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Abacavir Usage Patterns and Hypersensitivity Reactions (HSR) in the EuroSIDA cohort

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Background

- Potentially fatal hypersensitivity reactions (HSR) occurs in 5-8% of those initiating abacavir (ABC)
- We describe the proportion of individuals on cART receiving ABC-based regimens and factors associated with ABC utilization and discontinuation

Methods

- We calculated the proportion of EuroSIDA individuals receiving ABC-based cART among those receiving cART each year after 1/1/2009
- Multivariable Poisson regression was used to identify demographic, clinical and laboratory factors associated with ABC utilization and any discontinuation or due to HSR or HSR/any toxicity within 6 weeks of ABC initiation

Results

- 3,472 (34%) received ABC-based cART of 10,076 on cART
- Temporal trends of ABC utilization remained steady, with some variation across regions (**Figure 1**)
- Lower ABC utilization was associated with older individuals, higher CD4 cell-counts, higher cART lines, prior AIDS diagnosis, and 2014 had the lowest utilization (**Figure 2**)
- Higher ABC utilization was associated with higher HIV viral loads, CKD, and DAD-CKD risk. Persons from Central-East and Eastern Europe were more likely to utilize ABC compared to other regions (**Figure 2**)
- 2,139 started ABC after 1/1/2009; within 6 weeks of ABC initiation (**Table 2**)
  - 113 discontinued for any reason; IR per 100 person years =14.5 (95% CI = 12.1, 17.5)
  - 10 discontinued due to HSR; IR = 0.3 (0.1, 1.0)
  - 35 discontinued due to HSR/any toxicity; IR = 4.5 (3.2, 6.3)
  - 7 individuals died; no deaths were attributed to HSR
- No factors were associated with ABC discontinuation

Conclusion

- ABC remains a commonly used ARV across Europe
- There is a low incidence of ABC discontinuation due to HSR in our study population
- Decrease in reported rates of HSR could be attributed to HLAB*5701 screening uptake, although this data was not available in EuroSIDA

Table 1: Baseline characteristics, split by ABC use (total *vs.* no ABC *vs.* ever *ABC*) in the EuroSIDA cohort from 1/1/2009 to 4/1/2016

	Total N = 10076		No ABC N = 6604		ABC N = 3472		
	No.	%	No.	%	No.	%	p-value
Gender							
Male	7408	74	4926	75	2482	72	0.001
Female	2668	27	1678	25	990	29	
Region of Care in Europe							
South	2819	28	1962	30	857	25	<0.001
West	2478	25	1672	25	806	23	
North	2187	22	1348	20	839	24	
Central-East	1430	14	897	14	533	15	
East	1162	12	725	11	437	13	
HIV-Risk group							
MSM	4,054	40	2,701	41	1,353	39	0.171
IDU	2,198	22	1,438	22	760	22	
MSW	3,138	31	2,012	31	1,126	32	
OTH/NK	686	7	453	7	233	7	
Calendar year *†	2009	(2009, 2011)	2009	(2009, 2011)	2011	(2009, 2010)	0.001
Baseline Age †	45	(37, 52)	45	(37, 51)	51	(38, 52)	0.001
Baseline HIV-RNA †	49	(39, 74)	49	(39, 71)	71	(33, 90)	<0.001
Baseline CD4 cell count †	490	(337, 688)	488	(340, 679)	679	(333, 709)	0.385
CKD	172	2	106	2	66	2	<0.001
AIDS	3,228	32	2,045	31	1,183	34	0.001

Baseline defined study entry (1/1/2009 or enrolment into EuroSIDA, whichever occurred latest); % are column percentages; * calendar year of first ABC utilization; † values are median (IQR); Region of care in Europe - South: Argentina, Greece, Israel, Italy, Portugal, Spain; West: Austria, Belgium, France, Germany, Luxembourg, Switzerland, North: Denmark, Finland, Iceland, Ireland, Netherlands, Norway, Sweden, United Kingdom; Central-East: Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Poland, Romania, Serbia; Slovakia, Slovenia East: Belarus, Estonia, Georgia, Latvia, Lithuania, Russian Federation, Ukraine; MSM - sex between men; IDU - injection drug use; MSW - sex between men and women; OTH/NK - other, unknown

Figure 1: Percent (95% CI) prescribed ABC at the midpoint of each year overall and by region in the EuroSIDA cohort from 2009 to 2016

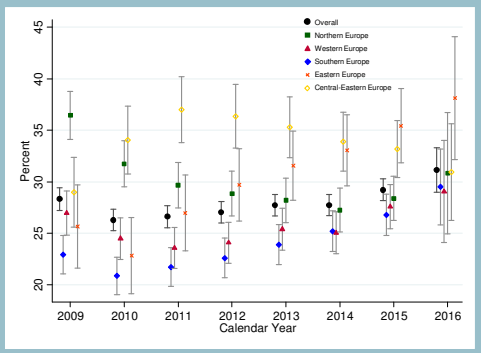
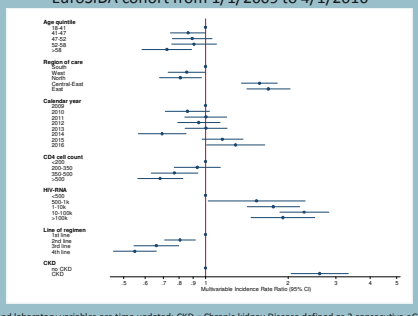


Figure 2: Multivariable incidence rate ratios for ABC utilization in the EuroSIDA cohort from 1/1/2009 to 4/1/2016



All clinical and laboratory variables are time updated; CKD = Chronic kidney Disease defined as 2 consecutive eGFRs >60 more than 3 months apart using the CKD EPI formula; Other variables in the model include Gender, Framingham CVD 10 year elevated risk, HCV, and HBV status, DAD CKD risk score and previous AIDS diagnosis

Table 2. Reasons and incidence rates for ABC discontinuation in the EuroSIDA cohort from 2009-2016. Individuals were censored at 6 weeks after ABC initiation, ABC discontinuation or death, whichever came first.

Reason for stopping treatment	Failures	Rate*	95% CI
Any Reason	113	14.51	(12.07, 17.45)
HSR or any toxicity	35	4.49	(3.23, 6.26)
Any toxicity	22	2.82	(1.86, 4.29)
Unknown	21	2.70	(1.76, 4.14)
Patient's wish/decision	20	2.57	(1.66, 3.98)
Other causes	17	2.18	(1.36, 3.51)
Physician's decision	16	2.05	(1.26, 3.35)
Toxicity - GI tract	16	2.05	(1.26, 3.35)
HSR	13	1.67	(0.97, 2.87)
Toxicity – Liver	2	0.26	(0.06, 1.03)
Toxicity, predominantly CNS	2	0.26	(0.06, 1.03)
Toxicity, predominantly kidneys	2	0.26	(0.06, 1.03)
Treatment Failure	1	0.13	(0.02, 0.91)
Concern of cardiovascular disease, including dyslipidaemia	1	0.13	(0.02, 0.91)
Other Toxicity	1	0.13	(0.02, 0.91)
Non-compliance	1	0.13	(0.02, 0.91)

*Total person years follow-up = 778; Rate = per 100 person years

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EuroSIDA