Abstract #61

Abacavir Weight-Band Dosing for Infants in the first 4 weeks of life

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Background

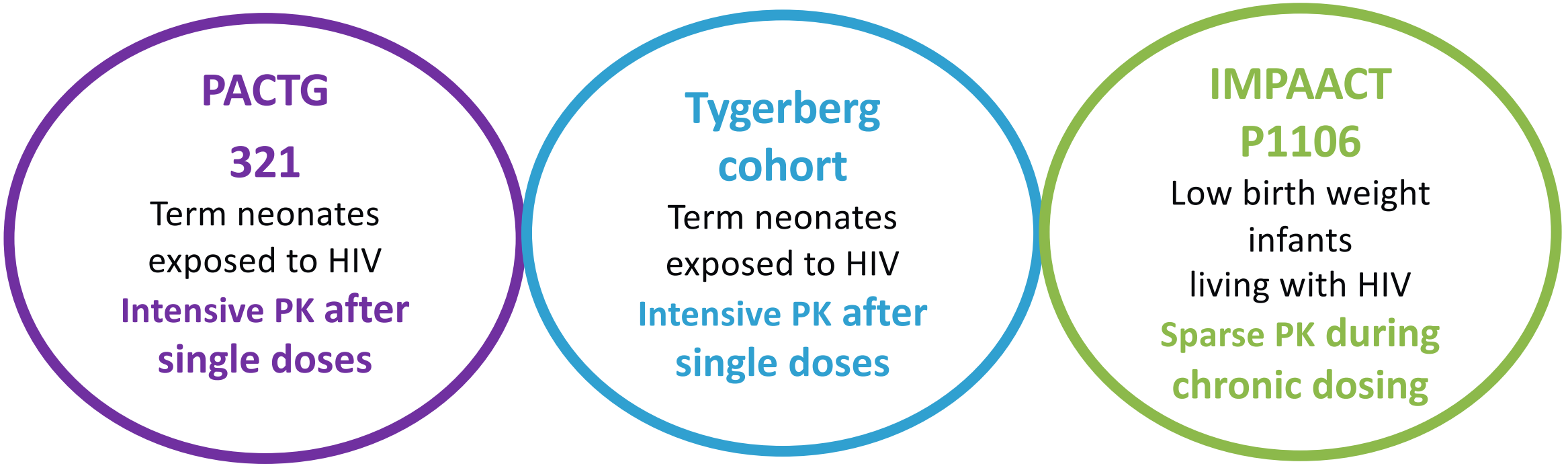
- **Abacavir (ABC)** is a 1st line antiretroviral for children per WHO guidelines
- ABC is licensed for infants >3 months of age at a dose of 8 mg/kg BID
- WHO recommends ABC use from 4 weeks of age and ≥ 3 kg **using weight band dosing**
- **Limited pharmacokinetic (PK) data** are available to inform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

Objective

Our objective was to determine the optimal weight-band doses for ABC liquid formulation in neonates

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

- 45 infants <3 months of age contributed 308 ABC concentrations
- Studies 1 & 2: 21 term neonates; Study 3: 24 infants living with HIV

Table 1: Characteristics of Infants on ABC (n=45)

	PACTG 321 (Study 1)	Tygerberg (Study 2)	P1106 (Study 3)	Total
Birth weight (kg)	3.1 (2.2-4.0)	3.2 (2.5-4·2)	2.2 (1.4.3.3)	2.6 (1.4-4.2)
LBW (<2500 gm)	3 (27)	0 (0)	18 (75)	21 (47)
GA at birth (weeks)	39 (39-39)	39 (38-42)	35 (27 - 39)	38 (27-42)
ABC Dose	2.0 (1.9-2.1)	8.1 (8.0-8.4)	10.8 (4.1-13.2)	NA
WT 1st PK Visit (kg)	3.1 (2.2-4.0)	3.3 (2.9-4.4)	3.8 (2.4-5.8)	3.5 (2.2-5.8)
PNA 1st PK Visit (days)	1 (1-8)	9.5 (6-15)	73 (41-190)	46 (1-190)

Pharmacokinetic Model: Maturation of ABC CL/F described using an exponential model as a function of PNA). ABC CL/F was low at birth but ~2-fold by 4 weeks of age

Safety: No hypersensitivity reactions reported. No major concerns but multi-doses in neoates lacking

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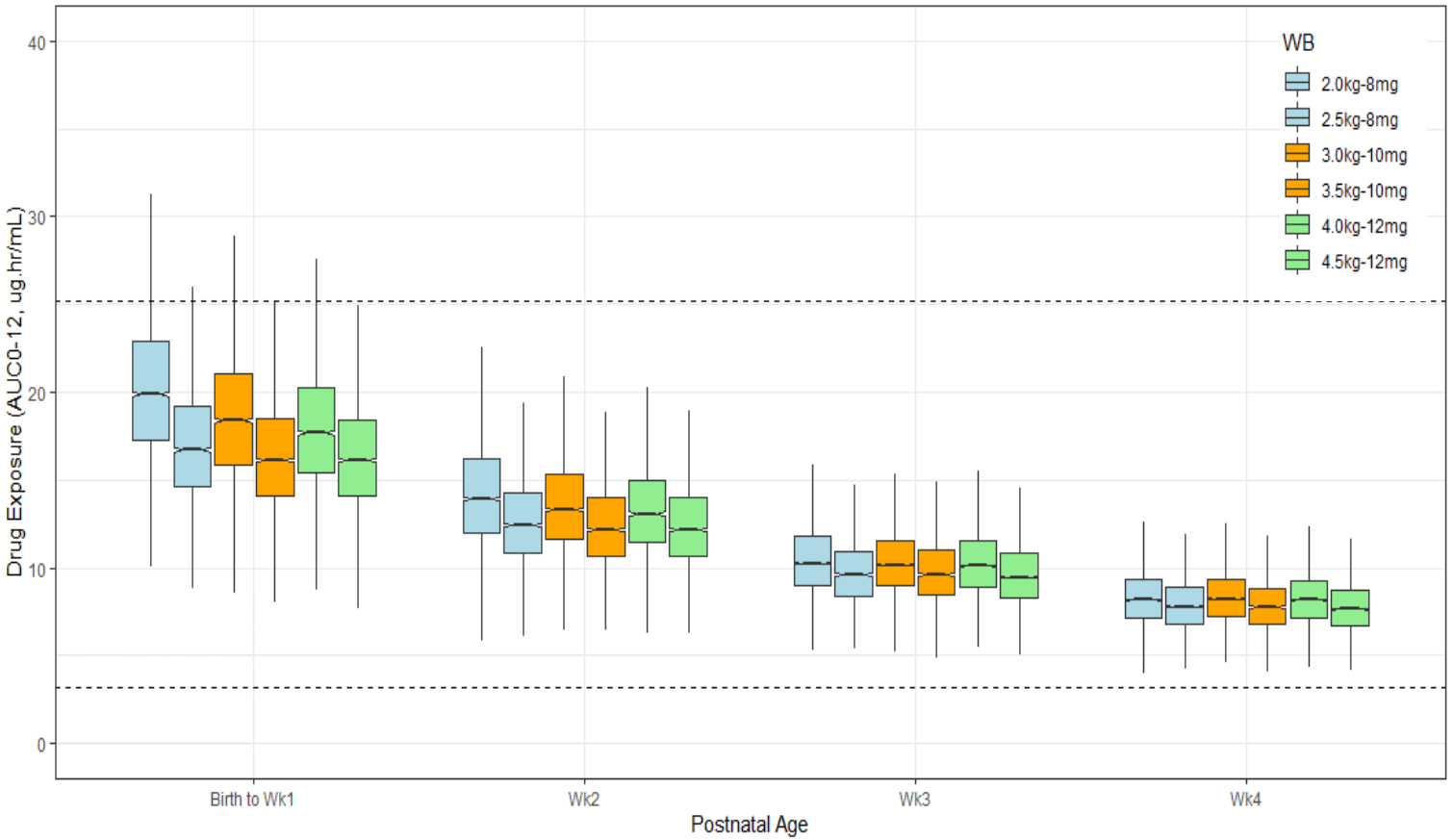
Neonatal ABC Dosing Per WHO-Weight Bands: Birth to 4 weeks of life

- ABC exposures **simulated** for neonates with birth weights of 2.0, 2.5, 3.0, 3.5, 4·0 and 4.5 kg

Drug	Strength of oral liquid	2-3 kg		3-4 kg		4-5 kg	
		AM	PM	AM	PM	AM	PM
ABC	**20 mg/mL**	**0.4 ml**	**0.4 ml**	**0.5 ml**	**0.5 ml**	**0.6 ml**	**0.6 ml**



- ABC $AUC_{0\text{-}12}$ were within the expected range, except for a small proportion (<15%) with higher exposures during the first week of life
- ABC $AUC_{0\text{-}12}$ decreased rapidly across all weight bands by ~25% at Week 2 and 55% at Week 4, consistent with the expected maturation of the enzymes that metabolize ABC

Conclusion

- Using ABC from birth aligns with current WHO 1st-line ART guidelines
- ABC weight-band dosing strategy of 8 mg (2-3 kg), 10 mg (3-4 kg) and 12 mg (4-5 kg) twice daily in infants less than 4 weeks of age provides therapeutic exposures for both treatment/prophylaxis during this period of rapid maturation and growth.
- Using the same dose from birth throughout the first 4 weeks of life will simplify implementation from a public health perspective
- Dosing and safety information on ABC within solid pediatric FDCs in neonates is forthcoming (*PETITE study,* ***Abstract #5***)

Acknowledgments

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Sponsor and Collaborators