Comparison of Florfenicol and Tulathromycin for the Treatment of Undifferentiated Fever in Alberta Feedlot Calves*

Joyce Van Donkersgoed, DVM, MVSa,†
Janice Berg, DVMb
Steven Hendrick, DVM, DVSc

aAlberta Beef Health Solutions, Inc.
Box 307
Picture Butte, Alberta T0K 1V0
Canada

bIntervet/Schering-Plough Animal Health
16750 Route Transcanadienne
Kirkland, Quebec H9H 4M7
Canada

cDepartment of Large Animal Clinical Sciences
Western College of Veterinary Medicine
52 Campus Drive
Saskatoon, Saskatchewan S7N 5B4
Canada

The purpose of this study was to compare the efficacy and cost-effectiveness of florfenicol versus tulathromycin for initial treatment of undifferentiated fever in fall-placed steer calves that received metaphylactic tilmicosin on arrival at the feedlot. No significant differences (P > .10) were observed in undifferentiated fever relapses or the crude case fatality rate. Calves treated with florfenicol had a lower case fatality rate (P = .04) for bovine respiratory disease and Histophilus disease than did calves treated with tulathromycin. The net economic advantage of florfenicol over tulathromycin (Can$17.70/treated animal) was based on differences in costs for the trial drug and calf replacement owing to bovine respiratory disease and Histophilus disease case fatality.

INTRODUCTION

Undifferentiated fever (UF), also known as bovine respiratory disease (BRD), is a common clinical disease in Canadian feedlot cattle. The term UF, which is commonly used in Alberta feedlots, has been described previously. Prevention, control, and treatment of UF involve the use of various respiratory vaccines and the administration of antimicrobials, either parenterally or orally. High-risk fall-placed feedlot calves are given long-acting metaphylactic antimicrobials (e.g., long-acting oxytetracycline, tilmicosin, tulathromycin) during on-arrival processing to reduce disease rates and improve performance. Florfenicol, a fluori-
A recent study compared the cost-effectiveness of florfenicol versus tulathromycin as a first-treatment drug for BRD when tulathromycin was used as a metaphylactic in very high risk calves in a Nebraska feedlot. Calves that received florfenicol had lower overall mortality and BRD mortality, but no significant differences were noted in performance, carcass traits, or other animal health variables. The overall net advantage for florfenicol versus tulathromycin was Can$41.19/treated animal.

The purpose of this study was to compare the efficacy and cost-effectiveness of florfenicol with that of tulathromycin when tilmicosin was used as the metaphylactic antimicrobial.
held approximately 225 head. Cattle were fed a balanced ration of barley or corn grain, corn or barley silage, corn dried distillers grains with solubles, and a mineral–vitamin supplement.

**Study Animals**

Animals enrolled in the study were crossbred beef steer calves (weight range, 650 to 750 lb) purchased from auction markets throughout Canada from October to December 2007. Within 24 hours of arrival at the feedlot, calves were processed and treated according to the feedlot’s standardized animal health protocols, which were the same for both facilities.

During on-arrival processing, calves were vaccinated with a modified-live virus vaccine containing bovine rhinotracheitis virus and bovine viral diarrhea virus (types 1 and 2) (Vista 3 SQ, Intervet); an *M. haemolytica* and *Haemophilus somnus* bacterin (Somnu-Star Ph, Novartis Animal Health Canada); and a clostridial bacterin–toxoid (Tasvax 8, Schering-Plough Canada). They also were given an antiparasitic (Ivermax Pour-On, RXV Veterinary Products) and a growth-promoting implant (Synovex C, Wyeth Animal Health). The cattle were fed monensin sodium throughout the feeding period to control coccidiosis and bloat and tetracycline for the first 56 days on feed to control hemophagosis. Calves received metaphylactic therapy with tilmicosin (Micotil, Elanco Animal Health; 10 mg/kg SC in the neck region). There was a 5-day posttreatment interval (after on-arrival processing) set for tilmicosin—pen riders could not pull and treat cattle for UF during the 5-day moratorium. All cattle were identified with a unique feedlot tag number and a Canadian Cattle Identification Agency ear tag.

**Experimental Design**

Feedlot pen riders monitored feedlot calves in their pens twice daily. Cattle exhibiting clinical signs of respiratory disease, including anorexia, depression, abnormal respiration, nasal discharge, and/or coughing, were removed from their pen and examined at the treatment facility. Those with clinical signs of respiratory disease and a rectal temperature ≥104.0˚F were assigned to the study and defined as having UF. Calves that had a history of treatment for any previous disease or that were moribund were excluded from the trial.

The target sample size for this trial was 250 animals/treatment group, a balance between trial power and practical and economic logistics of conducting the study. In moderately risked calves metaphylactically treated on arrival with tilmicosin, a first-pull respiratory disease treatment rate of 25% is not uncommon for the feedlots studied here. To reliably detect (power = 80%) a significant reduction (*P* < .05) in first-pull treatment rates from 25% to 15%, approximately 250 animals/treatment group are required. Similar sample sizes have been used to detect statistically significant respiratory disease outcomes between treatment groups in fall-placed feedlot calves.1

Cattle were systematically randomized to the treatment groups within each feedlot. A coin was flipped to determine whether the first animal in the trial would be treated with florfenicol or tulathromycin. The next animal was treated with the other drug. This pattern continued systematically until the desired sample size of 250 head/group was achieved.

The treatment groups were as follows:

- **Florfenicol** (Nuflor, Schering-Plough Canada), 40 mg/kg SC in the neck region
- **Tulathromycin** (Draxxin, Pfizer Animal Health), 2.5 mg/kg SC in the neck region

Calves were returned to their pen after being treated. Feedlot pen riders were blinded to the experimental status of each animal. Trial calves subsequently pulled by the pen riders for UF qualified for relapse treatment only if they had
exceeded the assigned posttreatment interval of 5 days for both drugs. Animals that exhibited clinical signs of depression, anorexia, abnormal respiration, nasal discharge, and/or cough, regardless of rectal temperature, were diagnosed as UF relapses. First UF relapses were treated with enrofloxacin (Baytril, Bayer Animal Health; 7.7 mg/kg SC in the neck region), and second UF relapses were treated with trimethoprim–sulfadoxine (Trivetrin, Intervet/Schering-Plough Animal Health; 16 mg/kg IM in the neck region for 3 to 5 days). Third UF relapses were deemed chronics and were not treated; instead, they were sent to the chronic pen and managed according to the feedlot’s chronic pen management protocol. All other diseases were treated according to a standard feedlot protocol.

All treatment data, including animal identification, treatment date, presumptive diagnosis, animal weight, drug used, dose, and route, were recorded in the chute-side computer system. Trial cattle were followed from allocation until slaughter. Any adverse events, such as anaphylactic reactions or sudden death following administration of the antimicrobials, were recorded. All mortalities were necropsied by the feedlot veterinarian to determine the cause of death based on gross pathology.

Data Analysis

Data were analyzed using an analytical software program (SAS System for Windows, Release 9.1, SAS Institute, Cary, NC). UF relapse rates were defined as previously described.1 With both variables treated as random effects. A binomial data distribution and logit link function were used in the modeling procedure. Calculation of the Wald-type CIs was done by using pseudo-likelihood estimation. The parameter estimates and CIs were converted to relative risks as previously described.3 Individual animals were the unit of analysis. The 5% level of statistical significance was used for all tests.

Differences in cost-effectiveness between the experimental groups were calculated using measured animal health variables that were statistically significant. The initial UF drug costs used in the economic calculation were based on the feedlot’s current drug costs when treating a 700-lb steer calf. Florfenicol cost Can$3.73/head less than tulathromycin. Differences in case fatality were based on a Can$735 replacement cost for a

There were no significant differences between florfenicol and tulathromycin in the first, second, or third UF relapse rate or crude case fatality rate.
700-lb steer calf. Performance and carcass traits were not assessed and thus were not included in the economic assessment.

## RESULTS

A total of 258 animals in the florfenicol group and 254 animals in the tulathromycin group were included in the final dataset. Eleven animals were removed from the dataset because of worker failure to follow the post-treatment interval for tilmicosin. There were no significant differences in the number of removals from either treatment group.

Results are presented in Table 1. There were no statistically significant differences between florfenicol and tulathromycin in the first, second, or third UF relapse rate or crude case fatality rate. In one feedlot, six animals died: one each of bronchointerstitial pneumonia, pericarditis, and waterbelly and two of unknown causes. In the other feedlot, 10 animals died: four of fibrinous pneumonia, two of myocarditis, three of pneumonia/arthritis, and one of unknown causes.

The case fatality rate for BRDHS was significantly lower ($P = .04$) in the florfenicol group (0.4%) than in the tulathromycin group (3.5%).

The average days on feed when first treated for UF was 13 days in both treatment groups. The median treatment interval between first UF treatment and first UF relapse was 17 days in the florfenicol group and 14 days in the tulathromycin group.

The economic advantage of florfenicol over tulathromycin was Can$17.70/head treated based on differences in trial drug costs and BRDHS case fatality replacement costs.

## DISCUSSION

This study suggests that florfenicol is more cost-effective than tulathromycin for initial UF treatment in moderately risked fall-placed calves given metaphylactic tilmicosin during on-arrival processing at the feedlot. These results are consistent with the recent findings of a study comparing florfenicol with tulathromycin for initial UF treatment following metaphylactic tulathromycin.1 The calves in the previous study had a

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### TABLE 1. Animal Health Data in Fall Steer Calves from Allocation to Slaughter

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Experimental Group</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FLOR</td>
<td>TULA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UF</td>
<td>258</td>
<td>254</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st UF relapse</td>
<td>16 (6.2%)</td>
<td>21 (8.3%)</td>
<td>0.75</td>
<td>0.44–1.42</td>
</tr>
<tr>
<td>2nd UF relapse</td>
<td>2 (12.5%)</td>
<td>0 (0%)</td>
<td>NC</td>
<td>NC</td>
</tr>
<tr>
<td>3rd UF relapse</td>
<td>0 (0%)</td>
<td>——</td>
<td>——</td>
<td>——</td>
</tr>
<tr>
<td>Crude CFR*</td>
<td>6 (2.3%)</td>
<td>10 (3.9%)</td>
<td>0.59</td>
<td>0.25–1.62</td>
</tr>
<tr>
<td>BRDHS CFR†</td>
<td>1 (0.4%)</td>
<td>9 (3.5%)</td>
<td>0.11</td>
<td>0.04–0.86</td>
</tr>
<tr>
<td>Other CFR‡</td>
<td>5 (1.9%)</td>
<td>1 (0.4%)</td>
<td>4.92</td>
<td>0.61–43.2</td>
</tr>
</tbody>
</table>

*The proportion of UF that died.
†The proportion of UF that died of BRD or histophilosis.
‡The proportion of UF that died of diseases other than BRD or histophilosis.

BRD = bovine respiratory disease; BRDHS = respiratory disease and histophilosis; CFR = case fatality rate; FLOR = florfenicol; NC = not calculable; TULA = tulathromycin; UF = undifferentiated fever.
much higher relapse rate (61%) than those in this study (7%). Contrary to the previous study, we found no significant differences in crude case fatality rate, which may be the result of the higher proportion of crude mortality due to BRD in the previous study than in our study. Failure to show statistically significant differences in some animal health outcomes may be related to a sample size that was too small to show statistically significant differences at low disease risks (type 2 error). Additional, larger scale studies in calves at low to medium risk for BRD should be conducted to add reliability to the findings presented here. We did not assess performance or carcass traits; therefore, we do not know the effect of the two trial treatments on these outcome variables.

The authors in the previous study speculated that differences in results between their study and that of Schunicht et al. were possibly due to changes in bacterial pathogens as a result of different vaccinations administered on arrival and the use of the same drug in metaphylaxis and treatment. The antigenic vaccines we used during on-arrival processing were similar to those used by Perrett et al. Both tilmicosin and tulathromycin are macrolides, and it is possible that the differences observed among studies are the result of acquired resistance to macrolides. Further research is warranted to evaluate this possibility.

Well-designed, large-scale field trials in commercial feedlots provide the best scientific data to feedlot veterinarians to help them make prudent decisions when designing treatment programs. It is important that practitioners review the type of cattle, management systems, level of disease risk, and methods of economic assessment in published studies to ensure that the results have external validity for extrapolation to their clients’ feedlot cattle.

In the study conducted in high-risk calves, the relative cost-effectiveness of florfenicol versus tulathromycin was Can$41.19/head treated. Their economic model included the price difference (Can$2.85/head treated) between the two trial drugs and the feeder purchase price (Can$102/100 lb). These values were less than our Can$3.73/head treated and Can$735 replacement cost because our trial cattle were heavier. The economic model used by Perrett et al. included morbidity and mortality rates, average daily gain, and carcass characteristics for the florfenicol group in the analysis and fixed values for all other factors. In our economic assessment, we did not include health variables that were not significantly different between the two groups; we also did not measure performance or carcass data, so those variables could not be assessed.

If in doubt about the cost–benefit of various therapeutic agents, the best way for practitioners to determine which product or management practice is more cost-effective than another in their client’s herds is to conduct in-house trials.

CONCLUSION

The results of this study suggest that it is more cost-effective to use florfenicol than tulathromycin for the initial treatment of UF in fall-placed feedlot calves at low to moderate risk for BRD that receive metaphylactic tilmicosin on arrival at the feedlot.
ACKNOWLEDGMENTS
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REFERENCES