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Virological response in HIV-infected-patients virologically-suppressed switching to a DTG-based regimen in an observational cohort based on the genotypic susceptibility score

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Objective

To assess, in a clinical cohort of virologically-suppressed patients, the potency of a dolutegravir containing regimen, according to genotypic susceptibility score (GSS), to maintain a VL supression up to W24.

Patients and methods

- Prospective observational single-center cohort enrolling all DTG naive patients with a plasma viral load (pVL) <50 c/mL initiating for the first time DTG-containing regimen between September and December 2015.
- Virologic failure was defined as 2 consecutive VL above 50 c/mL
- GSS of the antiretroviral regimen (including DTG) was calculated taking into account all historical genotypes, using the ANRS algorithm (V 25 September 2015) translating interpretations into :
  - susceptible: score 1
  - possible resistance: score 0.5
  - resistance: score 0

Results

- 254 patients switched to a DTG-containing regimen during the period
- 209 had available historical genotypes
- GSS 2 and 2.5 were pooled in the same category

GSS	1	1.5	2 and 2.5	3
N (%)	11 (5 %)	16 (8 %)	72 (34 %)	110 (53 %)
Median time (y) since last genotype	11 (7-14)	8 (4-11)	8 (3-13)	4 (2-8)

- 11 patients received only DTG as active drug as »functional » DTG monotherapy

Patients's characteristics at DTG initiation (1)

GSS	1 (n = 11)	1.5 (n = 16)	2 & 2.5 (n = 72)	3 (n = 110)
Male sex, n (%)	11 (100)	11(69)	41 (57)	80 (73)
Age, median years (IQR)	51 (49-60)	50 (45-53)	52 (46-59)	51 (40-59)
Time since HIV diagnosis, median years (IQR)	23 (21-25)	17 (10-22)	21 (16-24)	12 (6-21)
Duration of prior ART, median years (IQR)	20 (18-22)	13 (10-17)	17 (9-19)	10 (5-18)
Number of previous ART lines, median (IQR)	10 (9-12)	7 (4-9)	6 (3-10)	4 (2-7)
Duration of HIV-1 RNA <50 copies/mL before switch, median years (IQR)	3 (2-5)	6 (2-8)	4 (2-7)	3 (1-5)
Baseline CD4 cell count, median cells/mm^3 (IQR)	540 (400-798)	685 (560-908)	604 (513-828)	588 (393-785)
Nadir CD4 cell count, median cells/mm^3 (IQR)	70 (63-110)	197 (151-279)	234 (107-326)	213 (77-325)
Subtype B, n (%)	8 (73)	10 (59)	40 (55)	56 (51)

- Patients' characteristics at time of DTGinitiation were different according to the GSS
- GSS 1 was observed in more previously treated patients with the lowest CD4 nadir

Patients's characteristics at DTG initiation (2)

GSS	1 (n = 11)	1.5 (n = 16)	2 & 2.5 (n = 72)	3 (n = 110)
Associated antiretroviral drugs, n (%)				
ABC/3TC	5 (46)	14 (88)	12 (16)	67 (61)
TDF/FTC	0 (0)	1 (6)	6 (8)	27 (25)
3TC	0 (0)	0 (0)	7 (11)	0 (0)
RPV	3 (27)	0 (0)	26 (36)	0 (0)
DRV	0 (0)	0 (0)	5 (7)	0 (0)
ATV	1 (9)	0 (0)	6 (8)	0 (0)
RPV + NRTI	0 (0)	0 (0)	4 (6)	9 (8)
Other ARV drugs	2 (18)	1 (6)	6 (8)	7 (6)
Number of NRTI drug resistance mutations, median (IQR)	6 (3-7)	1 (1-3)	2 (1-4)	0 (0-0)
Number of M184V, n (%)	10 (100)	16 (100)	34 (47)	8 (7)
Number of NNRTI drug resistance mutations, median (IQR)	1 (0.5-3)	1 (0-2)	0 (0-2)	0 (0-1)
Number of major PI drug resistance mutations, median (IQR)	0 (0-3)	0 (0-0)	0 (0-0)	0 (0-0)
Time since last genotypic resistance test, median years (IQR)	11 (7-14)	8 (4-11)	8 (3-13)	4 (2-8)

- ABC/3TC/DTG and RPV/DTG were the most common regimens used
- M184V was the most prevalent resistance mutation

Virological outcome according to GSS

Patients with pVL<50c/mL	**GSS = 1 n = 11**	**GSS = 1.5 n = 16**	**GSS = 2/2.5 n = 72**	**GSS = 3 n = 110**
W12	11	15*	70**	108 **
W24	11	16	68 ****	106 ****

* Virologic failure * Blip * VL not controlled on 2nd specimen

- **During the follow up**
  - -All but one GSS 1 and 1.5 treated patients had a fully supressed VL
  - -9 patients experienced a blip: 3 patients at W12 & 6 patients at W24
  - -1 patient had virological failure at W12 (91c/mL) & W24 (64 c/ml) without acquisition of RAM (DNA)
  - -2 patients harbored a VL > 50 copies/ml at the last time of follow-up (W24)
  - -7 patients (3.3 %) discontinued DTG regimens between Day7 & W24
    - neuro-psychological side effects (n=1)
    - cutaneous side effects (n=1)
    - pregnancy (n=1)
    - renal toxicity (n=1)
    - headaches (n=1)
    - patients' decision (n=2).

Conclusions

- In this observational cohort, patients' characteristics at time of switching to a DTG-based regimen were different depending on the GSS

- However, short-term follow-up showed a high level of maintenance of virological suppression, regardless to the baseline GSS, even in patients treated by « functional DTG monotherapy.

- These data suggest that DTG remains potentially able to maintain viral suppression when combined with fully or incompletely active drugs in these long-term virologically-suppressed patients.

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