Predicting 2-drug antiretroviral regimen efficacy by genotypic susceptibility score: results from a cohort study

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BACKGROUND AND OBJECTIVE

HIV drug resistance has a deleterious effect on the virological outcome of antiretroviral therapy (ART). The aim of the study is to evaluate the ability of genotypic susceptibility score (GSS) to predict virological outcome following an ART switch to a 2-drug regimen in pretreated HIV-1 infected patients.

METHODS

From the ARCA database we selected HIV-1 infected treatment-experienced patients switching to 2-drug ART (2007-2017, time of switch=baseline), with pre-baseline resistance genotype and at least one HIV-1 RNA determination during follow up. Primary endpoint was virological failure (VF, defined as an HIV-1 RNA, VL, >400 copies/mL). Survival analysis was used to investigate predictors of VF. The genotypic susceptibility score (GSS) predicted by the latest and the cumulative genotype (CGSS, summing all the historical resistance mutations) was calculated using the Stanford hivdb (v.8.5) interpretation with respect to the 2-drug regimen started. Pre-baseline viremia copy-years (VCY) were calculated using the trapezoidal rule on the VL log10 scale using all the available VL results.

RESULTS

Tab.1 Patients characteristics (n=2,149)

Males, n (%)	1,380/2,032 (67.9)
Age, median (IQR)	50 (45-56)
Region of birth, n (%)	
Western Europe	1,723 (80.2)
Sub-Saharan Africa	72 (3.4)
Latin America and Caribbean	50 (2.3)
Eastern Europe	20 (0.9)
Other	18 (0.8)
Unknown	266 (12.4)
Geographic location of clinical sites, n (%)	
Northern Italy	1,197/2,148 (55.7)
Central Italy	864/2,148 (40.2)
Southern Italy/islands	87/2,148 (4.1)
Risk factors, n (%)	
Men who have Sex with Men	675 (31.4)
Injecting drug users	532 (24.8)
Heterosexual contacts	349 (16.2)
Other	69 (3.2)
Unknown	524 (24.4)
Viral subtype B, n (%)	1,340/1,552 (86.3)
Nadir CD4$^+$, cells/micrL, median (IQR)	166 (57-276)
Baseline CD4$^+$, cells/micrL, median (IQR)	577 (394-784)
Zenith HIV-1 RNA, Log_{10} cps/mL, median (IQR)	5.02 (4.39-5.53)
Baseline HIV-RNA, Log_{10} cps/mL, median (IQR)	1.57 (1.08-1.69)
Baseline HIV-RNA <50 cps/mL, n (%)	1,204/1,702 (70.7)
Viremia copy-years (log_{10} scale), median (IQR) (available in 1,330/2,149 pts)	22.62 (10.88-34.71)
Time since HIV diagnosis (years), median (IQR)	15 (8- 22)
Treatment discontinuation for any reason, n (%)	1,302/2,148 (60.6)

Fig.1 Previous antiretroviral classes used

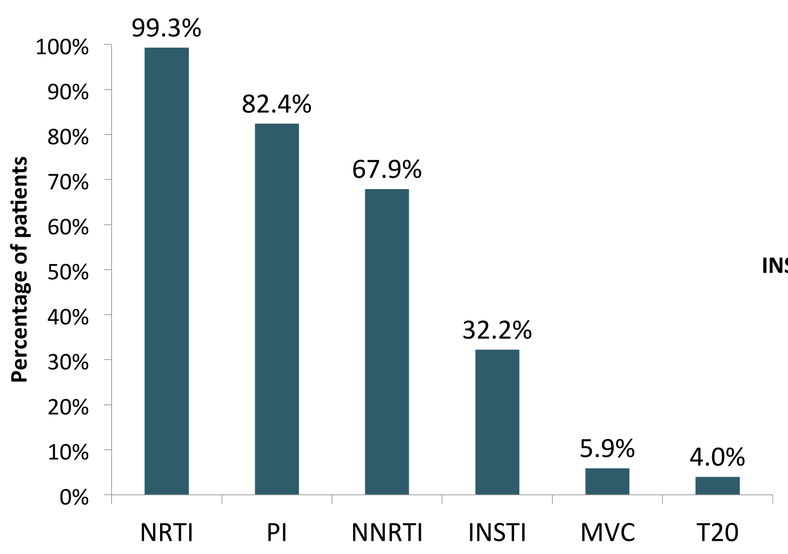


Fig.2 Two-drugs antiretroviral regimens

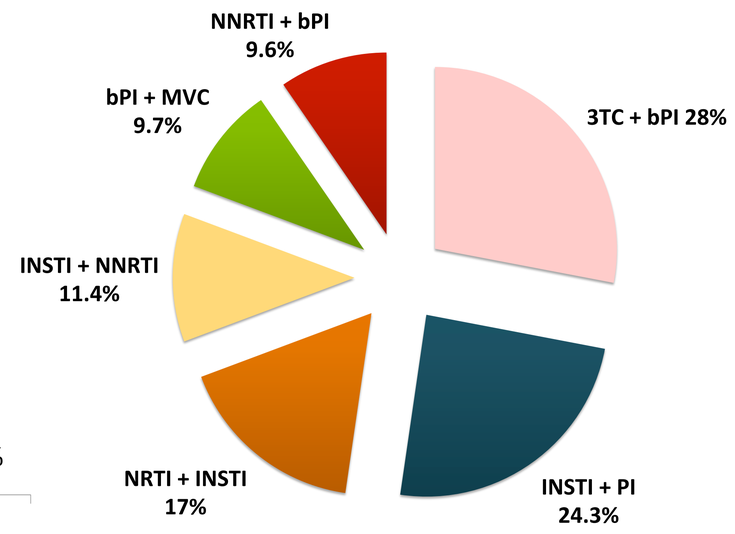
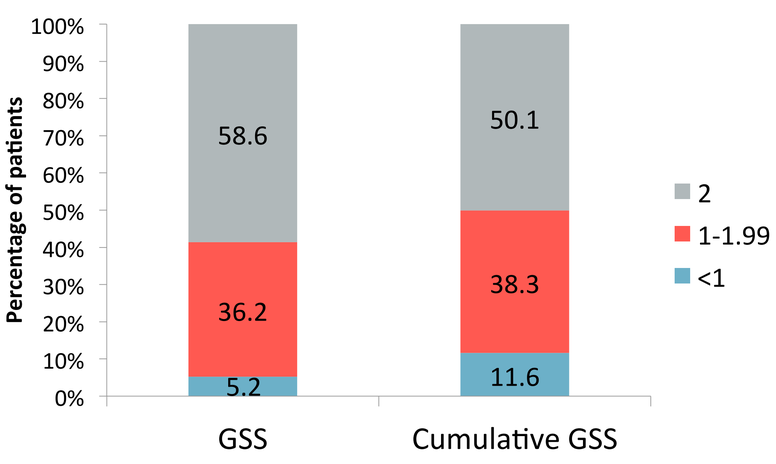


Fig.3 Strata of GSS and cGSS



Median GSS was 2 (1-2), with GSS <2 in 41% patients and median CGSS 2 (1-2), with CGSS <2 in 50% patients.

Fig.4 Reported reasons for 2-drug regimens discontinuation

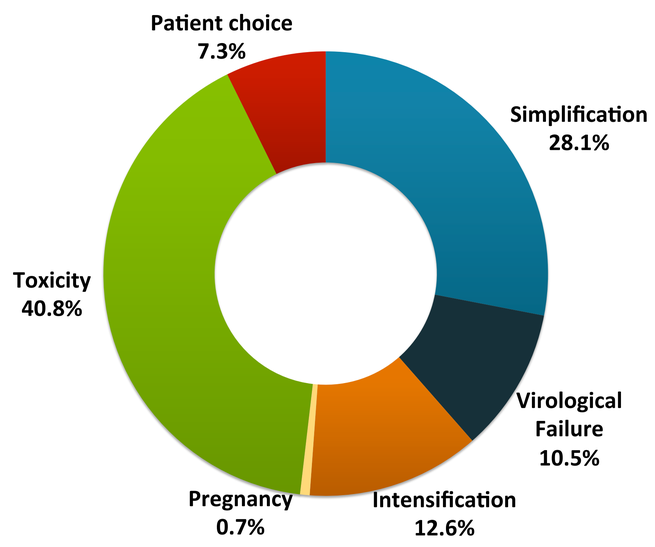
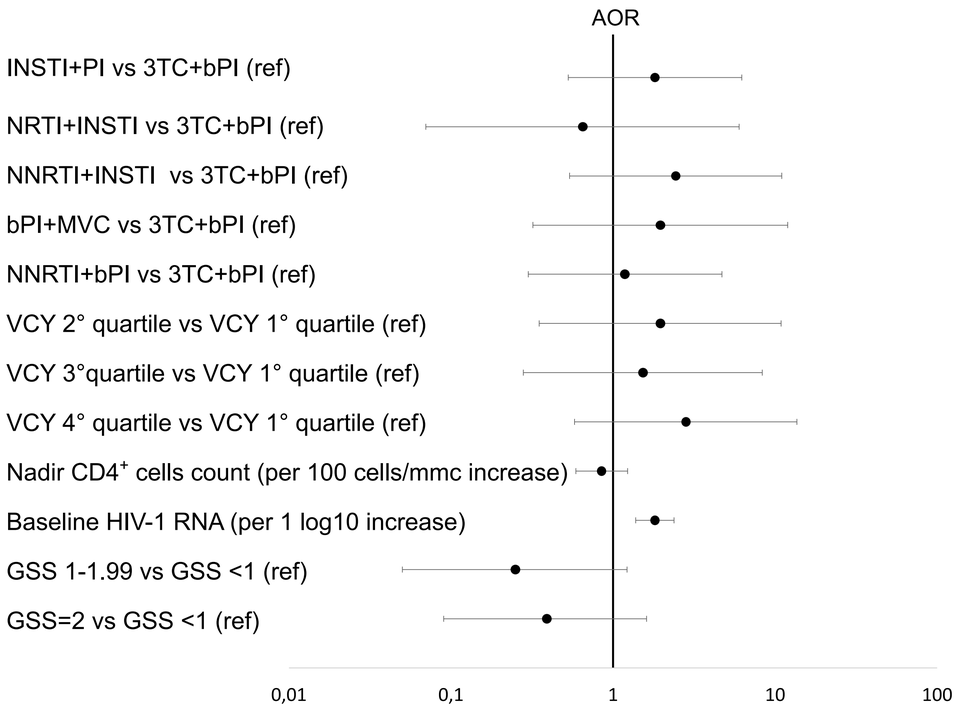
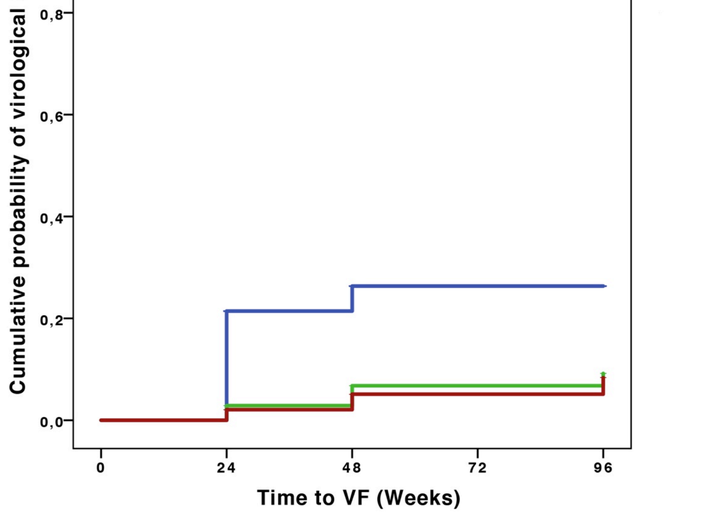


Fig. 5 Predictors of virological failure by multivariate Cox regression



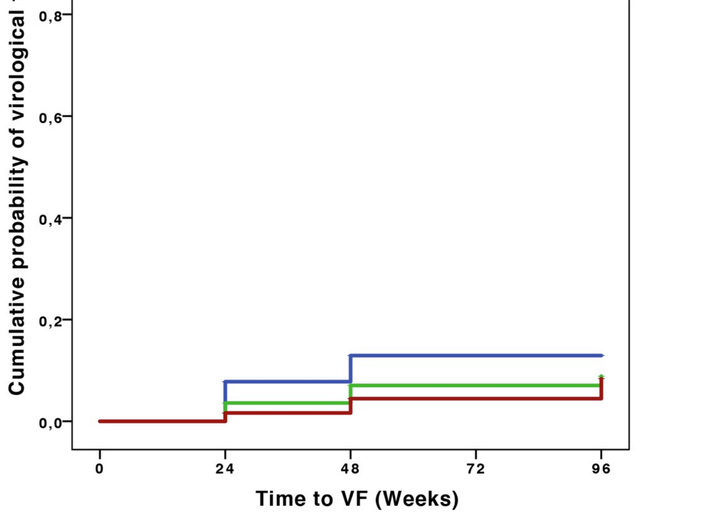
HIV-1 RNA was <50 cps/mL in 1,042/1,368 patients (76.2%) at 24 weeks, in 1,359/1,763 patients (77.1%) at 48 weeks and in 1,159/1,542 patients (75.2%) at 96 weeks.

Fig.6 Estimated probability of VF according to GSS



The estimated probability of virological failure at 48 weeks was 5.1% (95% CI 4-6.2) among patients with GSS=2, 6.8% (5.1-8.5) among patients with GSS 1-1.99 and 26.3% (17.6-35) among those with GSS <1 (log Rank p<0.001).

Fig.7 Estimated probability of VF according to cumulative GSS



According to cumulative GSS (CGSS), the estimated probability of VF at 48 weeks was 4.5% (95% CI 3.4-5.6) among patients with CGSS =2, 7.2% (5.7-8.7) among patients with CGSS 1-1.99 and 13% (9-17) among those with CGSS <1 (log Rank p=ns).

LIMITATIONS

- ✓ Retrospective design
- ✓ Lack of viremia copy-years in half of population

CONCLUSIONS

Higher viral load at switch and the presence of less than 1 fully active drug strongly influence virological efficacy of 2-drug regimens in treatment experienced HIV-1 infected patients. The most recent GSS seems more predictive of the outcome as compared to the cumulative GSS of these switch regimens.

ARCA was supported by unconditional educational grants from: **ViiV Healthcare, Gilead Sciences, Janssen, Hologic, MSD, Bristol-Myers Squibb, Siemens Healthineers**