NIHR | Cambridge Biomedical Research Centre

mulTi-Arm Therapeutic study in pre-ICu patients admitted with Covid-19 - Experimental drugs and mechanisms (TACTIC-E)

Site Initiation Visit: <date>; <time>

UK Site name/ Number: / Nxx

PI: <name>

TACTIC E

*E*valuating new drugs against COVID-19

Trial Processes

TACTIC-E

Randomisation

See also TACTIC-E Randomisation Manual

TACTIC-E
Evaluating new drugs against COVID-19

Unique Trial ID number

- The patient will be assigned a trial ID formatted as
- Nxx-xxxx where Nxx is the site specific ID and xxxx is the patient number at that specific site

- ID number will increase sequentially

- E.g. for your site:
  - <site name>: Nxx-0001, Nxx-0002, Nxx-0003…

This ID will be used to identify the patient in all documents throughout the trial

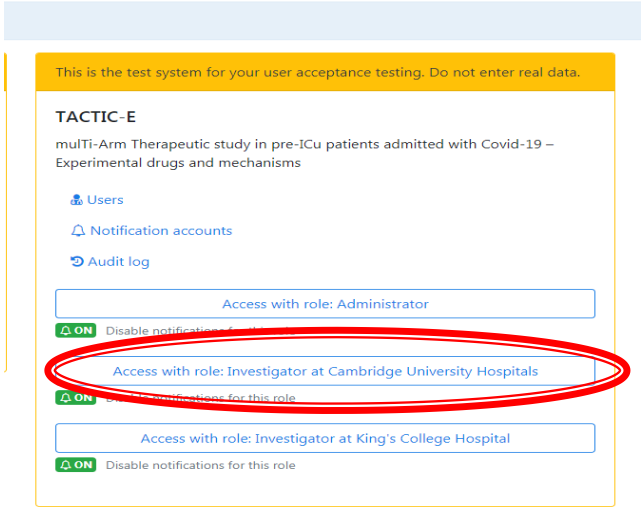
Randomisation

- Randomise patient at the **end of baseline** visit
- Investigators delegated to randomise participants will be given a log-in and a link to access Sealed Envelope (randomisation system)
- www.sealedenvelope.com/access/

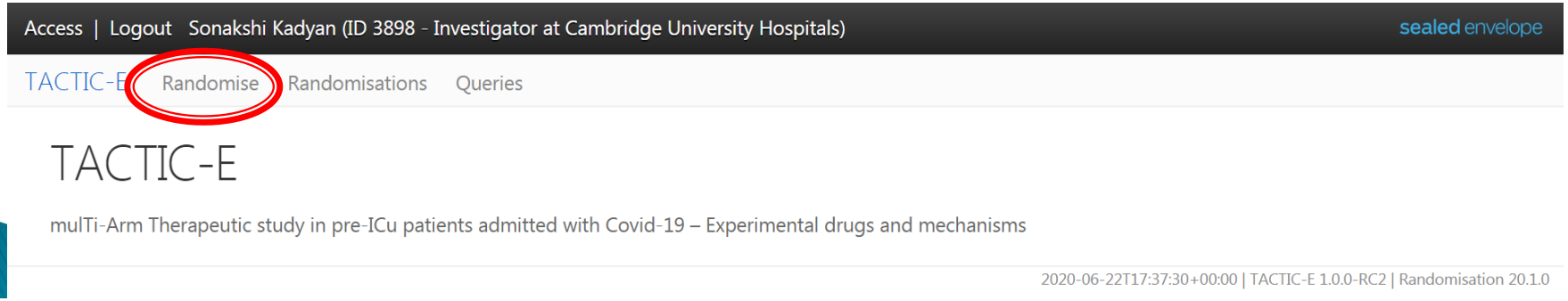
  www.sealedenvelope.com/redpill/tactice
- When you have been setup you will receive an email with a link to Sealed Envelope and your login details
- You will be prompted to change your password on your first login

Randomisation

1. Click on role as Investigator in the middle of the display screen to randomise a patient



2. Click on randomise



Randomisation

- Enter information required by the randomisation system
- Subject ID (participant unique trial ID e.g. Nxx-0001)
- Partial participant DoB (Month/Year)
- Initials XXX
- Date of informed consent
- A check against drug specific exclusion criteria for EDP1815/Ambrisentan + Dapagliflozin (image on next slide)
- Confirmation that participant meets all inclusion criteria (Yes/No)
- Confirmation that written informed consent has been obtained (Yes/No)
- Confirmation that none of the exclusion criteria apply (Yes/No)
- Site (drop-down menu, only your site will show)

Note. **Full inclusion/ exclusion must first be performed** (see Protocol or use CRF or eCRF) **before going to Sealed Envelope (SE)**

As SE only asks about the drug specific criteria for randomisation purposes

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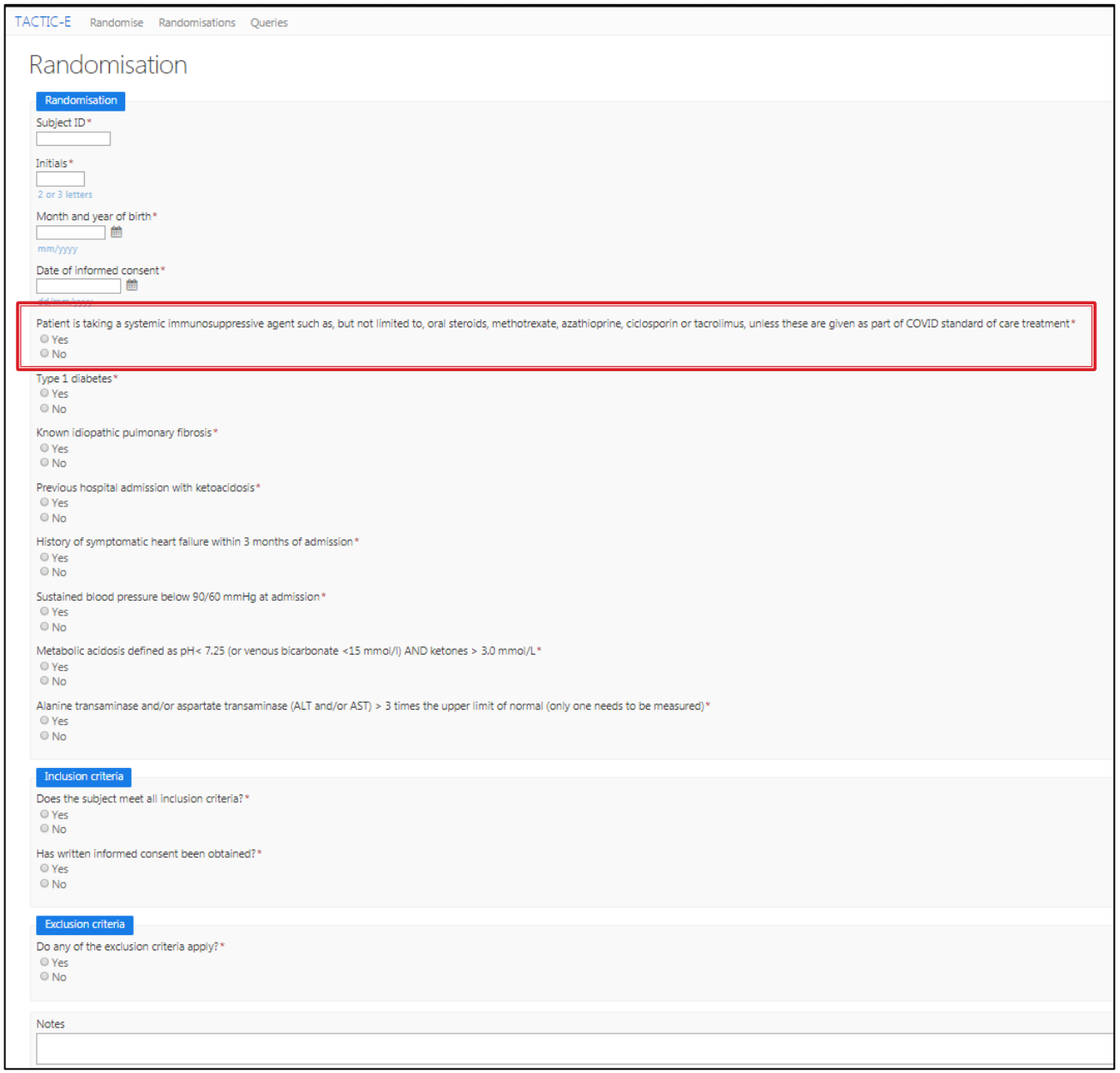

EDP1815 specific exclusion criterion

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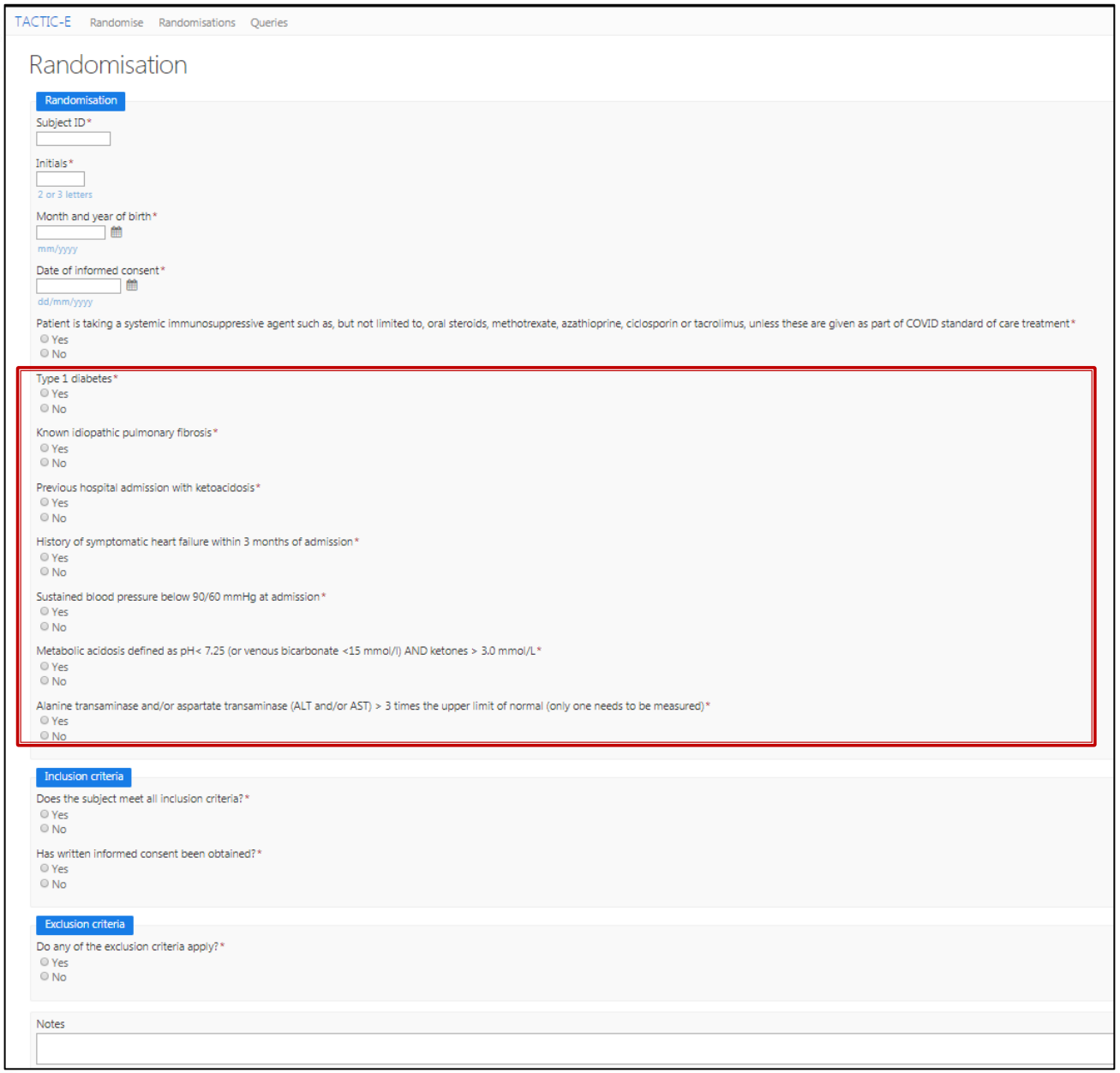

Dapagliflozin and Ambrisentan Specific Exclusions

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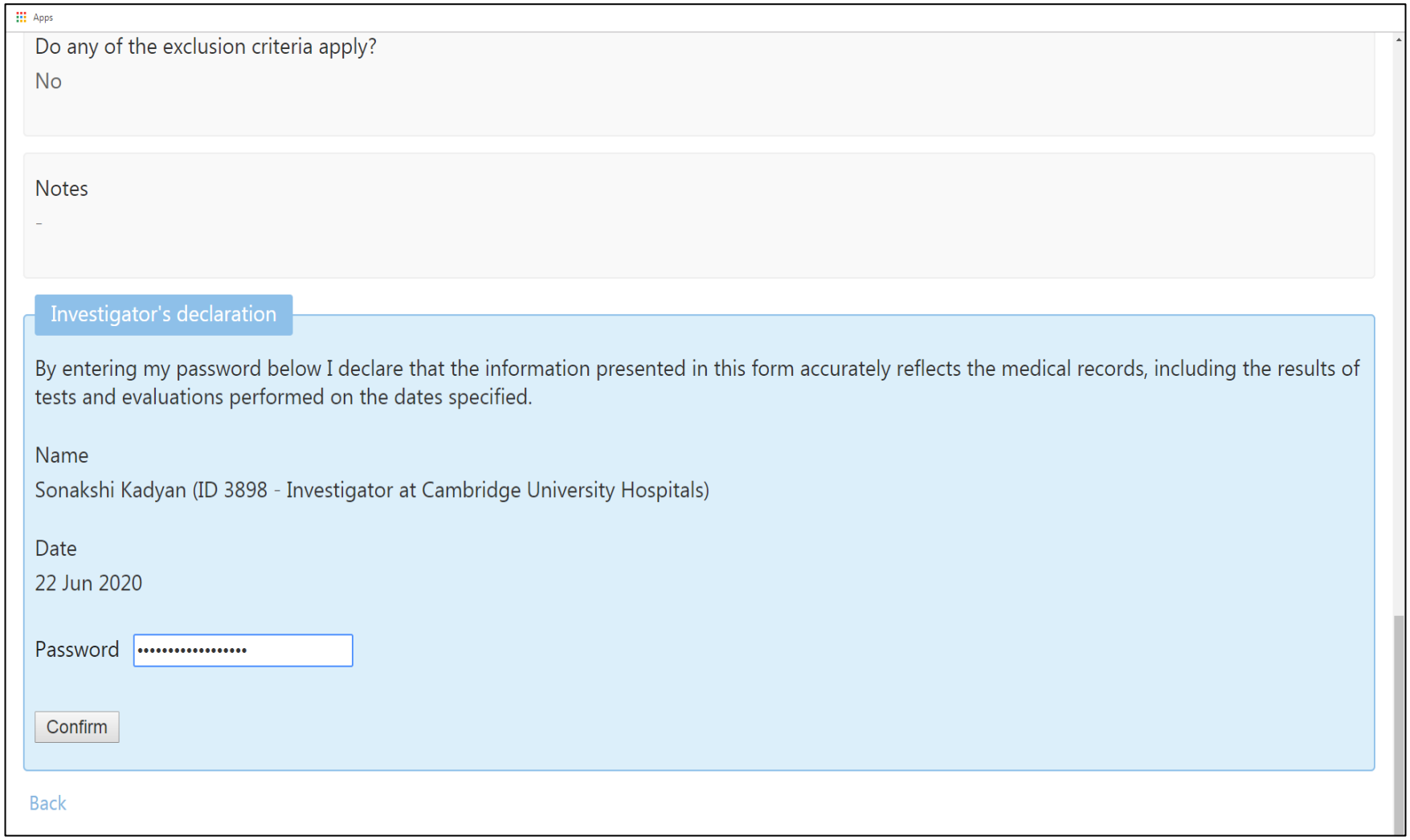
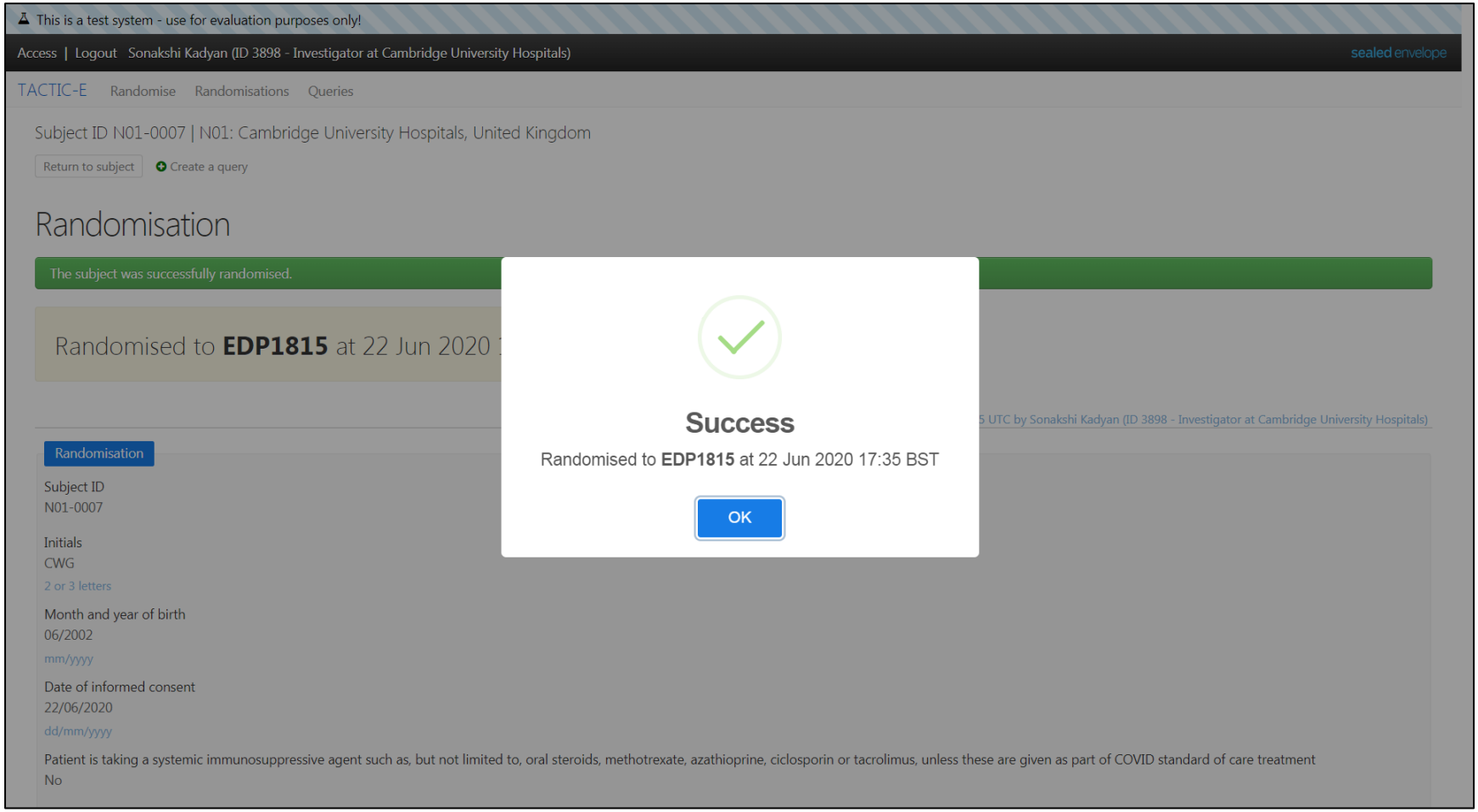


The randomiser will then be asked to re-enter their password to confirm



Screen when randomisation is successful.

Randomisation

- After a successful randomisation, an arm will be assigned to the patient. This will need to be added to the eCRF

- The following personnel will receive an email confirming the randomisation arm:
  - TACTIC-E Lead Site Trial office
  - Randomiser
  - Investigators at the randomising site (if delegated to randomise at the site)
  - Pharmacy at site (notification account can be set up)

- Email notification should be printed and filed in the ISF

Further information on randomisation can be found in the TPM

TACTIC-E
Data Entry / CRFs

TACTIC-E eCRF

- Electronic Case Report Form (eCRF) on MACRO
- Individual accounts / log in for TACTIC trial team members
- Electronic sign off of eCRFS for Trial PI:
  - **Eligibility confirmation**
  - **End of Trial participation form**
- Electronic sign off of eCRFS for trial PI or delegate:
  - **Clinical sign off**

Getting a MACRO account to use eCFR

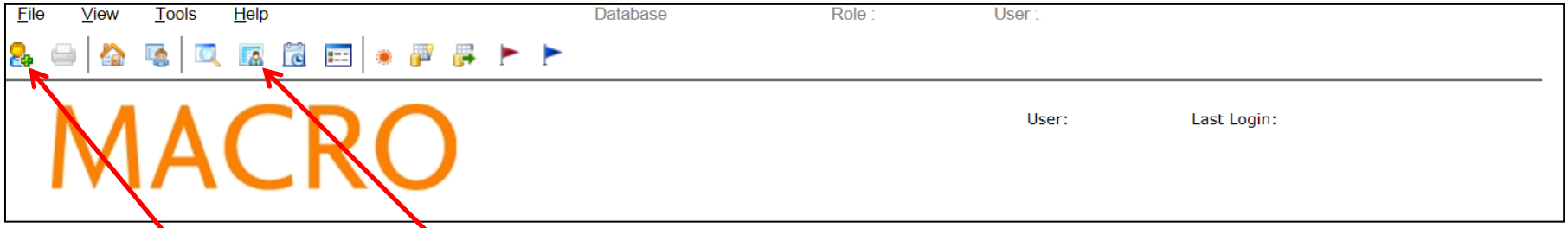
- **eCRF accounts can only be provided by the UK lead site/sponsor once MACRO training has been completed.**
- **PIs are required to sign of eCRFs so will need to complete training**
- You will receive an email containing your log in details when the account has been set up.
- Having an account allows you to :
  - add new patient to the database eCRF
  - continue to complete/add data to an eCRF for a previously entered TACTIC-E patient

Logging in to MACRO

You can access the MACRO system using the following web address.
(https://macro.infermed.com/macro4cuh)

Enter the username and password provided into the login/security window, as shown. The first time you access your MACRO account, you will be asked to create a new password. Once you have reset your password, you can
ess your Account.

Adding a NEW subject / patient

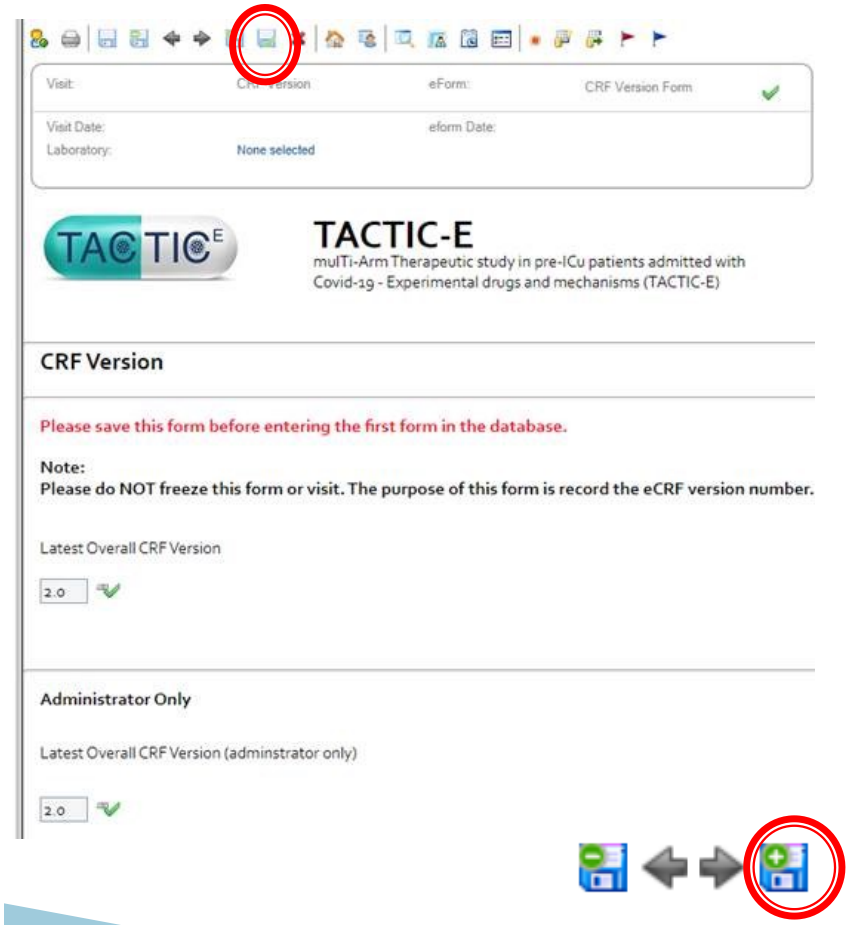


On homepage tool bar select the this ICON to create a new subject

Or select the this ICON to see list of existing subjects

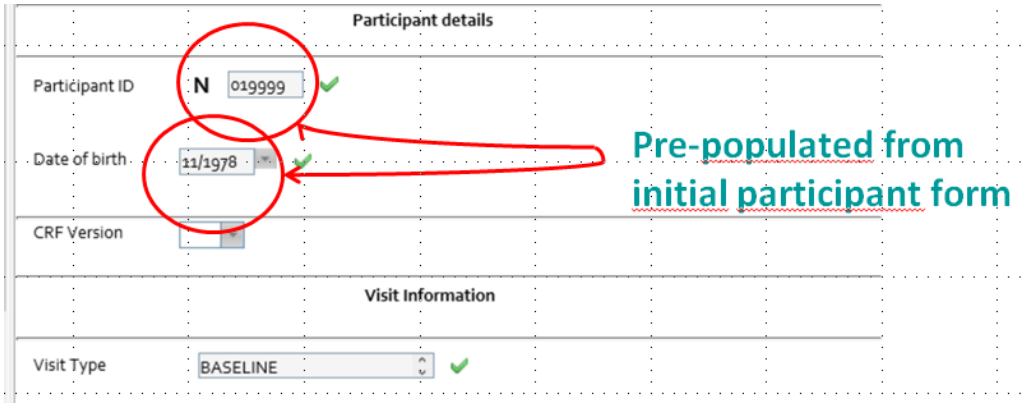
CRF version form completion

After creating a new patient/subject you will see the CRF version Form
click SAVE first before entering any other data.
This will only need to be done once per patient at the start



Completing visits

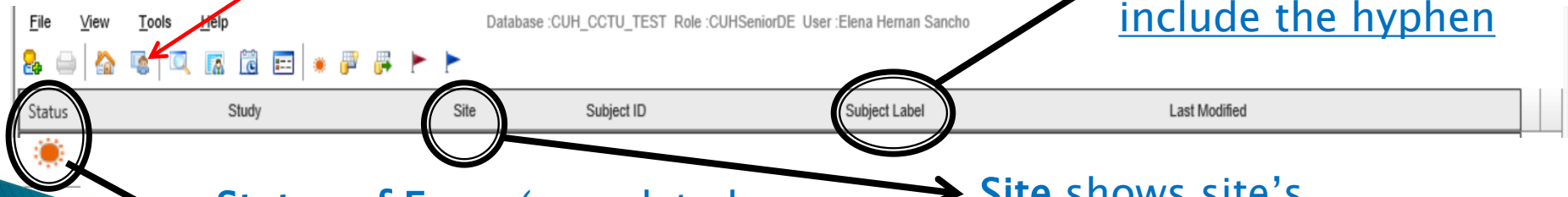
- Each Form (page) will have individual fields to complete for the data collected in that visit
- If a value is incorrect or outside range, an automatic warning will appear
- Patient ID and DOB are automatically pre-populated from what has been entered into the main “new patient” form



TACTIC-E eCRF:
Selecting a previously entered trial patient

- To find a subject / patient that has previously been entered into the DB, click the icon 

- A list of all the subjects which have been registered to TACTIC-E at your site will appear. Browse the list and select a subject by double clicking their subject ID.



Subject Label (Nxx-XXXX) – when entering ID in MACRO do not include the hyphen

Status of Form (completed, in progress etc

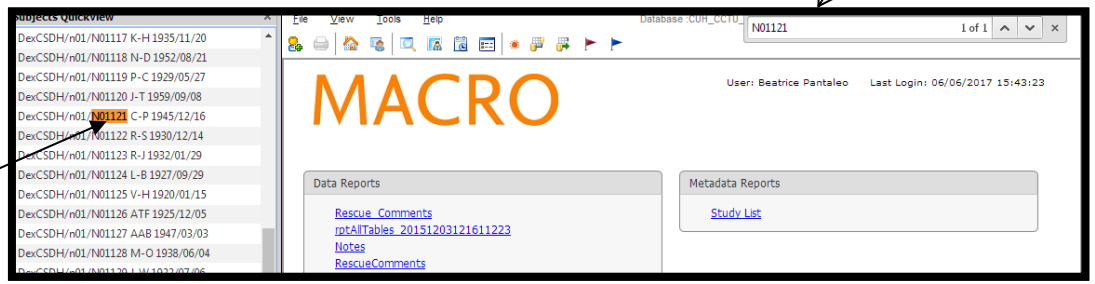
Site shows site's unique number, e.g. Nxx

TACTIC-E eCRF:
Selecting a previously entered trial patient

- If you are working with a large number of entered patients, it may be easier to use the **Subject Quick View** page by clicking the quick view icon 

and using the Ctrl+F function to search for the trial/subject ID you are looking for

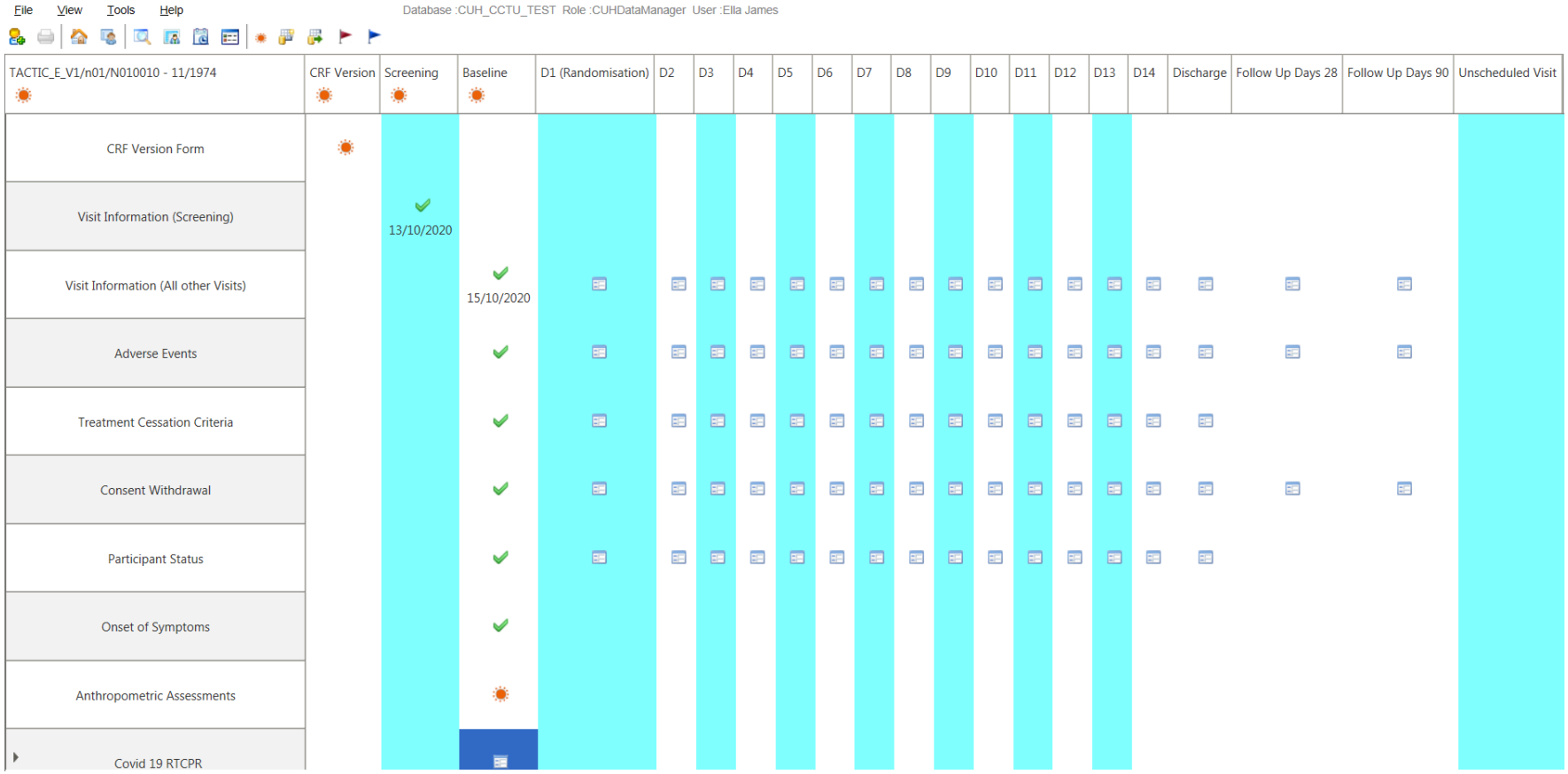
Type the subject ID that you wish to find here.



Searched label will highlight in orange.

TACTIC-E eCRF: Entering Data

Select a form inside a patient to begin data entry for a visit



Indicates an empty form that needs completing for that visit

Indicates form has been **partially completed**

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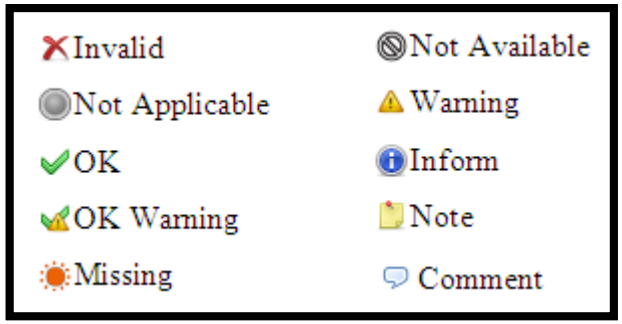
Entering Data



Once you have answered a question, click the next empty field, tab or Enter and a green tick should appear next to the completed field.

If the green tick does not show beside a question, the data will not be saved.

If the data is missing, leave this question and complete the rest of the form. An orange sun will show against the question and in the schedule view against that form as a reminder that data is missing.

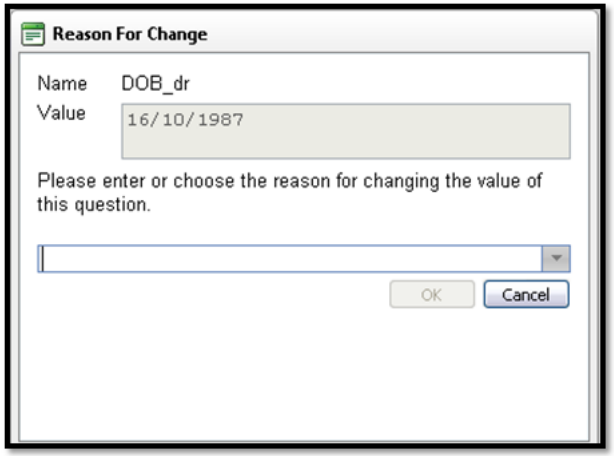
Missing/Questionable data can be queried and entered at a later date, However, overall **the return of data to the UK lead site should be as quick as possible**

Nb. Data regulatory checked (planned safety analysis) so needs to be entered as quick as possible

Amending data

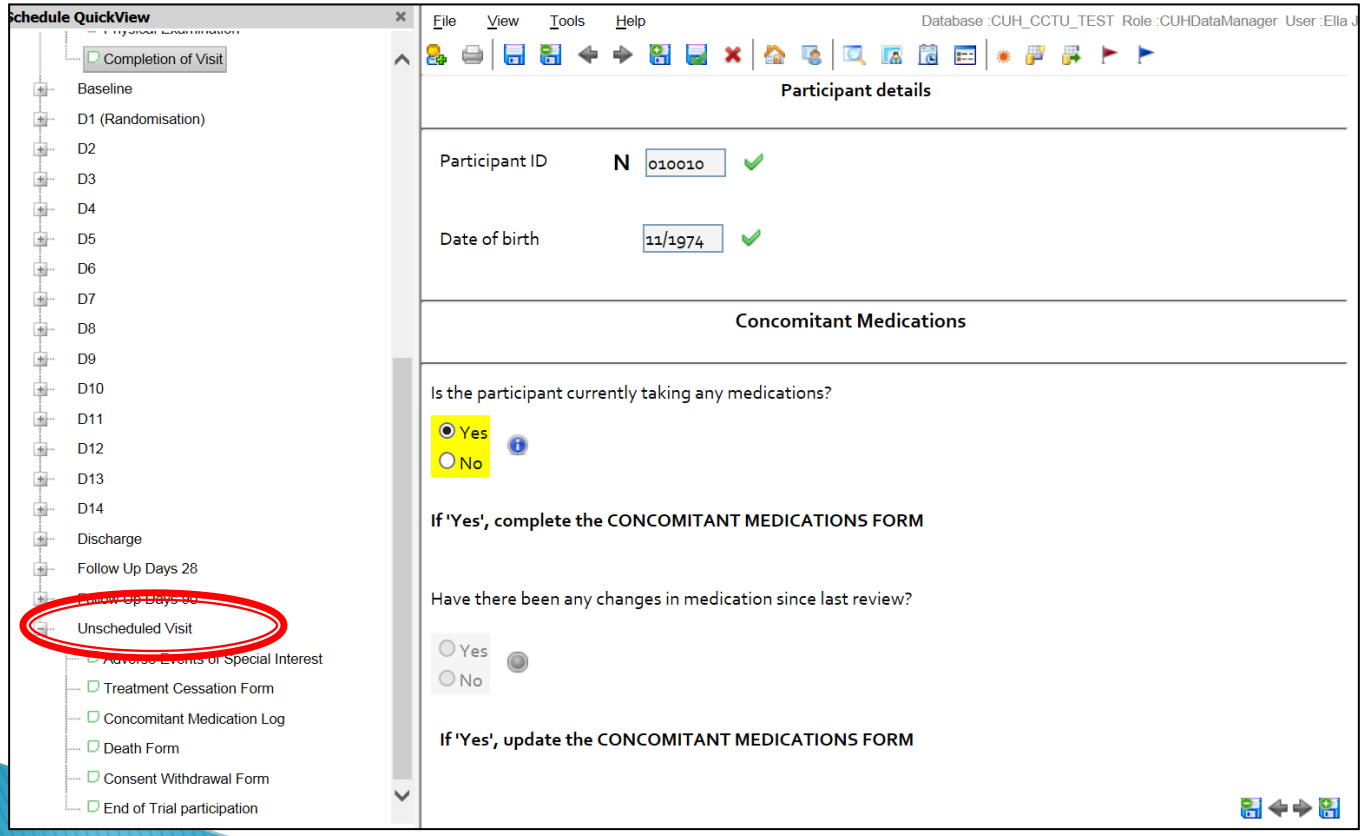
Most of the validations/edit checks work as soon as you enter the data.

If data needs to be changed after saving the e-form click on the data entry box, enter the correct data and save the form again. You will be asked the reason for the change. The new changes will be stored in the database and be used for the audit trail



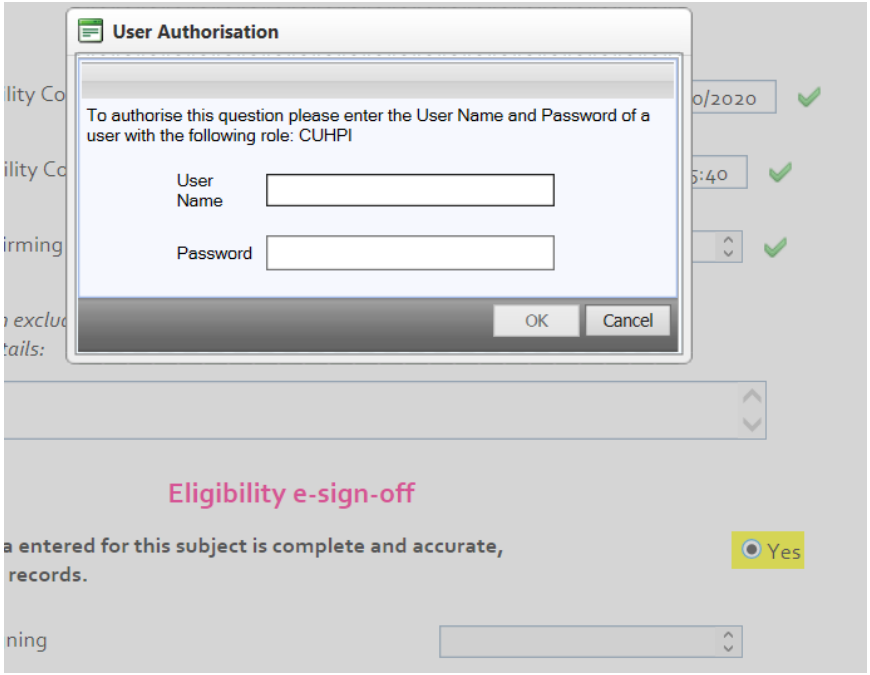
Other forms
e.g. concomitant medication, AESI, withdrawal etc

From left hand **Schedule QuickView** panel
navigate to **unscheduled visit** and click to reveal eCRF Forms



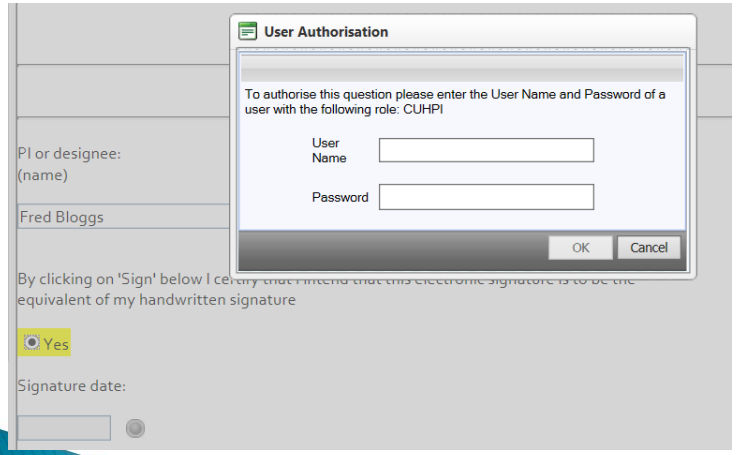
e-sign off: Eligibity → PI

"Eligibility" (screening visit)



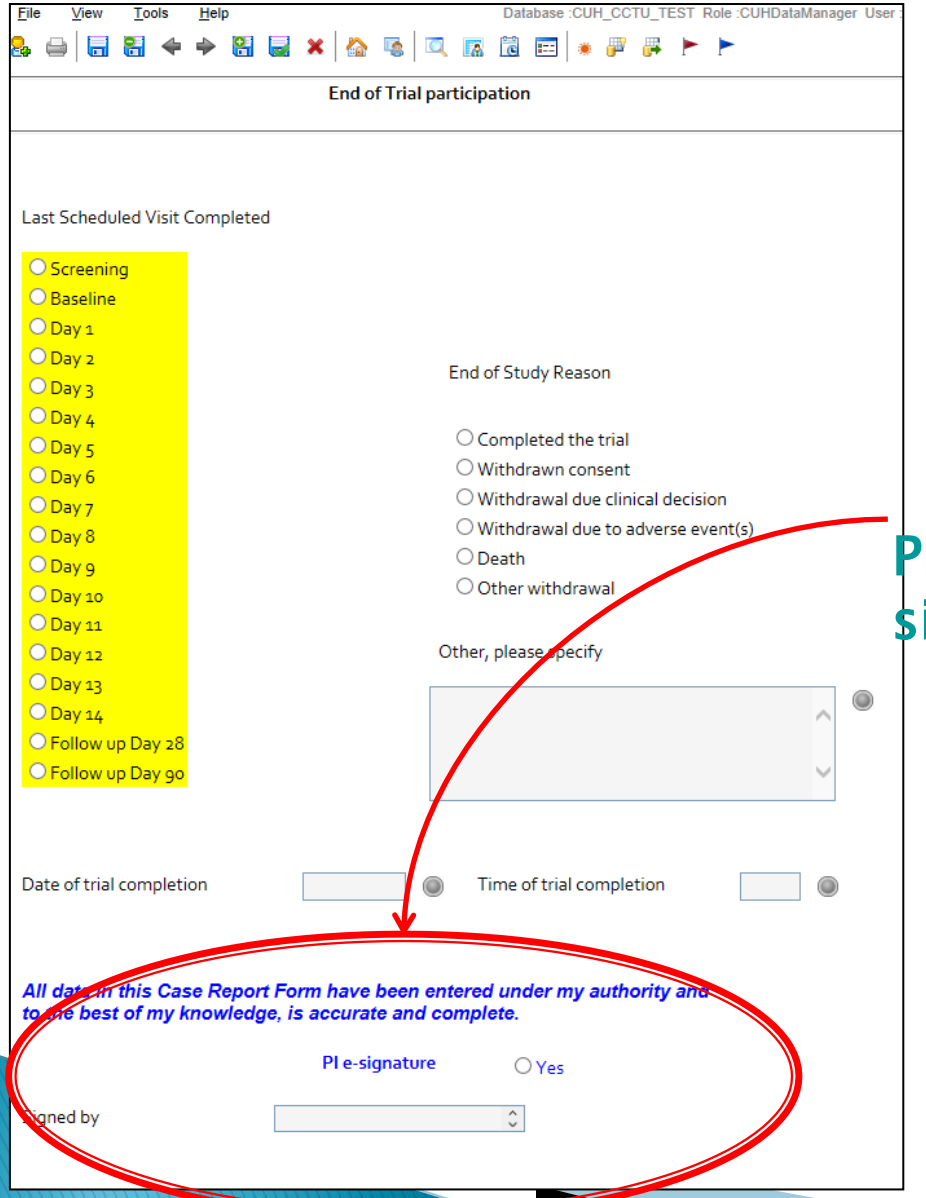
e-sign-off:
Completion of Visit + Clinical Sign-Off

Completion of Visit: Write name in visit conducted by field and click 'yes' for data to populate in Signature date field and for sign off to be completed for a visit.
UN / PW NOT required



Write name in PI or designee field and click 'yes' . User Authorisation by the PI or Delegate will then be required by entering PW / UN

End of trial participation sign-off

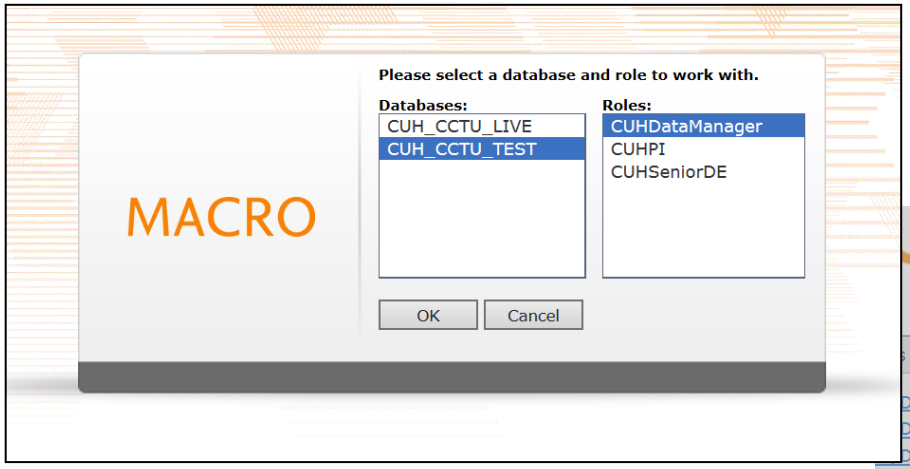


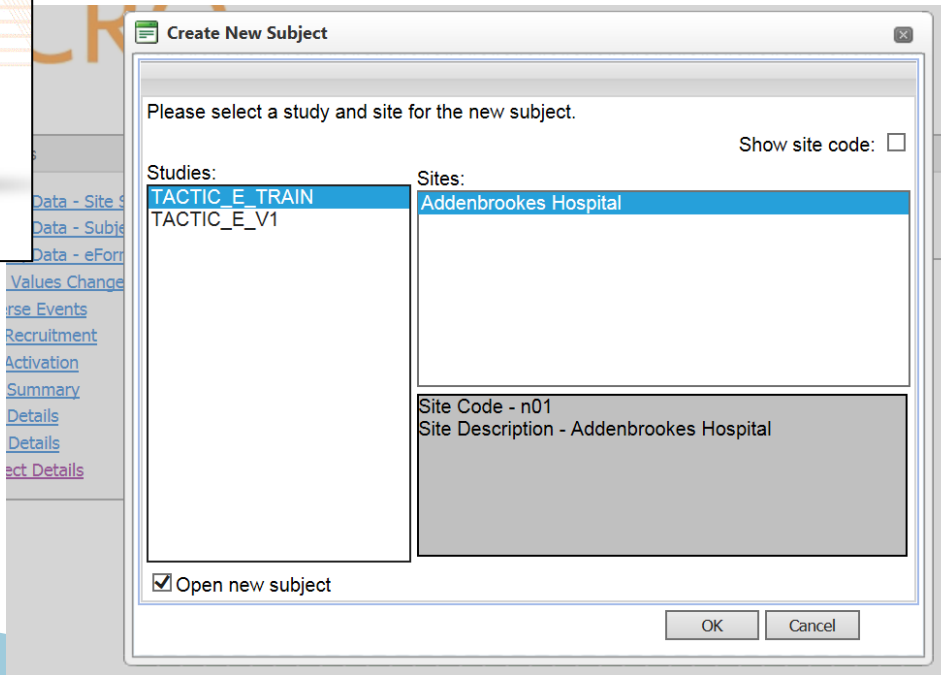
End of trial participation (in unscheduled visit forms) require PI e-sign off

PI electronic signature

Practice/Training

A test option is available to practice adding dummy data → once you get a MARCO account log in and go to TEST, create New Subject then TACTIC_E_Train





Prompt data entry key

AE of special interest Form
Dapa/Ambri arm
Diabetic ketoacidosis
New peripheral oedema

Complete in eCRF and inform
cambs.cardiovascular@nhs.net
(within 24h site awareness)

Were any of the Adverse Events considered to be an Adverse Event of Special Interest?

○ Yes
○ No

* New diabetic ketoacidosis in those patients on Dapagliflozin and Ambrisentan
* New peripheral oedema in those patients on Dapagliflozin and Ambrisentan

If 'Yes', complete the ADVERSE EVENT OF SPECIAL INTEREST FORM and scan and submit immediately by email to

cambs.cardiovascular@nhs.net and inform the UK lead site coordinator

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ADVERSE EVENT OF SPECIAL INTEREST FORM

Participant ID N☐☐-☐☐☐☐
Participant NHS/hospital number (first five digits) ☐☐☐☐☐
Partial DOB (Month/Year) ☐☐☐/☐☐☐☐

AESI No.	AESI type [a] (details on reverse side)	Date of onset (DD/MMM/YY)	Date of resolution (if applicable) (DD/MMM/YY)	Days from admission to AESI	Outcome [b]	Severity [c]	Is the AESI serious? [d]	Is the AESI related to the IMP? [e]
		☐☐/☐☐☐/☐☐	☐☐/☐☐☐/☐☐					
		☐☐/☐☐☐/☐☐	☐☐/☐☐☐/☐☐					
		☐☐/☐☐☐/☐☐	☐☐/☐☐☐/☐☐					
		☐☐/☐☐☐/☐☐	☐☐/☐☐☐/☐☐					
		☐☐/☐☐☐/☐☐	☐☐/☐☐☐/☐☐					
		☐☐/☐☐☐/☐☐	☐☐/☐☐☐/☐☐					

[a] AESI type	[b] Outcome	[c] Severity	[d] Is the AESI serious?	[e] Is the AESI related to the IMP?
1 = New diabetic ketoacidosis in those patients on Dapagliflozin and Ambrisentan 2 = New peripheral oedema in those patients on Dapagliflozin and Ambrisentan	1 = Resolved, no residual effects 2 = Resolved, with residual effects 3 = On-going 4 = Death	1 = Mild 2 = Moderate 3 = Severe	1 = Results in death 2 = Is life-threatening 3 = Requires hospitalisation 4 = Results in persistent or significant disability 5 = Results in congenital anomaly or birth defect 6 = Medically significant 7 = Non-serious	1 = Unrelated 2 = Unlikely 3 = Possibly 4 = Probably 5 = Definitely

PI or designee: (name)
PI or designee: (signature)
Date: ☐☐/☐☐☐/☐☐☐☐

Scan form and email immediately to: cambs.cardiovascular@nhs.net & include Trial name and 'AESI' in subject header; also inform UK lead site coordinator

TACTIC-E
ADVERSE EVENT OF SPECIAL INTEREST FORM
Page ☐☐ of ☐☐
Version 2.0
13/AUG/2020

Fig. Paper CRF: AESI form

eCRF AESI form located in unscheduled Visits section of Schedule QuickView for a patient.
eCRF requests the same information as paper AESI Form (with drop down menus)

Prompt data entry key

Planned Interim Analyses

- *n=10 per arm*: Review safety
- *n=30 per arm*: Variance of biomarkers (CRP, NLR, Ferritin, DDimer, LDH) + safety
- *n=100 per arm*: Biomarker futility endpoint + safety
- *n=125 per arm*: Clinical futility endpoint + safety
- *n=229 per arm*: Repeat Clinical futility endpoint + safety
- *n= 469 per arm*: Repeat Clinical futility endpoint + safety

Questions?

TACTIC-E

Pharmacy/ IMP

Trial Drugs

In accordance with the CTA granted by the Medicines and Healthcare Products Regulatory Agency (MHRA) the following medications are classed as Investigational Medicinal Products (IMPs) within this trial.

- EDP1815 oral 8 x 10^ 10
- Ambrisentan tablets
- Dapagliflozin tablets

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Trial Drugs

IMP	Route	Formulation	Strength(s)	Storage Requirements	Supply
EDP1815	Oral	Capsule	8 x 10^{10} cells per capsule in a carton of 70 capsules, containing 7 blisters of 10 capsules each	Store in the refrigerator between 2 – 8°C in the original container Protect from light	Clinical Trial Supply by Sponsor (Supplied by Evelo free of charge)
Dapagliflozin	Oral	Tablet	10mg film coated tablets in blister packs containing 28 tablets commercial product will be supplied	Room temperature below 25°C in the original container	Commercial product supplied by Sponsor (Supplied by Astra Zeneca free of charge)
Ambrisentan	Oral	Tablet	5mg film coated tablets	Room temperature below 25°C in the original container OR as per SmPC for brand used	Hospital local supply (reimbursed by Sponsor for the amount used) No specific brand is required

TACTICE
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DOSING SCHEDULE

IMP	Dose	Dose Frequency	Route of administration	Other requirements	Dispensing
EDP1815	16 x 10^{10} cells (2 capsules) TWICE a day for up to 7 days (increased to 14 days if required)	2 capsules TWICE a day for up to 7 days (increased to 14 days if required) or until discharge. DO NOT continue on discharge	Oral in fasted state. It should be taken on an empty stomach, at least 1 hour before or 2 hours after a meal.	Sites should dispense 3 blisters of 10 capsules for 7 days' supply of study medication	Attach dispensing label as per local procedure. **Ensure it is kept in a fridge on the ward (use within 24hr at room temperature)**
Dapagliflozin	10mg	ONCE a day up to a maximum of 14 days or until discharge. DO NOT continue on discharge	Oral can be taken with or without food	On receipt affix annex 13 compliant label and ring fence supplies – sample label provided in pharmacy manual	Additional dispensing label with instructions can be added as per local procedure
Ambrisentan	5mg	ONCE a day up to a maximum of 14 days or until discharge. DO NOT continue on discharge	Oral can be taken with or without food.	Dispense 7 days supply at a time . Do not require annex 13 compliant label (No requirement for ring fencing the medication)	Dispensing label with instructions required

All patients within this trial will be inpatients, please ensure that patients are identified as being on the trial and that the trial medication supplied is used .
This treatment will be in addition to standard of care treatment for these patients.

SAMPLE LABELS

Dapaglifozin or Ambrisentan Sample Label Or label with instructions can be added when dispensing

For Clinical Trial Use Only

TACTIC-E trial

EudraCT No: 2020-002229-27

Sponsor: Cambridge University Hospitals NHS Foundation Trust

Local Site Name:……

EDP1815 Sample Label each blister of 10 capsules will contain this label

TACTIC-E STUDY (EDP1815-204) **Participant ID:……**

Batch Number:……Expiry Date:……

This wallet contains 10 enteric-coated capsules for oral administration of

EDP1815 8.0×10^{10} cells/capsule

Take as directed by your doctor

Store refrigerated between 2^{0}C and 8^{0}C

For clinical Trial use only

Investigator:……

TACTIC-E
Evaluating new drugs against COVID-19

Dosing Modifications
No Dose Adjustments

Drug	Starting Dose	Dose level -1		Other instructions
EDP1815	2 capsules TWICE a day	No dose adjustments planned		Patients should not be on any immunosuppresive agents
Dapagliflozin	10mg ONCE a day	No dose adjustments planned		STOP treatment if metabolic acidosis occurs defined as **Venous pH< 7.3 (or venous bicarbonate <15 mmol/l) AND ketones > 3.0 mmol/L**
Ambrisentan	5mg ONCE a day	No dose adjustments planned		

Drug Interactions

Dapagliflozin

- may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension

EDP1815

- no anticipated drug-drug interactions

Ambrisentan

- There is a lack of inductive effect of Ambrisentan on the CYP3A4 isoenzyme

Trial Drug Accountability

It is the responsibility of the Clinical Trial Pharmacy Lead at each Site to maintain drug accountability records for all 3 Study medications

- Accountability Log(s) are provided for the trial; however, sites can use their own logs
- If using sites own logs then copies must be made available to Tactic-E co-ordinator upon request
- This is an open label trial
- **Sealed Envelope** randomisation system will be used for allocation of the drug (see earlier randomisation section and randomisation manual)

Ordering of EDP1815 and Dapagliflozin

Initial Orders

- The TACTIC-E co-ordinator will order the initial supply of study medications for each site upon opening to recruitment.

Subsequent orders

- It is the site pharmacy's responsibility to maintain adequate stocks of IMP. Sufficient supplies should be ordered by sites as needed in conjunction with the lead site coordinator, in order to meet the requirements of the trial population.
- Please ensure that sufficient time is allowed for delivery when requesting to place new orders.
- Sites must ensure the stock is within date and there is stock rotation of supplies to ensure the shortest expiry dates are used first. To minimise delivery costs, it is recommended that pharmacies order their stock on a quarterly basis.

Ordering process for Dapaglifozin and EDP1815

- Request an Order with the TACTIC-E trial lead site coordinator
- Ensure that you provided site delivery address correctly
- Email the Tactic-E Trial Co-ordinator with your request
- File a copy of the correspondence in the relevant section of the PSF
- Please allow up to 5 – 7 working days for delivery of the drug – check stock regularly

Ordering of Ambrisentan

- Locally supplied study medication

- Sponsor will re-imburse for the amount used within this trial

- It is the site pharmacy's responsibility to maintain adequate stocks of IMP. Sufficient supplies should be ordered by sites as needed, in order to meet the requirements of the trial population.
- Please do not over-order

IMP Destruction of Dapagliflozin

- Destruction of all unused or expired medication, may only be undertaken after written permission has been obtained from the sponsor (Tactic-E lead site co-ordinator)
- This destruction must be recorded on the Drug Destruction Log and the Accountability Log for each study medication to ensure the running balance is accurate.
- The completed logs and the confirmation of 'permission to destroy' email should be filed in the Tactic-E PSF. Supplies must be destroyed as per local destruction policies and procedures.
- Sites are permitted to use their own destruction log but this must ensure all the information required by the sponsor is available on the forms.

Patient returns

- Destruction of **patient surplus study medication** can occur at the site as per local procedure. No returns are expected to be sent to pharmacy
- Note: Authorisation is not required for patient returns destruction

IMP Destruction of EDP1815

1. EDP1815 should not be destroyed at site UNLESS the site is able to produce a certificate of destruction/local SOP for destruction processes and this is approved by Evelo. *Discuss with UK Sponsor coordinator to facilitate this*

2. All unused, expired stock and patient returns should be sent back to the Evelo

3. Sites should ensure all accountability for EDP1815 is completed and reconciliation of all drug has occurred before requesting to arrange a courier for collection.
   - Details will follow on how to manage returns

TEMPERATURE EXCURSIONS of IMPs

1. In case of temperature excursion the site must quarantine the IMP immediately under the correct storage conditions and as per local site procedure (if the IMP has been stored incorrectly by the participant it should be retrieved from the participant and a new supply should be dispensed)

2. The site must contact the TACTIC-E trial co-ordinator to inform of the temperature excursion or damage (giving the following information: dates, duration, and minimum/maximum temperatures as appropriate (including a temperature trace or printout where possible) quantity of packs and batch number of affected stock).

3. No affected IMP is to be given to participants until final decision and instruction is received from the TACTIC-E co-ordinator.

Pharmacy Monitoring

1. • Site Self-Assessment Monitoring/Central Monitoring
2. • A request will be sent to the site pharmacy periodically, by TACTIC-E Trial co-ordinator for drug accountability records
3. • Review of pharmacy site file (checklist provided periodically by TACTIC-E Trial co-ordinator)

TACTIC-E

Pharmacovigilance:

Safety Data Management

Evaluation of Safety Data: AEs, AR,SAEs, SARs, SUSARs

Seriousness Assessment	• Refer to the protocol section **11.1.4**
Causality Assessment	• Refer to the protocol section **11.3.2**
Expectedness Assessment	• Refer to the protocol RSI- protocol section **11.1.6**: • ***Section 4.8 of the SmPC Forxiga*** *(Dapagliflozin), dated 02 Jan 2020* • ***Section 4.8 of the SmPC Volibris*** *(Ambrisentan , dated 12 Nov 2018* • *Section 8 of* ***EDP1815*** *Investigator's Brochure Version 2.1 dated 28 January 2020*
Severity Assessments	• Refer to the protocol section 11.3.3

TACTIC-E AEs Collecting/Recording Details

Adverse events will be collected & assessed:

- *From: the point of Informed Consent*
- *To:* 90 (+/- 7 days) days after the baseline visit.

Adverse events will be recorded:

- ***AEs*** *– in medical notes only*
- ***ARs*** *– in the medical notes and AR log*
- ***All SAEs*** *– in the* ***study specific SAE reporting form***

The following AEs will be recorded as AESI using study specific CRF:

- *Diabetic ketoacidosis- for patients on Ambrisentan & Dapagliflozin*
- *New peripheral oedema -for patients on Ambrisentan & Dapagliflozin arm*

TACTIC-E SAEs Reporting Details

SAEs & SARs will be reported within 24 hours:

- *SAEs& SARs -since site awareness date to the CI / Coordination Team*
- *SARs -since CI/Coordination Team notification to Sponsor*

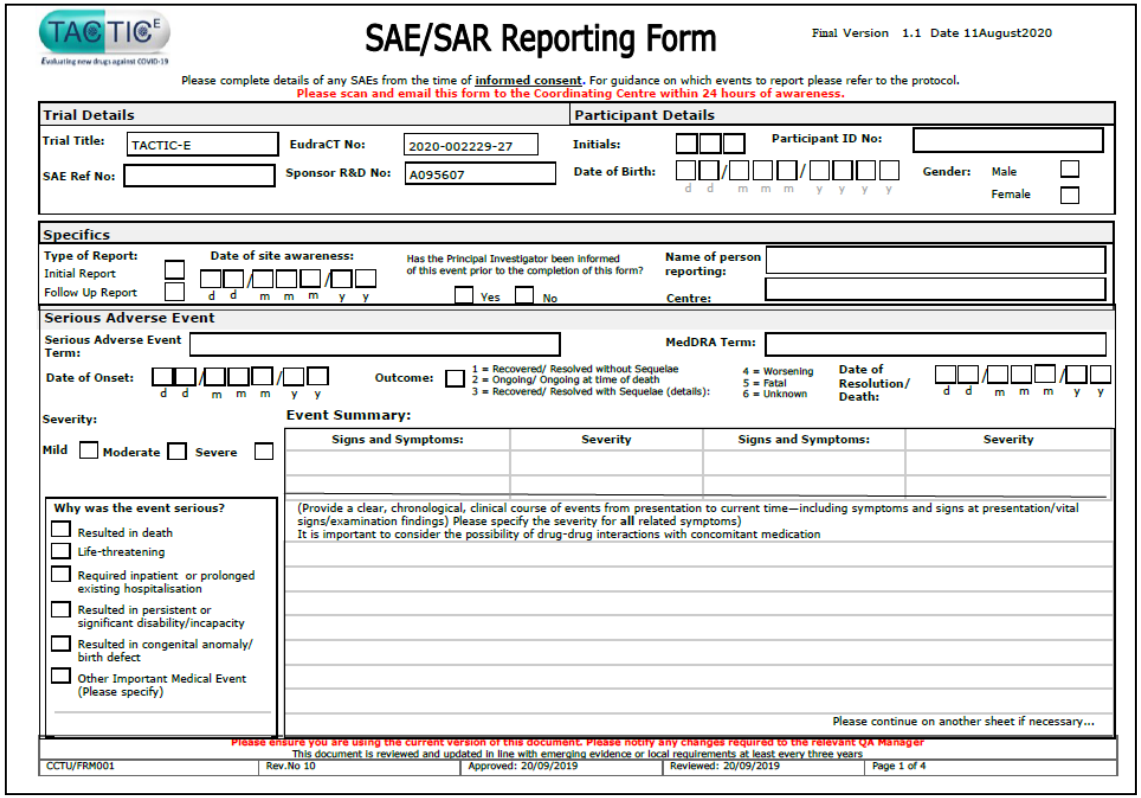
AESI reporting details:

- *ALL PIs must report all AESIs to the CI in a timely manner*
- *Serious AESI should be reported following procedure for an SAE reporting*

SAES, SARs, SUSARs for the Dapglifozin/Ambrisentan arm should ALSO be reported to:

- *ASTRAZENECA via: AEMailboxClinicalTrialTCS@astrazeneca.com*
- *Medpace via: safetynotification@medpace.com.*

TACTIC-E
Study Specific reporting form



SAE/SAR Reporting Form

Final Version 1.1 Date 11August2020

Please complete details of any SAEs from the time of **informed consent**. For guidance on which events to report please refer to the protocol.
Please scan and email this form to the Coordinating Centre within 24 hours of awareness.

Trial Details

Trial Title: TACTIC-E
EudraCT No: 2020-002229-27
SAE Ref No:
Sponsor R&D No: A095607

Participant Details

Initials:
Participant ID No:
Date of Birth: d d / m m / y y y y
Gender: Male / Female

Specifics

Type of Report: Initial Report / Follow Up Report
Date of site awareness: d d / m m / y y
Has the Principal Investigator been informed of this event prior to the completion of this form? Yes / No
Name of person reporting:
Centre:

Serious Adverse Event

Serious Adverse Event Term:
MedDRA Term:
Date of Onset: d d / m m / y y
Outcome: 1 = Recovered/ Resolved without Sequelae; 2 = Ongoing/ Ongoing at time of death; 3 = Recovered/ Resolved with Sequelae (details):; 4 = Worsening; 5 = Fatal; 6 = Unknown
Date of Resolution/ Death: d d / m m / y y

Severity:
Mild / Moderate / Severe

Event Summary:

Signs and Symptoms:	Severity	Signs and Symptoms:	Severity

(Provide a clear, chronological, clinical course of events from presentation to current time—including symptoms and signs at presentation/vital signs/examination findings) Please specify the severity for **all** related symptoms)
It is important to consider the possibility of drug-drug interactions with concomitant medication

Please continue on another sheet if necessary...

Why was the event serious?

- Resulted in death
- Life-threatening
- Required inpatient or prolonged existing hospitalisation
- Resulted in persistent or significant disability/incapacity
- Resulted in congenital anomaly/ birth defect
- Other Important Medical Event (Please specify)

Please ensure you are using the current version of this document. Please notify any changes required to the relevant QA Manager
This document is reviewed and updated in line with emerging evidence or local requirements at least every three years

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Complete form and email to TACTIC-E lead site within 24h of site awareness

Email: cambs.cardiovascular@nhs.net

TACTIC-E Pregnancy Reporting Requirements

Pregnancy (study participant or participant's partner) will be reported until the 3 month follow-up visit

Pregnancy should be reported within **24 hours of site awareness to:**

The Chief Investigator/ Trial Coordination team

The Sponsor

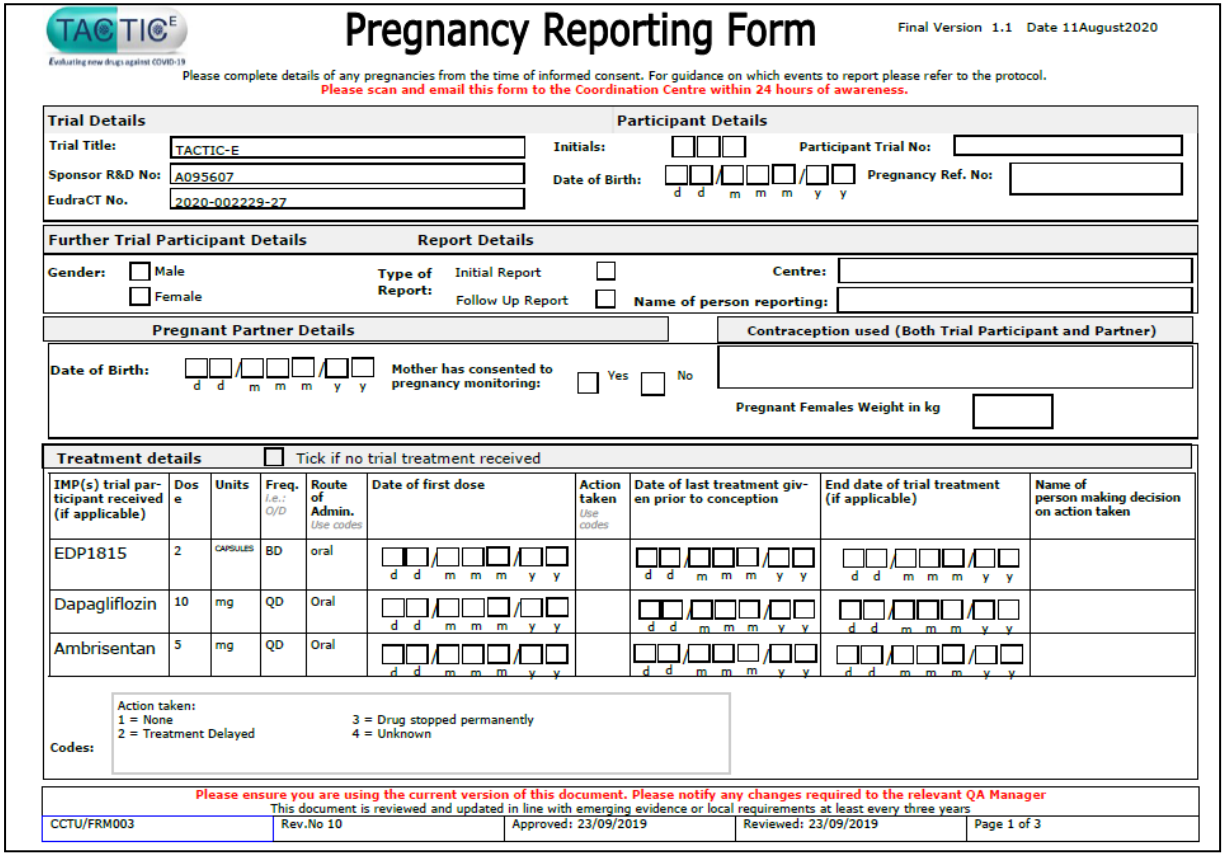
…s will be reported as SAE/SAR or SUSAR

- Spontaneous abortion
- Induced abortion (due to clinical/ foetal developmental reason)

- Still birth
- Neonatal death
- Birth defect(s)

TACTIC-E

Pregnancy Reporting Form



TACTIC-E
Evaluating new drugs against COVID-19

Pregnancy Reporting Form

Final Version 1.1 Date 11August2020

Please complete details of any pregnancies from the time of informed consent. For guidance on which events to report please refer to the protocol.
Please scan and email this form to the Coordination Centre within 24 hours of awareness.

Trial Details

Trial Title: TACTIC-E
Sponsor R&D No: A095607
EudraCT No. 2020-002229-27

Participant Details

Initials: ☐☐☐ Participant Trial No:
Date of Birth: ☐☐/☐☐/☐☐☐☐ (d d m m m y y) Pregnancy Ref. No:

Further Trial Participant Details

Gender: ☐ Male ☐ Female

Report Details

Type of Report: Initial Report ☐ Follow Up Report ☐
Centre:
Name of person reporting:

Pregnant Partner Details

Date of Birth: ☐☐/☐☐/☐☐☐☐ (d d m m m y y)
Mother has consented to pregnancy monitoring: ☐ Yes ☐ No

Contraception used (Both Trial Participant and Partner)

Pregnant Females Weight in kg

Treatment details ☐ Tick if no trial treatment received

IMP(s) trial participant received (if applicable)	Dose	Units	Freq. i.e.: Q/D	Route of Admin. Use codes	Date of first dose	Action taken Use codes	Date of last treatment given prior to conception	End date of trial treatment (if applicable)	Name of person making decision on action taken
EDP1815	2	CAPSULES	BD	oral	☐☐/☐☐/☐☐☐☐		☐☐/☐☐/☐☐☐☐	☐☐/☐☐/☐☐☐☐	
Dapagliflozin	10	mg	QD	Oral	☐☐/☐☐/☐☐☐☐		☐☐/☐☐/☐☐☐☐	☐☐/☐☐/☐☐☐☐	
Ambrisentan	5	mg	QD	Oral	☐☐/☐☐/☐☐☐☐		☐☐/☐☐/☐☐☐☐	☐☐/☐☐/☐☐☐☐	

Codes:
Action taken:
1 = None
2 = Treatment Delayed
3 = Drug stopped permanently
4 = Unknown

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TACTIC-E

Monitoring

Monitoring

The act of overseeing the progress of a clinical trial, and of ensuring that it is **conducted, recorded, and reported**

in accordance with the **protocol, SOPs, GCP, and the applicable regulatory requirement(s)**

Trial monitoring is an Integral Component of trial quality assurance process, and critical for GCP fulfilment.

Key monitoring activities
-- Participating Site: Remote Monitoring --

- Conducted approximately every 12 months from site activation

Logistics

- Remote monitoring will be initiated with site's PI in advance
- The site will be instructed to complete a remote monitoring form and questionnaire/checklist tailored to the TACTIC-E trial (provided by CTC).
- The site will have 4 weeks to return the completed form/checklist
- The CTC will provide the site with a report containing details of any findings and required actions to be taken by the site. These actions must be addressed within 4 weeks.

Site staff who complete remote monitoring tasks must be listed to do so on the delegation log

Trial team's involvement in monitoring visits

- **Preparation**
  - Ensuring all logs are up to date, including but not limited to screening/approach/subject ID logs, Delegation log, non-compliance log/forms, file note log etc.
  - Check filing is up to date and that findings from previous reports have all been addressed
  - Ensure all data is entered into eCRFs

The frequency of remote monitoring may change depending upon the rate of patient recruitment at the site, quality of the data and the findings from previous monitoring visits

If it wasn't documented, it wasn't done!

Document what is done as well as what is not done

Thank you

Questions?