

Randomized, Embedded, Multifactorial Adaptive Platform trial for Community- Acquired Pneumonia

Corticosteroid Domain



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Background: Corticosteroids



- There is significant uncertainty regarding the use of corticosteroids in patients with severe CAP (other than CAP caused by COVID-19) requiring hospital admission
- Several RCTs and meta-analyses have suggested benefit of treatment with corticosteroids, however existing evidence is not definitive and corticosteroids have a range of potentially adverse effects
- Potential benefit appears to be more likely for patients who are severely ill

Background: Corticosteroids



- Uncertainty about the use of corticosteroids in:
 - Patients with CAP due to influenza
 - Patients with septic shock vs those without septic shock
 - Patients with ARDS vs no ARDS.

Changes to Corticosteroid Domain



Major changes to the Corticosteroid Domain in V5:

1. Addition of new intervention, fixed course dexamethasone
2. Domain now available in Moderate State (i.e. patients who are not receiving organ failure support in an ICU)
 - Only where updated Core Protocol has been approved.
3. Domain now available to children aged ≥ 28 days
 - Only where updated Core Protocol has been approved.

Inclusion Criteria:

- Aged ≥ 28 days old
- If in the Moderate State, receiving some form of supplemental oxygen
 - Simple facemask, low- or high-flow oxygen, or non-invasive ventilation

Exclusion Criteria:

- Known hypersensitivity to any corticosteroid
- Intention to prescribe systemic corticosteroids for a reason that is unrelated to the current episode of CAP (or direct complications of CAP)
- More than 24h have elapsed since ICU admission (if in the Severe State)
- The treating clinician believes that participation in this domain is not in the best interests of the patient

- No corticosteroids
- Fixed duration hydrocortisone
(IV hydrocortisone, 50 mg 6 hourly for 7 days)
- Shock-dependent hydrocortisone
(IV hydrocortisone, 50 milligrams every 6 hours while patient is in shock)
- Fixed duration dexamethasone
(IV or enteral dexamethasone 6mg daily for 10 days)

No corticosteroid intervention



- Do not prescribe any systemic corticosteroid, including hydrocortisone or dexamethasone
- Withholding of corticosteroids is to continue until day 28 or hospital discharge (whichever occurs first)
- Administration of systemic corticosteroids for the treatment of new illnesses that develop in the course of a patient's ICU stay (i.e. not resulting from CAP or its direct complications) is permitted

Fixed-dose hydrocortisone



- Prescribe hydrocortisone IV 50 mg 6 hourly for 7 days
 - It is intended that a course of 28 doses is administered
- Commence immediately after randomisation
- Cease after 7 days or hospital discharge, whichever occurs first
- Prescribe to continue on ward if discharged from ICU before 7 days (not a protocol violation if ceased by ward staff)

Shock-dependent hydrocortisone



- Commence hydrocortisone IV 50 mg 6 hourly when patient is in septic shock
- Septic shock defined as:
 - Administration of any vasopressor by continuous infusion
 - The treating clinician believes the vasopressor requirement is due to the CAP and not another reason (e.g. hypovolaemia, sedation, mechanical ventilation)
- If septic shock is present at time of enrolment commence immediately
- Cease once clinician believes septic shock is resolved.
 - Note that septic shock is always considered to be resolved when vasopressors have not been administered via infusion in the preceding 24 h

Fixed-dose dexamethasone



- Prescribe dexamethasone (IV or enteral) 6mg daily for 10 days
- Commence immediately after randomisation
- In pregnancy, dexamethasone should be replaced by oral prednisolone 40mg once daily, or IV hydrocortisone 50mg 6 hourly
- In children, administer dexamethasone 0.15 mg/kg (max 6mg/day)
- Cease after 10 days or hospital discharge, whichever occurs first
- If patient develops septic shock, a switch from dexamethasone to hydrocortisone is permitted.

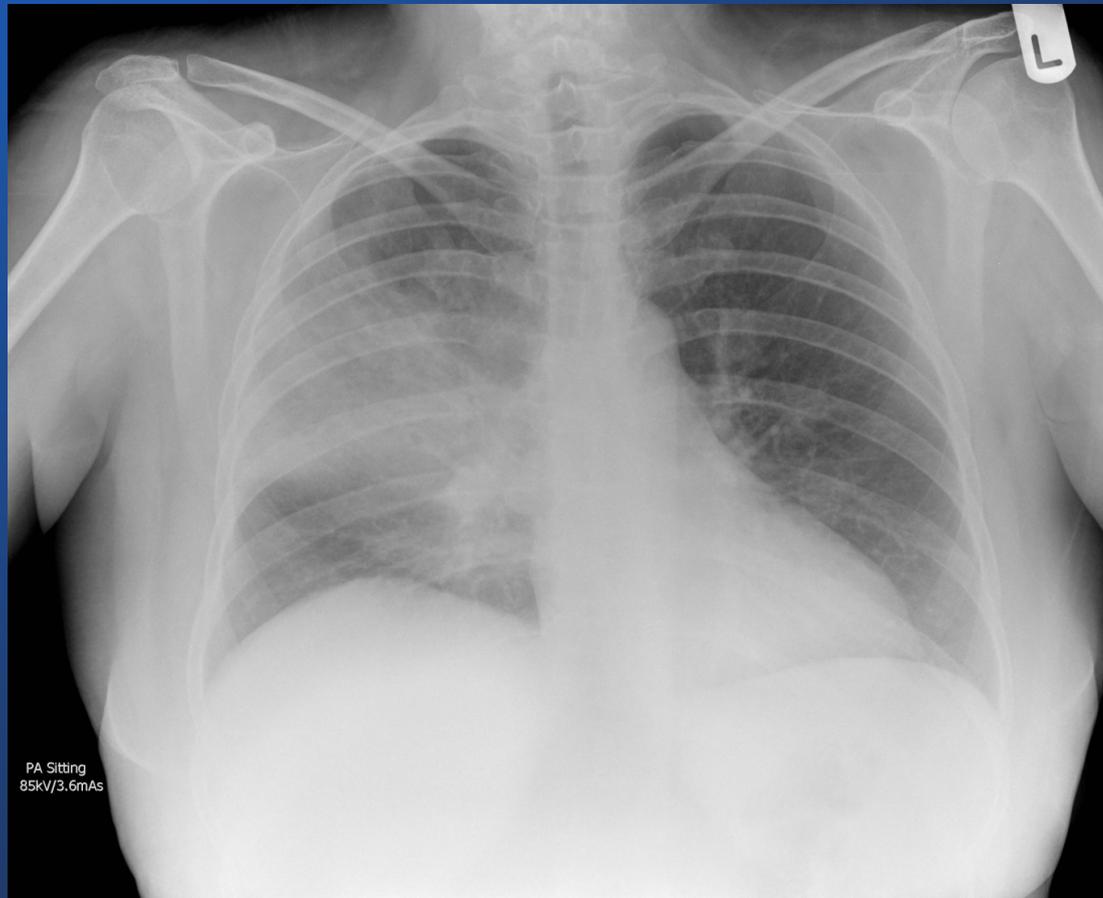
End-point



Primary endpoint

- REMAP-CAP primary endpoint, as defined in Core Protocol

Questions?



Randomized, Eembedded, Multifactorial, Aadaptive Platform
For Community-Acquired Pneumonia