

# Pharmacokinetics and clinical efficacy of a long-acting intramuscular Omeprazole in performance horses with gastric ulcers

**Provided for report submission to BET Pharmacy**

**L. Bass<sup>1</sup>, M. Lehman<sup>1</sup>, D. Gustafson<sup>1</sup>, S. Rao<sup>1</sup>, E. O'Fallon<sup>1</sup>**

<sup>1</sup>Department of Clinical Sciences, Colorado State University College of Veterinary Medicine and Biomedical Sciences, Fort Collins, CO

# Introduction

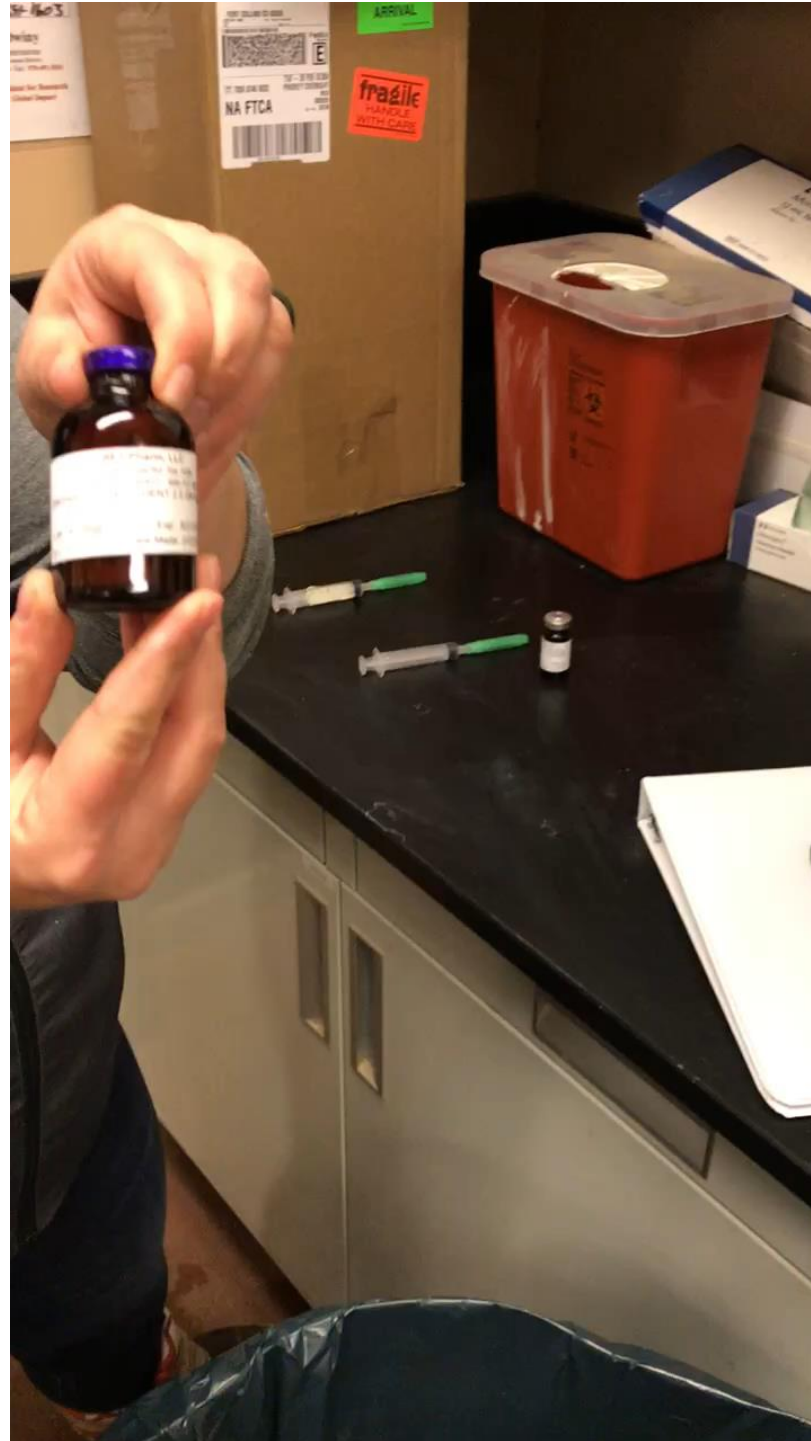
- Prevalence of Equine Gastric Ulcer Syndrome (EGUS) is high in horses, with some populations reporting prevalence of nearly 100%
- EGUS involves both squamous disease (ESGD) and glandular disease (EGGD)
- Current oral omeprazole formulation may have variable bioavailability depending on management techniques
- We seek to explore the BET long acting injectable omeprazole formulation in its safety and efficacy of treating both ESGD and EGGD as it will bypass bioavailability issues associated with feeding and management.



# Materials and Methods

- 23 horses with confirmed ESGD +/- EGGD were dosed every 7 days for 4 doses
  - Polo, English and western performance horses with the CSU Equine Sciences Program
  - Housed in dirt paddock; Fed Ad libitum grass hay diets
  - Dosed at 5 mg/kg, see following videos for reconstitution and dosing
- Recheck gastroscopy performed on Day 0, 14, and 28 to evaluate ESGD and EGGD
- Bloodwork (CBC/serum chemistry) and body weights assessed pre- and post-study
- PK study – 6/23 horses evaluated during the initial 7 day period
- Statistical analysis of efficacy data and PK analysis performed

# Drug Reconstitution



# Injection Administration



Injection site  
reactions  
were  
monitored  
daily:

- Scores were given to reactions, 0 being no inflammation, 3 being severe inflammation
- Signs of inflammation that were considered in scoring:
  - Pain
  - Heat
  - Swelling
  - Edema
  - Systemic response

# Results:

---

Gastroscopy images

---

Statistical Evaluation

---

Pharmacokinetic Data

---

Injection Site Reactions

---

Clinical Pathology/Body Weight Data

# Summary: Gastrosocopy Findings

---





**Clinical Case:** 15 year old breeding stallion not on study, but similar management and same treatment regime

Day 0 findings:

- Grade 4 ESGD seen at margo plicatus, greater and lesser curvatures
  - Grade 4 EGGD seen at ventral margin of pylorus
-



15 year old breeding stallion day 14 findings: Grade 1 ESGD, Grade 1 EGGD

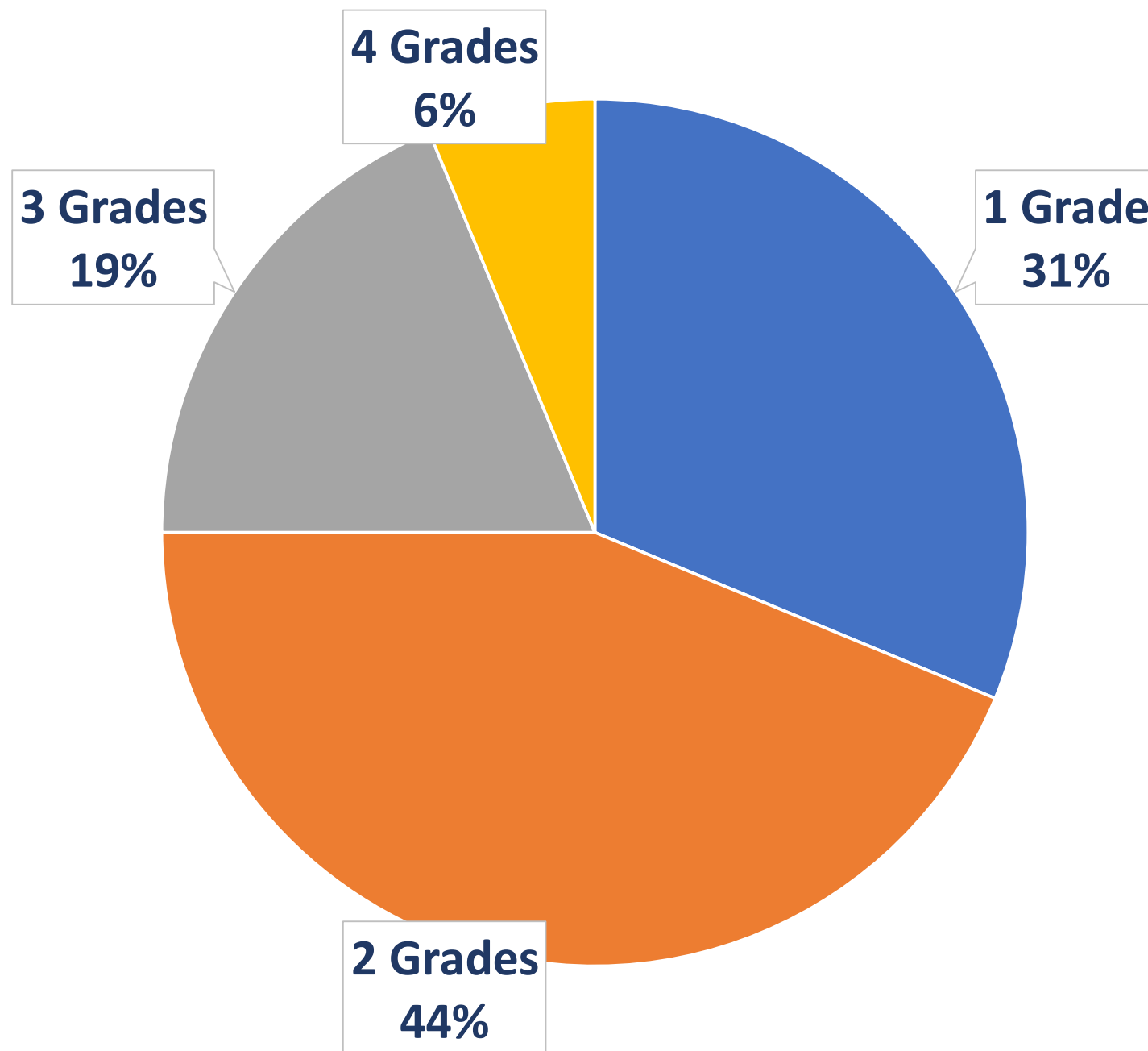
# Statistical Relevance: Gastroscopy Findings

---

## Improvement of Ulcers by Grade

78% of horses showed  
improvement in ESGD  
by Day 14, 74% by day  
28

Improvement is shown  
by how many grades  
were improved by Day  
14



# Change in Ulcer Grading from Day 0 to Day 28

ESGD*	n	Mean	Std Dev	EGGD*	n	Mean	Std Dev
Day 0	23	2.70	0.70	Day 0	21	0.38	0.67
Day 14	23	1.52	1.11	Day 14	18	0.56	0.87
Day 28	23	1.28	1.03	Day 28	23	0.26	0.62
Day 14 vs. Day 0	23	-1.17	1.28	Day 14 vs. Day 0	16	0.16	0.96
Day 28 vs. Day 0	23	-1.41	1.17	Day 28 vs. Day 0	21	-0.14	0.91

\*ESGD Grading: 0-4

\*EGGD Grading: 0-2

# Take homes: Change in Ulcer Grading

## Squamous disease:

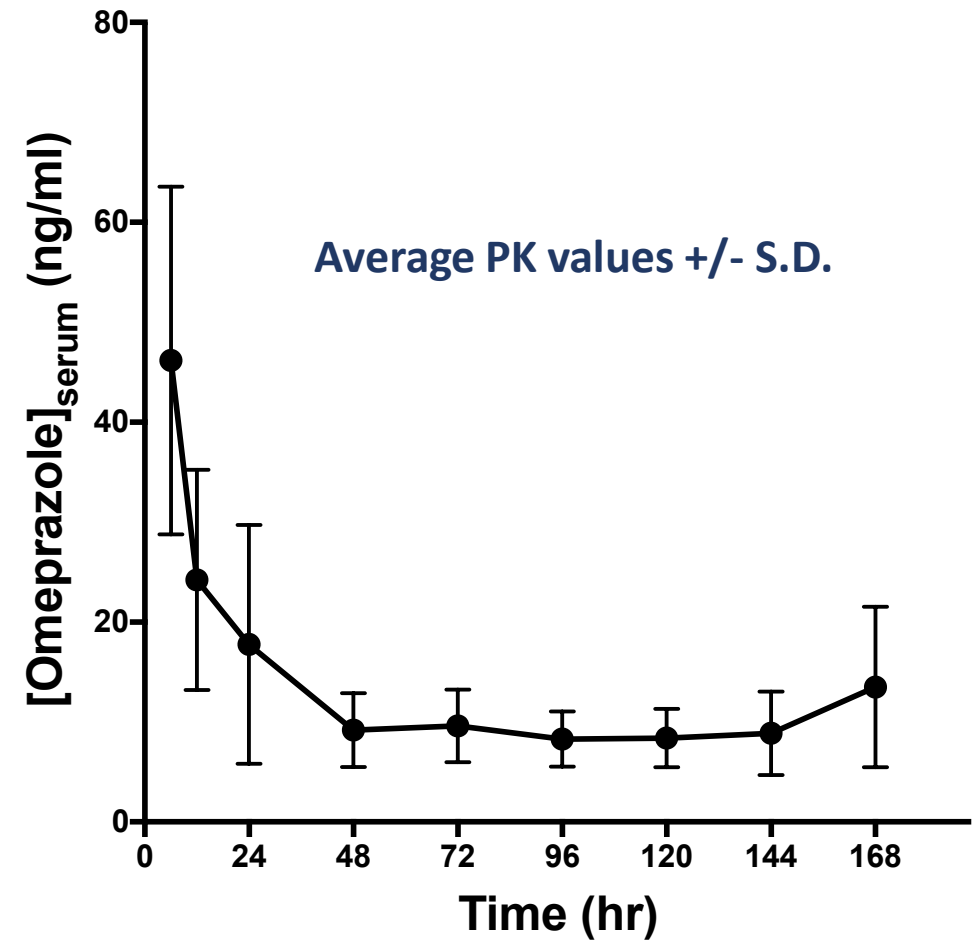
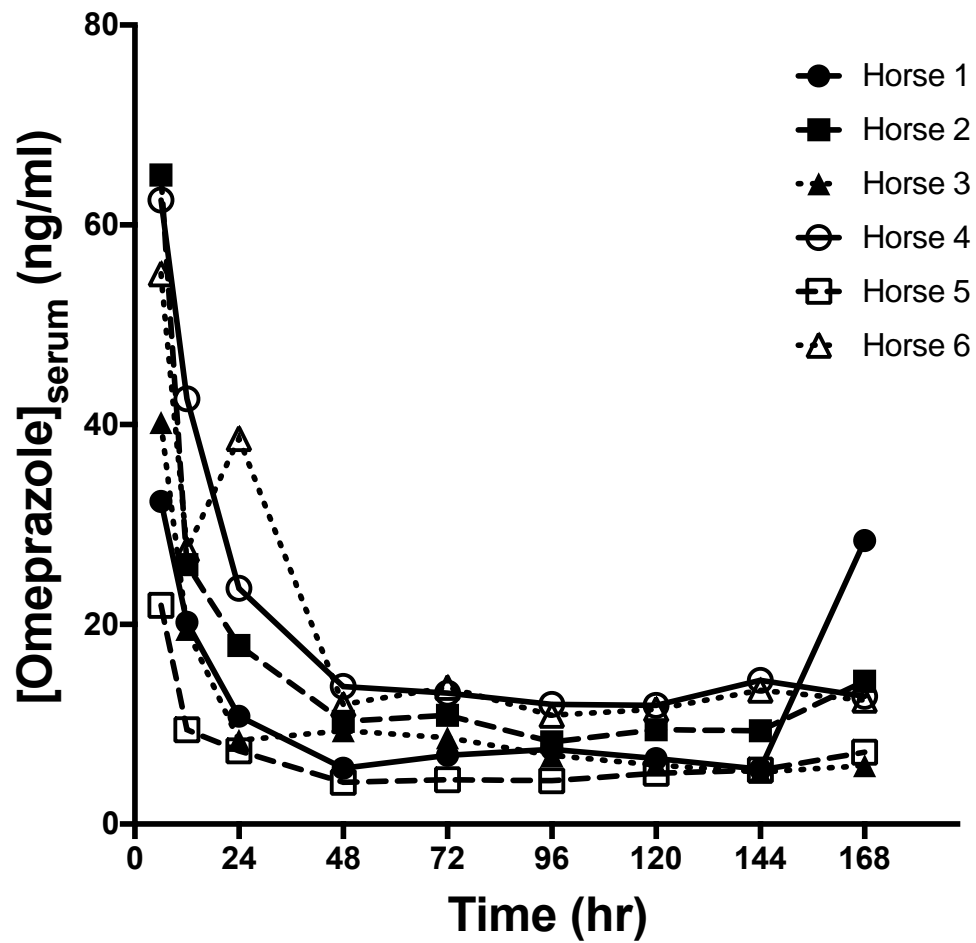
- Statistically significant decrease in grade (Avg decrease 1.17 grades) from Day 0-14
- Overall significant decrease in grade (Avg decrease 1.40 grades) from Day 0-28
- No statistically significant decrease from Day 14 to 28

## Glandular disease:

- No statistically significant change from Day 0-28

# Summary: Pharmacokinetic Data

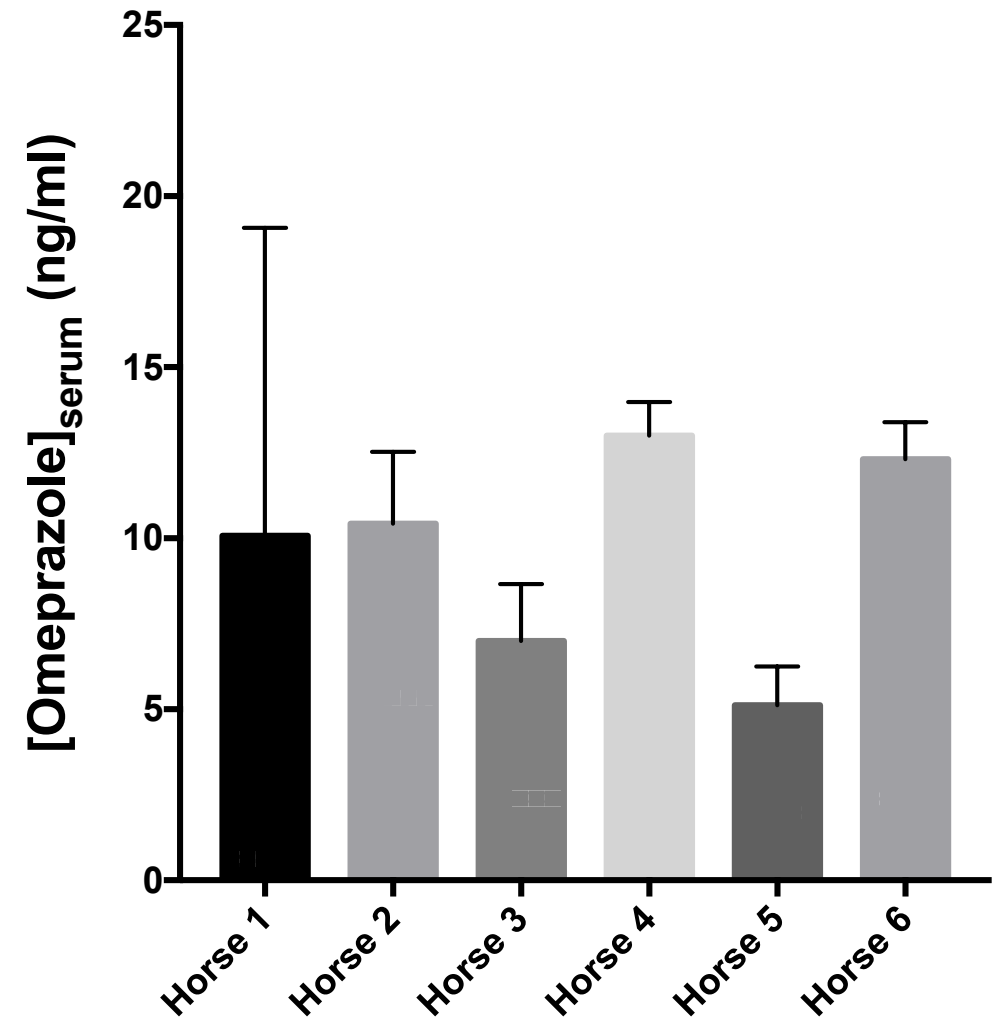
---





# PK Data Continued

- $C_{\max}$  21.9 – 65 ng/mL
- $T_{\max}$  occurred at 6 hrs
- AUC 933.7 – 2732 ng/mL\*hr
- All horses stayed above 4 ng/mL for 168 hrs
- Mean omeprazole levels following  $C_{\max}$ :
  - 9.6 mg/mL



Average serum concentrations from 48-168 hours following an initial dose. Values represent the mean +/- SD for each individual horse.

# Summary: Injection Site Reactions

---

Please note:

The number of photographs does not correlate with the number of injection site reactions. They are simply provided to provide visual documentation of the different degrees of reactions. Please refer to the data sheets for documentation of reactions.



# Injection reactions after Dose 3, same horse:



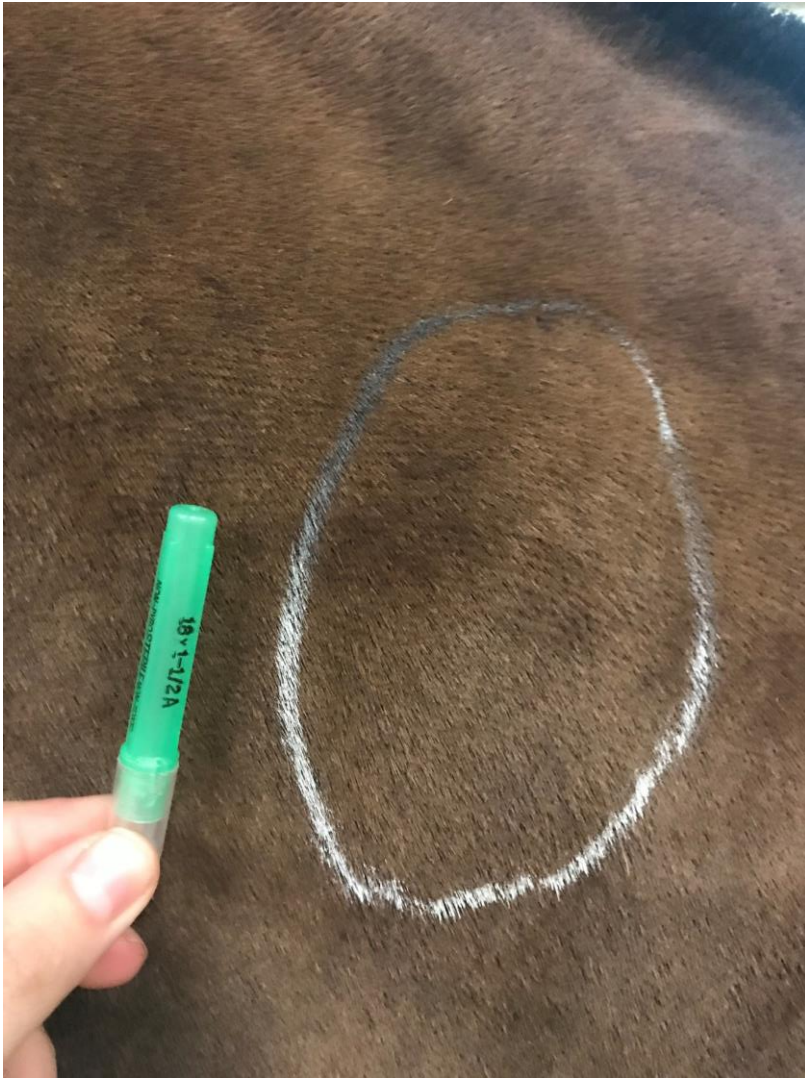
Day 1, Grade 2



Day 2, Grade 2



# Injection reactions after Dose 3, same horse:



Day 1, Grade 1



Day 2, Grade 1



# Injection reactions after Dose 4 (Day 3):



Grade 2



Grade 1



Grade 2



# Injection reactions after Dose 4, both Grade 2:



Small circles  
indicate size of  
reaction on Day 2

2 Different  
horses, 3  
days after  
injection 4





### Injection Site Monitoring Following Treatment 1 (Study Days 0-7):

	Horse	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
1	Dora	0	0	0	0	0	0	0	0
2	Lydia	0	0	0	0	0	0	0	0
3	Tammy	0	0	0	0	1	0	0	0
4	Zane	0	0	0	0	0	0	0	0
5	Frenchie	0	0	0	0	0	0	0	0
6	Capone	0	0	0	0	0	0	0	0
7	Recoletta	0	0	0	0	0	0	0	0
8	Wanda	0	0	0	0	1	0	0	0
9	Rasta	0	0	0	0	1	0	0	0
10	Bandito	0	0	0	0	0	0	0	0
11	Buoy	0	0	0	0	0	0	0	0
12	Rosie	0	0	0	0	0	0	0	0
13	Firefly	0	0	0	0	0	0	0	0
14	Cordial	0	0	0	0	0	0	0	0
15	Miss P	0	0	0	0	0	0	0	0
16	RC	0	0	0	0	0	0	0	0
17	Rayna	0	0	0	0	0	0	0	0
18	Cat's Lad	0	0	0	0	0	0	0	0
19	Playboy	0	0	0	0	0	0	0	0
20	Blue	0	0	0	0	0	0	0	0
21	Mona	0	0	0	0	0	0	0	0
22	Flip	0	0	0	0	0	0	0	0
23	Willow	0	0	0	0	0	0	0	0

\*\*Injection Site Scoring on a 0-3 Scale: 0 = no inflammation, 3 = severe inflammation



### Injection Site Monitoring Following Treatment 2 (Study Days 7-14):

	Horse	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
1	Dora	0	0	0	0	0	0	0	0
2	Lydia	0	0	0	0	0	0	0	0
3	Tammy	0	0	0	0	0	0	0	0
4	Zane	0	0	0	0	0	0	0	0
5	Frenchie	0	0	0	0	0	0	0	0
6	Capone	0	0	0	0	0	0	0	0
7	Recoletta	0	0	0	0	0	0	0	0
8	Wanda	0	0	0	0	0	0	0	0
9	Rasta	0	0	0	0	0	0	0	0
10	Bandito	0	0	0	0	0	0	0	0
11	Buoy	0	0	0	0	0	0	0	0
12	Rosie	0	0	0	0	0	0	0	0
13	Firefly	0	0	0	0	0	0	0	0
14	Cordial	0	0	0	0	0	0	0	0
15	Miss P	0	0	0	0	0	0	0	0
16	RC	0	0	1	1	0	0	0	0
17	Rayna	0	0	1	1	1	0	0	0
18	Cat's Lad	0	0	0	0	0	0	0	0
19	Playboy	0	0	0	0	0	0	0	0
20	Blue	0	0	0	1	0	0	0	0
21	Mona	0	0	0	0	0	0	0	0
22	Flip	0	0	0	0	0	0	0	0
23	Willow	0	0	0	0	0	0	0	0

\*\*Injection Site Scoring on a 0-3 Scale: 0 = no inflammation, 3 = severe inflammation

### Injection Site Monitoring Following Treatment 3 (Study Days 14-21):

	Horse	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
1	Dora	0	0	0	0	0	0	0	0
2	Lydia	0	1	0	0	0	0	0	0
3	Tammy	0	2	2	2	1	1	0	0
4	Zane	0	0	0	0	0	0	0	0
5	Frenchie	0	0	0	0	0	0	0	0
6	Capone	0	0	0	0	0	0	0	0
7	Recoletta	0	0	0	0	0	0	0	0
8	Wanda	0	1	1	0	0	0	0	0
9	Rasta	0	0	0	0	0	0	0	0
10	Bandito	0	0	0	0	0	0	0	0
11	Buoy	0	0	0	0	0	0	0	0
12	Rosie	0	0	0	0	0	0	0	0
13	Firefly	0	0	0	0	0	0	0	0
14	Cordial	0	0	0	0	0	0	0	0
15	Miss P	0	0	0	0	0	0	0	0
16	RC	0	0	0	0	0	0	0	0
17	Rayna	0	2	2	1	1	0	0	0
18	Cat's Lad	0	0	0	0	0	0	0	0
19	Playboy	0	0	0	0	0	0	0	0
20	Blue	0	0	0	0	0	0	0	0
21	Mona	0	0	0	0	0	0	0	0
22	Flip	0	0	1	1	1	0	0	0
23	Willow	0	0	0	0	0	0	0	0

\*\*Injection Site Scoring on a 0-3 Scale: 0 = no inflammation, 3 = severe inflammation

### Injection Site Monitoring Following Treatment 4 (Study Days 21-28):

	Horse	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
1	Dora	0	0	0	0	0	0	0	0
2	Lydia	0	0	0	0	0	0	0	0
3	Tammy	0	0	2	2	2	1	0	0
4	Zane	0	0	0	0	0	0	0	0
5	Frenchie	0	0	0	0	0	0	0	0
6	Capone	0	0	0	0	0	0	0	0
7	Recoletta	0	0	0	0	0	0	0	0
8	Wanda	0	0	2	0	0	0	0	0
9	Rasta	0	0	0	0	0	0	0	0
10	Bandito	0	0	0	0	0	0	0	0
11	Buoy	0	0	1	0	0	0	0	0
12	Rosie	0	0	2	2	2	1	0	0
13	Firefly	0	0	1	2	1	1	1	0
14	Cordial	0	0	0	0	0	0	0	0
15	Miss P	0	0	0	0	0	0	0	0
16	RC	0	0	2	2	1	1	1	1
17	Rayna	0	1	2	2	2	1	0	0
18	Cat's Lad	0	0	0	1	0	0	0	0
19	Playboy	0	0	0	1	0	0	0	0
20	Blue	0	0	0	1	0	0	0	0
21	Mona	0	0	0	0	0	0	0	0
22	Flip	0	0	1	2	0	0	0	0
23	Willow	0	0	0	0	0	0	0	0

\*\*Injection Site Scoring on a 0-3 Scale: 0 = no inflammation, 3 = severe inflammation

# Clinical Pathology Data

---

CBC Changes:  
No clinically  
significant  
changes

---

Value	Mean change	St Dev	P-value
Hgb	-2.58 ↓	1.82	<0.0001
Hgb cell	-2.71 ↓	1.66	<0.0001
<b>HCT</b>	<b>-10.00 ↓</b>	<b>6.07</b>	<b>&lt;0.0001</b>
RBC	-1.52 ↓	0.92	<0.0001
MCV	-2.43 ↓	1.25	<0.0001
RDW	-0.46 ↓	0.76	<0.0122
MCHC	1.76 ↑	1.04	<0.0001
CHCM	1.62 ↑	0.87	<0.0001
Nucleated cells	-1.95 ↓	0.99	<0.0001
Neutrophils	-0.98 ↓	0.92	<0.0001
Lymphocytes	-0.69 ↓	0.46	<0.0001
Monocytes	-0.08 ↓	0.10	0.0039
Basophils	-0.09 ↓	0.09	0.0004

Biochemistry  
Changes:  
No clinically  
significant  
changes

---

Value	Mean change	St Dev	P-value
Triglycerides	11.17↑	25.34	0.0327
Glucose	5.70↑	8.69	0.0047
BUN	-1.78↓	2.78	0.0055
P	1.30↑	1.31	0.0001
Ca	-1.06↓	0.37	<0.0001
Mg	-0.44↓	0.26	<0.0001
TP	0.26↑	0.32	0.0007
Alb	-0.15↓	0.17	0.0005
Glob	0.41↑	0.27	<0.0001
A:G Ratio	-0.14↓	0.08	<0.0001
T bili	1.31↑	0.56	<0.0001
AST	-128.80↓	503.49	0.0058
SDH	2.04↑	1.87	<0.0001
Na	-1.57↓	2.27	<0.0032
K	-0.95↓	0.90	<0.0001
HCO3	-1.54↓	2.21	0.0028
Anion Gap	-1.48↓	1.53	0.0001

## Summary: Body Weight Data

- Significant decrease of 20.9 kgs from Day 0 to Day 28
  - 3.8% decrease

## Discussion: Ulcer Grades

- Did see 1+ grade improvement with squamous ulcers
- The most significant decrease occurred day 0-14 with no significant change with the following doses
- No significant change in EGGD, however only 6 of 23 horses began the study with glandular disease, so the sample size for showing improvement of EGGD is small



# Discussion Continued

## PK Data

- All horses maintained omeprazole levels above 4 ng/mL for 7 days
- PK  $C_{max}$  values are within the reported PK values following GastroGard® administration, however maintained on lower than  $C_{max}$  levels for the 7 days following the  $C_{max}$

## Injection site reactions

- Reactions ranged from mild swelling and edema to moderate swelling, edema and pain
- Most significant reactions occurred following doses 3 and 4
- Horses were vaccinated in the opposite side of the neck on the same day as dose 4, unknown what contribution this has to the injection site reactions

## Discussion Continued

---

No clinically relevant changes to  
hematological parameters

---

Decrease in body weight seen may  
be due to change in exercise  
regimen, further study is needed  
here

## Conclusions

- Formulation is convenient in dosing and bypasses bioavailability variability seen with oral products
- Provides consistent levels of omeprazole for seven days
- Safe, effective drug for management of ESGD
  - Improve ESGD Grading by at least 1 grade
  - More data needed to determine any significant effects on EGGD
- Consider dosing for 2 doses instead of 4 as clinical efficacy may be reached by this point
  - Minimize injection site reactions by avoiding the 3<sup>rd</sup> and 4<sup>th</sup> doses?
- Some horses may be more “sensitive” to the injections than others
  - Manage owner expectations prior to dosing