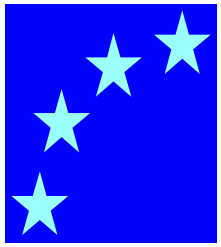

a multicentre study

EuroSIDA

High hepatitis C viremia is associated with an increased risk for mortality in HIV/Hepatitis C virus coinfected individuals

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on behalf of the EuroSIDA Study Group

Hepatitis C in the EuroSIDA Study

Background:

- In a previous multivariate analysis from the EuroSIDA cohort no increased risk for clinical progression (AIDS or death) associated with HCV status (determined by HCV antibodies alone) was found; the risk for liver-related death however, was increased in HIV/HCV-coinfected individuals
- HCV-coinfection did not influence virologic and immunologic response to HAART
- HCV-infection in most cohorts has solely been defined by presence of HCV antibodies only; information on HCV viral load and genotyope is mostly lacking

Rockstroh J et al., J Infect Dis 2005

Hepatitis C in the EuroSIDA Study

Objectives:

To investigate the influence of HCV RNA levels and HCV genotypes on

a) HIV or HCV disease progression and mortality

b) the response to highly active antiretroviral therapy

Hepatitis C in the EuroSIDA Study

Methods:

- Serum HCV-RNA testing was performed by a reliable quantitative assay (Versant HCV-RNA v3.0)
- HCV genotyping (LiPA) was carried out in all viremic subjects
- Poisson regression analyses were used to determine progression to death from any cause or from liver related disease adjusted for relevant confounding variables
- Cox proportional hazard models were used to compare virologic and immunologic response to cART

Hepatitis C in the EuroSIDA Study

Results 1: HCV viral load

- HCV viral load was determined for 1952 anti-HCV antibody positive individuals
- 415 patients (21%) had HCV-RNA ‹615 IU/ml (aviremic)
- 716 patients (36%) had HCV-RNA ›615 IU/ml but ‹$5x10^5$ IU/ml (low viral load)
- 821 patients (42%) had HCV-RNA › $5x10^5$ IU/ml (high viral load)

Hepatitis C in the EuroSIDA Study

	HCV viral load ‹615 IU/ml	HCV viral load 615-500000 IU/ml	HCV viral load ›500000 IU/ml
any death	n = 78	n = 96	n = 158
Incidence/100 PYFU (95% CI)	3.12 (2.42–3.81)	1.74 (1.39–2.08)	4.17 (3.52–4.82)
adj. IRR (95% CI)	1.13 (0.80–1.60)	1	1.94 (1.48–2.58)
p-value	p = 0.47		p ‹ 0.0001
liver-related death	n = 17	n = 32	n = 49
Incidence/100 PYFU (95% CI)	0.68 (0.40–1.09)	0.58 (0.38–0.78)	1.29 (0.95–1.66)
adj. IRR (95% CI)	0.73 (0.38–1.39)	1	1.77 (1.11–2.82)
p-value	p = 0.34		p = 0.016

Models were adjusted for gender, HIV-transmission category, region of Europe, HBV-coinfection, race, prior AIDS diagnosis, age, CD4 at genotype testing, date recruited to EuroSIDA, type of ART and date of HCV genotype testing

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Hepatitis C in the EuroSIDA Study

Results 3: HCV viral load and response to HAART

- The level of HCV viremia had no significant impact on immunologic and/or virological response to HAART in HIV/HCV coinfected individuals

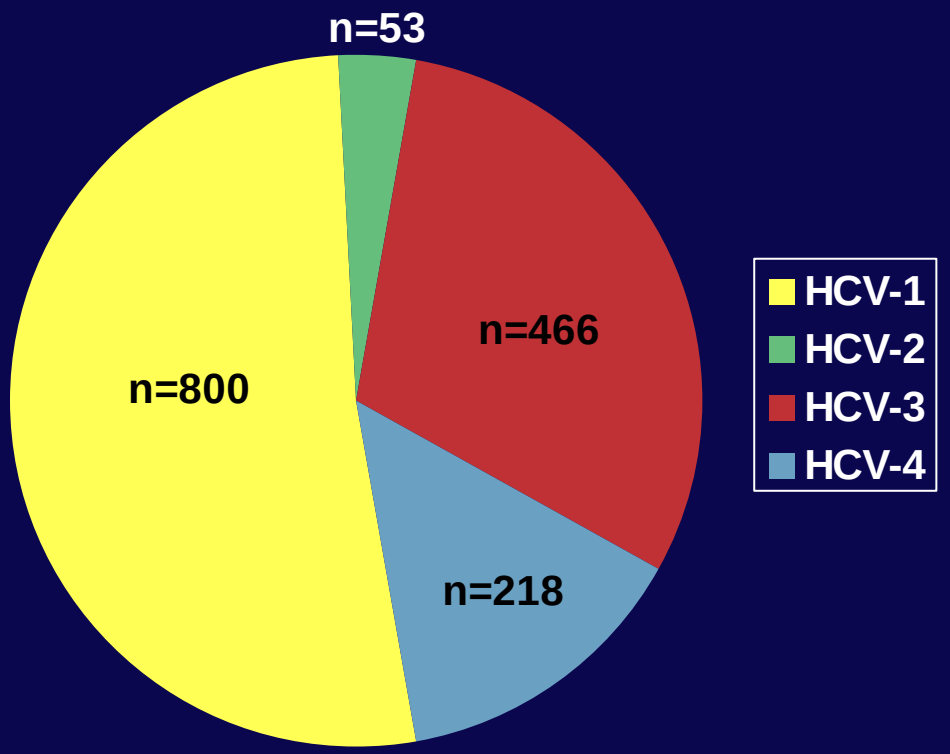
Conclusions 1: HCV viral load

- Patients with low HCV-RNA, have a similar incidence of all-cause-death and LRD compared to aviremic anti-HCV antibody positive subjects
- Patients with high HCV-RNA had a significantly increased incidence of death and LRD.
- HCV viral load had no significant effect for the host response to antiretroviral therapy

Hepatitis C in the EuroSIDA Study

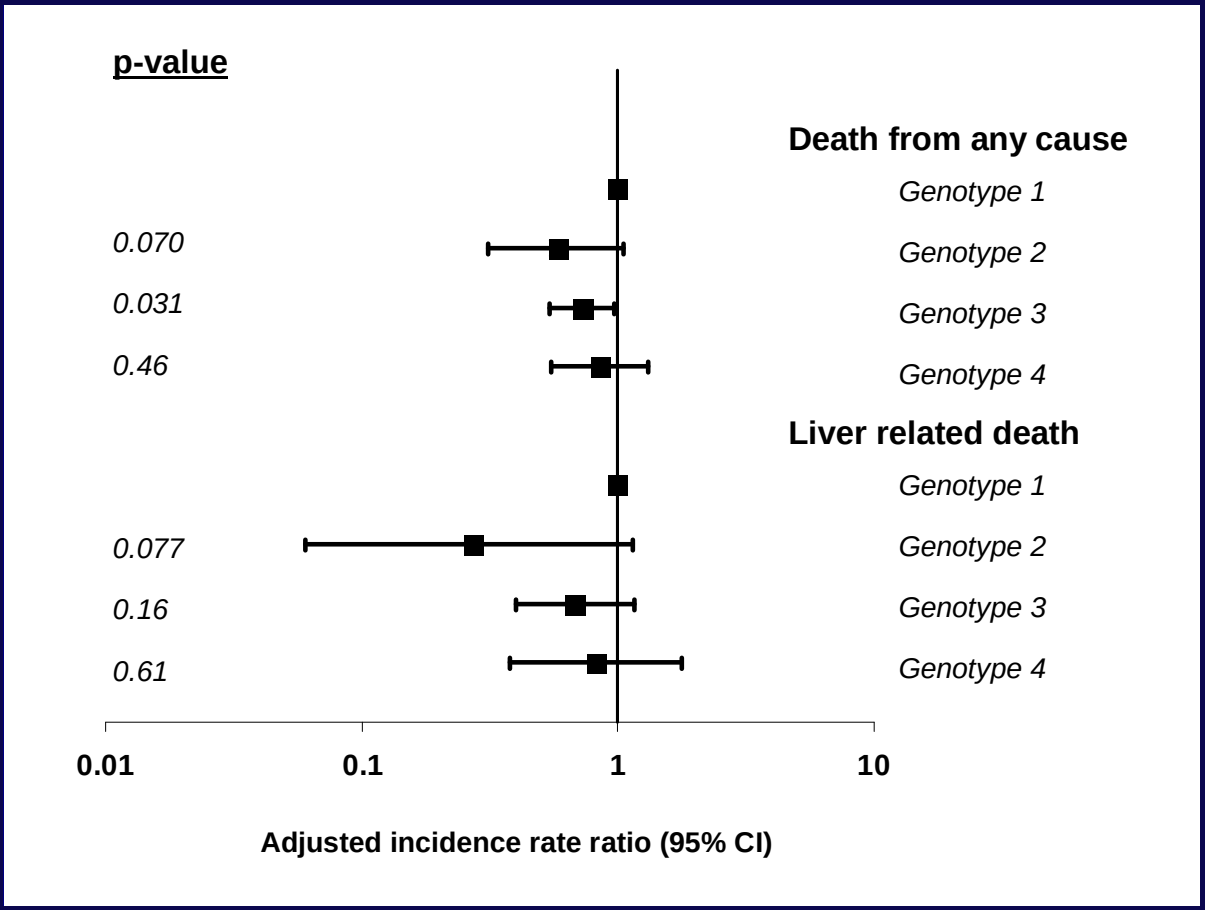
Results 4: HCV genotype

HCV genotype could be determined for 1537 HCV-RNA positive patients



Hepatitis C in the EuroSIDA Study

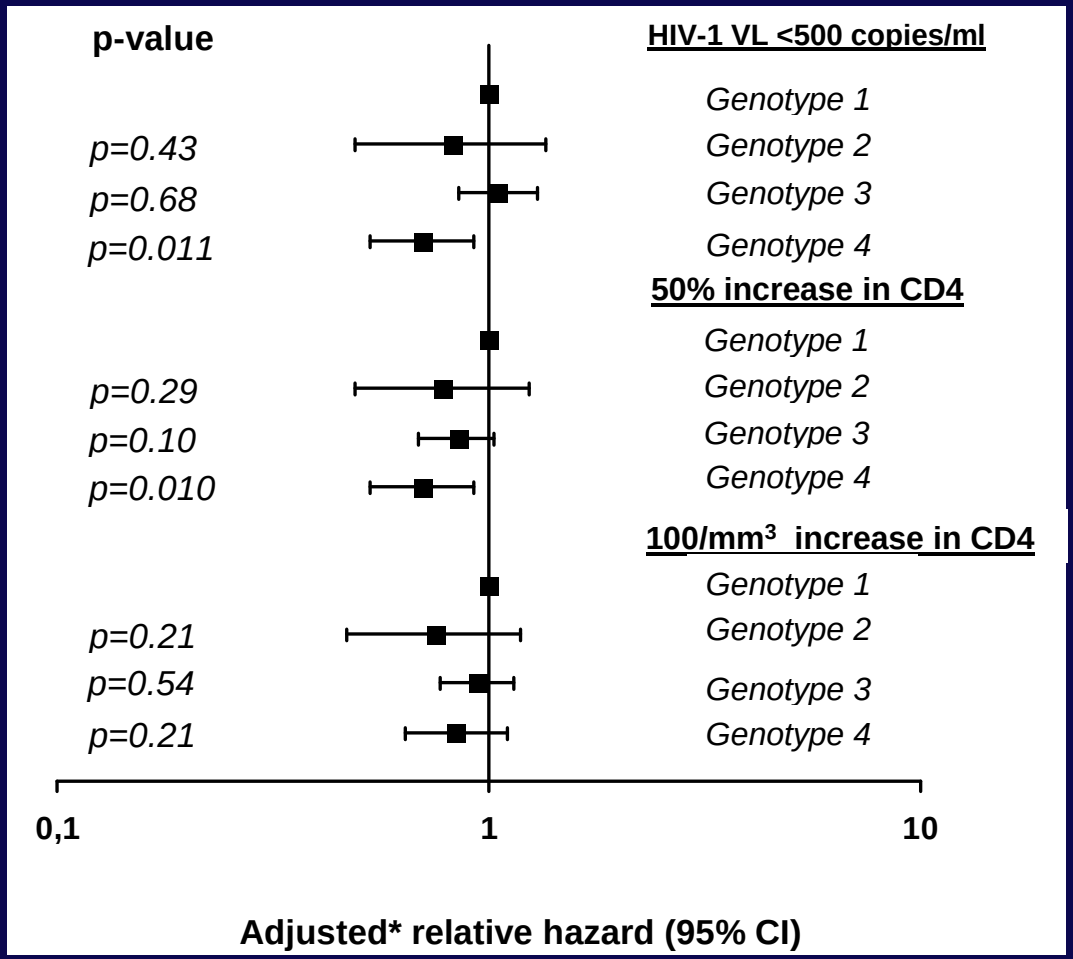
Results 5: HCV genotype and incidences of death



Multivariate IRR were adjusted for gender, exposure group, race, prior AIDS, region of Europe and Argentina, CD4+ T-cell nadir, age, and baseline date

Hepatitis C in the EuroSIDA Study

Results 6: HCV genotype and response to HAART



Multivariate models were adjusted for gender, age, exposure group, race, region of Europe and Argentina, HIV-RNA viral load, prior AIDS, date of cART initiation, cART regimen started, CD4+ T-cell nadir, baseline CD4+ T-cell count, and HBsAg status

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Conclusions 2: HCV genotype

- Patients with HCV genotype 3 had a significant lower incidence of death from any cause when compared to patients with HCV-1
- Despite lower incidences of liver-related death in patients with HCV genotypes 2 and 3, these incidences did not reach statistical significance.
- Coinfection with genotype 2, 3 or 4 was associated with a poorer virological and immunological response to HAART compared to genotype 1, but this only reached statistical significance for patients infected with genotype 4

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Baseline characteristics of study subjects I.

		All		HCV seronegative		HCV seropositive	
		N	%	N	%	N	%
All		10621	100	7630	71.8	2991	28.2
Gender	Male	8019	75.5	5930	77.7	2089	69.8
	Female	2602	24.5	1700	22.3	902	30.2
Race	White	9229	86.9	6488	85.0	2741	91.6
	Other	1392	13.1	1142	15.0	250	8.4
Risk	Homosexual	4414	41.6	4198	55.0	216	7.2
	IDU	2482	23.4	229	3.0	2253	75.3
	Heterosexual	2970	28.0	2636	34.6	334	11.2
	Other	755	7.1	567	7.4	188	6.3
HBV	Neg	8883	83.6	6540	85.7	2343	78.3
	Pos	605	5.7	407	5.3	198	6.6
	Unknown	1133	10.7	683	9.0	450	15.1
Region	Southern Europe/Argentina	3026	28.5	1946	25.5	1080	36.1
	Central Europe	2736	25.8	2202	28.9	534	17.9
	Northern Europe	2924	27.5	2387	31.3	537	17.9
	Eastern Europe	1935	18.2	1095	14.3	840	28.1
AIDS	Yes	2904	27.3	2214	29.0	690	23.1
ARVs ever Received	None	1745	16.4	1077	14.1	668	22.3
	ART	2650	25.0	1732	22.7	918	30.7
	cART	6226	58.6	4821	63.2	1405	47.0
HIV viral load	< 500 copies/mL	4162	53.7	3259	55.0	903	49.5

Abbreviations: IDU, intravenous drug users

Baseline characteristics of study subjects II

	Median	IQR	Median	IQR	Median	IQR
HIV viral load [log_{10}]	2.70	1.70-4.09	2.66	1.69-4.03	2.76	1.74-4.25
$CD4^+$ T cell count	324	181-490	334	189-500	303	167-462
Nadir $CD4^+$ T cell count	170	69-291	169	63-290	180	80-300
Age [years]	37.6	31.8-44.9	39.0	32.9-47.2	34.7	30.1-40.0