

# Potent Antiemetic Effect of GIP Analogue ZP6590 in ferrets, a gold standard model for emesis testing



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## AIM

- The aim of the study was to investigate the anti-emetic effects of the long-acting GIP analogue ZP6590 in morphine and PYY3-36 induced emesis in ferrets

## CONCLUSIONS

- ZP6590 has potent anti-emetic effects in an emesis model in ferrets utilizing two potent inducers of vomiting
- ZP6590 is a long-acting GIP analogue with potential for once-weekly dosing
- These data support the study of ZP6590 as a potential combination partner to other anorectic treatments that have demonstrated GI adverse affect (such as GLP-1) to alleviate these side-effects and ideally enhance dosing

## INTRODUCTION

- Glucose-dependent Insulinotropic Polypeptide (GIP) has potent incretin activity.
- GIP was recently shown to have anti-emetic effects in models of GLP-1 induced emesis in the musk shrew (Geisler C et al 2020).
- ZP6590 is a long-acting GIP analogue designed to allow for co-formulation with other peptides.
- More recently, GIP has been recently shown to attenuate PYY-induced nausea-like behavior in mice (Samms et al 2022).

## METHODS

- Ferrets (n=8/group) were dosed with ZP6590 at 10, 30, 100 or 300 nmol/kg. After 1 or 4 hours, emesis was induced by dosing animals with 3 mg/kg morphine or 100 nmol/kg PYY3-36. Animals were observed for 2 hours and number of vomits, retches and vomiting episodes were reported.

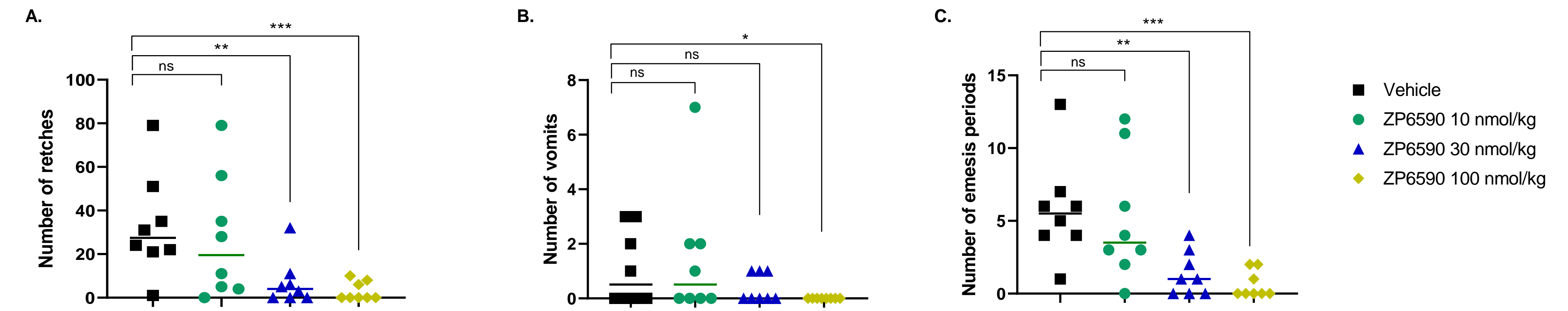
## RESULTS

ZP6590 is a long-acting molecule in ferrets with slow absorption following sc administration

	Dose (nmol/kg)	SC parameters	
		T <sub>1/2</sub> (h, Mean)	T <sub>max</sub> (h, Median)
ZP6590	50	24	24

Table 1: Pharmacokinetics of ZP6590 in ferrets (n=2)

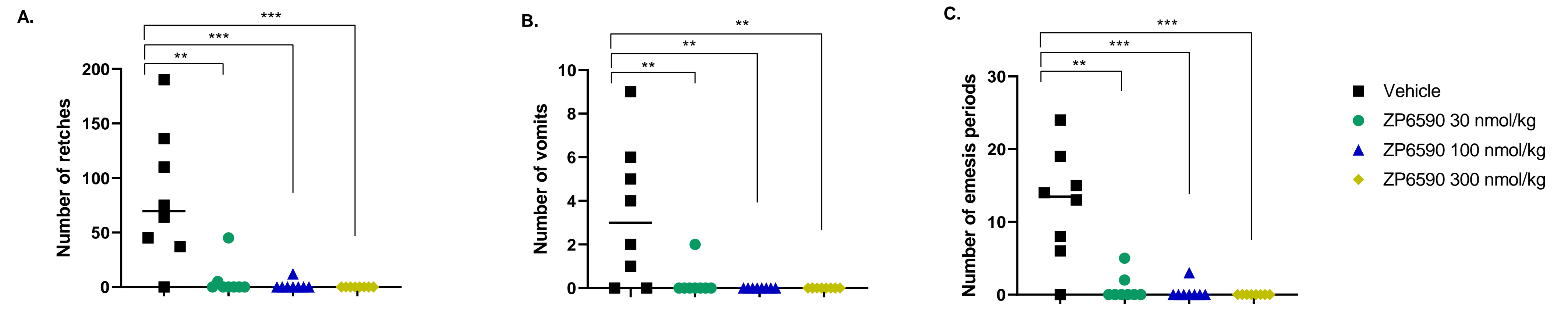
## RESULTS - Effect of ZP6590 on morphine-induced emesis.



Data are median values (n= 8/group). Data were compared by Mann-Whitney test. Statistics: comparison vs. vehicle group, Mann-Whitney test, \*p<0.05, \*\*p<0.01, \*\*\*p<0.001, ns=not significant

Figure 1: Number of retches (A), number of vomits (B) and number or emesis episodes (C)

## RESULTS - Effect of ZP6590 on PYY3-36-induced emesis.



Data are median values (n= 8/group). Data were compared by Mann-Whitney test. Statistics: comparison vs. vehicle group, Mann-Whitney test \*\*p<0.01, \*\*\*p<0.001.

Figure 2: Number of retches (A), number of vomits (B) and number or emesis episodes (C)

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