Viro-immunological efficacy and tolerability of dolutegravir-based regimens compared to regimens based on other INI, PI, NNRTI in patients with acute HIV infection (AHI): a multicenter cohort study

F. Lagi[1], G. Baldin[2], M. Colafigli[3], A. Capetti[4] A., G. Madeddu[5], S. T. Kiros[1], S. Di Giambenedetto[2], G. Sterrantino[6]

1 Infectious Disease Unit, Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy; | 2 Institute of Clinical Infectious Diseases, Catholic University of Sacred Heart, Policlinico Gemelli, Rome;| 3 Infectious Dermatology and Allergology Unit, IFO S. Gallicano Institute (IRCCS), Rome, Italy| 4 Division of Infectious Diseases, Department of Infectious Diseases, Luigi Sacco University Hospital, Milan, Italy| 5. Unit of Infectious Diseases, Department of Medical, Surgical and Experimental Sciences, University of Sassari| 6 Infectious and Tropical Disease Unit, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy;

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BACKGROUND

Dolutegravir (DTG)-based antiretroviral therapy (ART) is recommended in first-line regimens for all individuals with HIV-1 infection. However limited data are currently available in patients with acute HIV-1 infection (AHI). This study aims to compare the tolerability and viro-immunologic efficacy of dolutegravir-based regimens (DTG group) versus INI, PI, NNRTI (NODTG) based regimen in patients with AHI.

METHODS

This is a retrospective cohort study. We enrolled all AHI between 2015 -2017 who have started ART from 5 different Italian centers. The follow-up ending was 30th April 2018. AHI was defined by p24 antigen presence or indeterminate Western blot. We collected data regarding antiretroviral history, acquired drug resistance, and viro-immunologic outcome. Categorical variables were analyzed with X^2/Fisher's exact test and continuous variables with Wilcoxon signed rank test. Kaplan-Meier method was used to assess the probability of virological failure (>50 cp/ml).

RESULTS

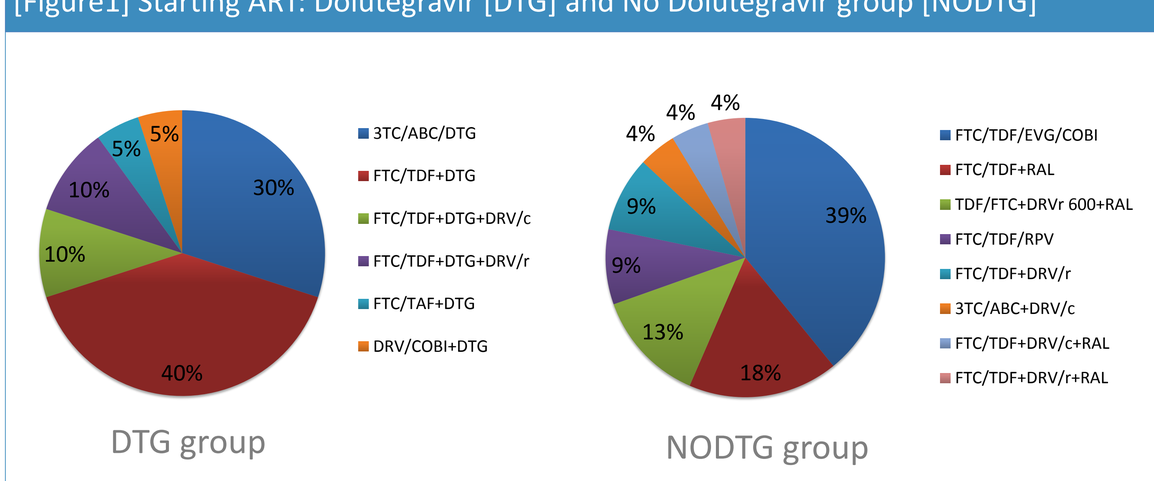
We retrospectively collected data from 43 patients with AHI : 20 on DTG, 23 in NODTG. In the follow-up no difference between the two groups was observed (median 1.8 years for both groups). Overall in the cohort, 81.4% were Italian and 83.7% men, with a median age of 41 years (IQR 31-48). Thirty-one (72.1%) were men who had sex with men (MSM). The median time between diagnosis and treatment initiation was 12 days [IQR 5-28]. Differences between the two groups are reported in Table 1. Three patients (7.0%) had detectable viremia at the end of the follow-up (EOF) (1 in NODTG, 2 in DTG) with no difference between the two groups (p=0.468). Regimens in details are showed in [Figure 1].

Nineteen subjects modified the ART, 15 for simplification, 4 for toxicity (2 on DTG due to neurological toxicity), (2 on Elvitegravir due to gastrointestinal toxicity). We reported ART changes during the follow-up in [Figure 2]. Six patients had transmitted mutations at baseline (none to INI) all in DTG group (p=0.005). In 2 patients the 184V mutation has been detected; both were undetectable at EOF, one of them achieved viral suppression after two years. In Figure 3 is shown the probability of achieving viral suppression in the two groups during the follow up (log rank: p= 0.5672). Both groups had a significant increase in CD4+ cell count, and CD4+/CD8+ ratio at 3, 6, 12, 24, and 36 months (p<0.05 for all comparisons) without significant differences between the two groups.

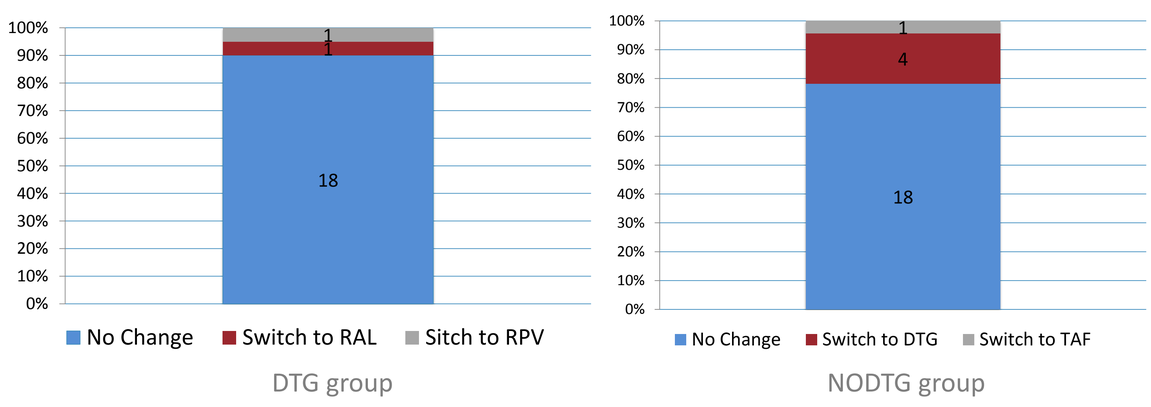
[Table1] Comparison of baseline charateristics	DTG N=20	NODTG N=23	P value
Sex Male n (%)	17 (85.0)	19 (82.6)	0.832
Median age, years [IQR]	33.5 [28-42]	45 [40-53]	**0.006**
Risk n (%)			
• **Heterosexual**	4 (20.0)	8 (34.8)	0.281
• **MSM**	16 (80.0)	15 (65.2)	
Country of origin n (%)			
• Italy	17 (85.0)	18 (78.3)	0.573
• Romania	2 (10.0)	2 (8.7)	
• Africa	0 (0.0)	1 (4.4)	
• Norway	1 (5.0)	0 (0.0)	
• Portugal	0 (0.0)	1 (4.4)	
• Peru	0 (0.0)	1 (4.4)	
Reason of HIV test n (%)			
• Risk perception	8 (40.0)	6 (26.1)	0.441
• Flu-like syndrome	6 (30.0)	6 (26.1)	
• HIV positive partner	3 (15.0)	2 (8.7)	
• Blood Donation	0 (0.0)	1 (4.4)	
• Screening for other diseases	0 (0.0)	3 (13.0)	
• Unknown	3 (15.0)	5 (21.7)	
HCV Ab positive n (%)	1 (5.0)	0 (0.0)	0.278
HBsAg potitive n (%)			
• Negative	19 (95.0)	14 (60.9)	**0.028**
• Positive	1 (5.0)	6 (26.1)	
• Unknown	0 (0.0)	3 (13.0)	
Positive Lue serology n (%)	3 (15.0)	3 (13.0)	0.853
Resistance at baseline n (%)			
• None	14 (60.0)	23 (100)	**0.005**
• NRTI	2 (10.0)	0 (0.0)	
• NNRTI	2 (10.0)	0 (0.0)	
• NRTI+NNRTI	1 (5.0)	0 (0.0)	
• PI	1 (5.0)	0 (0.0)	
Median CD4 cell/µL [IQR]	504 [311-710]	557 [339-717]	0.792
Median HIV-RNA Log $_{10}$ copies/mL [IQR]	6.0 [5.4- 6.4]	5.5 [4.9-6.3]	0.173
Median days from diagnosis to ART start [IQR]	10 [5-18]	22 [4-28]	0.387
Median days to achieve <50 copies/mL [IQR]	103 [58-190]	121 [60-197]	0.903
Number of drugs			
• 2	1 (5.0)	0 (0.0)	0.554
• 3	15 (75.0)	18 (78.3)	
• 4	4 (20.0)	5 (21.7)	
Single Tablet Regimen n (%)	6 (30.0)	11 (47.8)	0.233
Fever >38° n (%)	10 (50.0)	9 (39.1)	0.430
Lymphoadenopaty n (%)	10 (50.0)	12 (52.2)	0.887
GI symptoms (Diahrrea/vomiting) n (%)	5 (25.0)	2 (8.7)	0.149
CD4 < 350 cell/mm3 at diagnosis n (%)	6 (30)	6 (26.1)	0.081

GI: gastro-intestinal
MSM: men who have sex with men

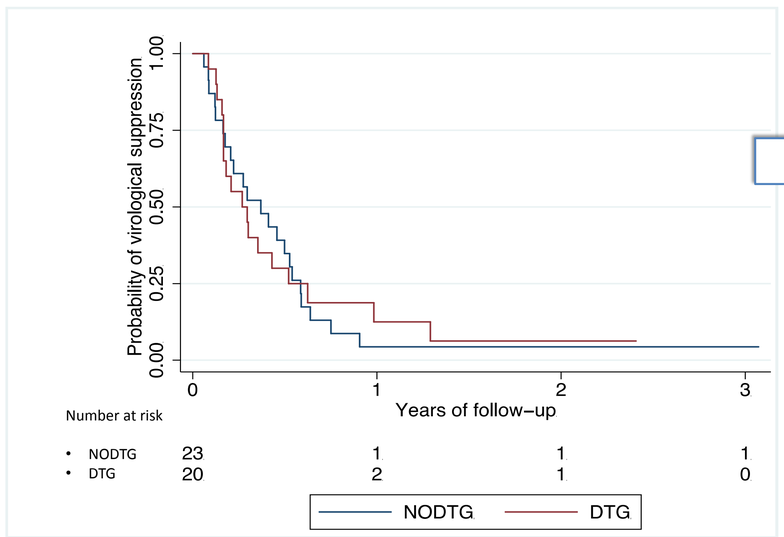
[Figure1] Starting ART: Dolutegravir [DTG] and No Dolutegravir group [NODTG]



[Figure2] Therapy change in Dolutegravir [DTG] and No Dolutegravir group [NODTG]



[Figure3] Kaplan-Meier for the probability of virologic suppression by group



CONCLUSION

In our setting, antiretroviral therapy in AHI has started very early. DTG showed excellent viro- immunologic efficacy even when NRTI transmitted mutations were present, interruptions rarely occured due to neurological toxicity.