ATOMIC2

A multi-centre open-label two-arm randomised superiority clinical trial of Azithromycin versus usual care In Ambulatory COVID-19 (ATOMIC2)

Training Slides

Based on Protocol V5.0

OCTRU
Oxford Clinical Trials Research Unit

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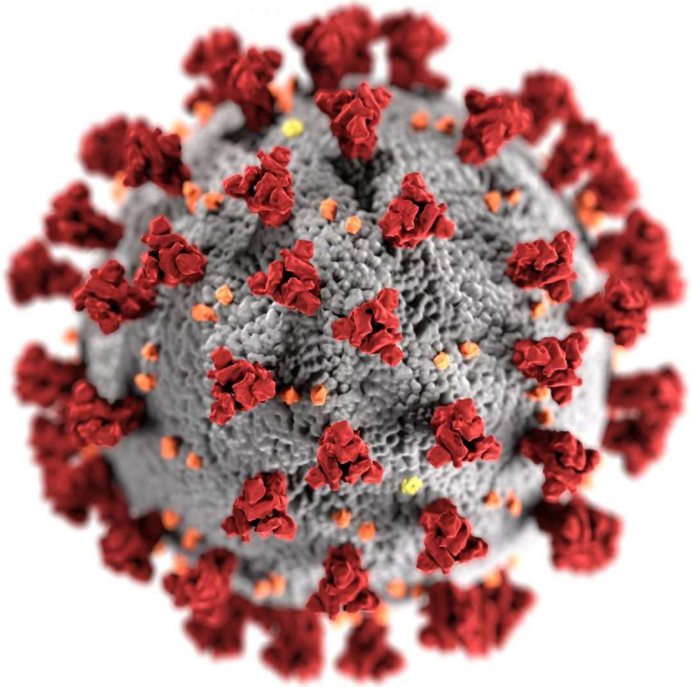

Trial organisation

- Sponsor: University of Oxford
- Trial management: Oxford Clinical Trials Research Unit
- Chief investigator: Timothy Hinks
- Funding:
  - NIHR Oxford BRC
  - Pfizer
  - University of Oxford
- Drug: Pfizer
- Swabs: Nankai University
- IRAS: 282892
- REC: 20/HRA/2105
- EudraCT: 2020-001740-26
- Local prioritisation: Oxford
- Portfolio adoption: Pending

Trial management team

- Trial manager: Lucy Cureton
- Chief investigator: Timothy Hinks
- Trial statisticians: Susan Dutton, Ariel Wang
- Quality assurance & Drug supply: Joanna Black
- TSC Chair: Paul Little
- DSMC Chair: James Chalmers

Background & Rationale

- Azithromycin (AZM) a synthetic macrolide antibiotic
- Used in SARS and 1/3 of MERS-CoV
- Antibacterial (WHO list of essential medicines)
- Antiviral
- Anti-inflammatory
- No randomised trial data in any coronoavirus to date

- Antiviral: efficacy against
  - Rhinovirus (↑ Type I & III IFN)[1-3]
  - Zika *in vitro*[4]
  - Enteroviruses *in vitro*[5]
  - Ebola *in vitro*[6,7]
  - SARS *in vitro*[5,6]
  - Influenza A (small RCT)[7]
  - 40% reduction in asthma exacerbations: mechanism unknown[8]

1. Gielen V Eur Respir J 2010
2. Shogler A Eur Respir J 2015
3. Porter JD J Antimicro Chemo 2016
4. Retallack H PNAS 2016
5. Madrid PB ACS Infect Dis 2015
6. Kouznetsova J Emerg Microbes Infect 2014
7. Kawamura K Int J Antimicrob Agents 2018
8. Lee N Antiviral Res 2017
9. Gibson PG Lancet 2017

Background & Rationale

- Anti-inflammatory effects
- Resp failure occurs after viral loads have fallen
- Related to late increase of IL-1b, IL-2, IL-6, IL-7, IL-8, GCSF, MCP, MIP1a, TNF[1]
- Associated with hemophagocytic lymphohistiocytosis[2]
- i.e. over-exuberant inflammatory cascade

- AZM
  - ↓ granulocyte activation[1-4]
  - ↓lymphocyte perforin[1-4]
  - ↓IL-1b, IL-6, TNF, IL-8, IL-18, G-CSF, GM-CSF[1-4]
- Effective clinically in asthma[5], COPD[6], cystic fibrosis[7], obliterative bronchiolitis, [1,2,8,9] post lung transplant bronchiolitis[10], diffuse pan bronchiololitis[1,2,8,9]

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3. Marjanovic N Pharmacol Res 2011
4. Shinkai Am J Physiol Lung Cell Mol Physiol 2006
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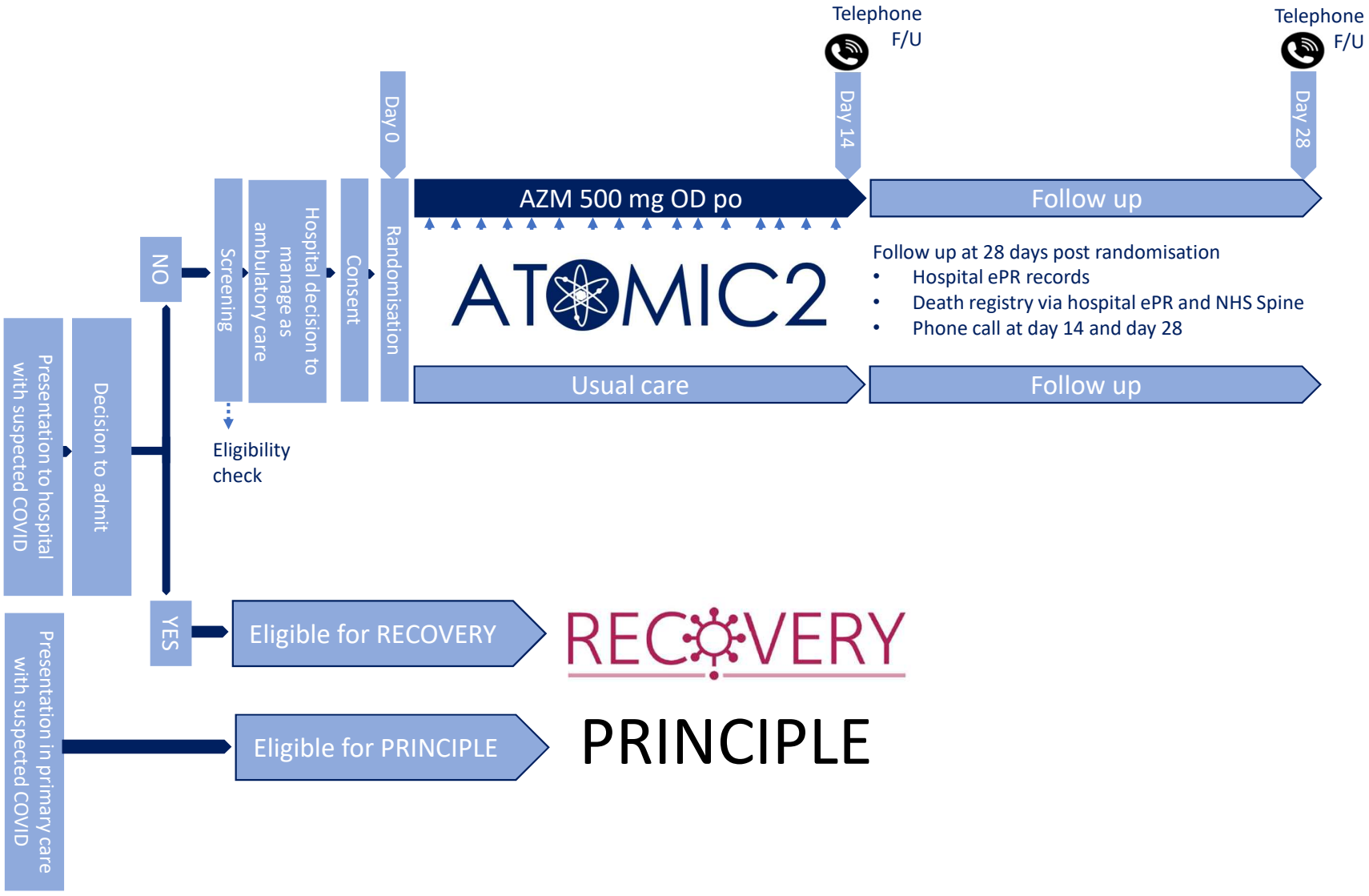

Telephone F/U
Telephone F/U
Day 0
Day 14
Day 28
Presentation to hospital with suspected COVID
Decision to admit
NO
Screening
Hospital decision to manage as ambulatory care
Consent
Randomisation
AZM 500 mg OD po
Follow up
ATOMIC2
Follow up at 28 days post randomisation
• Hospital ePR records
• Death registry via hospital ePR and NHS Spine
• Phone call at day 14 and day 28
Usual care
Follow up
Eligibility check
YES
Eligible for RECOVERY
RECOVERY
Presentation in primary care with suspected COVID
Eligible for PRINCIPLE
PRINCIPLE

PRINCIPLE

	PRINCIPLE	ATOMIC2	RECOVERY
Recruitment	Primary care	Secondary care ED, not admitted	Secondary care, admitted to hospital
Population	Patients ≥50-64 years with comorbidities and aged ≥65 with or without comorbidity presenting within 7 days since onset of symptoms with a new continuous cough and/or high temperature during time of prevalent COVID-19 infections	Adults, ≥18 years of age assessed in an acute hospital with clinical diagnosis of COVID-19 infection and where medically it is decided not to admit the patient and for the patient to be managed on an ambulatory (outpatient) care pathway	(i) Aged at least 18 years (ii) Hospitalised (iii) Confirmation of SARS-CoV-2 infection by PCR (This may be extended to include just clinically diagnosed)
Stage in disease	Early: </= 7 days	Middle / late: presenting to hospital with mild respiratory distress	Middle / late: presenting with severe disease requiring hospitalisation
Severity at time of enrolment	Mild (new cough or high temp)	Moderate (bad enough to warrant secondary care assessment but not requiring O2)	Severe (requires hospitalisation for O2 therapy)
Time line in care pathway	Recruits first in disease pathway so no competition from other studies	Recruits later if not already in PRINCIPLE	Recruits later ?can enrol if already in PRINCIPLE?
Scale	Large: 3000 patients	Smaller: Follow on up to total c 800 if good signal. If not, to be discontinued.	Very large: 1000s of patients, adaptive design
Geography	England/ Scotland / Wales / N Ireland +- Eire	Oxford/Banbury, Birmingham, Horton, Cardiff, Dundee, Stoke Mandeville initially.	UK

Study objectives

Hypothesis

- Use of Azithromycin 500 mg once daily for 14 days is effective in preventing and/or reducing the severity of lower respiratory illness of COVID-19 disease at 28 days.
- **Study design:** Multi-centre, prospective open label two-arm randomised superiority clinical trial of standard care and Azithromycin with standard care alone for those presenting to hospital with COVID-19 symptoms who are not admitted at initial presentation.

Study primary objective

Primary Objective

To compare the effect of Azithromycin in participants with a clinical diagnosis of COVID-19 in reducing the proportion with either death or hospital admission with respiratory failure requiring invasive or non-invasive mechanical ventilation over 28 days from randomisation.

Study secondary objectives

- To compare the effect of Azithromycin in participants with a PCR-confirmed diagnosis of COVID-19 in reducing the proportion with either death or hospital admission with respiratory failure requiring invasive or non-invasive mechanical ventilatory support over 28 days from randomisation (for those who had a COVID-19 swab at randomisation)
- To compare differences in all-cause mortality.
- To compare differences in proportion progressing to pneumonia.
- To compare differences in proportion progressing to severe pneumonia.
- To compare differences in peak severity of illness.
- To assess safety and tolerability
- Mechanistic analysis of blood and nasal biomarkers if available

Study design

Sample size

- 800 patients (subject to interim analysis at 100 pts)

Duration: 2-6 months depending on recruitment rate

Follow up duration: 28 days

Comparator: usual standard care

Study setting: Adult patients being assessed by approximately 20 secondary care NHS hospitals in the UK

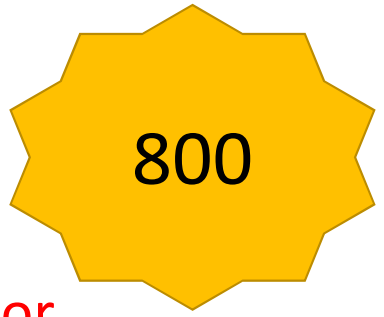
Inclusion criteria

- Male or Female, aged at least 18 years
- Assessed by the attending clinical team as appropriate for initial ambulatory (outpatient) management
- A clinical diagnosis of highly-probable or confirmed COVID-19 infection (diagnosis by the attending clinical team) with onset of first symptoms within the last 14 days
- No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in the trial
- Able to understand written English (for the information and consent process) and be able to give informed consent

Exclusion criteria

- Known **hypersensitivity** to any Macrolide including Azithromycin, Ketolide antibiotic, or the excipients including an allergy to soya or peanuts.
- Known fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase-insufficiency
- **Currently on a Macrolide** antibiotic (Clarithromycin, Azithromycin, Erythromycin, Telithromycin, Spiramycin)
- Elevated cardiac troponin at initial assessment suggestive of **significant myocarditis** (if clinically the clinical team have felt it appropriate to check the patient's troponin levels)
- Evidence of QTc prolongation: **QTc>480ms**
- Significant electrolyte disturbance (e.g. hypokalaemia K+<3.5 mmol/L)
- Clinically relevant bradycardia (P<50 bpm), non-sustained ventricular tachycardia or unstable severe cardiac insufficiency
- Currently on hydroxychloroquine or chloroquine

Screening and recruitment



- Eligibility MUST be confirmed by a medically qualified doctor
- Must be able to receive the first dose of Azithromycin within 4 hours of randomisation. Protocol waivers are not permitted.
- Patients will be screened by review of ePR/medical notes data for history of presentation, examination findings, ECG result, K^+ and, concomitant medications by anyone listed on the site study delegation log.
- Anyone considered for ATOMIC2 trial should be screened, even if not randomised.

Electronic consent, CRFs and randomisation

- Taken by a trained member of the study team (GCP not necessarily required) listed on the delegation of duties log
- Each recruiting site will be supplied with an iPad for taking eConsent, randomisation and completing eCRFs
- Two links: one for screening, one for main REDCap login to complete CRFs and view patients.

Screening survey URL: https://redcap-rrio.octru.ox.ac.uk/surveys/?s=3MCWXMXWAX

Main login: https://redcap-rrio.octru.ox.ac.uk/

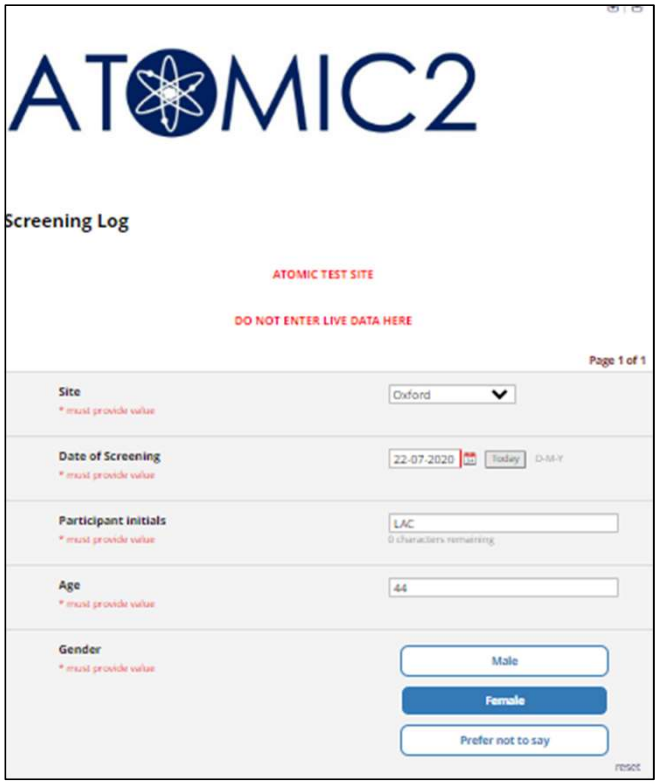
Apple iPAD 10.2” 128GB WiFi

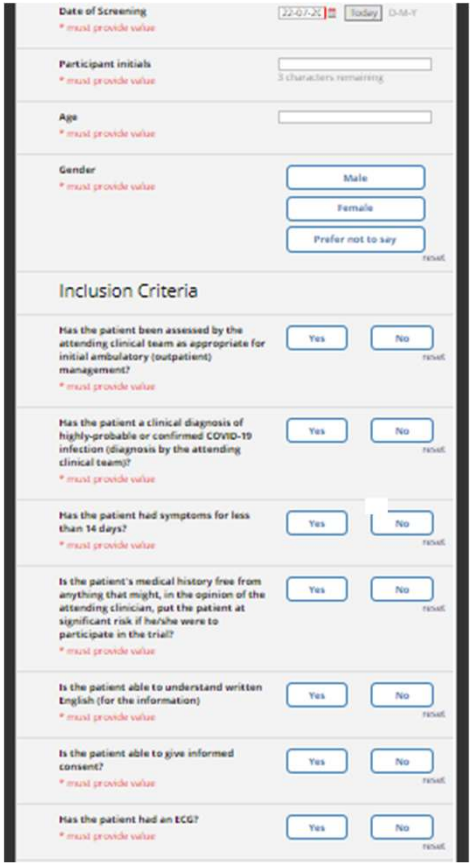
REDCap

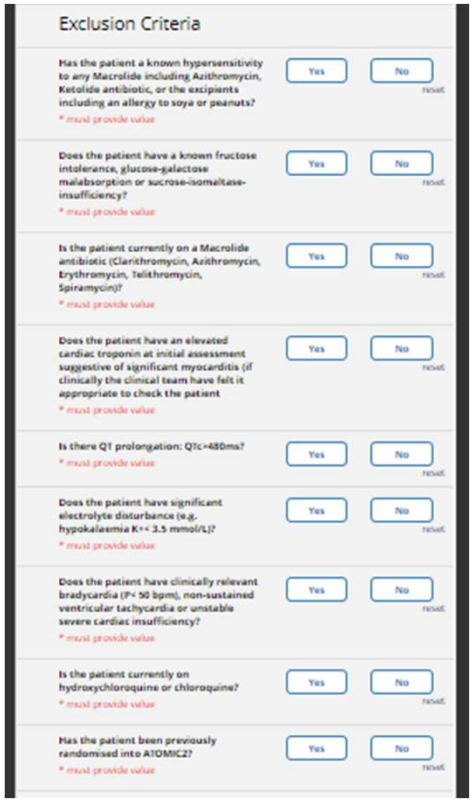
Screening log

- It is important to collect information about the patients who haven' entered the trial
- It is useful for i problems with and is essentia transparent rep trials

Think about… patient pathway - from coming to hospital to going home


ATOMIC2
Screening Log
ATOMIC TEST SITE
DO NOT ENTER LIVE DATA HERE
Page 1 of 1
Site
Oxford
Date of Screening
22-07-2020
Today
D-M-Y
Participant initials
LAC
Age
44
Gender
Male
Female
Prefer not to say

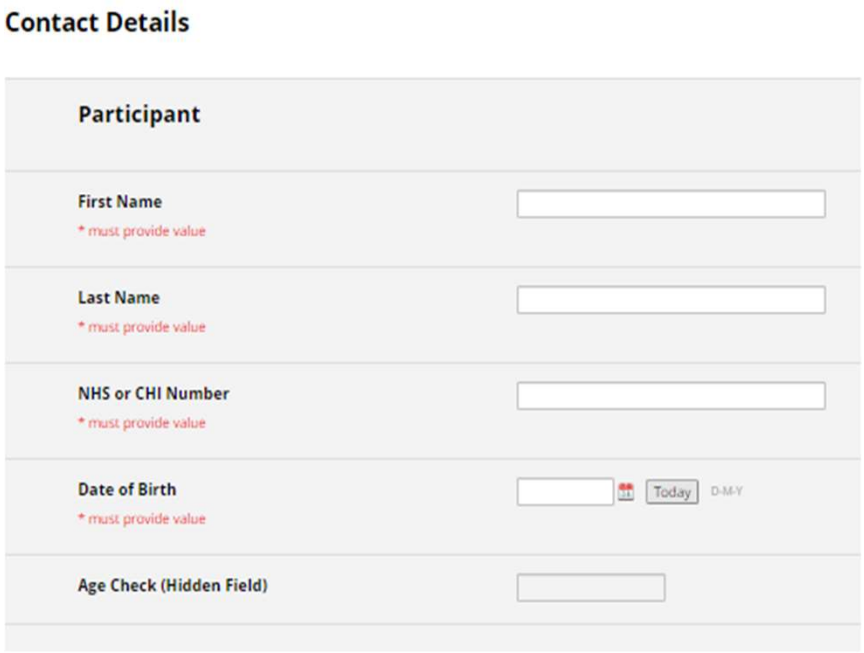

Date of Screening
Participant initials
Age
Gender
Male
Female
Prefer not to say
Inclusion Criteria
Has the patient been assessed by the attending clinical team as appropriate for initial ambulatory (outpatient) management?
Has the patient a clinical diagnosis of highly-probable or confirmed COVID-19 infection (diagnosis by the attending clinical team)?
Has the patient had symptoms for less than 14 days?
Is the patient's medical history free from anything that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in the trial?
Is the patient able to understand written English (for the information)
Is the patient able to give informed consent?
Has the patient had an ECG?
Yes
No


Exclusion Criteria
Has the patient a known hypersensitivity to any Macrolide including Azithromycin, Ketolide antibiotic, or the excipients including an allergy to soya or peanuts?
Does the patient have a known fructose intolerance, glucose-galectose malabsorption or sucrose-isomaltase-insufficiency?
Is the patient currently on a Macrolide antibiotic (Clarithromycin, Azithromycin, Erythromycin, Telithromycin, Spiramycin)?
Does the patient have an elevated cardiac troponin at initial assessment suggestive of significant myocarditis (if clinically the clinical team have felt it appropriate to check the patient
Is there QT prolongation: QTc>480ms?
Does the patient have significant electrolyte disturbance (e.g. hypokalaemia K+< 3.5 mmol/L)?
Does the patient have clinically relevant bradycardia (P< 50 bpm), non-sustained ventricular tachycardia or unstable severe cardiac insufficiency?
Is the patient currently on hydroxychloroquine or chloroquine?
Has the patient been previously randomised into ATOMIC2?
Yes
No


Clinician View
Is the patient suitable for ATOMIC2?
Eligibility confirmed by
Is the patient willing to consent?
Progress to Randomisation
Yes
No
Submit

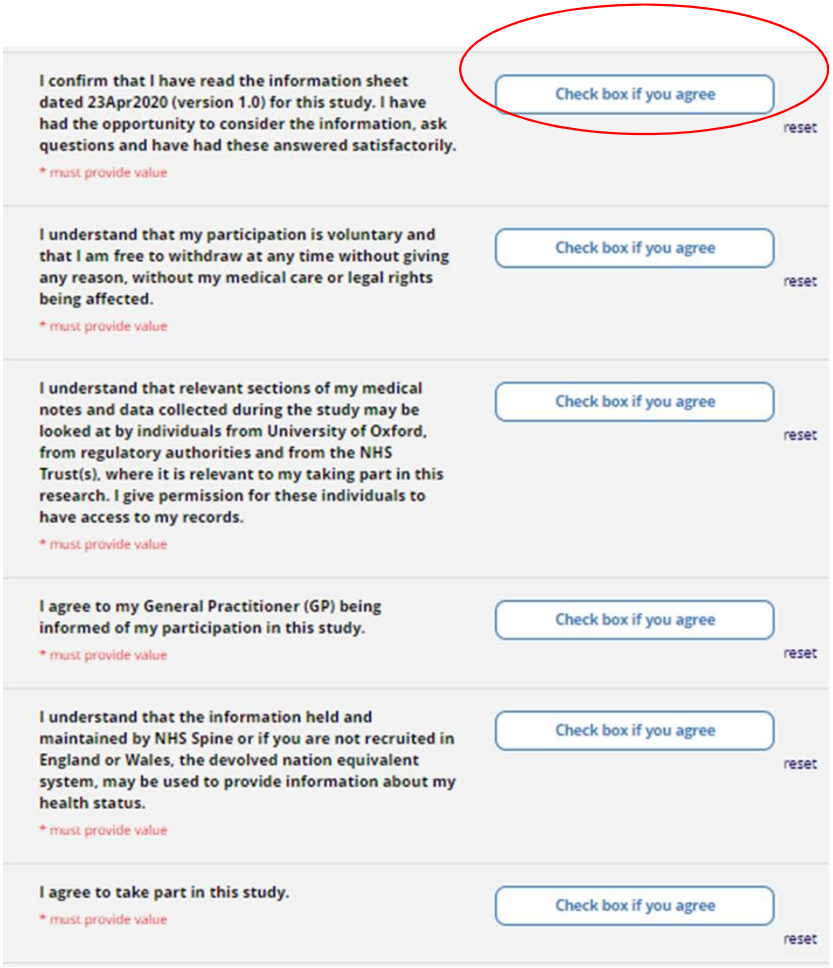
Informed consent

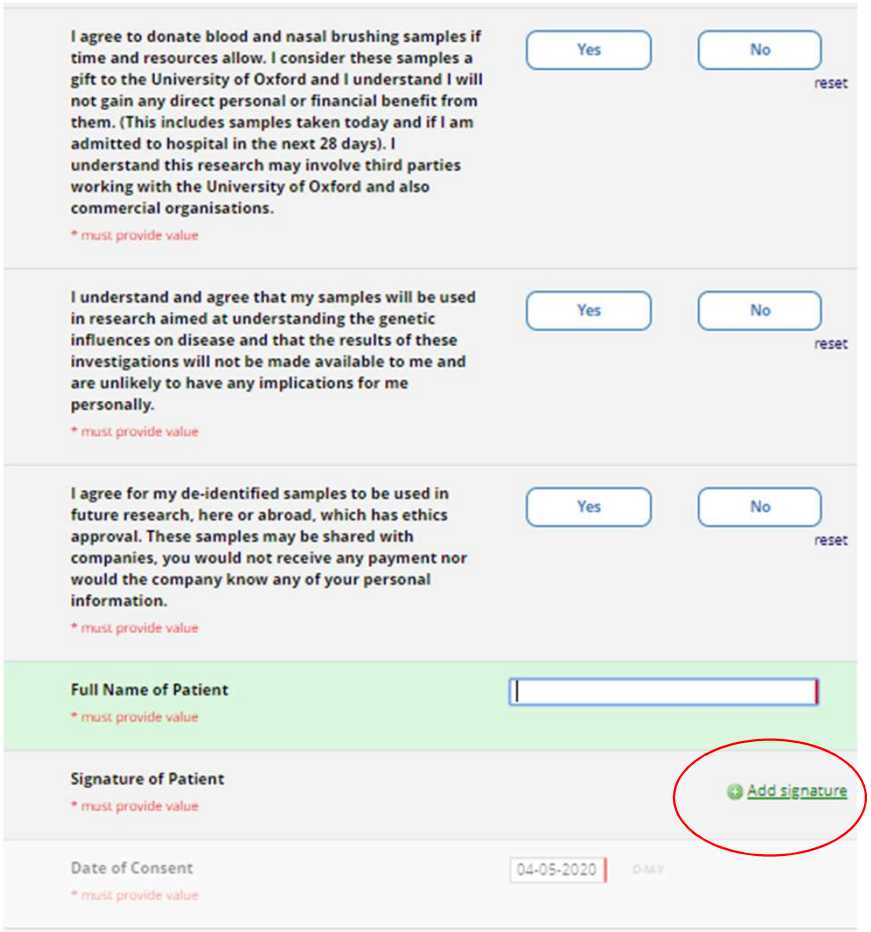
- The patient should have passed the eligibility checks before the consent process can start.
- Explain the exact nature of the ATOMIC2 study and what is involved.
- Ensure the patient has received the Participant Information Leaflet and been given time to think and ask questions. Due to the nature of the study, the usual 24 hour period does not apply.
- Ensure the patient is informed they can decline to participate and can withdraw from the study at any time.



Patient contact details are recorded as part of randomisation and consent. GP details are required as a letter is sent to the patient's doctor informing them of their involvement in the trial. Ensure telephone numbers are correct so that patients can be contacted for their follow-up calls

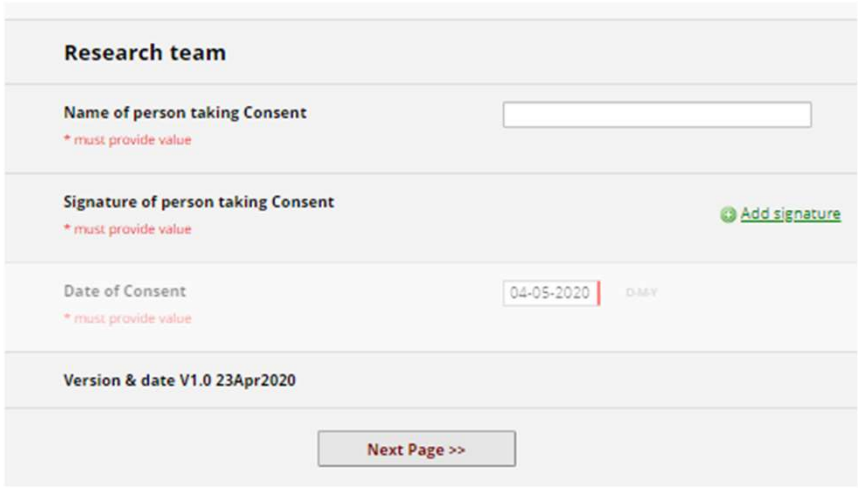
- If the patient is happy to join the study, the process of consent can continue.
- Give the patient the iPad or view of PC screen so that they can read the consent form.
- It is good practice to read each statement aloud to the patient
- Each statement on the Consent form should be discussed and **the box checked by the patient**





Optional samples consent

Researcher sign off



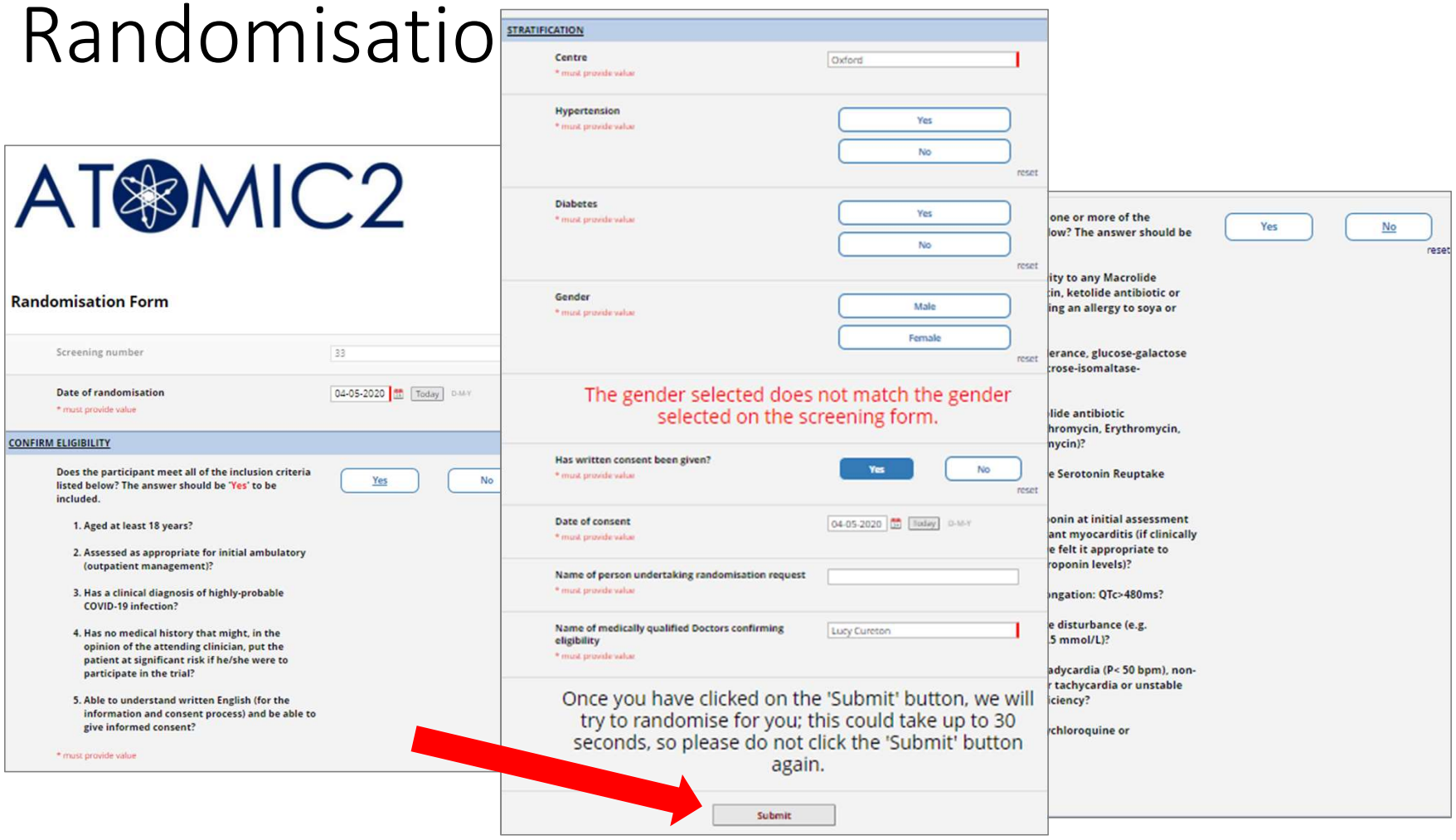
- The consent form should be signed and dated by the patient and the researcher, on the same date at the same time
- Signatures can be completed by finger on the iPad or mouse on a PC
- This is the legal equivalent of a written signature and should be treated as such

Informed consent

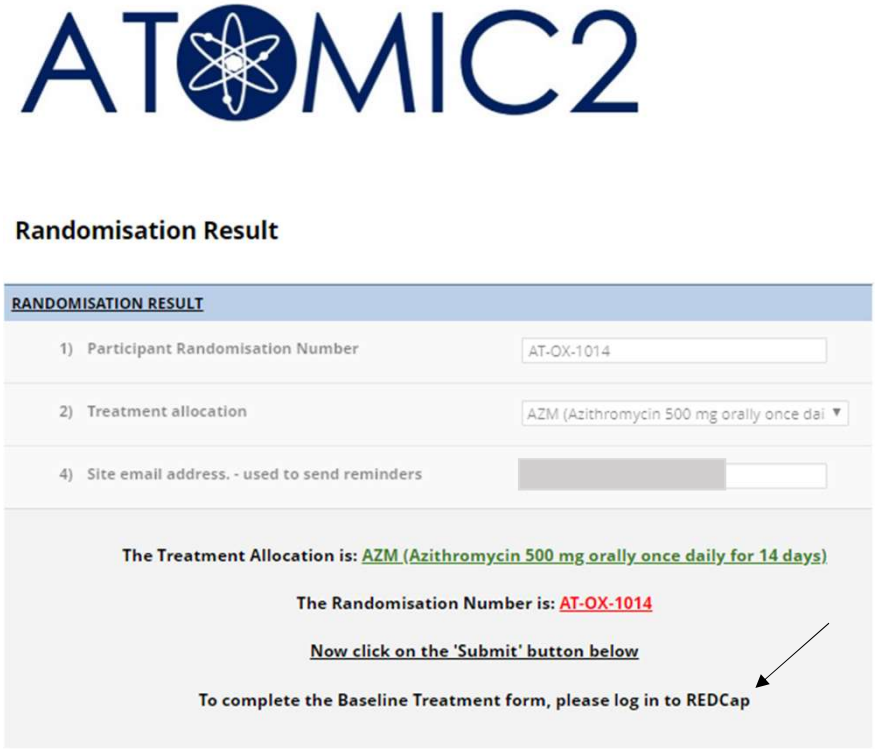
- Once the patient has been successfully consented, a PDF of the completed consent form will be sent to the email address recorded in the patient contact details section
- Ensure that there is a note of trial participation in the patient's medical records

REDCap then takes you to the randomisation page

Randomisatio



Patient randomised – well done!



- Once successfully randomised, you will see the randomisation result on screen
- You will also be sent an email alert with these details
- You can now complete the baseline CRF by logging into REDCap – please do this as soon as you can

ATOMIC2 Case Report Forms

💻 All CRFs completed online via REDCap 💻

List of CRFS:

Baseline CRF – completed as soon as possible after randomisation

Local swab CRF – for optional swabs processed via NHS pathway

Oxford swab CRF – for optional swabs being couriered to Oxford

Day 14 CRF – completed by telephone follow-up

Day 28 CRF - completed by telephone follow-up

Hospital admission CRF – to be completed on admission and daily thereafter

Hospital discharge CRF – to be completed when patient leaves hospital after admission

Withdrawal form – for stopping study treatment or withdrawing from follow-up

Death form – for non-COVID related deaths

SAE form – to be completed with in 24 hours of site being aware of an SAE as defined in protocol

Drug supply

- Supplied by Pfizer directly to sites in commercial packaging
- The CT label is MHRA approved – this will need to be printed by pharmacy
- 2 x 250mg capsules to be taken per day
- Patient will either be given 5 boxes of 6 capsules (=30 doses) or pharmacy can repack into one box of 28 or 30 doses
- If administering 30 doses, the last 2 capsules can be destroyed after day 14 phone call

CLINICAL TRIAL USE ONLY

ATOMIC2 **EudraCT No:** 2020-001740-26 **Patient ID:** xxxxxxxxxxxx

Sponsor: University of Oxford, Heather House: Clinical Trials and Research Governance, Joint Research Office, Boundary Brook House, Headington, Oxford, OX3 7GB.

Chief Investigator: Dr Timothy SC Hinks

Instructions for use: Take 2 capsules orally at least 1 hour before or 2 hours after food, and approximately the same time every day for 14 days.

Name of Site: xxxxxxxxxxxxxx

Name of Local Principal Investigator: xxxxxxxxxxx **Phone Number:** XXXXXXX

Date Dispensed: XXX **Batch no:** XXX **Expiry Date** XXXXXXXXXX

Drug supply

Drugs to be receipted in pharmacy and stored in Emergency Department for ease of dispensing – where will your drugs be stored?

- No standalone pharmacy manual
- We will provide a drug accountability log for pharmacy to receipt shipments and log what has been sent to ED
- Separate accountability log for person dispensing to complete with patient ID number and batch ID
- Central trials team request drug shipments based on how many patients randomised – but let us know if you think you are running out
- Initial supply ordered once confirmation of capacity and capability has been confirmed by R&D

Study Treatment

Explain to patient

- Indication for drug
- First dose to be taken at hospital in front of clinician completing the baseline CRF, and recorded on the CRF
- Potential interaction: to inform a clinician if another drug being started
- If on warfarin consider an INR check in 3-5 days
- May get diarrhoea (usually well tolerated, no need to discontinue)
- Discontinue if hearing disturbance or tinnitus
- Advise they will be contacted at days 14 and 28
- Remind them there is a study team contact number on the PIS

If side effects of study drug become intolerable, clinician or patient can make decision to withdraw

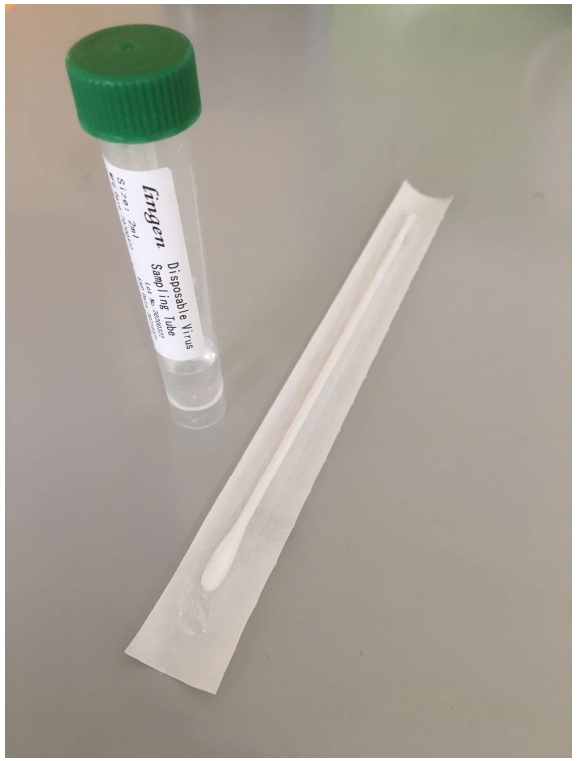
Withdrawals

- A participant may choose to withdraw from the trial treatment or follow-up at any time without having to give a reason
- Participants may choose to stop treatment but may remain on study follow-up
- In the event of a discontinuation from the trial during the 14 days following randomisation, participants will be asked to stop taking the IMP
- Participants may withdraw from follow-up and further communication but still allow the trial team to continue to access their medical records for key data
- Participants may request total withdrawal of consent and ask us to destroy their samples and/or erase any data we hold (this is unlikely)
- Principal Investigators may also choose to withdraw a participant

Always let the trials team know if a patient wants to withdraw. We will advise the best course of action

Oropharyngeal swabs

- **NHS COVID PCR** testing can be performed ***or***
- Research swabs may be used.
- Swabs will be provided to sites by the study team. 2ml viral transport media.
- Take Oropharyngeal swab, send to lab. Stable at room temp for up to 7 days, but on reaching lab should be frozen at < -70˚C for subsequent batched transfer for Oxford labs.
- **Results of research swabs will not be available to patients** (unless an NHS swab performed because clinically indicated)



Sample packs

Sample overview

All sites

Oropharyngeal swab

For PCR for SARS-CoV-2 and mycoplasma (non NHS)

How will this work at your site?
Are you able to store the samples safely?

All sites, optional (patient preference)

Nasal cytology brush

Blood RNA tube (Tempus)

Sample bag

Path lab

4˚C for ≤7 days

Weekly courier to Oxford for transfer to -80˚C

Optional samples (varies depending on site)

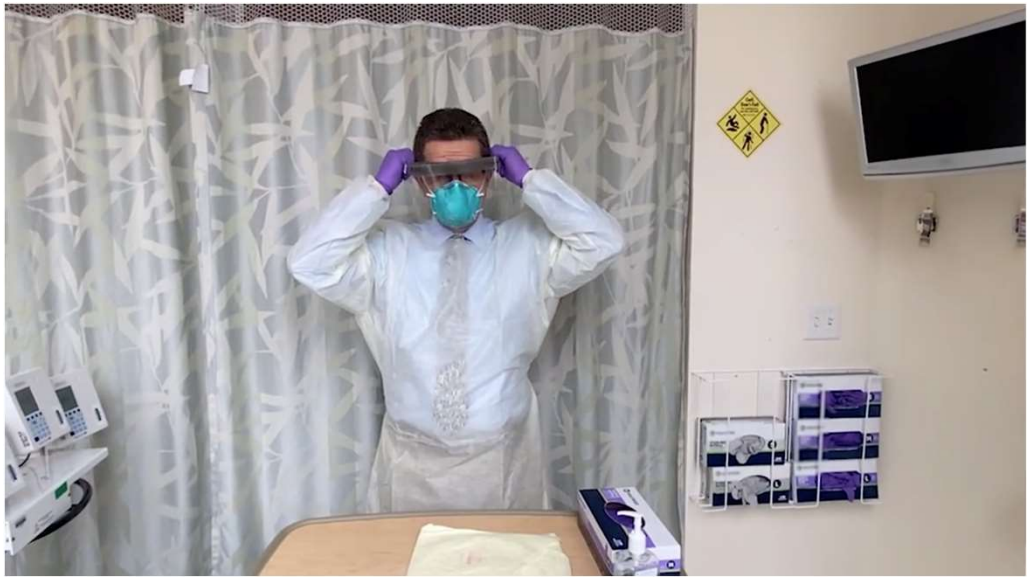
- **Serum SST** tube to be frozen (5ml blood)
- **Tempus blood RNA** tube to be frozen (3ml blood)
- **Nasal sampling** using a small brush into lysis buffer to be frozen
- **EDTA** tube to be frozen for subsequent DNA analysis. (4ml blood)
- EDTA tubes for cell preparation of peripheral blood mononuclear cells to be frozen (**2 x 10ml EDTA tubes, 1 x 4ml EDTA** tube)

How to take a nasal brush

- Contraindications: nil, but caution if: Recent nasal surgery, severe, coagulopathy, markedly deviated nasal septum
- Chose an appropriate area for swabbing and take at same time as the oropharyngeal swab.

https://www.nejm.org/doi/full/10.1056/NEJMvcm2010260

How to take a nasal brush



- Put appropriate PPE according to the standard protocol being followed in ED at the time

https://www.nejm.org/doi/full/10.1056/NEJMvcm2010260

How to take a nasal brush




- Ask patient to take off their mask
- Ask them to blow their nose
- Tilt head back slightly

https://www.nejm.org/doi/full/10.1056/NEJMvcm2010260

How to take a nasal brush

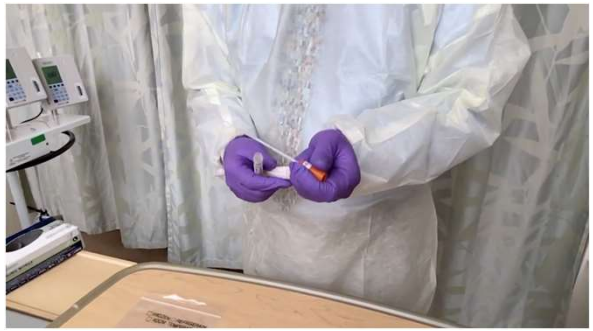



- Ask patient to close their eyes (comfort)
- Gently insert swab just above floor of nasal passage until resistance felt
- If resistance felt back off and reinsert at a different angle

https://www.nejm.org/doi/full/10.1056/NEJMvcm2010260

How to take a nasal brush



https://www.nejm.org/doi/full/10.1056/NEJMvcm2010260

- Insert to depth equal to length from nostril to ear
- Rotate swab 3 times before removing
- Pt to reapply mask.
- Open collection tube, cut tip off into tube with disposable scissors
- Close tube, place in biohazard bag and send to lab

Other antibiotics

- Not contraindicated
- Not usually indicated
- We would exclude people on current macrolide

Adjunctive antimicrobial therapy for suspected/ confirmed COVID-19

Coronavirus (Covid-19)

Interim guidelines for adjunctive antimicrobial therapy for suspected/ confirmed Covid-19 in adult patients

Principles:

Case definition of Covid-19 infection should be met Interim case definition of COVID-19

- Once daily medications are used where possible
- Secondary bacterial infection of viral pneumonitis is difficult to exclude in more severe cases and empirical antibacterials are often given
- Short courses are used, with regular review of results/ progress
- Influenza treatments are given during the "flu" season where indicated by national guidance until influenza infection can be proven
- Use paracetamol instead of NSAIDs for symptom relief in suspected/ confirmed covid-19 see MHRA advice here
- ACE inhibitors should be continued in line with ESC hypertension advice here

Usual duration 3 days (review iv daily)

If symptoms are mostly URTI

- No antibacterials indicated

For mild pneumonia:

CAP with no severe indicators
Preferred: doxycycline 200mg stat po then 100mg OD po
Alternative: amoxicillin 500mg po TDS
Review at 24h when results available

For severe disease:

Includes: severe pneumonia; Adult Respiratory Distress Syndrome (ARDS); Sepsis and Septic shock

- RR over 30 breaths per minute
- Severe respiratory distress
- Sats below 90% on room air

Preferred antibacterials
ceftriaxone 2g iv OD + **doxycycline** 200mg stat po then 100mg OD po IV if unable to receive enterally).

Severe penicillin allergy: moxifloxacin 400mg po OD (IV if unable to receive enterally.)
Moxifloxacin can result in prolonged QTc. Suggest baseline ECG.
Moxifloxacin - see BNF or SPC for contraindications, including concomitant use with other medicines associated with prolonged QTc.
Additional agents

- **oseltamivir** 75 mg BD po in line with NICE guidance if influenza confirmed on POC or other flu test
- other agents – only to be used in the setting of clinical trials

Follow up

- Study team to follow up at day 14 and day 28
- Before phoning patients check ePR and NHS spine for death or readmission
- Phone patient to ask: (14 and 28 day CRFs to be completed on REDCap system)
  - Drug compliance (dispose of last 2 capsules if dispensed 30)
  - Whether ambulatory or limitation of activities
  - COVID-19 symptoms and history
  - Concomitant medications
  - Hospital admissions – complete hospital admission CRF
  - Record any serious adverse events

Follow up: admissions

- If readmitted (20% of participants) complete readmission CRF on REDCap
- Offer repeat of the optional samples: these will be *very* useful if patient had these tests at baseline.

All sites

OUH sites only

- Whilst an inpatient complete eCRF daily: just basic vital signs and a few questions on disease severity: can be done by phone / ePR. Suggest same time each day eg 10:00 am

Safety reporting

Adverse Event (AE)	**Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.**
Adverse Reaction (AR)	An untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant. The phrase "response to an investigational medicinal product" means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect*. Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the trial treatments, based on the information provided.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse reaction, the nature and severity of which is not consistent with information in the MHRA approved Reference Safety Information

Adverse reactions

- Azithromycin is a very well known, commonly used drug with a good safety profile.
- Any difficulties with taking the study treatment will be recorded on the follow-up CRF and do not need to be reported separately. PI should follow these up.
- Advice is provided on the AZM patient information leaflet

Serious Adverse Events

- Defined in the protocol as …'serious events, which might reasonably occur as a consequence of the trial treatment…'
- All SAEs (other than those defined as foreseeable in next slide) occurring within the first **14 days** of the IMP administration will be reported
- Pfizer need to know about pregnancy or lactation
- If any cardiovascular events (related or unrelated) are recorded in follow-up CRFs the system will prompt you to complete an SAE form

Events exempt from reporting as SAEs

- Not to be recorded: events that are part of the natural history of the primary disease process, such as hospitalisation or death).
- Deaths due to COVID-19 disease under study are exempt from reporting as SAEs as they will be captured as part of the primary outcome.
- An AE should not be recorded for the positive SAR-CoV-19 infection, this will be known at time of inclusion into the study and should be recorded as medical history
- Worsening of COVID-19 symptoms is captured as an efficacy measure and in general will not be considered an adverse event.

All SAE information must be recorded on an ATOMIC2 Trial SAE form on REDCap within **24 hours** of the site observing or learning of the SAE(s)

SAEs must also be reported in the participant's medical notes, All sections of the SAE Reporting Form must be completed. Once the SAE form is completed in REDCap, an alert is sent to the Trials Team.

Investigator Site File

- Enables both the conduct of a clinical trial and the quality of the data at that site to be evaluated. Sub-section of TMF
- Investigator Site File will be provided electronically as a set of folders containing the relevant documents
- Should be stored on an NHS networked drive within the hospital with access only to the study team
- Please speak to your IT team for assistance
- Should be version controlled and maintained as you would with a paper site file

PI responsibilities

- Responsible for the conduct of the trial and for the leadership of the trial team at their site, although activities can be delegated to appropriate members of the trial team
- Delegation of duties log is a paper document to be signed by anyone undertaking ATOMIC2 duties. PI must ensure that the individual is appropriately qualified for the role they are to undertake & have been provided with appropriate GCP and protocol-specific training.
- Needs to ensure that sufficient staff are involved in the trial to ensure that all activities can be undertaken effectively
  - This includes both non clinical activities, such as CRF completion, data queries, management of the ISF, as well as subject-focused clinical care and medical cover.
- Review of safety information
- Sign-off of completed serious adverse event (SAE) forms

Site supplies

Supplies will be couriered to you. You will be provided with:

- an iPad (one for each recruiting hospital) – check you can log in and study staff know where it is located
- a box containing the necessary swabs and blood tubes – make sure these are stored correctly
- paper copies of localised Patient Information Sheets – to be handed to patients prior to consent process

iPads and Logins

- iPads are the property of the University and will be returned to Tim Hinks at the end of the trial.
- Keep them well charged and under lock and key. They are not to be used for any other purpose aside from ATOMIC2.
- They are set up with an individual password for use by all ATOMIC team members.
- It is the responsibility of the sites to keep the iPad and REDCap login details safe and secure.

- One generic log in per recruiting site
- Email alerts and confirmation of randomisation emails go to this email address
- The emails don't contain any patient identifiable information

What is the best email address to use for your REDCap generic site login?

Will you be recruiting at more than one site?

Contact details

- Chief Investigator: Timothy Hinks

  timothy.hinks@ndm.ox.ac.uk
- Trial manager: Lucy Cureton

  atomic2@ndorms.ox.ac.uk
- ATOMIC2 Website
  https://atomic2.octru.ox.ac.uk/
- REDCap
- https://redcap-rrio.octru.ox.ac.uk/

Mailing address

Oxford Clinical Trials Research Unit, University of Oxford, Botnar Research Centre, Windmill Road, Oxford, OX3 7LF

Tel: 01865 223469

When can you start seeing patients?

Site agreement fully executed?

Confirmation of Capacity & Capability?

Delegation of Duties log completed?

Received supplies and logged into iPad?

Received supply of study treatment?

Received site activation email from Trials Office?

Thank you

Funding

Oxford University Medical Sciences Division

COVID-19 Research Response Fund

NIHR Oxford Biomedical Research Centre

Pfizer

Questions?