



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

Laboratory Manual

Study Specific Supplement

Version and Date: Version 1.0 17 August 2017

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1 Communication, Contacts and Summary of Procedures Project Team Contact details:

Position	Name	Phone	Email
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Study Email	smartc@kirby.unsw.edu.	<u>au</u>	

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
	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 (
	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	To compare the proportion of participants with undetectable HCV RNA (HCV RNA <lloq) 12<="" at="" th=""></lloq)>						
Objective	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)		Х		Х	SVR12	3

Key:

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

† Collected from standard monitoring arm 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

^{*} At selected sub-study sites only

	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	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 AB).

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

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:

SMART-C Page 1 of 1

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16 May 2017

8 ATTACHMENT B: SAMPLE STORAGE DEVIATION FORM

LABORATORY SAMPLE STORAGE TEMPERATURE DEVIATION FORM

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

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	
ACTION Taken	
PLEASE ATTACH AN UP-TO-DATE LAB	ORATORY SAMPLE STORAGE TEMPERATURE LO
ignature of person reporting deviation	Date

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

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SMART-C						+	
			For Clinic use	only			
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Date of Collection:			Collectors' no Collection Tin	ne:			
(Format: 23/NOV/2009)	/	/	(Format: 24 hour	time, e.g. 15:30)	::		
Visit: (Please tick box)							
	2 x 10mL EDTA						
	1 X 4mL Whole Bloc	oa .					
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10 ATTACHMENT D: Laboratory Request Form (BSL/WK4/WK8 OR SVR12) - NON SUB-STUDY SITE

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□ BSL	2 x 10mL EDTA			
Screen ID): 3 3 3			
WK4 (standard arm only)	1 x 10mL EDTA			
☐ EoT (WK8)	1 x 10mL EDTA			
(standard arm only)	TX TOTAL EDIA			
□ SVR12	1 x 10mL EDTA			
LI SVKIZ				
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	For proce	ssing site use	only	
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Specimen processed: Da				
				_ 1 (1.8.10.00)
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(Please tick box)				
Samples specific commen	ts:			
Data recorded in	Processed by:			
Labkey	(Name and signa			
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STORE THIS COMPLETED FORMIN	COPY TO BE SENT TO KIR YOUR STUDY	RY LABORAL	OKY UPON INSTRU	CHONS
BINDER. DO NOT SHIP SAMPLES UNTIL REQ	Laboratory	Contact: ti/by.unsw.edu.au	SMART-C Research/ +61 2 93850203, <u>sm</u>	Assistant arto@kirby.unsw.edu.au

SMART-C COORDINATOR

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

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	For Clinic use only		
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SCICCII ID.	333 initials: Last name First nam	-	
	milias, costnane ristram	=	
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Date of Co	ollection: Collection Time:		
(Format: 23/I			
Visit: (Please			
VISII. (Please	e lick boxj		
	□ 2 x 10mL EDTA		
	SCR 1 X 4mL Whole Blood		
	☐ 6 X 10mL ACD (if consented to sub-study)		
Comments	51		
Committee	•		
	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	x1mL + 1 x mL EDTA plasma in round bottom cryotube vials	2000 to becat?	_
stored:	Day # DayFrage	Stored at -80°C	
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(Please tick	x1.8mL + 1 x mLEDTA whole blood in round bottom cryotube via	ls	
boxes)		Stored at -80°C	
DOXES	Box #: Positions:		
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	Up to 6 vials of PBMCs @cells/mL.		ш
	x1mL + 1 vial of mL PBMC in round bottom cryotube vials	OR	
		No ACD	_
	Box #: Positions:	collected	
		33.33.33	
Samples s	pecific comments:		
Data reco	rded in Processed by:		
LabKey	(Name and signature)		
	SITE KEEP YELLOW COPY - LABORATORY KEEP PINK CO)PV	
	WHITE COPY TO BE SENT TO KIRBY LABORATORY UPON INSTR	UCTIONS	
	OMPLETED FORM IN YOUR STUDY		
BINDER.	Laboratory Contact: SMART-C Research	Assistant	
	,		
	,	arto@kirby.unsw.edu.au	

12 ATTACHMENT F: Laboratory Request Form (BSL/WK4/WK8 OR SVR12) – SUB-STUDY SITE

SMART-C						
For Clinic use only						
Subject Study No.: 1701 Subject initials:/						
Date of Birth: (Format: 23/NOV/2009) Date of Collection:	//	Collectors' nam	Last nar	ne First name		
□ BSL	2 x 10mL EDTA					
Screen ID: 3 3 3						
WK4 (standard armonly)	☐ 1 x 10mL EDTA ☐ 6 x 10mL ACD (if consent	ed to sub-study)				
EoT (WK8) (standard arm only)	1 x 10mL EDTA					
SVR12	☐ 1 x 10mL EDTA ☐ 6 x 10mL ACD (if consent	ed to sub-study)				
Comments:						
For processing site use only						
Specimen received: Date	te://	(e.g. 23/NO	V/2009) Tir	me: :	(e.g. 15:30)	
Specimen received: Dafe: / (e.g. 23/NOV/2009) Time: : (e.g. 15:30) Specimen processed: Dafe: / (e.g. 23/NOV/2009) Time: : (e.g. 15:30)						
-tt-	1 x mL EDTA plas ositions:	ma in round bot	tom cryotube	e vials	Stored at -80°C	
(Please fick						
Up to 6 vials of PBMCs @cells/mLx 1mL + 1 vial ofmL PBMC in round bottom cryotube vials					Stored at -200°C OR	
Box #: Positions:					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 Y BINDER. DO NOT SHIP SAMPLES UNTIL REQUISMART-C COORDINATOR	OUR STUDY Laborato	IRBY LABORA ry Contact: @kirby.ursw.edu.au	SMART-	C Research Assist		