Is Response to Anti-HCV Treatment Predictive of Mortality in HCV/HIV Co-infected Patients?

Lars Peters for the hepatitis working group of COHERE in EuroCoord

Presenter disclosures

- The presenting author has no conflicts of interest

Background

- Observational studies of HCV mono-infected, a sustained virologic response (SVR) has been associated with reduced all-cause and liver-related mortality

- In HIV/HCV patients, mixed retrospective-prospective studies from Spain, have shown that, compared with patients who achieved SVR, non-responders to HCV treatment had
  - an almost nine-fold increased risk of liver-related clinical events[1]
  - reduced risk of HIV progression and non-liver-related death[2]

- Compared with HCV mono-infected patients, the benefit of HCV treatment of HIV/HCV patients could be
  - greater due to accelerated fibrosis progression in co-infected patients
  - lower due to higher prevalence of competing risk factors (both HIV-related and lifestyle factors) for mortality

[1]Berenguer, Hepatology 2009
[2]Berenguer, CID 2012

Objectives

- To compare the long-term risk of
  - all-cause mortality
  - liver-related death
  - Non-liver-related death

according to HCV treatment response in HIV/HCV co-infected patients in the prospective multi-cohort study COHERE

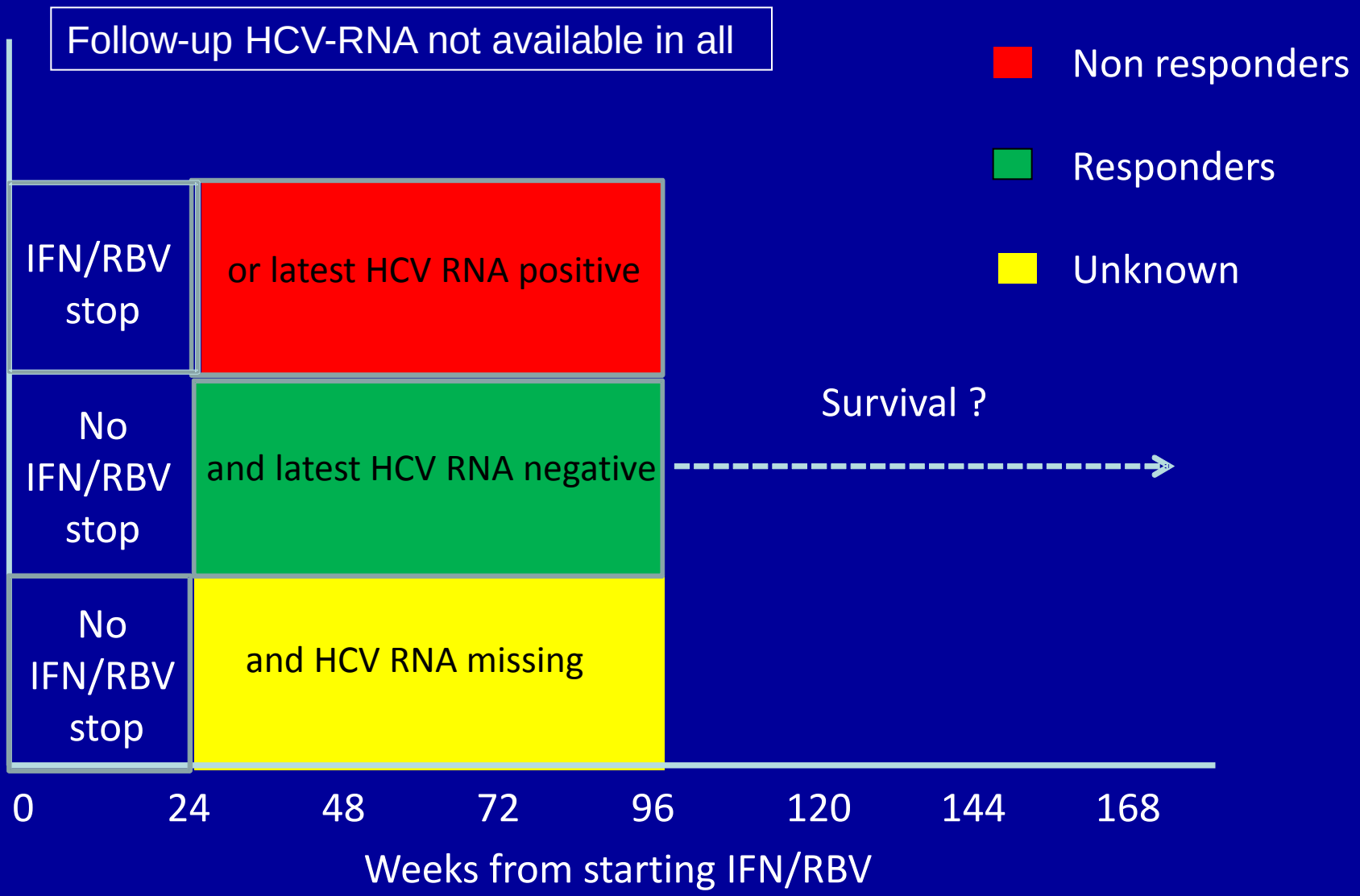
Methods

- The Collaboration of Observational HIV Epidemiological Research in Europe COHERE is a collaboration of 33 cohorts from across Europe and is part of the EuroCoord network
- Eighteen cohorts provided data for the present analysis.
- Analyses were based on data merged in July 2013

Inclusion criteria

- All HIV/HCV co-infected COHERE patients who had ever started interferon-based (IFN) therapy (baseline) and were followed-up for ≥96 weeks after baseline

Definition of HCV treatment response



Statistical methods

- Mortality rates in the three groups were compared using survival analysis.
- Survival times accrued from 96 weeks after baseline up to the date of death or last follow-up.
- Cox regression models were used to compare hazard ratios of death between response groups.

Results

- 3,500 patients had started HCV treatment and were included:
  - 996 (28.5%) responders
  - 1587 (45.3%) non-responders
  - 917 (26.2%) with unknown response

Patient characteristics at the date of HCV treatment initiation

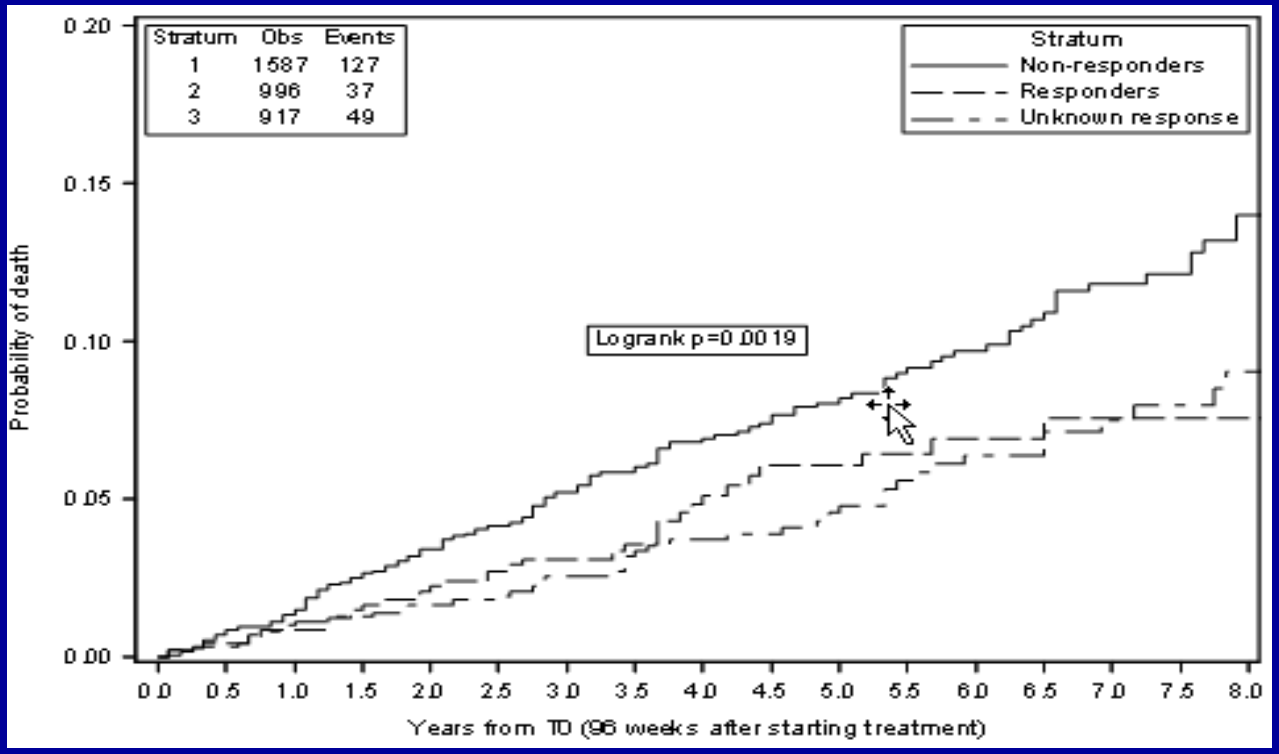
Characteristics	Responders N= 996	Non-responders N= 1587	Unknown response N= 917	p-value*	Total N= 3500
Age, median years (IQR)	42 (37, 46)	42 (37, 46)	41 (37, 46)	0.582	42 (37, 46)
Female, n (%)	209 (21.0%)	392 (24.7%)	210 (22.9%)	0.091	811 (23.2%)
Year of treatment initiation, median (IQR)	2007 (2005, 2009)	2005 (2003, 2007)	2005 (2002, 2007)	<.001	2006 (2003, 2008)
Injection drug use, n (%)	468 (47.0%)	1025 (64.6%)	581 (63.4%)	<.001	2074 (59.3%)
On ART, n (%)	838 (84.1%)	1387 (87.4%)	787 (85.8%)	0.065	3012 (86.1%)
CD4 count, median (IQR) cells/mm^3	461 (207, 653)	405 (167, 584)	453 (261, 620)	<.001	426 (203, 619)
HIV-RNA, median (IQR) log_{10} cp/mL	3.03 (2.00, 4.34)	3.05 (1.74, 4.15)	3.08 (1.94, 4.17)	0.411	3.05 (1.88, 4.17)
HCV RNA, median (IQR) log_{10} IU/mL	5.85 (5.11, 6.34)	6.04 (5.56, 6.60)	5.99 (5.60, 6.51)	<.001	5.95 (5.37, 6.51)
HCV genotype 1, n (%)*	262 (50.2%)	351 (62.2%)	138 (55.0%)	<.001	751 (56.2%)
HBsAg-positive, n (%)	87 (10.5%)	371 (33.8%)	23 (4.1%)	<.001	481 (19.3%)
APRI score, median (IQR)	0.9 (0.5, 2.1)	0.8 (0.5, 1.6)	0.8 (0.5, 1.4)	<.001	0.8 (0.5, 1.7)

*N with data: 1337

Incidence rates of all-cause death

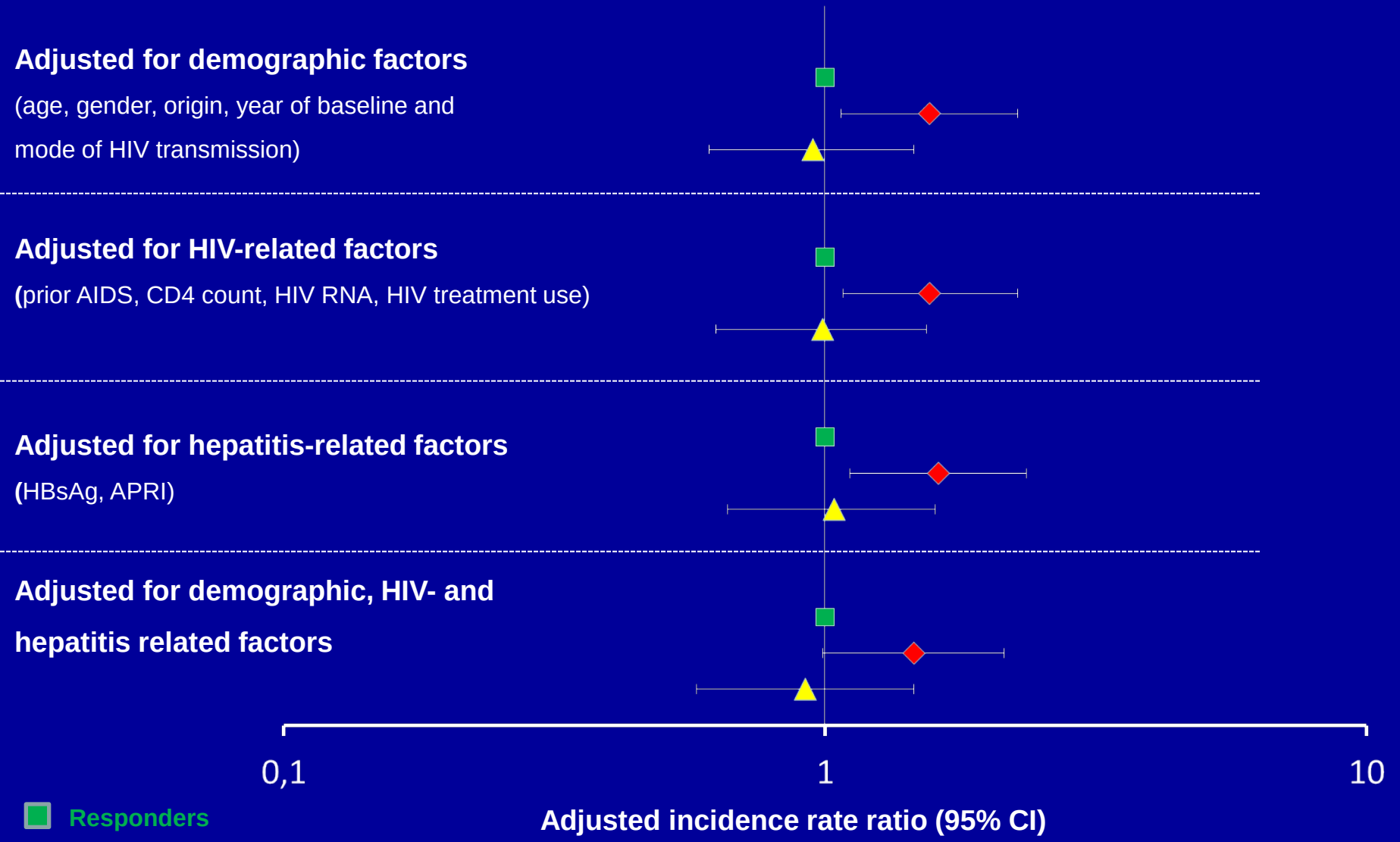
- After a median of 3.8 years of follow up, a total of 213 (6.1%) deaths had occurred.
  - The rates (per 1,000 PYFU, 95% CI) of all cause death were
    - 12.31 (10.35 - 14.65) for non-responders
    - 6.79 (4.92 - 9.37) for responders
    - 7.8 (5.86 - 10.26) for unknown responders

Cumulative risk of all-cause mortality



Non-responders	1587	1428	1222	998	814	626	479	334	201
Responders	996	818	646	472	342	256	174	114	65
Unknown response	917	828	736	632	518	408	308	225	151

Hazard ratio for all-cause death



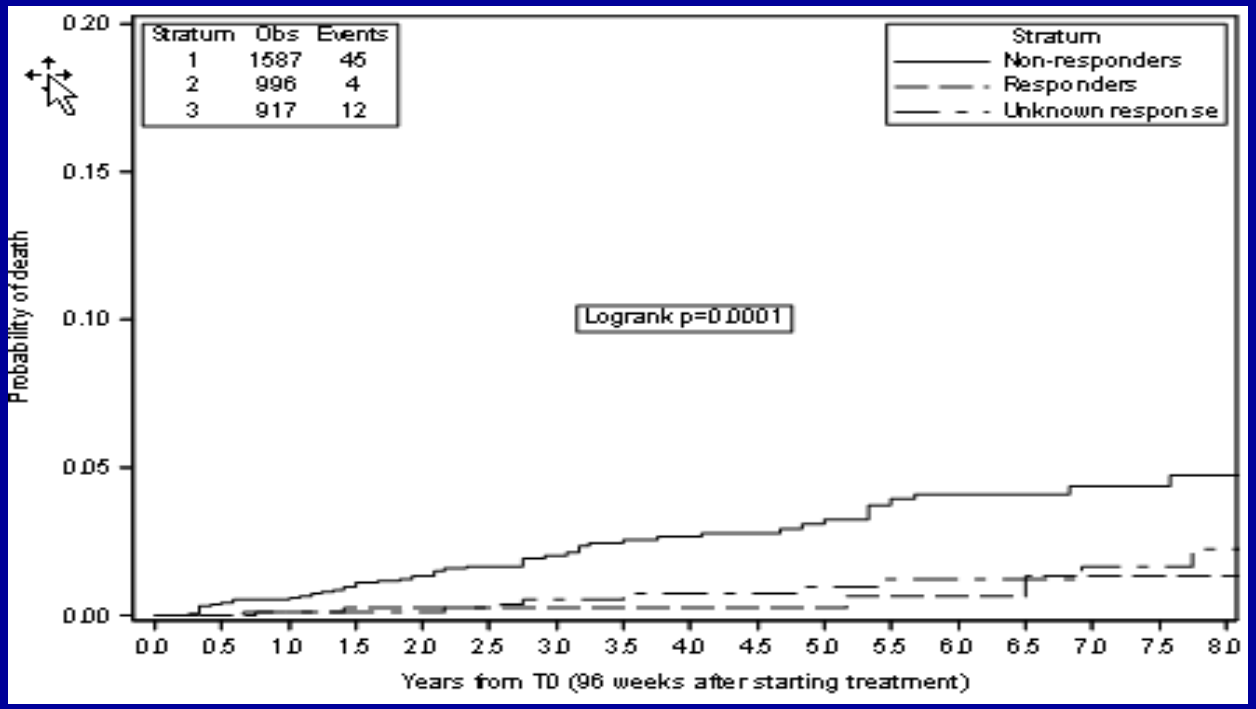
Incidence rates of liver-related death

- Liver-related death accounted for
  - 45/127 (35.4%) of all deaths among non-responders
  - 4/37 (10.8%) among responders
  - 12/49 (24.5%) among patients with unknown response

- Among responders with liver-related death, one out four had evidence of reinfection. None died from hepatocellular carcinoma

- Rates (per 1,000 PYFU, 95% CI) of liver-related death were
  - 4.17 (3.09 - 5.62) for non-responders
  - 0.73 (0.28 - 1.96) for responders
  - 1.9 (1.08 - 3.34) for unknown responders

Cumulative risk of liver-related death



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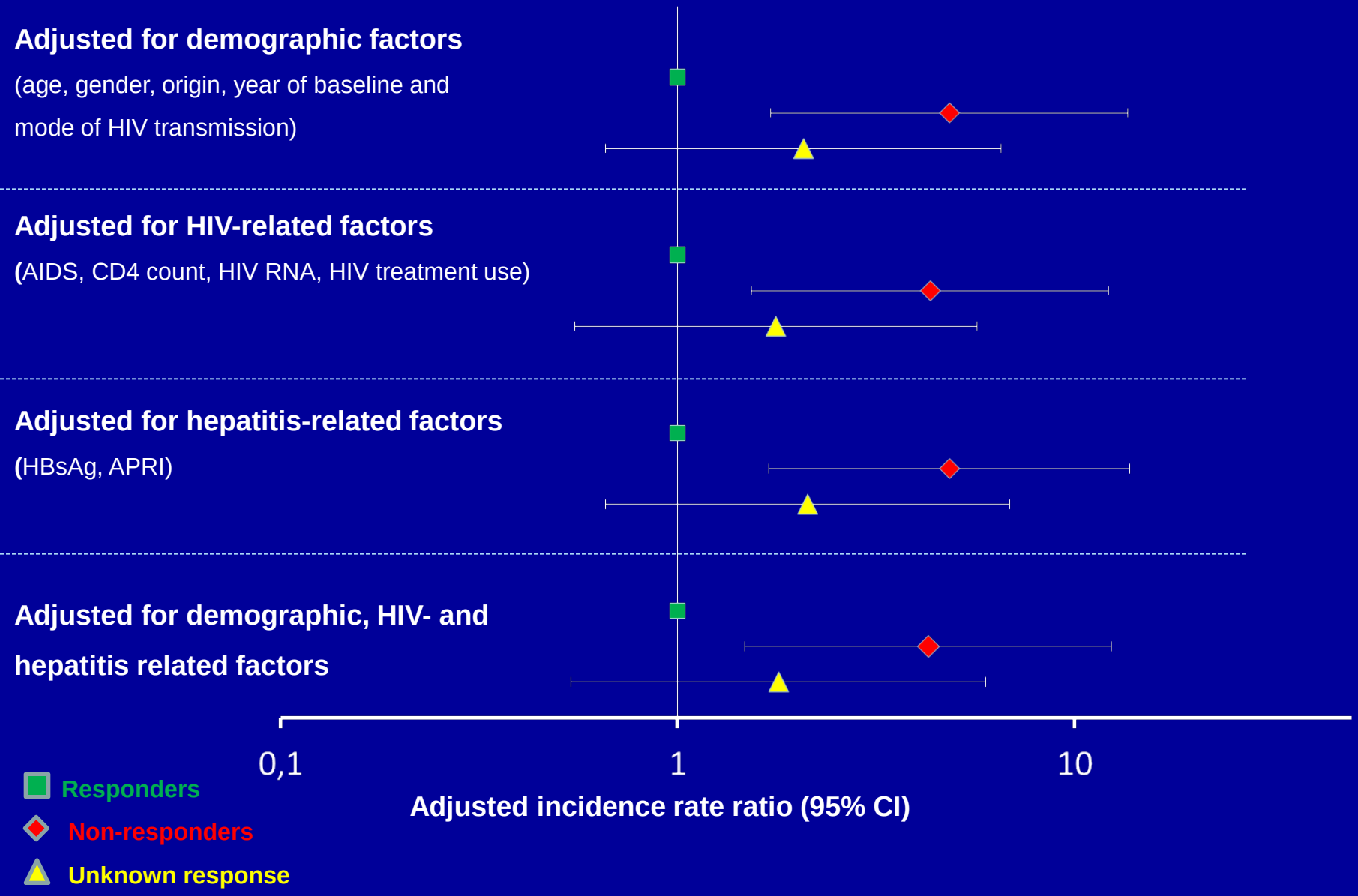

Non-liver-related mortality according to HCV treatment response

- All liver-related deaths excluded from analysis
- In unadjusted analysis there was no difference (non-responders vs. responders) in relative hazard of non-liver-related death (1.17, 95% CI 0.78 – 1.76).
- In fully adjusted model the relative hazard was 1.16 (95% CI 0.77 – 1.76)

Strengths and limitations

- Large prospective cohort study
- Lack of follow-up HCV-RNA measurements on all patients at least six months after end of therapy
  - some of the patients categorized as responders could have had HCV-RNA relapse
  - some patients categorized as non-responders could have achieved an SVR
- This limitation would only tend to underestimate the survival benefit of HCV therapy

Conclusions

- HIV/HCV co-infected patients with a favourable virological response to HCV treatment had
  - reduced risk of liver-related death and
  - improved overall survival

- There was no differences in risk of non-liver-related death between HCV treatment response groups

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Writing group

Lars Peters (EuroSIDA) Robert Zangerle (AHIVCOS),Giota Touloumi (AMACS), Frederic-Antoine Dauchy (AQUITAINE), Marc van der Valk (ATHENA), Gert Fätkenheuer (Cologne-Bonn), Antoni Noguera-Julian (CORISPE-cat), Juan Gonzales (CoRIS), Francois Dabis (HEPAVIH), Antonella Castagna (San Raffaele), Antonella d'Arminio Monforte (ICONA), Carlo Torti (MASTER), Christina Mussini (MODENA), Jordi Ceescat (PISCIS), Helen Kovari (SHCS), Stephane de Wit (St. Pierre), Jaime Cosin (VACH), Dorthe Raben (Copenhagen RCC), Genevieve Chene (Bordeaux RCC), Alessandro Cozzi-Lepri (EuroSIDA)

Steering committee:

Executive Committee: Stéphane de Wit (Chair, St. Pierre University Hospital), Jose Mª Miró (PISCIS), Dominique Costagliola (FHDH), Antonella d'Arminio-Monforte (ICONA), Antonella Castagna (San Raffaele), Julia del Amo (CoRIS), Amanda Mocroft (EuroSida), Dorthe Raben (Head, Copenhagen Regional Coordinating Centre), Geneviève Chêne (Head, Bordeaux Regional Coordinating Centre).).

Steering Committee - Contributing Cohorts: Ali Judd (AALPHI) Robert Zangerle (AHIVCOS),Giota Touloumi (AMACS), Josiane Warszawski (ANRS CO1 EPF/ANRS CO11 OBSERVATOIRE EPF), Laurence Meyer (ANRS CO2 SEROCO), François Dabis (ANRS CO3 AQUITAINE), Murielle Mary Krause (ANRS CO4 FHDH), Jade Ghosn (ANRS CO6 PRIMO), Catherine Leport (ANRS CO8 COPILOTE), Linda Wittkop (ANRS CO13 HEPAVIH), Peter Reiss (ATHENA), Ferdinand Wit (ATHENA), Maria Prins (CASCADE), Heiner Bucher (CASCADE), Diana Gibb (CHIPS), Gerd Fätkenheuer (Cologne-Bonn), Julia Del Amo (CoRIS), Niels Obel (Danish HIV Cohort), Claire Thorne (ECS), Amanda Mocroft (EuroSIDA), Ole Kirk (EuroSIDA), Christoph Stephan (Frankfurt), Santiago Pérez-Hoyos (GEMES-Haemo), Osamah Hamouda (German ClinSurv), Barbara Bartmeyer (German ClinSurv), Nikoloz Chkhartishvili (Georgian National HIV/AIDS), Antoni Noguera-Julian (CORISPE-cat), Andrea Antinori (ICC), Antonella d'Arminio Monforte (ICONA), Norbert Brockmeyer (KOMPNET), Luis Prieto (Madrid PMTCT Cohort), Pablo Rojo Conejo (CORISPES-Madrid), Antoni Soriano-Arandes (NENEXP), Manuel Battegay (SHCS), Roger Kouyos (SHCS), Cristina Mussini (Modena Cohort), Pat Tookey (NSHPC), Jordi Casabona (PISCIS), Jose M. Miró (PISCIS), Antonella Castagna (San Raffaele), Deborah_Konopnick (St. Pierre Cohort), Tessa Goetghebuer (St Pierre Paediatric Cohort), Anders Sönnerborg (Swedish InfCare), Carlo Torti (The Italian Master Cohort), Caroline Sabin (UK CHIC), Ramon Teira (VACH), Myriam Garrido (VACH). David Haerry (European AIDS Treatment Group)

Paediatric cohort representatives: Ali Judd, Pablo Rojo Conejo

•**European AIDS Treatment Group:** David Haerry.

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