Raltegravir PK in neonates – Modeling rising and declining PK profiles of newborns exposed to raltegravir in-utero

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Objectives: To develop a population PK model for neonates exposed to RAL in-utero.

Methods: The RAL clearance maturation profile in neonates develops from near-nil at birth to a maximum in approximately 4 months representing development of UGT-1A1 activity, which was implemented in a 2-compartment population PK-model for newborns exposed to RAL first time (naïves) [1]. Neonates exposed to RAL via the mother in-utero (non-naïves) [2], but without post-birth administration, showed striking PK with either declining (Figure, right-panel) or rising (left-panel) RAL levels during the first 36 hours of life. A non-naïve neonate PK-model was built mimicking fast RAL transport via the umbilical cord between mother (receiving RAL) and fetus assuming all RAL-clearance via the mother.

Results: The non-naïve PK-model elegantly explained that neonates could have rising or declining concentrations by tissue redistribution. Upon birth, the Vc mother-Vc neonate link is broken resulting in possible peripheral tissue back-flow where RAL cannot be cleared from Vc neonate.

Conclusions: A PK-model was developed explaining rising or declining RAL levels in non-naïve neonates through redistribution phenomena without having to assume a RAL depot (e.g. formation of RAL-glucuronides [2]).

References:
