



*11<sup>th</sup> International Congress on Drug Therapy in HIV Infection*

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

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The EuroSIDA study in EuroCoord

## Background

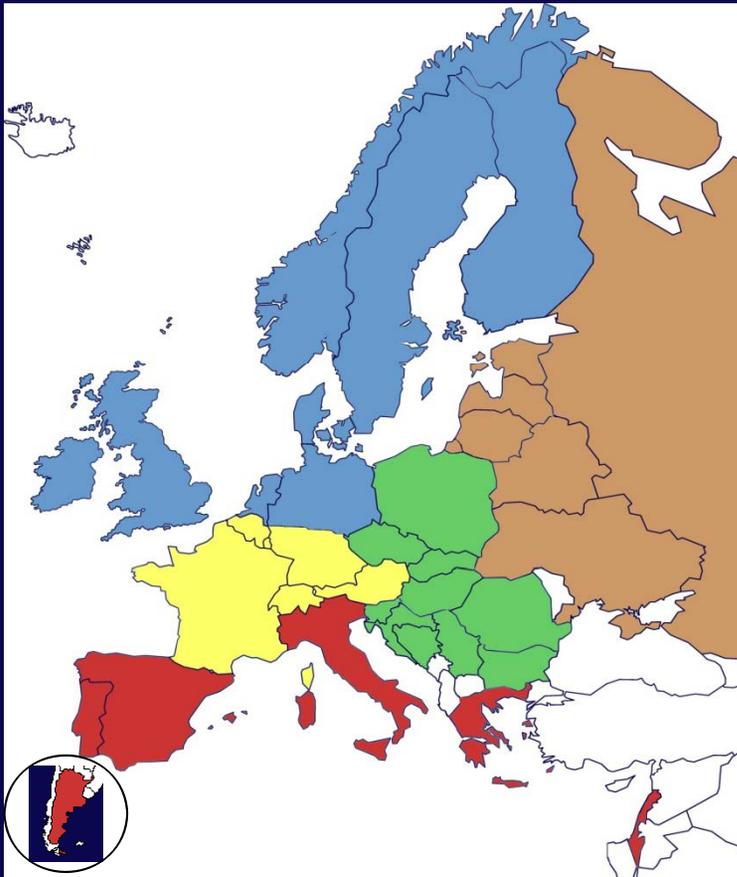
- CD4 and viral loads are used in clinical trials as surrogate endpoints for assessing efficacy of newly available antiretrovirals (ARVs)
- ARVs may also act through other pathways or negatively affect the risk of disease
- This would not be identified prior to licensing
- Risk of AIDS/death similar regardless of cART regimen being taken (older ARVs)<sup>1</sup>

# Objectives

- To investigate the CD<sub>4</sub> and viral load specific rates
  - of fatal and non-fatal AIDS and non-AIDS events
  - according to current ARVs

## Methods - EuroSIDA

EuroSIDA is a large prospective cohort with **16597** patients from 33 European countries, Israel and Argentina. Regularly collecting:



- HIV transmission risk group
- CD4 counts, HIV viral loads
- All treatment start/stop dates
- Clinical AIDS events
- Non-AIDS events (since 2001)
- Deaths and causes of death

EuroSIDA in EuroCoord

## Methods (patients)

- Patients starting an eligible regimen and with some CD<sub>4</sub> count and pVL measurements available
- Baseline: first time after 1 January 2001 when patients were on an eligible regimen
- Only regimens with >1000 person-years of follow-up (PYFU) were included

# Methods (regimens)

## 2 NRTIs together with a 3<sup>rd</sup> ARV

2 NRTIs	PYFU
ZDV/3TC	14607
D4T/3TC	4673
TDF/NRTI (excl FTC)	5985
TDF/FTC	9301
ABC/3TC	6973
ABC/NRTI (excl 3TC)	1580

3rd drug	PYFU
ABC	3064
NVP	7759
EFV	12256
IDV	1429
NFV	2090
ATV	1592
LPV/rtv	7054
APV/rtv	1176
ATV/rtv	4430
SQV/rtv	1967

## Methods (events)

- For specific regimens used, Poisson regression was used to compare overall events:
  - AIDS, non-AIDS events or death
  - AIDS events (fatal and non-fatal)
  - non-AIDS events (fatal or non-fatal)
    - malignancies, hepatic encephalopathy (grade 3-4), pancreatitis, cardiovascular events and end stage renal disease<sup>1</sup>
- Multiple events per person but recurrences of the same event excluded

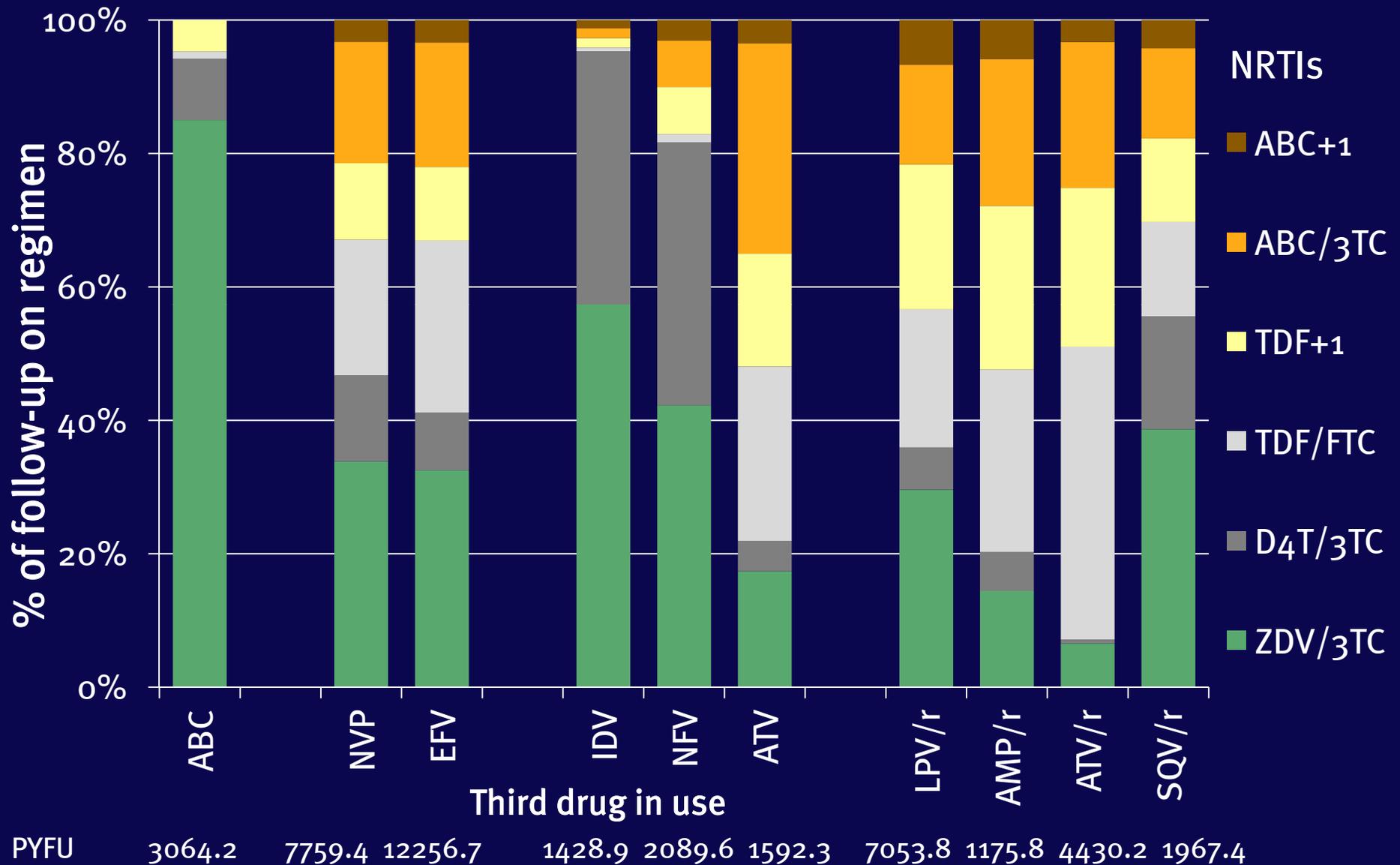
## Patient characteristics at baseline (1)

	<b>N</b>	<b>%</b>	<b>PYFU</b>
Total	9801	100	42373
Race (Caucasian)	8575	87.5	36949
Race (non-Caucasian)	1226	12.5	5424
Gender (Female)	2646	27.0	10852
Gender (Male)	7155	73.0	31520
Risk (MSM)	3836	39.1	17611
(IDU)	2171	22.2	8524
(HET)	3049	31.1	13108
(OTH)	745	7.6	3130
Region (South)	2563	26.2	11330
(West)	2169	22.1	9500
(North)	2295	23.4	11430
(East)	2364	24.1	8402
(Argentina)	410	4.2	1711
Prior AIDS	2961	30.2	12468
Prior non-AIDS	342	3.5	1337

## Patient characteristics at baseline (2)

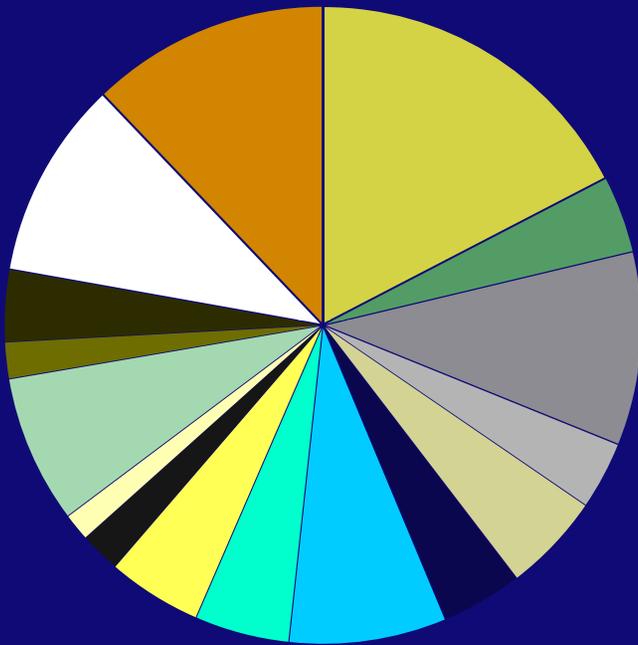
	Median	IQR
Baseline date	January 2004	January 2001 – February 2007
Age (years)	40.4	34.6-47.3
Nadir CD4 cell count (/mm <sup>3</sup> )	162	61-257
CD4 cell count (/mm <sup>3</sup> )	390	249-571
pVL (log <sub>10</sub> copies/ml)	1.9	1.7-3.3
Time since starting cART (years)	3.3	0.9-5.1

# cART regimens included during 42373 PYFU



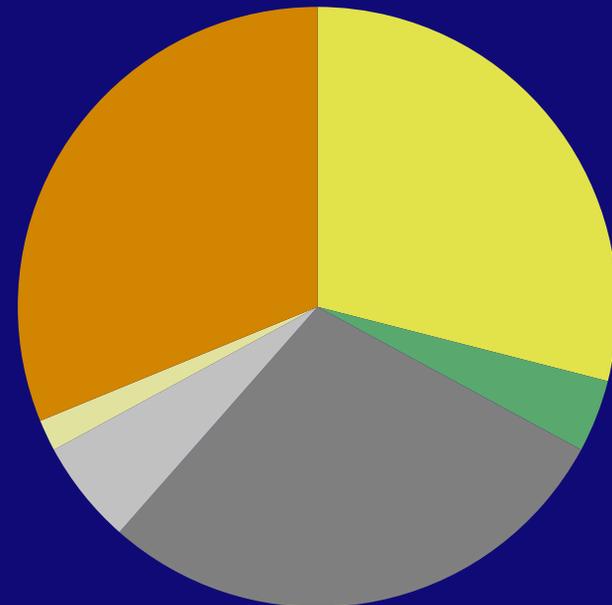
# Clinical events during follow-up

**AIDS events during follow-up**  
(n=437)



- CANO
- PCP
- MCP
- KS
- OTH
- WAS
- MCX
- TOX
- HERP
- DEM
- MAC
- NHL
- CMVR
- BPN
- CRCO
- AIDS death

**Non-AIDS events during follow-up**  
(n=766)

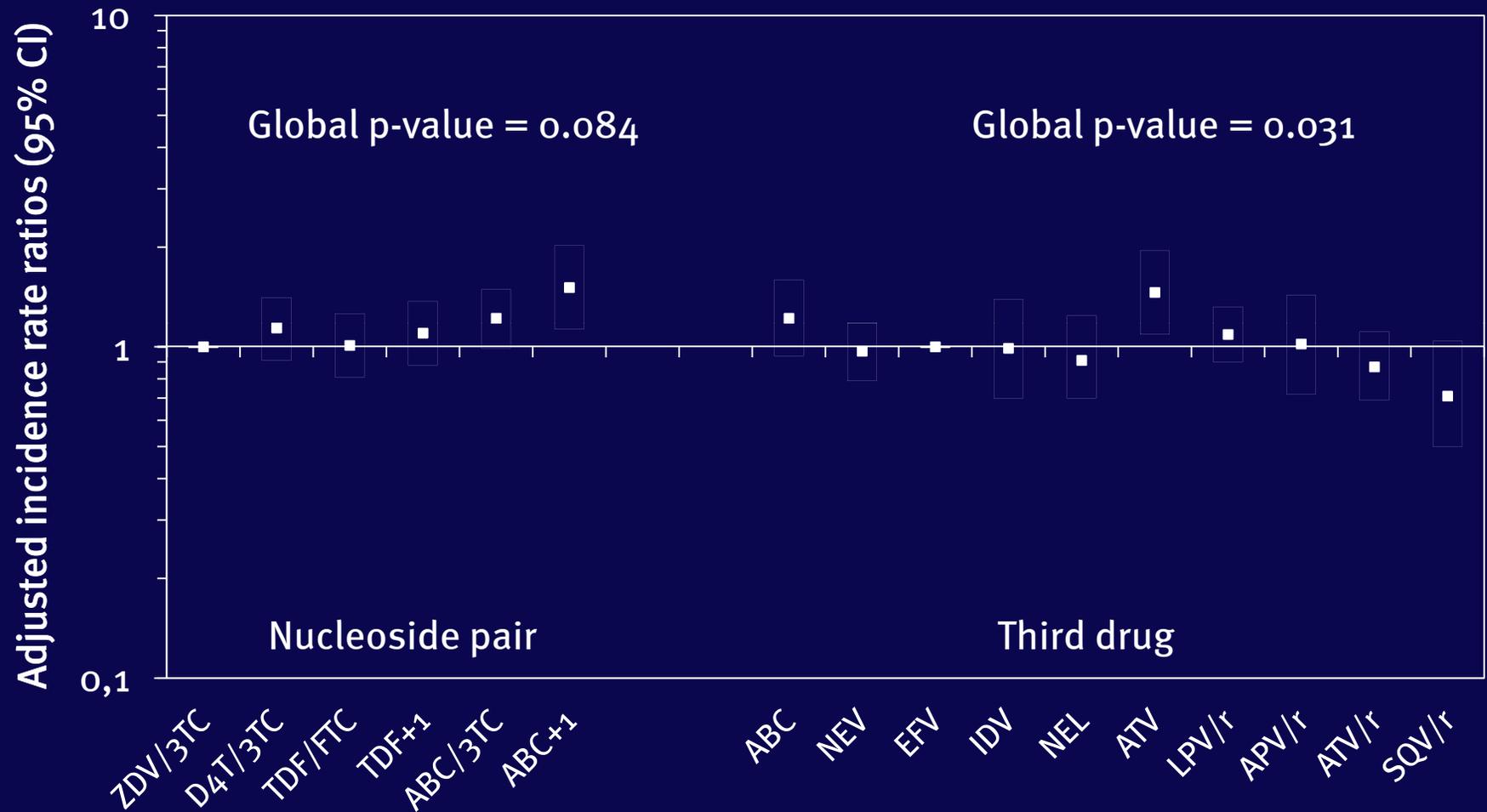


- CVD
- HEPENC
- NADM
- PANC
- ESRD
- non-AIDS death

## Incidence rates of fatal and non-fatal AIDS and non-AIDS events according to CD4

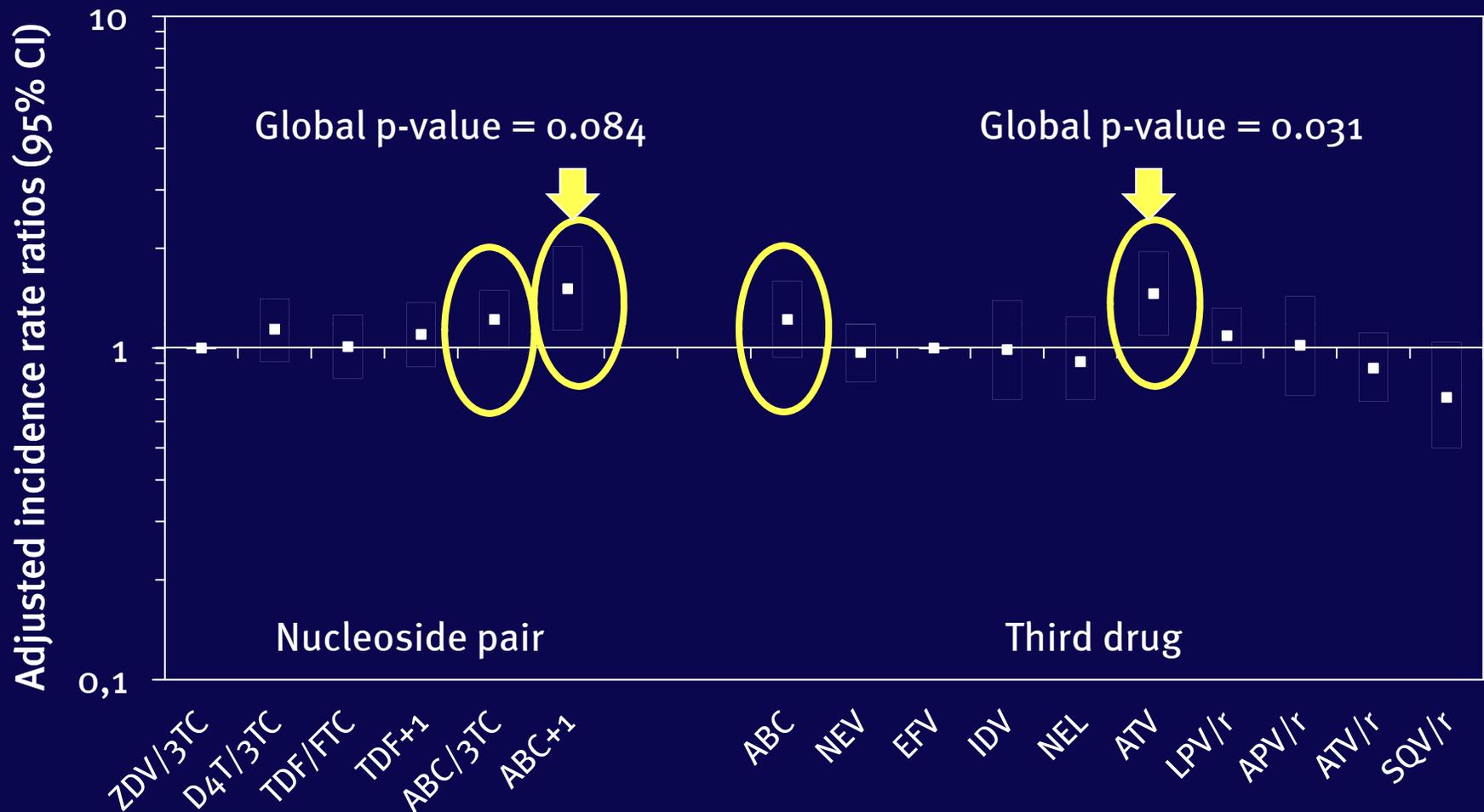
CD4 count:	<50	51-200	201-350	351-500	>500
ZDV/3TC	26.3 (16.5-36.0)	9.8 (7.9-11.7)	2.9 (2.3-3.6)	2.2 (1.7-2.7)	1.6 (1.3-1.9)
D4T/3TC	30.1 (17.2-48.9)	9.1 (6.2-12-.1)	3.8 (2.5-5.1)	2.7 (1.6-3.7)	1.2 (0.7-1.6)
TDF/FTC	31.0 (16.5-52.9)	7.8 (5.1-10.4)	2.5 (1.7-3.3)	1.5 (1.0-2.0)	1.7 (1.3-2.1)
TDF + 1	39.6 (24.9-54.3)	8.8 (6.1-11.6)	3.0 (1.9-4.0)	2.5 (1.7-3.4)	1.6 (1.2-2.1)
ABC/3TC	31.3 (16.6-53.4)	10.4 (6.9-13.9)	4.4 (3.1-5.7)	2.5 (1.7-3.3)	1.9 (1.5-2.4)
ABC + 1	37.5 (17.2-71.2)	10.4 (5.9-16.8)	4.8 (2.8-7.7)	2.6 (1.2-4.9)	3.5 (2.1-5.0)
ABC	72.7 (49.9-178.9)	12.0 (7.2-18.8)	5.3 (3.1-7.5)	2.1 (1.1-3.5)	2.1 (1.4-2.7)
NVP	43.5 (19.9-82.6)	9.0 (5.9-12.0)	2.4 (1.5-3.2)	2.8 (2.0-3.5)	1.2 (0.9-1.6)
EFV	24.8 (14.7-34.9)	9.4 (7.1-11.6)	2.7 (2.0-3.4)	2.0 (1.4-2.5)	1.7 (1.4-2.0)
IDV	27.4 (7.5-70.1)	13.0 (7.3-21.4)	2.4 (0.9-5.1)	2.7 (1.2-5.3)	1.3 (0.6-2.5)
NFV	37.7 (6.0-56.3)	5.6 (2.8-10.0)	3.9 (2.3-6.3)	1.3 (0.5-2.8)	1.7 (1.0-2.8)
ATV	37.7 (13.9-82.1)	20.4 (11.5-29.4)	5.5 (3.2-9.0)	2.4 (1.0-4.7)	2.5 (1.5-3.6)
LPV/r	32.5 (21.8-43.3)	9.6 (7.3-11.9)	3.5 (2.6-4.5)	2.3 (1.6-3.1)	2.3 (1.8-2.8)
APV/r	31.3 (8.5-88.0)	11.8 (6.1-20.7)	2.7 (1.1-5.5)	2.0 (0.7-4.3)	2.3 (1.1-4.1)
ATV/r	27.5 (12.6-52.3)	5.3 (3.0-8.7)	4.0 (2.6-5.4)	2.3 (1.4-3.2)	1.6 (1.0-2.1)
SQV/r	42.7 (13.9-99.7)	7.0 (3.2-13.3)	2.6 (1.2-4.9)	1.5 (0.6-3.2)	0.9 (0.4-1.7)

## Adjusted IRRs for AIDS & non-AIDS events according to current ARV use



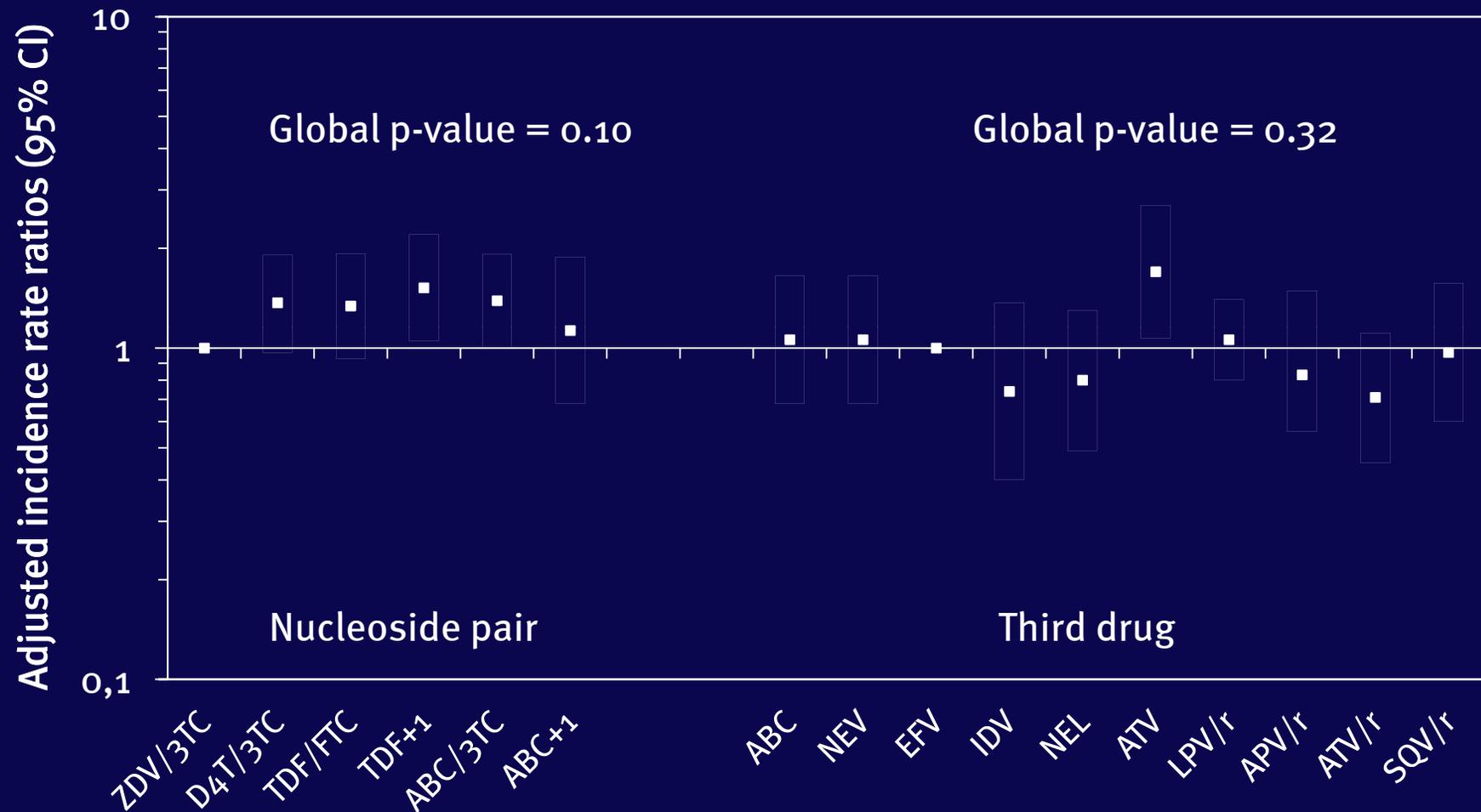
Also adjusted for gender, ethnic origin, risk group, region, prior AIDS, prior non-AIDS, age, CD4 nadir, time since starting third drug, year of follow-up, HBV/HCV status, CKD, anaemia, diabetes, hypertension and smoking status, current CD4 and viral load

## Adjusted IRRs for AIDS, non-AIDS and death according to current ARV use



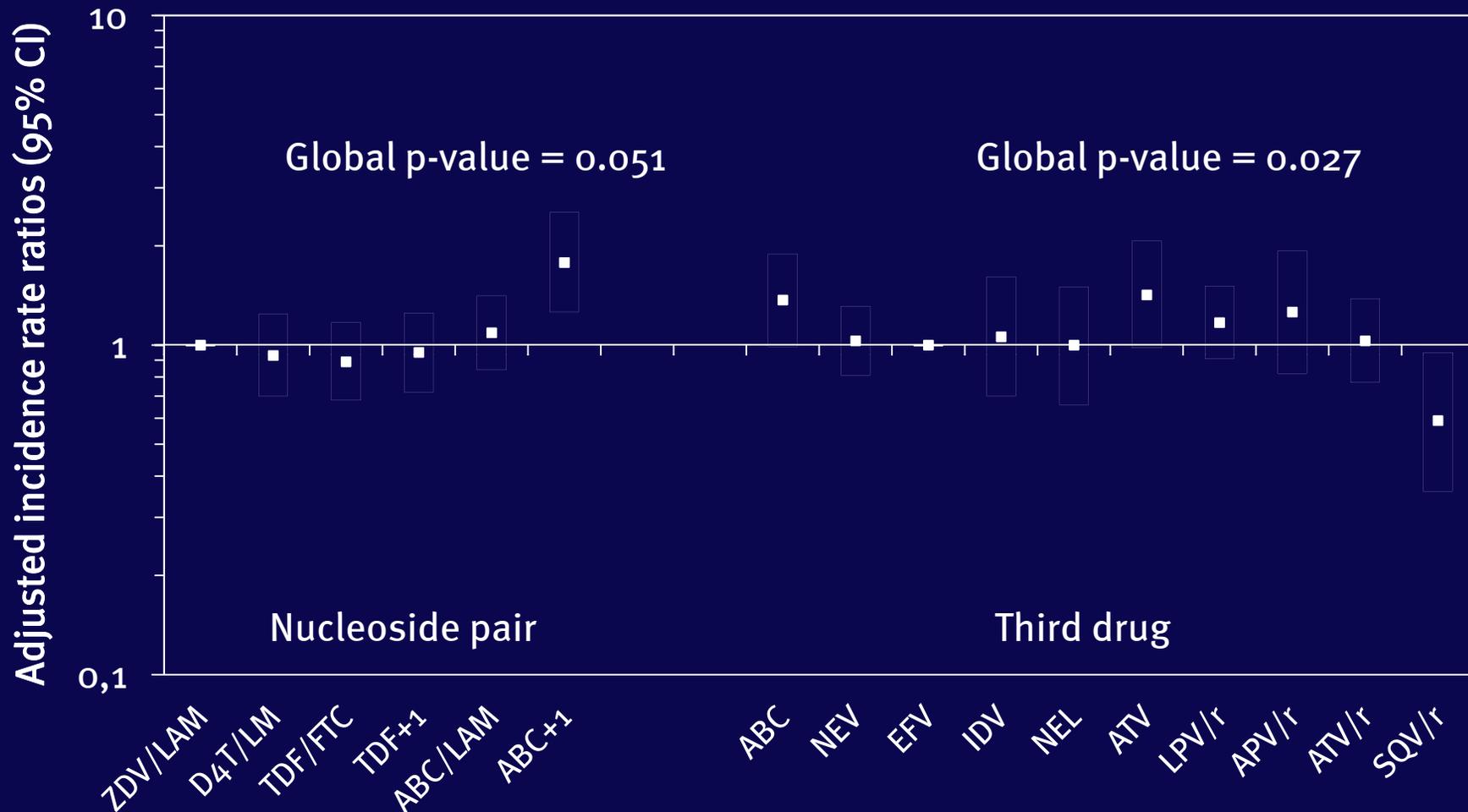
Also adjusted for gender, ethnic origin, risk group, region, prior AIDS, prior non-AIDS, age, CD4 nadir, time since starting third drug, year of follow-up, HBV/HCV status, CKD, anaemia, diabetes, hypertension and smoking status, current CD4 and viral load

## Adjusted IRRs: fatal and non-fatal AIDS events



Also adjusted for gender, ethnic origin, risk group, region, prior AIDS, prior non-AIDS, age, CD4 nadir, time since starting third drug, year of follow-up, HBV/HCV status, CKD, anaemia, diabetes, hypertension and smoking status, current CD4 and viral load

## Adjusted IRRs: fatal and non-fatal non-AIDS events



Also adjusted for gender, ethnic origin, risk group, region, prior AIDS, prior non-AIDS, age, CD4 nadir, time since starting third drug, year of follow-up, HBV/HCV status, CKD, anaemia, diabetes, hypertension and smoking status, current CD4 and viral load

## Limitations

- Until more follow-up has accumulated (>1000 PYFU), no results on the most recently available ARVs
  - Darunavir, tipranavir, raltegravir, maraviroc
- Wide confidence intervals for results
- Confounding by indication cannot be ruled out

## Summary

- There was little evidence of substantial differences between ARVs in the incidence of fatal and non-fatal AIDS and non-AIDS events for a given CD<sub>4</sub> or viral load
- Evidence that cART regimens which are licensed on the basis of changes in surrogate markers have similar risks of AIDS and non-AIDS events for a given CD<sub>4</sub> and pVL
- This suggests there are unlikely to be major unidentified adverse effects of specific ARVs

## Summary

- Some evidence that a NRTI regimen including ABC, or ABC or unboosted ATV as third drugs, had higher overall event rates for a given CD4 or viral load
- ABC plus one other NRTI or ATV or ABC as third drugs had a higher incidence of non-AIDS events, particularly cardiovascular events
- Larger studies are required to investigate the small differences found

# The EuroSIDA Study Group

The multi-centre study group of EuroSIDA (national coordinators in parenthesis).

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**Statement of Funding:** Primary support is provided by the European Commission BIOMED 1 (CT94-1637), BIOMED 2 (CT97-2713), the 5th Framework (QLK2-2000-00773), the 6th Framework (LSHP-CT-2006-018632), and the 7th Framework (FP7/2007-2013, EuroCoord n° 260694) programmes. Current support also includes unrestricted grants by Gilead, Pfizer, and Merck and Co. The participation of centres from Switzerland was supported by The Swiss National Science Foundation (Grant 108787).