describe ABC pharmacokinetic (PK) and safety data in HIV-infected normal and low birth weight (LBW) infants initiating ABC within the first 3 months of life.
Methods: IMPAACT P1106 is an opportunistic, multi-arm study of PK and safety in LBW infants conducted in South Africa on antiretroviral and antituberculosis medicines. Arm 5 included HIV-infected infants receiving ABC, lamivudine and lopinavir/ritonavir. Plasma samples for ABC PK assessment were collected pre-dose (C0), 1.5- and 4-hours post-dose at study weeks 2, 10, and 24, with C0 samples at weeks 6 and 16. ABC concentrations were measured by LC-MS/MS and ABC PK parameters estimated using a population approach. Adverse events (AE) were evaluated from entry to week 24.
Results: Twenty-five infants (18 LBW) were included in the analysis. Median entry age was 44 days (range 11 to 78 days). Twelve (48%) infants were male and 22 (88%) black African. Median ABC dose was 10 (6-13) mg/kg BID and ABC concentrations were available for 24 (195 observations) infants with median (range) birth weight 2190 g (1360-3260) and median gestational age 36 weeks (32-37). ABC plasma concentrations were described by a 1-compartment model. Infant body weight (BW) and post-menstrual age (PMA=gestational age+postnatal age [PNA]) influenced ABC PK parameters. ABC oral clearance (CL/F) increased by 2% per PMA week. Infant characteristics and ABC PK parameters per PK visit are shown in Table 1. One infant died of unknown cause 3 days after entry. Fourteen infants had Grade 3/4 AEs, among which most common were gastroenteritis (n=4) and respiratory infection (n=4) and all of which improved except for malnutrition (n=1), underweight (n=1) and a respiratory infection (n=1) present at the last study visit. No hypersensitivity was reported. All AEs were assessed as unrelated to ABC, except for one possibly related Grade 2 alanine aminotransferase where all antiretrovirals were stopped for 2 weeks until resolution then restarted without further complications.
Conclusion: ABC was well tolerated in LBW infants. ABC exposures were relatively high compared to older infants during the first 3 months of life but decreased rapidly as infants matured.

Table 1. Median (range) of Infant Characteristics and Abacavir PK parameters

Study Visit	ABC Dose (mg/kg)	Weight (kg)	PNA (Days)	PMA (Weeks)	CL/F (L/hr/kg)	*AUC_{0-12} (mg.hr/L)
Week 2 (n=16)	11 (6-13)	3.6 (2.4-5.4)	63 (41-93)	44 (38-50)	0.67 (0.24-1.42)	16.9 (4.6-48.7)
Week 10 (n=20)	9 (6-12)	5.2 (3.8-6.8)	118 (93-148)	52 (46-58)	0.79 (0.28-1.56)	10.7 (6.9-30.6)
Week 24 (n=20)	10 (7-12)	6.8 (5.1-8.9)	216 (186-247)	66 (59-71)	1.03 (0.34-1.97)	9.8 (4.4-33.9)

Historical ABC PK data in children 3 to 6 years old: AUC_{0-12}: 7.8 mg.hr/L [ARROW Trial: Musiime et al Antivir Ther. 2010;15(8):1115-24.]

844 ABACAVIR DOSING, EFFECTIVENESS, AND SAFETY IN YOUNG INFANTS LIVING WITH HIV IN EUROPE

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Background: The World Health Organization recommends abacavir (ABC) as the preferred/alternative backbone for 1st line regimens in children with HIV from age 28 days. There are limited data available on safety and tolerability of ABC in young infants aged <3 months.
Methods: All children in the European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC) who initiated ABC aged <3 months between 2000-2016 were included. We describe infant and regimen characteristics at the start of ABC (including drug combinations and dosing) and outcomes up to 12 months after first use of ABC. Outcomes include drug discontinuations (defined as interruption of treatment for >30 days), clinical adverse events (AE, reported from start of ABC up to 30 days after discontinuation) and viral suppression <400c/ml (VS) at 6 and 12 months of treatment for children who remained on ABC.
Results: Of 498 children in EPPICC who received antiretroviral therapy (ART) whilst aged <3 months, 139(28%) received an ABC-containing regimen (n=20 aged<28 days) and were followed for median 4.6 [IQR 1.5,9.7] years. Median year of birth was 2010 [2006,2012], age at HIV diagnosis was 39 [11,62] days and 84(60%) were female. 53(38%) were from UK and Ireland, 23(17%) Ukraine, 19(14%) Spain, 14(10%) Russia, 12(9%) Belgium and 18(13%) elsewhere in Europe. 63(45%) received post-exposure prophylaxis (PEP) prior to ABC-based treatment (4 PEP regimens included ABC, with the ABC continuing following HIV diagnosis). 54(39%) were taking ABC with lamivudine and lopinavir/ritonavir and for 44 infants with ABC dosing/weight data available, 30(68%) started on an 8mg/kg twice daily (BD) dose (Table).
Overall 66/92(70%) and 59/77(77%) on ABC-containing regimens had VS after 6 and 12 months, respectively. During the first 12 months on ABC, AEs were reported in 8 infants with 4 events leading to discontinuation of ABC, all occurring within the first 7 days of treatment (Table). By 12 months after start of ABC, cumulative incidence of discontinuation of ABC due to a safety concern was 3.6% (95% CI 1.4,7.8%). A further 11 infants discontinued ABC for other reasons (5 of 11 later restarted ABC) and the cumulative incidence of any discontinuation by 12 months was 11.8% (7.3,18.9%). There were no deaths reported during follow-up.
Conclusion: ABC is safe and well tolerated in infants, with rare discontinuations for safety concerns, supporting WHO treatment recommendation. More data on ABC use are required in neonates.

Table: Regimen characteristics, adverse events and drug discontinuations in infants who initiated abacavir aged <3 months

Characterises of ABC regimen		n(%)
Weight at start of ABC (n=71):	<3kg	8(11%)
	3 to <6kg	60(85%)
	6 to <10kg	3(4%)
Initial ABC dose (n=44):	<4mg/kg BD	3(7%)
	4-6mg/kg BD	6(14%)
	8mg/kg BD	30(68%)
	>8mg/kg BD	5(11%)
Initial regimen:	ABC+3TC+LPV/r	54(39%)
	ABC+3TC+AZT+NVP	45(32%)
	ABC+3TC +NVP	19(14%)
	Other	21(15%)

AEs and ABC discontinuations up to 12 months after ABC start	n
Treatment emergent AEs	8
Events leading to ABC discontinuation[1]	4
Other discontinuations	11
Non-compliance	3
Structured interruption	2
Treatment failure	2
More effective treatment available	1
Parents' wish	1
Unknown	2

Abbreviations: ABC – abacavir, 3TC – lamivudine, LPV/r – lopinavir/ritonavir, AZT – zidovudine, NVP – nevirapine
[1] Of 8 AEs, 4 led to ABC discontinuation within 7 days of starting ABC (1 in 2003, 1 in 2007 and 2 in 2011): 1 severe metabolic acidosis (initially thought to be ABC reaction, later confirmed rotavirus gastroenteritis; HLA-B 5701 negative); 1 diarrhoea and vomiting (considered unlikely related to ABC; HLA-B 5701 negative); 1 possible HLAB5701 positivity (unconfirmed); 1 hypersensitivity reaction. Other 4 AEs were: 3 pneumonia and 1 anaemia (possibly related to zidovudine).

845 ABACAVIR SAFETY AND EFFICACY IN YOUNG INFANTS IN SOUTH AFRICAN OBSERVATIONAL COHORTS

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Background: World Health Organization guidelines recommend abacavir as part of the preferred first line antiretroviral treatment (ART) regimen in children aged >28 days. However, there is no approved dose under 3 months of age, and with increasing access to early infant HIV diagnosis, more data are necessary to guide dosing recommendations in neonates. We describe the safety and effectiveness of abacavir in young infants in 9 South African cohorts participating in the IeDEA collaboration.
Methods: We included all infants who initiated ART (≥3 antiretroviral drugs from ≥2 classes) before 3 months of age, between 2006–2017. In those who received abacavir we described characteristics at abacavir initiation; the proportion who discontinued abacavir; and viral load suppression at 12 months. We compared infants who started abacavir aged <28 days with older infants, and those who weighed <3 kg with those who weighed ≥3 kg, in terms of abacavir discontinuations and viral load suppression, using Chi-squared or Fisher's exact tests.
Results: Of 1847 infants who started ART aged <3 months, 931 (50%) received abacavir: 96 were aged <28 days. At abacavir start, median (interquartile range, IQR) age was 67 days (48 to 80), CD4 percentage was 26.9 (19.0 to 37.0), viral load was 1 000 000 copies/mL (146 036 to 3 792 175), and weight was 4.2 kg (3.2 to 5.0). ART regimens included lamivudine and ritonavir-boosted lopinavir in 858 infants (92%), lamivudine and nevirapine in 9 (1%) and other antiretrovirals in 64 (7%). In those with ≥1 month's follow-up after abacavir initiation, 61/789 (8%) infants discontinued abacavir permanently, at a median of 13.3 months (IQR 6.4 to 26.8). There were no significant differences in the proportion of discontinuations by age or weight category (p=0.6 and 0.9 respectively, Table