HIV Multi-Drug Resistance is still a Clinical Relevant Issue Despite its Dramatic Drop over the Years

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Background

Despite modern antiretroviral regimens revolutionizing the treatment of HIV, drug-resistance remains a concern for the long-term success of antiretroviral-treatment (ART) both in low- (but also high-) income countries.

Aim

…Thus, we evaluated the prevalence of resistance among ART-experienced HIV-1 infected patients over the past 2 decades.

Methods

- We analyzed **12839** plasma genotypic resistance tests (GRTs) from **6147** ART-experienced HIV-1 infected patients followed in several clinical centers from Central and North Italy from 1999 to 2016.

- All plasma genotypic resistance tests (GRTs) performed from protease (PR), reverse transcriptase (RT) and integrase (IN, if available) were analyzed.

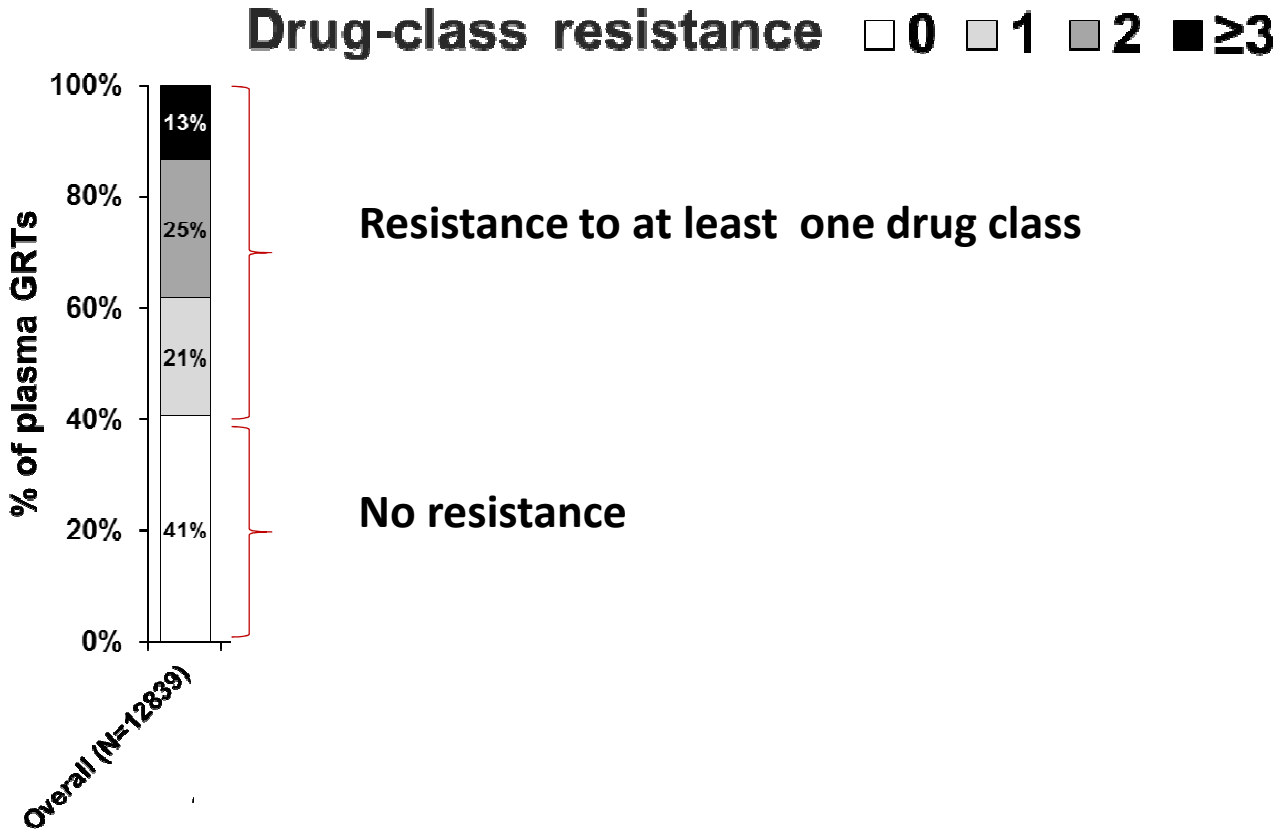
- Resistance to 1, 2 and ≥3 classes among nucleoside reverse-transcriptase inhibitors (NRTIs), non-NRTI (NNRTIs), protease (PIs) or integrase (INIs) inhibitors was evaluated over time by considering the major mutations paneled in the IAS-Stanford lists 2017.

- Viro-immunological parameters have been assessed in parallel with resistance.

- In patients having viremia follow-up available after the latest GRT with the highest resistance class level, subsequent virological suppression (VS, viremia <50 copies/mL) was evaluated by using Kaplan-Meier estimates.

Overall, 59% of plasma GRTs showed resistance.

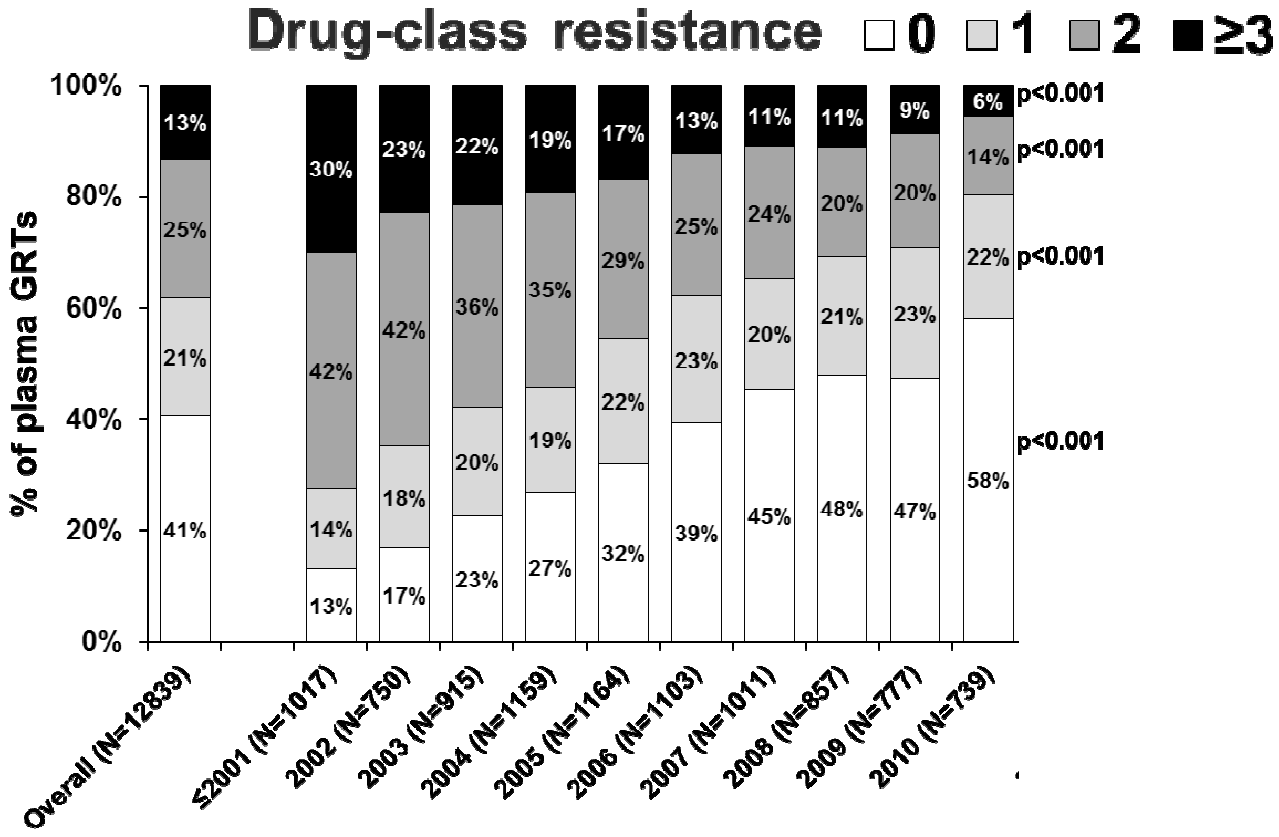
Prevalence of resistance to any drug-class among ART-experienced HIV-1 infected patients with virologic failure.



Analysis performed on 14497 sequences of protease/reverse transcriptase or integrase, from 12839 GRTs performed for routine clinical practice in ART-experienced HIV-1 infected patients (N=6147). P-values were calculated by Chi-squared test for trend; statistically significant tests ($p<0.05$) are indicated in boldface. Sequences performed from 1999 to 2001 were grouped.

Resistance at failure significantly decreased from 1999 to 2010 in conjunction with a remarkable increase of failures without resistance.

Prevalence of resistance to any drug-class among ART-experienced HIV-1 infected patients with virologic failure over the years.



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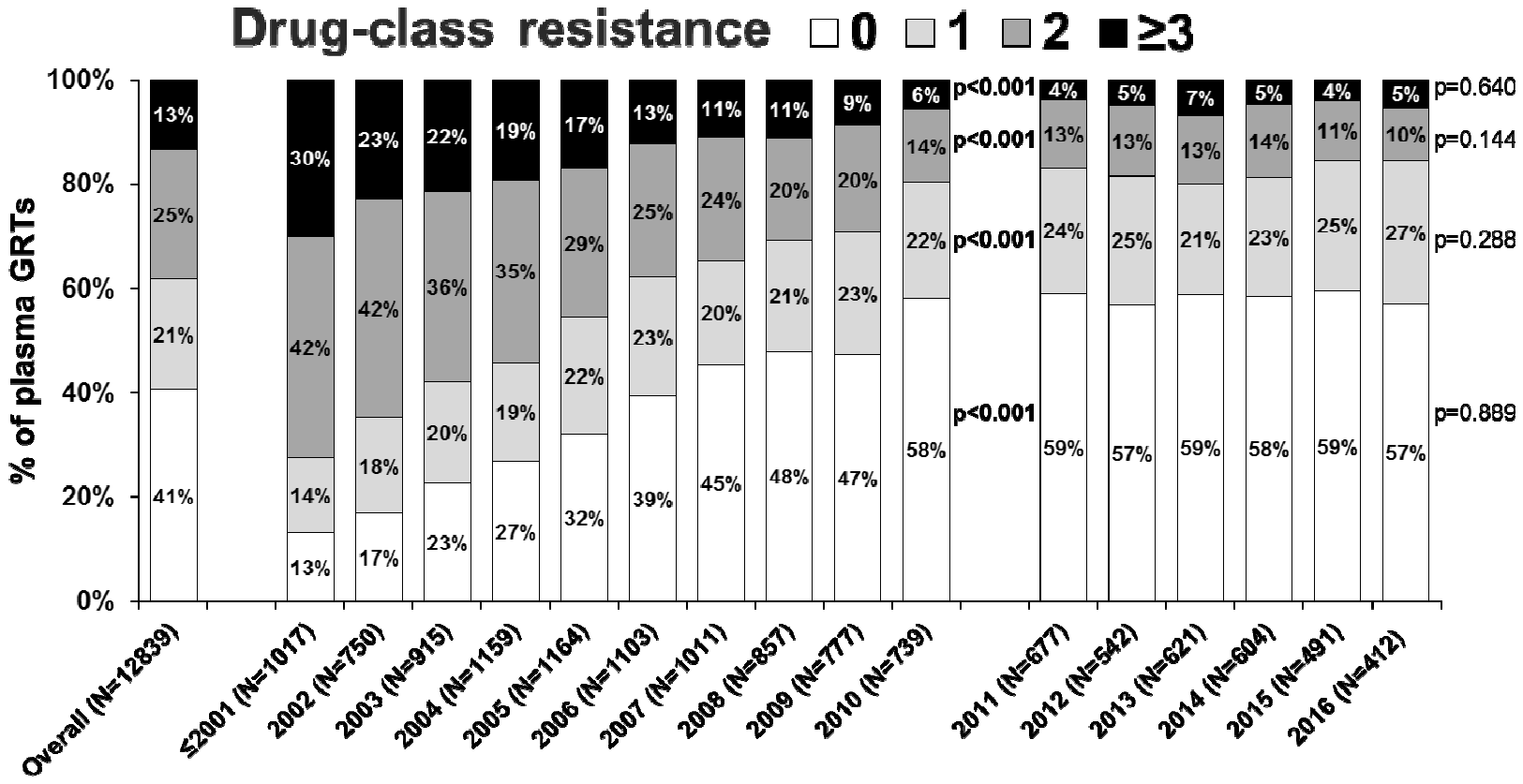
Beyond 2010, prevalence of resistance remained stable from 2011 to 2016.

Prevalence of resistance to any drug-class among ART-experienced HIV-1 infected patients with virologic failure over the years.



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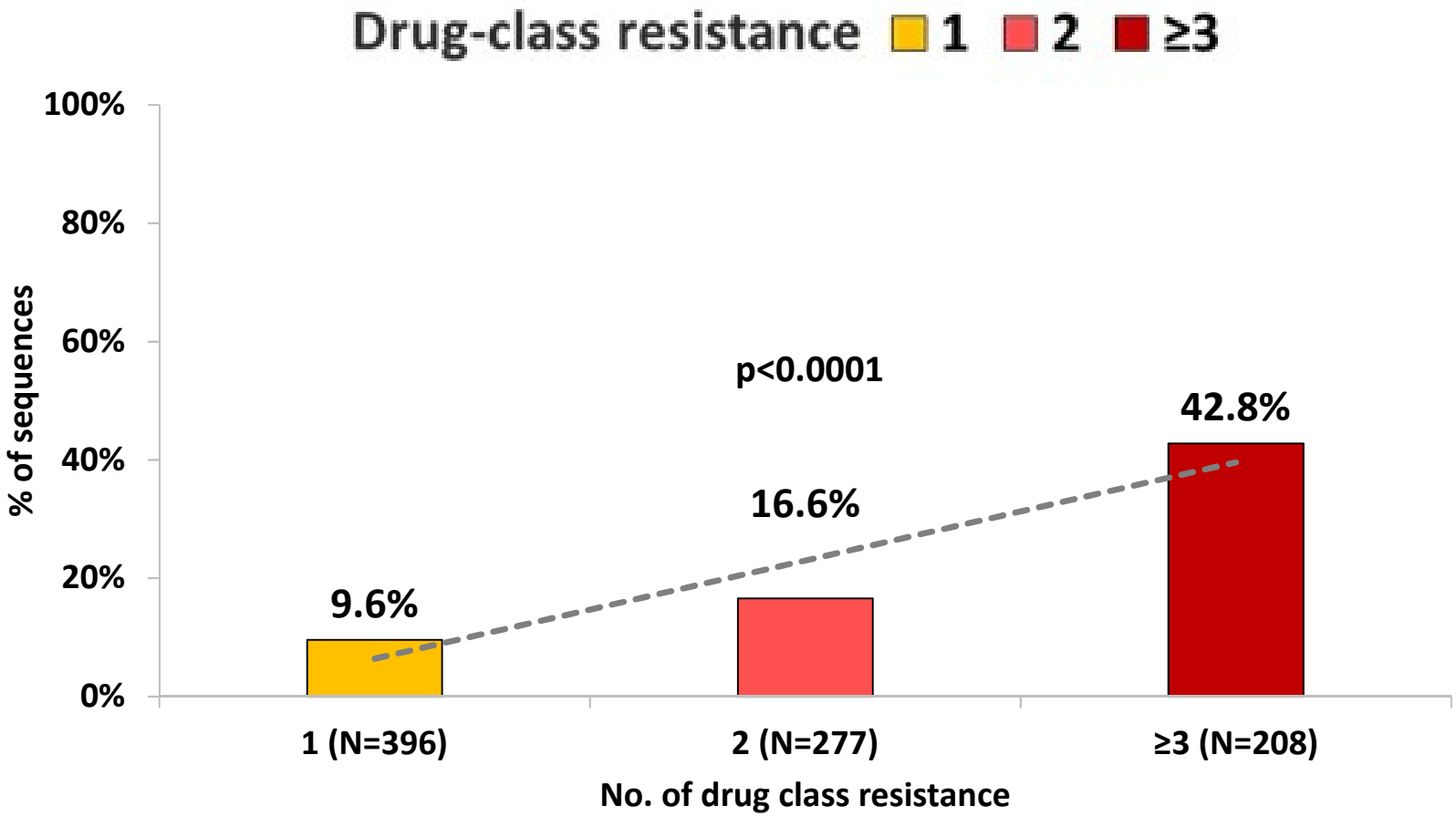
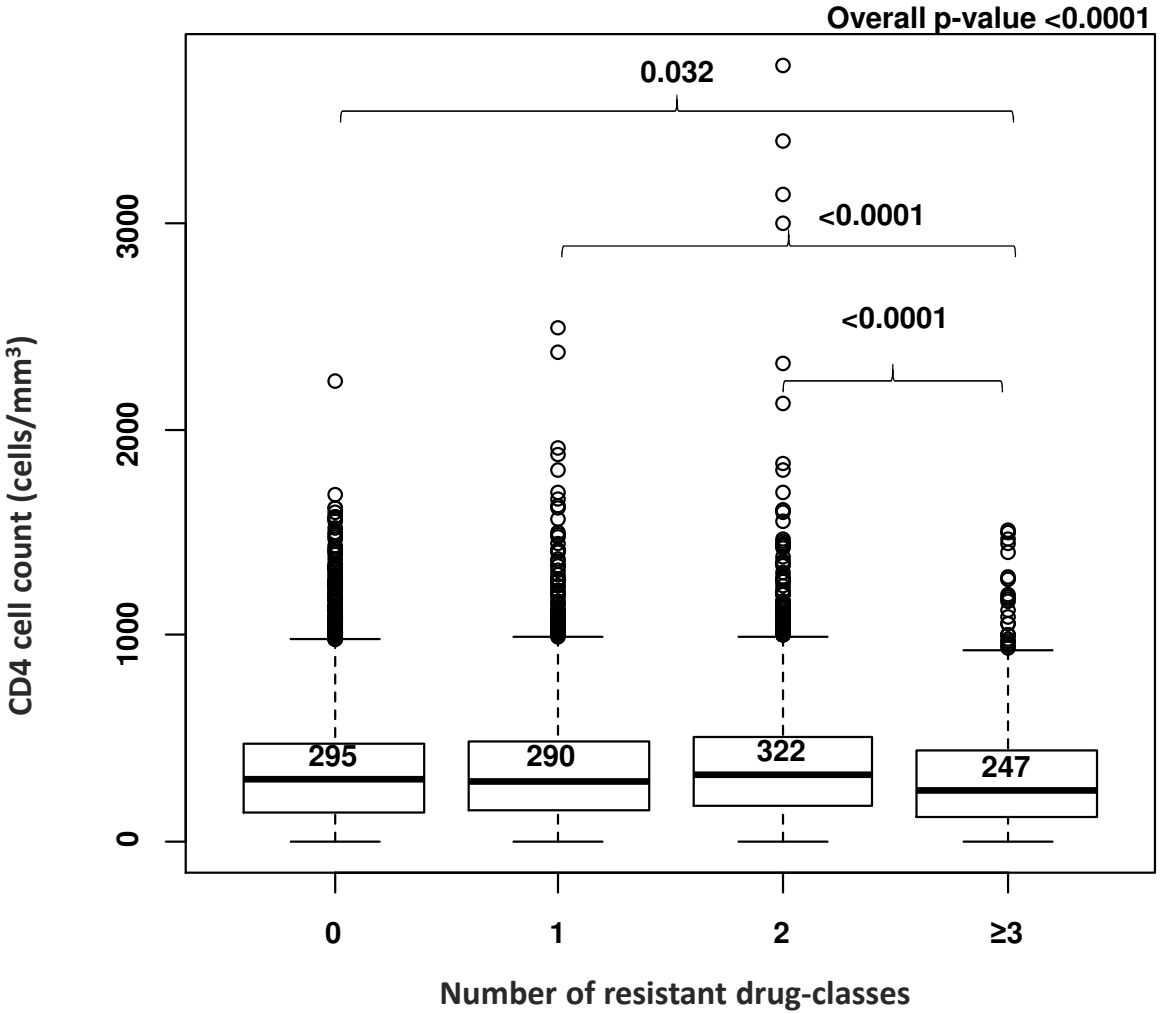
After 2008, INI-resistance contributed to resistance mostly in those GRTs with ≥3 class resistance.



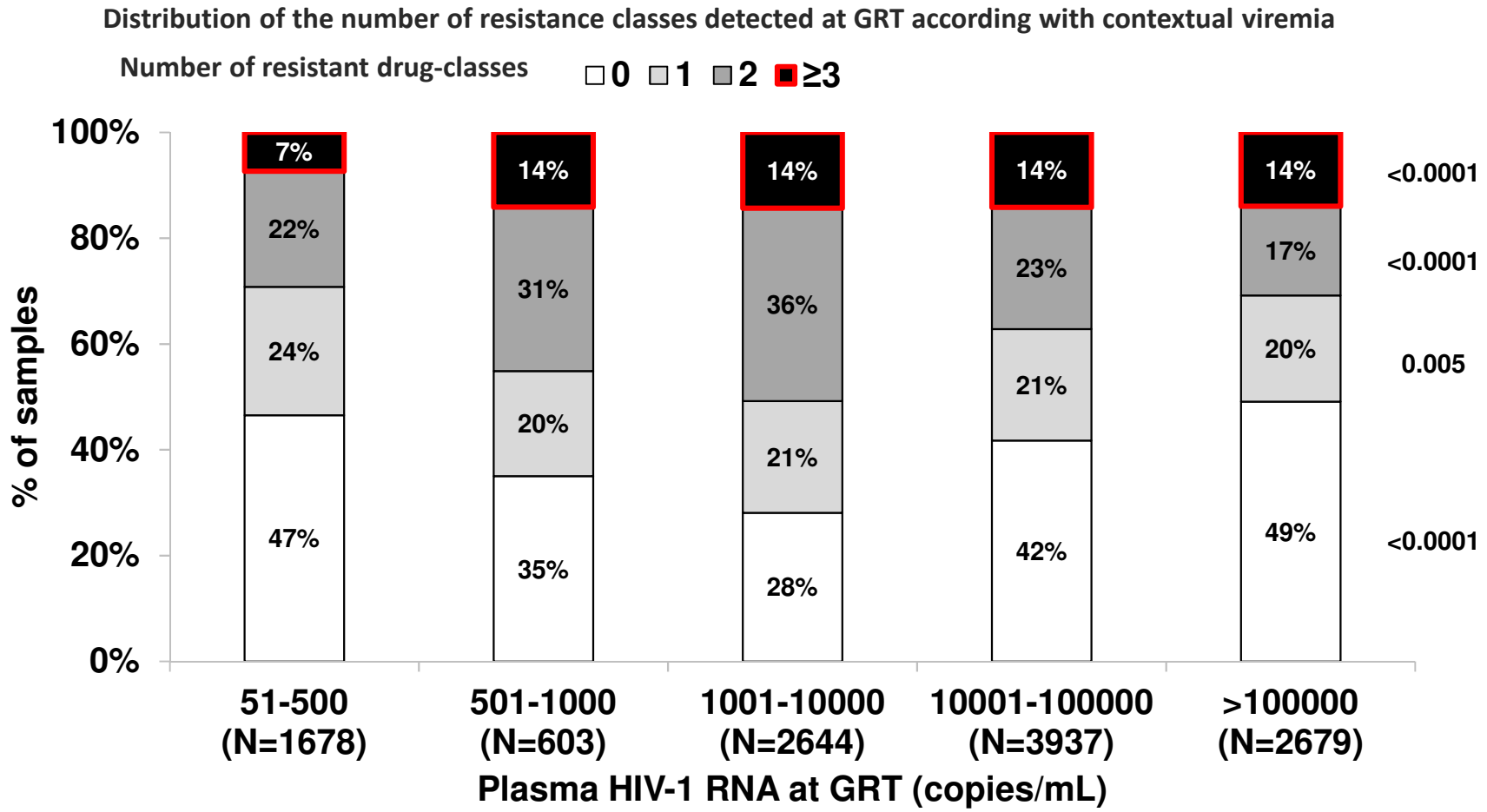
Analysis performed on 1658 protease/reverse transcriptase/integrase sequences from plasma samples of drug-experienced HIV-1 infected patients (1188). 777/1658 sequences had no drug-class resistance. P-values by Chi-squared test for trend. INI: integrase inhibitor.

Samples carrying ≥3 classes resistance showed the lowest CD4-count (cells/µl).



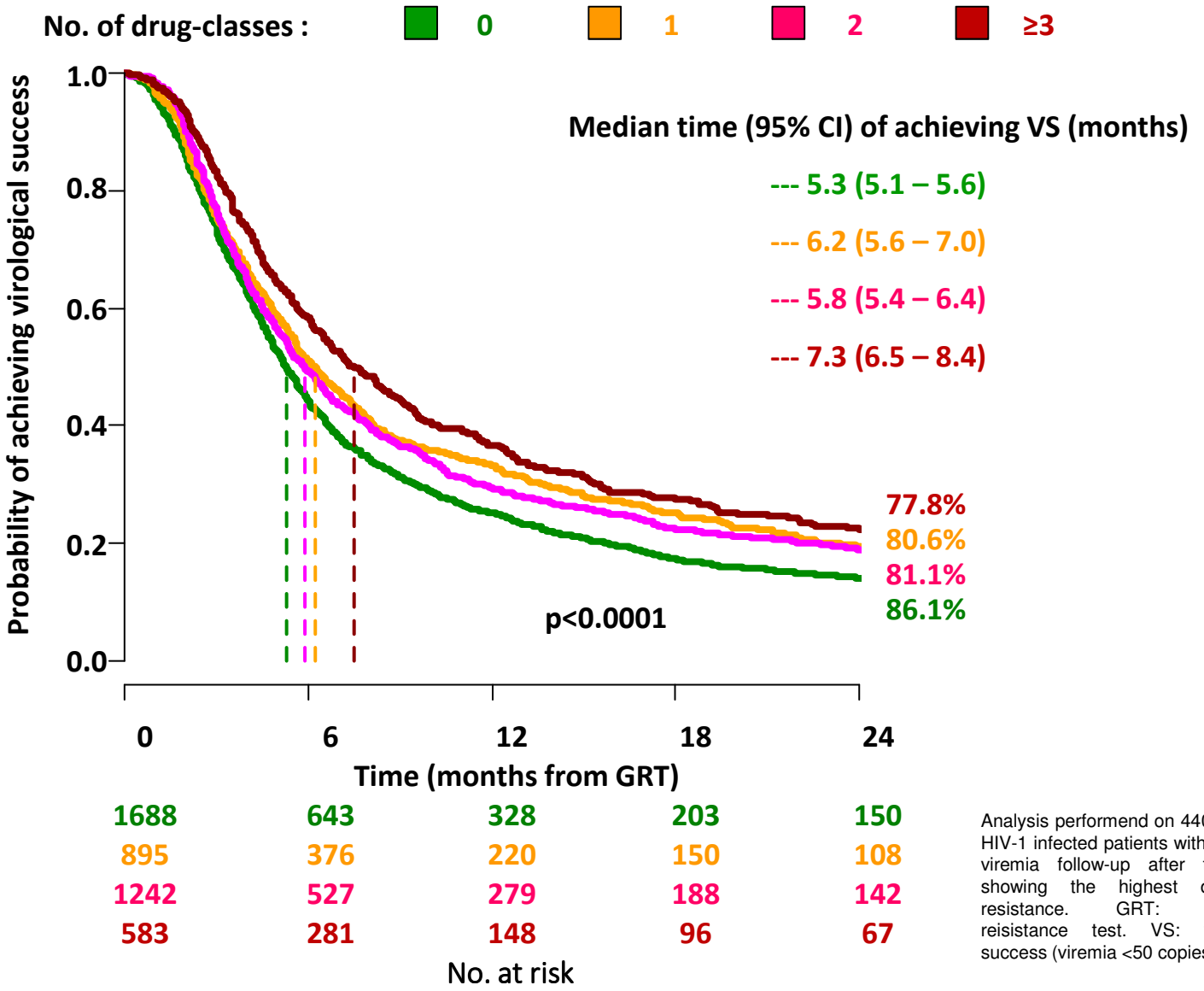
Analysis performend on 12032 sequences of drug-experienced HIV-1 infected patients from protease, reverse transcriptase or integrase with available CD4 cell count at GRT. P-values by Kruskal-Wallis (overall) and Mann-Whitney (paired test with Benjamini-Hockber correctioin) tests. GRT: genotypic resistance test.

The proportion of samples carrying ≥3 classes resistance was 7% at viremia levels <500 copies/mL and it significantly increased settling at 14% at higher viremia levels.



Analysis performend on 11541 sequences of drug-experienced HIV-1 infected patients from protease, reverse transcriptase or integrase with available viremia at GRT. P-values by Chi-squared test for trend. GRT: genotypic resistance test.

After the latest GRT with the highest resistance class levels, the probability of achieving virological success was significantly lower in patients having 3 drug-classes resistance compared to the others.



Analysis performend on 4408 treated HIV-1 infected patients with available viremia follow-up after the GRT showing the highest drug-class resistance. GRT: genotypic reisistance test. VS: virological success (viremia <50 copies/mL).

Conclusions

- A dramatic drop of drug-resistance has been achieved over time in high-income countries, confirming a good clinical-practice and ensuring a high number of treatment options for failing patients.

- However, in the last 5 years drug-resistance is stable!

- Resistance to ≥3 classes remains a recurrent concern deserving clinical attention.

  Its management requires an appropriate diagnostic and therapeutic approach.

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