Maraviroc Safety & Pharmacokinetics in HIV-Exposed Neonates

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Background

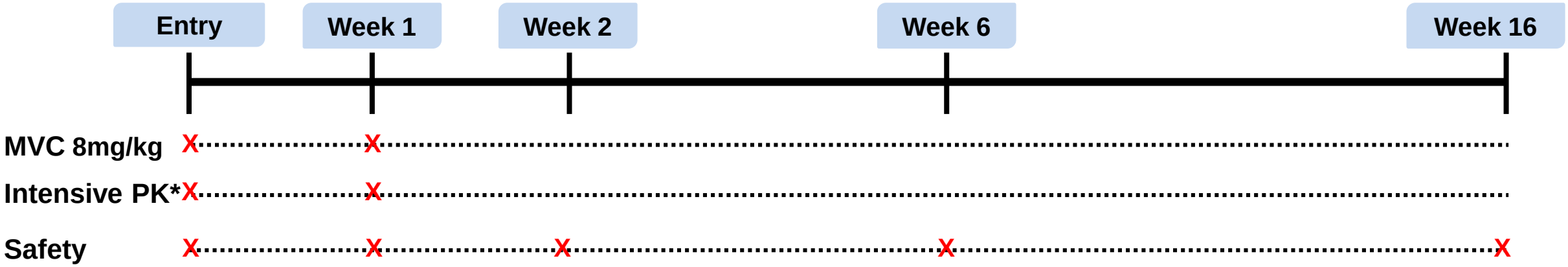
- Lack of safety and pharmacokinetic (PK) data limits options for HIV-1 prophylaxis and treatment in neonates.
- Maraviroc (MVC) is available as an oral solution licensed for treatment of HIV-1 in children ≥2yrs and ≥10kg.
- MVC is attractive as a potential component of neonatal ART.

IMPAACT 2007: Phase I, multi-center, open label study evaluating safety and PK of MVC in HIV-exposed neonates in addition to standard ARV prophylaxis.

Methods

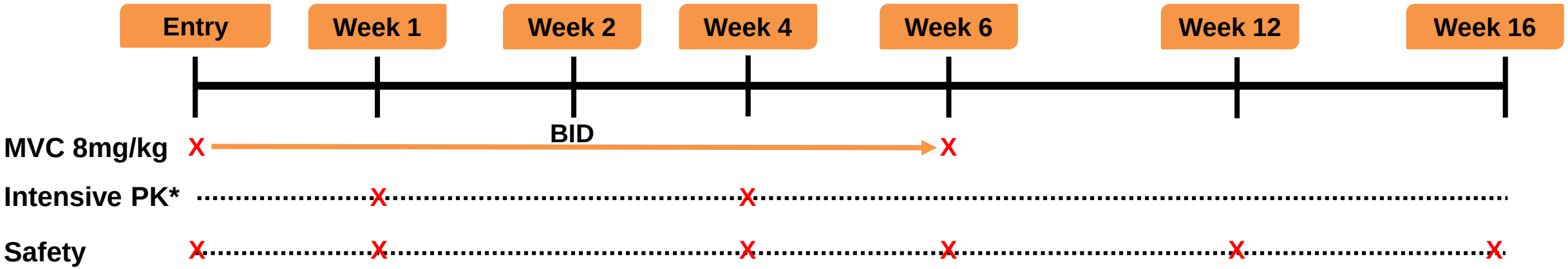
Cohort 1

* C_{avg}≥ 75ng/mL



Cohort 2

* C_{avg}≥ 75ng/mL



Results

Table 1. Infant Baseline Characteristics (All Treated Infants)

	Cohort 1	Cohort 2
	N=15 (%)	N=32 (%)
Sex		
Female	9 (60)	14 (43.8)
Race		
Black or African American	12 (80)	26 (81.3)
White	3 (20)	3 (9.4)
Asian	0 (0)	3 (9.4)
Gestational age (weeks)		
Median Q1, Q3	39.0 38.0, 39.0	39.0 38.5, 40.0
Birth Weight (kg)		
Median Q1, Q3	3.3 2.9, 3.5	3.0 2.8, 3.2

Safety*

- No participants met safety endpoints at week 6 and through week 16.
- No early study or early treatment discontinuations due to MVC.
- No enrolled infant acquired HIV-1 infection through the follow-up period.

*Standard NIH AE grading

Results (2)

Table 2: Cohort 2 PK Parameters by Study Strata[a]

		N	Dose (mg/kg)	AUC (ng*h/mL)	C_{avg} (ng/mL)	$C_{avg} \geq 75$ (ng/mL)	C_{max} (ng/mL)	T_{max} (h)	$t_{1/2}$ (h)
Week 1	EFV-naïve (2A)	13	8.5 [7.4-9.5]	1,827 [237-6,788]	152 [20-566]	**10 / 13 (77%)**	257 [52-1468]	1.5 [0.8-4.0]	3.6 [2.0-12.3]
	EFV-exposed (2B)	12	7.7 [6.8-8.3]	1,496 [205-6,610]	125 [17-551]	**8 / 12 (67%)**	309 [34-1274]	3.0 [1.0-6.2]	3.3 [2.2-5.6]
Week 4	EFV-naïve (2A)	13	7.5 [6.1-9.9]	1,123 [395-5,859]	94 [33-488]	**9 / 13 (69%)**	417 [125-793]	1.5 [1.0-4.0]	3.8 [2.0-16.1]
	EFV-exposed (2B)	12	7.4 [6.6-8.9]	1,217 [512-4,214]	101 [43-351]	**7 / 12 (58%)**	222 [77-739]	2.2 [0.0-11.4]	6.0 [2.3-144.0]

[a]Median [Min/Max] except for N, number of patients with $C_{avg} \geq 75$ ng/mL, number/total (% achieving PK target); AUC=Area under the concentration time curve to infinity to 12 hours for Cohort 2 (steady-state); Cavg = average concentration (AUC divided by tau set to 12 hours); C_{max} = maximum observed concentration; T_{max} = time of Cmax; $t_{1/2}$ = half-life.

Conclusions

Novel Aspects

- In the past 14 years, only 2 drugs have been licensed for use in neonates (FTC in 2006, RAL in 2018).
- Historically, new ARVs in neonates were studied in those at high-risk for HIV-1 acquisition. In this study, enrollment was regardless of risk status, facilitating earlier completion of this Phase I neonatal licensing trial.

Conclusions

- MVC appears safe and well-tolerated in this well-tolerated in this cohort of neonates treated over the first 6 weeks of life and followed through 16 weeks of age.
- MVC exposures met PK targets in ~2/3 of infants, but with considerable variability.
- MVC is a promising agent for prophylaxis and early treatment of HIV-1 exposed and infected neonates.

The study team would like to thank IMPAACT 2007 participants and their families in addition to ViiV Healthcare for their support of this trial.