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Comparative efficacy of ceftiofur crystalline free acid and florfenicol-flunixin meglumine for undifferentiated fever treatment in feedlot calves administered tulathromycin metaphylactically on arrival

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Abstract

A field study was conducted at commercial feedlots to compare the relative efficacy of ceftiofur crystalline free acid (CCFA) and florfenicol-flunixin meglumine (FFM) for undifferentiated fever (UF) treatment in calves that were administered tulathromycin metaphylactically on arrival. At the time of initial diagnosis of UF, experimental calves (n = 1,056) were randomly allocated to 2 experimental groups, CCFA and FFM. Calves in the CCFA group (n = 530) were administered 3.0 mg/lb (6.6 mg/kg) BW of ceftiofur crystalline free acid subcutaneously (SC) at the base of the ear. Calves in the FFM group (n = 526) were administered a combination of 18.1 mg/lb (40.0 mg/kg) florfenicol + 1.0 mg/lb (2.2 mg/kg) flunixin meglumine SC in the neck region. The first UF relapse treatment rate was lower in the CCFA group compared to the FFM group (P = 0.011). The third UF relapse treatment rate was also reduced in the CCFA group (P = 0.032), but no difference was detected in the second UF relapse treatment rate between the 2 groups. No differences in overall chronicity, wastage, salvage slaughter, or mortality rates were detected between the 2 groups at the $P \le 0.05$ level. There was a net economic advantage of \$10.35/treated animal in the CCFA group, driven primarily by the lower initial UF treatment cost when compared to the FFM group.

Key words: BRD, treatment, florfenicol, flunixin meglumine, ceftiofur, tulathromycin

Résumé

Une étude sur le terrain a été menée dans des parcs d'engraissement commerciaux afin de comparer l'efficacité relative du ceftiofur sous forme d'acide libre cristallin et d'une combinaison florfénicol et méglumine de flunixine pour le traitement de la fièvre non-spécifique chez les veaux recevant à leur arrivée de la tulathromycine en métaphylaxie. Au moment du diagnostic initial de fièvre non-spécifique, les veaux expérimentaux (n = 1056) ont été alloués aléatoirement dans deux groupes. Dans le groupe CCFA (n = 530) les veaux ont reçu une injection sous-cutanée à la base de l'oreille de ceftiofur sous forme d'acide libre cristallin à la concentration de 3.0 mg/lb (6.6 mg/kg) de poids corporel. Dans le groupe FFM, les veaux (n = 526) ont reçu une injection sous-cutanée dans la région du cou combinant du florfénicol à la concentration de 18.1 mg/lb 40.0 mg/kg) de poids corporel et de la méglumine de flunixine à la concentration de 1.0 mg/lb (2.2 mg/kg) de poids corporel. Le taux de première rechute pour la fièvre non-spécifique était moins élevé dans le groupe CCFA que dans le groupe FFM (P = 0.011). Le taux de troisième rechute était aussi moins élevé dans le groupe CCFA (P = 0.032), bien qu'il n'y avait pas de différence significative pour le taux de seconde rechute entre les deux groupes. Il n'y avait pas de différence entre les deux groupes au seuil de 5% pour le taux de chronicité, de perte, d'abattage de récupération ou de mortalité. L'avantage économique net de 10.35\$ par animal traité dans le groupe CCFA reflétait principalement le coût moindre du traitement initial de la fièvre non-spécifique dans ce groupe par rapport au groupe FFM.

Introduction

Bovine respiratory disease (BRD) remains the main health problem encountered by bovine practitioners in feedlot cattle in North America.⁸ One of the main challenges with this disease is its multifactorial nature, where a complex interaction of environmental, infectious, and host factors play a major role in the progression and outcome of the disease.¹⁰

In US feedlots, it was reported that BRD morbidity reaches to 70 to 80%, and 40 to 50% of mortality causes are attributed to BRD.⁸ In addition, the US Department of Agriculture's National Animal Health Monitoring System reported in a 2011 study that 16.2% of feedlot cattle were treated for BRD.⁴

Antimicrobials, alone or along with non-steroidal antiinflammatory drugs, continue to be the main BRD treatment method. A long list of antimicrobials has been used for treatment or prevention (metaphylactic use) of BRD in feedlot cattle. Field studies to compare their efficacy, reflected by economic loss reductions, are of utmost importance to feedlot veterinarians and their clients.

Combination florfenicol-flunixin meglumine^a is an antimicrobial and non-steroidal anti-inflammatory drug mixture product licensed in North America for the treatment of BRD complex – also known as undifferentiated fever (UF) – associated with *Mannheimia haemolytica*, *Histophilus somni*, and *Pasteurella multocida* infections and BRD-associated pyrexia.³

Florfenicol efficacy, alone or along with flunixin meglumine, for treatment of BRD in feedlot cattle has been examined.^{1,7,11} Its efficacy has also been compared with such other antimicrobials as tulathromycin and tilmicosin.9,11 When compared to tilmicosin in calves that had already received metaphylactic tilmicosin upon arrival at the feedlot, florfenicol was superior for treatment of UF because of lower chronicity, wastage, overall mortality, and BRD mortality rates.9 Similarly, in feedlot calves at ultra-high risk of developing BRD that have already received metaphylactic tulathromycin on arrival at the feedlot, it is more cost-effective to use florfenicol than tulathromycin for subsequent treatment of initial UF.11 In addition, in a study conducted to compare florfenicolflunixin meglumine with tulathromycin for treatment of UF in fall-placed feedlot calves that were administered metaphylactic tilmicosin on arrival, calves in the florfenicol-flunixin meglumine group had a lower crude case fatality rate compared to the calves in the group treated with tulathromycin.¹³

Ceftiofur crystalline free acid^b sterile injectable suspension is an antimicrobial product licensed in North America for treatment of BRD associated with *Mannheimia haemolytica*, *Histophilus somni*, and *Pasteurella multocida* infections in cattle.³ The efficacy of crystalline free acid was compared to that of florfenicol-flunixin meglumine for the treatment of UF in feedlot calves that were administered metaphylactic long-acting oxytetracycline on arrival.⁷ In that study, it was more cost-effective to administer florfenicol-flunixin meglumine than ceftiofur crystalline free acid for initial UF therapy because of a lower overall case fatality rate in the florfenicolflunixin meglumine group.⁷ However, in animals at ultra-high risk of developing UF/BRD, tulathromycin is commonly used metaphylactically on feedlot arrival as opposed to long-acting oxytetracycline. To the best of the authors' knowledge, no studies in the veterinary literature compare ceftiofur crystalline free acid to florfenicol-flunixin meglumine for the initial treatment of UF/BRD in feedlot calves that were administered tulathromycin metaphylactically on arrival. Therefore, this study's objective was to compare the relative efficacy of ceftiofur crystalline free acid to florfenicol-flunixin meglumine for initial treatment of UF/BRD in ultra-high risk feedlot calves administered tulathromycin metaphylactically on arrival at the feedlot. Efficacy parameters compared included animal health variables and economic analysis.

Materials and Methods

General Overview

The field study was conducted at commercial feedlots in Alberta, Canada. At the time of diagnosis of initial UF, steer and heifer calves (n = 1,056) were randomly allocated to 1 of 2 experimental groups: ceftiofur crystalline free acid (CCFA; n = 530) or florfenicol-flunixin meglumine (FFM; n = 526). Individual animal was the experimental unit, and animals were returned to their original pen immediately after initial UF treatment. Animals were followed from allocation (initial UF diagnosis) until exit from the feedlot premises to the slaughter house. Outcome variables were measured to evaluate relative effects of the UF treatment programs on animal health. Statistical analyses were used to determine the probability of whether differences in outcome variables between the experimental groups were due to differences in the disease control programs or random chance. Based on defined criteria, outcome variables were subsequently incorporated into economic models to determine the relative cost differences of the 2 programs. Animal use was approved by the Feedlot Health Management Services Ltd (Feedlot Health) Animal Care Committee, with informed consent from the animal owners.

Study Facilities

The study was conducted at 3 commercial feedlots in central Alberta with capacities of approximately 25,000 animals, 36,000 animals, and 45,000 animals for site 1, site 2, and site 3, respectively. The basic design of the feedlots is representative of standard designs used in western Canada. Animals were housed in open-air, dirt-floor pens arranged side by side with central feed alleys and 20% porosity woodfence windbreaks. There are 3 animal-handling facilities located at site 1, and 5 at sites 2 and 3. Each facility has a hydraulic chute equipped with an individual animal scale, a chute-side computer with individual animal data collection and management software^c, and separation alleys to facilitate the return of animals to the designated pens. Site 3 switched to a new animal data collection and management software program^d during the trial. Open-air containment pens are located adjacent to each facility.

Study Animals

Candidate animals for the study were auction marketderived, exotic crossbred steer and heifer calves at ultra-high risk of developing BRD that met the following 5 inclusion criteria at the time of initial UF diagnosis: 1) absence of abnormal clinical signs referable to organ systems other than the respiratory tract; 2) elevated rectal temperature \geq 105.0°F (> 40.5°C); 3) no previous treatment history for no fever (NF); 4) at least 72 hours (3 days) had elapsed from arrival metaphylactic tulathromycin^e administration; and 5) less than 80 days had elapsed from feedlot arrival.

At the time of feedlot arrival, each animal was processed as per standardized commercial feedlot procedures. Those included individual animal identification; an arrival metaphylactic antimicrobial (tulathromycin, at a dosage of 1.14 mg/lb (2.5 mg/kg) BW subcutaneously (SC) in the neck region); a multivalent modified-live viral vaccine; a 7-way clostridial with *H. somni* bacterin-toxoid vaccine; and a pour-on endectocide. Heifers received an abortifacient drug to terminate possible pregnancy. After receiving a multivalent clostridial bacterin including tetanus toxoid, intact bulls were banded and animals with retained testicles were surgically castrated with use of the appropriate anesthetic and/or analgesic products as per standard feedlot research protocols approved by the Feedlot Health Animal Care Committee. Animals were later re-vaccinated and implanted as per standardized feedlot protocols.

Experimental Design

Candidate steer and heifer calves that met the inclusion criteria were randomly allocated to 1 of 2 experimental groups at the time of initial UF diagnosis: CCFA or FFM. The random allocation was achieved utilizing a computergenerated randomization table created from a spreadsheet program customized to ensure equal distribution between the 2 groups^f. Animals in the CCFA group were administered 3.0 mg/lb (6.6 mg/kg) BW (1.5 mL/100 lb BW) of ceftiofur crystalline free acid SC at the base of the ear. Calves in the FFM group were administered a combination of 18.1 mg florfenicol + 1.0 mg flunixin meglumine/lb (40.0 mg florfenicol + 2.2 mg flunixin meglumine/kg) BW (6.0 mL/100 lb BW) SC in the neck region. First UF relapses were treated in the neck region with 3.5 mg/lb (7.7 mg/kg) BW of enrofloxacing SC. Second UF relapses were treated intramuscularly in the neck region with 13.6 mg/lb (30 mg/kg) BW oxytetracycline dihydrateh. Third UF relapses were treated with 3.0 mg/lb (6.6 mg/kg) BW of ceftiofur crystalline free acid SC at the base of ear. All individual treatment doses were determined based on body weight at the time of the respective UF relapse therapy.

Study animals were housed in commercial feedlot pens and followed from the time of initial UF diagnosis until exit from the feedlot premises to the slaughter house, with the individual animal as the experimental unit.

Feeding Program

Water and standard mixed complete feedlot diets, formulated to meet or exceed the National Research Council nutritional requirements for beef cattle, were offered *ad libitum* throughout the feeding period. The general diet composition was similar across the 3 study sites in that the concentrate component consisted primarily of barley grain, the forage component consisted of barley silage or barley straw, and all diets contained a granular supplement. Diet formulations and diet changes were based on commercial feedlot protocols and were consistent within each site. Feedlot diets were blended in truck-mounted mixer boxes equipped with electronic load cells. Diets were delivered to the pens once or twice daily.

Candidate animals for this study were conditioned to a high-concentrate diet over a 25 to 45 day period, with the step-up period being consistent within each site. Animals remained on the high-concentrate diet until harvest.

The feed offered to study animals from allocation until exit from the feedlots contained monensinⁱ at a level of 11.3 mg/lb (25 mg/kg) diet dry matter (DM) to control coccidiosis and bloat. Feed offered to heifers from allocation until at least 24 hours prior to slaughter contained melengestrol acetate^j to improve feed utilization and to suppress estrus. The feed offered to all study animals, from allocation until the start of the withdrawal feeding period, contained chlortetracycline^k at a level of 15.9 mg/lb (35 mg/kg) diet DM to control liver abscesses. During the withdrawal period, the feed offered to all study animals contained tylosinⁱ at a level of 5.0 mg/lb (11 mg/kg) diet DM to control liver abscesses.

Animal Health

Experienced animal health personnel blinded to the experimental status of each individual animal observed the study animals once or twice daily for evidence of disease. Animals deemed "sick" by the animal health personnel, based on subjective criteria such as general appearance, attitude, gauntness, or reluctance to move, were individually sorted from pen mates, and moved to the hospital facility where they were diagnosed and treated as per the standard feedlot protocol for all diseases other than UF. Animals diagnosed with UF were treated as per the experimental protocol provided. Treatment events, including date, presumptive diagnosis, drug(s) administered, and dose(s) used were recorded using individual animal data collection and management software.

The case definition for UF was a lack of abnormal clinical signs referable to organ systems other than the respiratory tract; a rectal temperature ≥ 105.0 °F (> 40.5°C); no previous treatment history for NF; a period of at least 72 hours (3 days) had elapsed from allocation/arrival metaphylactic tulathromycin administration; and less than 80 days had elapsed from feedlot arrival. All animals showing clinical signs of BRD, as reported by animal health personnel, subsequent to initial UF therapy were defined as relapses. Relapse treatment required an absence of abnormal clinical signs referable to organ systems other than the respiratory tract. Animals in the CCFA group had a post-treatment interval (PTI) of at least 7 days before they were eligible for first UF relapse therapy, whereas animals in the FFM group had a PTI of at least 3 days before they were eligible for first UF relapse therapy. The PTI for second and third UF relapses was at least 3 days for animals in both groups. The maximum number of UF treatments permitted for all animals on the study was 4. Animals identified as "sick" subsequent to third UF relapse therapy were deemed to be "chronics". Also, animals that were unsuitable for return to their designated feedlot pens, based on subjective appraisal of the attitude and appearance of each animal, were deemed to be "chronics". Chronics that did not die during the study were defined as wastage. All other diseases were treated as per standard feedlot protocols provided by the consulting veterinarians.

A gross necropsy examination was performed on each dead animal by trained personnel. In some instances, a Feedlot Health veterinarian conducted the post-mortem examination on site and determined the cause of death based on the findings of clinical history and gross post-mortem examination. In other instances, trained personnel prosected the dead animals using a standardized method to capture appropriate digital images as outlined in the written necropsy protocol provided by Feedlot Health.¹⁴ Subsequently, all digital images were electronically transferred to Feedlot Health and the cause of death for each experimental animal was determined based on clinical history and gross post-mortem examination by a Feedlot Health veterinarian. All animals that died were weighed by feedlot personnel.

Data Collection and Management

Over the course of the trial, data were collected using a chute-side computer with individual animal data collection and management software. All study data were entered or electronically imported into a spreadsheet program^f, collated, and verified. Outcome variables describing animal health were calculated for each individual animal. Definitions and formulae used to calculate animal health are summarized in Table 1.

Statistical Analysis

Data were analyzed using an analytical software program^m to compare the CCFA group to the FFM group. Statistical analyses were used to determine the probability of whether differences in outcome variables between the experimental groups were due to the respiratory disease control protocol. In all cases, the null hypothesis was that there was no difference between the experimental groups for the outcome variable in question.

The animal health data were analyzed using the GEN-MOD procedure in SAS using a Poisson regression in a log linear model for experimental group effects and correcting for intra-site clustering of disease with generalized estimating equations.¹² Potential interactions between experimental group and site or gender were explored and included in final models when significant (P < 0.05).

Table 1. Definitions and calculations for animal health variables used in a study comparing the efficacy of ceftiofur crystalline free acid (CCFA)* and florfenicol-flunixin meglumine (FFM)[†] for undifferentiated fever treatment in feedlot calves administered tulathromycin metaphylactically on arrival.

Animal health rates	
First UF relapse treatment	# of animals treated for first UF relapse divided by the # of animals treated for initial UF
Second UF relapse treatment	# of animals treated for second UF relapse divided by the # of animals treated for first UF relapse
Third UF relapse treatment	# of animals treated for third UF relapse divided by the # of animals treated for second UF relapse
Overall chronicity	# of animals with chronic disease (all causes) divided by the # of animals allocated
Overall wastage	# of animals with chronic disease (all causes) that did not die divided by the # of animals allocated
Overall salvage slaughter	# of animals sold for salvage slaughter (all causes) divided by the # of animals allocated
Overall mortality	 # of mortalities (all causes) divided by the # of animals allocated
BRD mortality	 # of mortalities due to BRD divided by the # of animals allocated
HS mortality	# of mortalities due to histophilosis divided by the # of animals allocated
Lameness mortality	# of mortalities due to lameness divided by the # of animals allocated
Metabolic mortality	# of mortalities due to metabolic disease divided by the # of animals allocated
Other mortality	# of mortalities (causes other than those previously listed) divided by the # of animals allocated

*CCFA = Excede[®], Zoetis Canada Inc., Kirkland, QC. Calves in the CCFA group (n = 530, 3 sites) were administered 3.0 mg/lb BW of ceftiofur crystalline free acid SC at the base of the ear.

⁺FFM = Resflor[®], Merck Animal Health, Intervet Canada Corp., Kirkland, QC. Calves in the FFM group (n = 526, 3 sites) were administered a combination of 18.1 mg florfenicol + 1.0 mg flunixin meglumine/lb BW SC in the neck region.

Ten animals in the CCFA group did not meet the protocol-indicated 7 day post-treatment interval when treated as a first undifferentiated fever relapse. These animals remained in the analysis because 5 of the animals went on to die, and removal from the analysis would have biased the results in favor of CCFA.

UF = undifferentiated fever, BRD = bovine respiratory disease, HS = histophilosis.

Economic Analysis

The relative cost-effectiveness of the respiratory disease control protocol was calculated using a computer spreadsheet program that simulates all economic aspects of feedlot production.^{2,11} Economic models were built to compare the CCFA group to the FFM group. The first UF relapse treatment regime cost (\$21.83) and third UF relapse treatment regime cost (\$18.13) were fixed for both experimental groups. The cost of initial UF treatment of calves in the FFM group was \$9.61 more than that of the CCFA group, which

was calculated based on the average allocation weight of 661 lb (300 kg). The input costs and sensitivity analysis are presented in Table 2.

Outcome variables describing animal health were incorporated into the model when significant differences (P < 0.05) existed between the 2 groups. When there were no significant differences ($P \ge 0.05$) between the experimental groups, the animal health values for the FFM group were used for both experimental groups in the comparison. All other factors were fixed in the economic simulations.

Table 2. Economic model input values and sensitivity analysis from a study comparing the efficacy of ceftiofur crystalline free acid (CCFA)* and florfenicol-flunixin meglumine (FFM)⁺ for undifferentiated fever treatment in feedlot calves administered tulathromycin metaphylactically on arrival.

			Change evaluated in	Economic advantage in
Description	Unit	Input value	sensitivity analysis	CCFA vs FFM
First UF relapse regime cost	\$/animal	\$21.83	\$5.00	\$0.09
Third UF relapse regime cost	\$/animal	\$18.13	\$5.00	\$0.08
Interest rate	%	4.0%	1.0%	\$0.03

*CCFA = Excede[®], Zoetis Canada Inc., Kirkland, QC. Calves in the CCFA group (n = 530, 3 sites) were administered 3.0 mg/lb BW of ceftiofur crystalline free acid SC at the base of the ear.

⁺FFM = Resflor[®], Merck Animal Health, Intervet Canada Corp., Kirkland, QC. Calves in the FFM group (n = 526, 3 sites) were administered a combination of 18.1 mg florfenicol + 1.0 mg flunixin meglumine/lb BW SC in the neck region.

Ten animals in the CCFA group did not meet the protocol-indicated 7 day post-treatment interval when treated as a first undifferentiated fever relapse. These animals remained in the analysis because 5 of the animals went on to die, and removal from the analysis would have biased the results in favor of CCFA.

UF = undifferentiated fever.

Table 3. Summary of morbidity and mortality data collected from a study comparing the efficacy of ceftiofur crystalline free acid (CCFA)* and florfenicol-flunixin meglumine (FFM)⁺ for undifferentiated fever treatment in feedlot calves administered tulathromycin metaphylactically on arrival.

	Experime		
Animal health variable	CCFA	FFM	P - value
Morbidity	4		
First UF relapse treatment (%)	18.11	19.96	0.011
Second UF relapse treatment (%)	46.88	34.29	0.182
Third UF relapse treatment (%)	37.78	58.33	0.032
Overall chronicity (%)	8.49	6.84	0.271
Overall wastage (%)	3.96	3.99	0.913
Overall salvage slaughter (%)	2.64	2.47	0.891
Mortality			
Overall mortality (%)	15.47	14.26	0.595
BRD mortality (%)	7.17	7.41	0.756
HS mortality (%)	4.15	3.04	0.440
Lameness mortality (%)	0.57	0.38	0.575
Metabolic mortality (%)	1.13	1.14	0.974
Other mortality (%)	2.45	2.28	0.651

*CCFA = Excede[®], Zoetis Canada Inc., Kirkland, QC. Calves in the CCFA group (n = 530, 3 sites) were administered 3.0 mg/lb BW of ceftiofur crystalline free acid SC at the base of the ear.

[†]FFM = Resflor[®], Merck Animal Health, Intervet Canada Corp., Kirkland, QC. Calves in the FFM group (n = 526, 3 sites) were administered a combination of 18.1 mg florfenicol + 1.0 mg flunixin meglumine/lb BW SC in the neck region.

Ten animals in the CCFA group did not meet the protocol-indicated 7 day post-treatment interval when treated as a first undifferentiated fever relapse. These animals remained in the analysis because 5 of the animals went on to die, and removal from the analysis would have biased the results in favor of CCFA.

Data were analyzed using the GENMOD procedure of SAS[®] software^m using a Poisson regression in a log linear model for experimental group effects and correcting for intra-site clustering of disease with generalized estimating equations.

UF = undifferentiated fever, BRD = bovine respiratory disease, HS = histophilosis.

Each "Morbidity" and "Mortality" variable is defined in Table 1.

Results and Discussion

The study included 1,056 calves. Of those, 264 calves were allocated at site 1 (107 heifers, 157 steers); 449 were allocated at site 2 (all steers); and 343 were allocated at site 3 (127 heifers, 216 steers). There was no difference in allocation weight between the groups (P = 0.302). In addition, there were no interactions between experimental group and site or gender detected at the P < 0.05 level for any of the outcome variables.

The animal health data are summarized in Table 3. Proportions of animals requiring first UF relapse and third UF relapse treatments were reduced in the CCFA group compared to the FFM group (absolute difference of 1.85%, P = 0.011 for first UF relapse and 20.55%, P = 0.032 for third UF relapse). However, there was no difference in the proportion of animals requiring second UF relapse treatment detected between the experimental groups at the P < 0.05 level. No differences in overall chronicity, overall wastage, overall salvage slaughter, overall mortality, BRD mortality, histophilosis mortality, lameness mortality, metabolic mortality, or other mortality were detected between the experimental groups at the P < 0.05 level.

The economic model input values and sensitivity analysis are presented in Table 2 and the economic analysis summary is presented in Table 4. There was a net economic advantage of \$10.35/treated animal for feedlot calves in the CCFM group, primarily driven by the lower initial UF treatment cost in the CCFM group when compared to the FFM group.

Undifferentiated fever, historically known as "shipping fever" or BRD, continues to be one of the most common animal health concerns in commercial feedlot production.^{5,6,15} Although beef feedlot operations have become more sophisticated in managing health problems, significant economic losses from UF continue to be related to morbidity and mortality rates, reduced feedlot performance, and metaphylactic and therapeutic treatment costs.⁶ Therefore, it is important to seek the most cost-effective UF treatment strategies, based on high-quality clinical trial data.

The relative cost effectiveness of various antimicrobial therapy options may change over time as standard commercial production procedures and/or the cost of antimicrobials change.

In the past, florfenicol for initial UF treatment in feedlot calves was reported to have a greater cost benefit compared to no treatment, tilmicosin, or tulathromycin.^{1,9,11} Additionally, florfenicol-flunixin meglumine was more cost-effective for UF treatment compared to either tulathromycin or ceftiofur crystalline free acid in animals receiving metaphylactic long-acting oxytetracycline at the time of feedlot arrival.⁷ At the time this study was conducted, the cost of initial UF treatment of calves in the FFM group in western Canada was approximately \$9 to \$10 more than that of the CCFA group, which was calculated based on the average allocation weight of 661 lb (300 kg). As such, the objective of this study was to compare the 2 antimicrobials in a commercial field trial setting in animals receiving metaphylactic tulathromycin at the time of feedlot arrival. Animals in the CCFA group had reduced first UF relapse and third UF relapse rates compared to animals in the FFM group, but all other animal health outcome parameters were similar between the 2 groups. These data suggest that ceftiofur crystalline free acid is more costeffective relative to florfenicol-flunixin meglumine for initial UF therapy in animals receiving metaphylactic tulathromycin at the time of feedlot arrival. This finding contrasts with previous work comparing florfenicol-flunixin meglumine to ceftiofur crystalline free acid for the initial treatment of UF/BRD in feedlot cattle. However, the metaphylactic antimicrobial used to control UF/BRD in the current study (tulathromycin) is from a different antimicrobial class than the metaphylactic antimicrobial used to control UF/BRD in the previous study (long-acting oxytetracycline),⁷ which may be a logical reason for the observed difference, as extensively discussed in a previous publication.¹¹ Additional research would be required to support or refute this hypothesis.

Table 4. Economic analysis summary from a study comparing the efficacy of ceftiofur crystalline free acid (CCFA)* and florfenicol-flunixin meglumine (FFM)⁺ for undifferentiated fever treatment in feedlot calves administered tulathromycin metaphylactically on arrival.

Outcome variable	Economic impact in CCFA vs FFM
Relative undifferentiated fever treatment program cost	\$9.61
First UF relapse rate	\$0.49
Third UF relapse rate	\$0.25
Net economic advantage for CCFA	\$10.35
*CCFA - Evendo® Zootic Canada Ina, Kirkland OC Calves in the CCFA group	n (n - E20, 2 sites) were administered 2.0 mg/lb BW/of actions in environmental

*CCFA = Excede[®], Zoetis Canada Inc., Kirkland, QC. Calves in the CCFA group (n = 530, 3 sites) were administered 3.0 mg/lb BW of ceftiofur crystalline free acid, SC at the base of the ear.

⁺FFM = Resflor[®], Merck Animal Health, Intervet Canada Corp., Kirkland, QC. Calves in the FFM group (n = 526, 3 sites) were administered a combination of 18.1 mg florfenicol + 1.0 mg flunixin meglumine/lb BW SC in the neck region.

Ten animals in the CCFA group did not meet the protocol-indicated 7 day post-treatment interval when treated as a first undifferentiated fever relapse. These animals remained in the analysis because 5 of the animals went on to die, and removal from the analysis would have biased the results in favor of CCFA.

UF = undifferentiated fever.

Conclusions

No differences were detected in second UF relapse treatment, overall chronicity, overall wastage, overall salvage slaughter, or overall mortality rates when comparing the use of ceftiofur crystalline free acid to florfenicol-flunixin meglumine for the initial treatment of UF in feedlot calves. Therefore, despite previous data indicating that florfenicolflunixin meglumine is more cost effective than ceftiofur crystalline free acid for initial UF treatment in feedlot calves that receive metaphylactic long-acting oxytetracycline at feedlot arrival for the control of UF/BRD, data from the present study indicate that this finding should not be automatically extrapolated to populations that receive metaphylactic tulathromycin at feedlot arrival for the control of UF/BRD. Rather, results from this study suggest that it is more cost-effective to use ceftiofur crystalline free acid than florfenicol-flunixin meglumine for initial UF treatment in feedlot calves at ultrahigh risk of developing UF/BRD that receive metaphylactic tulathromycin at feedlot arrival.

Endnotes

aResflor®, Merck Animal Health, Intervet Canada Corp., Kirkland, QC

^bExcede[®] 200, Zoetis Canada Inc., Kirkland, QC

ciFHMS[©], Feedlot Health, Okotoks, AB

^dparaDIAM, Western Feedlots Ltd., High River, AB and Feedlot Health, Okotoks, AB

eDraxxin®, Zoetis Canada Inc., Kirkland, QC

 ${}^{\mathrm{f}}\!\mathrm{Microsoft}^{\circledast}$ Office Excel 2010, Microsoft Corporation, Redmond, WA

Baytril[®] 100, Bayer Healthcare, Animal Health Division, Bayer Inc., Toronto, ON

^hOxymycine LA 300, Zoetis Canada Inc., Kirkland, QC

ⁱRumensin[®], Elanco Animal Health, Division of Eli Lilly Canada Inc., Guelph, ON

^jMGA[®] 100 Premix, Zoetis Canada Inc., Kirkland, QC

^kAureomycin[®] 220 G, Alpharma Canada Corporation, Mississauga, ON

¹Tylan® 40 Premix, Elanco Animal Health, Division of Eli Lilly Canada Inc., Guelph, ON

^mSAS[®] for Windows, Release 9.3, SAS Institute Inc., Cary, NC

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