

Scientific Update From Elanco Animal Health

Effect of Rumensin® on Health and Reproduction of Lactating Dairy Cows

Nine-trial Registration Summary

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Key Points

When Rumensin (monensin sodium) was fed to dairy cows:

- Services per conception, days open and calving interval were increased, and first-service conception rate was reduced in the 22 g/ton group. Pregnancy rates and successful calving rates were similar for all treatment groups. All measures of reproductive efficiency for all doses were well within accepted industry standards.
- The incidence of cystic ovarian disease and metritis was increased.
- There was no difference in somatic cell counts, or the incidence of clinical or sub-clinical mastitis.
- There was no difference in the involuntary removal rate of cows from the study.

Introduction

Reproduction and health are important considerations in the management of dairy cattle. There is an association between energy balance and the incidence of a number of postpartum diseases in the dairy cow¹⁻². Some studies³⁻⁵ have demonstrated a negative relationship between reproductive efficiency and the level of negative energy balance as measured by loss in body condition. Hammon et al.⁶ showed an inverse relationship in periparturient dry matter intake

(DMI), and the incidence of retained fetal membranes (RFM), subclinical endometritis and fever. Furthermore, they showed that cows with subclinical endometritis and fever had significantly higher periparturient serum nonesterified fatty acid (NEFA) and β -hydroxybutyrate (BHB) concentrations compared to cows without these conditions.

Improved reproductive performance associated with improved energy balance in early lactation could be anticipated in Rumensin-supplemented cows. However, three studies evaluating reproductive performance showed no difference between control cows and Rumensin-supplemented cows in days to first service, pregnancy rate or days open.

Objectives

A series of nine trials was conducted in the United States (Indiana, North Carolina, Michigan, New York, Florida and California) and Canada (Ontario, Quebec and Alberta) to determine the efficacy of Rumensin fed at inclusion rates of 0, 7, 15 or 22 g/ton in a total mixed ration (TMR) to primiparous and multiparous dairy cows. The primary objective of these trials was to determine the effects of Rumensin on milk production, dry matter intake and milk composition. Secondly, various reproduction and health parameters were also determined.

Materials and Methods

A total of 966 Holstein dairy cows, including 357 primiparous and 609 multiparous, were initially assigned to treatment at the nine trial sites throughout North America. Rumensin was fed beginning 21 ± 3 days before expected calving and continued through the full lactation to 7 to 9 days in milk (DIM) of the second lactation at all trial sites. Cows from three of the original nine trial sites continued on the trial to approximately 200 days in the second lactation. Treatments included 0 (control), 7, 15 and 22 g/ton Rumensin (100 percent dry matter basis) as part of a total mixed ration. Rumensin was fed continuously throughout the entire trial.

The voluntary wait period prior to breeding was 50 days for all study animals. Cows were observed twice daily for 30 minutes for estrous activity. All breedings were by artificial insemination. All inseminations within a 2-day period were considered a single service in this report. Cows were eligible for breeding up to 200 DIM. No estrus-detection aids (e.g., tail chalking, pressure-sensitive heat-detectors) or hormonal interventions (e.g., prostaglandins) for timing of estrus were used on study animals prior to 135 DIM.

All cows were monitored daily for health and reproductive events during the entire first lactation, the subsequent dry period (for pregnant cows) and from calving to 7 to 9 DIM of the subsequent lactation for all trial sites. Cows from the three second-lactation sites were monitored for health and reproductive events until approximately 200 DIM in a second lactation. Cows were routinely observed or examined for common health and reproductive conditions by trained trial-site personnel. The attending veterinarian for the individual trial site confirmed any suspected reproductive or health conditions observed by trial-site personnel. All personnel at the individual sites were blinded to treatment.

Health and reproductive conditions were summarized and analyzed by the following:

Animal Rate: Number of animals observed with the characteristic of interest relative to the number of animals at risk during the study period in question (an individual animal may contribute once per lactation)

Observation Rate: Number of days observed with the characteristic of interest relative to the number of days at risk

Incident Rate: Number of incidents for the characteristic of interest relative to the number of days at risk (individual animal may contribute a number of incidents)

Average Case Duration: Mean number of days that incidents persisted for the characteristic of interest

Occurrence of clinical mastitis (CM) was monitored on all cows throughout the study. A CM case was defined as an observation of abnormal milk and/or an abnormal mammary gland by trial personnel at a scheduled milking, or during an examination or observation period. Clinical mastitis was expressed as quarter rates (quarters with at least one case of CM per quarters at risk) as well as animal rate, incident rate (number CM per 1,000 quarter-days at risk) and average case duration. Clinical mastitis was also monitored by observation rate (number of days observed with CM per quarter-days at risk).

Quarter milk samples were collected for bacteriological culture during both lactations at the three second-lactation sites. Quarter samples were collected at specific events (e.g., calving and dry-off or removal) and the end of study. A second set of samples was collected at 56-day intervals throughout the lactation periods. Milk samples were collected weekly and submitted for determination of milk composition and of somatic cell count (SCC) during lactation 1 at all sites and to 200 DIM at the three second-lactation sites.

Statistical Analysis

This study was a randomized complete-block design. Each Rumensin treatment was compared to control in a pair-wise comparison with a statistical difference considered for health and reproductive parameters if $P \leq .10$. A parity-by-treatment interaction was considered significant if $P < .25$. If a significant parity-by-treatment interaction was determined, individual parity comparisons were examined. A dose-related linear trend was considered if a linear trend test was $P \leq .10$.

Table 1. Estrous Activity for Cows in Lactation 1

Variable	Rumensin (g/ton)				Industry Goal ¹⁰
	0	7	15	22	
Number of cows (50 DIM*)	218	211	219	221	
Days to first-observed standing estrus	74.5	73.8	68.6	73.0	
Days to first service	84.1	84.7	86.9	83.6	<80

*50-day voluntary wait period

Results

Reproductive Performance

All measures of reproductive efficiency of cows in the four treatment groups compared favorably with industry standards¹⁰.

Estrous activity was measured on 869 cows entering the breeding period (50 DIM) during Lactation 1. Days to first-observed standing estrus and days to first service were not different between any of the Rumensin treatment groups and controls (Table 1).

Eight hundred fifty-one cows were inseminated. First-service conception rate was reduced and days open were increased ($P \leq .05$) relative to controls at the highest (22 g/ton) level of Rumensin in the first lactation. Services per conception tended to be higher, and overall conception rates tended to be lower in Rumensin-supplemented cows. However, the rates at which eligible cows became pregnant (average 21-day pregnancy rates) ranged from 19.2 to 21.5, and were not different

($P > .10$) between treated and control cows. Pregnancy rates achieved in the study were considered to be good compared to industry standards (Table 2).

There were no differences in the percent of cows entering the breeding period that ultimately calved following a normal, full-length gestation (percent calving) or the multiple-birth rate following lactation 1.

Gestation length was normal and not different between treated animals and controls.

Birth weights of calves were heavier ($P \leq .10$) for calves born to Rumensin-treated cows (Table 3). The difference in birth weight was observed in female but not male calves.

Birth weights were within the anticipated range for Holstein calves. Differences in birth weights failed to produce any effect on calving-ease scores between treated and control animals.

Table 2. Breeding Efficiency in Lactation 1

Variable	Rumensin (g/ton)				Industry Goal ¹⁰
	0	7	15	22	
Cows inseminated	213	209	213	216	
Services per conception (all cows)	2.43	2.52	2.71	2.77	
Services per conception (pregnant cows)	1.79	1.90	1.75	1.97	≤ 2
First-service conception rate (%)	49.1	41.6	44.5	36.4 ^a	50
Overall conception rate (%)	42.8	41.4	40.0	37.6	50
Days open	99.8	104.6	100.4	107.7 ^a	85–115
Percent calving*	64.6	63.1	62.0	68.6	65–70
21-day pregnancy rate**	21.5	20.3	18.7	19.2	18–22

^a $P \leq .05$ compared to control

* Percent cows eligible for breeding that calved following a normal, full gestation

** Data on file

Table 3. Birth Ratio and Weights of Calves Born to Cows at the Completion of Lactation 1

Variable	Rumensin (g/ton)			
	0	7	15	22
Male:Female	52:48	47:53	52:48	53:47
All calves weight (lbs) ^b	94.8	97.7 ^a	97.2 ^a	97.4 ^a
Female calf weight (lbs) ^b	88.8	92.6 ^a	93.3 ^a	94.8 ^a
Male calf weight (lbs)	100.5	102.7	101.2	99.9

^aP≤.10 compared to control
^bP≤.10 for linear dose trend

Table 4. Animal Rate for Retained Fetal Membranes (RFM) in Lactations 1 and 2

Variable	Rumensin (g/ton)				Industry Goal ¹⁰
	0	7	15	22	
Lactation 1¹					
Number observed	32	36	37	25	
Animal rate	11.1	13.3	12.3	8.7	<8
Lactation 2^{1a*}					
Number observed	21	30	42	25	
Animal rate	10.0	18.0 ^a	22.6 ^a	12.2	<8

*Lactation 2a – Calving 2 to 7-9 DIM (9 sites)
^aP≤.10 compared to control
¹Lactations 1 and 2 on trial, not parity of the animals

Reproduction Conditions

There was no difference in the retained fetal membrane rate between treated and control animals in Lactation 1, but cows receiving rations containing 7 and 15 g/ton Rumensin had a higher (P≤.10) rate in Lactation 2. The RFM rate was not different from controls in the high (22 g/ton) Rumensin-dose group, so there was no dose-related trend for this condition (Table 4). The inci-

dence of other reproductive-tract conditions was not different between treated cows and controls in Lactation 2.

There was a linear trend (P≤.10) for an increase in the animal rate for metritis during Lactation 1. This trend was not observed in Lactation 2, but the number of observations in Lactation 2 was low (8–12 per treatment) (Table 5).

Table 5. Animal Rate for Metritis in Lactations 1 and 2

Variable	Rumensin (g/ton)				Industry Goal ¹⁰
	0	7	15	22	
Lactation 1¹					
Number observed	38	50	60	57	
Animal rate ^b	14.9	20.8	23.7 ^a	22.6	≤10
Lactation 2^{1b**}					
Number observed	8	9	12	9	
Animal rate	12.7	14.1	20.0	14.5	≤10

**Lactation 2b – Calving 2 to ~200 DIM (3 sites)
^aP≤.10 compared to control
^bP≤.10 for linear dose trend
¹Lactations 1 and 2 on trial, not parity of the animals

Table 6. Animal Rate for Cystic Ovarian Disease in Lactation 1

Variable	Rumensin (g/ton)				Industry Goal ¹⁰
	0	7	15	22	
Number primiparous observed	6	8	13	15	
Animal rate ^b	6.1	7.3	13.3 ^a	14.7 ^a	≤10
Number multiparous observed	22	21	23	24	
Animal rate	12.9	11.6	13.0	13.6	≤10

^aP≤.10 compared to control
^bP≤.10 for linear dose trend

Table 7. Animal Rate for Cystic Ovarian Disease in Lactation 2*

Variable	Rumensin (g/ton)				Industry Goal ¹⁰
	0	7	15	22	
Number observed	12	5	10	9	
Animal rate	19.0	7.8	16.7	14.5	<10

*Calving 2 to ~200 DIM (3 sites)

There was a dose-related trend ($P \leq .10$) for a higher animal rate for cystic ovarian disease (COD) as determined by rectal palpation in Lactation 1. There was also a significant parity-by-treatment interaction for COD in Lactation 1. Individual parity analysis indicated no difference in the animal rate in multiparous animals, but a significant linear trend for a higher animal rate in primiparous animals. The number of animals with COD in the primiparous group was 6, 8, 13 and 15 animals observed in the 0, 7, 15 and 22 g/ton treatment groups, respectively (Table 6).

There was no difference in the animal rate for COD in Lactation 2, but the total number of animals diagnosed with COD in Lactation 2 was insufficient for an accurate evaluation of this condition (Table 7).

Udder Health

Clinical Mastitis

There was no difference in the rates (animal, quarter, incidence or observation) or the average duration of clinical mastitis cases during Lactation 1. The microorganisms cultured from clinical cases were classified as environmental pathogens (primarily coliforms and environmental streptococci), contagious pathogens (*Staphylococcus aureus* and *Streptococcus agalactiae*), coagulase-neg-

ative staphylococci (CNS), others and negative (no growth). Most clinical cases during Lactation 1 were caused by environmental pathogens. There was no difference in the pathogens isolated across treatment groups in Lactation 1.

There was no difference in the clinical mastitis rates between Rumensin-treated and control animals in Lactation 2. There was a linear dose trend for a shorter ($P \leq .10$) duration of clinical cases during Lactation 2, but this observation was not considered clinically relevant. During Lactation 2, CNS was the most common pathogen group isolated from clinical cases. The relative incidence of CNS was higher in Lactation 2 than in Lactation 1.

Subclinical Mastitis

During the study, 15,370 routine quarter milk samples were collected from cows at the three two-lactation sites. Results for samples were reported by animal and quarter. Prevalence of infection was higher in multiparous cows compared to primiparous cows in Lactation 1. There were no differences in animal rate, quarter rate, incident rate or average case duration during Lactations 1 or 2 between any treatment level and control. During Lactation 2 the observation rate was lower ($P \leq .10$) in the 22 g/ton group compared to control.

Table 8. Animal Survival Rates in Lactations 1 and 2

Animal Survival at:	Rumensin (g/ton)			
	0	7	15	22
Treatment start to 7 DIM Lactation 1 ¹ , %	96.7	98.1	99.0 ^a	99.0 ^a
Treatment start to dry-off Lactation 1 ¹ , %	78.2	78.7	80.4	81.1
Treatment start to 7 DIM Lactation 2 ¹ (9 sites), %	64.1	62.1	61.0	68.0
Treatment start to 200 DIM Lactation 2 (3 sites), %	63.4	66.5	55.6	66.8

^aP≤.10 compared to control

¹Lactations 1 and 2 on trial, not parity of the animals

Somatic Cell Count

Somatic cell counts were low in all treatment groups, averaging less than 100,000 cells/mL. During Lactation 1, SCCs were similar for the control and the 15 and 22 g/ton groups. Average SCC was higher (P=.08) in the 7 g/ton Rumensin group than controls. There was no dose-related trend for higher SCC with Rumensin levels.

During Lactation 2, SCCs were similar for all groups. Cell counts tended to be lower in the 22 g/ton Rumensin group than other groups in the first 15 weeks of lactation, but were similar to other groups later in lactation.

Animal Survival

Animal survival, or the rate of involuntary removal from the trial, was measured for four time periods relative to treatment start. There was no difference between the animal-survival rates for control and treated animals for all periods measured, except for the treatment start to 7 DIM in Lactation 1. In this comparison, cows in the 15 and 22 g/ton treatment groups had higher (P≤.10) survival compared to control (Table 8).

There was no indication of a relationship between the feeding of Rumensin and any of the udder-health parameters monitored in the study.

Conclusions

The potential impact of any new technology on reproduction, health and milk quality are important considerations to dairy production. Technologies that increase milk production, especially early in lactation, should be scrutinized as

to their relative impact on energy balance in the dairy cow.

Excessive negative energy balance has been shown to decrease reproductive performance and increase the incidence or severity of some disease conditions. Duffield et al.¹¹ suggested that improved energy balance prior to calving is important in preventing energy-associated metabolic diseases such as clinical ketosis, retained placenta and left displaced abomasum (LDA). Rumensin provides additional energy from the ration by altering ruminal fermentation such that more propionate is produced relative to other volatile fatty acids (VFA). This mechanism should be particularly beneficial in early lactation when the dairy cow is in negative energy balance.

The incidence of some reproductive health conditions such as metritis, cystic ovaries and RFM were increased in some Rumensin treatment groups compared to controls. Additionally, some reproductive parameters such as services per conception, days open and calving interval were increased, and first-service conception rate was reduced in the 22 g/ton Rumensin group compared to controls in Lactation 1. However, pregnancy rates and calving rates were not different between any of the Rumensin treatments and controls, indicating that even though additional services were needed in the 22 g/ton group, these cows eventually became pregnant within the 50 to 200 DIM breeding window. Furthermore, the rate at which animals were removed (survival rate) was not different between treated and control cows. Other studies⁷⁻⁹ showed no difference in reproductive performance in Rumensin-treated compared to control cows.

Even though fertility appeared to be reduced in Rumensin-treated cows as reflected in services per conception, first-service conception rate and days open, the overall pregnancy rate did not differ, indicating that any reduction in fertility is manageable.

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