

TITLE

Integrase inhibitor-based antiretroviral treatment does not increase the risk of TB-IRIS in people with HIV treated for findings from the Reflate TB2 randomized trial

PRESENTER

Lara Esteves Coelho

AUTHORS

L.E. Coelho¹, C. Chazallon², D. Laureillard^{3,4}, R. Escada¹, J.-B. Ntakpe^{2,5}, I. Timana⁶, S.W. Cardoso¹, E. Messou^{5,7}, S. Eholie^{5,7}, Do Chau⁹, V.G. Veloso¹, X. Anglaret², C. Deaугerre^{10,11,12}, J.-M. Molina^{10,11,13}, B. Grinsztejn¹, O. Marcy², N. De Castro^{2,13}

INSTITUTIONS

¹National Institute of Infectious Diseases Evandro Chagas, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil, ²Universit National Institute for Health and Medical Research (INSERM) UMR 1219, Research Institute for Sustainable Developmer Bordeaux Population Health Centre, Bordeaux, France, ³Nimes University Hospital, Department of Infectious and Troj Nimes, France, ⁴University of Montpellier, Research Unit 1058, Pathogenesis and Control Chronical Infections, INSERM, Center, Montpellier, France, ⁵Programme PACCI/ANRS Research Center, Abidjan, Cote D'Ivoire, ⁶Instituto Nacional de S Marracuene, Mozambique, ⁷Centre de Prise en Charge de Recherche et de Formation, CePreF-Aconda-VS, Abidjan, C ⁸Université Félix Houphouët Boigny, Département de Dermatologie et d'Infectiologie, UFR des Sciences Médicales, Ab D'Ivoire, ⁹Pham Ngoc Thach Hospital, Ho Chi Minh City, Vietnam, ¹⁰INSERM U944, Paris, France, ¹¹Université Paris Cité, P ¹²AP-HP-Hôpital Saint-Louis, Virology Department, Paris, France, ¹³AP-HP-Hôpital Saint-Louis Lariboisière, Infectious Di Department, Paris, France

BACKGROUND: Antiretroviral therapy (ART) initiation in people living with HIV (PWHIV) treated for tuberculosis (TB) may due to the occurrence of tuberculosis-associated immune reconstitution inflammatory syndrome (TB-IRIS). Integrase i by providing a faster HIV-RNA decline than efavirenz, could increase the risk for this complication. We sought to assess determinants of TB-IRIS in PWHIV with TB on raltegravir or efavirenz-based ART.

METHODS: We conducted a secondary analysis of the ANRS 12300 Reflate TB 2 multicenter, phase 3 trial, that randomiz PWHIV on standard TB treatment, to receive raltegravir or efavirenz-based ART. TB-IRIS was defined according to the Ir Network for the Study of HIV-associated IRIS (INSHI) criteria. Incidence rates (IR) were estimated by 100 persons-year (P Kaplan-Meier curves (log-rank test) and cox regression models were used to assess determinants of TB-IRIS.

RESULTS: Of 460 trial participants, 453 participants from Brazil, Côte d'Ivoire, Mozambique and Vietnam were included Median age 35 years (IQR: 29-43), 40% female, 69% pulmonary TB only, median CD4 102 (IQR 38-239) cells/ μ L and media 5.0-5.8) \log_{10} copies/mL. Overall, 48 participants developed TB-IRIS (IR = 24.2/100 PY), 19 cases in the raltegravir arm and arm (log-rank test: $p=0.123$) (Figure). Factors associated with TB-IRIS were: CD4 count ≤ 100 cells/ μ L, HIV RNA $\geq 500,000$ cc pulmonary/disseminated TB (Table).

Figure. Stratified Kaplan-Meier curves for TB-IRIS-free survival probabilities by ART treatment (raltegravir arm versus efavirenz arm)

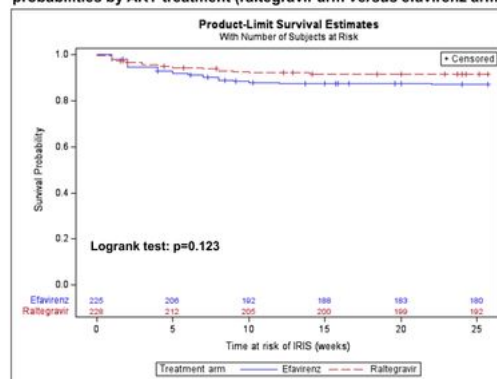


Table. Factors associated with TB-IRIS incidence.

	cHR	95% CI	aHR	95%CI
Country				
Ivory Coast	1			
Brazil	1.19	0.44-3.26		
Mozambique	0.47	0.18-1.19		
Vietnam	1.97	1.02-3.81		
CD4 (cells/mm3)				
CD4 >100	1		1	
CD4 ≤100	3.17	1.65-6.16	2.48	1.27-4.84
HIV VL (copies/mL)				
VL ≥ 500 000	1		1	
VL < 500 000	0.27	0.15-0.50	0.34	0.19-0.63
TB diagnosis at enrollment				
Pulmonary only	1			
Extrapulmonary/disseminated	2.22	1.25-3.93	2.17	1.23-3.85

VL: viral load; cHR: crude hazard ratio; aHR: adjusted hazard ratio; CI: confidence interval
ART treatment was not included in the cox regression models due to violation of proportional hazards assumption.

CONCLUSIONS: INSTI-based ART did not increase TB-IRIS risk. Low CD4 counts, high HIV RNA and extrapulmonary/disser risk factors for TB-IRIS.