508 Rilpivirine Pharmacokinetics With/Without Darunavir/r in Adolescents and Young Adults

Marc Foca[1], Ram Yogev[2], Andrew Wiznia[3], Rohan Hazra[4], Patrick Jean-Philipe[5], Bobbie Graham[6], Paula Britto[7], Vincent J. Carey[7], Jennifer King[8], Tim R. Cressey[9], for the IMPAACT P1058A team

[1]Pediatrics, Columbia University Medical Center, New York, NY, United States, [2]Pediatrics, Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL, United States, [3]Pediatrics, Jacobi Medical Center, Bronx, NY, United States, [4]National Institutes of Health, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Maternal and Pediatric Infectious Disease Branch, Bethesda, MD, United States, [5]Henry Jackson Foundation, National Institutes of Health, Division of Acquired Immunodeficiency Syndrome, International Maternal Adolescent Pediatric Branch, Bethesda, MD, United States, [6]Frontier Science & Technology, Amherst, NY, United States, [7]Harvard School of Public Health, Boston, MA, United States, [8]The University of Alabama at Birmingham, Birmingham, AL, United States, [9]Faculty of Associated Medical Sciences, Chiang Mai University, Chiang Mai, Thailand

Background: Rilpivirine (RPV), a second generation non-nucleoside reverse transcriptase inhibitor (NNRTI), is not recommended for patients <18 years of age. Once daily dosing of RPV makes it an attractive option for HIV-infected adolescents. We report the pharmacokinetic (PK) data of RPV once daily either alone or in combination with DRV/r as part of antiretroviral therapy in HIV-infected adolescents and young adults.

Methodology: IMPAACT P1058A is an ongoing observational study designed to evaluate the PK of antiretroviral drug combinations commonly used by HIV-infected children and adolescents. Patients <24 years old receiving RPV 25 mg once daily (with background NRTIs) either alone or combined with DRV/r 800/100 mg once daily were enrolled. Plasma samples were collected at pre-dose and 1, 2, 4, 6, 8, 12 and 24 hours after an observed dose. RPV and DRV plasma concentrations were determined using validated HPLC-UV and LC-MS/MS assays, respectively. The 90% confidence intervals (90% CI) for the geometric mean (GM) of the AUC and Cmin were compared with target ranges reported in adults.

Results: Data from 26 subjects were analyzed; 15 receiving RPV alone (8 male), and 11 receiving RPV in combination with DRV/r (7 males). The median (range) age and weight were 20 (13-23) years and 75 (40-117) kg, in the RPV alone group, and 20 (17-23) years and 68 (49-97) kg in the combination group. RPV and DRV PK parameters and adult target ranges are presented below:

The mean RPV AUC and Cmin for RPV alone were within the adult target ranges and the 90% CI had substantial overlap. In contrast, the mean and entire 90% CI for AUC and Cmin for RPV substantially exceeded the corresponding adult target when co-administered with DRV/r.

Conclusions: RPV alone in this age group provides similar exposure to adults. However, RPV exposure in patients receiving concomitant DRV/r was elevated two to three fold. It remains to be determined if this increased exposure leads to increased toxicity or side effect profiles, but currently, RPV dose reduction is not recommended. Further studies of this interaction are warranted.

PK Parameters GM (90% CI)	Rilpivirine 25 mg QD (n=15)	Rilpivirine 25 mg QD + DRV/r 800/100 mg QD (n=11)		Ratio of GM RPV With/Without DRV/r
	RPV	RPV	DRV	
AUC (µg.hr/mL)	2.38 (1.92,2.94)	6.93 (4.57,10.51)	76.6 (57.3,102.4)	2.91
Cmax (µg/mL)	0.14 (0.11,0.17)	0.42 (0.26,0.67)	6.06 (4.97,7.39)	2.98
Clast (µg/mL)	0.08 (0.06,0.10)	0.23 (0.15,0.35)	2.30 (1.43,3.69)	3.08
Cmin (µg/mL)	0.07 (0.05,0.09)	0.16 (0.10,0.27)	0.77 (0.40,1.50)	2.31
AUC Target range	1.4 to 2.2	1.4 to 2.2	48.8 to 76.3	
Cmin Target range	0.05 to 0.07	0.05 to 0.07	0.9 to 1.4	