Randomised Evaluation of COVID-19 Therapy: the RECOVERY trial

Collaborators' Meeting

6th October 2020

Agenda

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1. Introductions
2. Update on progress
3. REGN-COV2
4. Other developments
5. Future plans
6. Paediatric update
7. Q&A

Introductions

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- One of the central study team will talk to the agenda
- If you have questions please enter them into the “Q&A” on the right side of your screen.
- Questions may be answered directly or to the whole group

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PROGRESS UPDATE

New trial design

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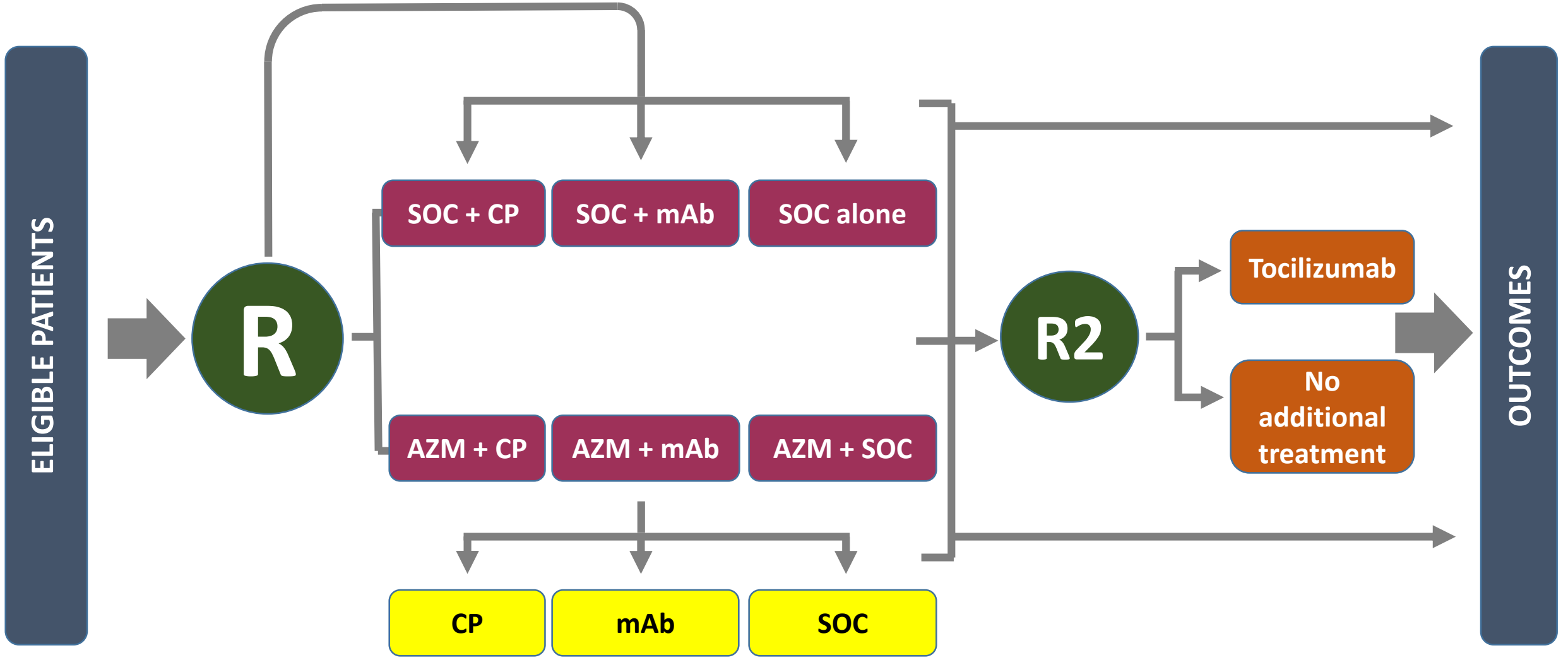

Recruitment by site and by time

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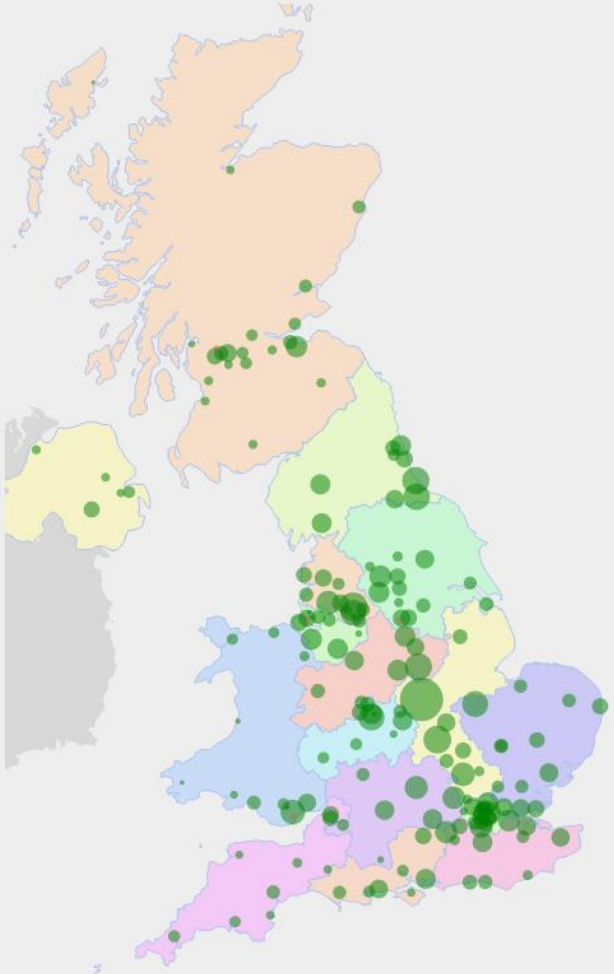
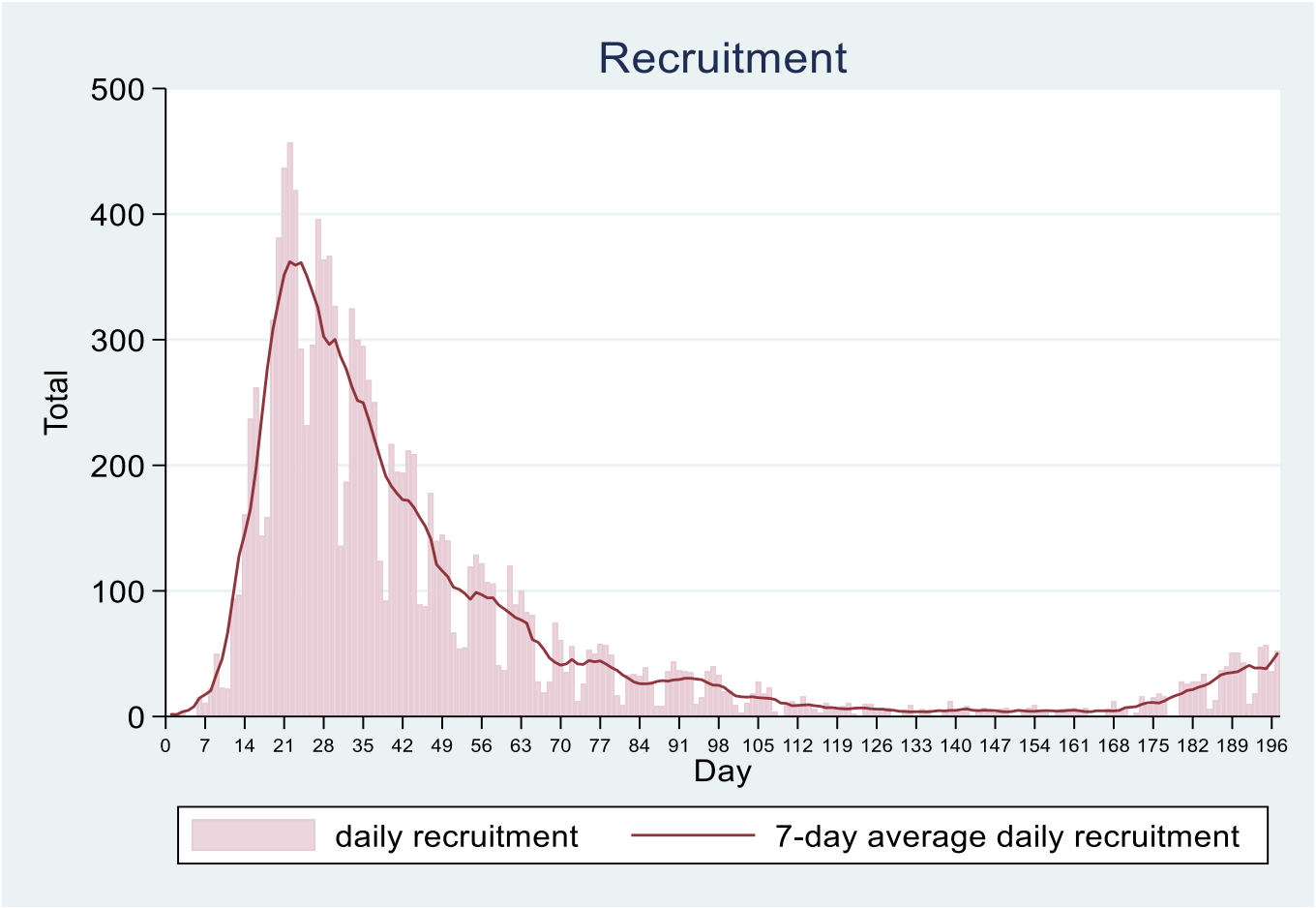
Active Sites	Recruiting Sites	Participants	Phase 2 rands.	Phase 3 rands.
176	172	13068	1018	963





Recruitment

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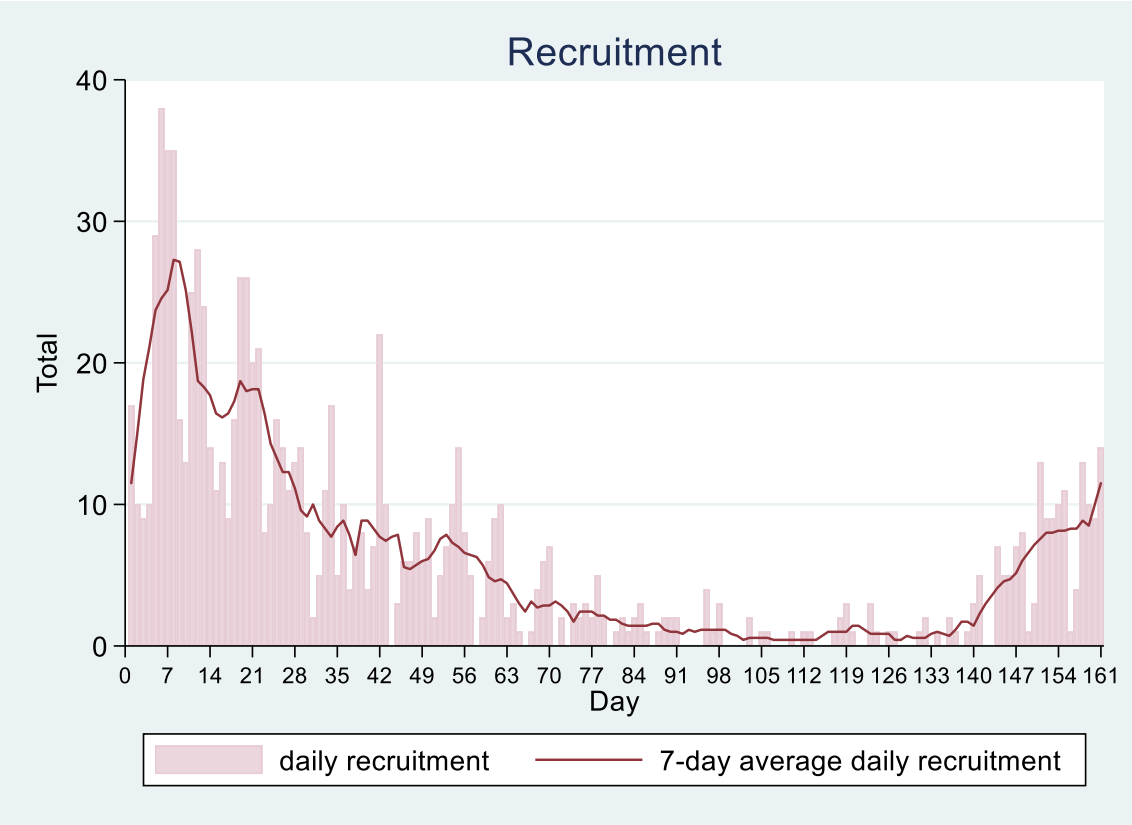
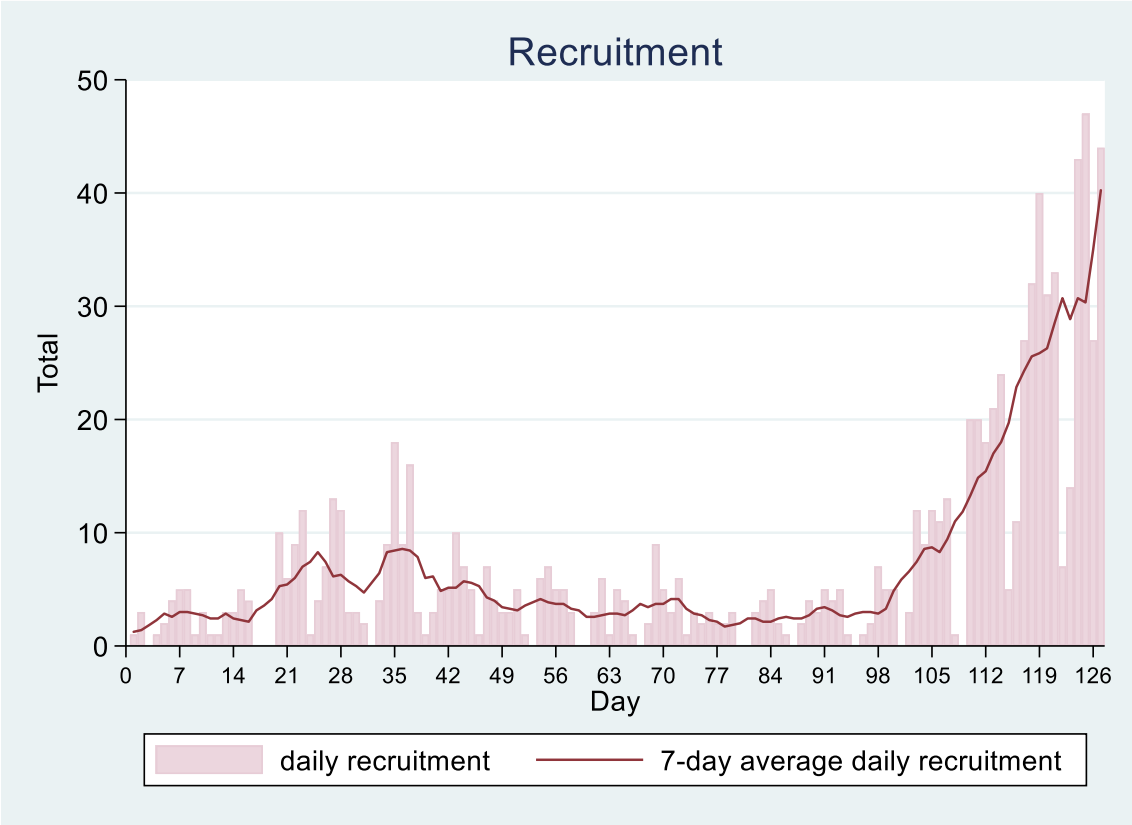
- Tocilizumab vs control



- Convalescent plasma vs control



Recruitment

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- Continued recruitment is essential

- As local outbreaks occur, please consider discussing with your teams how to ensure that all available admissions with Covid-19 are identified and enrolled if possible
  - Daily catch-up with admitting teams
  - Links with laboratory for all positive swabs among patients to be reported

- Please consider “re-launching” the trial at your site to refresh people and inform any new team members of how they can contribute

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REGN-COV2

REGN-COV2

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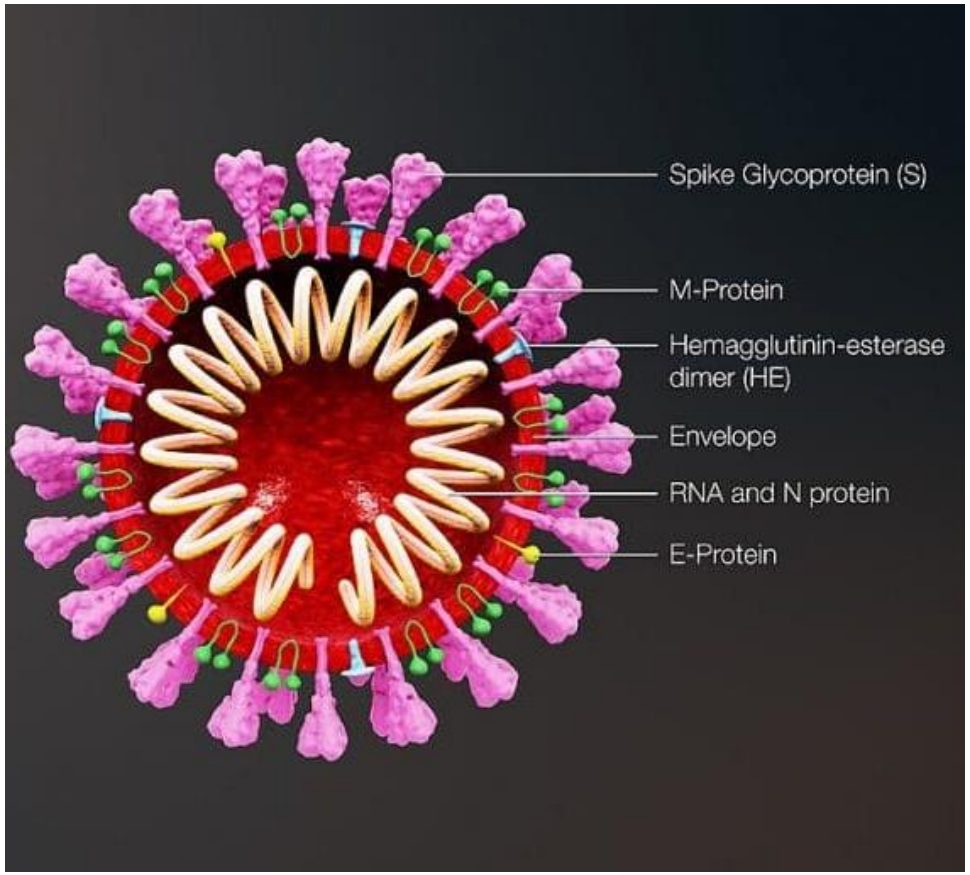
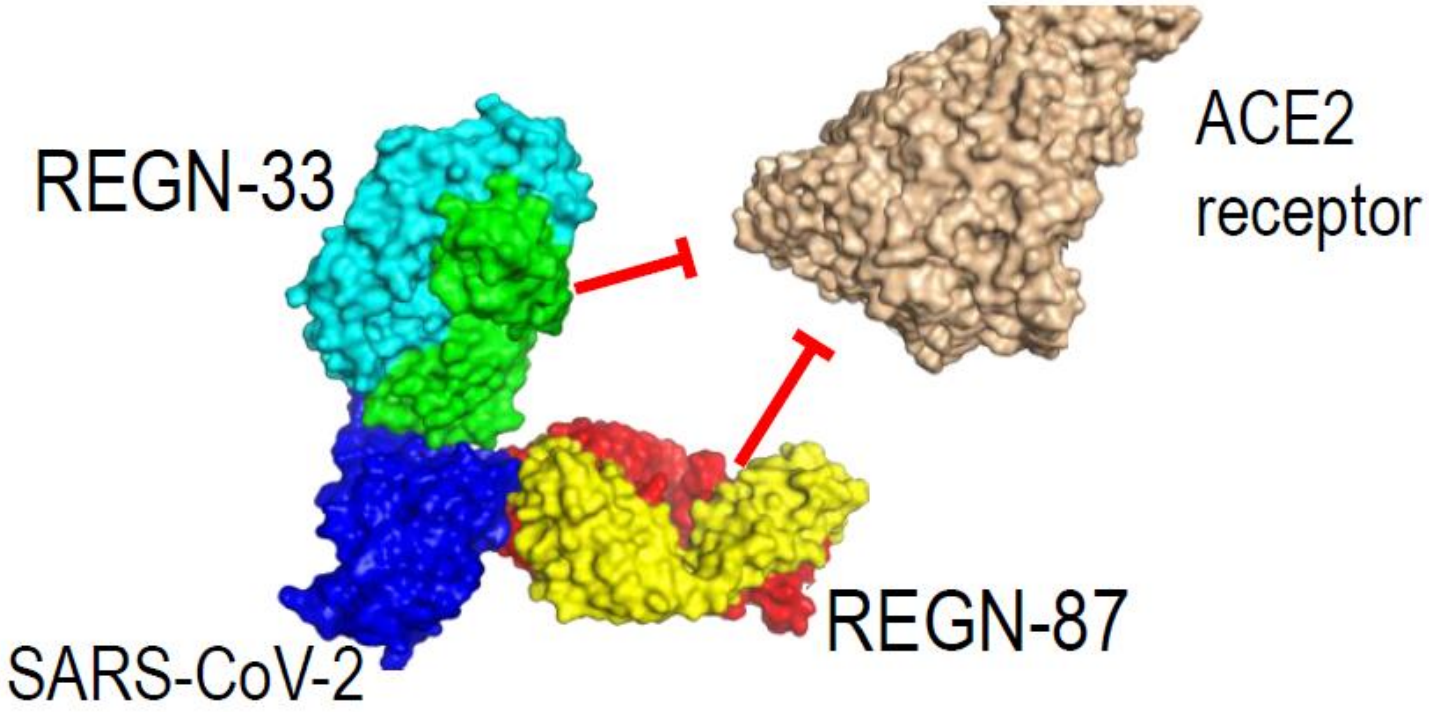
- Several companies are now producing monoclonal antibodies (mAbs) against SARS-CoV-2 “spike” protein





REGN-COV2

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- REGN-COV2 is a mixture of two monoclonal antibodies (mAbs: REGN10933 and REGN10987)

- These are fully human antibodies directed against spike protein

- Two different antibodies mean that if virus mutates its spike protein such that one antibody doesn't bind so well, the other antibody probably still will

Safety of REGN-COV2

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- REGN-COV2 mAb has been given to >1000 patients so far in early phase trials
  - No serious adverse reactions
  - Minor infusion reactions do occur during infusion

- Other trials ongoing in other clinical scenarios e.g. outpatient, prophylaxis
  - Preliminary results from outpatient trial suggest more rapid reduction in viral load and symptoms compared to placebo

It’s good enough for him…

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BBC | BBC Account | Home | News | Sport

Welcome to the BBC

LIVE Trump receives treatment as new cases emerge

REGN-COV2 site setup

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1. Local PIs need to complete online training and confirmation form
   - They should ask other staff involved at site to also do this, but not require before site activation

2. Pharmacy need to be ready to support new arm
   - Review Pharmacy Manual on website (V3.0 release today) and complete local risk assessment to determine where mAb will be prepared
   - Confirm staff details to RECOVERY team so user accounts on Cenduit websystem can be created (Cenduit user guide on website)
   - Indicate when they will be ready to:
     1. Receive drug
     2. Support allocation to a trial participant

REGN-COV2 dos and don’ts

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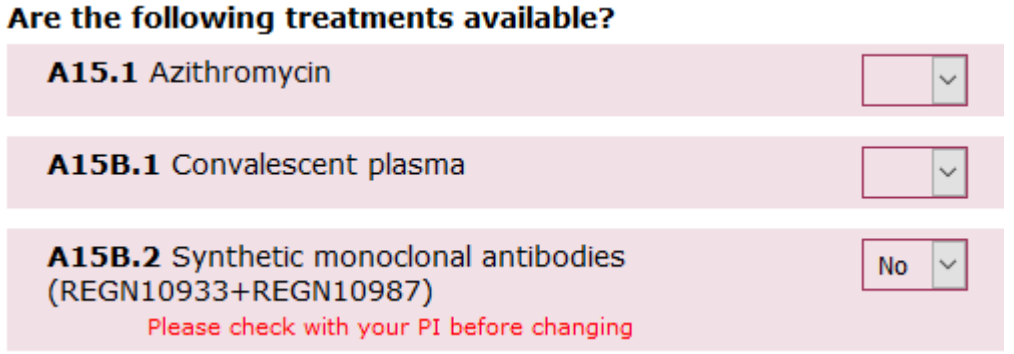
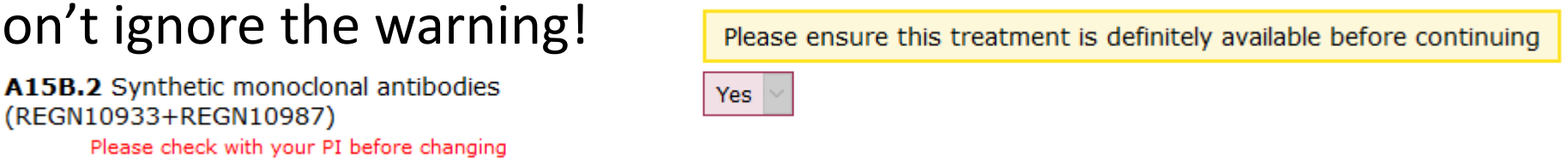
- Please **DO NOT** indicate REGN-COV2 is available if system suggests it is not *unless you are absolutely sure!*



- Please don’t ignore the warning!



- Otherwise the participant may be allocated a treatment they can’t have ☹

When to include REGN-COV2

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- REGN-COV2 should be administered as soon after randomisation as possible

- If being prepared in pharmacy, this may not be until next working day

- If delay is likely to be longer (e.g. at weekend), please indicate that mAb is unavailable on randomisation form so it will not be allocated

Administration

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- REGN-COV2 is reconstituted in 250 mL bag of normal saline and infused over 60 minutes
- Does not necessarily require delivery by research staff
- Observations and beginning, middle and end (as for blood product)
- Infusion should be stopped if reaction occurs
  - Reaction should be treated symptomatically
  - If severe, infusion should be abandoned
  - Otherwise can be restarted at half the original rate on medical advice

Safety assessments

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- Any suspected serious adverse reactions should be reported according to protocol
- 72h safety form to be completed for all participants received REGN-COV2 (or in control arm)
- Standard 28 day follow-up form to be completed

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OTHER DEVELOPMENTS

Outside RECOVERY

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- EMPACTA trial of tocilizumab among adults with hypoxia not on mechanical ventilation
  - Primary outcome: mechanical ventilation or death by day 28
  - HR 0.56 (95% CI 0.32-0.97)

- PLACID trial of convalescent plasma among hospitalized adults with hypoxia
  - Primary outcome: severe hypoxia or death
  - OR 1.09 (95% CI 0.67-1.77)
  - >1/3 donors had undetectable anti-SARS-CoV-2 neutralising antibodies

Other developments in RECOVERY: Phase 2

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Department of Health & Social Care

Guidance

Guidance: making a proposal for COVID-19 therapeutics clinical trials

Published 17 August 2020

Contents

Introduction

Given the success of the Phase III RECOVERY platform in delivering a single platform trial across the NHS, the UK Government has increased investment in an expanded platform which will operate for the next 24 months. This will include new treatments tested in Phase II and Phase III studies which will now be delivered through the RECOVERY platform (RECOVERY+) in patients admitted to hospital.

New treatments can be proposed for inclusion in the RECOVERY+ platform for both Phase II and Phase III trials. They will be considered by the UK COVID-19 Therapeutics Advisory Panel (UK-CTAP).

Subcommittees that have met to date:

- Antiviral
- Anticoagulation
- Immunomodulation
- Renin-angiotensin system

Other developments: RECOVERY international

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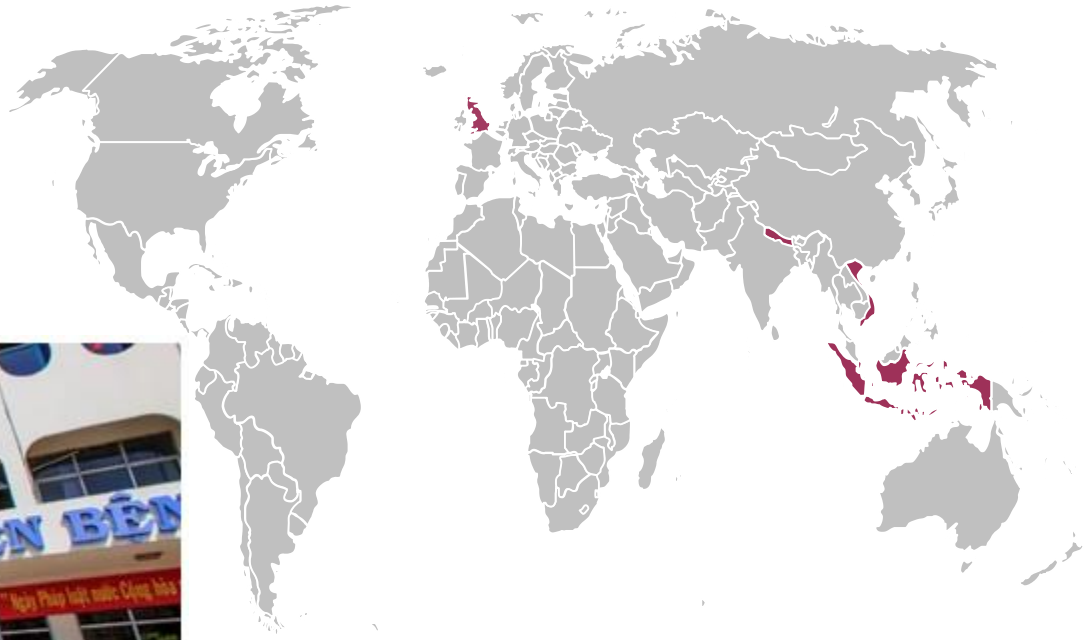
- RECOVERY has been approached by other countries asking to participate

- Discussions are progressing with Vietnam, Indonesia and Nepal



Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam

Pharmacogenomic substudy

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- Azithromycin known to prolong QT interval, but genetic determinants unknown

- Substudy for interested sites which requires:
  - ECG prior at baseline and 48h (uploaded to OpenClinica)
  - Co-enrolment into GenoMICC or ISARIC-4C encouraged (for genetic samples)

- Please e-mail recoverytrial@ndph.ox.ac.uk if interested

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TRIAL PROCEDURES

Serum samples

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- Participants entering antibody comparison (CP vs mAb vs control) need to have serum sample collected prior to randomisation

- Can be taken with G&S sample after consent prior to randomisation to limit venepunctures

- Must be taken for all participants in that comparison (regardless of allocation)

Completeness of follow-up

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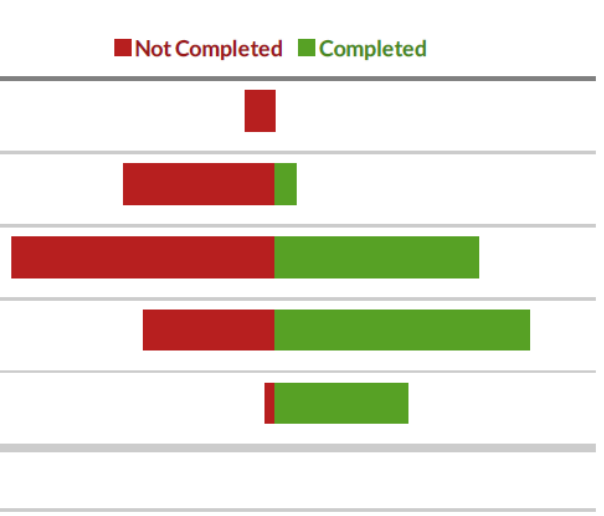
- Weekly reminders highlighting participants randomised >28 days ago without complete form **and also** those needing an Antibody Comparison 72h safety form

- Please do complete these as soon as possible

Follow-up form completion summary

Days Since Rand.	FU Not Completed	FU Completed	Total Rands.
7 ≤ 14	3 (100.0%)	0 (0.0%)	3
14 ≤ 21	15 (88.2%)	2 (11.8%)	17
21 ≤ 28	26 (56.5%)	20 (43.5%)	46
28 ≤ 35	13 (34.2%)	25 (65.8%)	38
> 35	1 (7.1%)	13 (92.9%)	14
Total	**58 (49.2%)**	**60 (50.8%)**	**118**



Carry on recruiting!

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- RECOVERY is expanding both in terms of therapies being tested and geography covered, so it is an exciting time for the trial.
- As admission rates rise, please ensure team are aware and prepared to recruit
- Need to continue recruitment and collection of follow-up information to provide DMC with information about efficacy and safety of study treatments
- Thank you for your support.