

Pharmacokinetics of a long-acting GLP-1 receptor agonist in minipigs

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Background & Aim

Minipigs are increasingly applied in preclinical drug safety testing and for prediction of human pharmacokinetics (PK). Also, studies in minipigs are most cost-effective and have fewer ethical implications as compared to non-human primates.

The present study evaluated the PK of a proprietary, long-acting GLP-1 receptor agonist in minipigs to enable dose prediction in humans.

Methods

See study outline. Female minipigs (n=3/group, 28-30 weeks of age and 14 kg at study start) were housed in Gubra's controlled minipig environment with tap water *ad libitum* and standard minipig diet (Altromin) being available twice a day.

Minipigs were dosed with the long-acting GLP-1 receptor agonist GUB021794 (2 nmol/kg), administered either as slow intravenously infusion (1 ml/kg, 5 min), or subcutaneous bolus (0.25 ml/kg).

Blood samples were collected from v. jugularis for up to 16 days post-dosing. Plasma samples were analysed using LC-MS/MS and PK parameters were estimated by non-compartmental analysis (NCA).

1 Study outline



3 PK profile

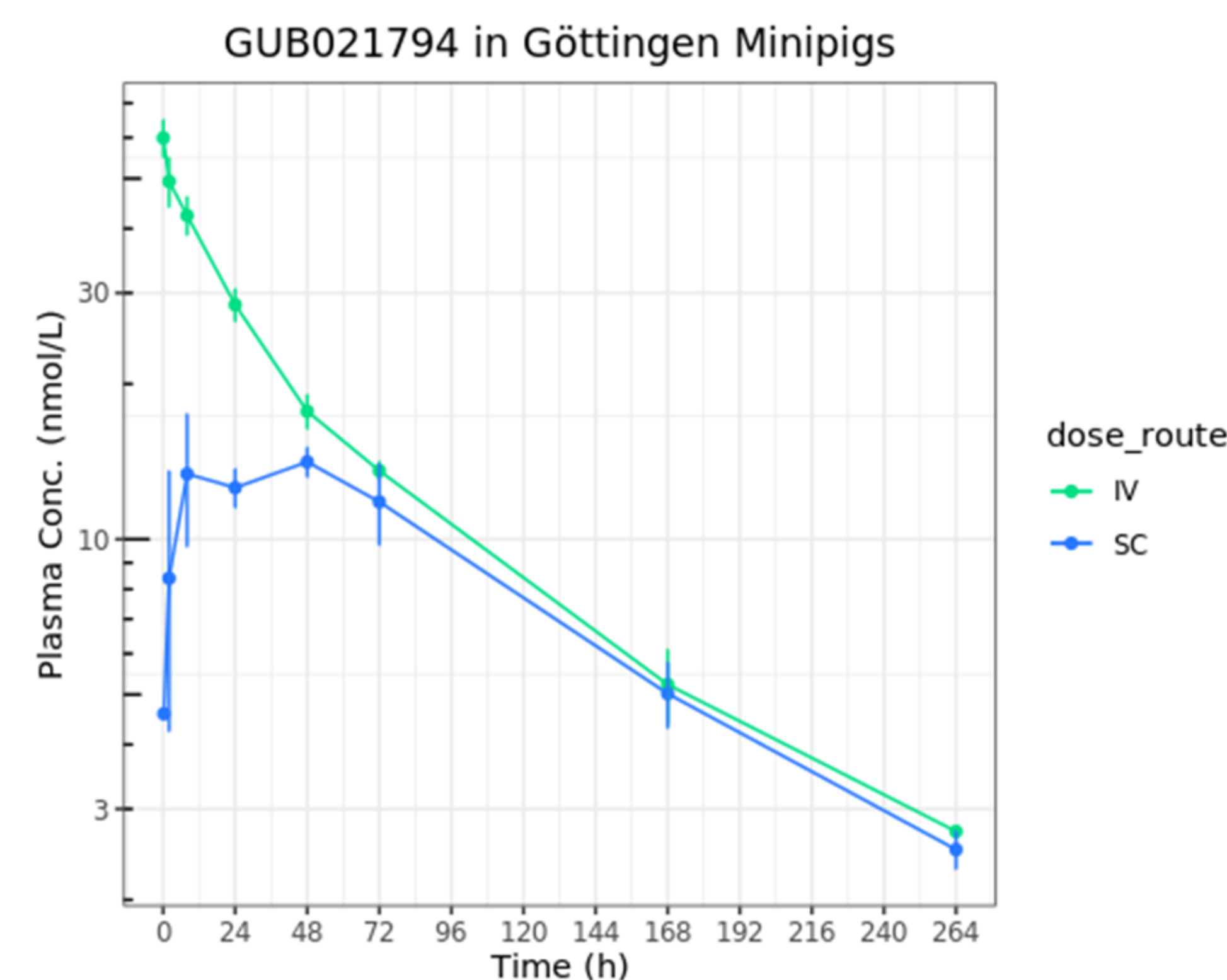


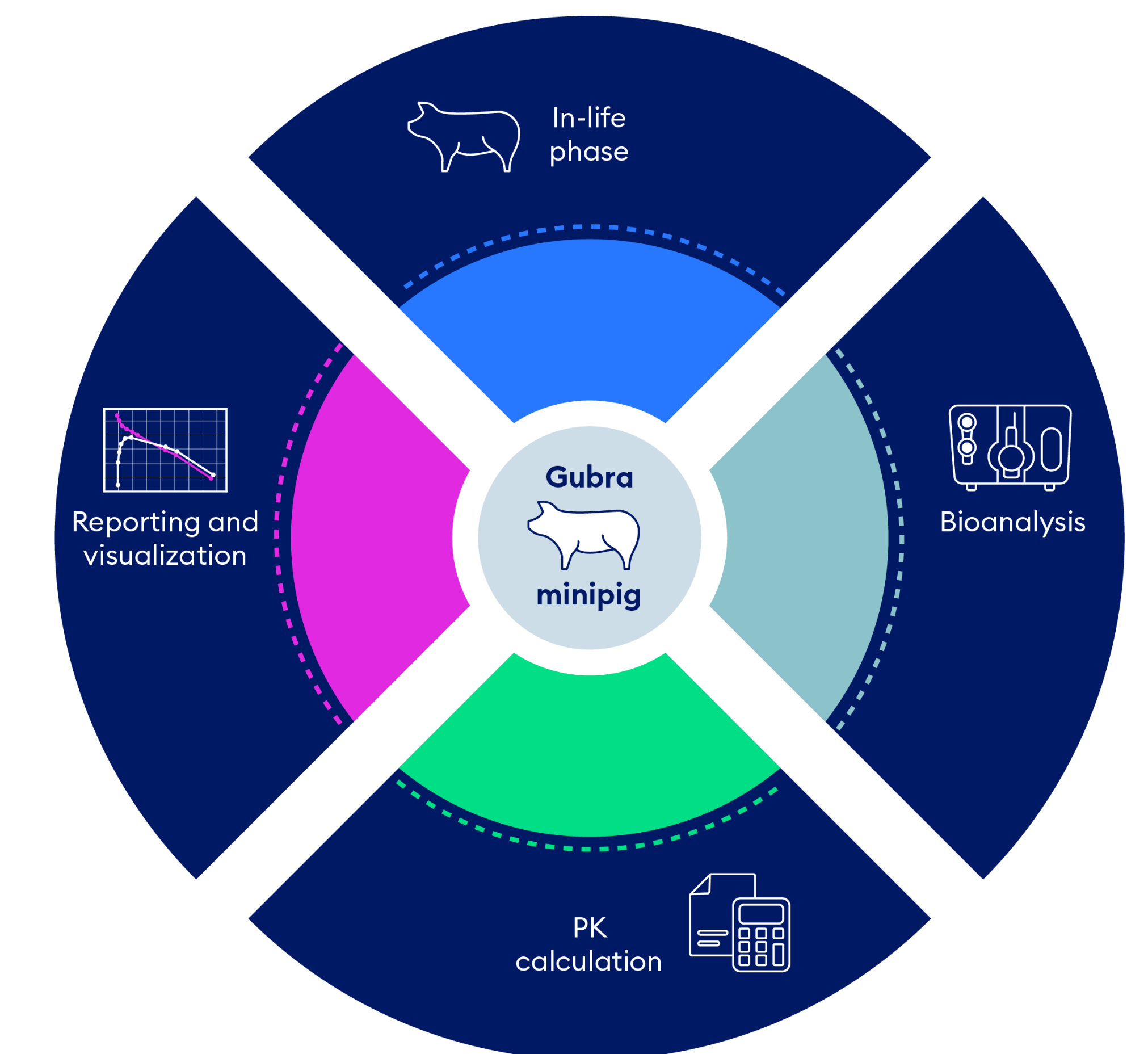
Figure 1. PK profile in minipigs of Gubra's long-acting GLP-1 receptor agonist GUB021794 after a 5 min intravenous infusion or subcutaneous injection (2 nmol/kg, n=3). Each data point represents the geometric mean, and the error bars represent the geometric standard deviation.

4 PK parameters

Parameter	Unit	GUB021794	
		IV infusion (5min)	SC bolus
Nominal Dose	nmol/kg	2	2
AUC _{inf}	nmol.h/L	3230	2330
AUC _{last}	nmol.h/L	2830	1900
%AUC _{extrapolated}	%	13	18
T _{last}	h	200	232
C _{max}	nmol/L	59	14.9
T _{max}	h	0.083	35
Cl	L/h/kg	0.00062	-
V _{ss}	L/kg	0.055	-
t _{1/2}	h	71	86
MRT	h	90	135
F	%	-	72

Figure 2. Calculated PK parameters in minipigs obtained by non-compartmental analysis. Abbreviations: AUC_{inf}, area-under-the-curve from time of dosing extrapolated to infinity; %AUC_{extrapolated}, percentage of the AUC being extrapolated; AUC_{last}, area-under-the-curve from time of dosing to last measurable concentration; C_{max}, highest measured concentration; Cl, total body clearance of the drug; F, calculated bioavailability of the SC route; MRT, mean residence time; T_{last}, timepoint of the last measurable concentration; T_{max}, time to maximum concentration; V_{ss}, volume of distribution at steady-state; T_{1/2}, terminal half-life.

2 Gubra workflow and capabilities



Conclusion

- + Pharmacokinetics of long-acting GLP-1 receptor agonist (GUB021794) was successfully evaluated in minipigs
- + The long-acting GLP-1 receptor agonist is applicable for once-weekly dosing in humans
- + Minipigs represent a suitable non-rodent species for clinical translation of peptide drug pharmacokinetics



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