Trial number: ☐☐☐☐

CONFIDENTIAL WHEN COMPLETE

UNIVERSITY OF BIRMINGHAM | BCTU Birmingham Clinical Trials Unit

CALIBRE

FOLLOW-UP FORM

IDENTIFYING DETAILS

Trial No.: ☐☐☐☐	Initials: ☐☐☐☐
Site Name: ……	
Date of follow-up visit: D D / M M M / Y Y Y Y	

TIME POINT

Please indicate which trial visit this form relates to:

6 months (*after randomisation*) ☐	12 months (*after randomisation*) ☐

HOW THE VISIT WAS CONDUCTED

Please state how the visit was conducted:

Face to Face ☐	Remote ☐

*Guidance: If a face to face visit is required **following** a remote visit, please only complete the CRF at face to face visit.*

CONFIRMATION OF CONSENT

Does the participant wish to continue taking part in the CALIBRE Trial?	No ☐	Yes ☐	*If no, please complete a Change of Status Form.* *If yes, please continue to next question.*

QUALITY OF LIFE QUESTIONNAIRE

Has the participant completed the EQ-5D-5L questionnaire:
If No please ask participant to complete and return to BCTU in the prepaid envelope provided

No ☐	Yes ☐

COVID-19 STATUS

Since the last visit has the participant been diagnosed with COVID-19?	No ☐	Yes ☐
Has the participant received <u>all</u> recommended doses of an initial COVID-19 vaccination?	No ☐	Yes ☐

GP VISITS

Since the last CALIBRE Trial visit, has the participant visited their GP in relation to liver cirrhosis/ oesophageal varices? No ☐ Yes ☐

If no, please continue to Blood Tests.

If yes, please complete the following question.

If yes, how many times did the participant visit their GP?
Please include the total for all GP visits that were required due to liver cirrhosis/oesophageal varices, since the last CALIBRE Trial visit: ☐☐

BLOOD TESTS

Please enter results from the most recent standard care blood tests:

Test		Date taken	Not available
Sodium	☐☐☐ mmol/L	D D / M M M / Y Y Y Y	☐
INR *(If unavailable then both PTT for patient and control needs completing*):	☐☐.☐	D D / M M M / Y Y Y Y	☐
PTT (Patient):	☐☐☐.☐ Seconds	D D / M M M / Y Y Y Y	☐
PTT (Control):	☐☐☐.☐ Seconds	D D / M M M / Y Y Y Y	☐
Albumin:	☐☐ g/L	D D / M M M / Y Y Y Y	☐
Creatinine:	☐☐☐ µmol/L	D D / M M M / Y Y Y Y	☐
AST:	☐☐☐ U/L	D D / M M M / Y Y Y Y	☐
ALT:	☐☐☐ U/L	D D / M M M / Y Y Y Y	☐
GGT:	☐☐☐ U/L	D D / M M M / Y Y Y Y	☐
Bilirubin:	☐☐☐ µmol/L	D D / M M M / Y Y Y Y	☐
Alkaline Phosphatase	☐☐☐ U/L	D D / M M M / Y Y Y Y	☐
eGFR:	☐☐☐ mL/min	D D / M M M / Y Y Y Y	☐
Ferritin:	☐☐☐ ug/L	D D / M M M / Y Y Y Y	☐
Platelets:	☐☐☐ U/L	D D / M M M / Y Y Y Y	☐

CONCOMITANT MEDICATIONS		
Is the participant taking any of the following medications currently?		
Class	**Yes**	**Agent**
Anticoagulants	☐	
Anti-platelets	☐	
ACE inhibitors	☐	
Angiotensin II receptor blockers	☐	
Calcium channel blockers	☐	
Statins	☐	
Alpha blockers	☐	
Beta blockers	☐	
Nitrates	☐	
Thiazide/ loop diuretics	☐	
Potassium-sparing diuretics	☐	
Sildenafil (if > 1 month)	☐	
Antibiotics (if > 1 month)	☐	
Antiviral agent	☐	
Ursodeoxycholic acid	☐	
Obeticholic Acid	☐	
Fibrate	☐	
Other (please specify)	☐	
I confirm that all above items have been considered and only those ticked are being taken	No ☐	Yes ☐

MEDICAL HISTORY

Past Medical History

Since the last CALIBRE visit, has the participant been diagnosed with any of the following? *Please tick all that apply:*

	Yes		Yes
Hypertension	☐	Peripheral vascular disease	☐
TIA	☐	Stroke	☐
Type 1 diabetes	☐	Type 2 diabetes	☐
Hypercholesterolaemia	☐	Myocardial infarction	☐

Please confirm all above items have been considered and only those ticked were present No ☐ Yes ☐

Smoking Status

If the participant has never smoked or is an ex-smoker, please continue to Alcohol Consumption.

Smoking status: Never smoked ☐ Ex-smoker ☐ Ex-smoker (<12 months) ☐ Current smoker ☐

If the participant is a current smoker or has smoked in the last 12 months, please complete the following question.

On average, how many cigarettes/ cigars/ cigarillos/ has the participant smoked daily for the last 12 months? ☐☐☐

Alcohol Consumption

Has the participant consumed alcohol in the last 12 months? No ☐ Yes ☐

If no, please continue to Coffee Consumption.

If yes, please complete the following questions.

On average, how many units of alcohol has the participant consumed per week over the last 12 months? ☐☐☐

Has an AUDIT – C assessment been undertaken? No ☐ Yes ☐

If no or not available, please continue to Coffee Consumption.

If yes, please complete the AUDIT questions below.

Please provide details of the participant's current alcohol consumption using the AUDIT-C, and if required, AUDIT assessment tool:

AUDIT – C score: ☐☐

Total AUDIT score ☐☐

If the participant's Audit C score is ≥ 5, using the guidance below please complete the remaining AUDIT questions and enter the total score.

Guidance:
AUDIT –C score:

Questions	Scoring system					Participant score
	0	1	2	3	4	
How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times per month	2-3 times per week	4+ times per week	
How many units of alcohol do you drink on a typical day when you are drinking?	1-2	3-4	5-6	7-9	10+	
How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	

Total AUDIT score:

Questions	Scoring system					Participant score
	0	1	2	3	4	
How often during the last year, have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year, have you failed to do what was normally expected from you because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year, have you needed an alcoholic drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year, have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often during the last year, have you been unable to remember what happened the night before because you had been drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Have you or somebody else been injured as a result of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
Has a relative or friend, doctor or other health worker been concerned about your drinking or suggested that you cut down?	No		Yes, but not in the last year		Yes, during the last year	

Coffee Consumption

Does the participant drink coffee daily? No ☐ Yes ☐

If no, please continue to Ultrasound Scan Report.

If yes, please complete the following question.

On average, how many cups of coffee does the participant drink per day? ☐☐

ULTRASOUND SCAN REPORT

Has the participant undergone an abdominal ultrasound since the last CALIBRE Trial visit? No ☐ Yes ☐

If no, please continue to FibroScan Report.

If yes, please complete the following questions.

Date ultrasound was undertaken: D D / M M M / Y Y Y Y

Hepatomegaly: No ☐ Yes ☐ Not available ☐

Splenomegaly: No ☐ Yes ☐ If yes, size: ☐☐.☐ cm

Was the hepatic vein patent? No ☐ Yes ☐ Not available ☐

Was the portal vein patent? No ☐ Yes ☐ Not available ☐

FIBROSCAN REPORT

Has the participant undergone a FibroScan since the last CALIBRE Trial visit? No ☐ Yes ☐

If no, please continue to Vital Signs.

If yes, complete the following questions and rest of form.

Date FibroScan was undertaken: D D / M M M / Y Y Y Y

Type of probe: Medium ☐ Extra Large ☐ Both ☐ Not available ☐

Liver stiffness measurement: ☐☐.☐ kPa Not available ☐

Liver stiffness measurement (IQR): ☐☐ % Not available ☐

Liver stiffness measurement (valid readings): ☐☐☐ % Not available ☐

Controlled attenuation parameter: ☐☐☐.☐ dB/m Not available ☐

Controlled attenuation parameter (IQR): ☐☐ dB/m Not available ☐

Vital signs, anthropometric measurements and ECG questions are only to be completed if visit is face to face.

VITAL SIGNS

Were Vital Signs taken? No ☐ Yes ☐ N/A ☐

Date vital signs taken: D D / M M M / Y Y Y Y

Blood pressure: ☐☐☐ / ☐☐☐ mmHg | Pulse: ☐☐☐ bpm

ANTHROPOMETRIC MEASUREMENTS

Please record measurements to the nearest <u>whole</u> number:

Were Anthropometric Measurements taken? No ☐ Yes ☐ N/A ☐

Date measurements taken: D D / M M M / Y Y Y Y

Height: ☐☐☐ cm | Weight: ☐☐☐ kg

ECG

Was an ECG performed? No ☐ Yes ☐

If no, please continue to Treatment Adherence.

If yes, please complete the following questions.

Was the ECG: Within normal limits ☐ Abnormal, not clinically significant ☐ Abnormal, clinically significant ☐

If abnormal and clinically significant, please indicate why:

Conduction abnormalities ☐ Rhythm abnormalities ☐

TREATMENT ADHERENCE

Since the last CALIBRE Trial Visit, has participant taken CARVEDILOL? No ☐ Yes ☐

Since the last CALIBRE Trial Visit, has participant had VBL? No ☐ Yes ☐

If yes to carvedilol, please complete the two carvedilol questions below
If yes to VBL, please complete the VBL and Endoscopy report questions
All participants to then continue to adverse events

PARTICIPANTS WHO HAVE TAKEN CARVEDILOL

Date first dose of carvedilol prescribed D D / M M M / Y Y Y Y

Please indicate participant percentage adherence for carvedilol (choose one):

Always (100%) ☐ Almost always (75-99 %) ☐ Most (50-74%) ☐

Some (25-49%) ☐ Hardly any (1-24%) ☐ Never (0%) ☐

PARTICIPANTS WHO HAVE HAD VARICEAL BAND LIGATION

Since the last CALIBRE Trial visit, has participant undergone **all** scheduled variceal band ligation procedures? No ☐ Yes ☐

If the participant has **not** undergone all scheduled variceal band ligation procedures, how many appointments have been missed? ☐☐

Have the participant's oesophageal varices been eradicated since the last CALIBRE Trial visit? No ☐ Yes ☐ *If **no,** please continue to endoscopy reports question.*

If **Yes**, What date were the participant's oesophageal varices eradicated? D D / M M M / Y Y Y Y

Have the participant's oesophageal varices recurred since the last CALIBRE Trial visit?

No ☐ Yes ☐ Unknown ☐

If **Yes**, What date did the participant's oesophageal varices reoccurred?

D D / M M M / Y Y Y Y Unknown ☐

Endoscopy Reports

Reports should be completed for each endoscopy undertaken since the last CALIBRE Trial visit (maximum of six), starting with the most recent

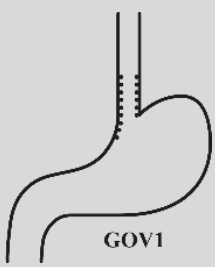
Have endoscopies been undertaken? No ☐ Yes ☐

If no, please continue to Adverse Events.

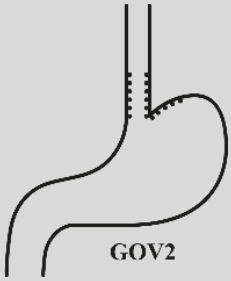
If yes, please complete a report for each endoscopy undertaken.

How many endoscopies have been undertaken? ☐☐

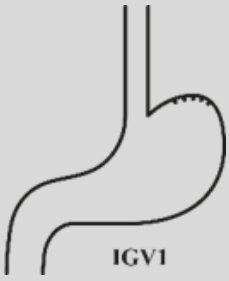
Guidance:



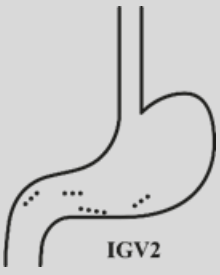
GOV 1: Oesophageal varices extending to lesser curve of stomach



GOV 2: Oesophageal varices extending to gastric fundus



IGV 1: Isolated fundal varices



IGV 2: Isolated varices in gastric antrum, body or pylorus

Endoscopy 1

Date of endoscopy: D D / M M M / Y Y Y Y

Banding undertaken: No ☐ Yes ☐

If no, please continue to the oesophageal varices questions

If yes, please complete the following question.

If there was a complication complete the complications during procedure question

Number of bands: ☐☐

Please specify the number of oesophageal varices present, per grade:

Grade I: ☐☐ Grade II: ☐☐ Grade III: ☐☐

Were red signs present: No ☐ Yes ☐

Were gastric varices present? No ☐ Yes ☐

If no, please continue to complications question below.

If yes, please complete the following questions.

Please specify the size of gastric varices identified, per grade:

Grade	Small	Medium	Large	Not present
GOV1	☐	☐	☐	☐
GOV2	☐	☐	☐	☐
IGV1	☐	☐	☐	☐
IGV2	☐	☐	☐	☐

Were red signs present: No ☐ Yes ☐

Were there any complications during the procedure? No ☐ Yes ☐

If no, please continue to the next endoscopy report (if required).

If yes, please complete the following questions. Please tick all that apply.

	Yes		**Yes**
Failed intubation	☐	Failed banding	☐
Bleeding	☐	Other (please specify)	☐ ……

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Endoscopy 2

Date of endoscopy: D D / M M M / Y Y Y Y

Banding undertaken: No ☐ Yes ☐

If no, please continue to the oesophageal varices questions

If yes, please complete the following question.

If there was a complication complete the complications during procedure question

Number of bands: ☐☐

Please specify the number of oesophageal varices present, per grade:

Grade I: ☐☐ Grade II: ☐☐ Grade III: ☐☐

Were red signs present: No ☐ Yes ☐

Were gastric varices present? No ☐ Yes ☐

If no, please continue to complications question below.

If yes, please complete the following questions.

Please specify the size of gastric varices identified, per grade:

Grade	Small	Medium	Large	Not present
GOV1	☐	☐	☐	☐
GOV2	☐	☐	☐	☐
IGV1	☐	☐	☐	☐
IGV2	☐	☐	☐	☐

Were red signs present: No ☐ Yes ☐

Were there any complications during the procedure? No ☐ Yes ☐

If no, please continue to the next endoscopy report (if required).

If yes, please complete the following questions. Please tick all that apply.

	Yes		**Yes**
Failed intubation	☐	Failed banding	☐
Bleeding	☐	Other (please specify)	☐ ……

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Endoscopy 3

Date of endoscopy: D D / M M M / Y Y Y Y

Banding undertaken: No ☐ Yes ☐

If no, please continue to the oesophageal varices questions

If yes, please complete the following question.

If there was a complication complete the complications during procedure question

Number of bands: ☐☐

Please specify the number of oesophageal varices present, per grade:

Grade I: ☐☐ Grade II: ☐☐ Grade III: ☐☐

Were red signs present: No ☐ Yes ☐

Were gastric varices present? No ☐ Yes ☐

If no, please continue to complications question below.

If yes, please complete the following questions.

Please specify the size of gastric varices identified, per grade:

Grade	Small	Medium	Large	Not present
GOV1	☐	☐	☐	☐
GOV2	☐	☐	☐	☐
IGV1	☐	☐	☐	☐
IGV2	☐	☐	☐	☐

Were red signs present: No ☐ Yes ☐

Were there any complications during the procedure? No ☐ Yes ☐

If no, please continue to the next endoscopy report (if required).

If yes, please complete the following questions. Please tick all that apply.

	Yes		**Yes**
Failed intubation	☐	Failed banding	☐
Bleeding	☐	Other (please specify)	☐ ……

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Endoscopy 4

Date of endoscopy: D D / M M M / Y Y Y Y

Banding undertaken: No ☐ Yes ☐

If no, please continue to the oesophageal varices questions

If yes, please complete the following question.

If there was a complication complete the complications during procedure question

Number of bands: ☐☐

Please specify the number of oesophageal varices present, per grade:

Grade I: ☐☐ Grade II: ☐☐ Grade III: ☐☐

Were red signs present: No ☐ Yes ☐

Were gastric varices present? No ☐ Yes ☐

If no, please continue to complications question below.

If yes, please complete the following questions.

Please specify the size of gastric varices identified, per grade:

Grade	Small	Medium	Large	Not present
GOV1	☐	☐	☐	☐
GOV2	☐	☐	☐	☐
IGV1	☐	☐	☐	☐
IGV2	☐	☐	☐	☐

Were red signs present: No ☐ Yes ☐

Were there any complications during the procedure? No ☐ Yes ☐

If no, please continue to the next endoscopy report (if required).

If yes, please complete the following questions. Please tick all that apply.

	Yes		**Yes**
Failed intubation	☐	Failed banding	☐
Bleeding	☐	Other (please specify)	☐ ……

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Endoscopy 5

Date of endoscopy: D D / M M M / Y Y Y Y

Banding undertaken: No ☐ Yes ☐

If no, please continue to the oesophageal varices questions

If yes, please complete the following question.

If there was a complication complete the complications during procedure question

Number of bands: ☐☐

Please specify the number of oesophageal varices present, per grade:

Grade I: ☐☐ Grade II: ☐☐ Grade III: ☐☐

Were red signs present: No ☐ Yes ☐

Were gastric varices present? No ☐ Yes ☐

If no, please continue to complications question below.

If yes, please complete the following questions.

Please specify the size of gastric varices identified, per grade:

Grade	Small	Medium	Large	Not present
GOV1	☐	☐	☐	☐
GOV2	☐	☐	☐	☐
IGV1	☐	☐	☐	☐
IGV2	☐	☐	☐	☐

Were red signs present: No ☐ Yes ☐

Were there any complications during the procedure? No ☐ Yes ☐

If no, please continue to the next endoscopy report (if required).

If yes, please complete the following questions. Please tick all that apply.

	Yes		**Yes**
Failed intubation	☐	Failed banding	☐
Bleeding	☐	Other (please specify)	☐ ……

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Endoscopy 6

Date of endoscopy: D D / M M M / Y Y Y Y

Banding undertaken: No ☐ Yes ☐

If no, please continue to the oesophageal varices questions

If yes, please complete the following question.

If there was a complication complete the complications during procedure question

Number of bands: ☐☐

Please specify the number of oesophageal varices present, per grade:

Grade I: ☐☐ Grade II: ☐☐ Grade III: ☐☐

Were red signs present: No ☐ Yes ☐

Were gastric varices present? No ☐ Yes ☐

If no, please continue to complications question below.

If yes, please complete the following questions.

Please specify the size of gastric varices identified, per grade:

Grade	Small	Medium	Large	Not present
GOV1	☐	☐	☐	☐
GOV2	☐	☐	☐	☐
IGV1	☐	☐	☐	☐
IGV2	☐	☐	☐	☐

Were red signs present: No ☐ Yes ☐

Were there any complications during the procedure? No ☐ Yes ☐

If no, please continue to the next endoscopy report (if required).

If yes, please complete the following questions. Please tick all that apply.

	Yes		**Yes**
Failed intubation	☐	Failed banding	☐
Bleeding	☐	Other (please specify)	☐ ………

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

ADVERSE EVENTS

Since the last visit, has the participant experienced any serious adverse events that are not defined as 'expected' (i.e. are recognised complications/ consequences of cirrhosis and oesophageal varices) in the protocol? **If yes, please complete a CALIBRE SAE FORM and return to the CALIBRE Trial Office within 24 hours** No ☐ Yes ☐

PARTICIPANTS WHO HAVE TAKEN CARVEDILOL

Since the last CALIBRE Trial visit, has the participant experienced/ been diagnosed with: *Please tick all that apply*

	Yes		Yes
Gastrointestinal upset	☐	Blurred vision	☐
Dizziness	☐	Lethargy	☐
Rash	☐	Headache	☐
Swelling in the feet or hands	☐	Upper respiratory tract infection	☐
Shortness of breath	☐	Sexual dysfunction	☐
Other (please specify)	☐	.....	

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Has the participant been put on a split dose of carvedilol because of adverse events? No ☐ Yes ☐

If no, please continue to the question regarding stopping carvedilol.

If yes, please complete the following questions.

Has the participant been put onto a reduced dose of carvedilol because of adverse events? No ☐ Yes ☐

		Not applicable
Date carvedilol dose was split:	D D / M M M / Y Y Y Y	☐
Date carvedilol was reduced:	D D / M M M / Y Y Y Y	☐

Please indicate which adverse events led to the dose of carvedilol being split or reduced: *Please tick all that apply*

	Yes		Yes
Gastrointestinal upset	☐	Blurred vision	☐
Dizziness	☐	Lethargy	☐
Rash	☐	Headache	☐
Swelling in the feet or hands	☐	Upper respiratory tract infection	☐
Shortness of breath	☐	Sexual dysfunction	☐
Other (please specify)	☐	.....	

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Has the participant stopped taking carvedilol because of adverse events? No ☐ Yes ☐

If no, please continue to the question regarding alternative treatment.

If yes, please complete the following questions.

Date carvedilol was stopped: D D / M M M / Y Y Y Y

Please indicate which adverse events have led to carvedilol being stopped: *Please tick all that apply*

	Yes		**Yes**
Gastrointestinal upset	☐	Blurred vision	☐
Dizziness	☐	Lethargy	☐
Rash	☐	Headache	☐
Swelling in the feet or hands	☐	Upper respiratory tract infection	☐
Shortness of breath	☐	Sexual dysfunction	☐

Other (please specify) ☐ .....

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Has an alternative treatment been commenced? No ☐ Yes ☐

If no, please continue to All Participants.

If yes, please complete following question.

Which alternative treatment has been commenced?

Propranolol ☐ Nadolol ☐ Variceal band ligation ☐

Other (please specify) ☐ .....

Not available

Date alternative treatment commenced: D D / M M M / Y Y Y Y ☐

PARTICIPANTS WHO HAVE HAD VARICEAL BAND LIGATION

Since the last CALIBRE Trial visit, has the participant experienced/ been diagnosed with: *Please tick all that apply*

	Yes		**Yes**		
Abdominal pain	☐	Banding-related dysphagia	☐	Other (*please specify*):	☐

……

Has treatment with variceal band ligation been stopped because of adverse events? No ☐ Yes ☐

If no, please continue to alternative treatment due to reasons other than adverse event question.

If yes, please complete the following questions.

Last variceal band ligation session: D D / M M M / Y Y Y Y

Please indicate which adverse events have led to variceal band ligation being stopped:

	Yes		**Yes**		
Abdominal pain	☐	Banding-related dysphagia	☐	Other (*please specify*):	☐

……

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Has an alternative treatment been commenced? No ☐ Yes ☐

If no, please continue to All Participants.

If yes, please complete the following question.

Which alternative treatment has been commenced?

Carvedilol ☐ Propranolol ☐ Nadolol ☐

Other (please specify) ☐ ……

Not available

Date alternative treatment commenced: D D / M M M / Y Y Y Y ☐

Since the last CALIBRE Trial visit, has the participant switched to an alternative treatment due to reasons other than adverse events: *Please tick all that apply*

Has an alternative treatment been commenced? No ☐ Yes ☐

If no, please continue to All Participants.

If yes, please complete following question.

Which alternative treatment has been commenced?

Carvedilol ☐ Propranolol ☐ Nadolol ☐

Variceal band ligation ☐ Other (please specify) ☐ ……

Reason alternative treatment commenced:

Participant choice ☐

Participant unable to attend hospital for variceal band ligation due to COVID-19 pandemic ☐

Other (please specify) ☐ ……

Date alternative treatment commenced: D D / M M M / Y Y Y Y **Not available** ☐

ALL PARTICIPANTS

Variceal Bleeding

Guidance:
The first variceal bleed is defined as hematemesis and/or melena with either: 1) endoscopic evidence of variceal bleeding or stigmata of recent haemorrhage and at least a 2 g/L reduction in haemoglobin within 24 hours of admission; or 2) massive upper gastrointestinal bleeding leading to death. The definition includes bleeding from banding ulceration.

Has the participant experienced variceal bleeding since the last CALIBRE Trial visit	No ☐	Yes ☐	*If no, please continue to Ascites.* *If yes, please complete the following questions.*
Was the bleeding banding related	No ☐	Yes ☐	

How many episodes of variceal bleeding has the participant experienced	☐☐ *Please complete the dates below with most recent first*	**Not available**
Episode 1:	D D / M M M / Y Y Y Y	☐
Episode 2:	D D / M M M / Y Y Y Y	☐
Episode 3:	D D / M M M / Y Y Y Y	☐
Episode 4:	D D / M M M / Y Y Y Y	☐

Since the last CALIBRE Trial visit, has the participant been hospitalised due to variceal bleeding? No ☐ Yes ☐

If no, please continue to outpatient visits below.

If yes, please complete the following questions.

Since the last CALIBRE Trial visit, how many times has the participant been hospitalised due to variceal bleeding?	☐☐	How many days in total, has the participant been hospitalised? *Please include the total for all hospitalisations that have occurred due to variceal bleeding, since the last CALIBRE Trial visit:*	☐☐
Since the last CALIBRE Trial visit, was the participant admitted to intensive care due to variceal bleeding?	No ☐ Yes ☐	If yes, how many days did the participant stay in intensive care? *Please include the total for all intensive care days that were required due to variceal bleeding, since the last CALIBRE Trial visit:*	☐☐
Since the last CALIBRE Trial visit, did the participant require additional outpatient visits due to variceal bleeding?	No ☐ Yes ☐	If yes, how many additional outpatient visits did the participant require? *Please include the total for all outpatient visits that were required due to variceal bleeding, since the last CALIBRE Trial visit:*	☐☐

Ascites

Guidance:
International Club of Ascites grading system

- *Grade 1: Mild ascites detectable only by ultrasound*
- *Grade 2: Moderate ascites manifested by moderate symmetrical distension of the abdomen*
- *Grade 3: Large or gross ascites with marked abdominal distension*

Has the participant experienced new or worsening ascites since the last CALIBRE Trial visit	No ☐	Yes ☐	*If no, please continue to Spontaneous Bacterial Peritonitis.* *If yes, please complete the following questions.*

How many episodes of new or worsening ascites has the participant experienced	☐☐ *Please complete the dates below with most recent first, grade and if new or worsening*	**Not available**
Episode 1:	D D / M M M / Y Y Y Y	☐
Grade	Grade 1: ☐ Grade 2: ☐ Grade 3: ☐	☐
New or worsening	New: ☐ Worsening: ☐	☐
Episode 2:	D D / M M M / Y Y Y Y	☐
Grade	Grade 1: ☐ Grade 2: ☐ Grade 3: ☐	☐
New or worsening	New: ☐ Worsening: ☐	☐
Episode 3:	D D / M M M / Y Y Y Y	☐
Grade	Grade 1: ☐ Grade 2: ☐ Grade 3: ☐	☐

New or worsening	New: ☐ Worsening: ☐	☐
Episode 4:	D D / M M M / Y Y Y Y	☐
Grade	Grade 1: ☐ Grade 2: ☐ Grade 3: ☐	☐
New or worsening	New: ☐ Worsening: ☐	☐

Since the last CALIBRE Trial visit, has the participant been hospitalised due to Ascites? No ☐ Yes ☐

If no, please continue to outpatient visits below.

If yes, please complete the following questions.

Since the last CALIBRE Trial visit, how many times has the participant been hospitalised due to Ascites? ☐☐

How many days in total, has the participant been hospitalised?
Please include the total for all hospitalisations that have occurred due to Ascites, since the last CALIBRE Trial visit: ☐☐

Since the last CALIBRE Trial visit, was the participant admitted to intensive care due to Ascites? No ☐ Yes ☐

If yes, how many days did the participant stay in intensive care?
Please include the total for all intensive care days that were required due to Ascites, since the last CALIBRE Trial visit: ☐☐

Since the last CALIBRE Trial visit, did the participant require additional outpatient visits due to Ascites? No ☐ Yes ☐

If yes, how many additional outpatient visits did the participant require?
Please include the total for all outpatient visits that were required due to Ascites, since the last CALIBRE Trial visit: ☐☐

Spontaneous Bacterial Peritonitis:

Since the last CALIBRE Trial visit, has the participant been diagnosed with spontaneous bacterial peritonitis? No ☐ Yes ☐

If no, please continue to Renal Dysfunction.

If yes, please complete the following questions.

How many episodes of spontaneous bacterial peritonitis have been diagnosed since the last CALIBRE Trial visit:	☐☐ *Please complete the dates below with most recent first*	**Not available**
Episode 1:	D D / M M M / Y Y Y Y	☐
Episode 2:	D D / M M M / Y Y Y Y	☐
Episode 3:	D D / M M M / Y Y Y Y	☐
Episode 4:	D D / M M M / Y Y Y Y	☐

Since the last CALIBRE Trial visit, has the participant been hospitalised due to spontaneous bacterial peritonitis? No ☐ Yes ☐

If no, please continue to outpatient visits below.

If yes, please complete the following questions.

Since the last CALIBRE Trial visit, how many times has the participant been hospitalised due to spontaneous bacterial peritonitis? ☐☐	How many days in total, has the participant been hospitalised? *Please include the total for all hospitalisations that have occurred due to spontaneous bacterial peritonitis, since the last CALIBRE Trial visit:* ☐☐
Since the last CALIBRE Trial visit, was the participant admitted to intensive care due to spontaneous bacterial peritonitis? No ☐ Yes ☐	If yes, how many days did the participant stay in intensive care? *Please include the total for all intensive care days that were required due to spontaneous bacterial peritonitis, since the last CALIBRE Trial visit:* ☐☐
Since the last CALIBRE Trial visit, did the participant require additional outpatient visits due to spontaneous bacterial peritonitis? No ☐ Yes ☐	If yes, how many additional outpatient visits did the participant require? *Please include the total for all outpatient visits that were required due to spontaneous bacterial peritonitis, since the last CALIBRE Trial visit:* ☐☐

Renal Dysfunction:

Since the last CALIBRE Trial visit, has the participant been diagnosed with Hepatorenal Syndrome per International Club of Ascites definitions?	No ☐ Yes ☐	*If no, please continue to Hepatocellular Carcinoma.* *If yes, please complete the following questions.*

How many episodes of Hepatorenal Syndrome have been diagnosed since the last CALIBRE Trial visit:	☐☐ *Please complete the dates below with most recent first*	**Not available**
Episode 1	D D / M M M / Y Y Y Y	☐
Episode 2	D D / M M M / Y Y Y Y	☐
Episode 3	D D / M M M / Y Y Y Y	☐
Episode 4	D D / M M M / Y Y Y Y	☐

Since the last CALIBRE Trial visit, has the participant been hospitalised due to Hepatorenal Syndrome? No ☐ Yes ☐

If no, please continue to outpatient visits below.

If yes, please complete the following questions.

Since the last CALIBRE Trial visit, how many times has the participant been hospitalised due to Hepatorenal Syndrome? ☐☐

How many days in total, has the participant been hospitalised?
Please include the total for all hospitalisations that have occurred due to Hepatorenal Syndrome, since the last CALIBRE Trial visit: ☐☐

Since the last CALIBRE Trial visit, was the participant admitted to intensive care due to Hepatorenal Syndrome? No ☐ Yes ☐

If yes, how many days did the participant stay in intensive care?
Please include the total for all intensive care days that were required due to Hepatorenal Syndrome, since the last CALIBRE Trial visit: ☐☐

Since the last CALIBRE Trial visit, did the participant require additional outpatient visits due to Hepatorenal Syndrome? No ☐ Yes ☐

If yes, how many additional outpatient visits did the participant require?
Please include the total for all outpatient visits that were required due to Hepatorenal Syndrome, since the last CALIBRE Trial visit: ☐☐

Guidance:

Diagnostic criteria of hepatorenal syndrome (HRS) type of acute kidney injury (AKI) in patients with cirrhosis
HRS-AKI

- *Diagnosis of cirrhosis and ascites*
- *Diagnosis of AKI according to ICA-AKI criteria**
- *No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin 1 g/kg bodyweight*
- *Absence of shock*
- *No current or recent use of nephrotoxic drugs (NSAIDs, aminoglycosides, iodinated contrast media, etc)*
- *No macroscopic signs of structural kidney injury#, defined as:*
  - *absence of proteinuria (>500 mg/day)*
  - *absence of microhaematuria (>50 RBCs per high power field)*
  - *normal findings on renal ultrasonography*

**Patients who fulfil these criteria may still have structural damage such as tubular damage. Urine biomarkers will become an important element in making a more accurate differential diagnosis between HRS and acute tubular necrosis.*
ICA, International Club of Ascites; NSAIDs, non-steroidal anti-inflammatory drugs; RBCs, red blood cells.

#Increase in sCr ≥0.3 mg/dL (≥26.5 µmol/L) within 48 h; or a percentage increase sCr ≥50% from baseline which is known, or presumed, to have occurred within the prior 7 days. (A value of sCr obtained in the previous 3 months, when available, can be used as baseline sCr. In patients with more than one value within the previous 3 months, the value closest to the admission time to the hospital should be used. In patients without a previous sCr value, the sCr on admission should be used as baseline).

Hepatocellular Carcinoma (HCC):

Since the last CALIBRE Trial visit, has the participant been diagnosed with HCC?	No ☐ Yes ☐	*If no, please continue to Hepatic Encephalopathy.* *If yes, please complete the following questions.*

BCLC stage: Stage 0 ☐ Stage A ☐ Stage B ☐ Stage C ☐ Stage D ☐

When was the participant diagnosed? M M M / Y Y Y Y Unknown ☐

Please indicate which treatment (if any) that the participant is on: *Please tick all that apply*

	Yes		Yes		Yes
Loco-regional therapy	☐	Systemic therapy	☐	Radiation therapy	☐
Surgery	☐	Other (*please specify*)	☐	…….	

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Since the last CALIBRE Trial visit, has the participant been hospitalised due to HCC?	No ☐ Yes ☐	*If no, please continue to outpatient visits below.* *If yes, please complete the following questions.*
Since the last CALIBRE Trial visit, how many times has the participant been hospitalised due to HCC? ☐☐		How many days in total, has the participant been hospitalised? *Please include the total for all hospitalisations that have occurred due to HCC, since the last CALIBRE Trial visit:* ☐☐
Since the last CALIBRE Trial visit, was the participant admitted to intensive care due to HCC?	No ☐ Yes ☐	If yes, how many days did the participant stay in intensive care? *Please include the total for all intensive care days that were required due to HCC, since the last CALIBRE Trial visit:* ☐☐
Since the last CALIBRE Trial visit, has the participant required additional outpatient visits due to HCC?	No ☐ Yes ☐	If yes, how many additional outpatient visits did the participant require? *Please include the total for all outpatient visits that were required due to HCC, since the last CALIBRE Trial visit:* ☐☐

Guidance:

BCLC Staging System

- *Stage 0: The tumour is less than 2 cm, the person feels well (performance status 0) and the liver is working normally*
- *Stage A: There is a single tumour less than 5 cm, or up to 3 tumours all less than 3cm. The person feels well and is active (performance status 0) and the liver is working well*
- *Stage B: There are many tumours in the liver, but the person feels well (performance status 0) and the liver is working well*
- *Stage C: The cancer has spread into the blood vessels, lymph nodes or other body organs. Or the person does not feel well (performance status 1 or 2). The liver is still working.*
- *Stage D: There is severe liver damage or the person is not well and needs help in being looked after (performance status 3 or 4)*

Hepatic Encephalopathy:		
Since the last CALIBRE Trial visit, has the participant been diagnosed with hepatic encephalopathy? No ☐ Yes ☐	*If no, please continue to Liver transplant question.* *If yes, please complete the following questions.*	
How many episodes of hepatic encephalopathy have been diagnosed since the last CALIBRE Trial visit:	☐☐ *Please complete the dates below with most recent first, grade and if new or worsening*	**Not available**
Episode 1:	D D / M M M / Y Y Y Y	☐
Grade	Grade 1: ☐ Grade 2: ☐ Grade 3: ☐ Grade 4: ☐	☐
New or worsening	New: ☐ Worsening: ☐	☐
Episode 2:	D D / M M M / Y Y Y Y	☐
Grade	Grade 1: ☐ Grade 2: ☐ Grade 3: ☐ Grade 4: ☐	☐
New or worsening	New: ☐ Worsening: ☐	☐
Episode 3:	D D / M M M / Y Y Y Y	☐
Grade	Grade 1: ☐ Grade 2: ☐ Grade 3: ☐ Grade 4: ☐	☐
New or worsening	New: ☐ Worsening: ☐	☐
Episode 4:	D D / M M M / Y Y Y Y	☐
Grade	Grade 1: ☐ Grade 2: ☐ Grade 3: ☐ Grade 4: ☐	☐
New or worsening	New: ☐ Worsening: ☐	☐

I confirm that all above items have been considered and only those ticked were present No ☐ Yes ☐

Since the last CALIBRE Trial visit, has the participant been hospitalised due to hepatic encephalopathy? No ☐ Yes ☐	*If no, please continue to outpatient visits below.* *If yes, please complete the following questions.*	
Since the last CALIBRE Trial visit, how many times has the participant been hospitalised due to hepatic encephalopathy? ☐☐	How many days in total, has the participant been hospitalised? *Please include the total for all hospitalisations that have occurred due to hepatic encephalopathy, since the last CALIBRE Trial visit:*	☐☐
Since the last CALIBRE Trial visit, was the participant admitted to intensive care due to hepatic encephalopathy No ☐ Yes ☐	If yes, how many days did the participant stay in intensive care? *Please include the total for all intensive care days that were required due to hepatic encephalopathy, since the last CALIBRE Trial visit:*	☐☐

Since the last CALIBRE Trial visit, did the participant require additional outpatient visits due to hepatic encephalopathy?	No ☐ Yes ☐	If yes, how many additional outpatient visits did the participant require? *Please include the total for all outpatient visits that were required due to hepatic encephalopathy, since the last CALIBRE Trial visit:* ☐☐

Guidance:
West Haven Criteria for hepatic encephalopathy grading

- *Grade 1: Trivial lack of awareness; euphoria or anxiety; shortened attention span; impaired performance of addition or subtraction*
- *Grade 2: Lethargy or apathy; minimal disorientation for time or place; subtle personality change; inappropriate behaviour*
- *Grade 3: Somnolence to semi stupor, but responsive to verbal stimuli; confusion; gross disorientation*
- *Grade 4: Coma*

Liver Transplant:

Since the last CALIBRE Trial visit, has the participant had a liver transplant?	No ☐ Yes ☐	*If no, there are no further questions to complete.* *If yes, please complete the following questions*

Not available

Date D D / M M M / Y Y Y Y ☐

CRF completed by:
You **must** have signed the CALIBRE site training log and CALIBRE delegation log

Name: ……..
(please print)

Date: D D / M M M / Y Y Y Y

Signature: ……..