

19. Visit 3 - Baseline - Date of Visit 3 - Baseline

Number	Question	Answers
19.1	Date of Visit 3 - Baseline	<input data-bbox="954 280 1050 315" type="text"/> <input data-bbox="1062 280 1158 315" type="text"/> <input data-bbox="1171 280 1294 315" type="text"/> (dd-mm-yyyy)
19.2	Is Visit 3 date 14 to 30 days after Visit 1 date and 4 to 10 days after Visit 2 date?	Automatic Calculation on Castor

20.2.9
Claustrophobia or inability to remain still during imaging. YES
 NO

20.2.10
Contra-indication to intravenous adenosine as judged by the investigator, i.e. asthma; severe chronic obstructive lung disease; decompensated heart failure; long QT syndrome; second- or third-degree AV block and sick sinus syndrome; severe hypotension. YES
 NO

20.2.11
Contra-indication/allergy to gadolinium contrast media.

20.2.12
Estimated glomerular filtration rate (eGFR) <30mL/min/1.73m². YES
 NO

YES
 NO

Eligibility

20.1.2.2
Is the participant eligible to take part in the sub-study? YES
 NO

20.1.2.2.1
Was eligibility signed off by a delegated doctor prior to MRI YES
 NO

20.1.2.2.2
Name of PI or delegated doctor

20.1.2.2.3
Date of signature

(dd-mm-yyyy)

MRI

20.2.14
Has MRI been done? YES
 NO

20.4 eligible and MRI

(dd-mm-yyyy)

20.4.1
Date of MRI

20.4.2
Haematocrit value (this will be from a full blood count test that is to be obtained at the time of the scan)

L/L

20.4.3
Systolic Blood Pressure before adenosine

mmHg

20.4.4
Diastolic Blood Pressure before adenosine

mmHg

20.4.5
Systolic Blood Pressure after 3 minutes adenosine

mmHg

20.4.6
Diastolic Blood Pressure after 3 minutes adenosine

mmHg

20.4.7

Heart rate before adenosine

bpm

20.4.8

Heart rate after 3 minutes adenosine

bpm

21. Visit 3 - Baseline - Weight

Number	Question	Answers
21.1	Weight	<input data-bbox="954 280 1321 313" type="text"/> kg

22. Visit 3 - Baseline - Concomitant Medications

Number	Question	Answers
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22.1	Concomitant Medications	
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Please complete Concomitant Medications Log

23. Visit 3 - Baseline - Adverse Events

Number	Question	Answers
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23.1	Adverse Events Please complete Adverse Events Log	
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24. Visit 3 - Baseline - Glucose Review

Number	Question	Answers
24.1	Was Glucose Management Assessed? <i>If Glucose Management not assessed, this is a Protocol breach.</i>	<input type="radio"/> YES <input type="radio"/> NO
24.2	Insulin administration	<input type="radio"/> Subcutaneous injections <input type="radio"/> Pump
24.3	Daily basal insulin dose (average of last 7 days)	<input type="text"/> units/day
24.4	Daily bolus insulin dose (average of last 7 days)	<input type="text"/> units/day
24.5	Total daily insulin dose (average of last 7 days)	Automatic Calculation on Castor
CGM summary data from previous 2 weeks		
24.6	Are summary data from CGM readings over the 2 weeks prior to this visit available?	<input type="radio"/> YES <input type="radio"/> NO
24.6.1	Number of days CGM worn over preceding 14 days	<input type="text"/> days
24.6.2	Percentage of time CGM was active over preceding 14 days	<input type="text"/> %

24.6.3	Mean blood glucose level over preceding 14 days	<input type="text"/>	mmol/L
24.6.4	Blood glucose percentage time above 13.9 mmol/L over preceding 14 days	<input type="text"/>	%
24.6.5	Blood glucose percentage time from 10.1 to 13.9mmol/L over preceding 14 days	<input type="text"/>	%
24.6.6	Blood glucose percentage time from 3.9 to 10.0 mmol/L over preceding 14 days	<input type="text"/>	%
24.6.7	Blood glucose percentage time from 3.0 to 3.8 mmol/L over preceding 14 days	<input type="text"/>	%
24.6.8	Blood glucose percentage time below 3.0 mmol/L over preceding 14 days	<input type="text"/>	%
24.6.9	Do blood glucose percentage times spent in each range add up to 100%?	Automatic Calculation on Castor	
24.6.10	Glycaemic variability index over preceding 14 days	<input type="text"/>	%CV

- 24.1.1 Does the participant report any level 2 or level 3 hypoglycaemic events since last visit? YES NO

If there has been a level 3 hypoglycaemic event since last visit, participant is ineligible for trial. Complete the hypoglycaemic repeating data.

Level 3 hypoglycaemic event is defined as requiring hospitalisation and/or assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions. These episodes may be associated with sufficient neuroglycopenia to induce seizure or coma. Plasma glucose measurements may not be available during such an event, but neurological recovery attributable to the restoration of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration

Hypoglycaemic Events

- 24.1.1.2 Hypoglycaemic Events
Please record any level 2 or 3 hypoglycaemic events in the Hypoglycaemic Events Log

- 24.1.3 Does the participant report any other symptomatic hypoglycaemic events in the last 2 weeks? YES NO

- 24.1.3.1 If Yes, specify

- 24.7 HbA1c performed? Automatic Calculation on Castor

- 24.7.1 HbA1c units used? Automatic Calculation on Castor

- 24.7.2 HbA1c level Automatic Calculation on Castor

- 24.7.1.1 Is HbA1c result lower than 58 mmol/mol? Automatic Calculation on Castor

- 24.7.1.2 Is HbA1c result lower than 7.5%?

- 24.7.1.2.1 If yes, was insulin reduced by 10%? YES NO
If insulin not reduced by 10%, this is a Protocol breach

- 24.7.1.1.1 If yes, was insulin reduced by 10%? YES
If insulin not reduced by 10%, this is a Protocol breach NO

25. Visit 3 - Baseline - Ketone Review

Number	Question	Answers
Ketone Readings		
25.1	Have there been Ketone measures since the last visit?	<input type="radio"/> YES <input type="radio"/> NO
25.1.1	Number of ketone measurements taken since last visit	<input style="width: 150px; height: 20px;" type="text"/>
25.1.2	Number of episodes with ketone levels between 0.6 and 1.5 mmol/L (inclusive of endpoints).	<input style="width: 150px; height: 20px;" type="text"/>
<p>A distinct episode is a period where ketones have gone above the threshold (0.6mmol/L) and then come down below this. If it then went up again that would be a new distinct event.</p>		
25.1.4	Number of episodes with ketone levels greater than 1.5 mmol/L	<input style="width: 150px; height: 20px;" type="text"/>
<p>A distinct episode is a period where ketones have gone above the threshold (1.5mmol/L) and then come down below this. If it then went up again that would be a new distinct event.</p>		
25.1.6	Have there been any DKA events since the last visit?	<input type="radio"/> YES <input type="radio"/> NO
<p>If there has been a DKA event since last visit, participant is ineligible for trial. Complete the DKA Log.</p> <p>If the participant has experienced any DKA events please complete the DKA Events Log</p>		

Repeating Data 'Vital Signs'

Form Vital Signs

Number	Question	Answers
	Complete Vital Signs form	
1.1	Blood Pressure - Systolic	<input type="text"/> mmHg
1.2	Blood Pressure - Diastolic	<input type="text"/> mmHg
1.3	Pulse	<input type="text"/> bpm

27. Visit 3 - Baseline - Questionnaires

Number	Question	Answers
27.1	Has the KCCQ questionnaire been completed?	<input type="radio"/> YES <input type="radio"/> NO
27.1.1	Add KCCQ	Performed in Castor
27.2	Has the DTSQs questionnaire been completed?	<input type="radio"/> YES <input type="radio"/> NO
27.2.1	Add DTSQs	Performed in Castor
27.3	Has the EQ-5D-5L questionnaire been completed?	<input type="radio"/> YES <input type="radio"/> NO
27.3.1	Add EQ-5D-5L	Performed in Castor

28. Visit 3 - Baseline - 6-Minute Walk Test

Number	Question	Answers
Please complete 6-Minute Walk Test		
28.1	Was 6-Minute Walk Test completed?	<input type="radio"/> YES <input type="radio"/> NO
28.1.1	Distance walked in 6 minutes?	<input style="width: 150px; height: 15px;" type="text"/> m
28.1.2	Number of stops?	<input style="width: 150px; height: 15px;" type="text"/>

Repeating Data 'Safety Bloods'

Visit 3 - 29. Samples - Form Safety Bloods

Number	Question	Answers
1.1	Date of blood sample	<input type="text"/> <input type="text"/> <input type="text"/> (dd-mm-yyyy)
1.2	Haemoglobin	<input type="text"/>
1.3	Haemoglobin Unit	<input type="radio"/> g/L <input type="radio"/> g/dL
1.4	Is the haemoglobin value within the expected range?	
1.5	Sodium	<input type="text"/> mmol/L
1.6	Potassium	<input type="text"/> mmol/L
1.7	Urea	<input type="text"/> mmol/L
1.8	Creatinine	<input type="text"/> μ mol/L
1.9	Glucose	<input type="text"/> mmol/L
1.10	eGFR	<input type="text"/> mL/min/1.73m ²

29. Visit 3 - Baseline - Samples

Number	Question	Answers
29.1	Urine Pregnancy Test	
	Pregnancy test performed	
29.2		<input type="radio"/> YES <input type="radio"/> NO <input type="radio"/> N/A
29.2.1	Pregnancy test result	<input type="radio"/> Positive <input type="radio"/> Negative
	Without a negative pregnancy test result, the participant is not eligible to take part in the trial.	
29.2.2	Is the participant either permanently sterilized or post-menopausal?	<input type="radio"/> YES <input type="radio"/> NO
Urine Sample		
29.3	Urine Sample	
29.4	Were research bloods taken and processed as per laboratory manual?	<input type="radio"/> YES <input type="radio"/> NO
29.4.1	If answered No, give reason	<div style="border: 1px dashed black; height: 80px; width: 100%;"></div>

Repeating Data 'Urine Sample'

Form Urine sample

Number	Question	Answers
1.1	Date of urine sample	<input type="text"/> <input type="text"/> <input type="text"/> (dd-mm-yyyy)
1.2	Albumin	<input type="text"/> mg/L
1.4	Creatinine	<input type="text"/>
1.5	Creatinine Units	<input type="radio"/> µmol/L <input type="radio"/> mmol/L
1.6	Urine albumin/creatinine ratio	<input type="text"/> mg/mmol creat
1.7	Sodium	<input type="text"/> mmol/L

30. Visit 3 - Baseline Inclusion Criteria

Number	Question	Answers
30.2	Age 18 years to less than 85 years	<input type="radio"/> YES <input type="radio"/> NO
30.3	Type 1 Diabetes	Automatic Calculation on Castor
30.4	Insulin dose greater than or equal to 0.5 units/kg body weight at screening or BMI greater than or equal to 25kg/m ² at screening	Automatic Calculation on Castor
30.5	Using continuous glucose monitor at screening or willing to use one for the duration of the trial	Automatic Calculation on Castor
30.1.2	<p>Diagnosis of heart failure (HF) or high risk for HF defined as any of the following:</p> <p>NT-pro-BNP greater than or equal to 250 ng/L for those in atrial fibrillation/flutter, greater than or equal to 125 ng/L for those in all other rhythms</p> <p><u>or</u></p> <p>Previous HF hospitalisation where HF was documented as the primary cause of hospitalisation and there was a requirement for loop diuretics.</p> <p><u>or</u></p> <p>Impaired left ventricular function (i.e. LVEF less than 50% by any imaging modality) at any time</p> <p><u>or</u></p> <p>Preserved LV systolic function (LVEF greater than or equal to 50%) with left atrial enlargement (2-dimensional measurement of left atrial width greater than or equal to 3.8 cm or left atrial length greater than or equal to 5.0 cm or left atrial area greater than or equal to 20 cm² or left atrial volume index greater than 29 ml/m²) within the last 24 months.</p>	<input type="radio"/> YES <input type="radio"/> NO

or

Preserved LV systolic function (LVEF greater than or equal to 50%) with left ventricular hypertrophy (2-dimensional measurement of end-diastolic interventricular septal diameter greater than or equal to 1.2 cm or end-diastolic left ventricular posterior wall diameter greater than or equal to 1.2 cm) within the last 24 months

or

Preserved LV systolic function (LVEF greater than or equal to 50%) with diastolic dysfunction (septal e' less than 7 cm/sec or lateral e' less than 10 cm/sec or average E/e' greater than or equal to 15) within the last 24 months

30.6	New York Heart Association Class II-IV at screening	Automatic Calculation on Castor
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30.7	Kansas City Cardiomyopathy clinical summary score less than 85 at screening.	Automatic Calculation on Castor
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31. Visit 3 - Baseline - Exclusion Criteria

Number	Question	Answers
31.1	Cardiac surgery (coronary artery bypass graft or valve replacement), type 1 myocardial infarction, implantation of cardiac device (including biventricular pacemaker) or cardiac mechanical support implantation within 1 month of screening, or between screening and randomisation, or planned during the trial.	<input type="radio"/> YES <input type="radio"/> NO
31.2	End-stage heart failure requiring left ventricular assist devices, intra-aortic balloon pump, or any type of mechanical support at the time of randomisation.	<input type="radio"/> YES <input type="radio"/> NO
31.3	Documented primary severe valvular heart disease, amyloidosis or hypertrophic cardiomyopathy as principal cause of heart failure as judged by the local investigator.	<input type="radio"/> YES <input type="radio"/> NO
31.4	Respiratory disease thought to be the primary cause of dyspnoea as assessed by the local investigator.	<input type="radio"/> YES <input type="radio"/> NO
31.5	Chronic kidney disease with estimated glomerular filtration rate <25ml/min/1.73m ² at screening.	<input type="radio"/> YES <input type="radio"/> NO
31.6	Moderate or severe hepatic impairment (e.g. Child-Pugh B and C) at screening as judged by the local investigator.	<input type="radio"/> YES <input type="radio"/> NO
31.7	Use of sotagliflozin or any SGLT2 inhibitor within 1 month of screening or between screening and randomisation.	<input type="radio"/> YES <input type="radio"/> NO
31.8	Previous hypersensitivity/intolerance to SGLT2 inhibitors.	<input type="radio"/> YES <input type="radio"/> NO
31.9	Presence of malignancy with expected life expectancy less than 1 year at screening	

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- 31.10 Severe hypoglycaemia (hospitalisation for hypoglycaemia or episode requiring external assistance to treat) within 1 month prior to screening or between screening and randomisation. YES
 NO
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- 31.11 One episode of diabetic ketoacidosis or nonketotic hyperosmolar state within 1 month of screening or between screening and randomisation, or greater than or equal to 2 diabetic ketoacidosis or nonketotic hyperosmolar state events within 6 months of screening. YES
 NO
-
- 31.12 Pregnant or lactating women YES
 NO
-
- 31.13 Women of childbearing age or male partners of women of childbearing age and not practicing a method of acceptable birth control.
-
- 31.14 On a ketogenic diet. YES
 NO
-
- 31.15 Unwilling/unable to share glucose and ketone monitoring data. YES
 NO
-
- 31.16 Use of any investigational drugs within five times of the elimination half-life after the last dose or within 30 days, whichever is longer. Current enrolment in non-interventional, observational studies will be allowed. YES
 NO

32. Visit 3 - Baseline - Eligibility

Number	Question	Answers
Eligibility must be checked prior to randomisation by a doctor delegated this task in the Delegation Log.		
32.1	Is the participant eligible to take part in the trial?	<input type="radio"/> YES <input type="radio"/> NO
32.2	Was eligibility signed off by a delegated doctor prior to randomisation?	<input type="radio"/> YES <input type="radio"/> NO
32.3	Name of PI or delegated doctor	<input type="text"/>
32.4	Date of signature	<input type="text"/> / <input type="text"/> / <input type="text"/> (dd-mm-yyyy)
32.5	Date of signature between date of visit 3 and date of randomisation?	Automatic Calculation on Castor

33. Visit 3 - Baseline - Randomisation

Number	Question	Answers
33.1	Has the participant been randomised?	<input type="radio"/> YES <input type="radio"/> NO
33.1.1	Date of Randomisation	<input type="text"/> <input type="text"/> <input type="text"/> (dd-mm-yyyy)
33.1.2	Is date of randomisation after date of consent (Visit 1) and on or after date of eligibility sign-off (Visit 3)?	Automatic Calculation on Castor

34. Visit 3 - Baseline - Dispensing of IMP

Number	Question	Answers
34.1	Was IMP dispensed at visit?	<input type="radio"/> YES <input type="radio"/> NO
34.1.1	If answered No, give reason?	<div style="border: 1px dashed black; height: 100px; width: 100%;"></div>