DESMOPRESSIN

WHAT IS NEW?

Paediatric drug development: towards maturity
Desmopressin: Intro

- Complete response (1/3)
  - 100% reduction
- Partial response (1/3)
  - 50 to 99% reduction
- No-response (1/3)
  - <50% reduction
Why do we observe no or partial anti-enuretic effect?
DESMOPRESSIN: INTRO

Timing of administration?

Formulation?

Dose?

Age-dependency?

Fluid intake?

Food interaction?
DESMOPRESSIN: INTRO

Timing of administration?

Need for PK/PD characteristics of desmopressin

Food interaction?
WP 1
Identification of the needs

WP 2
Clinical trials the importance of surrogate parameters

WP 3
Juvenile animal model

WP 4
PK/PD modelling

WP 5
Critically ill children

WP 6
Neonates

WP 7
Guidelines

WP 8
Ethical and legal aspects

WP 9
Management and coordination
**Desmopressin: Problem Setting**

Children grow and mature
⇒ Size/age dependency of PK?

**Food effect was shown on the PK in adults (Rittig et al., 1998)**
⇒ Children are often not fasted 1h before bedtime (recommended dosing time)!

**Bioequivalence of two formulations (melt and tablet) in adults (120µg/200µg)**
⇒ Is this true in the paediatric population?

**Difficult to perform full PK studies**
⇒ Can the piglet be a suitable animal model?
DESMOPRESSIN: AGE-DEPENDENCY

Pharmacokinetics of desmopressin administered as tablet and oral lyophilisate formulation in children with monosymptomatic nocturnal enuresis

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Age-dependency only for the melt
DESMPRESSIN: FOOD INTERACTION

Food effect

\[
\frac{\text{AUC}_{\text{fasted}}}{\text{AUC}_{\text{fed}}} = 191\% \ [180\% - 202\%] \\
\frac{\text{C}_{\text{max,fasted}}}{\text{C}_{\text{max,fed}}} = 195\% \ [177\% - 211\%]
\]

Michelet et al. (2016)
Desmopressin: Bioequivalence

Formulation effect

\[ \frac{AUC_{\text{tab}}}{AUC_{\text{melt}}} = 137\% \ [129\% - 145\%] \]

\[ \frac{C_{\text{max,tab}}}{C_{\text{max,melt}}} = 140\% \ [128\% - 150\%] \]

Michelet et al. (2016)
DESMOPRESSIN: COMPARISON CHILDREN-PIGLETs

Gasthuys et al. (2018)

Two absorption peaks

Osterberg et al. (2006)

Two absorption peaks
**Desmopressin: Conclusions**

**Children grow and mature**
- Size/age dependency of PK? **YES (melt)**

**Food effect was shown on the PK in adults (Rittig et al., 1998)**
- Children are often not fasted 1h before bedtime (recommended dosing time)! **YES (melt superior to tablet)**

**Bioequivalence of two formulations (melt and tablet) in adults (120µg/200µg)**
- Is this true in the paediatric population? **NO (150 µg/200µg)**

**Difficult to perform full PK/PD studies**
- Can the piglet be a suitable animal model? **YES (PK)**