

Safety of stopping primary *T. gondii* prophylaxis with suppressed viremia and CD4>100/mm3

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Background/Objective: Current guidelines recommend that primary *Toxoplasma gondii* prophylaxis can be safely discontinued in HIV and *T. gondii* co-infected patients with suppressed viraemia on antiretroviral therapy (ART) and a CD4 cell count >200 cells/mm3. Whether such a policy can be extended to patients with CD4 cell counts between 100-200 cells/mm3 is unknown.
Methods: The Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) included data from 10 European cohorts on 11,015 HIV and *T. gondii* co-infected patients who started taking ART after 1997.

Table 1: Patients characteristics at baseline.

	Incidence risk factors Toxo		Stopping prophylaxis		
	N	%	N	%	
All patients	11015	100	1484	100	
Gender					
Male	8084	73.4	1069	72.0	
HIV exposure group					
MSM	3783	34.3	417	28.1	
IDU	1895	17.2	219	14.8	
Heterosexual	4446	40.4	720	48.5	
Other	455	4.1	50	3.4	
Unknown	436	4.0	78	5.3	
Ethnic					
White/Caucasian	6948	63.1	851	57.3	
Other	1401	12.7	24	1.6	
Unknown	2666	24.2	391	26.3	
Prior AIDS	1600	14.5	484	32.6	
Viral load <400	2326	21.1	960	64.7	
On cART	3584	32.5	1484	100	
	Median	IQR	Median	IQR	
Age	Years	37.8	32.1-45.6	41.1	35.5-49.6
CD4	cells/μL	353	190-533	257	188-340
Viral load	log ₁₀ copies/ml	4.2	2.8-5.0	2.0	1.7-2.9

Table 2: Factors associated with CNS Toxoplasmosis

	CD4<=100 cells/μL			CD4>100 cells/μL			
	IRR	95% CI	p	IRR	95% CI	p	
Toxo prophylaxis	Yes vs no	0.80	0.47 - 1.35	0.3977	0.79	0.33 - 1.87	0.5876
cART	Yes vs no	0.80	0.46 - 1.37	0.4106	0.72	0.35 - 1.46	0.3635
CD4	Per doubling	0.75	0.64 - 0.87	0.0001	0.30	0.19 - 0.47	<0.0001
Viral load<400	<400 vs ≥400	0.08	0.02 - 0.34	0.0006	0.24	0.11 - 0.51	0.0002
Prior AIDS		0.75	0.43 - 1.31	0.3129	2.87	1.40 - 5.87	0.004

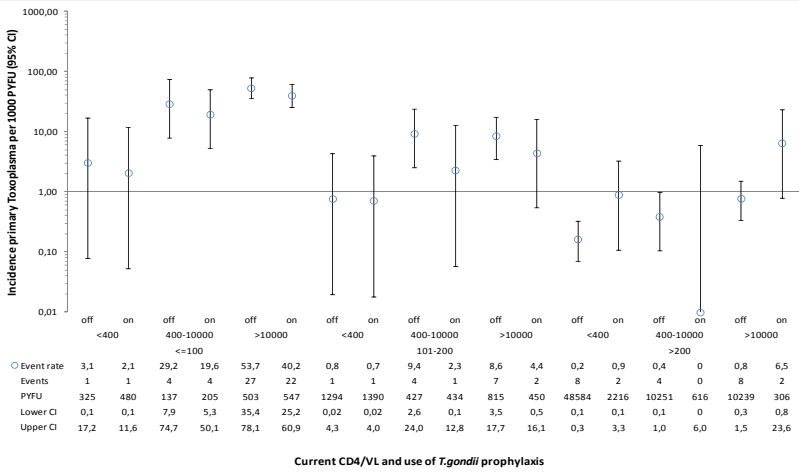
Analysis was adjusted additionally for sex, ethnic origin, HIV transmission group, hepatitis B and C status and age.

T. gondii infection was considered present if patients were *T. gondii* IgG antibody seropositive. Central nervous system (CNS) toxoplasmosis was diagnosed according to the 1993 CDC case definition. Multivariate Poisson regression models were used to model incidence rate ratios (IRRs) of CNS toxoplasmosis.

Results:

- There were 99 CNS toxoplasmosis episodes during 79,220 person-years of follow-up (PYFU). The characteristics of the patients at baseline are shown in **Table 1**.
- The incidence of CNS toxoplasmosis stratified by current CD4 cell count, viral load (VL), and use of prophylaxis is shown in the **Figure 1**.

Figure 1: Incidence rate of CNS toxoplasmosis according to current CD4 cell count, viral load (VL) and use of anti-*T. gondii* prophylaxis.



- Among patients who had a current CD4 cell count of 100-200 cells/mm3 and a VL<400 copies/mL, incidence of CNS toxoplasmosis was 0.7 episodes per 1000 PYFU (95% CI, 0.02-4.0; 1 event during 1,390 PYFU) in those receiving *T. gondii* prophylaxis and 0.8 episodes per 1,000 PYFU (95% CI, 0.02-4.3; 1 event during 1,294 PYFU), in those who stopped prophylaxis.
- The predictors of CNS toxoplasmosis among patients with a current CD4 cell count >100 cells/mm3 (**Table 2**) were: previous AIDS diagnosis; doubling CD4 cell count/year; and, detectable viral load, whereas primary prophylaxis was not a significant predictor.
- **Table 3** shows the incidence of primary CNS toxoplasmosis after stopping prophylaxis while on ART, respectively.

Table 3: Incidence of primary CNS toxoplasmosis after stopping prophylaxis while on ART.

CD4 cell count, cells/μL	cART	Viral load, copies/mL	Toxoplasmosis prophylaxis	Events	PYFU	Incidence rate (per 1000 PYFU)	95% CI
<=100	On or off	Any	On or off	14	282.8	49.5	27.1 - 83.1
<=100	On	Any	On or off	9	214.7	41.9	19.2 - 79.6
<=100	On	<400	On or off	0	123.2	0	0 - 29.9
<=100	On	<400	Off	0	48.5	0	0 - 76.1
101-200	On or off	Any	On or off	3	818.8	3.7	0.8 - 10.7
101-200	On	Any	On or off	2	697.4	2.9	0.3 - 10.4
101-200	On	<400	On or off	1	534.5	1.9	0 - 10.4
101-200	On	<400	Off	0	291.7	0	0 - 12.6
>200	On or off	Any	On or off	7	9289.8	0.8	0.3 - 1.6
>200	On	Any	On or off	6	8508.3	0.7	0.3 - 1.5
>200	On	<400	On or off	4	7968.2	0.5	0.1 - 1.3
>200	On	<400	Off	2	7714.6	0.3	0 - 0.9

Conclusions

- The incidence of primary CNS toxoplasmosis among virologically suppressed patients on ART and who had CD4 cell counts >100 cells/mm3 was very low regardless of prophylaxis use.
- Extending current guidelines for safely discontinuing primary *T. gondii* prophylaxis to patients with CD4 counts of 100-200 cells/mm3 and suppressed VL would be appropriate.

COHERE Acknowledgements: Executive Committee: Stéphane de Wit (Chai; St. Pierre University Hospital), Jose M Miro (PISCIS), Dominique Costagliola (FHID), Antonella d'Arminio-Monforte (ICONA), Antonella Castagna (San Raffaele), Julia del Amo (CoRIS), Amanda Mocroft (EuroSida), Dorthe Raben (Head, Copenhagen Regional Coordinating Centre), Genevieve Chêne (Head, Bordeaux Regional Coordinating Centre). **Steering Committee:** Robert Zangerle (AHIVCO), Giota Touloumi (AMACS), Josiane Warszawski (ANRS CO1 EPF/ANRS CO11 OBSERVATOIRE EPF), Laurence Meyer (ANRS CO2 SEROCO), François Dabis (ANRS CO3 AQUITAINE), Marilee Mary Krause (ANRS CO4 FHDH), Jade Ghon (ANRS CO5 PRIMO), Catherine Lepout (ANRS CO6 COPLITE), Linda Witkop (ANRS CO13 HEPAVIR), Peter Reiss (ATHENA), Ferdinand Wit (ATHENA), Maria Prins (CASCADE), Heiner Bucher (CASCADE), Caroline Sabin (CHIC), Diana Gbb (CHPE), 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-Hernández (GEMES-Haem), Osamah Hamouda (German ClinSurv), Barbara Bartmeyer (German ClinSurv), Nikozi Chkharitishvili (Georgian National HIV/AIDS), Antoni Noguera-Julian (CORISPE-Cat), Andrea Anticori (ICC), Antonella d'Arminio-Monforte (ICONA), Hubert Brokmeier (KOMNET), Luis Prieto (Madrid PMCT Cohort), Pablo Rojo Conejo (CORISPE-Madrid), Antoni Soriano-Arandes (NENEPI), Manuel Battegay (GHCS), Roger Kouyou (GHCS), Cristina Masari (Modena Cohort), Pat Tookev (NSHPC), Jordi Casabona (PISCIS), Jose M. Miro (PISCIS), Antonella Castagna (San Raffaele), Deborah Konopnicki (St. Pierre Cohort), Tessa Goethgebuer (St. Pierre Paediatric Cohort), Anders Sonnenberg (Swedish InCare), Carlo Torti (Italian Master Cohort), Ramon Teira (VACH), Myriam Garrido (VACH), David Haery (European AIDS Treatment Group). **Project Leads and Statisticians:** Juan Beneringuer, Julia Bohlius, Vincent Bouletoup, Heiner Bucher, Alessandro Cozzi-Vergari, François Dabis, Antonella d'Arminio-Monforte, Mary-Anne Davies, Julia del Amo, Maria Dorrucci, David Dunn, Matthias Egger, Hansjakob Furrer, Marguerite Gugut, Sophie Grabar, Ali Judd, Ole Kirk, Olivier Lambert, Vahneane Leroy, Sara Lodi, Sophie Matheron, Laurence Meyer, Jose M Miro, Amanda Mocroft, Susana Monge, Olivier Nakagawa, Vahneane Leroy, Roger Parades, Andrew Phillips, Massimo Puoti, Michael Schomaker, Colette Smit, Jonathan Sterne, Rodolphe Thiebaut, Claire Thorne, Carlo Torti, Marc van der Valk, Linda Witkop, Natasha Wyras. **Paediatric cohort representatives:** Ali Judd, Pablo Rojo Conejo. **Regional Coordinating Centres:** Bordeaux RCC; Diana Barger; Christine Schwimmer; Monique Termolis; Linda Witkop; Copenhagen RCC; Maria Gambotti; Nina Fritsch; Jørgen Kjær; Dorthe Raben; Rikke Sabot Brandt. **European AIDS Treatment Group:** David Haery. **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 from «name of specific funder». A list of the funders of the participating cohorts can be found at www.cohere.org.