Virological outcome after switching a suppressive HAART to Dolutegravir with 2 NRTIs among HIV-1 infected patients: potential effects of previous suboptimal therapies or previous virological failures

Mohamed N'dongo SANGARE[1,2], Jean-Guy BARIL[3,4,5], Alexandra DE POKOMANDY[6,7], Claudie LAPRISE[8,9], Réjean THOMAS[10], Marina KLEIN[6], Cécile TREMBLAY[11], Louise LAPORTE[2], Zoe GREENWALD[10], Costa PEXOS[6], Nima MACHOUF[3], Madeleine DURAND[11], Helen TROTTIER[1,2]

[1]Department of Social and Preventive Medicine, Université de Montréal; [2]Sainte Justine University Hospital Center.; [3]Clinique de médecine urbaine du Quartier latin; [4]Faculty of Medicine, Université de Montréal; [5]Centre hospitalier de l'Université de Montréal;[6]Chronic Viral Illness Service, McGill University Health Centre; [7]Faculty of Family Medicine, McGill University. [8]Division of Cancer Epidemiology, McGill University ;[9]Division of Oral Health and Society, McGill University; [10]Clinique Médicale L'Actuel; [11]Department of Microbiology, Infectious Diseases and Immunology, Université de Montréal.

BACKGROUND AND OBJECTIVE

Switching antiretroviral regimen in the context of suppressed HIV viral load since at least 6 months but with prior history of virological failure or suboptimal therapy is often desired for simplification or toxicity reasons. However, few studies documented the risk of failure following these switches. The objective was to study the virological outcome following a switch to Dolutegravir (DTG) +2 NRTIs (Nucleoside reverse transcriptase inhibitor) in patients virologically suppressed for at least 6 months, and to compare whether previous virological failure or past suboptimal regimen increased the risk of post-switch virological failure.

MATERIALS AND METHODS

Study design: Observational cohort study.

Data collection: Regular monitoring of patients living with HIV, representing more than 78% of patients presently followed in the Quebec province. The inclusion criteria was as follow: having been switched to a DTG + 2 NRTIs regimen, having a suppressed viral load (VL) (<50 copies) for at least 6 months before switching and having at least one VL after switch.

Statistical analyses: Previous virological failure was defined as a VL>1000 copies/ml after 16 weeks of therapy, or VL>400 copies/ml after 24 weeks or two consecutive VL>50 copies/ml after 48 weeks or after having been suppressed. Blips were not considered as failure. Suboptimal therapies consisted of exposure to a single-NRTI or two-NRTIs for at least one month. Cox regression models were used to estimate the association between previous virological failure or suboptimal therapies with post-switch virological failure (defined as two consecutive VL>50 copies/ml, or the last VL available >50 copies/ml). Hazard ratios (HR) were adjusted for the following variables measured at switch: age, treatment duration, time since HIV diagnosis, number of treatment changes, lifetime Hepatitis B and C using 6% change in estimate Method.

RESULTS

Among the 1209 eligible patients with suppressed viral load for at least 6 months, who were switched to DTG + 2NRTIs, 478 were previously exposed to mono or dual NRTIs therapy or had previous virological failure whereas 731 were only exposed to triple therapies without previous virological failure.

Table 1 shows the characteristics of patients according to exposure status. Patients exposed to optimal therapy (triple therapy) without virological failure were younger (48.6 years) than those with previous virological failure and/or suboptimal therapy (53.2 years). Very few cases of virological failure were observed after switch. One year after switch, only 2.8% and 3.0% have a virological failure among patients exposed to optimal therapy without previous virological failure and among patients exposed to previous suboptimal therapy or previous virological failure, respectively.

Table 2 presents the crude and adjusted hazard ratio for the association between post-switch virological outcome and exposure. The incidence rate of virological failure among patients with prior virological failure and/or suboptimal therapy versus those without were 0.019 years^{-1} (95% CI: 0.011-0.034 and 0.013 years^{-1} (0.008-0.022), respectively. The crude and adjusted HR shows no statistically significant difference between groups (crude HR=1.48 (95% CI: 0.70-3.12) and adjusted HR=1.33 (95% CI: 0.53-3.29)).

CONCLUSION

Our study shows a low incidence rate of virological failure among patients who were switched to DTG and a lack of association between these virological failure and previous virological failure and/or exposition to suboptimal therapy. These findings can help clinicians in the management of patients living with HIV.

Table 1: Characteristics of patients exposed to suboptimal therapy (monotherapy or dual therapy) or virological failure before Dolutegravir switch and patients exposed to optimal therapy (triple therapy) only without previous virological failure

PATIENT CHARACTERISTICS*		Patients exposed to suboptimal therapy or virological failure before Dolutegravir switch (N=478)	Patients exposed to optimal therapy (triple therapy) only without virological failure before Dolutegravir switch (N=731)
Socio-demographic characteristics*			
Age Mean (SD)		53.2 (9.3)	48.6(11.2)
Sex (%)	Male	411 (86.0%)	632 (86.5%)
	Female	67 (14.0%)	99 (13.5%)
Acquisition factors			
MSM (%)	Yes	327 (68.4%)	532 (72.8%)
	No	151 (31.6%)	199 (27.2%)
Bisexual (%)	Yes	12 (2.5%)	14 (1.9%)
	No	466 (97.5%)	717 (98.1%)
Heterosexual (%)	Yes	100 (20.9%)	107 (14.6%)
	No	378 (79.9%)	624 (85.4%)
From endemic countries (%)	Yes	60 (12.5%)	61 (8.3%)
	No	418 (87.5%)	670 (91.7%)
Vertical transmission (%)	Yes	2 (0.4%)	1 (0.1)
	No	476 (99.6%)	730 (99.9%)
Viral load (VL) one-year post-switch (%)	≥1000 copies/ mL	3 (1.1%)	4 (0.8%)
	≥50 copies/ mL	9 (3.0%)	14 (2.8%)
ARV treatment duration prior DTG switch§	≥10.9 years	367 (76.8%)	202 (27.6%)
Time since HIV diagnosis before switch§	≥13.2 years	363 (75.9%)	240 (32.8%)
Number of treatment changes prior DTG switch	≥2	476 (99.6%)	715 (97.8%)
Hepatitis B before switch	Positive for HBsAg	19 (4.0%)	16 (2.2%)
Hepatitis C before switch	Positive anti-HCV	48 (10.0%)	42 (5.7%)
Pre-switch virological failure	Yes	437 (91.4%)	0 (0%)

*At DTG switch unless reported differently
§categorized with the mean

Table 2: Univariable and multivariable Cox regression analysis. Crude and adjusted Hazard ratio for the association between post-switch virological failure and exposure

Exposure	Person-year	Incidence rate years^{-1} (95% CI)	Crude HR (95% CI) n=1131**	Adjusted HR* (95% CI) n=1055***
Exposure to optimal therapy (triple therapy) only without virological failure before Dolutegravir switch	1100.3	0.013 (0.008-0.022)	1 (Reference)	1 (Reference)
Exposure to previous suboptimal therapy (monotherapy or dual NRTIs therapy) or virological failure before Dolutegravir switch	654.0	0.019 (0.011-0.034)	1.48 (0.70-3.12)	1.33 (0.53-3.29)

*Multivariate model adjusted for age, treatment duration, and Hepatitis C (variables among the list described in the method section that changed the HR by 6%).
** 78 patients excluded because they had no VL measures after switch
***Patients were excluded because of missing data on covariates

DISCLOSURE

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