**BACKGROUND**

- Drug resistance testing for individuals infected with HIV-1 is a key component of the management of antiretroviral (ARV) therapy.
- We examined phenotypic drug resistance patterns in protease- (PI), nucleoside-reverse-transcriptase- (NRTI), and non-nucleoside-reverse-transcriptase-inhibitors (NNRTI) as well as 1-, 2-, and 3-class resistance over time by surveying Monogram Biosciences commercial database.

**METHODS**

- We examined fully de-identified samples submitted for routine phenotypic and genotypic patient testing that show phenotypic resistance to at least one drug within PIs, NRTIs, and NNRTIs as measured by fold-change of IC50 (FC) - lower cutoff (CO).
- A total of 68587 resistant samples collected from 2003 through 2010 were grouped into 3-classes since 2007, from 2003 to 2007 grouped into 2-classes.
- We studied the temporal trends of % phenotypic drug resistance in each drug-class.
- We examined phenotypic drug resistance for individuals infected with HIV-1 and NNRTI mutations L100I, K103N and P225H.
- We evaluated the significance of trends.
- Each dot represents the percentage of samples that have the specified amino acid at that position, compared to the sum total of all samples that exhibited reduced susceptibility to the drug class of interest.

**RESULTS**

- Marked decrease in the fraction of drug resistant HIV-1 strains with reduced susceptibility to all 3 drug classes since 2007, from 29% to 11% (p=0.001).
- Steady increase in reduced susceptibility to a single drug class, from 31% to 54% (p=0.0015).
- Double-class resistance remained relatively stable (40% to 35%).
- Decrease in the percentage of resistant viruses that exhibited reduced susceptibility to PIs since 2007, from 49% in 2007 to 26% in 2010 (p=0.02).
- Reduced susceptibility to NRTI and NNRTI remained relatively stable: NNRTI decreased from 70% to 61% and NRTI decreased from 77% to 70%.
- The frequency of the PI RAMs associated with first-generation PIs (e.g. L10I, D30N, M46I/L, G48V, V82, V82M) declined, whereas the frequency of mutations V11I, V32I, L54I, T74R, and T74F and N88S is increasing.
- Major Reverse-Transcriptase (RT) RAMs are declining over time, except for NRTI mutations K65R and Y115F and NNRTI mutations L10I, K201I and P233H.

**CONCLUSIONS**

- These observations suggest that the downward trend in 3-class drug resistance since 2007 is driven by the decrease in the fraction of resistant viruses with reduced susceptibility to the PI class.
- These trends also highlight a decrease in the number of patients with multi-drug resistant virus: a group for whom very little treatment options were available until 2006.
- The improved efficacy of the standard of care and the continual availability of antiretroviral treatments utilizing novel anti-HIV targets or with favorable cross-resistance profiles and evolving prescription patterns of PI, NNRTI, and NRTIs may have relevance to the decreasing prevalence of multi-drug resistance in this clinical database.
- These results may have important implications for antiretroviral drug selection, clinical trial design as well as future drug discovery and development.

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