



Immune Recovery After Starting ART in HIV-Infected Patients Presenting and Not Presenting With Tuberculosis in South Africa

6th South African Aids Conference, ICC Durban

20 June 2013

Michael Schomaker, Matthias Egger, Mhairi Maskew, Daniela Garone, Hans Prozesky, Christopher Hoffmann, Andrew Boulle, Lukas Fenner

Background

Methods

Results

Discussion

Conclusions

References



- Tuberculosis (TB) is the most common HIV-associated illness in resource-constrained settings
- TB may play an important role in immune recovery after ART initiation
- A recent European study (Cingolani et al., 2012, *CID*) reported impaired CD4 count recovery among HIV-infected patients presenting with TB at ART initiation
- However, there is no evidence on the influence of TB on immune recovery after starting ART in sub-Saharan Africa

Background

[Methods](#)

[Results](#)

[Discussion](#)

[Conclusions](#)

[References](#)

Aim

We study the immune response, defined as CD4 slope/increase after starting ART, in patients presenting and not presenting with TB in South Africa



- Data from three treatment programs participating in IeDEA-SA and systematically collecting OIs
- 15,646 ART-naive adults (>16 yr.) starting ART between January 2003 and December 2010 and having at least 6 months of follow-up were included
- CD4 slopes were calculated as **the relative change between two consecutive CD4 counts per day**
- To account for missing CD4 counts and viral loads at baseline and during follow-up, as well as missing WHO stage data, we used longitudinal multiple imputation

[Background](#)

[Methods](#)

[Results](#)

[Discussion](#)

[Conclusions](#)

[References](#)

Main analysis

We study the association between CD4 slope/increase and presenting with TB by means of mixed models– adjusted for age, sex, CD4, time on ART, WHO stage, treatment program.



Characteristic	All	TB	no TB
TB at ART start	1052 (6.7%)		
Site of TB			
<i>pulm.</i>	718 (4.6%)		
<i>extra-pulm.</i>	334 (2.1%)		
CD4 cell count	98 (41-161)	45 (18-98)	102 (45-163)
WHO stage IV	2989 (28.1%)	399 (39.3%)	2590 (26.9%)
Age	34 (29-40)	34 (29-39)	34 (29-40)
Female	10622 (67.9%)	621 (60%)	10001 (68.5%)
Follow-up (days)	710 (428-1075)	645 (389-970)	716 (433-1081)

[Background](#)

[Methods](#)

[Results](#)

[Discussion](#)

[Conclusions](#)

[References](#)

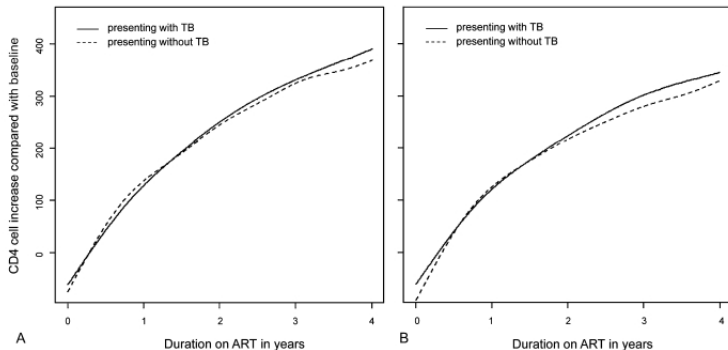
CD4 increase compared to baseline¹



Modeled CD4 trajectories (adjusted) defined as CD4 cell count increase from baseline by TB status at ART start, according to CD4 cell count at the start of ART

(A) of CD4 count <50

(B) of CD4 count 50 - 199



[Background](#)

[Methods](#)

[Results](#)

[Discussion](#)

[Conclusions](#)

[References](#)

¹From Schomaker et al. (2013), *JAIDS*; adjusted results from an additive linear mixed model refer to a male reference population aged 35-45 years with stage I/II



Characteristics	Cells/ μ L per 6 mo. TB vs. not TB	p-value
<i>Unrestricted</i>		
Overall	4.9 (0.2; 9.7)	0.04
First 6 mo. after ART start	-3.3 (-15.3; 8.8)	0.58
> 6 mo. after ART start	6.5 (2.0; 11.1)	0.01
<i>Time under viral suppression</i>		
Overall	4.9 (0.1; 9.7)	0.05
First 6 mo. after ART start	-1.3 (-13.5; 10.9)	0.83
> 6 mo. after ART start	6.2 (1.5; 10.9)	0.01

[Background](#)

[Methods](#)

[Results](#)

[Discussion](#)

[Conclusions](#)

[References](#)

²Linear mixed models were adjusted for age, sex, baseline CD4 count, current CD4, early time on ART, WHO stage, treatment site



- TB patients do not have worse immune recovery than other patients because
 - i) TB treatment alone has positive effect on immune system
 - ii) survival bias: very sick patients die before starting ART
 - iii) underascertainment bias: undiagnosed TB patients count as TB free
- Immune recovery was also poorer in man and older patients, as previously shown in other studies
- We obtained very similar results when looking at log VL slope
- Probably no adherence issue → time under viral suppression
- Our study contrasts with European study for various reasons:
 - i) different setting with different patients, public health systems, TB screening practices, clinical follow-up
 - ii) methodological differences in analyzing the data

[Background](#)

[Methods](#)

[Results](#)

[Discussion](#)

[Conclusions](#)

[References](#)



HIV-infected patients presenting with TB did not have a worse immune recovery after ART initiation compared with other patients

References

Cingolani, A., A. Lepri, A. Castagna, D. Goletti, A. De Luca, P. Scarpellini, I. Fanti, A. Antinori, A. Monforte, and E. Girardi (2012). Impaired CD4 t-cell count response to combined antiretroviral therapy in antiretroviral-naive HIV-infected patients presenting with tuberculosis as AIDS-defining condition. *Clinical Infectious Diseases* 54(6), 853–861.

Schomaker, M., M. Egger, M. Maskew, D. Garone, H. Prozesky, C. Hoffmann, A. Boulle, and L. Fenner (2013). Immune recovery after starting ART in HIV-infected patients presenting and not presenting with tuberculosis in South Africa. *Journal of Acquired Immune Deficiency Syndromes* 63(1), 142–145.

Background

Methods

Results

Discussion

Conclusions

References