

**Online supplemental table 1. Summary of variables included in the PRESTIGIO Registry from the date of evidence of 4-class drug resistance.**

<b>Socio-demographic data</b>	
<i>General</i>	date of birth, sex at birth, country of birth, ethnicity
<i>Lifestyle</i>	height, weight, smoking habit
<i>HIV-specific</i>	mode of HIV transmission, date of last negative HIV test, date of first positive HIV test, date of 4-class drug resistance
<b>Laboratory results</b>	
<i>HIV-specific</i>	HIV-1 RNA (copies/mL), HIV-1 RNA before ART start (copies/mL) CD4 <sup>+</sup> T-cell count (cells/ $\mu$ L, %), CD8 <sup>+</sup> T-cell count (cells/ $\mu$ L, %), CD4 <sup>+</sup> /CD8 <sup>+</sup> ratio, CD4 <sup>+</sup> nadir (cells/ $\mu$ L) RNA- and DNA-based genotypic resistance testing ( <i>collected since the first test available, also before evidence of 4-class drug resistance</i> ) subtype, viral tropism ( <i>collected since the first available, also before evidence of 4-class drug resistance</i> )
<i>Other</i>	hepatitis B and C serologies, HBV DNA, HCV RNA complete blood cell count plasma glucose, triglycerides, total/HDL-/LDL-cholesterol, creatinine, transaminases, direct and indirect bilirubin
<b>Treatment</b>	
<i>Antiretroviral therapy</i>	date of antiretroviral therapy start, date of highly active antiretroviral therapy (defined as a combination of drugs from at least 2 different classes) start

	regimens from baseline to the last available visit (including start and stop dates, dose and mode of administration, reason for switch)
<i>Other medications</i>	specific drugs (including start and stop dates, dose and mode of administration, reason for stop)
<i>Vaccines</i>	date and type of vaccinations
<b>AIDS diagnoses</b>	date and type of AIDS events
<b>Comorbidities</b>	non-AIDS malignancies, diabetes, arterial hypertension requiring treatment, major adverse cardiovascular events, chronic liver or kidney diseases, osteoporosis and related fractures, neurocognitive disorders, chronic obstructive pulmonary disease, etc. (including dates of diagnosis and eventually resolution)
<b>Hospitalizations</b>	dates and reason for hospitalization
<b>Pregnancies</b>	dates of pregnancy, date of delivery, etc.
<b>Sexually transmitted infections</b>	date of diagnosis, type, and treatment of sexually transmitted infections
<b>Death</b>	date and reason of death

**Online supplemental figure 1.** Resistance-associated mutations present in  $\geq 20\%$  of 4DR-PLWH from the PRESTIGIO Registry. All RNA-based genotypic resistance tests through Sanger sequencing were considered cumulatively. Percentages evaluated on 229 PLWH for NRTI, NNRTI, and PI resistance-associated mutations, on 175 PLWH with at least one available integrase genotype for INSTI resistance-associated mutations. INSTI: integrase strand transfer inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor; PI: protease inhibitor; 4DR-PLWH: people living with 4-class drug-resistant HIV.

