The neonatal Göttingen Minipig as translational model for perinatal asphyxia and therapeutic hypothermia

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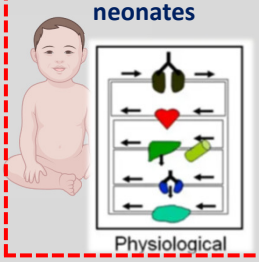
Introduction

Perinatal asphyxia (PA)

Therapeutic Hypothermia (TH): cooling core body temperature (T°) at 33.5°C for 72h

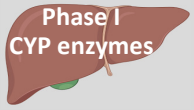
Decreased body T° slows metabolic rate, preventing further **brain damage**

Physiology-Based Pharmacokinetic (PBPK) cooling framework as integrative predictive model in **neonates**



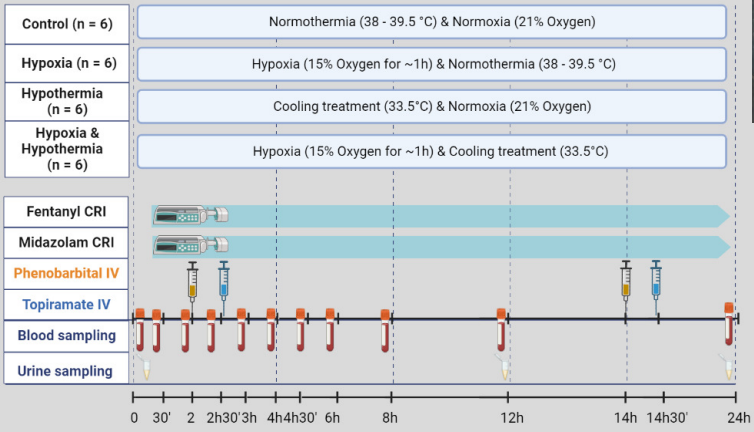
Investigation of cooling and asphyxia on **pharmacokinetics (PK)** in **neonatal Göttingen Minipigs**

Add-on drug treatment:
Fentanyl
Midazolam
Topiramate
Phenobarbital



We hypothesized that **TH and PA** have an impact on CYP-mediated drug disposition. Because TH and PA cannot be studied separately in the clinical context, we used the **neonatal Göttingen Minipig** as translational model.

Methods



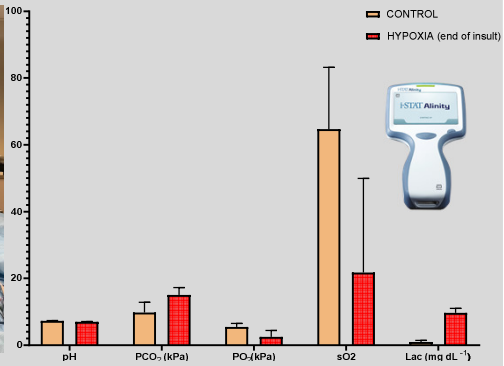
- **Hypoxia** was induced by setting the **inspiratory oxygen fraction (FiO2) at 15%, using nitrogen gas.**

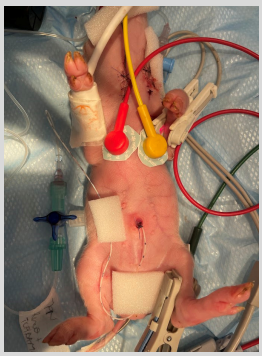
Conclusions

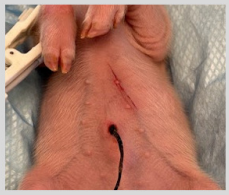
- We showed that **perinatal asphyxia (PA)** can be induced in **the neonatal Göttingen Minipig**, in a setting comparable to human **NICU,** and the effect of **PA and TH on drug disposition** can be studied separately, **for 24h**.
- These data reveal the potential of the neonatal Göttingen Minipig as **promising in vivo animal model** in safety assessment for conditions for the human paediatric population.

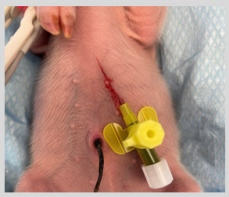
Results

Study procedures were well tolerated for **24h** in **24 neonatal Göttingen Minipigs** of **551.12g (± 60.32g)**. **Cooling** was easy to control and to maintain at a target rectal temperature of **33.5°C**. **Hypoxia** could be established for **51 (±34.82) min**. **Increased** blood **lactate 9.56 (±2.27) mmol/L** and **decreased pH 7.00 (±0.16)** were used as key parameters for PA.

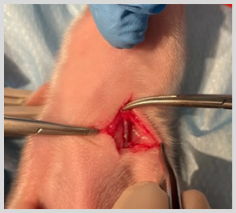


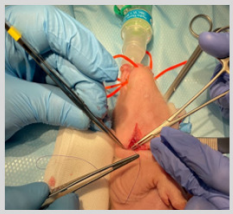


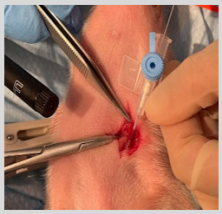


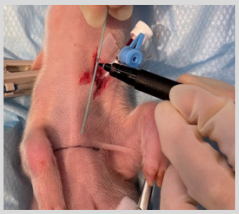


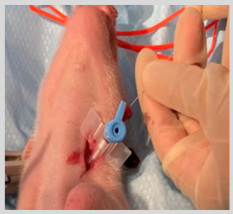
- **Peripheric catheterisation** was easiest in the **epigastric vein,** whereas catheterization of the **umbilical vein** depended on whether the umbilical cord was still wet or not.
- **Central venous catheterisation via Modified Seldinger technique, showed to be the main method for vascular access, either for sampling or administration.**

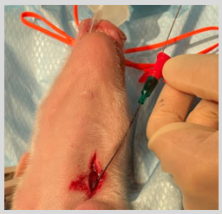












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