CROI 2019
Poster 712

Withholding primary PCP prophylaxis in virally suppressed HIV patients from COHERE

Andrew Atkinson*, on behalf of the Opportunistic Infections Project Team of COHERE in EuroCoord

*Department of Infectious Diseases, Bern University Hospital, University of Bern, Switzerland.

Andrew Atkinson
Dept of Infectious Diseases
Bern University Hospital
University of Bern, Switzerland
andrew.atkinson@insel.ch

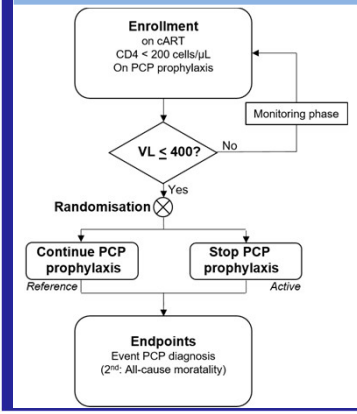
Introduction

- Analyses using COHERE data previously suggested (Clin Infect Dis 2010:51: 611) that primary Pneumocystis Pneumonia (PcP) prophylaxis could be withdrawn in patients with CD4 counts of 100-200 cells/µL if HIV-RNA is suppressed, suggesting HIV replication as major risk factor for PcP.
- Given the wealth of new data available in COHERE we investigated whether primary prophylaxis might be withheld or stopped in all patients on antiretroviral therapy with suppressed plasma HIV RNA (<400c/mL), irrespective of CD4 count.

Methods

- Inclusion: HIV infected individuals are eligible to enter the hypothetical target trial if they began follow-up in their cohort after 1.6.98, started cART on or after 1.6.98 (any combination of 3 or more antiretrovirals of any type), be 16 years or older, and have no history of previous PCP.

Figure 1. Enrollment, monitoring phase, randomisation and end-points for the hypothetical trial



- **Goal:** Estimate the risk of PcP in COHERE patients on cART including time-updated CD4 counts, HIV-RNA and use of PcP prophylaxis.
- We emulated a hypothetical randomised trial using established causal inference methods in which inverse probability (IP) weighting adjusts for censoring selection bias.
- **Figure 1:** Eligibility criteria were plasma HIV RNA (<400c/mL) and CD4 counts ≤200 cells/µL.
- We estimated the hazard ratio (HR) fitting a pooled logistic model which included baseline characteristics (CD4, RNA, gender, age, transmission, geographical origin calendar year), used restricted cubic splines to capture CD4/RNA trajectories, and included polynomial time for modelling the baseline hazard.

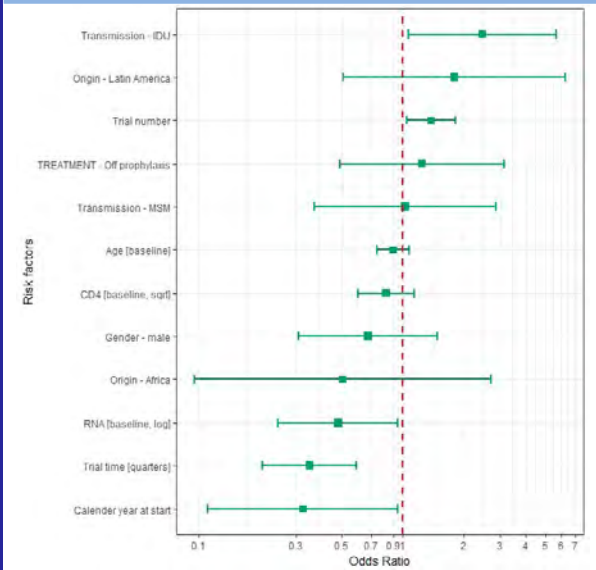
Results

- **Table 1**: There were 9,743 patients eligible for the emulated trials with a total of 18,550 person years followed-up during 1998-2015. The unadjusted incidence rate of PCP diagnosis was 1.5 per 1000py on PCP prophylaxis compared to 2.8 off PCP prophylaxis.
- We emulated three trials
  - **A.** Continue PCP prophylaxis versus stop
  - **B.** Start PCP prophylaxis versus no prophylaxis
  - **C.** On PCP prophylaxis versus off PCP prophylaxis
- The HR estimates for the PCP outcome from the 3 emulated trials were 2.0 ([0.61 6.4], p=0.3) for Trial A, 2.8 ([0.8 9.9], p=0.1) for Trial B, and 1.2 ([0.5, 3.2], p=0.8) for Trial C (**Figure 2**).

Table 1. Patient baseline characteristics by study arm

	Continue PCP prophylaxis	(%) / [IQR]	Stop PCP prophylaxis	(%) / [IQR]	p-value
Number	3150	(32%)	6593	(68%)	
PCP diagnosis	11	(0.3%)	28	(0.4%)	0.9
Male	2371	(75%)	4794	(73%)	0.008
MSM/IDU/Hetero.	961/666/1200	(31/21/38%)	1835/1863/2157	(28/28/33%)	<0.001
Europe/Africa/Latin America	2470/341/183	(78/11/6%)	4555/555/272	(69/8/4%)	<0.001
Age (yrs) (median [IQR])	41	[35, 48]	42	[36, 49]	0.001
baseline CD4 (median [IQR])	133	[84, 170]	149	[101, 180]	<0.001
baseline HIV RNA (median [IQR])	90	[50, 204]	50	[49, 199]	<0.001
Calendar year at baseline (median [IQR])	2005	[2001, 2009]	2006	[2002, 2010]	<0.001
Follow-up (years) (median [IQR])	1.0	[0.4, 3.1]	0.7	[0.3, 2.1]	<0.001
Death / LTFU (%)	573/542	(18%/17%)	830/931	(13%/14%)	<0.001

Figure 2. Adjusted hazard ratios for risk of PCP diagnosis



Conclusions & further study

- These preliminary results suggest that in virologically suppressed patients, irrespective of CD4 levels, the risk of PcP appears to be low, and similar for individuals on and off prophylaxis, although the precision of the results was limited due to the overall low incidence of PCP.
- Further study will include more closely modelling the hypothetical trial encompassing the dynamic nature of treatment adherence.

COHERE Acknowledgements:
Executive Committee: Stéphane de Wit (Chair, St. Pierre University Hospital), Jose Mª Miró (PISCIS), Dominique Costagliola (FHDH), Antonella d'Arminio-Monforte (ICONA), Antonella Castagna (San Raffaele), Julia del Amo (CoRIS), Amanda Mocroft (EuroSida), Dorthe Raben (Head, Copenhagen Regional Coordinating Centre), Geneviève Chêne (Head, Bordeaux Regional Coordinating Centre).
Steering Committee: Robert Zangerle (AHIVCOS),Giota Touloumi (AMACS), Josiane Warszawski (ANRS CO1 EPF/ANRS CO11 OBSERVATOIRE EPF), Laurence Meyer (ANRS CO2 SEROCO), François Dabis (ANRS CO3 AQUITAINE), Murielle Mary Krause (ANRS CO4 FHDH), Jade Ghosn (ANRS CO6 PRIMO), Catherine Leport (ANRS CO8 COPILOTE), Linda Wittkop (ANRS CO13 HEPAVIH), Peter Reiss (ATHENA), Ferdinand Wit (ATHENA), Maria Prins (CASCADE), Heiner Bucher (CASCADE), Caroline Sabin (CHIC), Diana Gibb (CHIPS), Gerd Fätkenheuer (Cologne-Bonn), Julia Del Amo (CoRIS), Niels Obel (Danish HIV Cohort), Claire Thorne (ECS), Amanda Mocroft (EuroSIDA), Ole Kirk (EuroSIDA), Christoph Stephan (Frankfurt), Santiago Pérez-Hoyos (GEMES-Haemo), Osamah Hamouda (German ClinSurv), Barbara Bartmeyer (German ClinSurv), Nikoloz Chkhartishvili (Georgian National HIV/AIDS), Antoni Noguera-Julian (CORISPE-cat), Andrea Antinori (ICC), Antonella d'Arminio Monforte (ICONA), Norbert Brockmeyer (KOMPNET), Luis Prieto (Madrid PMTCT Cohort), Pablo Rojo Conejo (CORISPES-Madrid), Antoni Soriano-Arandes (NENEXP), Manuel Battegay (SHCS), Andri Rauch (SHCS), Cristina Mussini (Modena Cohort), Pat Tookey (NSHPC), Jordi Casabona (PISCIS), Jose M. Miró (PISCIS), Antonella Castagna (San Raffaele), Deborah_Konopnick (St. Pierre Cohort), Tessa Goetghebuer (St Pierre Paediatric Cohort), Anders Sönnerborg (Swedish InfCare), Carlo Torti (Italian Master Cohort), Ramon Teira (VACH), Myriam Garrido (VACH). David Haerry (European AIDS Treatment Group)
Project Leads and Statisticians: Juan Berenguer, Julia Bohlius, Vincent Bouteloup, Heiner Bucher, Alessandro Cozzi-Lepri, François Dabis, Antonella d'Arminio Monforte, Mary-Anne Davies, Julia del Amo, Maria Dorrucci, David Dunn, Matthias Egger, Hansjakob Furrer, Marguerite Guiguet, Sophie Grabar, Ali Judd, Ole Kirk, Olivier Lambotte, Valériane Leroy, Sara Lodi, Sophie Matheron, Laurence Meyer, Jose Mª Miró, Amanda Mocroft, Susana Monge, Fumiyo Nakagawa, Roger Paredes, Andrew Phillips, Massimo Puoti, Michael Schomaker, Colette Smit, Jonathan Sterne, Rodolphe Thiebaut, Claire Thorne, Carlo Torti, , Marc van der Valk, Linda Wittkop, Natasha Wyss *Paediatric cohort representatives:* Ali Judd, Pablo Rojo Conejo
Regional Coordinating Centres: Bordeaux RCC: Diana Barger, , Christine Schwimmer, Monique Termote, Linda Wittkop; Copenhagen RCC: Maria Campbell, Nina Friis-Møller, Jesper Kjaer, Dorthe Raben, Rikke Salbøl Brandt.
European AIDS Treatment Group: David Haerry
OI Working Group: H. Furrer, A. Atkinson, M. Zwahlen (SHCS), P. Reiss (ATHENA), R. Teira (VACH), O. Hamouda (ClinSurv), O. Kirk, A. Mocroft (EuroSIDA), J. M. Miró (PISCIS), N. Obel (DHK), Ph. Morlat (AQUITAINE), A. d'Arminio Monforte (ICONA), R. Zangerle (AHIVCOS), A. Anatoniadou (AMACS), A. Castagna (San Raffaele), J. Del Amo (Co-RIS), G. Fätkenheuer (Bonn), P. Rojo Conejo (CO-RISMD), L. Wittkop (HEPAVIH), C. Mussini (Modena), D. M. Gibb (CHIPS), G. Fätkenheuer (Cologne), A. Noguera-Julian (CORISPE-cat), G. Chêne (Bordeaux RCC), D. Raben (Copenhagen RCC)
Funding sources: The COHERE study group has received unrestricted funding from: Agence Nationale de Recherches sur le SIDA et les Hépatites Virales (ANRS), France; HIV Monitoring Foundation, the Netherlands; and the Augustinus Foundation, Denmark. The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under EuroCoord grant agreement n° 260694. The group has also received project specific funding Swiss National Science Foundation. A list of the funders of the participating cohorts can be found at www.COHERE.org.