Risk of extensive triple-class virologic failure of the three original antiretroviral drug classes among people followed from therapy initiation with NNRTI or ritonavir-boosted Protease Inhibitor regimens

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METHODS

COHERE (Collaboration of Observational HIV Epidemiological Research Europe) is a collaboration of most HIV observational cohorts in Europe. The 28 cohorts participating in the PLATO II project submitted data in a standardized format to one of two regional co-ordinating centres, where error checks were performed and duplicate records removed.

The analysis was restricted to patients aged 16 or over, who started ART from 1998 onwards with an initial regimen of 2 NRTIs and either an NNRTI or a PI or a PI+r.

In a large European multi-cohort collaboration, we studied the rate of triple class virologic failure (TCVF) in patients who started ART with 2 NRTIs and either an NNRTI or a PI.

We also specifically focused on TCVF in a subgroup of patients who started ART-containing (as first PI) after having virologically failed a first-line NNRTI regimen.

RESULTS

Analysis of patients starting a PI-r as second line ART

- A subgroup of 2042 patients were included in the analysis of patients starting a PI-r as second line ART (TABLE 2).
- In these patients, the median (IQR) time from starting ART to failure of the NNRTI was 0.9 (0.5-1.5) years and the median (IQR) time from failing an NNRTI to starting a PI-r was 0.8 (0.3-3.2) years.
- Of a total of 2945 person-years of follow-up from failure of the NNRTI to initiation of the PI-r, 353 person-years (12.0%) were spent on ART, 1028 person-years (65.5%) were spent on ART with viral load >500copies/ml, and 664 person-years (22.5%) were spent on ART with viral load ≤500 copies/ml.
- 575 (28.2%) patients developed TCVF, in all cases on the date of virologic failure of a PI-r. The Kaplan-Meier estimates of the cumulative proportions of patients who had developed TCVF by 5 and 9 years from the start of ART were 3.4% (95% CI: 3.1%-3.6%) and 8.6% (95% CI: 7.5%-9.8%).
- Hazard ratios for factors associated with the risk of TCVF after the start of ART are shown in FIGURE 2. Lower pre-ART CD4 count and higher pre-ART viral load were associated with an increased risk of TCVF. A lower risk of TCVF was observed in homosexual men than in the other combined gender/risk groups, and older age at the time of starting ART was found to be associated with a lower risk of TCVF.
- There was no significant difference in the risk of TCVF according to the drug class used in the initial ART regimen (adjusted HR for PI-r compared with NNRTI: 0.88, 95% CI: 0.75-1.03, p=0.11).

COMMENTS

- The rate of development of TCVF was very similar according to whether ART was started with NNRTI-containing regimens or PI-containing regimens.
- For those patients who experienced first-line virologic failure, the time to the start of a regimen containing the third class was surprisingly long at a median of 0.8 years.
- Factors in our analysis associated with slower development of TCVF after starting ART included being in the homosexual male risk group and older age, in addition to lower pre-ART viral load and higher pre-ART CD4 count.
- In those starting a PI-r as second-line ART, homosexual men also experienced a slower rate of TCVF, as did those with lower viral load and higher CD4 count at the time of starting the PI-r, and those who spent less than 3 months on ART with viral load >500 copies/ml had a lower risk of TCVF.

SUMMARY AND CONCLUSIONS

- The rate of virologic failure of the three original drug classes is low, but not negligible, and does not appear to diminish from time with start of ART. If this trend continues many patients are likely to eventually need newer drugs in order to maintain viral suppression.
- The rate of triple class failure from start of a PI-r after NNRTI failure (46% with failure by 5 years overall, 55% in the heterosexual risk groups) provides a comparator for studies of response to second-line regimens in developing countries.