SMART-C

Simplified Monitoring – A Randomised Trial in hepatitis C

A phase IIIb, open-label, multicentre, international randomised controlled trial of simplified treatment monitoring for 8 weeks glecaprevir (300mg)/pibrentasvir (120mg) in chronic HCV treatment naïve patients without cirrhosis

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Laboratory Manual

Study Specific Supplement
Version and Date:
Version 1.0
17 August 2017

Table of Contents

1 Communication, Contacts and Summary of Procedures

Project Team Contact details:

Position	Name	Phone	Email
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Laboratory Coordinator	Danica Martinez	+61 2 9385 0203	dmartinez@kirby.unsw.edu.au
Study Email	smartc@kirby.unsw.edu.au		

For all protocol, study or site management related questions, please contact your Project Coordinator.

For laboratory specific questions please contact the Laboratory Coordinator

2 Study and Participant Identifiers

Protocol number: 1701 (used in participant ID number from baseline onwards)

Screening Number: 333 (used in screening ID at screening visit only)

At sites where regulations restrict the collection of participant's full date of birth and/or initials, the following conventions will be used:

- Date of birth will be entered as 01/01/YYYY

- Initials will be entered as AA-AA, BB-BB, CC-CC etc.

3 Protocol Synopsis

Rationale	Current standard on-treatment monitoring in clinical trials involves clinic-based visits every 4 weeks. In the DAA era where treatments are highly tolerable, effective and short duration, this intensive monitoring strategy may no longer be required. A simplified on-treatment monitoring strategy is hypothesised to be non-inferior to the standard clinical trial on treatment monitoring strategy. If successful, a simplified on-treatment monitoring strategy is likely to be highly attractive to patients, clinicians and health care payers. It has the potential to improve the rapid scale up of treatment providing population level benefits in the reduction of global hepatitis C disease burden.
Study Design	Phase IIIb, randomised, controlled, multicentre, international trial.

	Eligible patients will be randomised into one of two on-treatment monitoring strategies; standard clinical trial monitoring (4-weekly on-treatment visits) vs simplified monitoring (no on-treatment visits). Randomisation will be 1:2 (standard vs simplified) and all participants will receive treatment with glecaprevir (300mg)/pibrentasvir (120mg) for 8 weeks.
Primary Objective	To compare the proportion of participants with undetectable HCV RNA (HCV RNA <LLOQ) at 12 weeks post-treatment (SVR12) following 8 weeks treatment with glecaprevir (300mg)/pibrentasvir (120mg) in HCV treatment naïve non-cirrhosis chronic HCV patients who have received a standard versus simplified schedule of safety and virological monitoring
Hypotheses	In treatment naïve non-cirrhosis patients with chronic HCV (genotypes 1-6) the sustained virological response rate 12 weeks following treatment with glecaprevir (300mg)/pibrentasvir (120mg) among those receiving a simplified monitoring schedule will be non-inferior to that in those receiving a standard monitoring schedule based on the intention-to-treat (ITT) population.

4   Specimen collection and documentation

The following samples are collected for research at the time points specified below.

Visit Name	EDTA Whole Blood (4mL)	EDTA Plasma (10mL)	EDTA Plasma (20mL)	PBMC* (60mL)	Visit Abbreviation	Kit Type
Screening	X		X	X	SCR	1
Baseline			X		BSL	2
Week 4		†		†	WK4	3
EoT (Week 8)		†			EoT	3
SVR12 (Week 20)		X		X	SVR12	3

Key:

X Collected from all participants (i.e. both study arms)

† Collected from standard monitoring arm only

* At selected sub-study sites only

4.1   Lab Kit Descriptions

The 3 lab kit types for SMART-C are described in the following table.

	Kit Type 1	Kit Type 2	Kit Type 3
Visits	**SCR**	**BSL**	**WK4/EoT/SVR12**
All Sites	1 x Laboratory Request Form 3 x specimen tube label 1 x spare cryovial label 1 x spare site log cryovial label	1 x Laboratory Request Form 2 x specimen tube label 1 x spare cryovial label 1 x spare site log cryovial label	1 x Laboratory Request Form 1 x specimen tube label 1 x spare cryovial label 1 x spare site log cryovial label

	EDTA Collection 2 x 10mL EDTA blood collection tubes 8 x 1.8mL cryovials (purple top) 8 x EDTA Plasma cryovial labels *Whole Blood Collection* 1 x 4mL EDTA whole blood collection tube 2 x 1.8mL cryovials (red top) 2 x EDTA Whole Blood cryovial labels	*EDTA Collection* 2 x 10mL EDTA blood collection tubes 8 x 1.8mL cryovials (purple top) 8 x EDTA Plasma cryovial labels	*EDTA Collection* 1 x 10mL EDTA blood collection tube 4 x 1.8mL cryovials (purple top) 4 x EDTA Plasma cryovial labels
Sub-study Sites	As above with the addition of: *PBMC Collection:* 6 x 10mL ACD blood collection tubes 6 x 1.8mL cryovials (yellow top) 6 x PBMC cryovial labels		For WK4 and SVR12 visit only, as above with the addition of: *PBMC Collection:* 6 x 10mL ACD blood collection tubes 6 x 1.8mL cryovials (yellow top) 6 x PBMC cryovial labels

4.2   Sample Storage

Sites will be supplied with 10x10 cryoboxes for sample storage. EDTA Plasma AND EDTA whole blood samples must be stored at -80°C. PBMC samples (if applicable) must be stored in vapour phase tanks at -200°C. You are required to keep a daily temperature log for the freezer/tank where the samples are stored. You can document this with your local laboratory freezer temperature log or the temperature log provided. Your SMART-C Project Coordinator must be notified as soon as possible of any deviations above -60°C for samples that are stored at -80°C (EDTA plasma, EDTA whole blood), or a vapour phase tank failure for PBMC samples stored at-200°C, using the sample storage temperature deviation form (see ATTACHMENT A**B**).

You will be provided with a file note to document where the samples are stored and who is responsible for maintaining the samples (see ATTACHMENT A).

It is essential that you complete the number and types of samples stored, box number and position of samples and confirmation of sample tracking in LabKey Offsite Repository. The comments section can be used to record any details of problems with the sample. Refer to the VHCRP Local Laboratory Manual for instructions on using LabKey.

4.3   Laboratory Request Form

The laboratory request form differs depending on the study visit (i.e. Screening Visit or any other visit) and whether or not the site is participating in the sub-study. Samples of laboratory request forms are shown in ATTACHMENT C. The top half of the form should be completed by the person responsible for blood collection. The bottom half of the form is to be completed by the person responsible for processing and storage of the samples.

5   LabKey Visit Name

The visit name for the end of treatment appears as ETR on the LabKey repository. For all specimens related to EoT from SMART-C participants (as noted on labels and request forms), please enter them into LabKey using the ETR visit name.

6   Sample Shipping

Samples are to be stored at the processing site until the conclusion of the study. The SMART-C Project Coordinator will arrange the shipment of samples to Sydney Australia and will contact you to arrange a suitable date and provide all shipping instructions and materials.

7   ATTACHMENT A: ISF file note for sample storage

SMART-C

Protocol Title: A phase IIIb, open-label, multicentre, international randomised controlled trial of simplified treatment monitoring for 8 weeks glecaprevir (300mg)/pibrentasvir (120mg) in chronic HCV treatment naïve patients without cirrhosis

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ISF FILE NOTE

Hospital Name:

EDTA plasma and EDTA whole blood samples must be stored at -80 °C (-112 °F) and PBMCs samples must be stored at -200 °C (-328 °F). It is the responsibility of the site principal investigator or designee to ensure that the study central laboratory specimens are stored appropriately.

- A daily temperature log for the freezer where the specimens are stored is

  maintained by: _____

  located at: _____

- The freezer is alarmed and a procedure is in place to ensure continued correct storage of the specimens should the freezer fail. The procedure is: _____

  _____

  _____

- The SMART-C Coordinating Centre will be notified as soon as possible of any deviations above at -60 °C (-76 °F) for EDTA plasma and EDTA blood samples or a vapour phase tank failure for PBMCs samples, using the sample storage temperature deviation form as per the Manual Of Operations (MOOP)

Name: _____ Signature: _____ Date: _____

Monitor: _____ Signature: _____ Date: _____

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8   ATTACHMENT B: SAMPLE STORAGE DEVIATION FORM

LABORATORY SAMPLE STORAGE
TEMPERATURE DEVIATION FORM

Please **SCAN and EMAIL** this notification to HepBank: HepBank@kirby.unsw.edu.au

Site_____   Investigator_____

Date of start of temperature deviation	_ _ / _ _ _ / _ _ _ _ (dd/mon/yyyy)
Sample affected by temperature deviation	☐ -80°C EDTA plasma; EDTA whole blood ☐ -200°C PBMCs
Duration of temperature deviation	
Maximum temperature reached (°C)	
Action taken	

PLEASE ATTACH AN UP-TO-DATE LABORATORY SAMPLE STORAGE TEMPERATURE LOG

_____

Signature of person reporting deviation   **Date**

9 ATTACHMENT C: Laboratory Request Form (SCR) – NON SUB-STUDY SITE

SMART-C

Study Nurse/Coordinator to complete

For Clinic use only

Screen ID: 333 – __ __ __	**Subject initials:** ___ ___ / ___ ___ Last name First name

Date of Birth: (Format: 23/NOV/2009) ___ ___ / __ ___ / ___ ___ ___ **Collectors' name:** _____

Date of Collection: (Format: 23/NOV/2009) ___ ___ / __ ___ / ___ ___ ___ **Collection Time:** (Format: 24 hour time, e.g. 15:30) ___ ___ : ___ ___

Visit: (Please tick box)

☐ SCR	2 x 10mL EDTA 1 X 4mL Whole Blood	

Comments:

Laboratory staff to complete

For processing site use only

Specimen received: Date:___ / __ ___ / ___ ___ ___ (e.g. 23/NOV/2009) Time: ___ ___ : ___ ___ (e.g. 15:30)

Specimen processed: Date:___ / __ ___ / ___ ___ ___ (e.g. 23/NOV/2009) Time: ___ ___ : ___ ___ (e.g. 15:30)

Samples stored: _____ x 1mL + 1 x _____ mL EDTA plasma in round bottom cryotube vials   Stored at -80°C ☐
Box #:____ Positions: _____

(Please tick boxes) _____ x 1.8mL + 1 x _____ mL EDTA whole blood in round bottom cryotube vials   Stored at -80°C ☐
Box #:____ Positions: _____

Samples specific comments:

Data recorded in LabKey ☐   **Processed by:** (Name and signature)

SITE KEEP YELLOW COPY - LABORATORY KEEP PINK COPY
WHITE COPY TO BE SENT TO KIRBY LABORATORY UPON INSTRUCTIONS

STORE THIS COMPLETED FORM IN YOUR STUDY BINDER.
DO NOT SHIP SAMPLES UNTIL REQUESTED BY THE SMART-C COORDINATOR

Laboratory Contact: HepBank@kirby.unsw.edu.au

SMART-C Research Assistant +61 2 9385 0203, smartc@kirby.unsw.edu.au

10 ATTACHMENT D: Laboratory Request Form (BSL/WK4/WK8 OR SVR12) – NON SUB-STUDY SITE

SMART-C

For Clinic use only

Subject Study No.: 1701 – _ _ _ _ _ _ – _ _   **Subject initials:** _ _ / _ _
                                                                                          Last name First name

Date of Birth:
(Format: 23/NOV/2009)   _ _ / _ _ _ _ / _ _ _ _   **Collectors' name:** _____

Date of Collection:
(Format: 23/NOV/2009)   _ _ / _ _ _ _ / _ _ _ _   **Collection Time:**
                                                    (Format: 24 hour time, e.g. 15:30)   _ _ _ : _ _

Visit: (Please tick box)

☐ **BSL**	2 x 10mL EDTA	
Screen ID: 3 3 3- _ _ _		
☐ **WK4** (standard arm only)	1 x 10mL EDTA	
☐ **EoT (WK8)** (standard arm only)	1 x 10mL EDTA	
☐ **SVR12**	1 x 10mL EDTA	

Comments:

For processing site use only

Specimen received: Date: _ _ / _ _ _ _ / _ _ _ _ (e.g. 23/NOV/2009)   **Time:** _ _ _ : _ _ _ (e.g. 15:30)

Specimen processed: Date: _ _ / _ _ _ _ / _ _ _ _ (e.g. 23/NOV/2009)   **Time:** _ _ _ : _ _ _ (e.g. 15:30)

Samples stored: _____ x 1mL + 1 x _____ mL EDTA plasma in round bottom cryotube vials   Stored at -80°C ☐

Box #: ____ Positions: _____

(Please tick box)

Samples specific comments:

Data recorded in Labkey	☐	Processed by: (Name and signature)

SITE KEEP YELLOW COPY - LABORATORY KEEP PINK COPY
WHITE COPY TO BE SENT TO KIRBY LABORATORY UPON INSTRUCTIONS

STORE THIS COMPLETED FORM IN YOUR STUDY
BINDER.
DO NOT SHIP SAMPLES UNTIL REQUESTED BY THE
SMART-C COORDINATOR

Laboratory Contact:
HepBank@kirby.unsw.edu.au

SMART-C Research Assistant
+61 2 9385 0203, smartc@kirby.unsw.edu.au

11 ATTACHMENT E: Laboratory Request Form (SCR) – SUB-STUDY SITE

SMART-C

For Clinic use only

Screen ID:	333 – __ __ __
Subject initials:	__ __ / __ __ __ Last name First name

Date of Birth:
(Format: 23/NOV/2009)   __ __ / __ __ __ / __ __ __ __   **Collectors' name:** _____

Date of Collection:
(Format: 23/NOV/2009)   __ __ / __ __ __ / __ __ __ __   **Collection Time:**
(Format: 24 hour time, e.g. 15:30)   __ __ __ : __ __ __

Visit: (Please tick box)

☐ **SCR**
   ☐ 2 x 10mL EDTA
   ☐ 1 X 4mL Whole Blood
   ☐ 6 X 10mL ACD (if consented to sub-study)

Comments:

For processing site use only

Specimen received: Date:__ __ / __ __ __ / __ __ __ __ (e.g. 23/NOV/2009)   Time: __ __ __ : __ __ __ (e.g. 15:30)

Specimen processed: Date:__ __ / __ __ __ / __ __ __ __ (e.g. 23/NOV/2009)   Time: __ __ __ : __ __ __ (e.g. 15:30)

Samples stored:

(Please tick boxes)

_____ x 1mL + 1 x _____ mL EDTA plasma in round bottom cryotube vials
Box #:____ Positions: _____   Stored at -80ºC ☐

_____ x 1.8mL + 1 x _____ mL EDTA whole blood in round bottom cryotube vials
Box #:____ Positions: _____   Stored at -80ºC ☐

Up to 6 vials of PBMCs @_____cells/mL.
_____ x 1mL + 1 vial of _____ mL PBMC in round bottom cryotube vials
Box #:____ Positions: _____

Stored at -200ºC ☐
OR
No ACD collected ☐

Samples specific comments:

Data recorded in LabKey ☐	**Processed by:** (Name and signature)

SITE KEEP YELLOW COPY - LABORATORY KEEP PINK COPY
WHITE COPY TO BE SENT TO KIRBY LABORATORY UPON INSTRUCTIONS

STORE THIS COMPLETED FORM IN YOUR STUDY BINDER.
DO NOT SHIP SAMPLES UNTIL REQUESTED BY THE SMART-C COORDINATOR

Laboratory Contact:
HepBank@kirby.unsw.edu.au

SMART-C Research Assistant
+61 2 9385 0203, smartc@kirby.unsw.edu.au

SMART-C

For Clinic use only

Subject Study No.: 1701 – __ __ __ __ __ __ – __ __ __   **Subject initials:** __ __ __ / __ __ __ __
Last name First name

Date of Birth:
(Format: 23/NOV/2009)   __ __ / __ __ __ / __ __ __ __ __   **Collectors' name:** _____

Date of Collection: **Collection Time:**
(Format: 23/NOV/2009)   __ __ / __ __ __ / __ __ __ __ __   (Format: 24 hour time, e.g. 15:30)   __ __ __ : __ __ __

Visit: (Please tick box)

☐ **BSL**   2 x 10mL EDTA

Screen ID: 3 3 3- __ __ __ __

☐ **WK4**   ☐ 1 x 10mL EDTA
(standard arm only)   ☐ 6 x 10mL ACD (if consented to sub-study)

☐ **EoT (WK8)**   1 x 10mL EDTA
(standard arm only)

☐ **SVR12**   ☐ 1 x 10mL EDTA
    ☐ 6 x 10mL ACD (if consented to sub-study)

Comments:

For processing site use only

Specimen received: Date: __ __ / __ __ __ / __ __ __ __ __ (e.g. 23/NOV/2009)   Time: __ __ __ : __ __ __ (e.g. 15:30)

Specimen processed: Date: __ __ / __ __ __ / __ __ __ __ __ (e.g. 23/NOV/2009)   Time: __ __ __ : __ __ __ (e.g. 15:30)

Samples stored: _____ x 1mL + 1 x _____ mL EDTA plasma in round bottom cryotube vials   Stored at -80°C ☐

(Please tick boxes)   Box #: ____ Positions: _____

Up to 6 vials of PBMCs @ _____ cells/mL.
_____ x 1mL + 1 vial of _____ mL PBMC in round bottom cryotube vials   Stored at -200°C ☐

Box #: ____ Positions: _____   OR

No ACD collected ☐

Samples specific comments:

Data recorded in Labkey ☐   **Processed by:**
    (Name and signature)

SITE KEEP YELLOW COPY - LABORATORY KEEP PINK COPY
WHITE COPY TO BE SENT TO KIRBY LABORATORY UPON INSTRUCTIONS

STORE THIS COMPLETED FORM IN YOUR STUDY
BINDER.   Laboratory Contact: SMART-C Research Assistant
DO NOT SHIP SAMPLES UNTIL REQUESTED BY THE   HepBank@kirby.unsw.edu.au   +61 2 9385 0203, smartc@kirby.unsw.edu.au
SMART-C COORDINATOR