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Acute HCV Treatment - European Perspective

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International HIV/Viral Hepatitis Co-Infection Satellite Meeting

18-19 July 2014
Melbourne, Australia

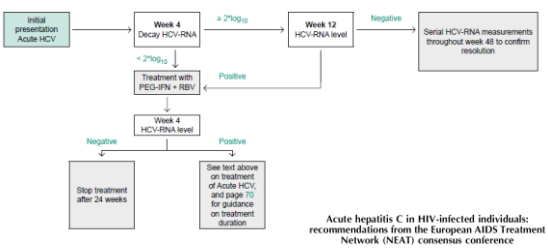
ashm
Supporting the HIV, Viral Hepatitis and Sexual Health Workforce

AIDS 2014

NEAT

EACS European AIDS Clinical Society

EACS Recommendations for treatment of acute HCV in HIV co-infection



Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference

The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel

AIDS 2011, 25:399–409

Clinical Practice Guidelines

CrossMark

EASL European Association for the Study of the Liver | JOURNAL OF HEPATOLOGY

EASL Clinical Practice Guidelines: Management of hepatitis C virus infection

European Association for the Study of the Liver*

Treatment of acute hepatitis C

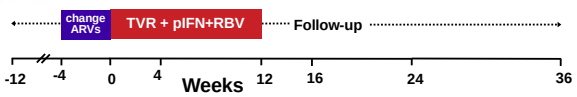
Consensus guidelines for the management of acute HCV in HIV-infected individuals were published in 2011 [151]. Regardless of infecting genotype, the guideline recommended the combination of pegylated IFN-α and weight-based ribavirin for treatment. Duration of treatment can be determined by kinetics of response, with 24 weeks of treatment given to those with serum RNA negativity at 4 weeks (RVR), and 48 weeks for those with first serum RNA negativity delayed beyond 4 weeks.

Journal of Hepatology **2014** vol. 60 | 392–420

Treatment strategies:
Beyond pegIFN + RBV

- pegIFN / RBV + HCV PI
  - Boceprevir
  - Telaprevir
- 1 DAA + RBV
  - Sofosbuvir + RBV
- 2 DAAs
  - Sofosbuvir + Ledipasvir

Telaprevir in AHC



	ETR	SVR 4	SVR 12	SVR 24
Total	16/19	16/19	16/19	16/19
Success rate	84%	84%	84%	84%

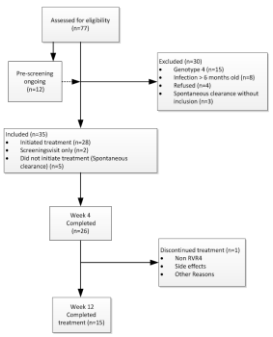
63% (30/48) in the comparator group:
Treated prior to the availability of, or ineligible for, telaprevir

Fierer et al., CID 2014

Current & future studies
with DAAs in acute HCV

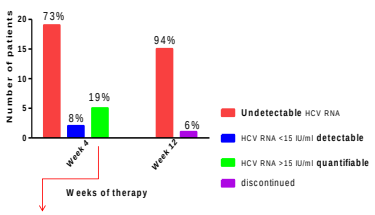
Study name	Coordinator	DAAs	HCV genotype	Duration (weeks)	HIV Status
DAHHS	Erasmus MC	BOC + pegIFN + RBV	1	12	pos
CHAT	UKB	TPV + pegIFN + RBV	1	12	pos
SWIFT-C	ACTG	SOF + RBV	all	8 vs. 12	pos
DARE C III	Kirby Institute	SOF + RBV	all	6	neg + pos
SOL	UKB	SOF + LDV	1, 4	6	pos
Hep-Net Acute HCV	MHH	SOF + LDV	1	6	neg

Dutch Acute HCV in HIV Study:
Boceprevir + pegIFN/RBV in AHC co-infection



Hullegie et al, 10th Co-Infection Workshop 2014, #O_02

Dutch Acute HCV in HIV Study:
On treatment responses



15,15,15,50,12400 IU/ml

Hullegie et al, 10th Co-Infection Workshop 2014, #O_02

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Clinical Protocol

NEAT

Section #1	
Study Title (Acronym)	An open label, randomised, non-inferiority trial of pegylated interferon, ribavirin and telaprevir versus pegylated interferon and ribavirin alone in the response guided treatment of acute hepatitis C genotype 1 virus infection in patients with HIV-1 co-infection (CHAT Study)
Protocol Date	January 16th 2013
Protocol Version	Version 9
Protocol Number	TPVAHC2012
Eudra-CT Number	2012-001419-21

Study design

THE CHAT STUDY

[A] patients who do not achieve an RVR will be treated for 48 weeks

[B] patients who do not achieve an RVR will be treated for 24 weeks (12 weeks TPV/Peg-IFN/RBV followed by 12 weeks Peg-IFN/RBV)

[C] patients with a HCV RNA > 1000 IU/ml at week 4 will be discontinued from Telaprevir and continued with Peg-IFN/RBV for additional 44 weeks

[D] patients who do not achieve a ≥ 2 $\log_{10}$ drop in HCV RNA at week 12 will stop treatment

[E] patients who do not achieve an undetectable HCV RNA at week 24 will stop

Interim analysis

THE CHAT STUDY

- 14 pts. screened (1 screening failure); UK: 9 pts
- SVR: 3 pts (arm 2)
- 4 ETR (2 arm 1, 2 arm 2)
- 1 Tx discontinuation due to AE (arm 2)
- 1 re-infection under Tx (arm 2)
- 4 virologic failures (2 arm 1, 2 arm 2)

CHAT patient: HCV kinetics

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HCV RNA Baseline: 10.852.811 IU/ml
HCV RNA Week 2: 355 IU/ml
HCV RNA Week 4: 28.762 IU/ml
HCV RNA Week 5: 996.909 IU/ml –> Tx discontinuation

2 reasons for non-response:
Reinfection -> again GT 1a infection
HCV PI resistence

Resistence analysis @ week 4

geno2pheno®

HCV resistance prediction from genotype (version 1.0)

II. Substitutions

NS3 region	V36M, T40A, V71I, Q80K, S91A, L153I, R155K

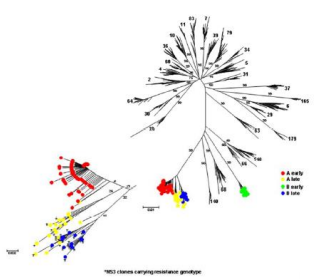
III. Resistance analysis

Drug	Prediction		Scored Mutations	Fold change
Boceprevir	resistant		36M,155K,80K	5.1
Telaprevir	resistant		36M,80K,155K	62
Simeprevir	resistant		80K,155K	420
Faldaprevir	resistant		36M,80K,155K	360

-> Pre-existent?

Detection of a Sexually Transmitted HCV Protease Inhibitor-Resistance Variant in a HIV-infected Homosexual Man

Sandra Franco[1], Cristina Tural[2-5], Maria Nevot[2], José Moltó[2-5], Jürgen Kurt Rockstroh[6], Bonaventura Clotet[1-5], and Miguel Angel Martinez[1]



To appear in: *Gastroenterology*
Accepted Date: 9 May 2014

Resistence analysis @ baseline

geno2pheno®

HCV resistance prediction from genotype (version 1.0)

II. Substitutions

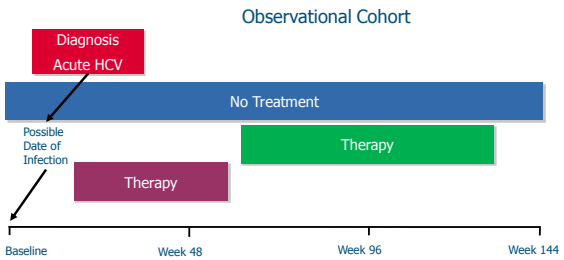
NS3 region	T40A, V71I, Q80K, S91A, L153I

III. Resistance analysis

Drug	Prediction		Scored Mutations	Fold change
Boceprevir	susceptible		none	-
Telaprevir	susceptible		none	-
Simeprevir	resistant		80K	14
Faldaprevir	resistant		80K	2.2

HCV RNA Baseline: 10.852.811 IU/ml

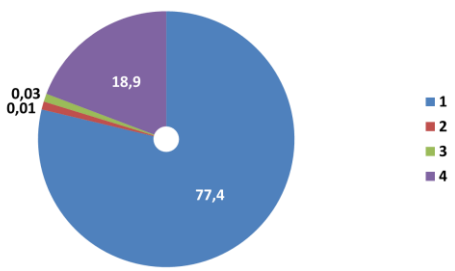
PROBE-C Study



probec@ukb.uni-bonn.de

HCV Genotype Distribution

478 AHC episodes in 459 pts. (19 reinfections)



Interim analysis

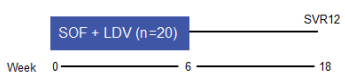
- Spontaneous clearance in 12.7%, in 58,4% (279/478) treatment was initiated
- 278 pegIFN + RBV
- 1 SOF + RBV (GT2)
- SVR: 68% (83/122)

Studies with 2 DAAs

NEAT Clinical Protocol neatid

Section #1	
Study Title (Acronym)	A pilot trial of **so**fosbuvir and **l**edipasvir for 6 weeks in the treatment of acute hepatitis C genotype 1 and 4 infection in patients with HIV-1 co-infection (**SOL** Study)
Protocol Date	June 1st, 2014
Protocol Version	Version 2
Protocol Number	n/a
Eudra-CT Number	n/a
Sponsor	NEAT ID Foundation, London House, 266 Fulham Road, London SW10 9EL, UK

SOL study design



ACTG: SOF + LDV for 12 wks (if successful -> 8 wks)

2015+

But, in the meantime …

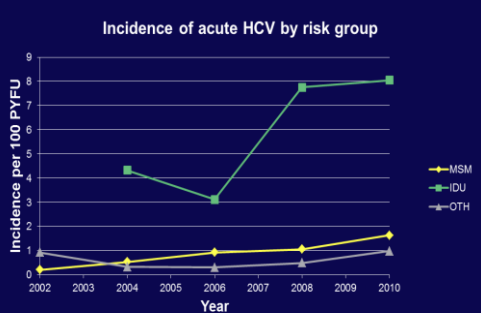
Rapid fibrosis progression after AHC?

	Median age [years] (IQR)	Transmission risk [%]		Median CD4-cells [/µl] (IQR)	HIV-RNA <50copies /ml [%]	cART [%]	Median HCV-RNA [IU/ml] (IQR)	HCV-RNA >800.000 IU/ml [%]	HCV-Genotype [%]		Median maximum ALT [U/l] (IQR)	Clinical symptoms* [%]	Median Fibrosis Score [kPa] (IQR)	Median Follow-up [weeks] (IQR)
		MSM	IVDU						1	4				
All (n=41)	43 (37-47)	97.6	2.4	491 (360-736)	85	95	1.989.500 (633.000-6.670.000)	72.5	78	22	401 (153-616)	20	8 (5.9-10.2)	179 (120-276)

Years since AHC diagnosis (# of available measurements)	1 (n=20)	2 (n=23)	3 (n=17)	4 (n=14)	5 (n=10)	6 (n=3)	7 (n=4)	8 (n=3)
Median liver stiffness [kPa] (IQR)	7.7 (6-10)	7.0 (6-10)	6.3 (5-8)	6.4 (5-8)	4.4 (4-5)	7.7 (6-20)	7 (5.1-10)	8 (5-49.6)

Boesecke C et al, CROI 2014

AHC Incidence in HIV+ MSM

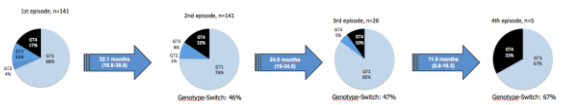


Interaction between transmission group and year p-value=0.044

EuroSIDA in EuroCoord

Rockstroh, JIAS 2012

HCV Reinfection in HIV+ MSM



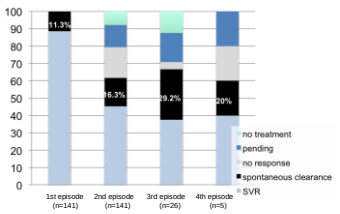
553 patients from 7 NEAT centers with cured acute HCV since 6/2001

141 with at least one reinfection (25.5%)

1509 patient-years of FU, median 2.1 years

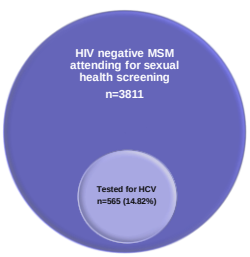
Incidence rate: 7.82/100 patient-years

Treated patients: 7.9/100 patient years
Spontaneous clearers: 3.3/100 patient-years



Ingiliz et al, EASL 2014, Martin et al, AIDS 2013

Acute HCV in HIV negative MSM



Nelson M, 10th Co-Infection Workshop 2014