HEPATITIS C VIRUS CORE ANTIGEN: A SIMPLIFIED TREATMENT MONITORING TOOL AMONG THOSE WITH RECENT HCV INFECTION, INCLUDING FOR POST-TREATMENT RELAPSE

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Introduction

❑ Simplified, affordable diagnostic tools are essential to facilitate global access to interferon-free directly acting antiviral (DAA) hepatitis C virus (HCV) treatment.

❑ Tools to monitor treatment response and recurrent viraemia due to relapse or reinfection remain critical.

❑ HCV core antigen (HCVcAg) provides an alternative tool to detect active HCV viraemia in recent HCV infection

Aim

To prospectively evaluate the clinical performance of HCV core antigen detection in plasma to monitor HCV treatment efficacy and recurrent viraemia among those with recent HCV infection

Method

Study participants: The DARE-C II study

(Martinello M, Hepatology 2016, doi: 10.1002/hep.28844)

❑ Participants from DARE-C II (NCT0215670), an open label pilot study conducted in Australia and New Zealand to assess the efficacy of sofosbuvir and ribavirin for six weeks in adults with recent infection, were eligible.

❑ Recent infection was defined as duration of infection <12months, with initial HCV anti-HCV antibody and/or HCV RNA within 6 months of enrolment and either
- (i) recent HCV seroconversion (anti- HCV antibody negative result in the 18 months prior to enrolment), or
- (ii) acute clinical hepatitis within the previous 12 months

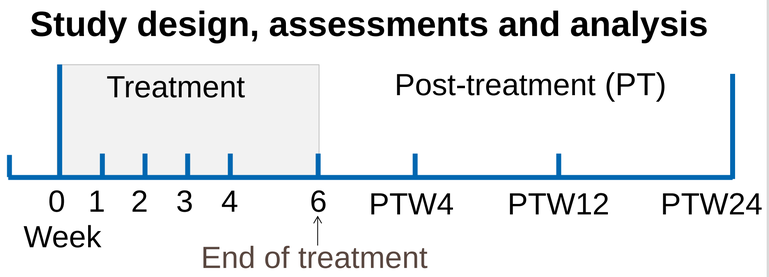

***Figure 1:* Study design and assessments.** HCV RNA and HCVcAg were assessed at baseline, on weeks 1, 2, 3, 4, 6, and post-treatment (PT weeks 4, 12, 24).

❑ RNA in plasma - AmpliPrep/COBAS Taqman assay (Roche). Lower limit of quantitation 15IU/mL (Gold standard)

❑ Core antigen - ARCHITECT HCV Ag (Abbott Diagnostics). Lower limit of detection 12 fmol/L

❑ Samples having HCVcAg from 3-10 fmol/mL (ie. the "grey-zone") were retested where sample was available

❑ The sensitivity (true positives) and specificity (true negatives) of HCVcAg assay (>3fmol/L) were calculated for quantifiable HCV RNA (>15IU/mL)

Results

Participants characteristics: 19 DARE-C II participants were included. The median age was 41 (IQR 31-50), 89% were male, 68% had genotype 1a, and 74% had HIV coinfection. HCV was acquired via injection drug use (53%) and sexual exposure in men who-have-sex-with-men (MSM) (47%). Median estimated duration of infection at screening was 32 (range 9–51) weeks. Twelve participants demonstrated virological failure: two non-response, nine post-treatment relapse and one reinfection. One participant was lost to follow up at week 2.

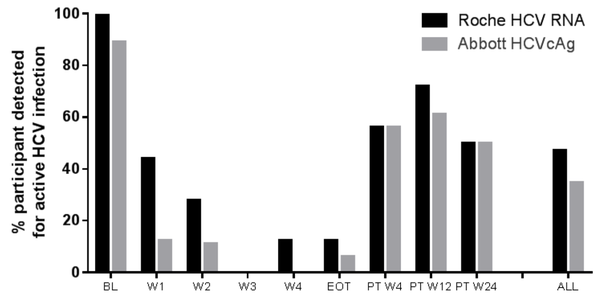

***Figure 2:* Percentage of participants detected for active HCV infection in the DARE-C II study.** Active infection is detected either quantifiable HCV RNA by - AmpliPrep/COBAS Taqman assay (Roche) or HCVcAg ARCHITECT HCV Ag (Abbott Diagnostics)detectable

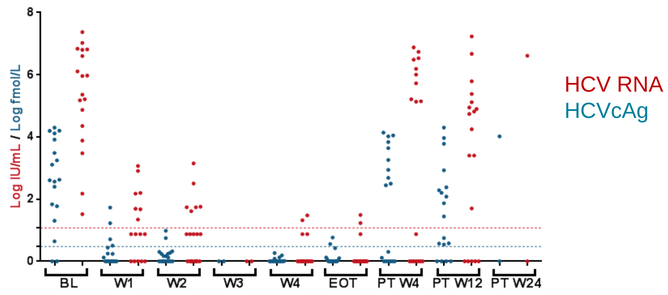

***Figure 3:* Distribution of HCV RNA and core antigen levels at each on treatment and post-treatment timepoint.** Horizontal lines represent the limit of quantification of HCV RNA (red line, 15IU/mL) and reactive core antigen levels (blue line, 3fmol/L).

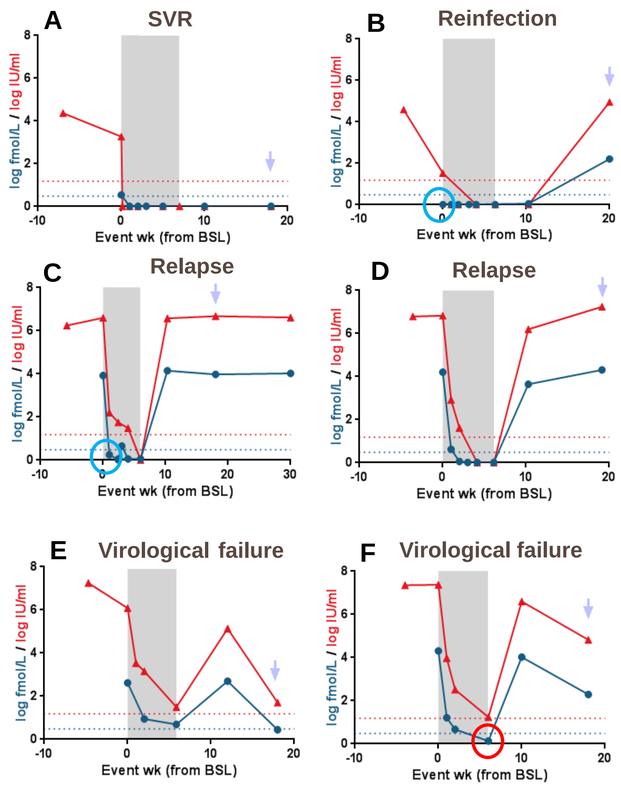

***Figure 4:* RNA and core antigen levels in a subset of patients during treatment (grey box) and post-treatment follow-up.** Example of patients with SVR (A), reinfection (B) relapse (C and D) and virological failure (E and F). Participant from panel 4F had detectable HCV RNA and negative core antigen at end of treatment. Time points at which HCV RNA was detectable, but HCVcAg was not, are highlighted at baseline (blue circle) and EOT (red circle). PT W12 is shown by the arrow.

For those samples not detected by HCVcAg at baseline (n=2) and EOT (n=1), low level HCV RNA was quantifiable (baseline: 33 and 150 IU/mL, EOT: 17 IU/mL), as highlighted in Figure 4 and Table 1.

***Table 1:* The numbers of samples detectable by HCVcAg (≥3fmol/L) and quantifiable by HCV RNA in participants.**
HCVcAg non-detected: NR: Non-responder R: Relapse

	HCV RNA (≥15IU/mL)	ND VL (<15IU/mL)	Sensitivity (Lower and upper limit)	Specificity (Lower and upper limit)
Baseline n=18	**18**	**0**		
HCVcAg det (≥3fmol/L)	16	0	88.9	NA
HCVcAg ND (<3fmol/L)	2	0	(63.9-98.1)	NA
Week 4 n=16	**2**	**14**		
HCVcAg det (≥3fmol/L)	0	0	0	100
HCVcAg ND (<3fmol/L)	2 (NR / R)	14	(0-80.2)	(73.2-100)
ETR n=16	**2**	**14**		
HCVcAg det (≥3fmol/L)	1	0	50.0	100
HCVcAg ND (<3fmol/L)	1 (NR)	14	(2.7-97.3)	(73.2-100)
PT W4 n=18	**10**	**8**		
HCVcAg det (≥3fmol/L)	10	0	100	100
HCVcAg ND (<3fmol/L)	0	8	(65.5-100)	(59.8-100)
PT W12 n=18	**13**	**5**		
HCVcAg det (≥3fmol/L)	11	0	84.6	100
HCVcAg ND (<3fmol/L)	2 (NR / R)	5	(53.7-97.3)	(46.3-100)
PT W24 n=2	**1**	**1**		
HCVcAg det (≥3fmol/L)	1	0	100	100
HCVcAg ND (<3fmol/L)	0	1	(5.5-100)	(5.5-100)
All timepoints n=124	**58**	**66**		
HCVcAg det (≥3fmol/L)	43	1	74.1	98.5
HCVcAg ND (<3fmol/L)	15	65	(60.7-84.4)	(90.7-99.9)

Conclusion

These preliminary data indicate core antigen

❑ **May be used to diagnose recent HCV infection in a new diagnostic clinical algorithm where a confirmatory RNA tests would be required for HCVcAg negative results among those considered at high risk.**

❑ **Consistently demonstrated high specificity when compared with HCV RNA**

❑ **Demonstrated lower sensitivity, which may provide a clinical advantage while monitoring treatment.**

❑ **Accurately identifies post-treatment viraemia, including first detection of relapse at PT WK4 (n = 1) or PT W12 (n=8), and reinfection at PT WK 12 (n = 1).**

❑ **Core antigen may facilitate HCV treatment scale-up, including low and middle income countries**

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