BACKGROUND
In the years prior to 1997, drug approval for antiretroviral therapy (ART) relied on trials according to latest HIV-RNA levels and specific drugs effect of a drug regimen on the immunologic/virologic, surrogate markers, i.e. CD4 count/ HIV-RNA levels, strongly correlated to the risk of clinical progression to AIDS or death. As a result, the FDA decided in 1997 that it was sufficient for clinical trials to show that a new drug resulted in sustained suppression of plasma HIV-RNA levels and to rises in peripheral CD4 lymphocyte count. Since 1997, the HIV-1 community, industry and regulatory authorities have relied completely on the general assumption that the relationship between the HIV RNA & CD4 count levels and the risk of clinical disease continues to hold true for newer antiretroviral drugs (released after 1997), and that there is no additional effect of such drugs leading to a higher or lower AIDS death risk for given HIV RNA/CD4 count levels compared to others.

HYPOTHESIS
The risk of clinical disease progression to AIDS or death according to specific CD4 counts or HIV-RNA levels is similar in new ARTs.

OBJECTIVE
To determine and compare rate ratios of AIDS and death at given, latest CD4 count and HIV-RNA levels, according to various nucleoside pairs and specific third drugs.

METHODS
The EuroSIDA study is a prospective European cohort study initiated in 1994 of 9,802 HIV-1 infected patients followed in 72 clinics from 26 European countries. Patients included are those consecutively referred to 72 clinics from 26 European countries. Patients included are those consecutively referred to 72 clinics from 26 European countries.

RESULTS
A total of 3,246 patients contributed observation time to the analysis, representing 92% of all the patients that had started cART; 6% were taking regimens not fixed. There was a total of 45,269 person-years of follow-up. The median date of starting cART was 1997, and 4,735 patients (25%) had used nucleoside mono- or dual therapy before starting cART. A total of 4401 events of AIDS or death were observed, of which 457 were deaths.

CONCLUSION
The crude incidence rates of AIDS/death for given, latest CD4 count strata (figure 1) and HIV-RNA levels and other factors listed in figure 3.

HIV-RNA and CD4 levels are individual patients receiving newer drugs have the same meaning in terms of AIDS/death risk, regardless of the specific antiretroviral regimen. Our results support the assumption that these markers have the same prognostic significance, regardless of the antiretroviral drugs being used.

Sensiative analyses
The results of the main analysis were consistent with the results of the different sensitivity analyses performed, e.g. when restricting analyses to:
- person-time in which the third drug had been used for at least 6 months
- person-months when CD4 and HIV-RNA were known within at least the past 3 years
- person-time with a CD4 < 200 /mm3 or above the defined on the third drug
- person-time when the specific third drug had been started when HIV RNA was <500 copies/mL
- persons with CD4 counts < 200 /mm3 at ART initiation and a latest CD4 count > 350 /mm3

The crude incidence rates of AIDS/death for given, latest CD4 count strata (figure 1) and latest HIV-RNA levels and other factors listed in figure 3.

Please note that the figures cannot be used to compare efficacy of drug regimens.