IMPAACT P1106
ARV AND TB PHARMACOKINETICS (PK) IN PREMATURE/ LOW BIRTH WEIGHT (LBW) INFANTS

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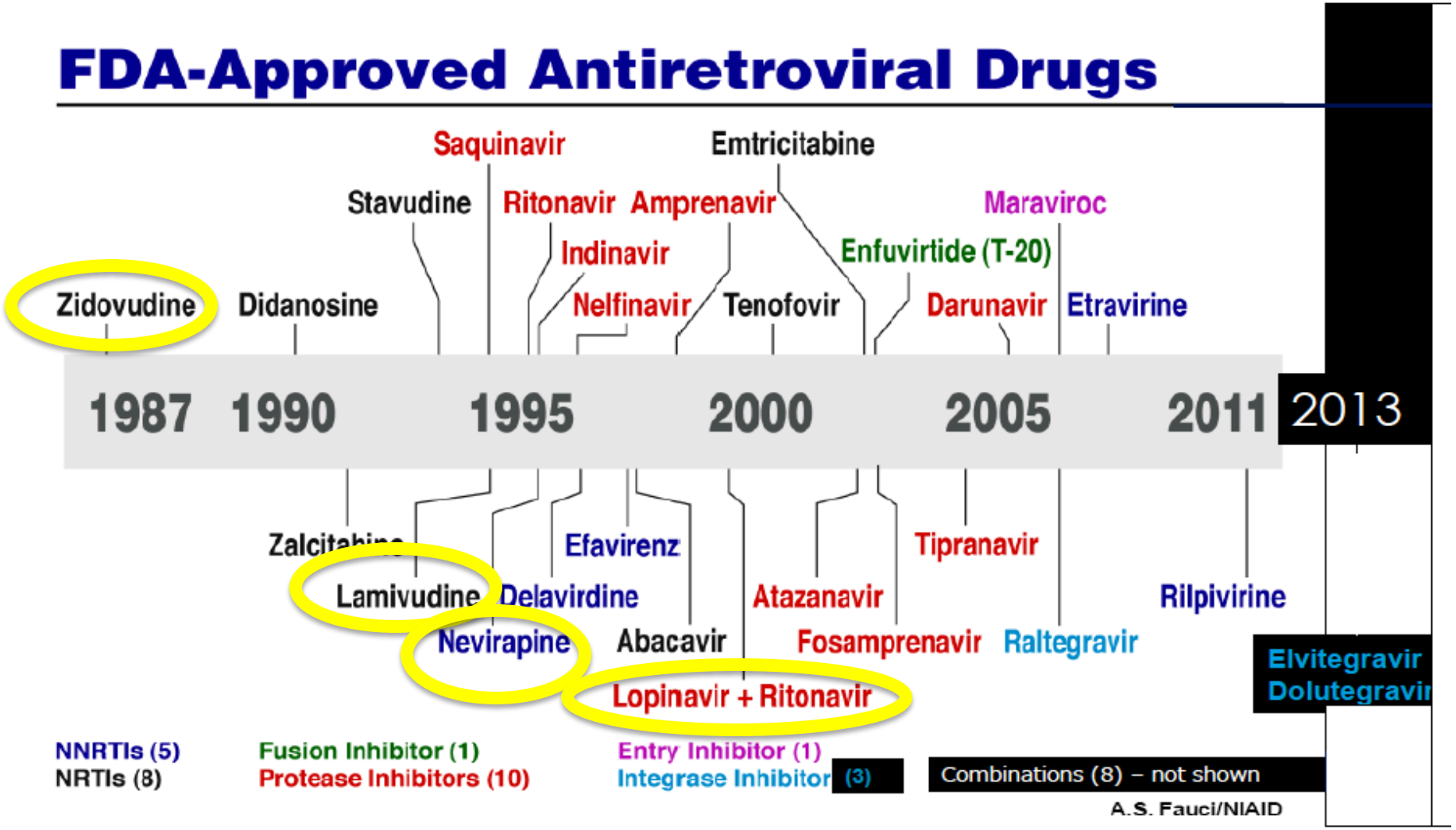
ARVs available for newborns in LMICs



P1106: Phase IV Prospective PK Study

Primary Objective

To describe PK and safety of ARV and TB drugs in LBW infants

Study Arms		(planned n=158)
1	NVP	40
2	NVP + INH	18
3	NVP + INH + RIF	28
4	INH ± RIF	18-36
5	LPV/r + 2NRTIs ± INH	24
6	LPV/r + 2NRTIs +RIF ± INH	12

Opportunistic study design (infant dosing – clinician choice)
PK visits at Entry and Weeks 4, 6, 10, 16, and 24

2 South African sites:
FAMCRU - Cape Town; PHRU - Johannesburg

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Accrual

91 infants enrolled from August 2015 - March 2018
(82 LBW and 9 NBW)

	Study Arms	Accrual target	Accrual
1	**NVP**	**40**	**40**
2	NVP + INH	36	**18**
~~3~~	~~NVP + INH + RIF *~~	~~28~~	~~0~~
4	INH ± RIF	18 - 36	**7**
5	**LPV/r + 2NRTIs ± INH**	**24**	**25**
~~6~~	~~LPV/r + 2NRTIs +RIF ± INH~~	~~12~~	~~1~~
	New total	Max of 136	**91**

PK data are available for NVP, LPV/r,
PK assays are planned for ABC, 3TC, ZDV and TMP-SMX
(INH arms - still recruiting)

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Baseline Characteristics (n=91)

Infant Characteristics (n=91)	
Male (n, %)	38 (42%)
Race (Black African) (n,%)	77 (85%)
Birth weight, g (median, Q1-Q3)	1860 (1525 - 2250)
Gestational age, weeks (median, Q1-Q3)	34 (32 - 36) *
Enrollment age, days (median, Q1-Q3)	13 (10 – 35)

*missing data (gestational age) for 4 infants

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NVP PK

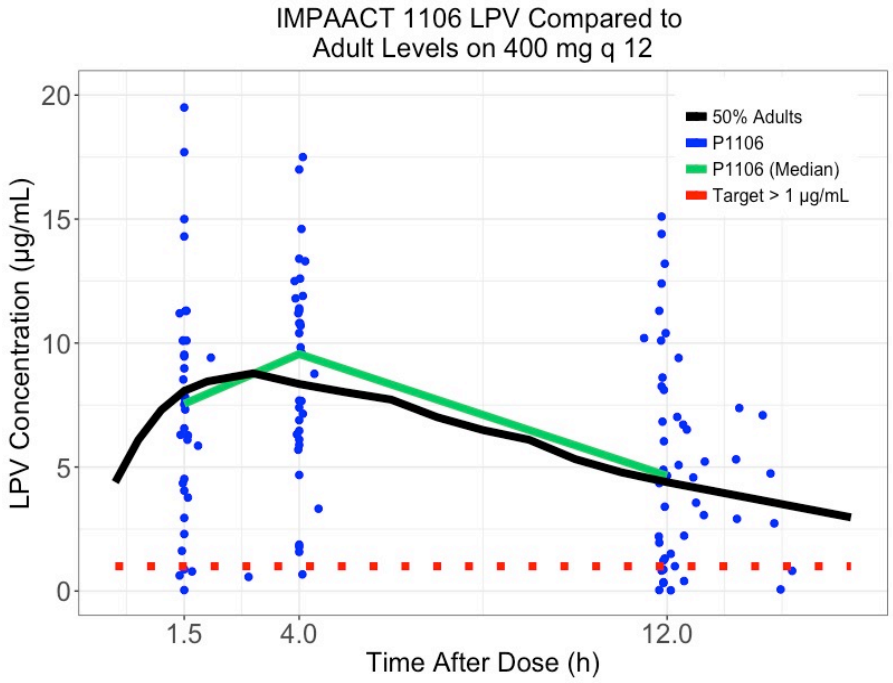
Removed as presented data pending publication

NVP

Removed as presented data pending publication

LPV/r PK (n=23)

LPV/r solution at 300/75 mg/m^2 twice daily



LPV/r trough concentrations (C_0)

- low at 2 weeks
- similar to adults from 6 weeks

- 13/23 (57%) started LPV/r *before* 42 weeks PMA range (33.9 - 41.9 weeks)

Characteristic	Week 2	Week 6	Week 10	Week 16	Week 24
Current WT (kg)	3.6	4.5	5.0	5.6	6.8
Dose (mg/kg)	27.1	23.7	22.6	22.7	20.8
PNA (weeks)	8.9	12.9	17.0	23.0	31.2
PMA (weeks)	**43.5**	47.5	51.8	57.2	65.8
C_0 (µg/mL)	**1.8**	4.6	4.5	3.1	4.0

LPV/r safety (n=23)

No treatment related adverse events were observed

Alanine transferase (IU/L)	16 (13 – 21)
Osmolality (mOsm/kg)	290 (288 – 294)
Calcium (mmol/L)	2.61 (2.53 – 2.66)
Creatinine (µmol/L)	24 (20 – 27)

Electrocardiogram (ECG) and Echocardiogram (ECHO) findings

- None had a QTc prolongation of > 450 msec (4 had QTc changes from baseline > 60 msec, but were asymptomatic throughout)

- All newborn ECHOs were normal except 2 with mild abnormalities; a slightly thickened interventricular septum (5-6 mm) and mild pulmonary valve stenosis.

Conclusions

- **91 infants** on ARV and TB drugs have successfully been enrolled
- **All NVP** concentrations within the target range for prophylaxis
- **Postmenstrual age & CYP2B6 status** influenced NVP clearance
- **LPV concentrations** were similar to adult target values (no safety signals)
- **No treatment related adverse events** were observed
- **PK assays** are scheduled for secondary outcome drugs - **ABC, 3TC, ZDV, TMP-SMX and INH**

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