HIV-DNA decrease during treatment in Primary HIV-1 Infection: a randomized clinical trial with 3 different drug regimens.

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Background and aim of the study

Antiretroviral therapy (ART) initiation during primary HIV-1 infection (PHI) could restrict establishment of HIV reservoirs. Multitarget ART including protease inhibitor (PI) and integrase strand transfer inhibitors (INSTIs) could reduce the reservoir even more.
The aim of the study is to assess the effect of three different ART regimens on HIV-DNA load in people who started ART during PHI.

Methods

PHI (an incomplete HIV-1 western blot and detectable plasma HIV-RNA) was the inclusion criterion of this randomized, open-label, multicentric Italian study initiated by INACTION (Italian Network of Acute HIV Infection). Participants were randomly assigned (10:10:8) to a fixed-dose combination of tenofovir alafenamide (TAF) 25 mg plus emtricitabine (FTC) 200 mg, darunavir 800 mg, and cobicistat 150 mg once daily (group 1), or TAF 25 mg plus FTC 200 mg, dolutegravir 50 mg once daily (group 2), or an intensive four-drug regimen (TAF 25 mg plus FTC 200 mg, dolutegravir 50 mg, darunavir 800 mg, and cobicistat 150 mg once daily) (group 3) . The primary endpoint was the decrease of HIV-DNA copies/10^6 peripheral blood mononuclear cells (PBMC) at weeks (W) 12 and 48. HIV-DNA was quantified by Droplet digital PCR (Biorad QX100) and normalized to RPP30 reference gene. Secondary endpoints were increase in CD4+ cells, increase in CD4+/CD8+ ratio, percentage of participants reaching undetectable HIV-RNA. This study is registered in ClinicalTrials.gov, number NCT04225325. Figure 1 shows study design.

Table 1 Characteristics of patients enrolled in INACTION study

Baseline Characteristics	TAF/FTC + DRV/c (N=22)	TAF/FTC + DTG (N=23)	TAF/FTC + DRV/c+DTG (N=16)	p
Males	100%	100%	100%	
Age (years), median	34,5	36	40,5	0,719
CD4 (cells/µL), median	619	705	682	0,884
CD4%	30%	30%	28%	0,620
CD4/CD8, median	0,63	0,57	0,55	0,898
HIVRNA (copies/mL) , median	441.559	282.150	113.000	0,608
HIVDNA (log_{10} copies 10^6 PBMCs) , median	4,22	4,48	4,47	0,166
Fiebig (%)				
I	0%	8,7%	0%	0,248
II	27,3%	17,4%	18,8%	
III	4,5%	13%	0%	
IV	22,7%	0%	18,8%	
V	31,8%	43,5%	37,%	
VI	13,6%	17,4%	25%	

Results

Sixty-four participants were enrolled: 22 were randomly assigned at group 1, 23 at group 2 and 16 at group 3. Median CD4+ count was 682/uL (467- 801), HIV-RNA 5.47 (4.70, 6.14) log10 copies/mL. Table 1 shows baseline characteristics; no differences were observed between groups. At W12 and W48 respectively 30% and 66.7% of patients achieved HIVRNA<50 copies/mL (Figure 2). At W12 and at W48, HIV-DNA loads were similar between groups (p=0.189 and p=0.747 respectively). At W48, HIV-DNA decrease was more evident in the intensive four-drug regimen, although not significantly (Figure 3). At W12 CD4+ (median [IQR]) were 655.00 [495.50, 853.50]; at W48 CD4+ 688.50 [565.50, 850.00; CD4+/CD8+ at W12 0.82 [0.61, 1.13], at W48 0.87 [0.63, 1.22]; no differences observed between the treatment groups.

At multivariate analysis, difference in HIV-DNA delta at W12 was -0.098 (-0.383;0.187) p=0.490 between group 1 and 3, -0.246 (-0.517;0.024) p=0.073 between group 2 and 3. Difference at W48 was -1.322 (-2.688;0.044) p=0.057 between group 1 and 3 and -0.891 (-2.098;0.316) p=0.135 between group 2 and 3.

Figure 1 Study design

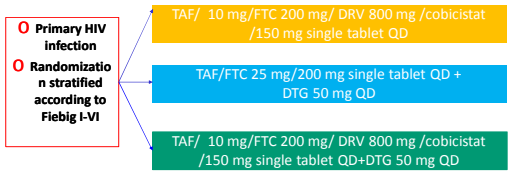


Figure 2 Proportions of pts with HIV-RNA<50 copies/mL over time.

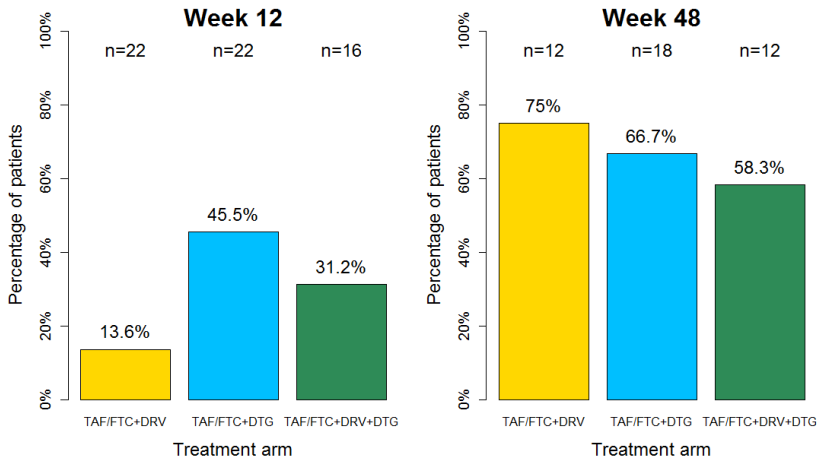
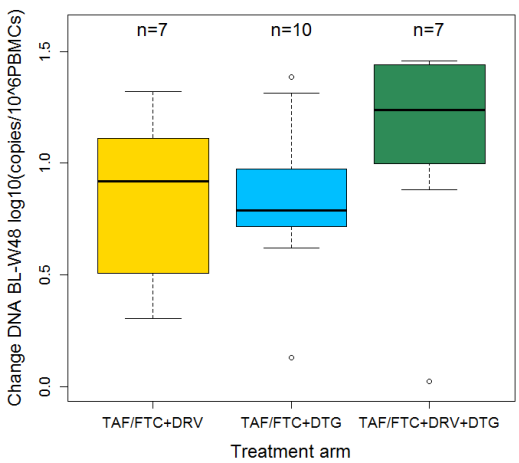


Figure 3 Change in HIV-DNA at week 48 in the 3 drug regimens



Conclusions

We observed a decrease in HIV-DNA from baseline to W48 in treatment during PHI. The results suggest a potential, although not significant, effect of the 4-drug regimen on HIV blood reservoirs.

References

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Acknowledgments

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