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PREVALENCE OF RESISTANCE AND LIMITED THERAPEUTIC OPTIONS IN PATIENTS VIREMIC ON ART

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BACKGROUND

Although current ART has led to improved rates of prolonged virologic suppression, some patients remain viremic under ART. Reasons of this uncontrolled viremia could be due to resistance to treatment, sub-optimal ART combination or poor adherence to treatment.

Although most patients with multi-drug resistant (MDR) HIV-1 can be offered ART combinations allowing viremia suppression, the prevalence of multi-drug resistance and/or limited therapeutic options in patients remaining viremic on ART is not fully assessed.

Such information would be useful to know the number of patients in need of new ARVs, *specially* with new mechanism of action (attachment *inhibitor,* maturation inhibitor, capsid inhibitor, etc.)

MAIN OBJECTIVE

To evaluate prevalence of resistance, MDR and therapeutic options among viremic subjects on ART in a large multicentric study.

METHODS

- Retrospective multicentric cross-sectional survey in 3 French referral *centers* for HIV care belonging to the Dat'AIDS cohort (NCT02898987). Study was approved by Nantes Ethic Committee.
- Population : PLWHIV with follow-up between October 2017 and October 2018
- Time point of analysis : latest visit closer to 1 Oct 2018
- PLWHIV with HIV RNA >50 copies/mL after at least 6 months of ART were compared to PLWHIV with HIV RNA <50 copies/mL
- For PLWHIV with HIV RNA >50 copies/mL we assessed :
  - cumulative data for all plasma RNA genotypes
  - Number of active drugs (AD)
  - Genotype sensitivity score (GSS) defined by the number of active ART in the ongoing treatment

Resistance to ARV was defined *on the cumulative data for all plasma RNA genotypes analysis,* based on ANRS algorithm ﴾(http://www.hivfrenchresistance.org version 29; 2018).

Limited therapeutic option (TO) was defined as resistance to ≥3 of 4 ARV classes (maraviroc and enfuvirtide were not considered) and ≤2 AD among 5 specified drug groups (3TC or FTC, ABC or TDF, ≥1 NNRTI, ≥1 PI/b, ≥1 INSTI).

χ2 and Mann-Whitney tests were used for comparisons.

RESULTS

- ***Population***

- Of 5,429 individuals under follow-up, 215 (4%) had HIV RNA >50 c/mL. We excluded 7 subjects with no available genotype (Table 1)
- Of the 208 viremic subjects, 84 had HIV RNA 50-200 c/mL and 124 HIV RNA > 200 c/mL.

- ***Risk factors of HIV RNA >50 c/mL***

- Reported adherence issues : 65%
- Social problems : 50%
- Non-French native : 41.5%

- ***Current cART in individuals with HIV RNA >50 c/mL***
  - 62% on PI (52.4% 2 NRTIs + PI/r)
  - 37.1% on INSTI
  - Only 5.3% on NNRTI

- ***Resistance to ART in individuals with HIV RNA >50 c/mL***

- 8.2% (17) of viremic subjects had resistance to 3 or 4 ARV classes
- 50.4 % had no resistance;
- Susceptibility to TDF, ETR, DRV/r and DTG was 92.8%, 86.1%, 98.6% and 95.7%, respectively (Table 2).

- ***Remaining active drugs in 208 subjects with HIV RNA > 50 c/mL (figure 1)***

- Number of AD ≥3 : 85.6%
- Ongoing treatment had :
  - a GSS ≥3 in 68%
  - a GSS = 2 in 24%
- Limited therapeutic option : 9 subjects
  - 4.3% of subjects with HIV RNA > 50 c/mL
  - 0.17% (95% CI : 0.06-0.27) of the total population
  - Only 2 had GSS = 0 **and** AD = 0.

Table 1: Patients characteristics (5,429 subjects with > 6 months of cART)

	RNA > 50 c/mL N = 208	RNA < 50 c/mL N = 5,214	p
Gender : female	38.0%	32.1%	0.07
Mean age, years	47.2	48.9	0.06
MSM	25.0%	43.5%	<0.0001
Non-French native	41.4%	29.8%	0.0004
CDC Stage C	41.4%	20.2%	<0.0001
Zenith HIV RNA >5 log_{10} c/mL	73.1%	18.7%	<0.0001
Nadir CD4 <200/mm³	63.9%	43.4%	<0.0001
Last CD4 <200/mm³	22.1%	3.4%	<0.0001

Table 2: % of resistance to each ARV in the population with HIV RNA > 50 c/mL

Class	ARV	n (%) N=208	Class	ARV	n (%) N=208
NRTI	All	81 (38.9%)	PI	All	16 (7.7%)
	3TC - FTC	73 (35.1%)		Lopinavir/r	12 (5.8%)
	Abacavir	26 (12.5%)		Atazanavir/b	15 (7.2%)
	Tenofovir	15 (7.2%)		Darunavir/b	3 (1.4%)
	Zidovudine	24 (11.5%)			
NNRTI	All	75 (36.1%)	INSTI	All	21 (10.1%)
	Efavirenz	58 (27.9%)		Raltegravir	18 (8.7%)
	Nevirapine	55 (26.4%)		Elvitegravir	21 (10.1%)
	Etravirine	29 (13.9%)		Dolutegravir	9 (4.3%)
	Rilpivirine	53 (25.5%)		Bictegravir	NA NA

Figure 1: Ongoing active treatment (GSS) and therapeutic options in subjectswith HIV RNA > 50 copies/mL



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Key points

- PLWHIV with HIV RNA > 50 c/mL on cART and limited therapeutic options are rare :
- 0.17 % of patients on cART
- 4.33 % of patients on cART with HIV RNA >50 copies/mL
- Resistance or MDR to treatment and sub-optimal ART strategies are not the main reasons of treatment failure.
- Adherence seems to be the biggest challenge.

DISCUSSION/CONCLUSION

- **In this cross-sectional survey, we estimated the ongoing treatment efficacy and therapeutic options based on cumulative data resistance genotype in a population with absence of virological suppression.**
- **After 6 months of follow-up, few (4%) individuals on ART ≥6 months had HIV RNA >50 copies/mL.**
- **Resistance to ART was similar to a 2014 French nationwide survey, adding *consistency* to our results (MULTIVIR STUDY)**
- **Therapeutic options still remain for the vast majority of patients**
- **Ongoing treatment failure is mainly not explained by resistance profile of ART, or MDR, suggesting a lack of adherence, as documented in many cases**
- **Extrapolating our results to all patients under care in France (2016 estimation : 112,877; 95% CI: 111,635- 114,053), we would obtain an estimate of 192 (95% CI: 190-194) HIV-1 infected adults with limited therapeutic options.**

Ce tableau de la dernière version me pose problème
Pourquoi calcul sur 76 pts et non 208 ?
Les % de résistance ne correspondent pas à aux chiffres de sensibilité (100 −R) du texte.

Class	Molecules	Number of patient (%) N=76	Class	Molecules	Number of patient (%) N=76
INTI	Overall	18 (23,7%)	INNTI	Overall	12 (15,8%)
	3TC - FTC	16 (21,1%)		EFAVIRENZ	9 (11,8%)
	ABACAVIR	6 (7,9%)		NEVIRAPINE	11 (14,5%)
	TENOFOVIR	5 (6,6%)		ETRAVIRINE	6 (7,9%)
	ZIDOVUDINE	5 (6,6%)		RILPIVIRINE	8 (10,5%)
PI	Overall	4 (5,3%)	INI	Overall	6 (7,9%)
	LOPINAVIR	4 (5,3%)		RALTEGRAVIR	5 (6,6%)
	ATAZANAVIR	4 (5,3%)		EVILTEGRAVRIR	6 (7,9%)
	DARUNAVIR	1 (1,3%)		DOLUTEGRAVIR	5 (6,6%)