RESPOND International Cohort Consortium of Infectious Diseases

Recent Abacavir Use and Incident Cardiovascular Disease in Contemporary Treated PLWH within the RESPOND Cohort Consortium

Nadine Josephine Jaschinski on behalf of the RESPOND study group

CHIP, Section 2100, Rigshospitalet, Copenhagen, Denmark

Co-authors: L. Greenberg; B. Neesgaard; J. M. Miró; K. Grabmeier-Pfistershammer; G. Wandeler; C. Smith; S. De Wit; F. Wit; A. Pelchen-Matthews; C. Mussini; A. Castagna; C. Pradier; A. d'Arminio Monforte; J. J. Vehreschild; A. Sönnerborg; A. Volny-Anne; A. Carr; L. Bansi-Matharu; J. D. Lundgren; H. Garges; F. Rogatto; R. Zangerle; H.F. Günthard; L. D. Rasmussen; C. Necsoi; M. van der Valk; M. Menozzi; C. Muccini; A. Mocroft; L. Peters and L. Ryom.

18th European AIDS Conference (EACS)

October 27-30, 2021, London, United Kingdom

Presenter Disclosure Information

RESPOND International Cohort Consortium of Infectious Diseases

Nadine Josephine Jaschinski

Disclosed no conflict of interest

Introduction

RESPOND International Cohort Consortium of Infectious Diseases

Background:

- An increased risk of myocardial infarction (MI) with recent abacavir (ABC) use was first reported by the D:A:D study in 2008 [1]
  - The association persisted in the period from 2008-2013 [2]
- Somewhat inconsistent findings across other studies [3-5]
- Increased platelet reactivity suggested as a possible causal mechanism [6]

Purpose:

- To assess whether the association between ABC and cardiovascular disease (CVD) remained amongst contemporarily treated PLWH within RESPOND
- To investigate whether the association depends on the estimated 5-year CVD or chronic kidney disease (CKD) risk score strata

1. Sabin CA, et al. Lancet. 2008; 2. Sabin CA, et al. BMC Med. 2016; 3. J Lundgren, et al. AIDS. 2008;
4. Brothers CH, et al. JAIDS. 2009; 5. Ding X, et al. 2012; 6. Baum PD, et al. AIDS. 2011

Methods

RESPOND International Cohort Consortium of Infectious Diseases

Inclusion:

- RESPOND [1] participants aged ≥18 years were followed from latest of cohort enrolment or 1st of January 2012 (baseline)

Outcomes:

- Cardiovascular disease (CVD) - rigorously defined composite endpoints: MIs, strokes, invasive cardiovascular procedures (ICP)

Statistical analysis:

- Individuals followed to the first CVD event, last follow-up or 31st of December 2019, whichever occurred first
- Recent ABC use: current use or use within six months [2]

1. Neesgaard et.al. Microorganisms, 2020; 2. Sabin CA, et al. Lancet. 2008

Methods

RESPOND International Cohort Consortium of Infectious Diseases

Statistical analyses:

- Logistic regression to assess the odds of initiating ABC by the estimated D:A:D 5-year CVD and 5-year CKD risk score strata
- Negative binomial regression to assess the association between recent ABC use and risk of CVD, adjusted for:
  - Age, sex, ethnicity, region, BMI, HIV transmission risk group, CD4 count, hypertension, diabetes, AIDS, CVD, CKD and dyslipidemia – all fixed at baseline
  - Calendar year, smoking status, exposure to INSTI, cumulative exposure to boosted lopinavir and darunavir, indinavir, didanosine and stavudine – all time updated
- Interaction analyses between relative CVD risk with recent ABC use and 5-year CVD and 5-year CKD risk score

Results

RESPOND International Cohort Consortium of Infectious Diseases

Demographics:

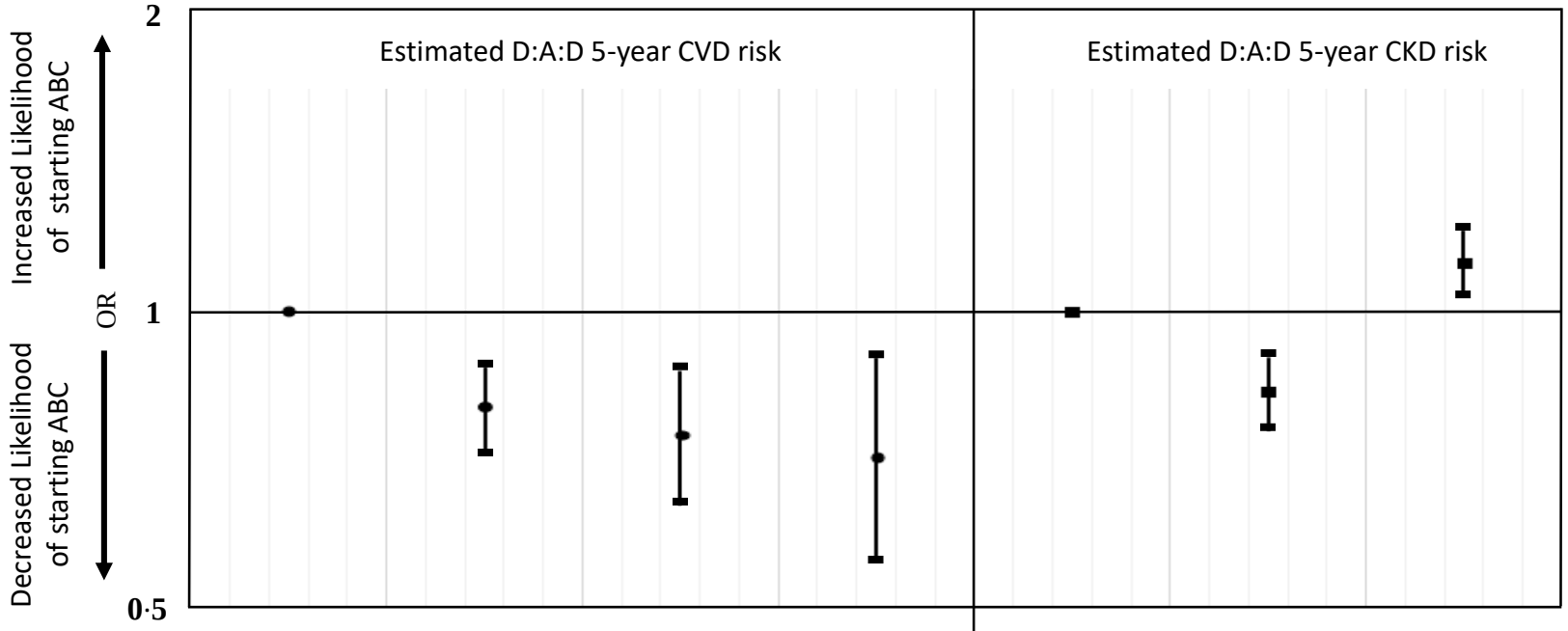
- A total of **29,340** individuals included: median age **44 years** (IQR 36 – 51) and median CD4 count **524 cells/µL** (IQR 357-715)
- Predominantly male (**74%**), White (**70%**) with MSM as primary mode of transmission (**45%**)
- Baseline CVD risk factors: Diabetes (**4%**), hypertension(**19%**), current smoking (**28%**), any dyslipidemia (**61%**)
- Overall, **34%** were recently using ABC; of those, **32%** were on boosted protease inhibitors

CVD events:

- During **6.16 years** median follow-up (IQR 3.87-7.52; 160,252 person-years of follow-up, PYFU), **748 CVD events: 299 MIs**, **228 strokes** and **221 ICPs**
  - Incidence rate **4.7/1000 PYFU** (95% CI 4.3-5.0)

Results

Odds of iniating ABC by 5-year CVD and CKD risk score:



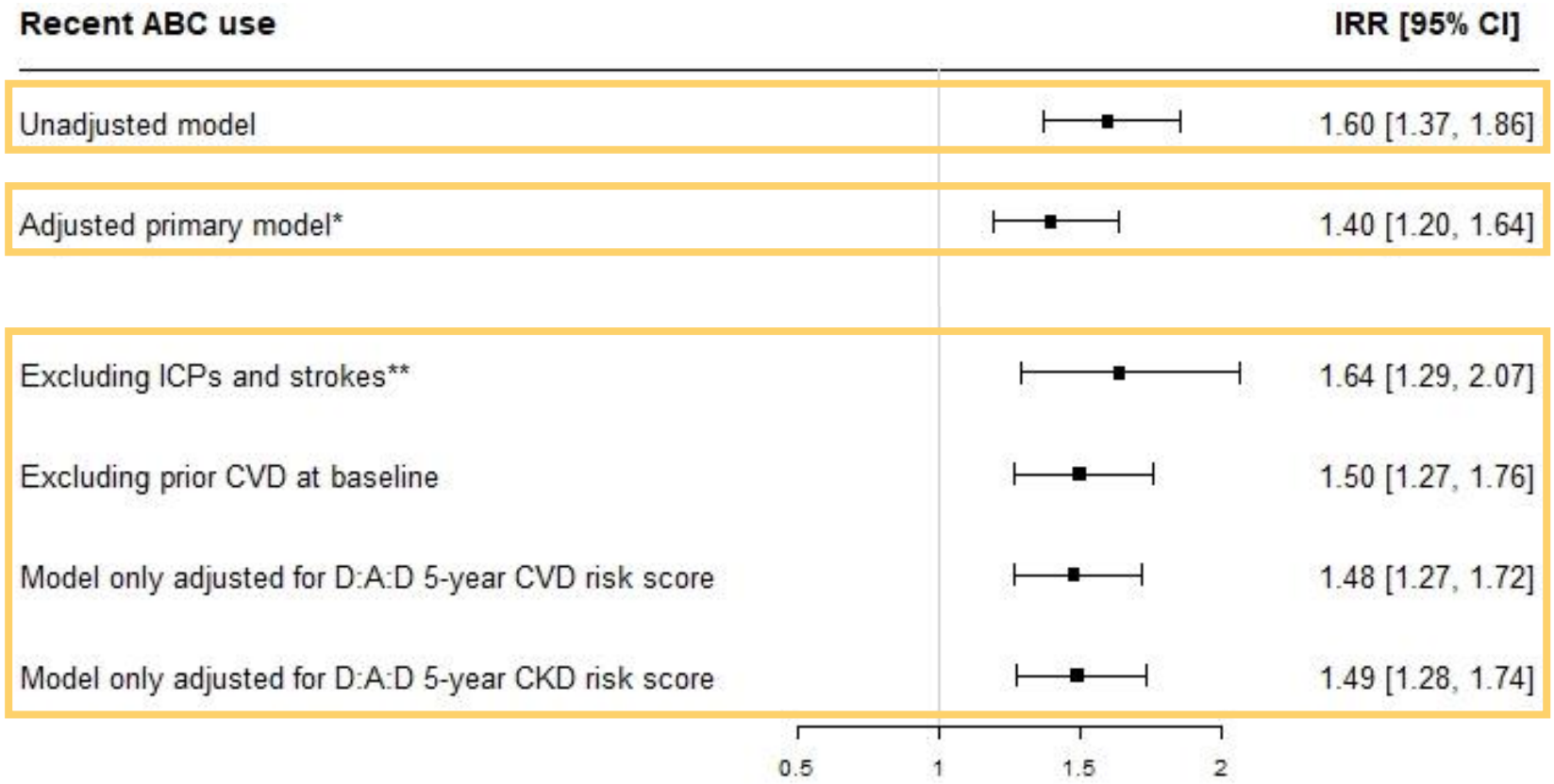
	Low (<1%)	Moderate (≥1 – <5%)	High (≥5 – <10%)	Very high (≥10%)	Low (< 0)	Moderate (≥0 – <5)	High (≥5)
Adjusted odds ratio* (95% CI)	**1**	**0.80** (0.72–0.88)	**0.75** (0.67–0.87)	**0.71** (0.56–0.90)	**1**	**0.83** (0.76–0.90)	**1.12** (1.04–1.21)
p-values	(ref)	<0.001	<0.001	<0.001	(ref)	<0.001	<0.001

*adjusted for baseline year

Results

RE SPOND International Cohort Consortium of Infectious Diseases

Incidence rate ratios (IRR) of CVD: recent ABC use compared to no recent ABC use



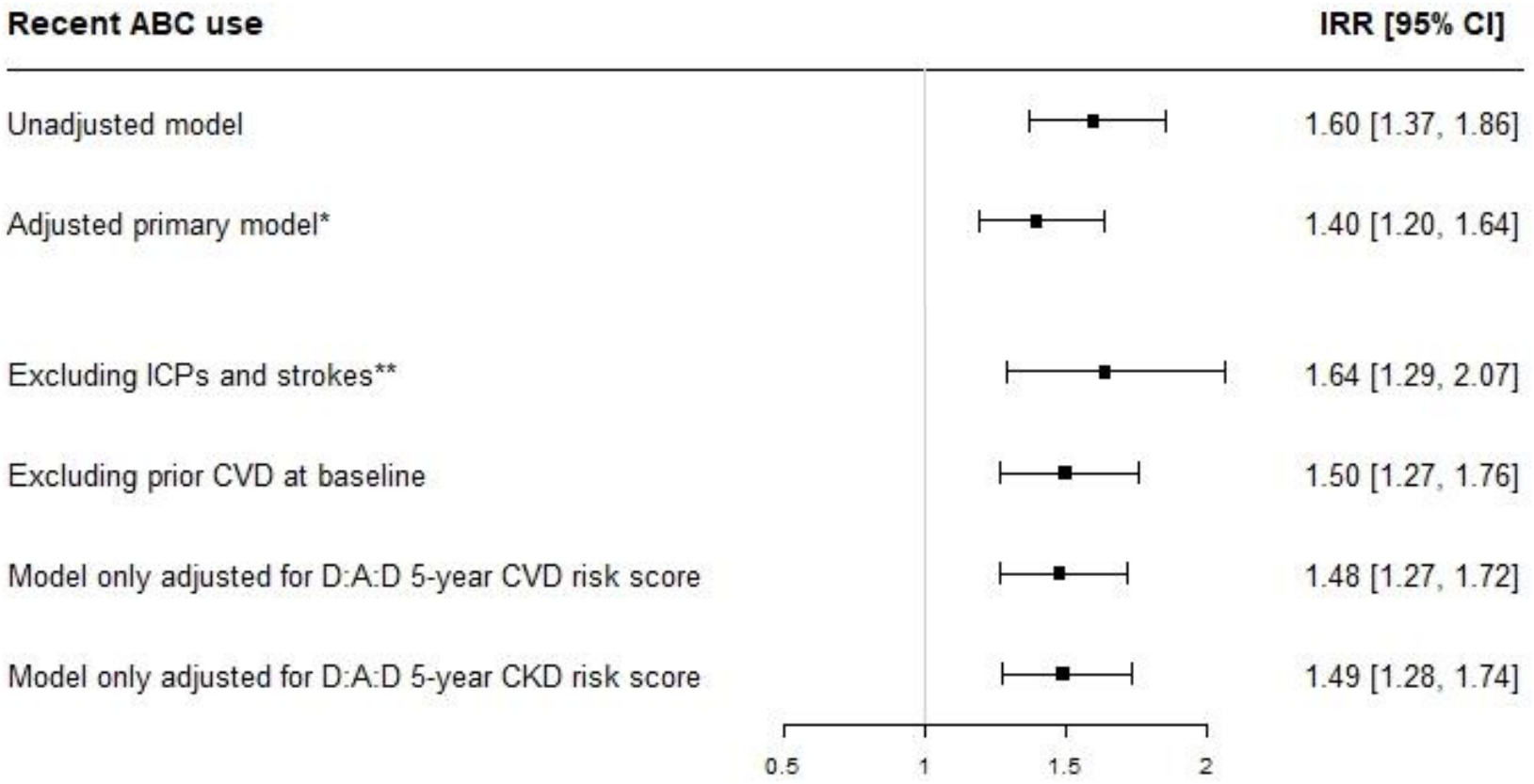
*Adjusted for age, sex, ethnicity, region, BMI, HIV risk, CD4 count, hypertension, diabetes, AIDS, CVD, CKD, dyslipidemia (all fixed at baseline), calendar year, smoking status, exposure to INSTI, cumulative exposure to boosted lopinavir and darunavir, indinavir, didanosine and stavudine (all time updated)

**Only adjusted for age, CD4 nadir, smoking status and prior CVD

Results

RESPOND International Cohort Consortium of Infectious Diseases

Incidence rate ratios (IRR) of CVD: recent ABC use compared to no recent ABC use



No evidence suggesting relative CVD risk with recent ABC use differed according to CVD or CKD risk score strata; p-value for interaction: CVD: 0.56, CKD: 0.98

Limitations and Conclusions

RESPOND International Cohort Consortium of Infectious Diseases

Limitations:

- Potential confounding by indication and residual confounding

Conclusions:

- Within RESPOND, after adjustment for potential confounders, recent ABC use was associated with a 40% increased CVD rate, compared to no recent ABC use
  - Robust results when only including MIs
- Despite individuals with increased estimated CKD risk had higher odds of starting ABC compared to those with low risk, the association between CVD and ABC was unchanged after adjustment for renal function and did not differ according to estimated CVD or CKD risk

ACKNOWLEDGEMENTS

RESPOND International Cohort Consortium of Infectious Diseases

Cohort principal investigators:.

S. De Wit (St. Pierre, Brussels), R. Zangerle (AHICOS), M. Law (AHOD), F. Wit (ATHENA) G. Wandeler (EuroSIDA), C. Stephan (Frankfurt), N. Chkhartishvili (IDACIRC), C. Pradier (Nice HIV cohort), A. d'Arminio Monforte (ICoNA), C. Mussini (Modena), J. Casabona & J.M. Miro (PISCIS), H. Günthard (SHCS), A. Sönnerborg (Swedish InfCare), C. Smith (Royal Free HIV cohort), A. Castagna (St. Rafael, Milano), J.C. Wasmuth (Bonn, HIV Cohort) and J.J. Vehreschild (Cologne, HIV cohort).

Cohort Coordinators, operational team members and data management:

C. Necsoi, M. Delforge (st. Pierre, Brussels), H. Appoyer, U. Dadogan, G. Leierer (AHIVCOS), J. Hutchinson, N. Rose. (AHOD), M. van der Valk, M. Hillebregt, T. Rutkens, D. Bergsma (ATHENA), F. Ebeling, M. Bucht, (Frankfurt), O. Chokoshvili, E. Karkashadze (IDACIRC), E. Fontas, K. Dollet, C. Caissotti (NICE, HIV cohort), J. Fanti, A. Tavelli, A. Rodanò (ICoNA), V. Borghi (Modena), A.Bruguera, J. Reyes-Urueña, A. Montoliu (PISCIS), H. Bucher, Kusejko, Y Schaefer (SHCS), V. Svedhem-Johansson, L. Mattsson, K. Alenadaf, (Swedish InfCare), F. Lampe, C. Chaloner (Royal Free, HIV cohort), A. Lazzarin, A. Poli, S. Nozza (St. Rafael, Milano), K. Mohrmann, J. Rockstroh (Bonn, HIV cohort), G. Fätkenheuer, N. Schulze, B. Frank, M. Stecher and H. Weiler (Cologne HIV cohort).

RESPOND Scientific Steering Committee:

J. Lundgren (Co-chair), H. Günthard (Co-Chair), C. Mussini, R. Zangerle, A. Sönnerborg, V. Vannappagari, J. Rooney, I. McNicholl, J.C. Wasmuth, M. Law, F. Wit, H. Bucher, C. Pradier, H. Garges, C. Necsoi, G. Wandeler, C. Smith, J.J. Vehreschild, F. Rogatto, C. Stephan, N. Chkhartishvili, A. d'Arminio Monforte, A. Bruguera, J. Begovac , A. Castagna, L. Ryom, A. Mocroft, L. Peters, J. Rockstroh, J. Kowalska, D. Raben, O. Kirk, D. Podlekareva.

Community representatives:

A. Volny-Anne, N. Dedes, L. Mendoza (European AIDS Treatment Group), E. Dixon Williams (UK).

RESPOND Executive committee:

L. Ryom (Chair), J. Lundgren, R. Zangerle, H. Günthard, G. Wandeler, M. Law, I. McNicholl, C. Smith, V. Vannappagari , S. De Wit, J. Rooney, H. Garges.

RESPOND coordination office, data management and quality assurance:

B. Neesgaard, J.F. Larsen, L. Peters, N. Jaschinski, O. Fursa, O. Valdenmaiier, A. Bojesen, M.L. Jacobsen, E. Hansen. D. Kristensen, T. Elsing, S. Thomsen T. Weide, A. Traytel, SHW Krøyer.

Scientific interest group moderators:

L. Ryom, A. Mocroft (Outcomes with antiretroviral treatment), L. Peters, J. Rockstroh (Hepatitis), D. Raben and J. Kowalska (Public Health), O. Kirk, D. Podlekareva (Tuberculosis) A. Philips, V. Cambiano and J. Lundgren (PrEP).

Members of the scientific interest group:

The Outcomes with antiretroviral treatment scientific interest group; details at:
https://chip.dk/Research/Studies/RESPOND/SIGs/Outcomes-with-ARVs

Statistical Staff:

A. Mocroft, L. Greenberg, L. Bansi-Matharu, A. Pelchen-Matthew, K. Petoumenos, N. Rose, D. Byonanebye.

Funding:

The International Cohort Consortium of Infectious Disease (RESPOND) has received funding from ViiV Healthcare LLC and Gilead Sciences. Additional support has been provided by participating cohorts contributing data in-kind: Austrian HIV Cohort Study (AHIVCOS), The Australian HIV Observational Database (AHOD), CHU Saint-Pierre, University Hospital Cologne, The EuroSIDA cohort, Frankfurt HIV Cohort Study, Georgian National AIDS Health Information System (AIDS HIS), Modena HIV Cohort, San Raffaele Scientific Institute, Swiss HIV Cohort Study (SHCS), Royal Free HIV Cohort Study.