AASV Foundation – First Quarterly Report

Title:

• Investigating the plasma pharmacokinetics and tissue residues of oral firocoxib following transmammary delivery from sows to piglets.

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Statement of problem:

• In the US, no drugs are currently labeled by the Food and Drug Administration (FDA) to alleviate pain in swine. Therefore, the development of pain mitigation strategies that address consumer concerns about animal welfare while still being safe, effective, practical and economical to administer are urgently needed for the swine industry to address emerging animal welfare challenges. In a recent study evaluating a transmammary route of administration for firocoxib, we reported a significant reduction in plasma cortisol concentrations and an increase in average daily gain in bodyweight (ADG) from processing to weaning in piglets nursing sows that received 2 mg/kg IM of firocoxib. However, this required intramuscular injection volumes of 20 to 30 mL of firocoxib. This dose volume may be inconvenient for caregivers to administer in many commercial pork production systems. Furthermore, this could potentially create challenges in regards to compliance with Pork Quality Assurance (PQA) standards, specifically due to muscle damage and the potential for broken injection needles. Therefore, we are proposing to investigate the pharmacokinetics of oral firocoxib in sows. The pharmacokinetic data can then be used to further optimize an oral dose of firocoxib intended for transmammary delivery to piglets.

Objective(s):

- Describe the pharmacokinetics (PK) of oral firocoxib in sows.
- Describe the tissue residue concentrations of firocoxib in sows following oral administration.

Brief materials and methods:

• Seven sows will be enrolled onto the study. The study will be conducted in two phases with a 28 day washout period between the IV dosing of 0.5 mg/kg in phase 1, and oral dosing of 4 mg/kg in phase 2. Whole blood will be obtained at predetermined time points for plasma firocoxib determination. Following oral firocoxib administration at 4 mg/kg, sows will humanely euthanized and tissue samples collected for firocoxib concentrations. Plasma and tissue firocoxib concentrations will be determined using a validated LC-MS method developed and published by our research group. The pharmacokinetics of firocoxib in sows following IV and oral dosing will be determined via non-compartmental analysis using commercial computer software. Bioavailability will be dose adjusted by multiplying the AUC after oral administration with the IV dose and dividing this by the AUC after IV administration multiplied by the oral dose. Tissue residue data will be analyzed using a regression analysis in R-software.

Significant results: *No results to report at this point in the study.*
• Progress: Study protocol is finalized.
• Plasma samples from 7 sows given IV and oral firocoxib have been obtained and are awaiting analysis.
• Tissues from firocoxib treated sows (4 mg/kg PO) have been collected for tissue firocoxib analysis as well as histopathology for indication of toxicity. Tissue samples have not been analyzed.

Discussion of how results can be applied by practitioners: *No results to report at this point in the study.*
• Expected outcome: We expect to determine the oral bioavailability of firocoxib administered at 4 mg/kg. This data will be compared to our previous work describing the pharmacokinetics of firocoxib in sows following a single IM dose of 0,5; 1.0; 1.5 and 2 mg/kg. Tissue concentrations will be used to estimate a tissue withhold period for oral administration of firocoxib.