



*a
multicentre
study*

EuroSIDA

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Immuno-virological discordance (ID) is associated with a higher frequency of fatal and non-fatal AIDS and non-AIDS

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on behalf of EuroSIDA in EuroCoord

Background

- ~ 30% late presenters with advanced immunodeficiency (<200 CD4 cells)*
- Failing immune recovery despite suppressive ART (immunovirological discordance, ID) in up to 15% of cases**
- ID is associated with AIDS/death[†] even if risk is greatly reduced with longer viral suppression
- Impact of ID on composite of fatal and non-fatal AIDS and non-AIDS has not been thoroughly investigated

*Battegay M et al, Antivir Ther. 2007

**Borghi V et al, JAIDS 2008

†COHERE collab., PLOS Med 2012

§Zoufaly et al, JID 2011

Objectives

- To determine the rates of fatal and non-fatal AIDS/non-AIDS in the EuroSIDA cohort stratified according to whether or not ID is present
- To compare these rates over time
- To analyse other factors associated with this outcome

Methods

- Inclusion of patients with CD4 count < 200 when starting one or more new antiretroviral drugs after enrollment in EuroSIDA
- Definition of immuno-virological discordance (ID) as remaining on a CD4 < 200 while virologically suppressed
- Follow-up from first day of VL < 50 cop/ml (baseline) to new fatal or non-fatal AIDS/non-AIDS* or viral rebound > 50 cop/ml
- Poisson Regression Models included
 - Time-updated ID
 - Demographic factors
 - Risk factors for mortality
 - Number of drugs, time to viral suppression

Baseline characteristics (n=1349, 5247 PYFU)

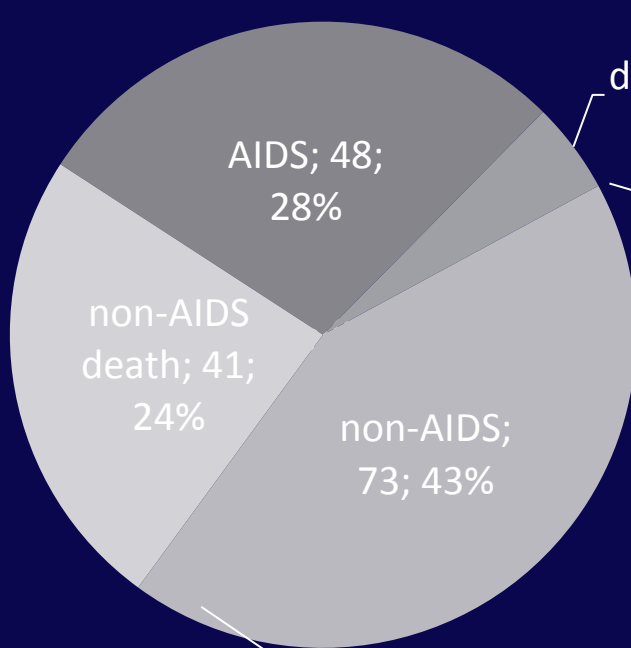
	%
Male sex	75
Transmission risk – MSM / IDU / heterosexual	35/25/32
CD4 cell count 0-49 / 50-99 / 100-200	20/19/60
previous AIDS / non AIDS	42/4
ART naïve	28
Hepatitis C positive	26
Diabetes present	3
Hypertension present	21
Anaemia present	36
Estimated GFR<90 present	21
Current smoker	36
	Median (range)
Age, years	43 (20-80)
Viral load at start of new regimen (log cop/ml)	4.9 (2.7-7.8)
Year of viral suppression	2006 (2001-2011)

Rates and relative rates of fatal and non-fatal AIDS/non-AIDS

Exposure	No. events	PYFU	Rate (95%CI)	Crude RR (95% CI)	Adjusted** RR (95% CI)
Fatal or non-fatal <u>AIDS and non-AIDS</u>					
Not ID	106	4418	24.0 (19.6-29.0)	1	1
ID	64	830	77.1 (59.4-98.5)	3.22 (2.34-4.41)	2.15 (1.40-3.30)
Fatal or non-fatal <u>non-AIDS</u>					
Not ID	79	4473	17.7 (14.0-22.0)	1	1
ID	43	847	50.7 (36.7-68.4)	2.87 (1.98-4.17)	2.07 (1.26-3.41)
Fatal or non-fatal <u>AIDS</u>					
Not ID	32	4595	7.0 (4.8-9.8)	1	1
ID	27	863	31.3(20.6-45.5)	4.49 (2.67-7.54)	3.46 (1.54-7.75)

*adjusted for gender, age, smoking, ART naive status, year of suppression, HBV/HCV coinfection, risk, race, region, current cART, change of ART before viral suppression, time to viral suppression, presence of diabetes, hypertension, anemia, current eGFR<90, cd4 nadir, cd4 count at first viral suppression, viral load at baseline, previous AIDS/non AIDS event

Type of event

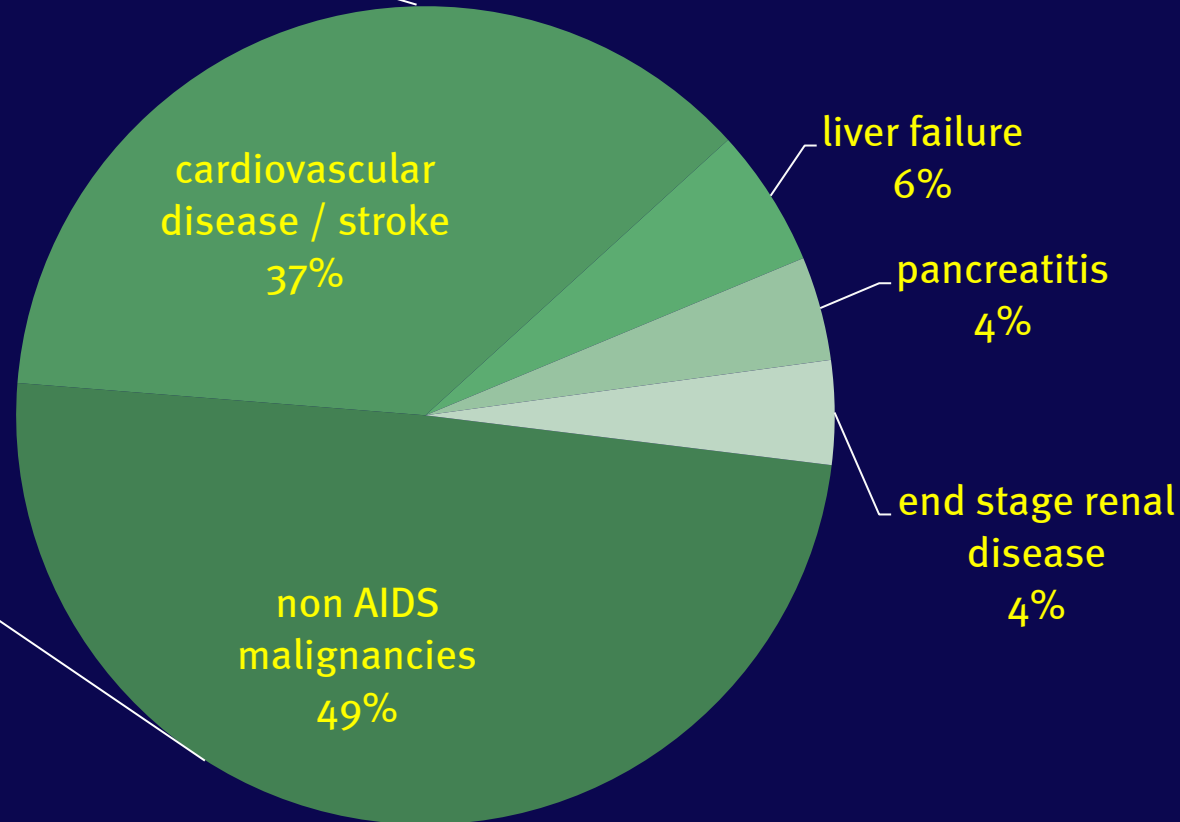


AIDS death; 8; 5%

AIDS; 48; 28%

non-AIDS death; 41; 24%

non-AIDS; 73; 43%



cardiovascular disease / stroke 37%

liver failure 6%

pancreatitis 4%

end stage renal disease 4%

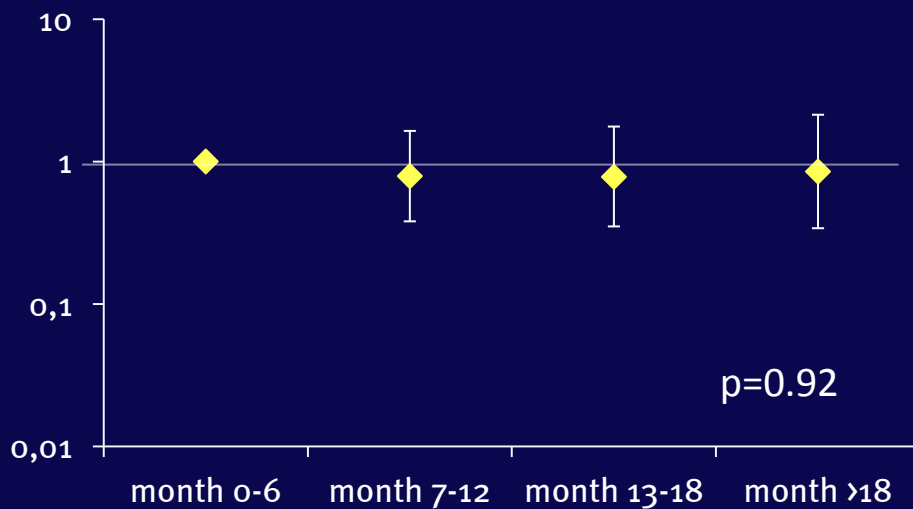
non AIDS malignancies 49%

Rates of fatal and non-fatal AIDS/non-AIDS in patients with and without ID

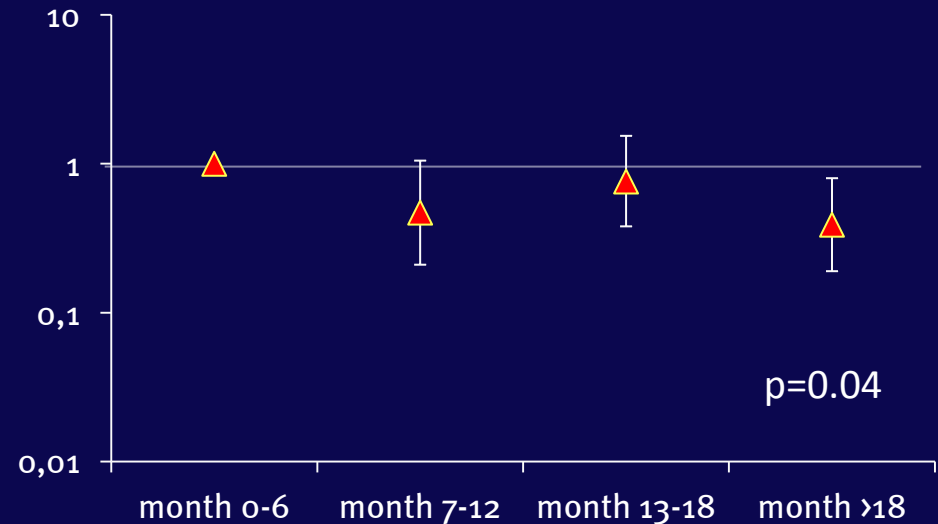
Immuno-virological Discordance (ID)					
Months	Events	PYFU	Rate	95%CI	
0-6	22	229	96.2	60.3	145.7
7-12	11	153	72.1	36.0	128.9
13-18	8	106	75.7	32.7	149.2
>18	23	343	67.1	42.5	100.7
No Immuno-virological Discordance					
Months	Events	PYFU	Rate	95%CI	
0-6	18	436	41.3	24.4	65.2
7-12	9	455	19.8	9.0	37.6
13-18	15	443	33.9	19.0	55.9
>18	64	3084	20.8	16.0	26.5

Relative Rates of fatal and non-fatal AIDS/non-AIDS by duration of viral suppression and ID status

Patients with ID



Patients without ID



Other risk factors for fatal and non fatal AIDS/non-AIDS in the multivariable analysis

Risk factor	IRR*	95%CI		p
Anaemia present	2.29	1.66	3.15	<0.001
Age (per 10 years older)	1.44	1.18	1.76	<0.001
Diagnosis of Diabetes	1.75	0.93	3.30	0.084
Previous non-AIDS	2.50	1.41	4.44	0.002

* adjusted for ID, gender, ART naive status, year of suppression, HBV/HCV co-infection, risk, race, region, current cART, change of ART before viral suppression, time to viral suppression, smoking, estimated GFR, presence of hypertension, current, CD4 nadir, CD4 at baseline, viral load at baseline, previous AIDS

Sensitivity analyses

- Results similar after stratifying for ART naive status
- Results similar after restricting to those who achieved viral load suppression within 1 year

Summary and Conclusion I

- Immuno-virological discordance is a risk factor for fatal and non-fatal AIDS/non-AIDS
- The association of ID and fatal and non fatal AIDS is stronger than for other considered outcomes
- Risk of fatal and non fatal AIDS/non-AIDS decreased with longer viral suppression in the non ID group but not in ID

Summary and Conclusion II

- Majority of events are non-AIDS (mainly malignancies)
- The fact that current CD4 count is a stronger predictor of AIDS than non-AIDS was previously shown in EuroSIDA*; this finding is consistent with the results of our analysis focussing on ID in people starting a new regimen with a CD4<200
- This analysis suggests that ART alone is not sufficient to remove the risk of fatal and non-fatal AIDS/non-AIDS in people identified as ID

*Mocroft A et al, Antivir Ther 2012

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