Comparative virological efficacy, tolerance and immunological recovery at 3 years of different antiretroviral regimens initiated during acute/recent HIV infection.

HIV Drug Therapy GLASGOW 2018

P058

Juan Ambrosioni[1&], Júlia Farrera[2&], Elisa de Lazzari[1], David Nicolás[1], Christian Manzardo[1], Mar Mosquera[3], Carmen Ligero[1], M Ángeles Marcos[3], Sonsoles Sánchez-Palomino[4], Emma Fernández[1], Montserrat Plana[4], José M Miró[1] and the Hospital Clinic Acute/Recent HIV Study Group. [&]Equivalent merits.

1- Infectious Diseases Service, Hospital Clinic-IDIBAPS, University of Barcelona. Barcelona, Spain.
2- School of Medicine, University of Barcelona, Barcelona, Spain.
3- Laboratory of Virology, Microbiology Service, Hospital Clinic-ISGLOBAL, University of Barcelona, Barcelona, Spain.
4-Laboratory of Retrovirology and Viral Immunopathology, AIDS Research Group, IDIBAPS, Barcelona, Spain

Contact:
ambrosioni@clinic.cat
jmmiro@ub.edu

BACKGROUND AND OBJECTIVES

Background: Acute HIV infection is defined as infection of <30 days, and recent infection as <180 days post-infection. Antiretroviral treatment (ART) in this period reduces the viral reservoir, preserves the immune system, decreases transmission and optimizes immune recovery. Guidelines recommend starting ART in all patients; however, the optimal antiretroviral regimen in terms of immunological recovery and tolerability in this setting is unknown.

Objectives: To analyze the virological efficacy, tolerance and the immunological reconstitution at 1 and 3 years after starting ART during recent HIV infection. Regimens based on boosted-protease inhibitors (PI), integrase inhibitors (InSTI) and non-nucleoside reverse transcriptase inhibitors (NNRTI) were compared.

METHODS

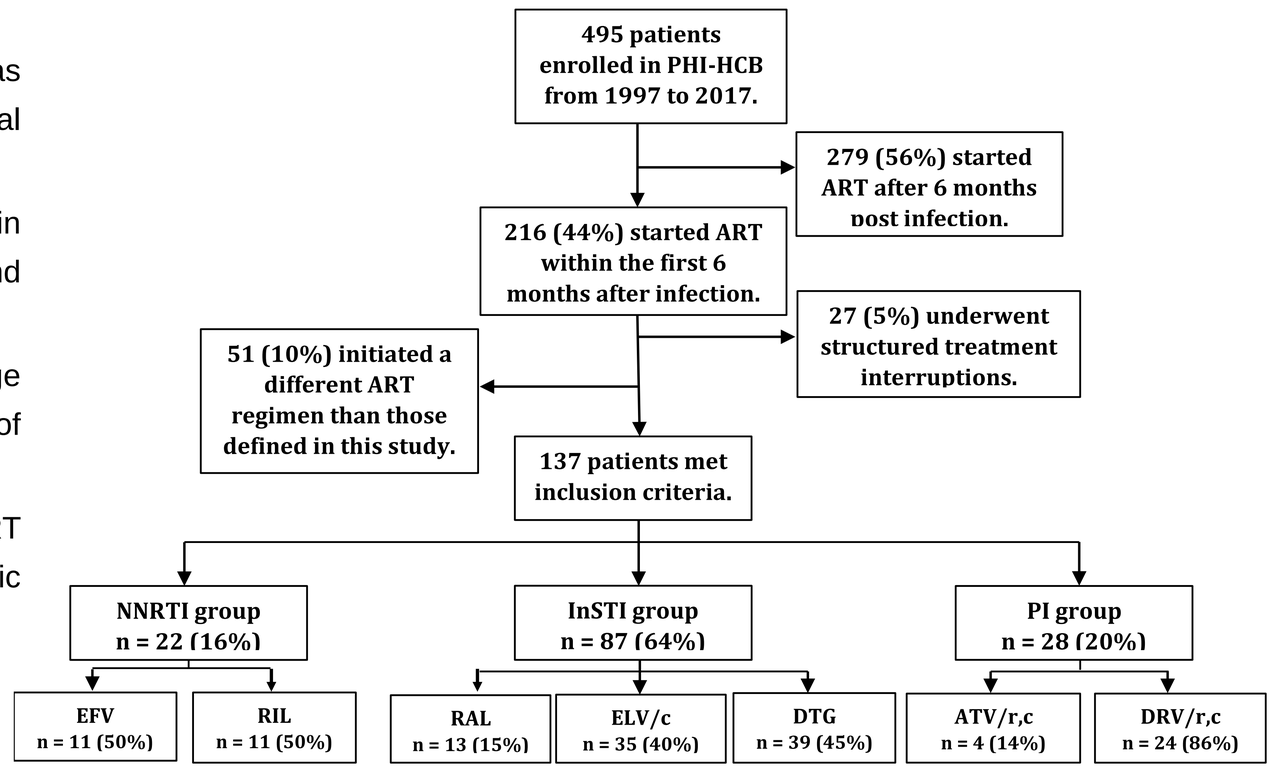
- Retrospective study of 137 patients with confirmed acute/recent infection who started ART within 6 months post-infection, between 2003 and 2017 (Figure 1). We compared regimens based on: ritonavir/cobicistat boosted-PI (darunavir or atazanavir, N=28), InSTI (elvitegravir/cobicistat, raltegravir, dolutegravir, N=87) and NNRTI (efavirenz, rilpivirine, N=22), all combined with two nucleoside reverse transcriptase inhibitors (abacavir/lamivudine or TDF-TAF/emtricitabine).

- Primary endpoints were virologic suppression (VL <50 copies/mL) and immune reconstitution (CD4+ T cell count >900 cells/µL and CD4/CD8 ratio >1) at 1 and 3 years. Secondary endpoints were adverse events (AE) leading to ART discontinuation at 1 and 3 years. ITT and PP analysis were performed.

RESULTS

- Baseline characteristics were comparable among groups (table 1)
- Viral suppression (overall suppression of 96% at 1 year and 99% at 3 years) was comparable in all ART regimens (ITT, table 2). Among the InSTI group, levels of viral suppression were comparable for dolutegravir and elvitegravir-based regimens.
- At 1 year there was an increment of 350 CD4+ T cells/µL, which was comparable in all ART regimens. Overall 36% and 39% achieved CD4>900 cells/µL and 43% and 66% a CD4/CD8>1 at 1 and 3 years, respectively (table 3).
- In a subanalysis of immune recovery comparing Fiebig stages I-V with Fiebig stage VI, starting ART during the earliest Fiebig stages was associated with higher rates of CD4>900 cells/µL at 3 years (p=0.027).
- Discontinuation due to AE was more frequent with NNRTI compared to other ART families (p=0.036 at 1 year, p=0.040 at 3 years) with high rates of neuropsychiatric AE (table 4).
- Results were comparable by ITT and PP analysis

Figure 1: Study design and included patients



1-Baseline characteristics	Total (N=137)	NNRTI (N=22)	PI (N=28)	InSTI (N=87)	p-value
Age [median (IQR)]	34 (31,40)	34 (32,38)	37 (29,44)	34 (30,39)	0.718
Gender [n (%)]					
- Male	130 (95%)	22 (100%)	26 (93%)	82 (94%)	0.546
- Female	7 (5%)	0	2 (7%)	5 (6%)	
Transmission group [n (%)] N=128					
- MSM	115 (90%)	21 (95%)	23 (85%)	71 (90%)	0.931
- HTSX	10 (8%)	1 (5%)	4 (15%)	5 (6%)	
- IDU	2 (2%)	0	0	2 (3%)	
- Unknown	1 (1%)	0	0	1 (1%)	
CD4+T cells absolute count cells/mm3 [median (IQR)]	475 (335,583)	491 (368,572)	538 (262,638)	470 (333,578)	0.904
CD4/CD8 ratio [median (IQR)]	0.48 (0.31,0.72)	0.67 (0.35,0.82)	0.38 (0.17,0.69)	0.50 (0.33,0.71)	0.061
HIV RNA, log10copies/ml [median (IQR)]	4.80 (3.81,5.52)	4.53 (3.78,5.05)	5.20 (4.78,5.83)	4.67 (3.56,5.52)	0.063
Fiebig at cohort inclusion [median (IQR)]	5 (4,6)	6 (4,6)	5 (5,6)	5 (4,6)	0.241
Fiebig at ART initiation [median (IQR)]	6 (5,6)	6 (5,6)	6 (5,6)	6 (5,6)	0.400

2-Virological outcomes	Total	NNRTI	PI	InSTI	p-value
VL<50 at 1 year of follow up [n (%)] N=119	114 (96%)	21 (95%)	27 (100%)	66 (94%)	0.686
VL<50 at 3 years of follow up [n (%)] N=57	70 (99%)	18 (100%)	25 (100%)	27 (96%)	1.000

3-Immunological outcomes	Total	NNRTI	PI	InSTI	P-value
CD4+ T cell delta at 1 year [mean (SD)] N=114	350 (274)	330 (264)	332 (319)	364 (261)	0.724
CD4+ T cell delta at 3 years [mean (SD)] N=57	348 (279)	367 (268)	383 (266)	298 (304)	0.518
CD4+ T cell >900 at 1 year [n (%)] N=114	41 (36%)	6 (29%)	8 (31%)	27 (40%)	0.419
CD4+ T cell >900 at 3 years [n (%)] N=57	22 (39%)	6 (40%)	7 (33%)	9 (43%)	0.745
CD4/CD8 >1 at 1 year [n (%)] N=114	52 (46%)	10 (48%)	11 (42%)	31 (46%)	0.986
CD4/CD8 >1 at 3 years [n (%)] N=57	36 (63%)	8 (53%)	13 (62%)	15 (71%)	0.518

4-Toxicity	Total	NNRTI	PI	InSTI	P-value
At least one adverse event at 1 year [n (%)]	36 (26%)	8 (36%)	10 (36%)	18 (21%)	0.146
At least one adverse event at 3 years [n (%)]	49 (36%)	11 (50%)	12 (43%)	26 (30%)	0.145
Discontinuation rate# at 1 year [n (%)]	**13 (9%)**	**5 (23%)**	**3 (11%)**	**5 (6%)**	**0.036**
Discontinuation rate# at 3 years [n (%)]	**20 (15%)**	**6 (27%)**	**6 (21%)**	**8 (9%)**	**0.040**

CONCLUSIONS

- **Viral suppression and immunological recovery were excellent in acute/recent patients, with no differences between ART regimens.**
- **Earlier ART initiation (<100 days) was associated with a higher proportion of immunological recovery, favoring Fiebig stages I to V compared to stage VI.**
- **NNRTIs-based regimens were associated with higher treatment discontinuation rates due to AE.**
- **Among InSTI regimens, dolutegravir and elvitegravir-based regimens showed comparable efficacy.**