tively (p>0.05). ADGs were 2.93, 2.91 and 2.85 lb/day for the 3, 5 and 7-day groups, respectively (p>0.05) for cattle that completed the study. Mortality due to BRD was 1.57, 1.57 and 1.17% for cattle in the 3, 5, and 7-day groups, respectively. Two animals died immediately after CCFA-SS administration. These deaths were determined to be due to inadvertent administration of the formulation into the middle auricular artery. This resulted in retrograde movement of the formulation into the arterial supply of the brain, causing cerebral infarction.

Conclusions

The 12 percentage point increase in the single administration durable cure rate observed with a 7-day retreatment moratorium in this initial non-pivotal GCP multi-location clinical study supports the hypothesis that retreatment based on clinical signs, when therapeutic plasma concentrations of ceftiofur are present (relative to the target pathogens *Mannheimia haemolytica, Pasteurella multocida* and *Haemophilus somnus*), does not improve treatment success rates. These observations provide opportunities to alter the management of BRD and reduce the total number of treatments administered while improving durable cure rates. This study also confirms the necessity for the correct injection technique for this unique formulation and route of administration.

Ceftiofur Crystalline Free Acid Sterile Suspension (CCFA-SS) in Cattle: Pharmacokinetics after Injection in the Middle Third of the Ear and Importance of Injection Technique

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Introduction

Ceftiofur, a time-dependent, bactericidal antibiotic active against bovine respiratory disease pathogens, is effective when the concentrations remain above the minimum inhibitory concentration (MIC) for at least 3-5 days. A new product, CCFA-SS, is a prolonged release formulation of ceftiofur, intended to provide single dose efficacy in cattle. It is administered subcutaneously (SC) in the ear, eliminating any injection in edible tissue. The objective of this study was to generate plasma ceftiofur concentration data following administration of CCFA-SS SC in the middle third of the posterior aspect of the ear.

Materials and Methods

Angus and Angus crossbred beef cattle (n=24; 590-880 lb [270-400 kg]) were administered a single dose of 3.0 mg CE/lb (6.6 mg ceftiofur equivalents ([CE] /kg) BW in the middle one-third of the ear, inserting the needle approximately 1/3 of the length of the ear from the tip, pointed toward the base of the ear. An alternative site is on the rostral third of the caudal surface of the ear. These two locations are parallel to the rostral branch of the middle auricular artery. The needle should be fully inserted, the thumb positioned perpendicular to the needle to allow deposition in the middle third of the ear. Once the full dose is administered, the bleb should be massaged away from the injection site. The consequence of the inadvertent arterial injection could be retrograde delivery of the product to the external carotid artery, which in the bovine continues as the internal carotid artery and is a major blood supply to the brain (this description is in contrast to the description of Sisson and Grossman). Blood samples were collected at 0, 2, 4, 8, 12, 24, 36, 48, 72, 96, 120, 168 and 240 h after treatment administration. Plasma was harvested and stored at -20∞C before being assayed for ceftiofur and desfuroylceftiofur-related metabolites using the validated HPLC-DCA method. The LOQ of the assay is 0.150 mg CE/mL plasma. The $AUC_{0\text{-}LOQ}$ (by trapezoidal summation) and $t_{>0.2}$ (the time plasma concentrations remained above the therapeutic level of 0.2 mg/mL) were evaluated using the WinNonlin' nonlinear modeling software.

Results

All animals remained healthy during the study, and tolerated injection of the product in the ear well. Plasma concentrations over time will be shown during our presentation. Maximum concentrations were 6.3 ± 2.3 mg/mL, observed from 4-24 hours after drug administration. The $AUC_{0\text{-}LOQ}$ was 376 mg•h/mL, and the $t_{>0.2}$ was 183 hours, or over seven days above the therapeutic concentrations for bovine respiratory disease (BRD) pathogens. These concentrations provide therapeutic concentrations for sufficient time to allow single dose efficacy for BRD.

Conclusions

The data from this study supports the hypothesis that one dose of NAXCEL XT 200 Sterile Suspension (3.0 mg/lb; 6.6 mg/kg BW) will provide therapeutic concentrations in plasma for at least seven days after SC injection in the ear of cattle. Therefore, the use of this formulation of ceftiofur will ensure that a full course of therapy is provided with the convenience of a single injection.

Reproductive Performance Following Timed Artificial Insemination in Silage-fed Beef Cows: the Effects of Synchronization Method and Postpartum Energy Intake

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Many studies have examined methods for estrous synchrony in beef cows, yet very little controlled research has addressed the interaction between postpartum energy intake and synchrony system. The objectives of this study were to compare the effectiveness of two estrous synchronization methods (Ovsynch or CIDR®) for use in timed artificial insemination (TAI) programs in silage-fed beef cows, and to examine interactions between synchronization method and postpartum energy intake. It was hypothesized that a modified CIDR program[1], which utilizes progesterone and estradiol benzoate (EB), would result in enhanced reproductive efficiency in underfed cows when compared to an Ovsynch program.

Prior to calving, Hereford-cross cows (53 and 64 head for years 1 and 2, respectively) were assigned to one of six treatments arranged in a 3 x 2 factorial design: three levels of silage (Low, Medium and High) and two methods of estrus synchronization (Ovsynch or CIDR) stratified by parity and predicted calving date. Cows were fed grass / clover silage, with dry matter intakes of 1.4%, 1.7% and 2.0% of body weight for the Low, Medium and High groups, respectively. Ovsynch treatment consisted of 100 µg of gonadotropin-releasing hormone (GnRH, Cystorelin®) IM on day 0, 25 mg of prostaglandin $F_{2\alpha}$ (Lutalyse®) IM on day 7 and 100µg of GnRH IM again on day 9, with insemination 16 hours later. CIDR treatment consisted of intravaginal insertion of a CIDR® implant with 1 mg EB (estradiol benzoate 0.5mg/ml in alcohol) IM and 100mg of progesterone (progesterone 50mg/ml in alcohol) IM on day 0, 25mg of prostaglandin $F_{2\alpha}$ (Lutalyse®) IM and removal of the implant on day 7, followed by 1 mg of EB IM 24 hours later, and insemination 28 hours after the final EB injection.

Percent pregnant following TAI tended to be greater for CIDR cows (69%) when compared to Ovsynch cows (53%, P=0.07). The probability of pregnancy depended on diet (P<0.05) and was subject to a diet-year interaction (P<0.05); specifically, cows with higher postpartum energy intakes performed better in year 1, but not in year 2. In year 1, conception rates were 59, 75 and 89% for the Low, Medium and High groups, respectively; in year 2 conception rates were 55, 50 and 47%, respectively (P=0.9). The reason for the difference between years is not readily apparent, but average body condition score was lower for the second year of the study (data not shown). Breed, parity, pen, insemination sire, AI technician, calving-to-insemination interval, body condition score or live weight at treatment were not associated with the probability of reproductive success following TAI.