Case studies | Lessons from the pandemic

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Repetita **NON** iuvant!

Case Report Forms (CRF) should be carefully designed to streamline data acquisition and avoid repetition

More is not necessary better & can slow down QC of data

Rapidly designed data capture in a rapidly evolving global pandemic, lessons to be learnt

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BACKGROUND

With the emergence of a global pandemic we rapidly set up a platform trial to evaluate whether specific immuno-modulatory interventions could reduce the composite of progression of patients with COVID-19-related disease to organ failure or death. Understandably the trial was clinically-driven but the consequently rapidly-designed CRF presented with major challenges in the collection, management, and quality control of the data. This impacted adversely the speed of the analysis and ultimately the dissemination of results. Data management and/or statistics' input would have been largely beneficial at the design stage with a focus to rationalise and streamline data capture.

Primary endpoint

Time to incidence
(up to and including day 14)
of any of the following events,
whichever comes first:

- DEATH
- MECHANICAL VENTILATION
- CV ORGAN SUPPORT
- RENAL FAILURE
- DISCHARGE *
- WITHDRAWAL **

CRF design & data acquisition

66 different CRF forms were used in the trial. Of these, 11 contained 18 different variables of 3 types (binary, categorical and dates) needed to determine the primary endpoint. Scheduled forms were filled at each visit, while unscheduled forms were filled only when needed/relevant.

Participant Status	Binary (Yes/No)	Scheduled
Respiration, Cardiac and Renal Status	4 x Binary (Yes/No)	
7-Point Ordinal Scale	Categorical (7 levels)	
Treatment Cessation Criteria	Binary (Yes/No)	
Consent Withdrawal	Binary (Yes/No)	
Death Form	Date	Unscheduled
Treatment Cessation Form	Categorical (10 levels) + Date	
Consent Withdrawal Form	Categorical (2 levels) + Date	
End of Trial Participation Form	2 x Categorical (18 & 6 levels) + Date	
Adverse Events of Special Interest	Categorical (7 levels) + Date	
Serious Adverse Events	Categorical (6 levels) + Date	

Visit schedule

- SCREENING
- BASELINE
- D1 RANDOMISATION
- D2
- D3
- D4
- D5
- D6
- D7
- D8
- D9
- D10
- D11
- D12
- D13
- D14
- DISCHARGE
- FOLLOW-UP D28
- FOLLOW-UP D90

* The statistical analysis treated the composite of primary events and discharge as competing risk. Discharge meant “discharge from hospital”.

** Withdrawal before day 14 or LTFU patients were right-censored at the time of their last completed scheduled visit

6 Events (type & time)

FOCUS ON THE MINIMUM AMOUNT OF DATA NECESSARY TO DETERMINE THE PRIMARY ENDPOINT

ACTUAL: 11 CRF pages + 18 variables * (18 scheduled visits + ? unscheduled visits)

PROPOSED: 4 CRF pages + (6 binary variables & 6 dates) + (3 unscheduled visits + 14 scheduled visits)

- ✓ **COLLECT DATA WITH CLEAR PURPOSE** (clearly identify and group separate CRF forms used for efficacy, safety or patient disposition)
- ✓ **DON’T DUPLICATE DATA SOURCES** (cross-checking different CRFs takes time & effort)
- ✓ **KEEP VARIABLES SIMPLE & USE A CLEAR CRF LAYOUT** (keep variables on the same page)
- ✓ **CLARIFY TERMINOLOGY** (i.e. “Discharge from hospital”, don’t confuse events & visit names)

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https://github.com/mnodale/ICTMC-2022

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