the study days was compared between vaccinated and control groups with the 2-tailed Fisher exact test. The BRSV virus isolation (VI) data was summarized by time point and treatment. Frequency distributions of presence of BRSV (sample with VI value <10) were summarized by treatment and time point. Duration of presence of BRSV shed was determined for each animal and was calculated as "last time point present minus first time point present +1." Duration of virus shed was set to zero for animals that had no time points with positive BRSV isolated. Duration of virus shed was calculated as "last scheduled time point of VI collection minus first time point present + 1" for animals that were removed from the study prior to the last scheduled VI collection time point. Data on virus shedding, challenge-phase rectal temperatures, and challenge-phase antibody titers were each compared between groups with a general linear mixed model with repeated measures, with treatment, assessment point, and the interaction between these 2 variables as fixed effects and individual calf and residuals as random effects. The comparisons with $P \leq 0.05$ were considered significant for all analyses. Whether an animal was a challenge related mortality for BRSV was analyzed using Fisher's Exact Test to compare frequencies between vaccinated and control groups. Percentage of consolidation of the lung was compared between groups with a linear mixed model, with treatment as a fixed effect and residual as a random effect.

Results

Vaccine Safety and Post-challenge Mortality

Total of 32 calves were dosed at ~60 d of age with either the 5-way MLV vaccine + *M. haemolytica* toxoid, or placebo without *att*BRSV. None of the animals showed signs of an adverse reaction, including but not limited to injection site reactions, fever, anaphylaxis, and tremor, post-administration of corresponding treatments (vaccine or placebo). There was a significant ($p<0.0001$) difference between groups in mortality as defined by death or requirement for euthanasia prior to termination of the study on d 8 after challenge. In the placebo group, 81.3% of animals (13/16) died or were euthanized before the end of the study due to severity of respiratory disease following challenge, while none (0/16) in the vaccinated group died or were euthanized (Figure 1). From the placebo group, 1 animal was removed on d 6, 11 animals were removed on d 7, and 1 animal was removed on d 8 prior to the end of the study (study d 27-29).

Clinical Observation

Calves in both groups developed variable signs of respiratory disease characteristic of BRSV infection, including pyrexia, cough, dyspnea, and increased respiratory rates. There were no significant differences between the 2 groups in individual clinical variables such as cough and respiratory rate (Table 2). However, there was a significant difference in the prevalence of clinical signs of depression and dyspnea. The vaccinated group had a significantly lower proportion of calves that developed signs of depression (0%, $p=0.0445$) and dyspnea (29.4%, $p=0.0013$) compared to calves in the placebo group (29.4% depression and 88.2% dyspnea; Table 2). Furthermore, there was a statistically significant differ-

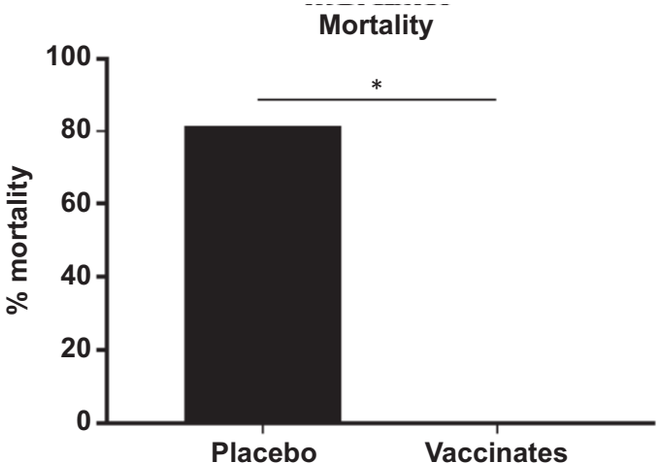

Figure 1. Percentage mortality in ~60 d old calves following vaccination with combination ML BHV-1, BVDV (types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* toxoid (vaccinates) or ML BHV-1, BVDV (types 1 and 2), PI3V vaccine + *Mannheimia haemolytica* toxoid (placebo) and challenged with virulent BRSV.
*Data points significantly different (p<0.0001)

Table 2. Summary of percent incidence (%) of clinical signs ever observed in placebo and vaccinated animals post-challenge with virulent BRSV. Data points significantly different if p<0.001 (**); or p<0.05 (*).

	Placebo†	Vaccinates†	P-value
Cough	64.7	47.1	0.495
Depression	29.4	0	**0.0445***
Dyspnea	88.2	29.4	**0.0013****
Respiratory rate	94.1	94.1	1.0

†Vaccinates administered a modified-live BHV-1, BVDV types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* (Bovi-Shield Gold One Shot, Zoetis, Parsippany, NJ). In the placebo vaccine, test antigen fraction *att*BRSV was removed.

ence in percentage of calves with individual clinical signs (depression, dyspnea, respiratory effort) on particular days post-challenge (Table 3). More calves in the placebo group showed depression at 6 d post-challenge (26.7%, p=0.04), dyspnea on d 5 to 7 post-challenge (93.8%, p<0.0001; 93.3%, p<0.0001; 75%, p=0.013), and in respiratory rate on d 6 post-challenge (100%, p=0.0068; Table 3).

There were no significant differences in mean rectal temperatures between the groups until d 5 post-challenge. On study d 26 to 28 (5 to 7 post-challenge), mean rectal temperatures in the placebo group were significantly higher than in vaccinates (Figure 2). This time period coincides with the significant number of animals with pyrexia (103.5°F; 39.7°C) observed in the placebo group following challenge (62.5%, 80%, and 50%) compared to vaccinated animals (0% pyrexia on d 26 to 28).

Virus Shedding

Vaccine efficacy was assessed by comparing the viral counts and duration of virus shedding post-challenge between placebo-control and vaccinated groups. All animals were negative for BRSV virus presence before the challenge phase as determined by virus isolation (VI).

All placebo (100%) and 15 of 16 vaccinated calves (93.8%) shed BRSV from nasal secretions following challenge (data not shown). From d 5 through d 7 (challenge phase), vaccinated calves showed a significant reduction in the amount of virus shed each day compared to placebo-treated calves (Figure 3). In addition, a significantly lower percentage of vaccinates shed virus on d 5 and 6 post-challenge compared to the placebo group (Table 3). Under the curve analysis (total virus shed) demonstrated a 61.2% reduction in geometric LSM virus titers shed by the vaccinates compared to the control group during the post-challenge period (p=0.0371). In addition, LSM duration of virus shedding post-challenge was significantly shorter in the vaccinated

Table 3. Analysis of presence clinical signs at each time point post-challenge with virulent BRSV; significance values for contrasts among treatments.

Study day		**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**
Post-challenge		**-1**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Cough	**Placebo†**	**0**	0	0	**6.3**	**12.5**	**18.8**	**25**	**6.7**	**25**	**66.7**
	Vaccinates†	0	0	0	0	**18.8**	**12.5**	0	**18.8**	**6.3**	**6.3**
	P value	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*	*Ns*	*ns*	*ns*	*ns*
Depression	**Placebo**	0	0	0	0	0	0	**6.3**	**26.7**	**0**	**0**
	Vaccinates	0	0	0	0	0	0	0	0	0	**0**
	P value	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*	*Ns*	***0.04***	*ns*	*ns*
Dyspnea	**Placebo**	0	0	0	0	**6.3**	**25**	**93.8**	**93.3**	**75**	**66.7**
	Vaccinates	0	0	0	0	0	0	**12.5**	**18.8**	**6.3**	**12.5**
	P value	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*	***0.0001***	***0.0001***	***0.013***	*ns*
Respiratory rate	**Placebo**	0	0	**25**	**43.8**	**62.5**	**75**	**100**	**100**	**100**	**66.7**
	Vaccinates	0	0	**18.8**	**50**	**50**	**43.8**	**75**	**56.3**	**37.5**	**50**
	P value	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*	*Ns*	***0.0068***	*ns*	*ns*

†Vaccinates administered a modified-live BHV-1, BVDV types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* (Bovi-Shield Gold One Shot, Zoetis, Parsippany, NJ). In the placebo vaccine, test antigen fraction *att*BRSV was removed. *significant difference (P <= 0.05)

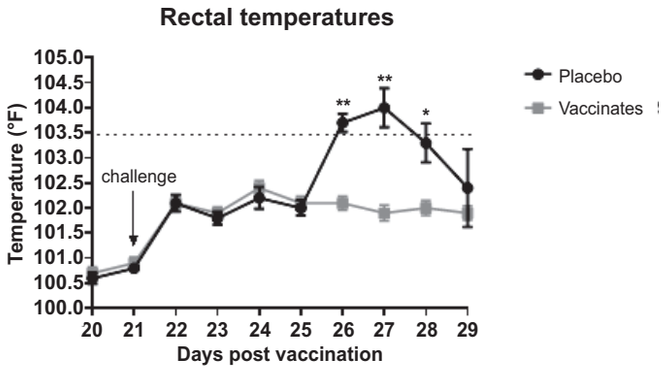

Figure 2. Least squares means (LSM) of rectal temperatures in ~60 d old calves following vaccination with either a combination ML BHV-1, BVDV (types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* toxoid (vaccinates; Bovi-Shield Gold One Shot, Zoetis, Parsippany, NJ) or a vaccine formulated in the same way as the study vaccine but without the *att*BRSV fraction (placebo) and challenged with virulent BRSV. *Data points significantly different if p<0.0001(**) and p<0.05.

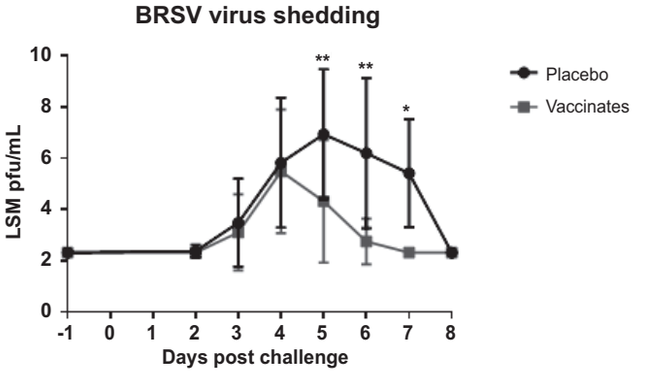

Figure 3. LSM of BRSV virus titer in nasal secretion samples collected from the ~60 d old calves following vaccination with either a combination ML BHV-1, BVDV (types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* toxoid (vaccinates; Bovi-Shield Gold One Shot, Zoetis, Parsippany, NJ) or a vaccine formulated in the same way as the study vaccine but without the *att*BRSV fraction (placebo) and challenged with virulent BRSV. *Data points significantly different if p<0.0001(**) and p<0.05 (*).

calves, with 2 (±0.27) days of shedding compared to placebo calves 5.1 (±0.27) days of shedding (p<0.0001), representing a strong protective vaccine effect (Figure 3).

PaO2 and Pneumonic Lesions

Arterial blood oxygen concentrations on d 6 after challenge were significantly (P < 0.001) higher in the vaccinated group (back-transformed LSM ± SE, 79.97 ± 1.82 mm Hg), compared with the placebo group (52.62 ± 2.02 mm Hg; Figure 4A).

Calves in all groups had pneumonic lesions typical of acute BRSV infection, but the percentage of pneumonic lung tissue in the vaccinates (back-transformed LSM ± SE, 5% ± 1%) was significantly (p < 0.001) lower than that in the placebo group (59% ± 7%; Figure 4B).

Serology

Antibody Responses and Correlation Analyses

Antibody responses are summarized in Figures 5A and 5B. There was no significant difference in LSM SN titers between the 2 groups prior to vaccination or prior to challenge. However, post-challenge geometric LSM titer in vaccinated animals rose to 11 vs 2 in placebo calves (p=0.0003). Similarly, LSM titer of anti-BRSV specific IgG antibodies were significantly higher (p<0.0006) in the vaccinated group (20±3.5) compared to the placebo group (1±3.5).

Discussion

Respiratory disease caused by BRSV virus has a significant economic impact on cattle populations worldwide, with a seroprevalence of 30 to 70% in many cattle populations.

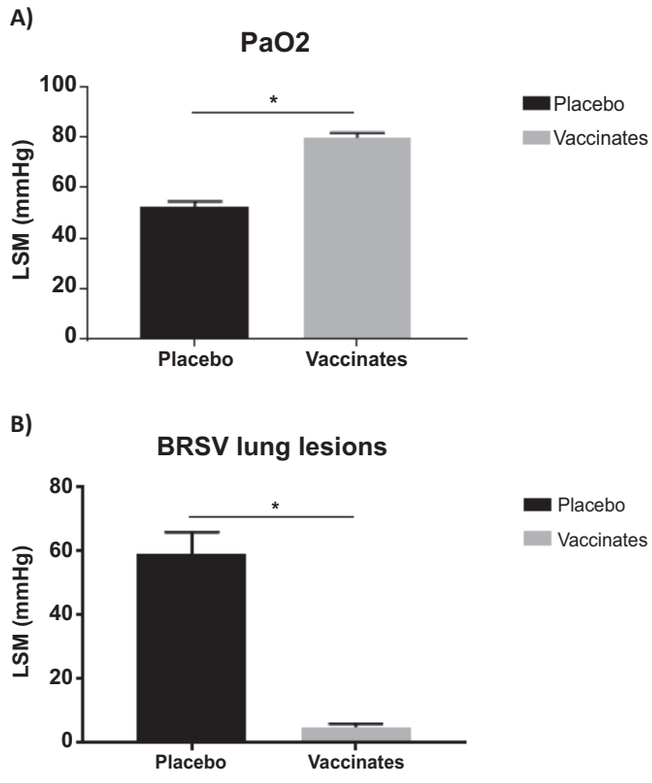

Figure 4. LSM of PaO2 (A) and lung lesions (B) from the ~60 d old calves following vaccination with either a combination ML BHV-1, BVDV (types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* toxoid (vaccinates; Bovi-Shield Gold One Shot, Zoetis, Parsippany, NJ) or a vaccine formulated in the same way as the study vaccine but without the *att*BRSV fraction (placebo) and challenged with virulent BRSV. *Data points significantly different if p<0.001 (*).

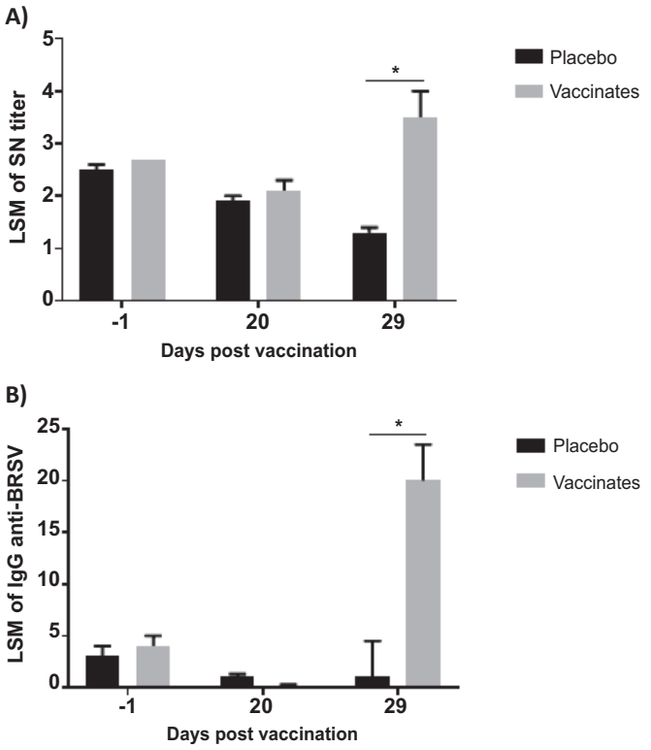

Figure 5. LSM of serum neutralizing (A) and serum IgG anti-BRSV antibodies (B) from the ~60 d old calves following vaccination with either a combination ML BHV-1, BVDV (types 1 and 2), PI3V, BRSV vaccine + *Mannheimia haemolytica* toxoid (vaccinates; Bovi-Shield Gold One Shot, Zoetis, Parsippany, NJ) or a vaccine formulated in the same way as the study vaccine but without the *att*BRSV fraction (placebo) and challenged with virulent BRSV. *Data points differ ($p<0.001$).

Due to this high level of seroconversion, BRSV infections are considered responsible for more than 60 to 70% of the epizootic respiratory diseases observed in dairy and beef herds.[1,17] In temperate zones, BRSV regularly causes winter and autumn outbreaks of respiratory disease in cattle; the most susceptible age group is day-old to 5-month-old calves. It is associated with high morbidity (>60%) and a mortality rate of 20%.[17] BRSV infects the upper and lower respiratory tract causing mild to severe respiratory disease characterized by coughing, fever, tachypnea, dyspnea, and bronchopneumonia. Infected animals shed virus in nasal secretions from 3 to 7 d after infection. Recovered animals typically do not show clinical disease upon reinfection. Hence it is important to protect animals during their most vulnerable age and time of the year. Prevention or control of BRSV respiratory disease has been attempted by use of both inactivated and MLV vaccines. The history of exacerbation of disease after BRSV challenge, especially using formalin inactivated vaccines with alum adjuvant, is well documented and highlights the importance of induction of appropriate protective immune responses.[8] Exacerbation of disease following challenge correlated with induction of IL-4 cytokine and IgE antibodies, i.e., a Th-2 type of immune response. Protective immunity to BRSV is essentially cell-mediated, delivered by $CD4^+$ and $CD8^+$ T cell lymphocytes. Mucosal IgA antibodies also have a role in protection.[4,5] A comparison of efficacy of an inactivated BRSV vaccine against MLV vaccine demonstrated that the former was less efficient in inducing neutralizing IgG antibodies to the protective antigens F and G proteins compared to the latter.[4,5] Vaccination with inactivated vaccines induced less neutralizing antibody titer than vaccination with MLV vaccines, which is not surprising as the latter type mimics an infection without causing disease.

In the current study, we explored efficacy of a 6-way MLV-toxoid vaccine[c] to confer protection against experimentally induced BRSV respiratory disease in young seronegative calves at ~ 60 d of age following single SC vaccination. All calves were exposed to a virulent strain of BRSV by a natural aerosol route of transmission. The data presented demonstrated that a single dose of this vaccine protected vaccinated calves against severe BRSV respiratory disease and induced protection, as evidenced by significantly less respiratory clinical signs, pneumonic lesions, and mortality in vaccinates compared to the placebo controls. Although CMI responses were not measured in this study, the virus neutralizing antibody responses were significantly higher at time of challenge and on the last day of the study in vaccinates vs controls. These titers correlated with higher PaO2 levels in the vaccinates on d 6 of challenge, which is an indication of oxygen levels in the blood and supports the conclusion that the 6-way MLV-toxoid vaccine induced a strong disease-sparing effect. Furthermore, virus shedding data demonstrated that vaccinates shed significantly less virus and for a shorter duration compared to the placebo controls. These data compare well with the protective effect of MLV when administered via the IN route,[5] confirming that different routes of vaccination can deliver robust protection against BRSV respiratory disease.

Proper timing of vaccination is of paramount importance for success of vaccine efficacy and disease control.[14] The earliest opportunity to vaccinate beef and dairy calves is at birth; however, this time point is often challenging both logistically and immunologically.[14,20] Preconditioning is a longstanding management practice that includes a series of vaccinations and management practices at various age stages in order to better prepare beef calves for their transition to subsequent production sectors, such as backgrounding and/or feedlots.[14,15] Sixty days of age corresponds with many of the preconditioning procedures.[14] In this report, we demonstrated that 6-way MLV-toxoid vaccine is safe and efficacious in young calves 60 d of age following a single SC vaccination. As in virtually all efficacy studies conducted for licensure-related purposes, this study was conducted, as mandated by regulatory agencies, in BRSV-seronegative calves, which would be different than its application in most instances in the field. Nevertheless, calves were vaccinated at an age when there was likely significant decay of maternal

antibodies in calves with good passive immunization from colostrum,[2] making it relevant to the timing of vaccination in many commercial operations.

Conclusions

This study confirmed that a single SC dose of the combination 6-way MLV-toxoid vaccine, modeled on a commercial vaccine, was safe as no adverse effects were noted associated with vaccination of 60-d old calves. Furthermore, a single dose of this vaccine induced a level of protection that significantly reduced mortality, and provided clinically relevant disease sparing protective immunity against a BRSV respiratory challenge in naïve 60-d old calves. This age is linked to preconditioning activities, and is convenient timing for dosing calves, building immunity against key pathogens ahead of their next phase of life. Additional research is required to better characterize the duration of immunity and vaccine efficacy in the presence of maternal antibodies.

Endnotes

[a]CalfGuard®, Zoetis, Parsippany, NJ
[b]SAS/STAT User's Version 9.4, SAS Institute, Cary, NC
[c]Bovi-Shield Gold® One Shot, Zoetis, Parsippany, NJ
[d]Model 288, Ciba-Corning, Medfield, MA

Acknowledgement

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