CD4 count and viral load specific rates of AIDS, non-AIDS and deaths according to current antiretroviral use

Mocroft, A ; Phillips, A ; Gatell, J ; Horban, A ; Ledergerber, B ; Zilmer, K ; Jevtovic, D ; Maltez, F ; Kirk, O ; Lundgren, J

Abstract: Background: CD4 and viral loads are used in clinical trials as surrogate endpoints for assessing efficacy of newly available antiretrovirals. If antiretrovirals act through other pathways or negatively affect the risk of disease this would not be identified prior to licensing. The aims of this study were to investigate the CD4 and viral load specific rates of fatal and non-fatal AIDS and non-AIDS events according to current antiretrovirals. Methods: Poisson regression was used to compare overall events (fatal or non-fatal AIDS, non-AIDS or death), AIDS events (fatal and non-fatal) or non-AIDS events (fatal or non-fatal) for specific nucleoside pairs and third drugs used with>1000 person-years of follow-up (PYFU) after January 1st 2001. Results: 9801 patients were included. The median baseline date was January 2004 (interquartile range [IQR] January 2001-February 2007), age was 40.4 (IQR 34.6-47.3 years), and time since starting cART was 3.3 (IQR 0.9-5.1 years). At baseline, the median nadir CD4 was 162 (IQR 71-257/mm3), baseline CD4 was 390 (IQR 249-571/mm3), viral load was 1.9 (IQR 1.7-3.3 log10copies/ml) and 2961 (30.2%) had a prior AIDS diagnosis and 6.4 years) prior to baseline. During 42372.5 PYFU, 1203 (437 AIDS and 766 non-AIDS) events occurred. The overall event rate was 2.8 per 100 PYFU (95% confidence interval [CI] 2.7-3.0), of AIDS events was 1.0 (95% CI 0.9-1.1) and of non-AIDS events was 1.8 (95% CI 1.7-1.9). Of the AIDS events, 53 (12.1%)were fatal as were 239 (31.2%) of the non-AIDS events. After adjustment, there was weak evidence of a difference in the overall events rates between nucleoside pairs (global p-value=0.084), and third drugs (global p-value=0.031). Compared to zidovudine/lamivudine, patients taking abacavir/lamivudine (adjusted incidence rate ratio [aIRR] 1.22; 95% CI 0.99-1.49) and abacavir plus one other nucleoside (aIRR 1.51; 95% CI 1.14-2.02) had an increased incidence of overall events. Comparing the third drugs, those taking unboosted atazanavir had an increased incidence of overall events compared to those taking efavirenz (aIRR 1.46; 95% CI 1.09-1.95)(Figure). Conclusions: There was little evidence of substantial differences between antiretrovirals in the incidence of fatal and non-fatal AIDS and non-AIDS events for a given CD4 or viral load, suggesting there are unlikely to be major unidentified adverse effects of specific antiretrovirals, although confounding by indication cannot be ruled out.

DOI: https://doi.org/10.7448/IAS.15.6.18191

Originally published at:
Mocroft, A; Phillips, A; Gatell, J; Horban, A; Ledergerber, B; Zilmer, K; Jevtovic, D; Maltez, F; Kirk, O; Lundgren, J (2012). CD4 count and viral load specific rates of AIDS, non-AIDS and deaths according to current antiretroviral use. Journal of the International Aids Society, 15(6):18191.
DOI: https://doi.org/10.7448/IAS.15.6.18191

Abstracts of the Eleventh International Congress on Drug Therapy in HIV Infection
Mocroft A et al. *Journal of the International AIDS Society* 2012, **15(Suppl 4)**:18191
http://www.jiasociety.org/index.php/jias/article/view/18191 | http://dx.doi.org/10.7448/IAS.15.6.18191

JIAS Journal of the International AIDS Society

Oral Abstract – O412

CD4 count and viral load specific rates of AIDS, non-AIDS and deaths according to current antiretroviral use

Mocroft, A[1]; Phillips, A[1]; Gatell, J[2]; Horban, A[3]; Ledergerber, B[4]; Zilmer, K[5]; Jevtovic, D[6]; Maltez, F[7]; Kirk, O[8] and Lundgren, J[8]

[1]University College London, London, UK. [2]Hospital Clinic i Provincial, Barcelona, Spain. [3]Terapii AIDS, Warsaw, Poland. [4]University Hospital Zurich, Zurich, Switzerland. [5]West-Tallinn Central Hospital, Tallinn, Estonia. [6]Institute for Infectious and Tropical Diseases, Belgrade, Serbia and Montenegro. [7]Hospital Curry Cabral, Lisbon, Portugal. [8]University of Copenhagen, Copenhagen, Denmark.

Background

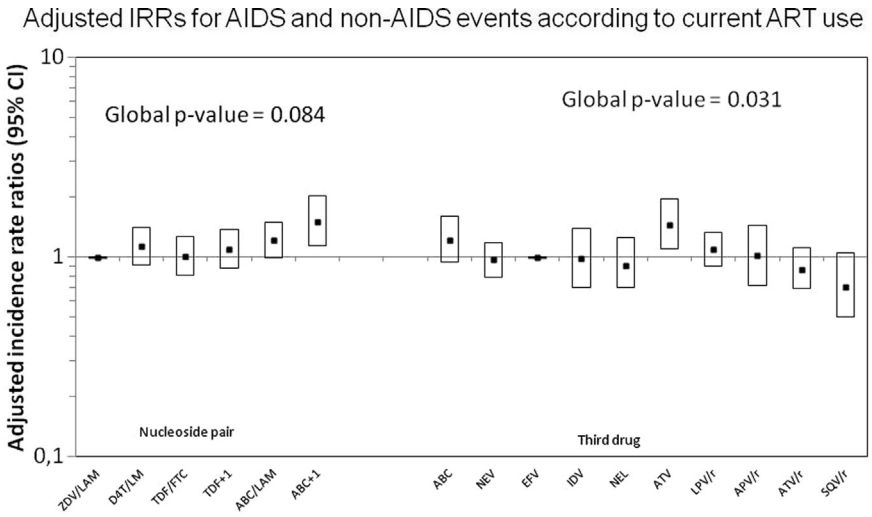
CD4 and viral loads are used in clinical trials as surrogate endpoints for assessing efficacy of newly available antiretrovirals. If antiretrovirals act through other pathways or negatively affect the risk of disease this would not be identified prior to licensing. The aims of this study were to investigate the CD4 and viral load specific rates of fatal and non-fatal AIDS and non-AIDS events according to current antiretrovirals.

Methods

Poisson regression was used to compare overall events (fatal or non-fatal AIDS, non-AIDS or death), AIDS events (fatal and non-fatal) or non-AIDS events (fatal or non-fatal) for specific nucleoside pairs and third drugs used with >1000 person-years of follow-up (PYFU) after January 1st 2001.

Results

9801 patients were included. The median baseline date was January 2004 (interquartile range [IQR] January 2001–February 2007), age was 40.4 (IQR 34.6–47.3 years), and time since starting cART was 3.3 (IQR 0.9–5.1 years). At baseline, the median nadir CD4 was 162 (IQR 71–257/mm^3), baseline CD4 was 390 (IQR 249–571/mm^3), viral load was 1.9 (IQR 1.7–3.3 $\log_{10}$copies/ml) and 2961 (30.2%) had a prior AIDS diagnosis and 6.4 years) prior to baseline. During 42372.5 PYFU, 1203 (437 AIDS and 766 non-AIDS) events occurred. The overall event rate was 2.8 per 100 PYFU (95% confidence interval [CI] 2.7–3.0), of AIDS events was 1.0 (95% CI 0.9–1.1) and of non-AIDS events was 1.8 (95% CI 1.7–1.9). Of the AIDS events, 53 (12.1%)were fatal as were 239 (31.2%) of the non-AIDS events. After adjustment, there was weak evidence of a difference in the overall events rates between nucleoside pairs



Multivariate models also adjusted for gender, ethnic origin, risk group, region, prior AIDS, prior non-AIDS, age and CD4 nadir, time since starting third drug, plus year of follow-up, hepatitis B/C status, development of CKD, anaemia, diabetes, hypertension and smoking status, current CD4 and viral load as time-updated variables

Published 11 November 2012

(global p-value = 0.084), and third drugs (global p-value = 0.031). Compared to zidovudine/lamivudine, patients taking abacavir/lamivudine (adjusted incidence rate ratio [aIRR] 1.22; 95% CI 0.99–1.49) and abacavir plus one other nucleoside (aIRR 1.51; 95% CI 1.14–2.02) had an increased incidence of overall events. Comparing the third drugs, those taking unboosted atazanavir had an increased incidence of overall events compared to those taking efavirenz (aIRR 1.46; 95% CI 1.09–1.95)(Figure).

Conclusions

There was little evidence of substantial differences between antiretrovirals in the incidence of fatal and non-fatal AIDS and non-AIDS events for a given CD4 or viral load, suggesting there are unlikely to be major unidentified adverse effects of specific antiretrovirals, although confounding by indication cannot be ruled out.