Stopping secondary TE prophylaxis in suppressed patients with CD4 100-200 is not safe

Poster # 646

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Background/Objective: Current guidelines recommend that secondary Toxoplasma gondii prophylaxis can be safely discontinued in HIV-infected patients with suppressed viremia 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 101-200 cells/mm3 is unknown.

Methods: The Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) included data from 10 European cohorts on 1151 HIV-infected patients who developed a toxoplasmic encephalitis (TE) and started ART after 1997. TE was diagnosed on the basis of the 1993 CDC case definition. A relapse was defined as a new TE episode after 4 months of the initial TE. Patient followup began at the date of the first TE and ended at the time of first TE relapse, last visit, or death,whichever occurred first. Incidence rates of TE relapses were calculated after stratification by current use of prophylaxis, current CD4 cell count, and current viral load (VL). Multivariate Poisson regression models were used to model incidence rate ratios (IRRs) of TE.

Results:

- There were 79 TE relapses during 6,030 person-years of follow-up (PYFU).The characteristics of the patients at baseline are shown in **Table 1**.
- The incidence of TE relapses stratified by current CD4 cell count, detectable or undetectable VL, and use of prophylaxis is shown in **Figure 1.**
- Among patients who had a current CD4 cell count of 101-200 cells/mm3 and an undetectable VL (<400 copies/mL), incidence of TE relapses was 0.9 episodes per 100 PYFU (95% CI, 0.11-3.2; 2 episodes during 224 PYFU) in those receiving *T. gondii* prophylaxis and 1.9 relapses per 100 PYFU (95% CI, 0.75-3.8; 7 episodes during 376 PYFU), in those who stopped prophylaxis (P=0.349).
- Among virologically suppressed patients on ART without secondary *T. gondii* prophylaxis, the incidence of TE relapses in patients with CD4 101-200 (1.9 [95% CI, 0.75-3.8] episodes per 100 PYFU) was significantly higher than that seen in patients with CD4>200 cells/mm3 (0.5 [95% CI, 0.3-0.8] episodes per 100 PYFU; P=0.0019) (**Figure** 2).
- To be on ART (IRR, 0.33; 95% CI, 0.12–0.94; P=.038) was the only TE relapse predictor in patients with CD4 cell count between 100 and 200 cells/mm3; whereas detectable VL, CD4 T cell count and prophylaxis were not predictors (**Table 2**).

Table 1: Characteristics of patients at the time of the first TE episode.

		Overall		No relapse		Relapse		
		N	%	N	%	N	%	p
All patients		1151	100	1072	100,0	79	100	
Gender	Male	836	72.6	779	72.7	57	72.2	0.9209
HIV exposure group	MSM	324	28.1	301	28.1	23	29.1	0.5259
	IDU	201	17.5	182	17.0	19	24.1	
	Heterosexual	424	36.8	399	37.2	25	31.6	
	Other	199	17.3	187	17.4	12	15.2	
	Unknown	3	0.3	3	0.3	0	0.0	
Ethnic	White/Caucasian	384	33.4	363	33.9	21	26.6	0.0583
	Other	64	5.6	63	5.9	1	1.3	
	Unknown	703	61.1	646	60.3	57	72.2	
Viral load <400		139	12.1	130	12.1	9	11.4	0.8467
ART	Naive	613	53.3	582	54.3	31	39.2	0.0158
	Before TE	112	9.7	99	9.2	13	16.5	
	at TE episode	426	37.0	391	36.5	35	44.3	
		Median	IQR	Median	IQR	Median	IQR	p
Age	Years	38.4	32.9-45.8	38.8	33.0-45.9	36.0	30.7-43.5	0.0159
CD4	cells/µL	46	18-109	46	18-109	43.0	14-112	0.8257
Viral load	log10 copies/ml	5.1	3.9-5.6	5.1	3.9-5.6	4.9	4,0-5,5	0.3890

Table 2: Analysis of risk factors for TE relapses

		CD4 cell count, 100-200 cells/µL			CD4 cell count, >200 cells/µL		
		IRR	95% CI	p	IRR	95% CI	p
Toxo prophylaxis	Yes vs no	1.03	0.39 - 2.76	0.9524	0.99	0.37 - 2.68	0.9807
cART	Yes vs no	0.33	0.12 - 0.94	0.0382	2.42	0.57 - 10.30	0.2329
CD4	Per doubling	0.57	0.10 - 3.11	0.5145	0.93	0.50 - 1.70	0,8042
Viral load<400	<400 vs ≥400	1.24	0.44 - 3.49	0.6851	1.85	0.65 - 5.29	0.2506

Analysis was adjusted additionally for sex, ethnic origin, HIV transmission group, hepatitis B and C status and age. Prophylaxis, combination antiretroviral therapy (cART), viral load and CD4 cell count are included as time-updated (current) values

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

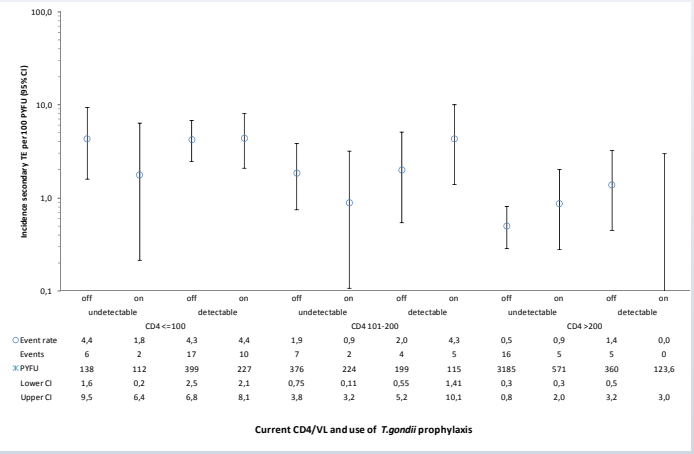
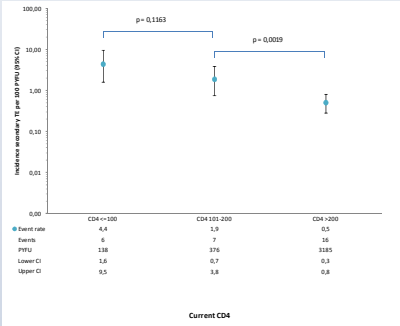


Figure 2: Incidence rate of TE relapses according to current CD4 cell count in patients with undetectable viral load and who are not on prophylaxis.



Limitations

- The TE episodes and relapses are not validated and we do not know their clinical characteristics

Conclusions

- In suppressed HIV-infected adult patients on ART, secondary TE prophylaxis can be safely discontinued in patients with CD4 cell counts >200 cells/mm3.
- However, in patients with detectable HIV RNA the risk of relapse may be substantial, even if the CD4 cell count is >200 cells/mm3 and prophylaxis should be maintained.
- Secondary TE prophylaxis should not be stopped in virologically suppressed patients on ART with CD4 cell counts of 101-200 cells/mm3.

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