

Assessment of maternal and fetal dolutegravir exposure by integrating ex vivo placental perfusion data and physiologically-based pharmacokinetic modeling



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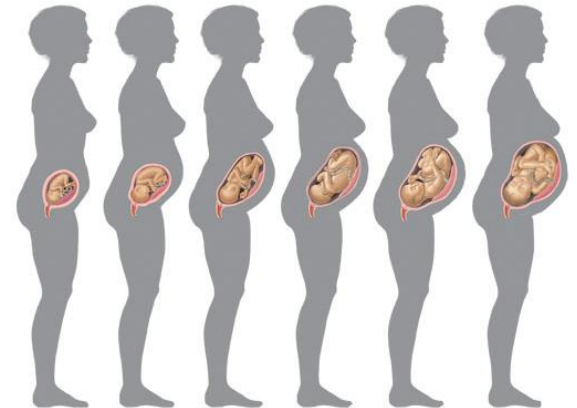
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Background

- About 1.4 million HIV-infected women give birth every year
- Mother-to-child transmission is linked to viral load
- Antiretroviral therapy reduces MTCT to $<2\%$

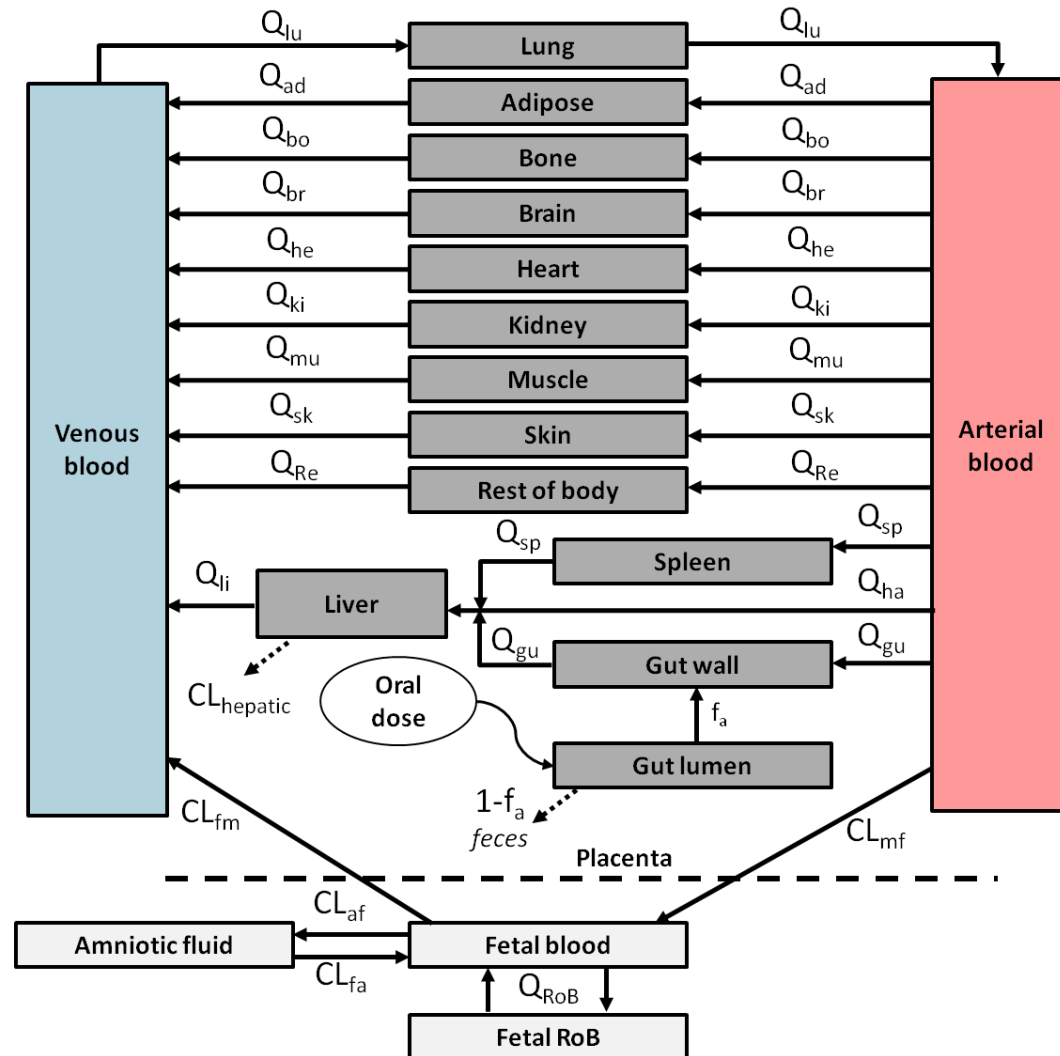


**Optimal dosing in
pregnancy is challenging!**



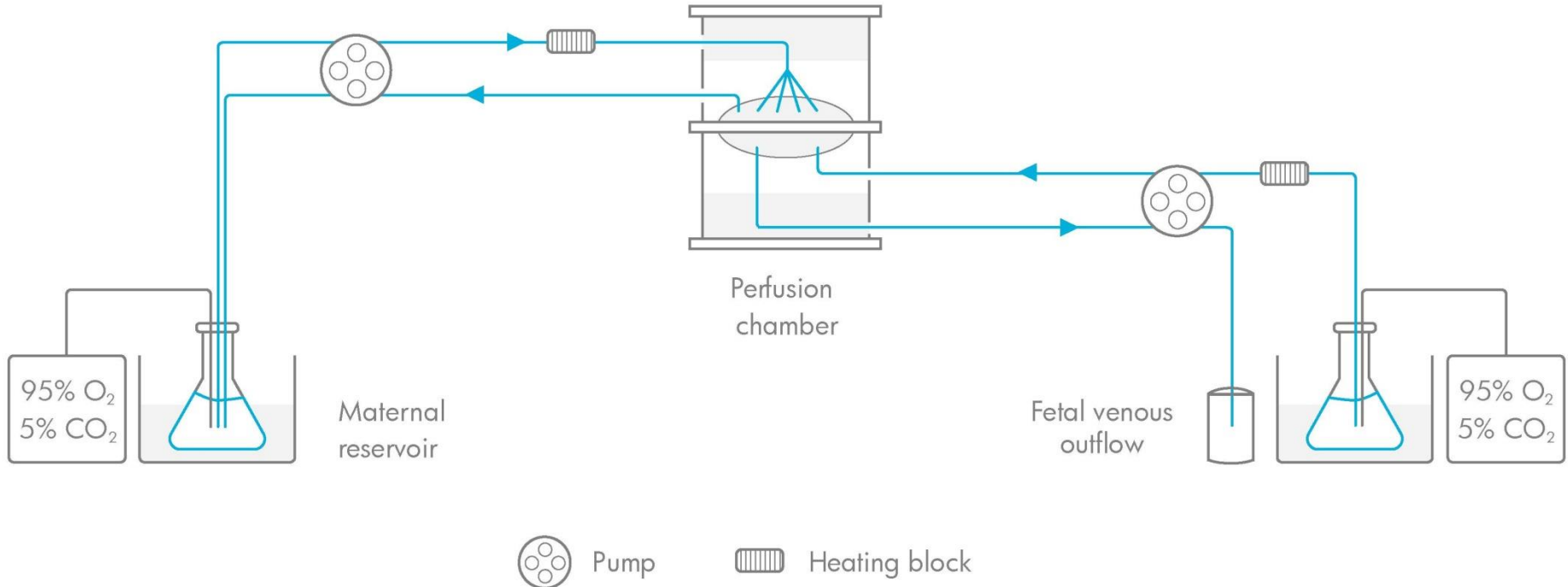
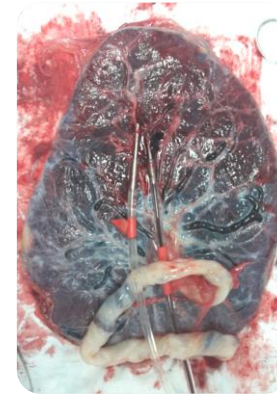
Methods

✓ Pregnancy physiologically-based pharmacokinetic model (p-PBPK)

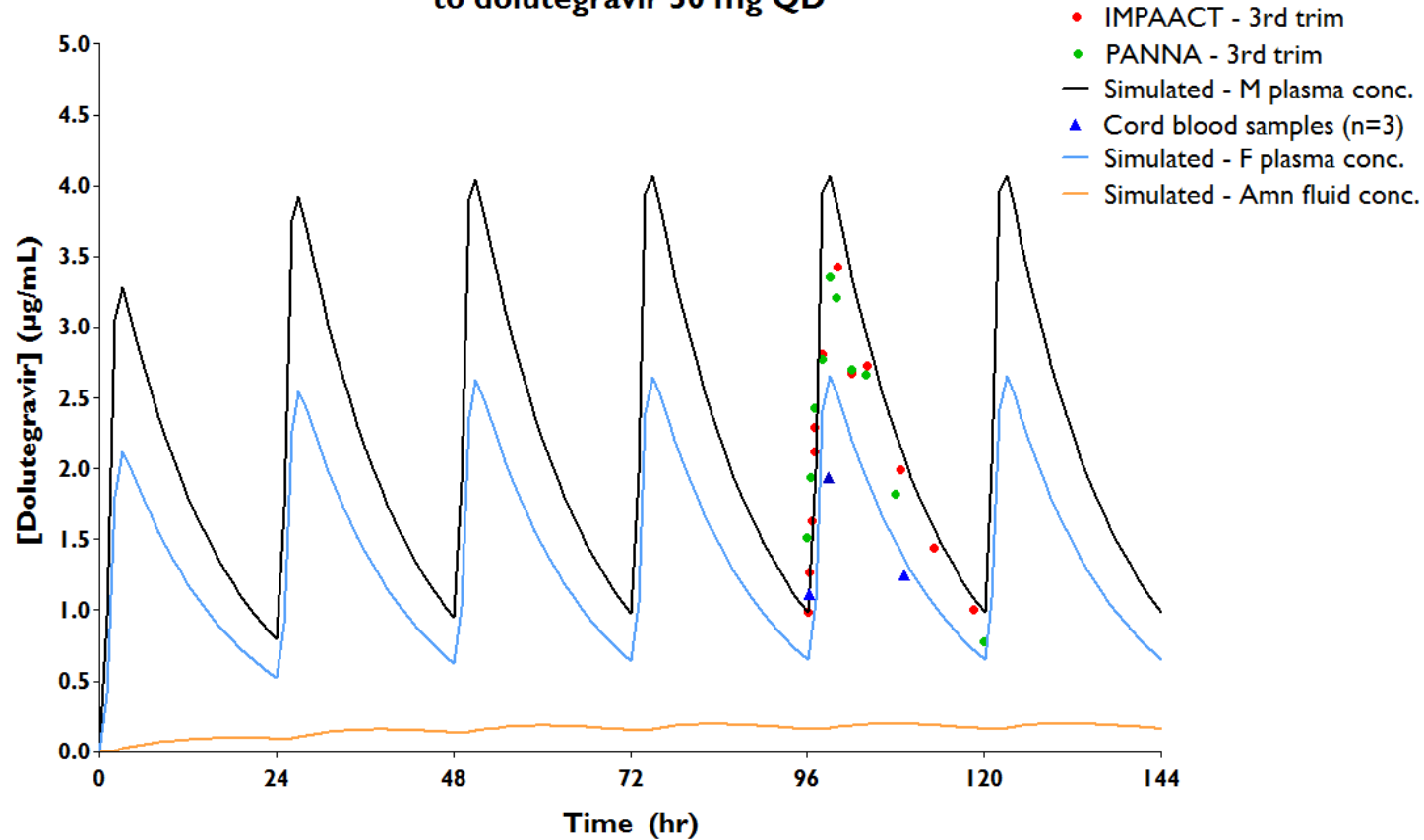


Methods

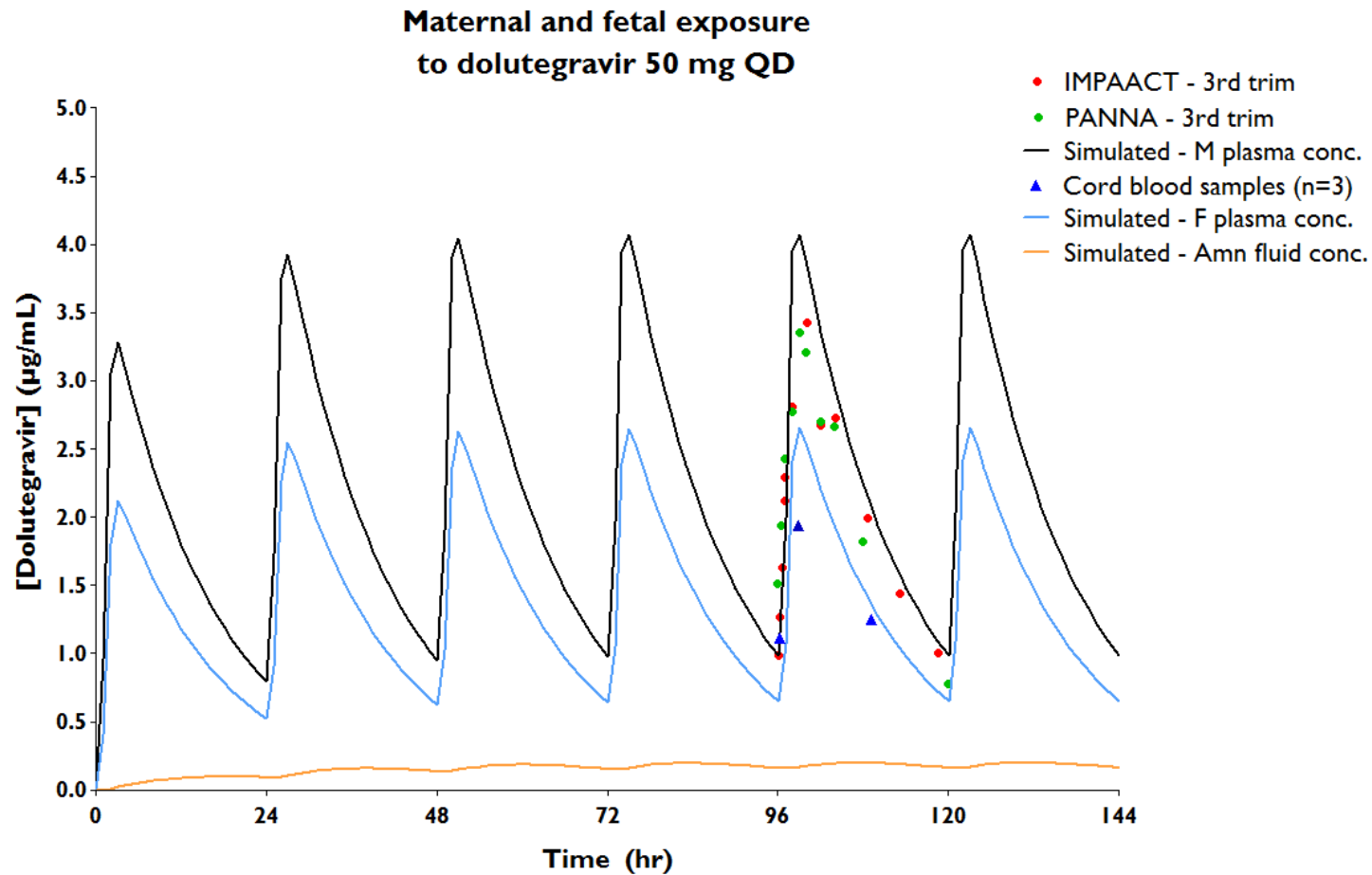
- ✓ Pregnancy physiologically-based pharmacokinetic model (p-PBPK)
- ✓ Perform *ex vivo* dual-side placental perfusion experiments



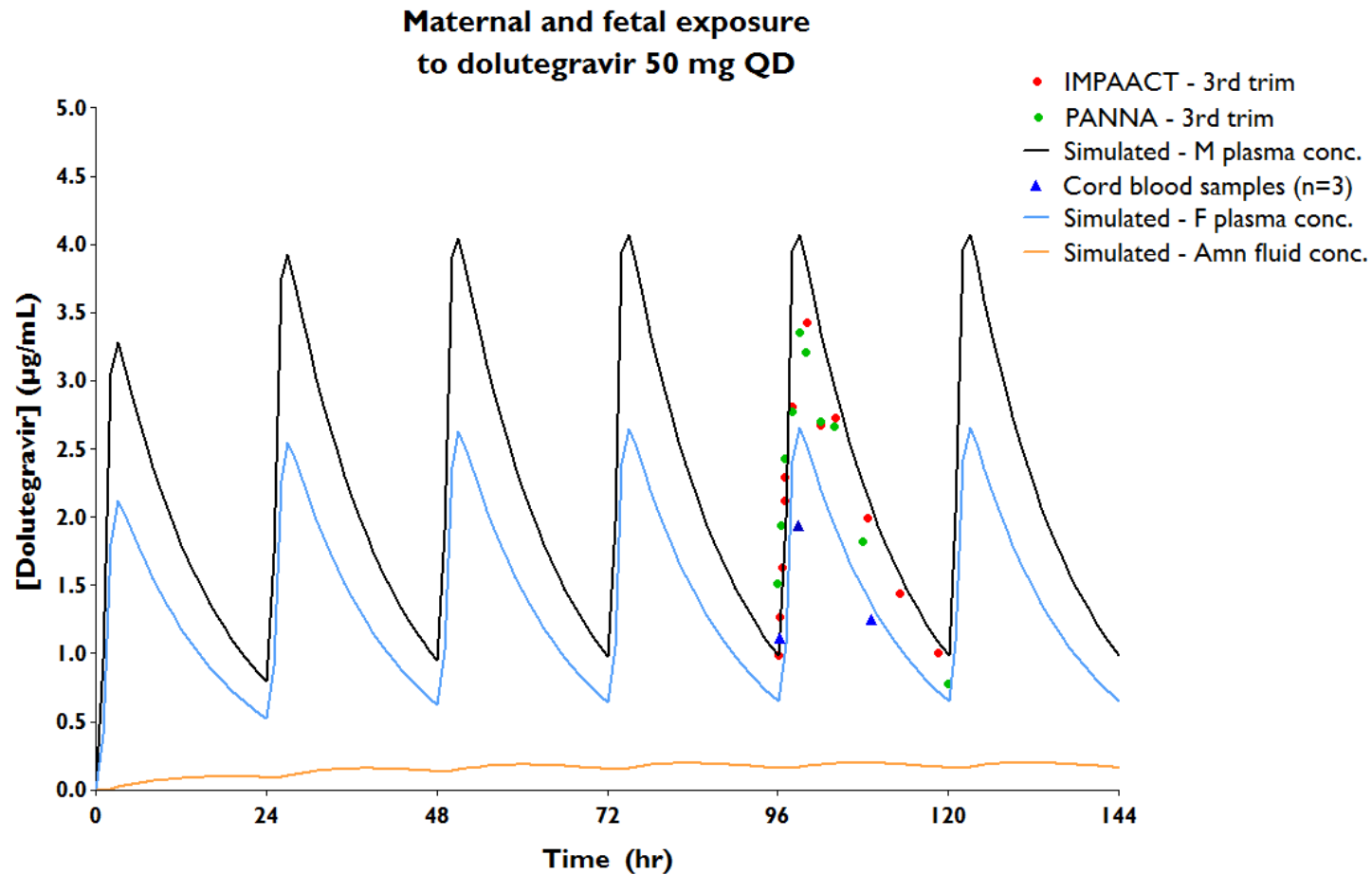
Maternal and fetal exposure to dolutegravir 50 mg QD



- Simulations were able to capture maternal clinical pharmacokinetics



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- Dolutegravir crosses the placenta *in vivo* and *ex vivo*



- Simulations were able to capture maternal clinical pharmacokinetics
- Dolutegravir crosses the placenta *in vivo* and *ex vivo*
- Predicted fetal $C_{24h} > EC90$ for viral inhibition → pre-exposure prophylaxis

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Poster #14

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