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Incidence of transmitted drug resistance mutations among newly diagnosed HIV-1 patients: a 6-month retrospective analysis

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Introduction

- Approximately 10% to 17% of cART-naive HIV-positive patients have drug resistance mutations (DRMs) to at least one antiretroviral drug.
- The aim of our study is to describe the incidence of DRMs in the ART-naive HIV-1 patients population attending our Hospital and evaluate the clinical relevance of these findings.

Methods

- We performed a retrospective analysis on a small group of newly diagnosed HIV-1 patients attending the Infectious Diseases Unit of S. Orsola Hospital (Bologna, Italy) between September 2023 and March 2024. The baseline data (age, sex, ethnicity, and transmission routes) were collected.
- HIV-1 genotyping analysis was performed using Next Generation Sequencing (NGS) with the Illumina MiSeqTM platform. The target genomic regions were amplified by One-Step PCR with AD4SEQ HIV-1 Solution v.2 kit. The Fastq analysis obtained was conducted with the HIVdb Program software, available from the Stanford University HIV Drug Resistance Database: we considered sequences with a minimum of 100 reads at each known drug resistance position and a 10% threshold.
- Pending the NGS results, ART was started and afterwards modified, if needed.

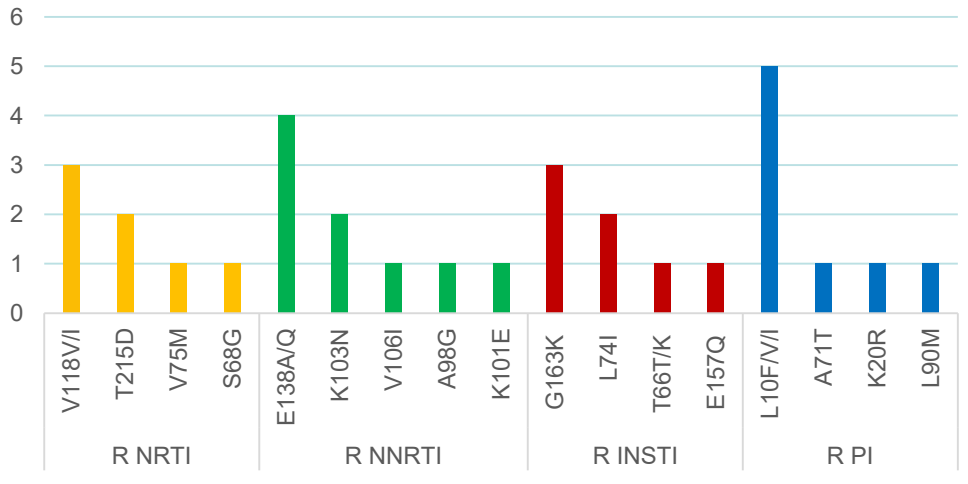
Results

- The patients enrolled in this study were reported in Table 1.
- DRMs to any class of antiretroviral agents were detected in 15 viral sequences (44%). The distribution in the major antiretroviral agents were: 3 (9%) for NRTI, 8 (24%) for NNRTI, 6 (18%) for INSTI with 1 (3%) major mutation, 1 (3%) major mutation for PI.
- The most common and relevant DRMs identified were (Figure 1):
  - 3 V118V/I (9%) for NRTI;
  - 2 K103N (6%), 4 E138A (12%), 1 A98G (3%), 1 K101E (3%) for NNRTI;
  - 3 G163K (9%), 2 L74I (6%) and 1 T66T/K (3%) for INSTI;
  - 1 L90M (3%) for PI.
- The incidence of DRMs for RPV and DOR was 18% (n=6) and 3% (n=1) respectively, the incidence of DRMs for BIC or DTG was 3% (n=1). No DRMs detected for DRV/r.
- We opted for an INSTI-based regimen in 28 patients (82%).
- The result of the genotyping analysis led to a modification of the ART in only 2 patients (6%).

Table 1: characteristics of the study population

	Total (n = 34)
Age at diagnosis [mean ± std]	38,4 ± 3,9
Gender	
Male	25 (74%)
Women	6 (18%)
MtF	3 (9%)
Caucasian	30 (88%)
HIV transmission risk category	
MSM	16 (53%)
Heterosexual	11 (37%)
IDU	1 (3%)
PrEP	2 (6%)
CD4+ LC (cells/mmc) [mean ± std]	439 ± 113
HIV RNA (log10 cp/mL)	5,8
AIDS diagnosis	7 (21%)
Viral subtype B	13 (41%)

Figure 1: prevalence of detected mutations



Conclusions

- We found a higher transmitted DRMs rate in our group compared to other Italian or European cohort studies.
- The use of NGS sequencing instead of Sanger technology has increased sensitivity to detect more DRMs, including low-frequency variants with uncertain clinical potential.
- We found only a small number of DRMs for first-line ART recommended regimens, which led to ART adjustments in only 2 patients (6%).
- Our study is limited by the small sample size, therefore other large-scale clinical studies are needed for the standardization of NGS assays and the definition of the prevalence and clinical relevance of NGS identified DRMs.

References

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