Vaccine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Comparison of reproductive protection against bovine viral diarrhea virus provided by multivalent viral vaccines containing inactivated fractions of bovine viral diarrhea virus 1 and 2

Paul H. Walz [a], Kay P. Riddell [a], Benjamin W. Newcomer [a], John D. Neill [b], Shollie M. Falkenberg [b], Victor S. Cortese [c,*], Daniel W. Scruggs [d], Thomas H. Short [d]

[a] College of Veterinary Medicine, Auburn University, Auburn, AL 36849, USA
[b] USDA, Agricultural Research Service, National Animal Disease Center, Ruminant Diseases and Immunology Research Unit, Ames, IA 50010, USA
[c] Zoetis INC., 746 Veechdale Road, Simpsonville, KY 40067, USA
[d] Zoetis INC., Parsippany, NJ 07054, USA

ARTICLE INFO

Article history:
Received 17 November 2017
Received in revised form 28 March 2018
Accepted 3 April 2018
Available online xxxx

Keywords:
Bovine viral diarrhea virus
Cattle
Vaccine efficacy
Inactivated vaccine
Reproductive protection
Fetal protection

ABSTRACT

Bovine viral diarrhea virus (BVDV) is an important viral cause of reproductive disease, immune suppression and clinical disease in cattle. The objective of this study was to compare reproductive protection in cattle against the impacts of bovine viral diarrhea virus (BVDV) provided by three different multivalent vaccines containing inactivated BVDV. BVDV negative beef heifers and cows (n = 122) were randomly assigned to one of four groups. Groups A-C (n = 34/group) received two pre-breeding doses of one of three commercially available multivalent vaccines containing inactivated fractions of BVDV 1 and BVDV 2, and Group D (n = 20) served as negative control and received two doses of saline prior to breeding. Animals were bred, and following pregnancy diagnosis, 110 cattle [Group A (n = 31); Group B (n = 32); Group C (n = 31); Group D (n = 16)] were subjected to a 28-day exposure to cattle persistently infected (PI) with BVDV (1a, 1b and 2a). Of the 110 pregnancies, 6 pregnancies resulted in fetal resorption with no material for testing. From the resultant 104 pregnancies, BVDV transplacental infections were demonstrated in 73 pregnancies. The BVDV fetal infection rate (FI) was calculated at 13/30 (43%) for Group A cows, 27/29 (93%) for Group B cows, 18/30 (60%) for Group C cows, and 15/15 (100%) for Group D cows. Statistical differences were observed between groups with respect to post-vaccination antibody titers, presence and duration of viremia in pregnant cattle, and fetal infection rates in offspring from BVDV-exposed cows. Group A vaccination resulted in significant protection against BVDV infection as compared to all other groups based upon outcome measurements, while Group B vaccination did not differ in protection against BVDV infection from control Group D. Ability of inactivated BVDV vaccines to provide protection against BVDV fetal infection varies significantly among commercially available products; however, in this challenge model, the inactivated vaccines provided unacceptable levels of BVDV FI protection.

1. Introduction

Bovine viral diarrhea virus (BVDV) is an important viral cause of reproductive disease in cattle. Consequences of BVDV exposure during pregnancy can range from abortion outbreaks affecting large populations of pregnant cattle to more subtle reproductive losses including early embryonic death, premature birth, congenital defects, weak calves, stillbirths, and the birth of persistently infected (PI) offspring [1–3]. Maintenance of BVDV in cattle populations is through the generation of PI offspring, and the economic impact associated with PI animals in cattle populations has been demonstrated for beef and dairy operations [1,2]. Vaccination provides an important contribution to limiting reproductive losses associated with BVDV infections. Vaccines licensed for use against BVDV are often multivalent, containing both viral and bacterial antigens, and are available in North America as either modified-live viral (MLV) or killed viral (kV) vaccines [4]. While both MLV and kV BVDV vaccines have been demonstrated to provide fetal protection, MLV BVDV vaccines provide higher protection and

Abbreviations: kV, killed viral; MLV, modified live viral; FI, fetal infection; BVDV, Bovine viral diarrhea virus.

* Corresponding author.
E-mail address: victor.cortese@zoetis.com (V.S. Cortese).

https://doi.org/10.1016/j.vaccine.2018.04.005
0264-410X/

longer durations of immunity [3,5,6]. In spite of evidence of superior protection afforded by MLV vaccines, kV vaccines continue to be widely used by cattle producers [7] because of perceived safety concerns associated with MLV vaccination in close time proximity to breeding or during gestation [8]. While some users of kV BVDV vaccines consider this class undifferentiated, kV vaccines vary among manufacturers with respect to BVDV strains and adjuvants employed, and comparative reproductive efficacy data between kV vaccines are lacking. This study examined reproductive efficacy among commercially available kV BVDV vaccines against BVDV when challenge-exposed to PI calves comprising all three genotypes present in North America.

2. Materials and methods

2.1. Experimental design

The study was designed as a randomized, controlled clinical trial and all study procedures were reviewed and approved by the Institutional Animal Care and Use Committee of Auburn University (PRN #2015-2795). Cattle enrolled in the study consisted of 63 nulliparous heifers and 59 primiparous cows and were blocked and randomized to study groups. For the randomization, nulliparous heifers were sorted by age in nine blocks of seven heifers, and then within block randomly assigned such that two heifers were assigned to each of Groups A, B, and C and one to Group D. Primiparous cows were sorted by ID tag, from lowest to highest and then grouped into three blocks of eight cows and five blocks of seven cows. Within each block, cows were randomly assigned such that two cows were assigned to each of Groups A, B, and C, while two cows were assigned to Group D in the first three blocks and one cow assigned to Group D in the last five blocks. Upon completion of randomization of heifers and cows to treatments, resulting treatment group sizes were 34 each for groups A-C and 20 for group D (Fig. 1). Twelve cows were removed from study between enrollment and BVDV exposure. Thus, 110 pregnancies were subjected to BVDV exposure, and consisted of 31, 32, 31, and 16 cattle for groups A-D, respectively.

All animals were administered vaccinations on days 0 and 21 and then subjected to synchronization of estrus and bull breeding for a period of 60 days. Pregnancy exam was performed by transrectal ultrasonography; however, pregnancy results were only 77% (92/120), and not at the level expected. The 92 pregnant cattle were continued in the study and constituted phase I of the study. Since the 28 remaining cattle had been maintained in strict biosecurity, a second opportunity was afforded for the remaining 28 open study cows to conceive through a second 60-day breeding exposure to fertile bulls. Of these 28 study cows, 64% (18/28) became pregnant, and these 18 pregnant cattle were continued in the study and constituted phase II of the study. The days between booster vaccinations on study day 21 to the first day of BVDV exposure were 111 days for Phase I and 210 days for Phase II (Fig. 1). In both phases, the time from bull removal to the first day of BVDV exposure was 33 days.

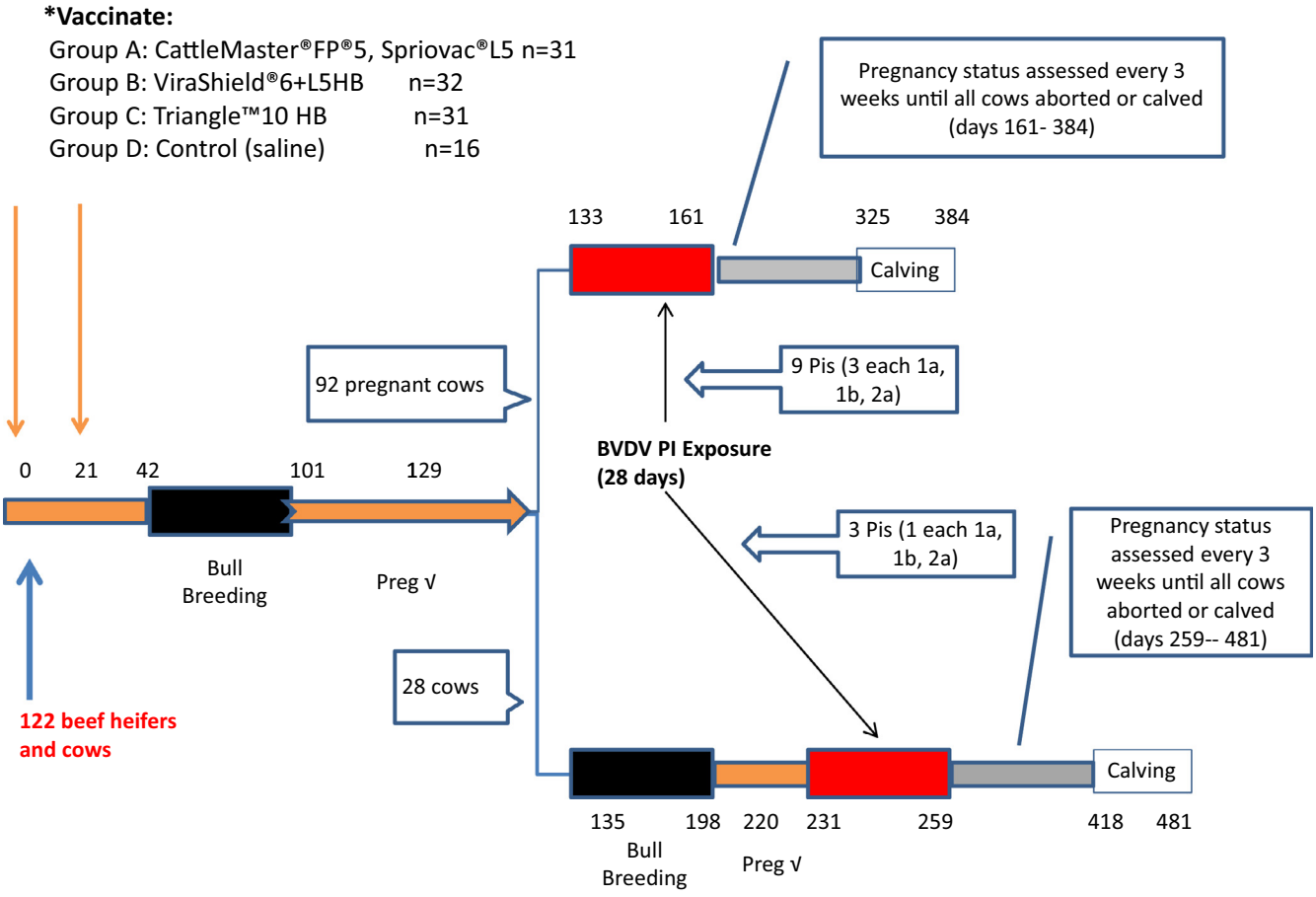

Fig. 1. Timeline for events occurring throughout the study (numbers represent day of event). *number of pregnant cattle per group exposed to persistently infected cattle. A CattleMaster® Gold FP®5; 105292/106571B; 8-Nov-16; 105292/A518642B;27-Sep-16; Spirovac®L5; A407769 8-Nov-16; 22-Jun-16; A518533B 22-Mar-17. B ViraShield® 6 + L5 HB 221-1032C 12-May-18; 221-1030A 7-Oct-17. C Triangle™ 10 HB 6120091A 3-Dec-16; 6120091A 3-Dec-16.

Please cite this article in press as: Walz PH et al. Comparison of reproductive protection against bovine viral diarrhea virus provided by multivalent viral vaccines containing inactivated fractions of bovine viral diarrhea virus 1 and 2. Vaccine (2018), https://doi.org/10.1016/j.vaccine.2018.04.005