Abacavir Dosing, Effectiveness and Safety in Young Infants Living with HIV in Europe

Siobhan Crichton[1], Intira Jeannie Collins[1] , Anna Turkova[1], Luminita Ene[2], Luisa Galli[3], Magdalena Marczynska[4], Marisa Navarro[5], Lars Naver[6], Antoni Noguera-Julian[7], Yulia Plotnikova[8], Henriette Scherpbier[9], Alla Volokha[10], Evgeny Voronin[11], Ali Judd[1] on behalf of the European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC)

[1]MRC Clinical Trials Unit at UCL, University College London, London, UK. [2]Victor Babes Hospital, Bucharest, Romania. [3]Department of Health Sciences, University of Florence, Meyer Children's University Hospital, Italy. [4]Medical University of Warsaw, Hospital of Infectious Diseases, Warsaw, Poland. [5]Hospital General Universitario "Gregorio Marañón", Complutense University, Madrid, Spain. [6]Karolinska Institutet and University Hospital, Sweden. [7]Unitat d'Infectologia, Servei de Pediatria, Hospital Sant Joan de Deu, Universitat de Barcelona, Barcelona, Spain. [8]Irkutsk Regional Centre for Prevention and Control of AIDS and Infectious Diseases, Irkutsk, Russian Federation. [9]Emma's Children Hospital, Amsterdam University Medical Centers, Netherlands. [10]Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine. [11]Republican Hospital of Infectious Diseases, St Petersburg, Russia

0844

s.crichton@ucl.ac.uk

Background

The World Health Organization (WHO) recommends abacavir 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 abacavir in young infants aged <3 months.

Inclusion criteria

All children in the European Pregnancy and Paediatric Infections Cohort Collaboration (EPPICC) who initiated abacavir aged <3 months between 2000-2016 were included.

Methods

We describe infant and regimen characteristics at the start of abacavir (including drug combinations and dosing) and outcomes up to 12 months after first use of abacavir.

Outcomes include:

- drug discontinuations (defined as interruption of abacavir for >30 days),
- clinical adverse events (AE, reported from start of abacavir, and up to 30 days after discontinuation of abacavir) and
- viral load at 6 and 12 (±3) months after start of abacavir.

Characteristics of infants initiating abacavir

- Of 498 children in EPPICC who initiated antiretroviral therapy (ART) aged <3 months, 139 (28%) received an abacavir containing regimen and were followed for median 4.6 [IQR 1.5,9.7] years.
- Characteristics of these 139 infants are shown in Table 1 and weight bands and regimen characteristics in Table 2.

Table 1: Characteristics of infants initiating abacavir age <3 months

	n(%) or median [IQR]
Year of birth	2010 [2006, 2012]
Female sex	84 (60%)
Age at HIV diagnosis (days)	39 [11,62]
Age at start of abacavir (days)	62 [35,78]
Age <28 days at start of abacavir	20 (14%)
Post-exposure prophylaxis received*	63 (45%)

*63 infants received post-exposure prophylaxis (PEP) prior to abacavir-based treatment. 4 of the 63 PEP regimens included abacavir, with the abacavir continuing following HIV diagnosis).

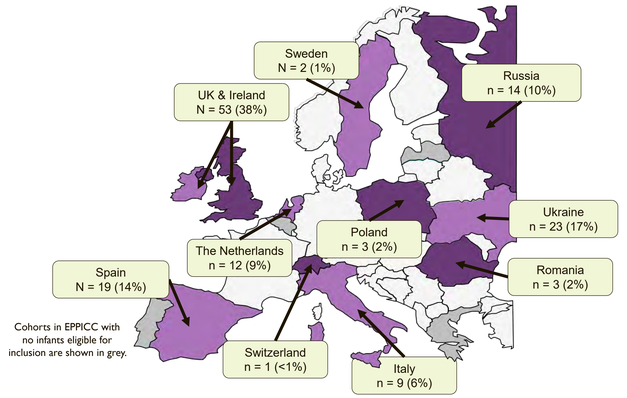


Figure 1: Location of infants included in analyses

- The 139 infants were from 13 cohorts in 11 countries across Europe (Figure 1).

Table 2: Weight bands and dosing at start of abacavir

	n(%)
Weight at start of abacavir (n=71)	
<3kg	8(11%)
3 to <6kg	60(85%)
6 to <10kg	3(4%)
Initial abacavir 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%)

Abbreviations: ABC – abacavir, 3TC – lamivudine, LPV/r – lopinavir/ritonavir, AZT – zidovudine, NVP – nevirapine
*The EMA recommend a dose of 8mg/kg BD from age 3 months but due to limited data do not provide dosing recommendations for those <3 months old. Excludes agacavir containing PEP regimend

Adverse events and drug discontinuations

- By 12 months after start of treatment 3.6% (n=4) had discontinued abacavir due to an ART safety concern and 11.8% (n=15) discontinued for any reason (Figure 2).
- During the first 12 months, 8 infants had one AE each (Table 3). Four of these AEs led to discontinuation of abacavir, all occurred within 7 days of starting abacavir (1 in 2003, 1 in 2007 and 2 in 2011). The AEs were:
  - 1 severe metabolic acidosis (initially thought to be abacavir reaction, later confirmed rotavirus gastroenteritis; HLA-B 5701 negative);
  - 1 diarrhoea and vomiting (considered unlikely related to abacavir; HLA-B 5701 negative);
  - 1 possible HLAB5701 positivity (unconfirmed);
  - 1 hypersensitivity reaction (HLAB5701 status unknown).
- The other 4 AEs reported (which did not lead to abacavir discontinuation) were 3 pneumonia and 1 anaemia (possibly related to zidovudine):
- There were no deaths reported during follow-up of the 139 children who initiated abacavir in infancy.

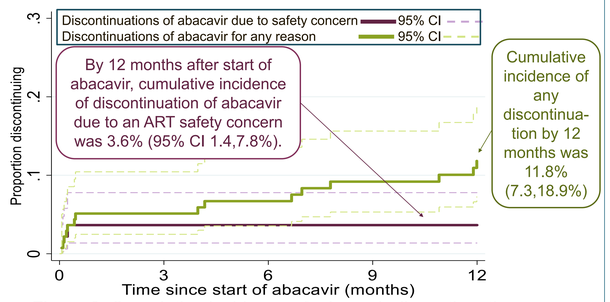


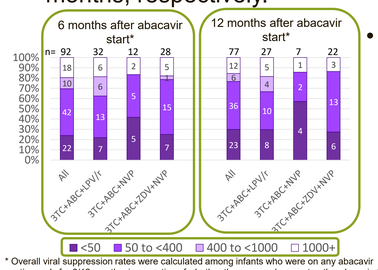
Figure 2: Cumulative incidence of abacavir discontinuations

Table 3: AEs and discontinuations up to 12 months after abacavir start

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

Viral suppression at 6 and 12 months

- 64/92(70%) and 59/77(77%) on abacavir containing regimens had viral load <400 copies/mL at 6 and 12 months, respectively.



* Overall viral suppression rates were calculated among infants who were on any abacavir continuously for 6/12 months, irrespective of whether there were changes to other drugs in the regimen. Suppression rates by regimen were restricted to those who remained on their initial regimen for 6/12 moths,

- Viral load at 6 and 12 months of treatment did not differ significantly by regimen type (p=0.433 and 0.319, respectively)

Figure 3: Viral load at 6 and 12 months after start of continuous abacavir by regimen

Conclusions

- Across children initiating abacavir in early life in Europe, it was safe and well tolerated, and discontinuations for safety concerns were rare.
- Viral suppression was below the UN-AIDS 90% target which may reflect challenges of treatment in infancy.

Acknowledgements

Cohorts participating in EPPICC: Hospital St Pierre Cohort, Brussels, Belgium (T Goetghebuer); Greece Cohort, Greece (V Spoulou); Italian Register for HIV infection in children, Italy (L Galli, M de Martino); Latvian Cohort, Latvia (S Ansone); ATHENA Cohort, Netherlands (P Reiss, H Scherpbier, C Smit); Paediatric Cohort, Poland (M Marczynska); "Victor Babes" Hospital Cohort, Romania (L Ene); The Republican Hospital of Infectious Diseases, St Petersburg, Russia (E Voronin, L Okhonskaia); The City HIV Centre, St Petersburg, Russia (A Samarina); Irkutsk AIDS Centre (Y Plotnikova, V Rozenberg); CoRISPE-cat, Catalonia, Spain (A Noguera Julian); CoRISPES, rest of Spain cohort, Spain (P Rojo Conejo , J Tomas Ramos Amador); Karolinska University Hospital, Stockholm, Sweden (L Naver); Swiss Mother and Child HIV Cohort Study, Switzerland (C Kahlert); Thailand Program for HIV Prevention and Treatment (PHPT) Study Group, Thailand (G Jourdain, N Ngo-Giang-Huong); National Study of HIV in Pregnancy and Childhood, UK and Ireland (C Thorne); Collaborative HIV Paediatric Study, UK and Ireland (A Judd, Di Gibb); Paediatric HIV Cohort Study, Odessa, Ukraine (R Malyuta). **Funding:** PENTA Foundation