

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

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

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.

## 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 Anson); ATHENA Cohort, Netherlands (P Reiss, H Scherpbier, C Smit); Paediatric Cohort, Poland (M Marczyńska); "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 Kahler); 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 Maljuta). **Funding:** PENTA Foundation

## 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.

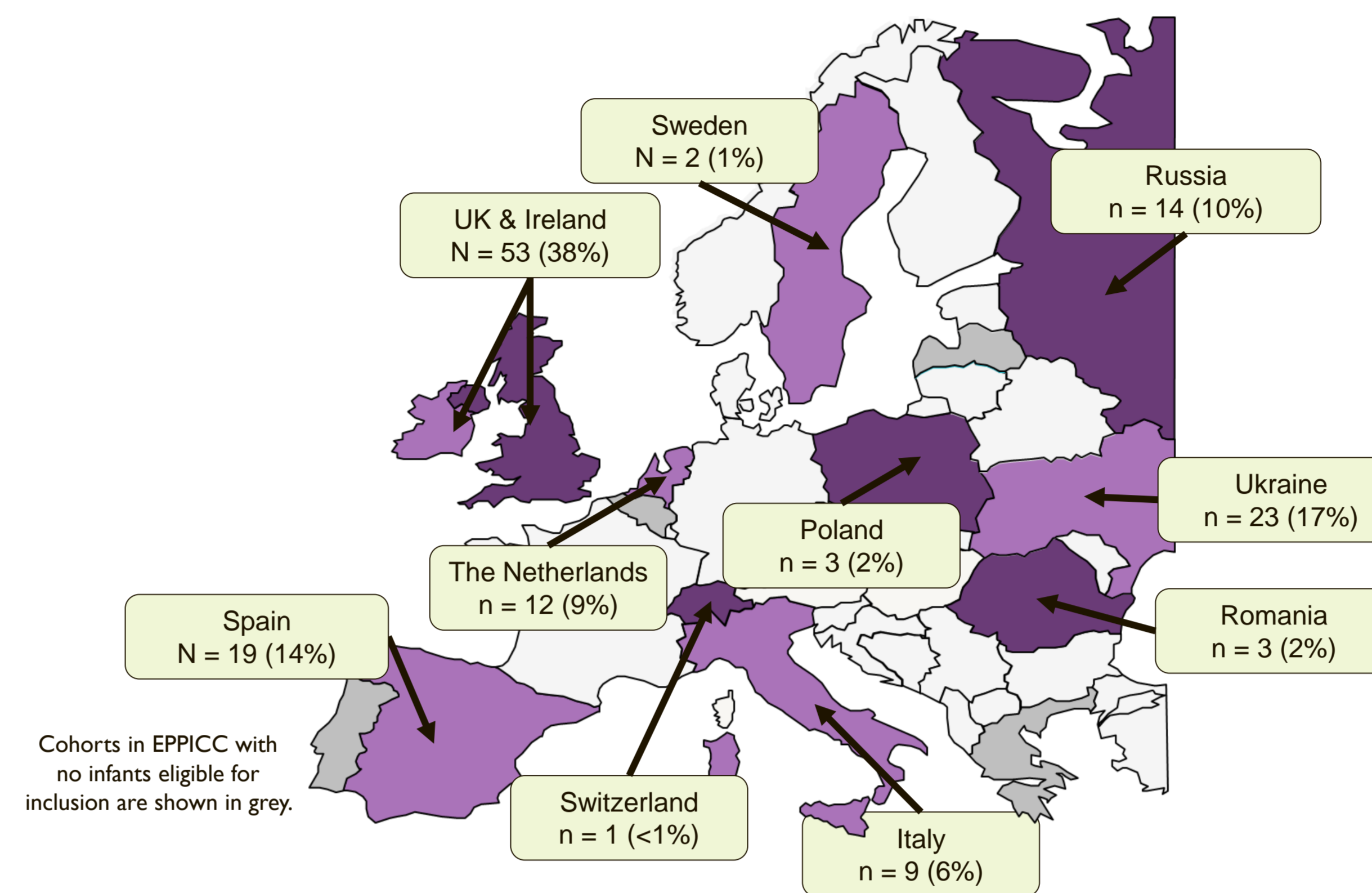


Figure 1: Location of infants included in analyses

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

Table 2: Weight bands and dosing at start of abacavir

Weight at start of abacavir (n=71)	n(%)
<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 regimen

## 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.

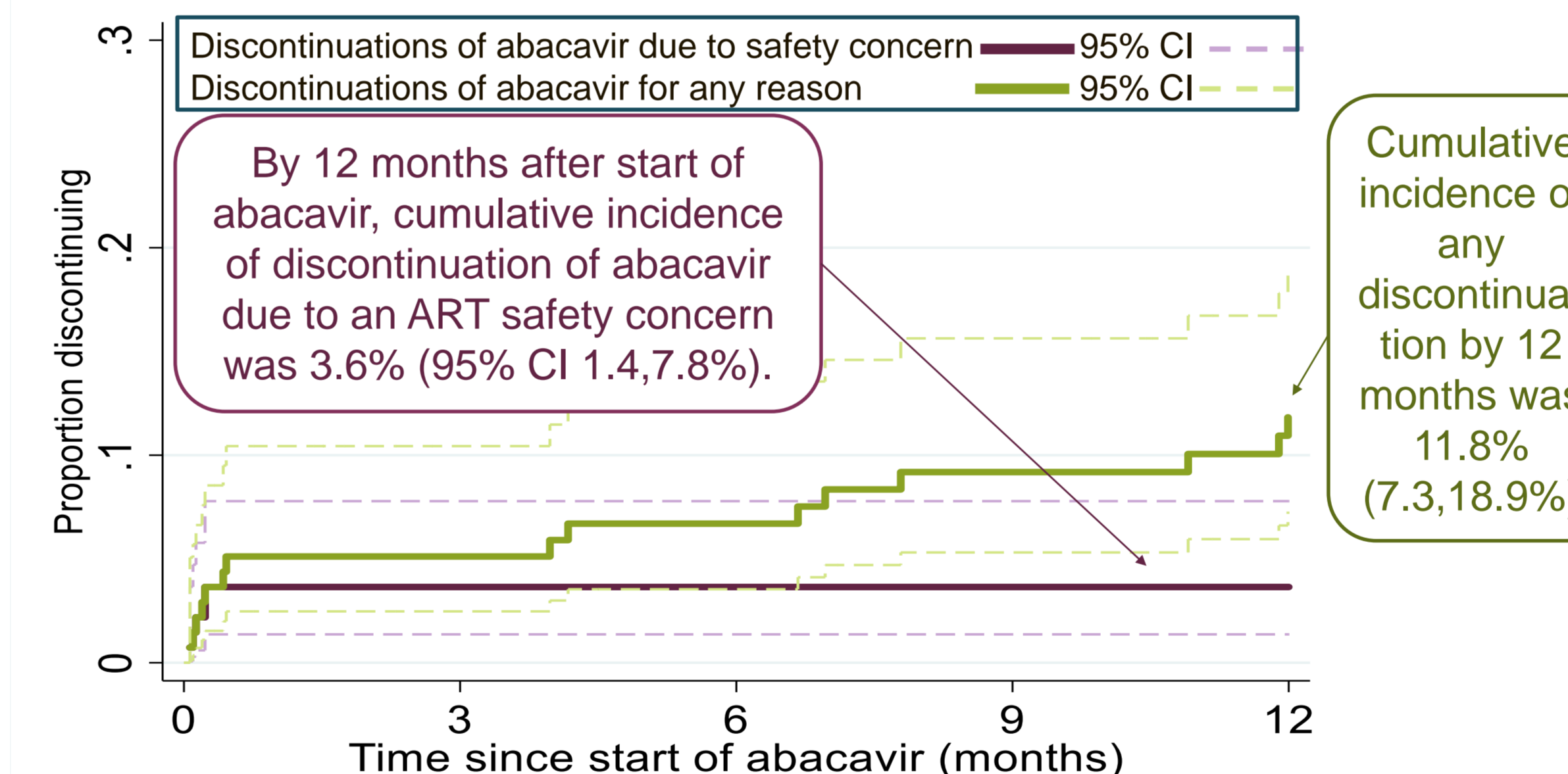


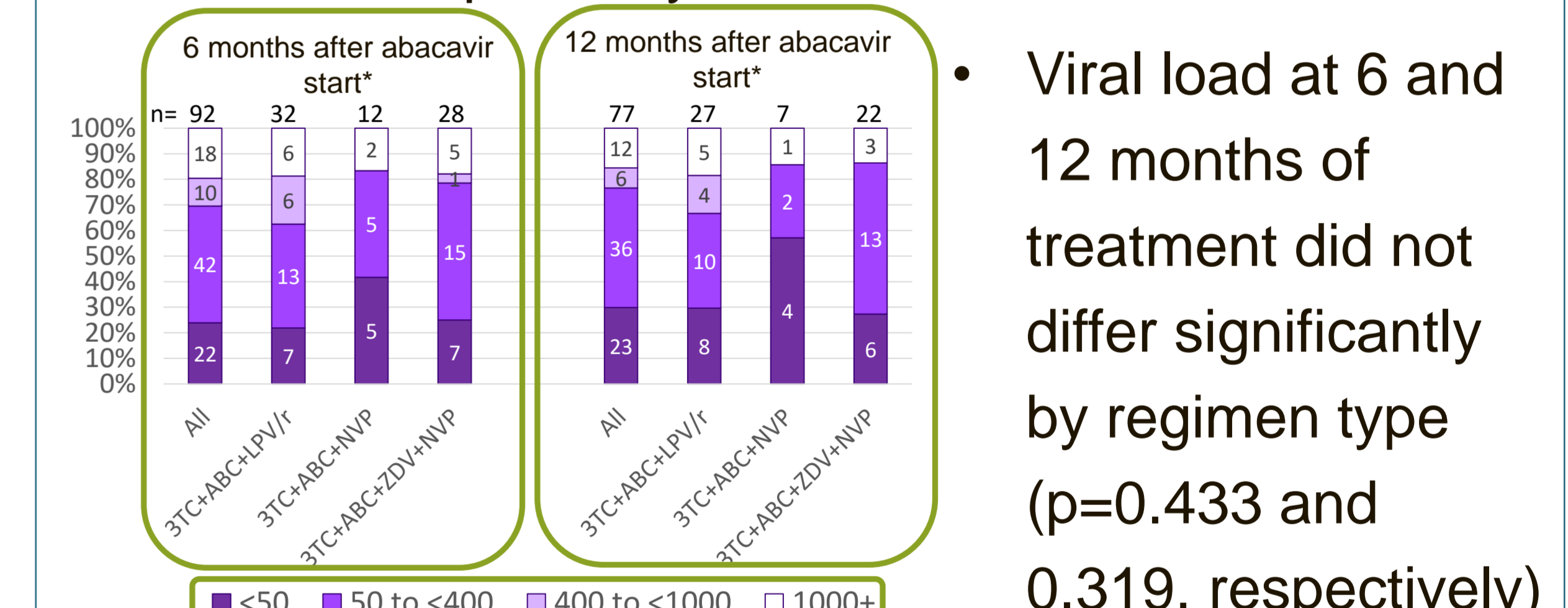
Figure 2: Cumulative incidence of abacavir discontinuations

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

AEs and abacavir discontinuations up to 12 months after abacavir start	n
<b>Treatment emergent AEs</b>	8
Events leading to abacavir discontinuation <sup>1</sup>	4
<b>Other discontinuations</b>	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 months.

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.