# Abacavir (ABC) use and risk of recurrent myocardial infarction (MI)

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## INTRODUCTION

D:A:D

- Previous analyses of the D:A:D Study, published in 2008, have demonstrated that current exposure to ABC is associated with an increased risk of MI<sup>1,2</sup>. However, associations between exposure to the drug and the risk of a subsequent MI in persons who have already experienced an MI have not yet been investigated.
- Our objective was to describe associations between ABC use and subsequent MI among people having experienced at least one MI during prospective D:A:D follow-

## **METHODS**

- We considered the rate of recurrent MI among D:A:D participants who had experienced an MI during study follow-up and who remained under follow-up at 28 days post-MI
- Follow-up was considered from 28 days post-MI to the date of next new (recurrent) MI, death, 1st February 2014 or 6 months after last clinic visit
- Poisson regression models considered associations between recurrent MI and exposure to ABC before and after adjusting for calendar year and age (both timeupdated)
- Three different exposures to ABC were considered:
- Use at the time of initial MI (time-fixed);
- Current, post-MI use (time-updated); and
- Cumulative use (time-updated, including exposure both pre- and post-MI)

#### **RESULTS**

- 816 people who developed an MI during prospective follow-up remained alive and under follow-up for at least 28 days.
- Included individuals were largely male (91.4%), infected with HIV through sex between men (59.6%) and had a median age of 51 years (inter-quartile range [IQR] 44-58) at initial MI. 80.1% of participants were current/ex-smokers (**Table 1**).
- Median CD4 count at initial MI was 503 (IQR 340-728) cells/mm<sup>3</sup>. Most people (793, 97.2%) had received antiretroviral therapy (ART), with 719 (88.1%) receiving ART at the time of MI; 544 people (66.8%) had an HIV RNA <50 copies/ml.
- 415 (50.9%) people had received ABC prior to initial MI for a median of 3.1 years (IQR 0.1-13.9) and 277 (34.0%) were still on ABC at the time of initial MI. Of these, 204 (73.7%) subsequently stopped using the drug after their initial MI (Table 2). Of the 139 people who, after their initial MI, either started ABC for the first time or restarted ABC after a previous use, 120 (86.3%) did so prior to the publication of the D:A:D study findings in 2008 demonstrating an association between ABC and MI.

Modian (IQR) age (years) at MI	Total number of persor	ns		816	(100.0)
Mode of infection, n (%)	Male gender, n (%)			746	(91.4)
Mode of infection, n (%)	Median (IQR) age (ye	ars) at MI		51	(44, 58)
n (%)   Injection drug use   109   (13.4)   Heterosexusi   175   (21.5)   C21.5)			sex with men	486	
Other/not known   46   (5.6)	n (%)		ction drug use	109	(13.4)
Race, n (%)    White   459   (56.3)     Black African   24   (2.9)     Other   13   (1.6)     Not known   320   (39.2)     Year of MI   1999-2001   95   (11.6)     2002-2004   203   (24.9)     2005-2007   200   (24.5)     2008-2010   178   (21.8)     2008-2011   178   (21.8)     2008-2011   178   (21.8)     2018-2011   178   (21.8)     2018-2011   178   (21.8)     2018-2011   178   (21.8)     2018-2011   178   (21.8)     2018-2011   178   (21.8)     2018-2011   178   (21.8)     30   (3.7)     Smoking, n (%)   Lurrent smoker   464   (56.9)     Ex-smoker   189   (23.2)     Diabetes, n (%)   113   (13.9)     Diabetes, n (%)   113   (13.9)     Diabetes, n (%)   525   (64.3)     High Carrent   189   (23.2)     Pervious MI before D:A:D entry, n (%)   124   (19.3)     Pervious MI before D:A:D entry, n (%)   124   (19.3)     Pervious MI before D:A:D entry, n (%)   195   (23.9)     Moderate (10-20%)   263   (32.2)     High (≥20%)   228   (27.9)     Not known   130   (15.9)     ABC   Ever received, n (%)   793   (97.2)     ABC   Ever received, n (%)   415   (50.9)     Median (IQR) years   3.1   (0.0, 13.9)     On at the time of MI, n (%)   277   (34.0)     PIs   Ever received, n (%)   695   (85.2)     Median (IQR) years   2.8   (0.0, 17.7)     NNRTIS   Ever received, n (%)   695   (85.2)     Median (IQR) years   2.8   (0.0, 17.7)     NNRTIS   Ever received, n (%)   571   (70.0)     Median (IQR) years   2.8   (0.0, 17.7)     On at the time of initial MI   (n=277)   Remained on ABC   73 (26.3)     Stopped ABC   204 (73.7)     Restarted ABC   204 (73.7)     Never received ABC prior to initial Started ABC   63 (15.7)		_			
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- People with an MI were followed for a median of 4.2 (range 0.1-13.2) years after their MI (total person-years of follow-up (PYFU): 3863). Over this time, there were 102 recurrent MIs, giving a rate of 2.64/1000 PYFU (95% Confidence Interval [CI] 2.13-3.15).
- Rates of recurrent MI were 2.75 (1.90-3.60) and 2.57 (1.93-3.21)/1000 PYFU in those who were and were not on ABC at initial MI. Rates were 3.47 (2.37-4.57) and 2.31 (1.75-2.88)/1000 PYFU in those who were/were not currently receiving ABC post-MI (Figure 1).
- Whilst neither cumulative exposure to ABC nor receipt of ABC at initial MI were significantly associated with recurrent MI risk, current post-MI exposure was associated with an increased risk (Figure 1). With the exception of age, there were no significant associations between demographic or lifestyle factors and recurrent MI. Earlier calendar year was, however, associated with an increased risk (Table 3).
- The association between recent ABC use and recurrent MI risk was similar after controlling for age (adjusted relative hazard: 1.51 [95% CI 1.01, 2.25], p=0.04), but was attenuated after controlling for calendar year (1.19 [0.79, 1.79], p=0.40).

# **CONCLUSIONS**

- Whilst we found some evidence that use of ABC post-MI was also associated with an elevated risk of a recurrent MI, this effect was attenuated after adjusting for calendar
- This suggests that the apparent increased risk may be explained by greater use of ABC in those with an initial MI in the earlier years of the study, although our findings should be interpreted cautiously given the collinearity between current ABC use and calendar year.

#### REFERENCES

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- 2. Sabin C et al. Poster 957c. 15th Conference on Retroviruses and Opportunistic Infections, Feb 3-6, 2008, Boston

## Acknowledgements

ACKNOWIEGEMENTS

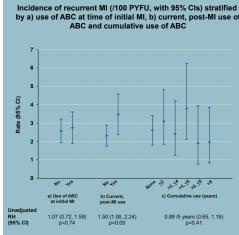
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6 Abb/le, Bristol-Myers Squibb, Gilead Sciences, XiVI Healthcare, Merck and Janssen Pharmaceuticals.



Results from univariable analyses of association between non-ABC factors and recurrent MI

Factor		Relative Rate (RR)	95% CI	p-value
Year	1999-2001	12.32	(5.17, 29.37)	0.0001
	2002-2004	4.91	(2.53, 9.54)	0.0001
	2005-2007	3.74	(1.98, 7.04)	0.0001
	2008-2010 2011-2013	2.34	(1.23, 4.46)	0.01
	2011-2013	1	•	-
Gender	Male	0.98	(0.48, 2.03)	0.97
	Female	1	-	-
Age (/5 years older)		1.02	(1.00, 1.04)	0.06
Smoking	Current	0.93	(0.49, 1.76)	0.83
	Ex-	1.13	(0.60, 2.15)	0.71
	Never	1		
	Unknown	0.89	(0.29, 2.77)	0.85
Ethnicity	White	1		-
	Non-white	0.75	(0.50, 1.12)	0.16
Mode of infection	MSM	1		
	IDU	0.55	(0.26, 1.14)	0.11
	Heterosexual	0.83	(0.49, 1.38)	0.47
	Other/unknown	3.03	(1.67, 5.51)	0.0003
Dyslipidaemia		0.76	(0.43, 1.37)	0.36
Body mass index	<18	1.21	(0.49, 3.01)	0.68
	>18, <26	1		-
	>26, <30	0.83	(0.47, 1.45)	0.51
	>30	0.86	(0.35, 2.14)	0.75
	Not known	2.81	(1.48, 5.32)	0.002
Diabetes		1.34	(0.82, 2.18)	0.24
Hypertension		0.74	(0.46, 1.19)	0.21
Gender, ethnic group, movariates; calendar year, ecent exposure to ABC w	age, smoking status,	dyslipidaemia,	BMI, diabetes, hype	

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