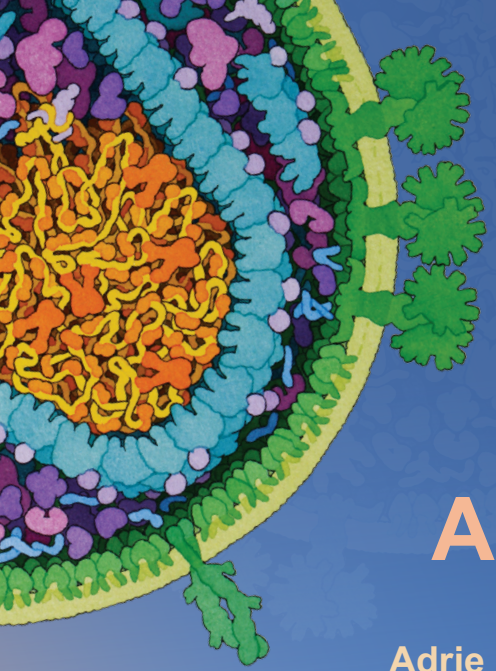

SCIENCE SPOTLIGHT™

ABACAVIR DOSING IN NEONATES FROM BIRTH: A PHARMACOKINETIC ANALYSIS

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Disclosure: None

CROI 2021

Background

- **Abacavir (ABC)** is a 1st line antiretroviral for children per WHO guidelines
- ABC is licensed for infants > 3 months of age at a dose of 8 mg/kg BID, with the WHO recommending use from 4 weeks of age and ≥ 3 kg
- **Limited pharmacokinetic (PK) data** are available to inform dosing from birth

Objective

- We performed a **PK analysis** using ABC plasma concentrations from neonates and young infants **to determine ABC dosing guidelines for neonates,** using the liquid formulation

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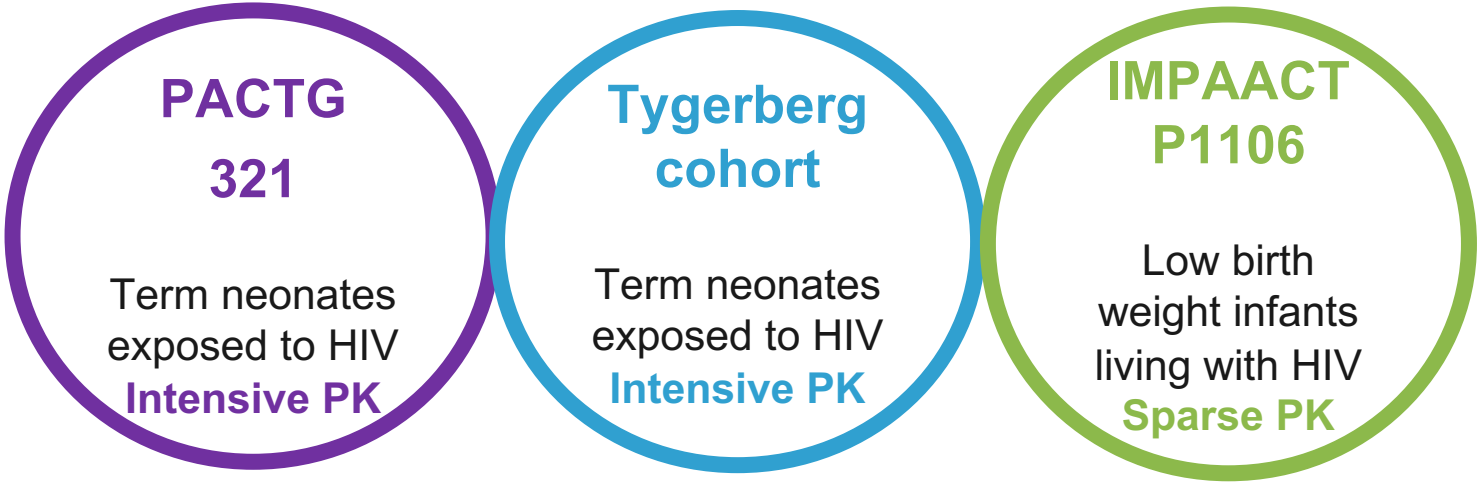
Methods

- Data were **pooled from 3 studies** administering ABC liquid formulation



- Population PK approach + Monte Carlo simulations **to identify the optimal ABC dose** to achieve **exposures in the range** expected in older children dosed per WHO weight band (***$AUC_{0\text{-}12}$ range: 3.2 to 25.2 mcg.hr/mL***, *US FDA submission: Ref ID: 3702679*)

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Results

Study	PACTG 321	Tygerberg cohort	P1106
Participants (n)	11	10	24
Samples (n)	60	50	198
Dosing strategy	Single dose	Single Dose	Multi-dose
ABC Dosing (mg/kg)*	2.0 (1.9 - 2.1)	8.1 (8.0 - 8.4)	10.8 (4.1 -13.2)
Gestational age at birth* (weeks)	39 (39 – 39)	39 (38 - 42)	35 (27 - 39)
Low birth weight (<2500 gm), n(%)	3 (27)	0 (0)	18 (75)
Weight at PK Visit (kg)*	3.1 (2.2 - 4.0)	3.3 (2.9 - 4.4)	3.8 (2.4 – 5.8)
Postnatal age (PNA) at PK Visit (days)*	1 (1 - 8)	9.5 (6 - 15)	73 (41 – 190)
Clearance (L/hr/kg)*	0.17 (0.15 – 0.24)	0.22 (0.18 – 0.3)	0.54 (0.3 – 0.87)

*Median (range)

Population PK results

- ABC clearance (CL/F) was allometrically scaled for body weight
- **ABC clearance was low at birth, but increased ~ 5X by 6 months of age**
- ABC CL/F in LBW infants at 6 weeks postnatal age was similar to term infants of similar chronological age

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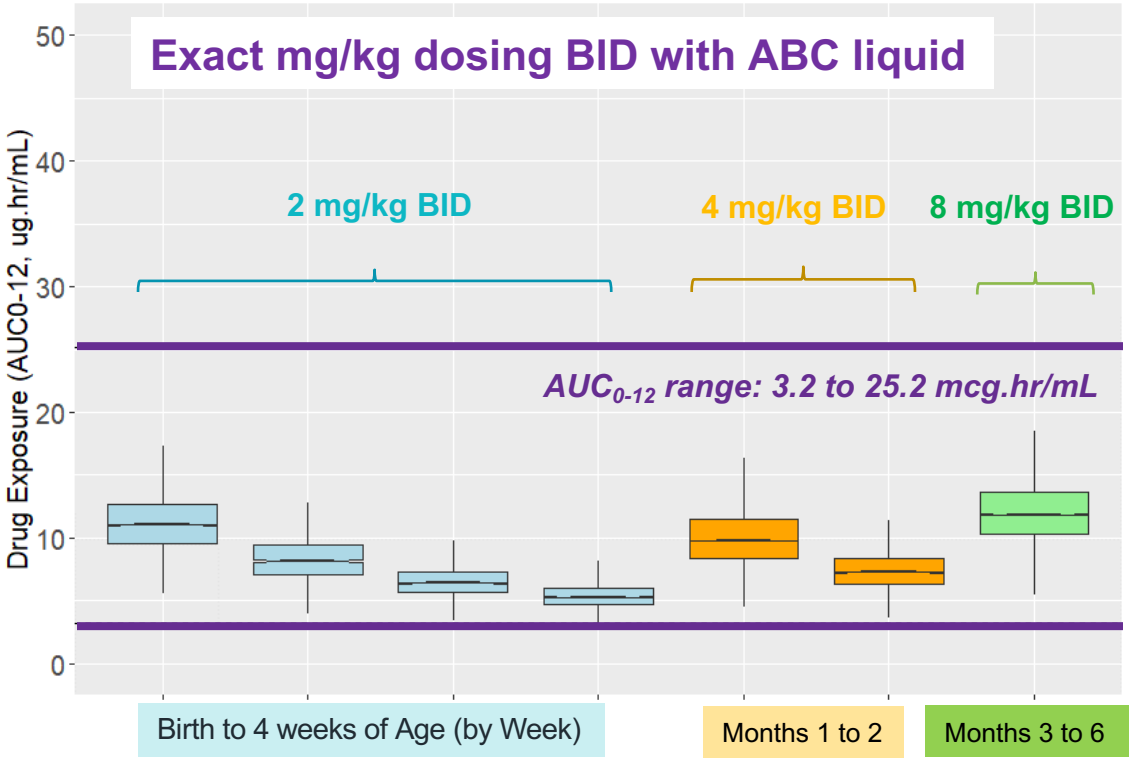
Impact of Postnatal Age on Predicted ABC exposures in term neonates (0-6 months)



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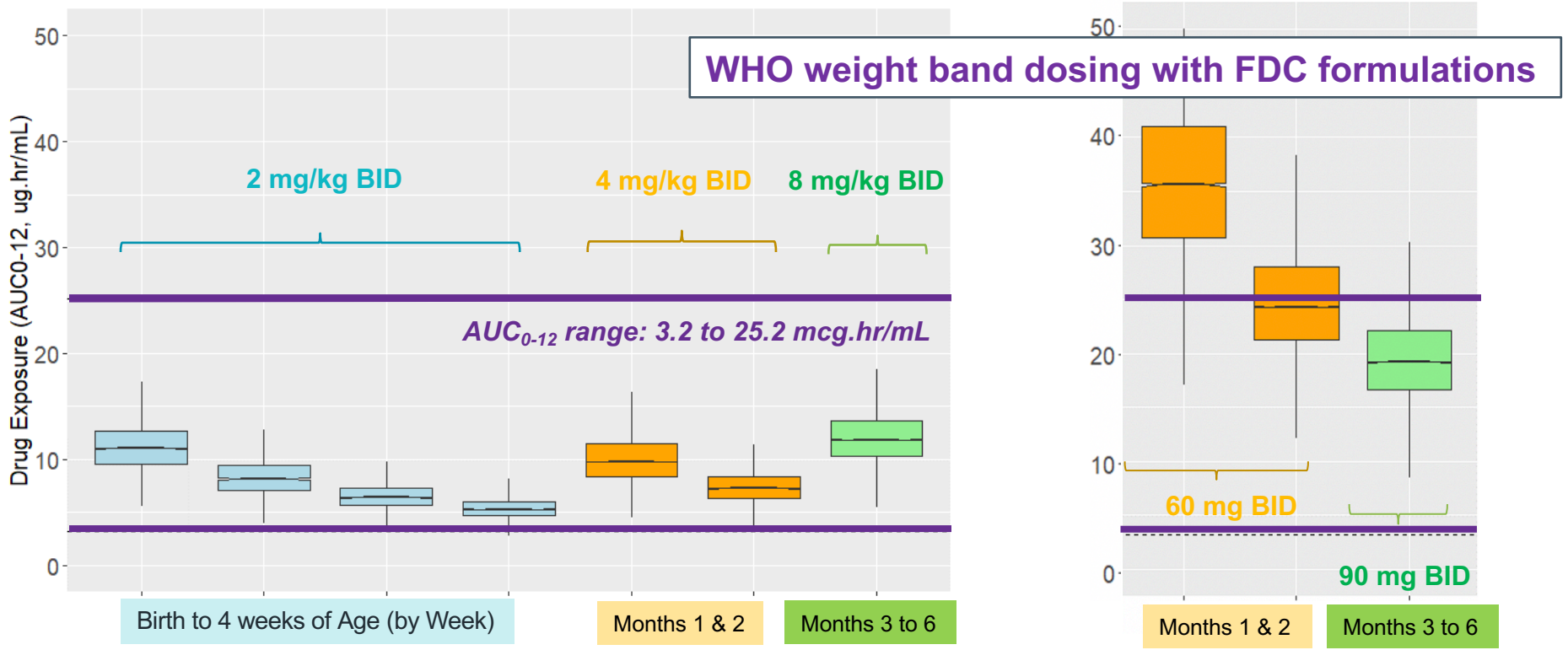

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Conclusions

- ABC elimination is greatly reduced at birth but rapidly increases over the 1st weeks of life
  - ABC clearance in LBW infants at 6 weeks postnatal age is equivalent to that in term infants at that age

Age	Dose
0 – 4 weeks	2 mg/kg BID
4 – 12 weeks	4 mg/kg BID

- Our proposed mg/kg dosing regimen achieved exposures within the expected range for older children

- Current WHO weight band dosing with fixed-dose combinations for infants (4 weeks and ≥ 3 kg) results in high ABC exposures
  - But only for short duration as clearance continues to increase rapidly over the next few weeks

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Acknowledgments

The IMPAACT team wish to thank the participants on the P1106 trial and the study staff conducting the protocol at FAMCRU and PHRU in South Africa

Overall support for the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) was provided by the National Institute of Allergy and Infectious Diseases (NIAID) with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH), all components of the National Institutes of Health (NIH), under Award Numbers UM1AI068632-15 (IMPAACT LOC), UM1AI068616-15 (IMPAACT SDMC) and UM1AI106716-09 (IMPAACT LC), and by NICHD contract number HHSN275201800001I. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

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