a multicentre study

EuroSIDA

Does Hepatitis C virus (HCV) genotype or viral load predict the risk of all-cause mortality of HIV/HCV coinfection ?

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on behalf of the EuroSIDA Study Group

Background

- Previous analyses from EuroSIDA showed:
  - No increased risk for clinical progression (AIDS or death) associated with HCV status (determined by HCV antibodies alone)
  - Increased risk for liver-related death in HIV/HCV-coinfected individuals
  - HCV-coinfection did not influence virological and immunological response to HAART

Rockstroh J et al., J Infect Dis 2005

Objectives

- To investigate the relationship between HCV-genotype and/or HCV-RNA level and the risk for developing liver disease related death, or all cause mortality within the EuroSIDA cohort.

EuroSIDA - information collected

- Core information:
  - *Demographics*
  - *All CD_4 cell counts/plasma viral loads*
  - *Treatments (HIV and OI's)*
  - *AIDS-related clinical events*
  - *Death and cause of death*

- Other:
  - Potential toxicity
  - Admission to hospital
  - *Hepatitis*, pregnancy, etc
  - Plasma bank

Methods

- Serum HCV-RNA testing was performed by a reliable quantitative assay for distinct genotypes (Versant)
- HCV genotyping (LiPA) was carried out in all viremic subjects

- All patients with known HCV-genotype were included (n=1677)
- An additional 586 patients were included who had a HCV-RNA < 615 IU/ml but were HCV-antibody positive (HCV cleared = HCV-c)
- Data on genotype was available from 2 sources: the sample repository testing and EuroSIDA follow-up forms; where data was available from both sources, the results from the sample repository were used.

Statistical Analyses

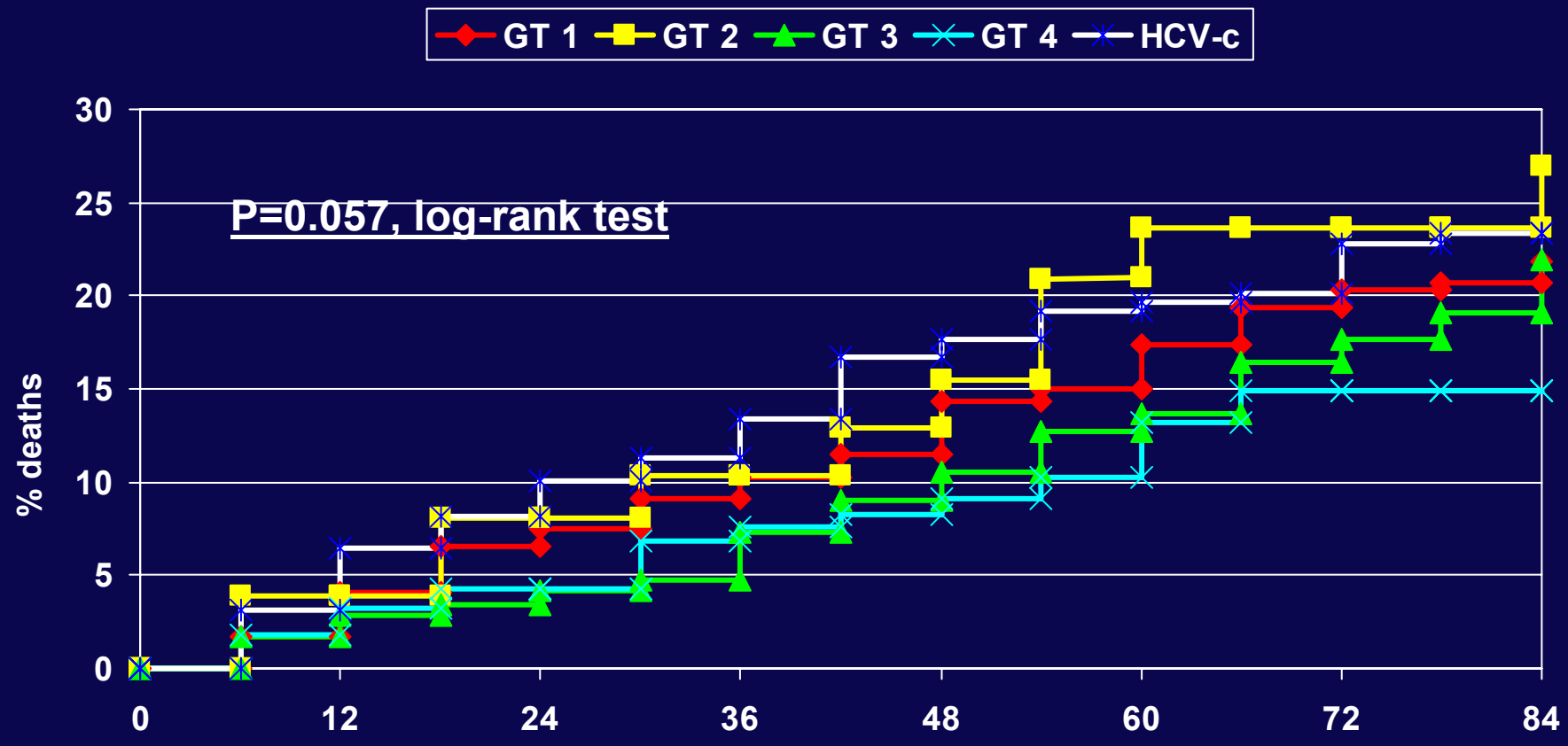
- Kaplan-Meier and Poisson regression analyses were used to determine progression to death from any cause or from liver related disease and compared between genotypes and patients with positive HCV-antibodies but undetectable HCV-RNA (HCV-c)
- Models were adjusted for demographic variables (gender, exposure group, region of Europe), data source (sample repository or EuroSIDA follow-up forms), source of HCV+ test, prior AIDS diagnosis, treatment regimen started at or before baseline, age, CD4, CD4-nadir, date of HCV genotype test or HCV-RNA measurement and date enrolled in EuroSIDA

Results

- 340 patients (15%) died during follow-up (Total PYFU 9048)
- 91 died from liver disease
- After adjustment no other HCV genotype nor HCV infected patients who cleared HCV infection had a significantly different incidence of death compared to HCV genotype 1 infection (p>0.01).
- Risk of liver related deaths did not differ depending on HCV-c status nor HCV genotype and HCV-RNA level, although the power of detecting differences using this outcome was lower.

Kaplan-Meier progression to death (any cause)

(univariate analysis)



N under follow-up								
1	890	738	621	515	411	301	246	192
2	51	48	42	36	32	28	26	19
3	500	406	340	277	225	164	131	101
4	236	194	170	124	102	64	51	41
HCV-c	586	451	374	288	236	172	146	117

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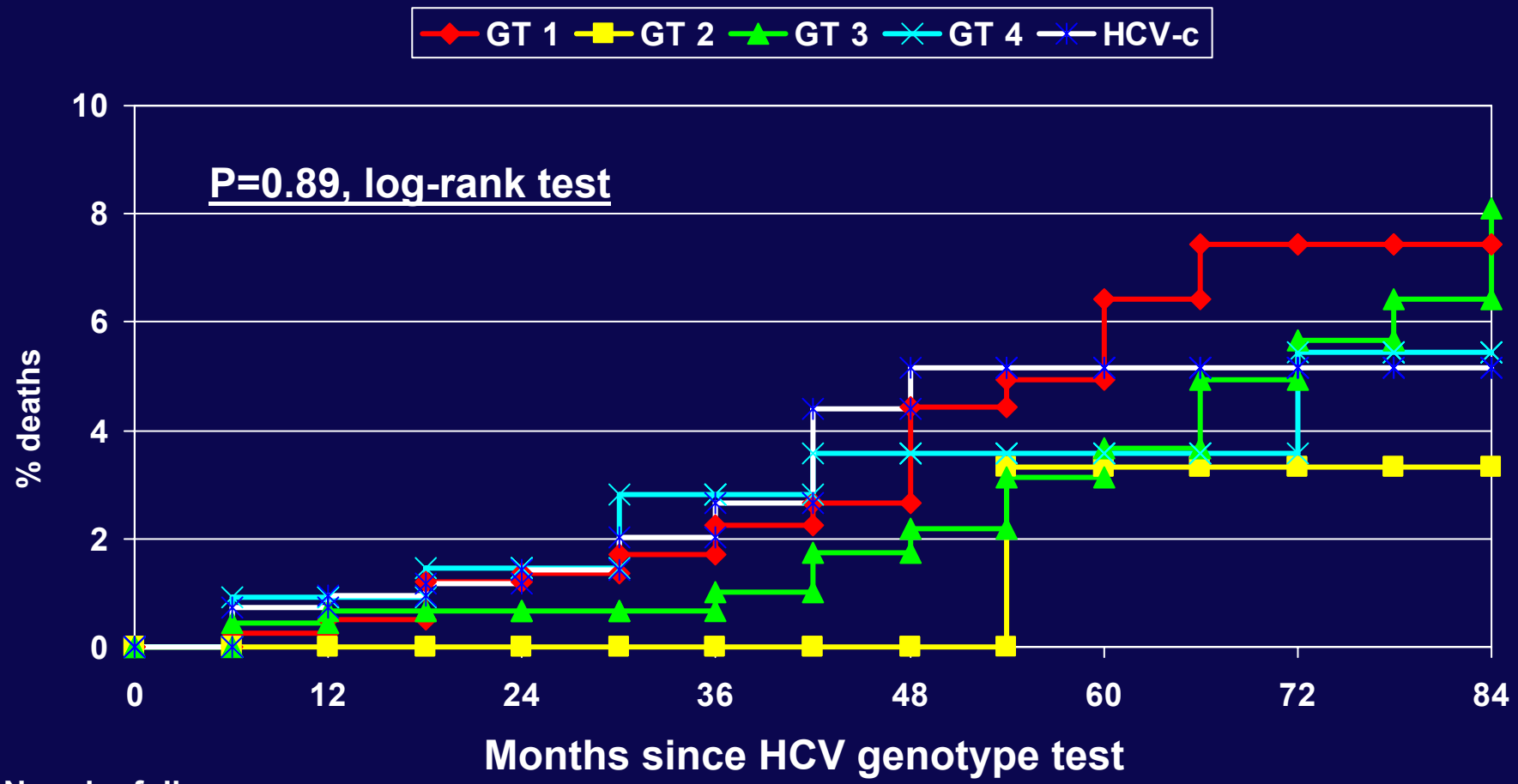
Kaplan-Meier progression to death (LRD) (univariate analysis)



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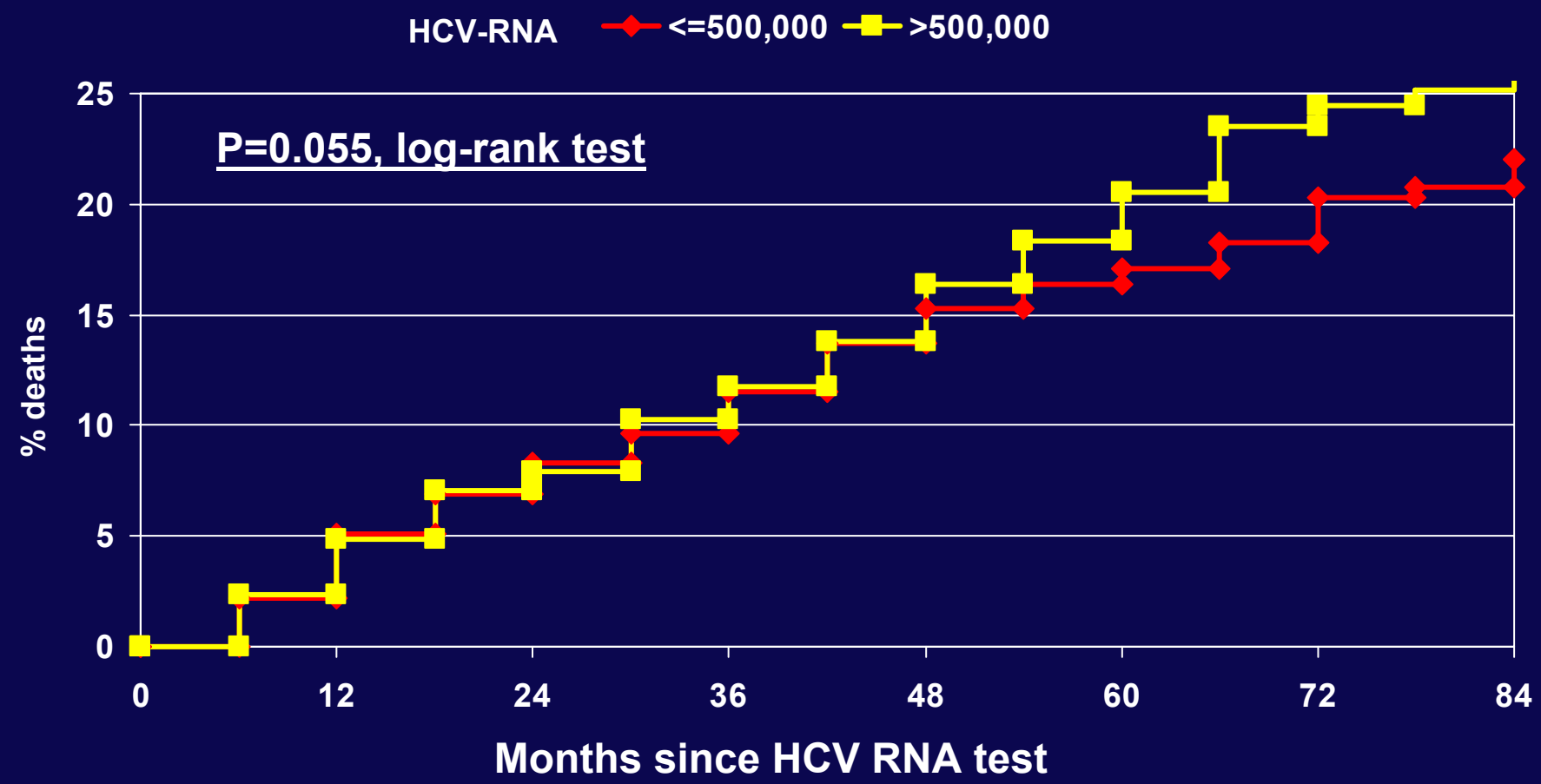
Event rates and incidence rate ratios (IRR per 100 PYFU)

HCV Genotype	1	2	3	4	HCV-c
PYFU	3684.2	287.9	2008.0	885.3	2182.7
Deaths (any cause)					
N	142	13	67	22	96
% progressed at 5 years (95% CI)	17.4 (14.2 – 20.5)	23.6 (10.6 – 36.7)	13.7 (9.8 – 17.6)	10.3 (5.4 – 15.2)	19.6 (15.5 – 23.7)
Incidence rate (95% CI)	3.85 (3.22 – 4.49)	4.52 (2.40 – 7.70)	3.34 (2.54 – 4.14)	2.49 (1.45 – 3.52)	4.40 (3.52 – 5.28)
IRR (95% CI)	1.00	1.23 (0.70 – 2.18)	0.86 (0.64 – 1.15)	0.63 (0.40 – 0.99)	1.19 (0.92 – 1.54)
p-value	-	0.47	0.31	0.045	0.19
Adjusted IRR* (95% CI)	1.00	1.13 (0.55 – 2.34)	1.09 (0.77 – 1.53)	1.04 (0.61 – 1.78)	0.80 (0.56 – 1.14)
p-value	-	0.73	0.63	0.89	0.22

*Analysis adjusted for data source, gender, exposure group, region of Europe, coinfection with HBV, race, prior AIDS, age, CD4 at GT, data recruited to ES, treatment regimen and date of HCV GT testing

Kaplan-Meier progression and HCV-RNA

(univariate analysis; patients with undetectable HCV-RNA are included)



N under follow-up

<500k	1365	1090	933	741	619	458	375	300
≥500k	705	610	532	445	374	270	234	181

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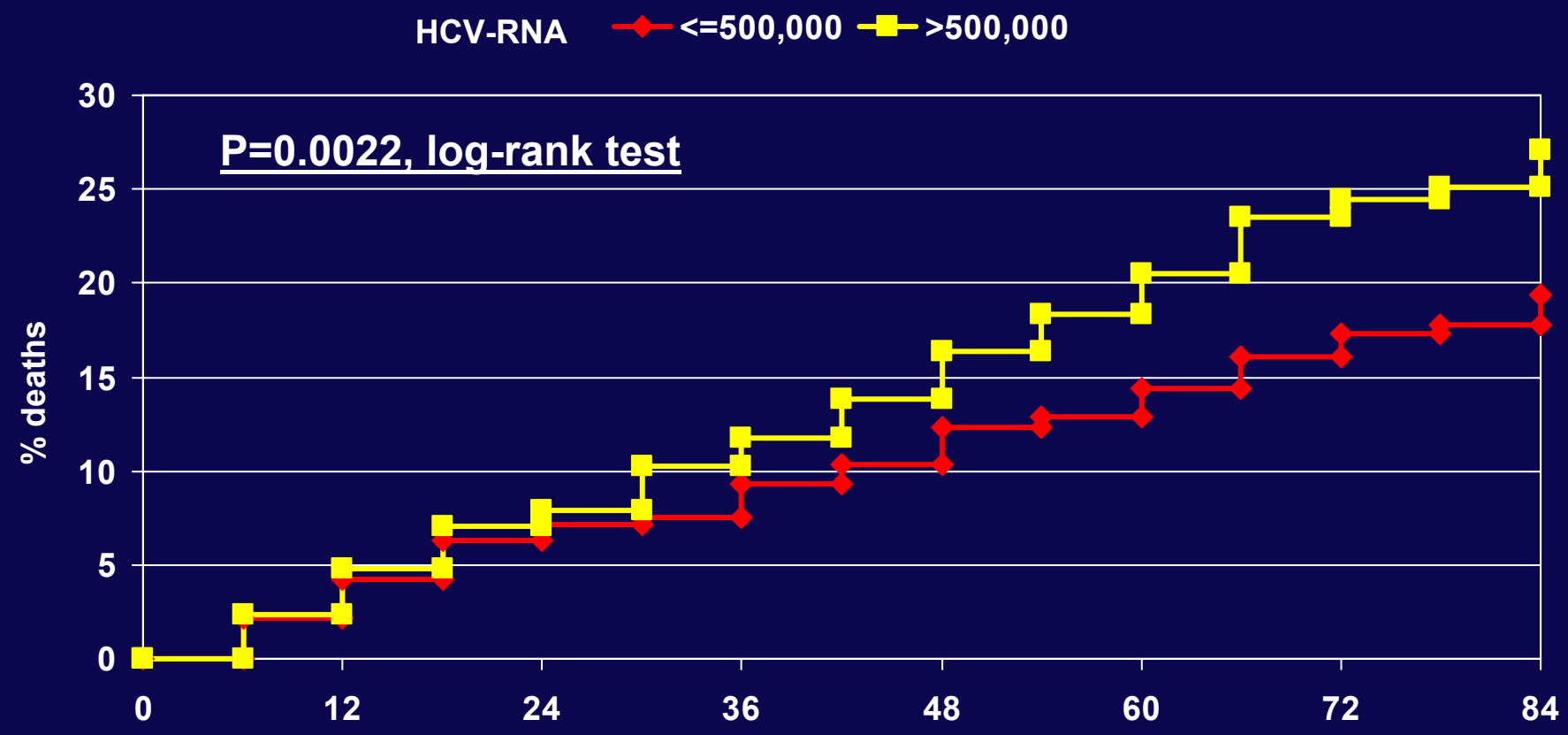
Kaplan-Meier progression and HCV-RNA

(univariate anaylsis; only including viremic patients)



N under follow-up

<500k	667	565	482	391	327	237	193	151
≥500k	705	610	532	445	374	270	234	181

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Results : HCV Viremia

- **Results:**
  - Per log10 increase in HCV-RNA the risk of all cause mortality increased by 23% (IRR=1.23 (1.05-1.45), p=0.01), but after adjustment for confounders, this was no longer significant (IRR=1.06 (0.90-1.25), p=0.46).

Conclusion

- Within the EuroSIDA cohort no association between HCV-RNA levels nor HCV genotype and risk of all cause mortality was detected

- Risk of liver related deaths did not differ depending on HCV-c status nor HCV genotype and HCV-RNA level, although the power of detecting differences using this outcome was lower.

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