Studying corticosteroid utilization in the treatment of community-acquired pneumonia in Japan through an international adaptive platform trial, REMAP-CAP

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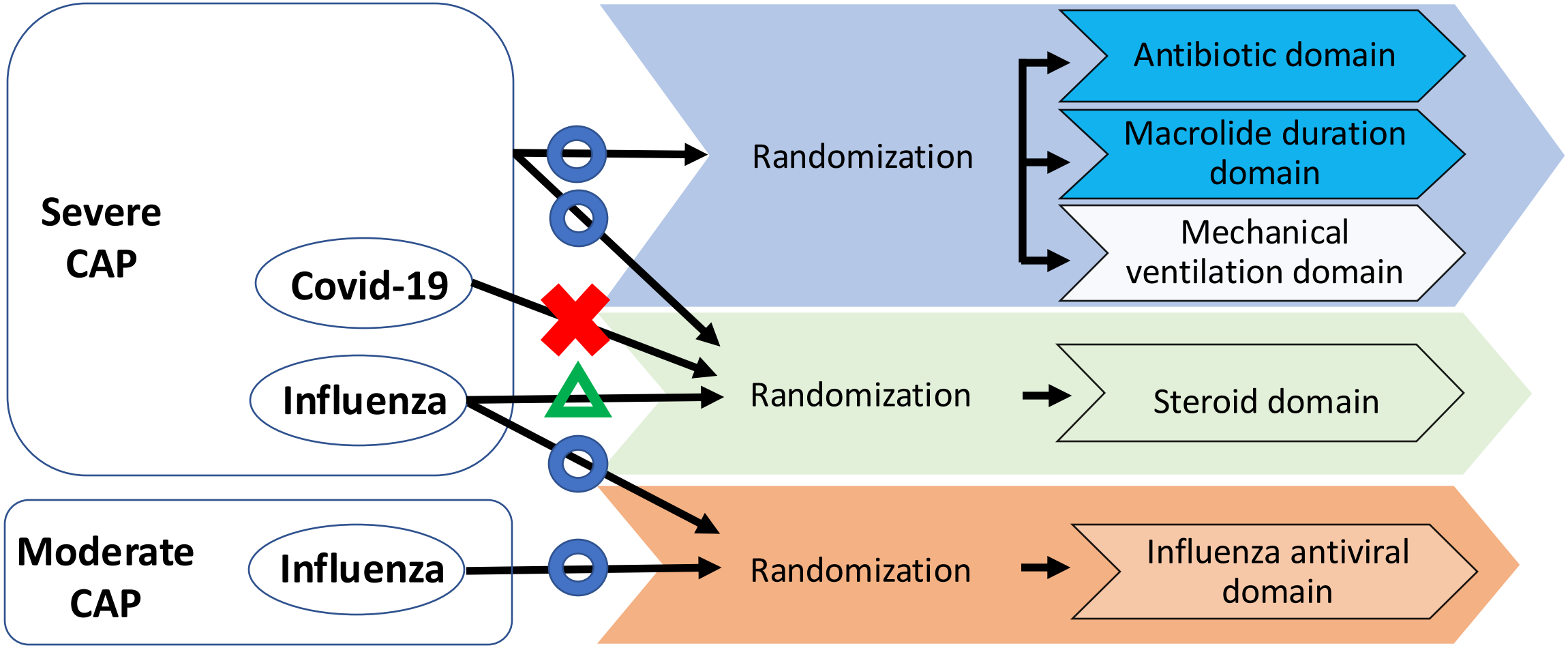
- I have nothing to disclose

Introduction

- REMAP-CAP: A Randomised, Embedded, Multi-factorial, Adaptive Platform trial for Community-Acquired Pneumonia
- REMAP-CAP enables the simultaneous assessment of multiple therapeutic strategies on community-acquired pneumonia (CAP) across domains.
- A total of 325 sites across 25 countries have participated in the trial, including 32 sites in Japan.
- REMAP-CAP findings contributed to evidence regarding therapeutic options for COVID-19, such as anticoagulation, tocilizumab and sarilumab therapies.[1)2)3)]

References
1) N Engl J Med 2021; 385: 777
2) N Engl J Med 2021; 385: 790
3) N Engl J Med 2021; 384: 1491

Interventions addressed by REMAP-CAP JAPAN



Background

- CAP leads to pulmonary and systemic inflammation.
- Corticosteroids are expected to have an anti-inflammatory role that mitigates the consequences of pneumonia.
- There is a clinical equipoise about the role of corticosteroids among patients hospitalized due to CAP.

Aim

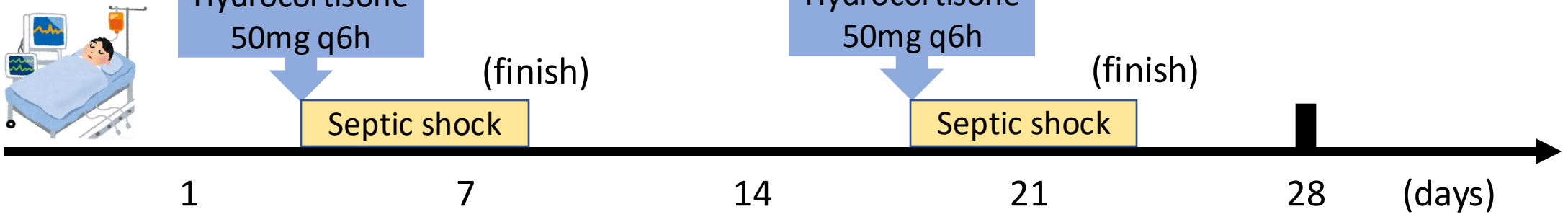
- To determine the effective strategies of different corticosteroid interventions for severe CAP.
- To share some experiences of practical operations when we incorporate the REMAP-CAP for the steroid domain protocol in Japan.

Material and method

The overview of steroid domain	
Patients	Severe CAP ＊not including patients in the pandemic infection
Intervention	□Shock-dependent hydrocortisone while patients are in septic shock □Dexamethasone 10 days
Endpoints	Primary endpoint：All-cause mortality at 90 days Secondary endpoint：ICU mortality, ICU length of stay(LOS), hospital LOS, ventilator free days, Organ failure free days at 28 days etc.

Differences in the two interventions of steroid domain

Shock-dependent hydrocortisone



Dexamethasone

Results

- Through the local implementation process of the corticosteroid domain, we are able to develop the ability to respond immediately against next pandemic.
- Additionally, we can discuss with researchers globally about the domain.

Discussion

- REMAP-CAP enrolled patients very rapidly during the pandemic.
- A global-network clinical trial is essential to respond to future outbreaks.[4)]
- Every county must ensure REMAP-CAP operation aligns with local ethical guidelines and regulations.

Reference
4) Lancet Infect Dis 2022; 22: e153

Discussion

The overview of steroid domain in global		
Patients	Moderate CAP	Severe CAP
Intervention	☐No corticosteroids ☐Fixed duration dexamethasone	☐No corticosteroids ☐Fixed duration hydrocortisone ☐Shock-dependent hydrocortisone ☐Fixed duration dexamethasone

The overview of steroid domain in Japan	
Patients	Severe CAP
Intervention	☐Shock-dependent hydrocortisone ☐Fixed duration dexamethasone

Why Japan Regional Management Committee(RMC) modified Japan Regional Specific Appendix as above?

- Fixed duration hydrocortisone was cancelled globally.
- Corticosteroids is widely used in patients with septic shock in Japan.
- Dexamethasone is approved for severe states alone in Japan.

Conclusion

- When introduced to Japan, local adaptation is important to address operational issues and to ensure feasibility of the trial.
- This exercise will facilitate better understanding of the local adaptation of the global protocol and lead to improved pandemic preparedness.