Randomised Evaluation of COVID-19 Therapy: the RECOVERY trial

Collaborators' Meeting

27th April 2021

Agenda

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1. Introductions
2. Update on progress
3. REGN-COV2
4. Dimethyl fumarate
5. Baricitinib
6. New international arms
7. Trial procedures
8. 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

Current design (adults)

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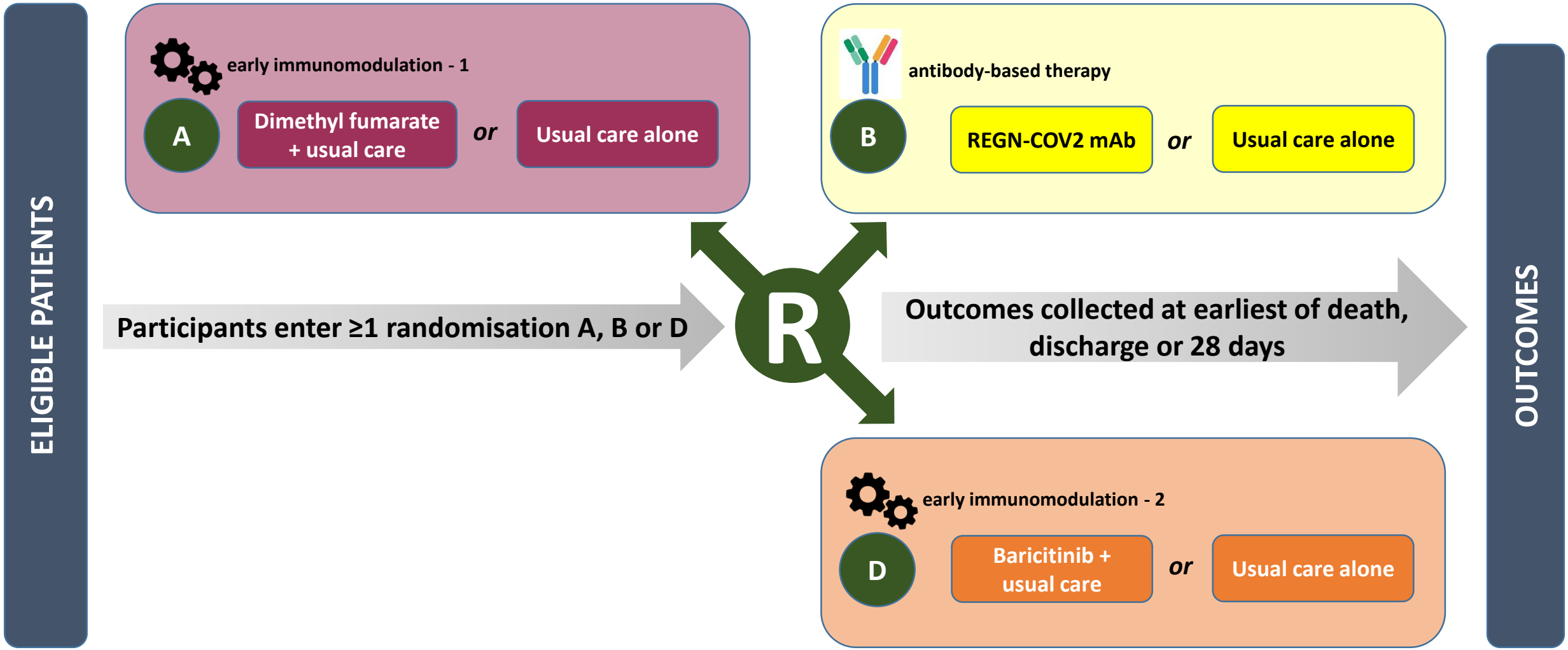

Recruitment by site and by time

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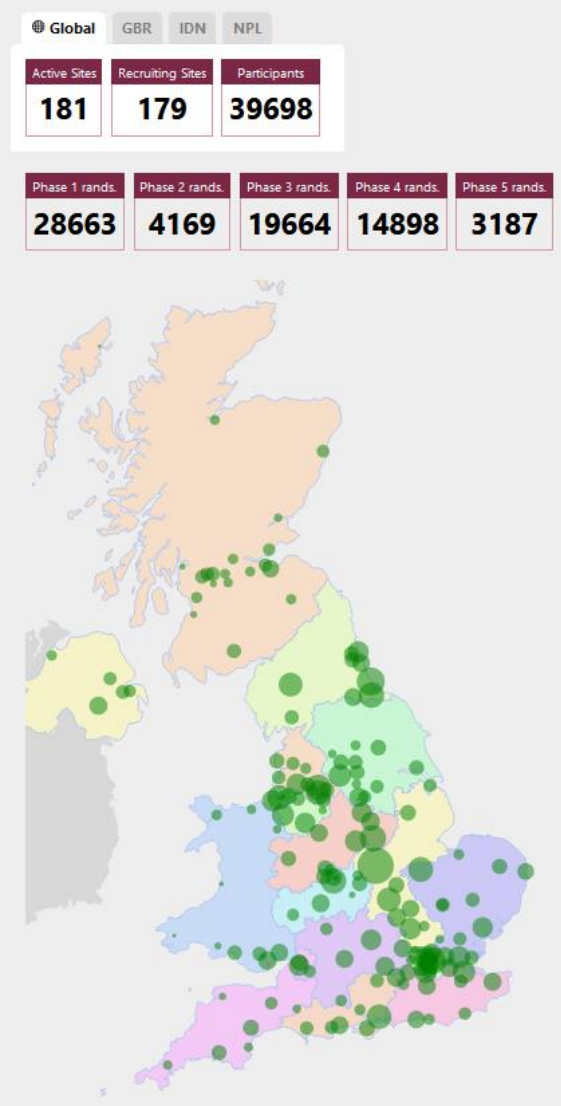

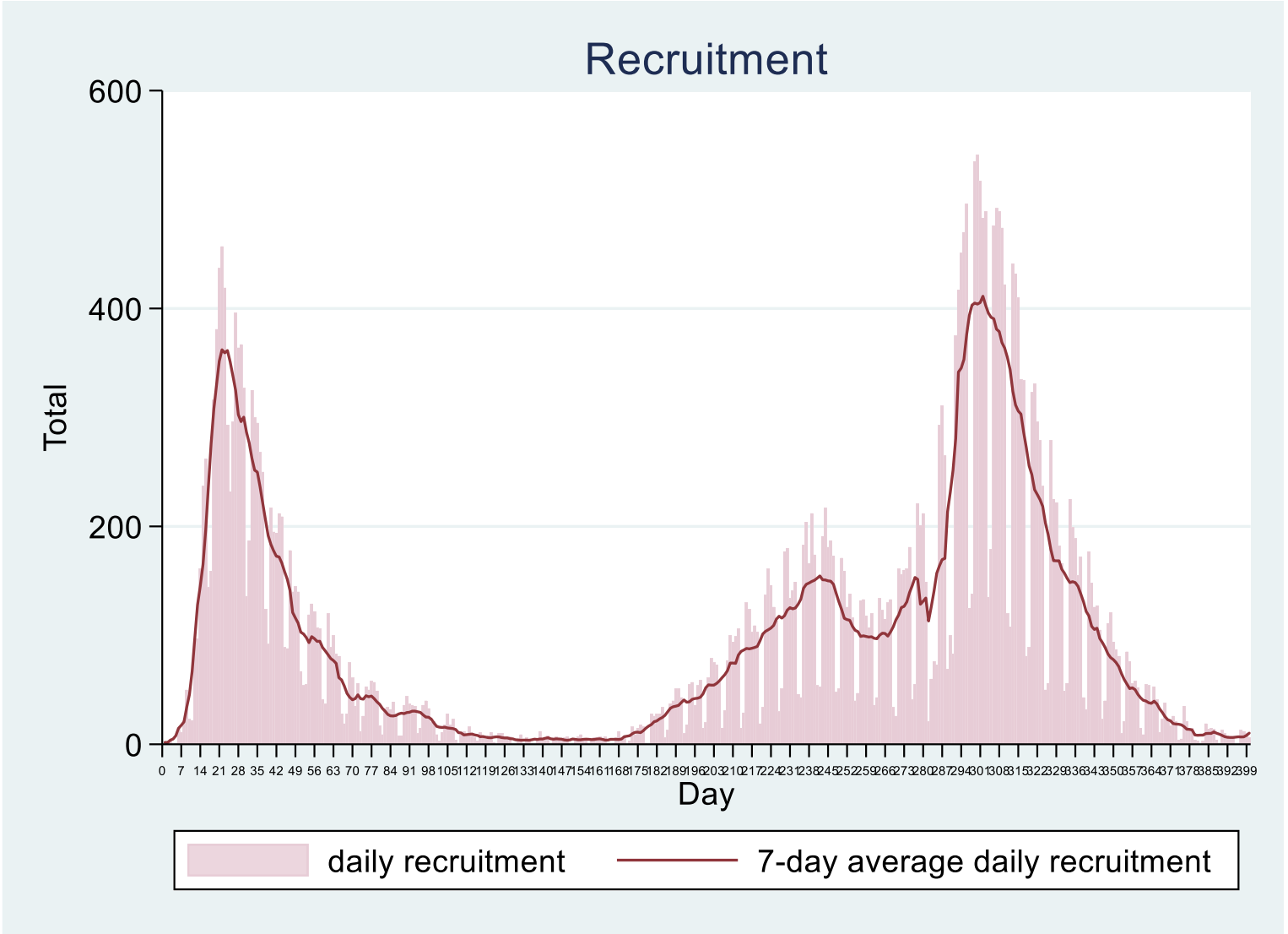

Current numbers in comparisons

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- REGN-COV2 *vs* usual care: ~9700
- Baricitinib *vs* usual care: ~3200
- Dimethyl fumarate *vs* usual care: 70

Recruitment

- Recruitment will be a challenge over the coming weeks
- Many staff will be returning to previous research studies, but please do ensure that your site continues to have a strategy to identify, invite and recruit patients presenting with COVID-19
- It remains to be seen whether there will be a ‘third wave’ in the summer, but RECOVERY will remain open

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REGN-COV2

REGN-COV2

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- 9700 people in comparison to date
- Other data on REGN-COV2 suggests the biggest effect might be expected in antibody negative patients (but these cannot be identified reliably on admission)
- Original aim was to recruit 12,000 participants; currently under review

REGN-COV2 in outpatients

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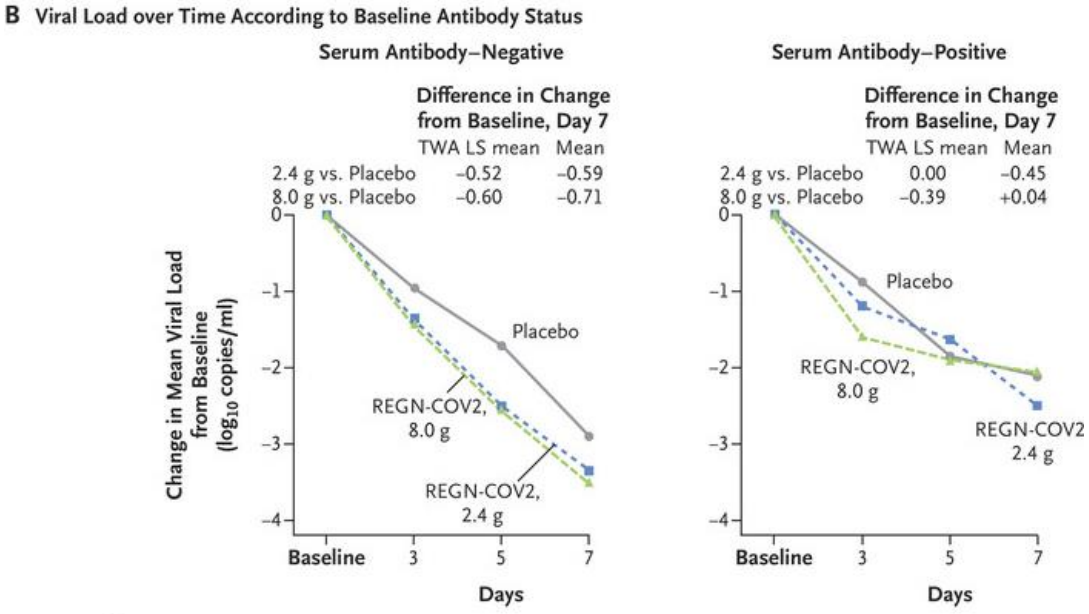
- Data presented in *NEJM* recently
  - 275 patients with PCR-proven SARS-CoV-2 infection not in hospital
  - Randomised between placebo, 2.4g or 8g (RECOVERY dose) of REGN-COV2 (1:1:1)
  - Key outcome: viral load



Serum samples

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- **All** participants entering REGN-COV2 comparison need to have serum sample collected prior to randomisation

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

- **Please check whether any samples have not been returned to the central lab**

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DIMETHYL FUMARATE

Dimethyl fumarate

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- Recently added to protocol and has been piloted at some sites

- Includes extra data collection on:
  - S/F_{94} (measurement of oxygenation function of lungs)
  - Lab results
  - Tolerability of DMF

- Sites can still express an interest in participating in this arm

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BARICITINIB

Baricitinib in COVID-19

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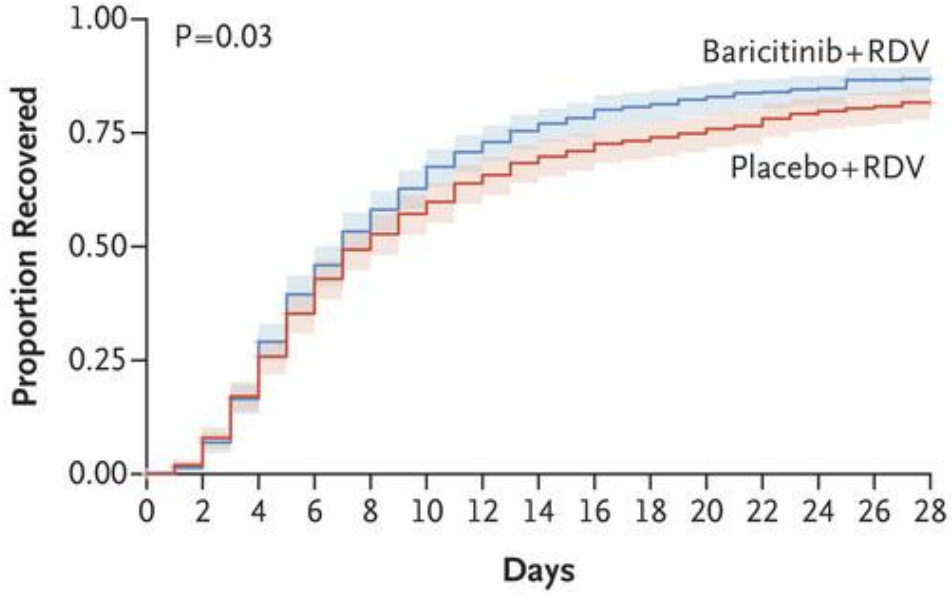
- JAK/STAT system is key to immune activation so modulating it may be beneficial

- Data from ACTT-2 show quicker time to recovery



No. at Risk

Baricitinib+RDV	515	497	418	302	233	186	145	121	107	95	87	80	76	63	30
Placebo+RDV	518	495	417	322	251	211	178	156	143	131	123	115	102	92	44

Baricitinib in COVID-19: COV-BARRIER

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- 1525 patients hospitalised with COVID-19 and at least one marker of inflammation (but not receiving invasive mechanical ventilation)
  - 79% on corticosteroids
- Randomised between baricitinib 4mg once daily and placebo
- Primary outcome: Progression to ventilation or death within 28 days

Baricitinib in COVID-19: COV-BARRIER

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- Trial results announced on 8 April:
  - Non-significant reduction in primary outcome:
    - aOR 0.85; 95% CI 0.67 – 1.08
  - Reduction in death (secondary outcome): 162 deaths in total
    - 8.1% *vs* 13.1%: HR 0.57, 95% CI 0.41 – 0.78
  - Reassuring safety data: similar proportions with SAEs (14.7% *vs* 18.0%)
    - Serious infection 8.5% *vs* 9.8%
    - VTE 2.7% *vs* 2.5%

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PROTOCOL V15.0

Protocol V15.0

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- Officially removes aspirin and colchicine from protocol

- Adds two new arms:
  - Infliximab (single dose 5 mg/kg IV)
  - High-dose dexamethasone (20mg for 5d then 10mg for 5d)

- New arms being started at international sites:
  - Would delay completion of baricitinib
  - Removal of aspirin and colchicine leaves no IMPs for international sites
  - Will be brought back to UK if another wave does occur

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TRIAL PROCEDURES

Completeness of follow-up

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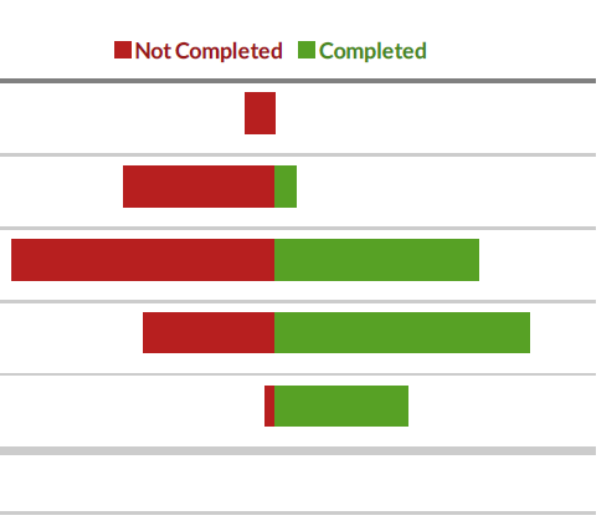
- Weekly reminders highlighting participants randomised >28 days ago without complete form

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**



Baseline samples

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- Please don’t forget baseline samples for participants in REGN-COV2 comparison!

- These will be key to interpreting the results

Carry on recruiting!

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- RECOVERY remains the largest global trial in COVID-19 and is an exemplar of what trials can do (both in and after pandemic)
- Current therapies are exciting, but need reliable data before they should be used routinely
- THANK YOU for all your support to date and please don't forget RECOVERY!