Therapeutic strategies for acute HCV
Past, current and future:
an Australian perspective

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Therapeutic strategies for acute HCV

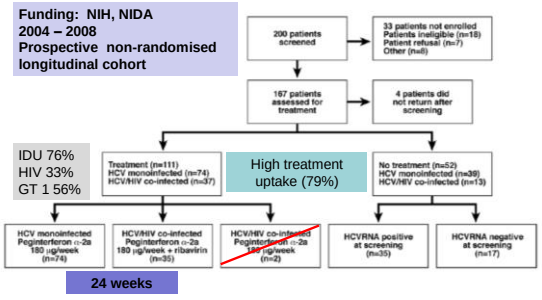
Key issues

- Small proportion of HCV infections diagnosed during acute phase
- Potential for "over-treatment" of spontaneous clearance cases
- Slow disease progression in chronic HCV infection
- IFN-based treatment outcomes superior in acute HCV
- Rapid development of HCV DAA therapy
- Potential for 'treatment as prevention'

ATAHC I: Australian Trial in Acute Hepatitis C

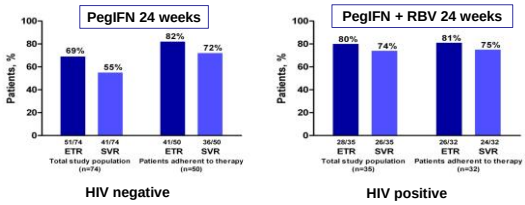
Funding: NIH, NIDA
2004 – 2008
Prospective non-randomised longitudinal cohort

IDU 76%
HIV 33%
GT 1 56%



High treatment uptake (79%)

ATAHC I: Treatment outcomes



HIV negative **HIV positive**

Low rate of re-infection (n = 7, 4.3%)

ATAHC recall: re-infection incidence 1.7/100py (95%CI 0.6—4.5)

Dore GJ et al. Gastroenterology 2010;138:123-135, Doyle IAC 2014

Current guidelines for acute treatment

- EASL 2014
  - PEG (+RBV if HIV) : 24 weeks
- AASLD
  - Due summer 2014
- EACS (HIV)
  - PEG/RBV : 24 weeks if RVR, 48/individualise if no RVR
- BHIVA (HIV)
  - PEG/RBV : 24 weeks if RVR, 48 weeks if no RVR

Ongoing and future studies in recently acquired HCV
ATAHC II, DARE-C I and II, REACT

ATAHC II

NIH R01 renewal grant 2010 – 2015

ATAHC entry criteria – estimated duration up to 18 months
Planned 120 subjects, including HIV positive and negative

Individualized response guided therapy

- PEG for acute HCV mono
- PEG/RBV for early chronic HCV mono and HIV co-infection

	HCV RNA BDL at:	Duration therapy
Group A	Week 2	8 weeks
Group B	Week 4	16 weeks
Group C	Week 6	24 weeks
Group D	Week 8	36 weeks
Group E	Week 12	48 weeks

DARE-C I: DAA-based therapy for recently acquired HCV

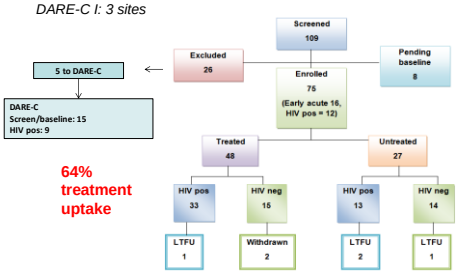
Sub-study of ATAHC II
February 2012 – July 2014

Prospective open label multi-centre pilot study
Response guided therapy: PEG/RBV/TVR
Genotype 1
Early chronic infection (estimated duration 6-18 months)
HIV negative and HIV positive; n=20

	HCV RNA BDL at:	Duration
Group A	Week 2	8 wks PEG/RBV/TVR
Group B	Week 4	12 wks PEG/RBV/TVR
Group C	Week 8	12 wks PEG/RBV/TVR + 12 wks P/R

ATAHC II and DARE-C I: Progress

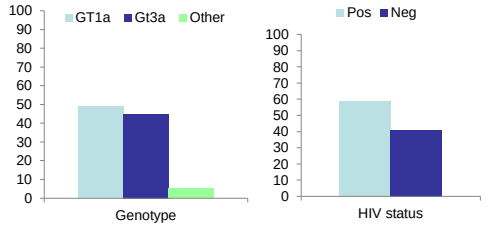
ATAHC II: Enrolment commenced late 2011; 8 sites
DARE-C I: 3 sites



64% treatment uptake

Aim to complete enrolment June 2014

Genotype and HIV distribution



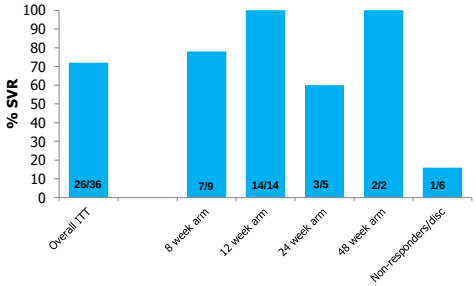
- Median estimated duration of infection 35 weeks
- Predominant modes of infection: IDU 60% and sexual 33% (partner of the same sex of unknown HCV status)

Treatment duration allocation

Group	Duration of treatment	No. (n=48)
A	8 wks	12 (25%)
B	16 wks	15 (31%)
C	24 wks	9 (19%)
D	32 wks	0
E	48 wks	2 (4%)
Non-responder		5 (10%)
Discontinued/withdrew		4 (8%)
Duration pending		1 (2%)

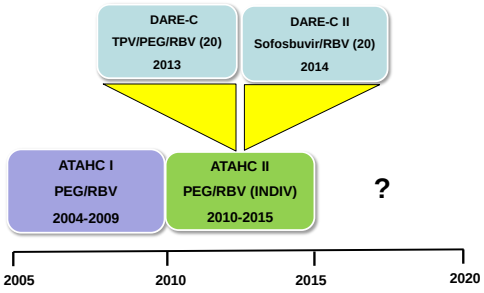
58% allocated to shortened therapy arms (8 or 16 weeks)

Interim SVR 12 results



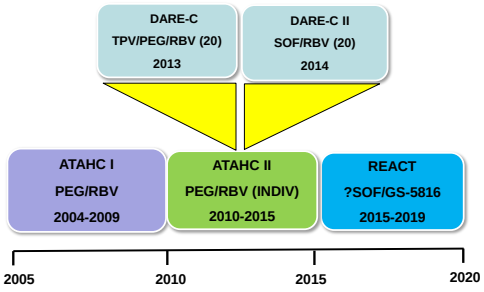
DARE-C II: DAA-based therapy for recently acquired HCV

- Sub-study of ATAHC II
- June 2014 – June 2015
- Prospective open label multi-centre pilot study
- Short course IFN-free therapy
- Sofosbuvir + ribavirin (weight-based) for 6 weeks
- Acute and early chronic infection (</= 12 months)
- HIV negative and HIV positive
- N = 20



Acute HCV: Future directions

- Highly potent, pan-genotypic IFN-free regimens
- No individualization
- Very short course therapy (4-8 weeks) : ? shorter
- Potential for significant individual and population level benefits
- Treatment as prevention?



? REACT

A Randomised Controlled trial of IFN-free therapy for HEpatitis C during Recent infection

- International multicentre RCT 2015 - 2020
  - Australia, Canada, US, Europe
- Short (4/6 wks) vs standard (8/12 wks) IFN-free DAA-based therapy for recent HCV infection
- ? Sofosbuvir + GS5816
- Non-inferiority design, n= 250
- Primary endpoint: SVR12
- Primary AND re-infections
- Nested substudies – immunology/behavioural etc