2022/12/2 AMED Platform Trial Symposium

# Concept of Today's Symposium

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# A trial based on Master Protocol


The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

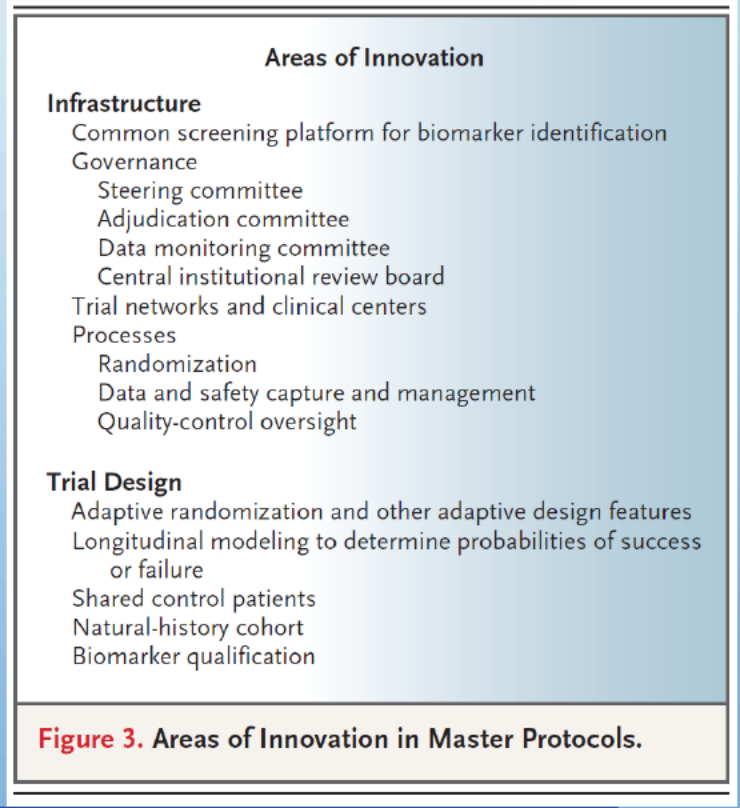
THE CHANGING FACE OF CLINICAL TRIALS

Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both

Janet Woodcock, M.D., and Lisa M. LaVange, Ph.D.

- A trial based on a master protocol
  - With a **common system** of patient selection, operational administration, and data management
  - With each sub-study conducted in parallel (Woodcock&LaVange, 2017)
- Areas of **Innovation** in Master Protocols
  - **Infrastructure**: common system to get data
  - **Trial Design**: adaptation, shared control, etc.


**Areas of Innovation**

**Infrastructure**
- Common screening platform for biomarker identification
- Governance
  - Steering committee
  - Adjudication committee
  - Data monitoring committee
  - Central institutional review board
- Trial networks and clinical centers
- Processes
  - Randomization
  - Data and safety capture and management
  - Quality-control oversight

**Trial Design**
- Adaptive randomization and other adaptive design features
- Longitudinal modeling to determine probabilities of success or failure
- Shared control patients
- Natural-history cohort
- Biomarker qualification

**Figure 3. Areas of Innovation in Master Protocols.**

# Three types of master protocol trials

- Umbrella: to study multiple therapies in a single disease
- Basket: to study a single therapies in multiple subtypes
- **Platform:** to study **multiple therapies** allowing **add on or drop** an arm at interim over a **long period**

- Basically a **big screening trial** for effective treatments that should be moved to a confirmatory study

# January 7, 2021: Preliminary study report released

- REMAP-CAP: **Adaptive Platform** Trial
  - Published results showing the efficacy of IL-6 receptor antagonists in COVID-19 patients **requiring organ support** in the ICU

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



**Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 – Preliminary report**

The REMAP-CAP Investigators

https://pulmonary.exblog.jp/29367726/

https://www.nikkei.com/article/DGXZQODG29DY50Z20C21A1000000/

# When was REMAP-CAP prepared and initiated ?

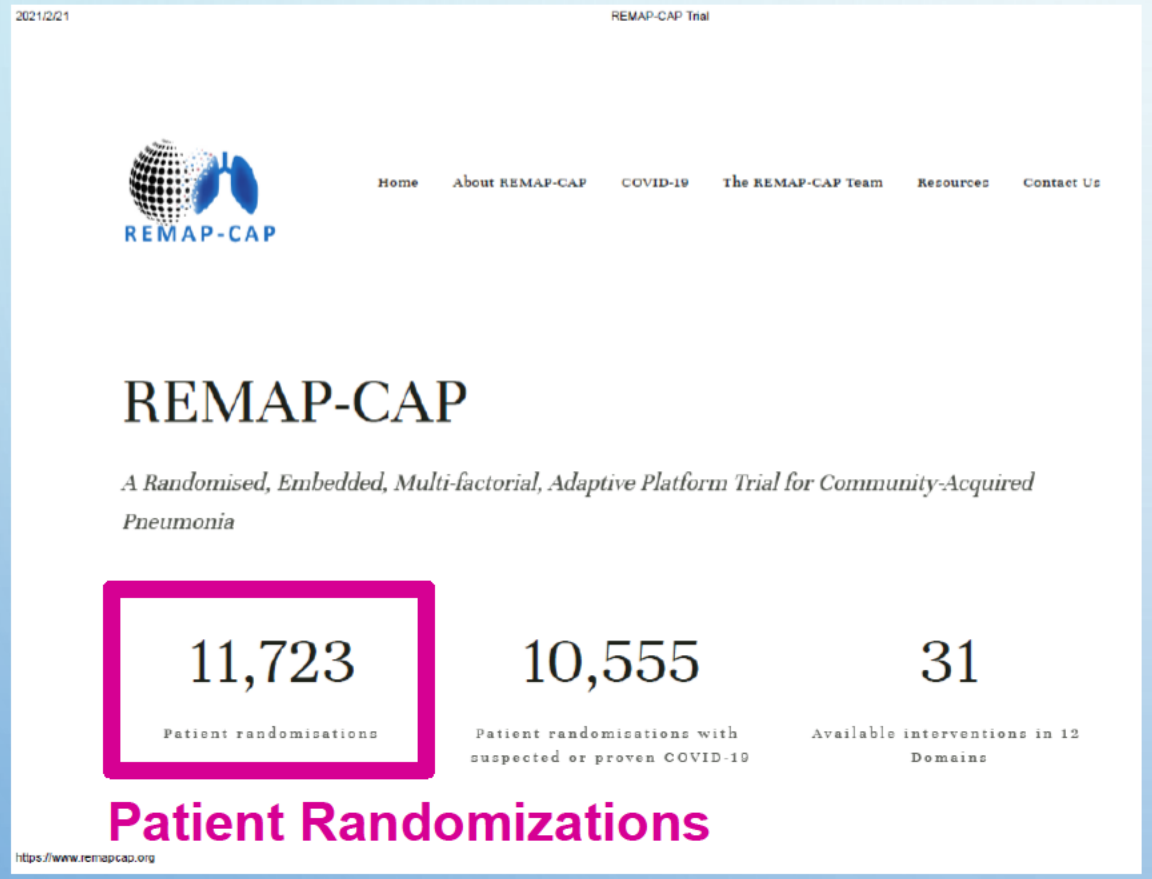
- Protocol Version 1.0 on **January 31**, 2020
- First Patient In for COVID-19 on **March 9**, 2020

横浜港に停泊するクルーズ船「ダイヤモンド・プリンセス」前を、サイレンを鳴らして移動する救急車両（2020年2月）＝共同

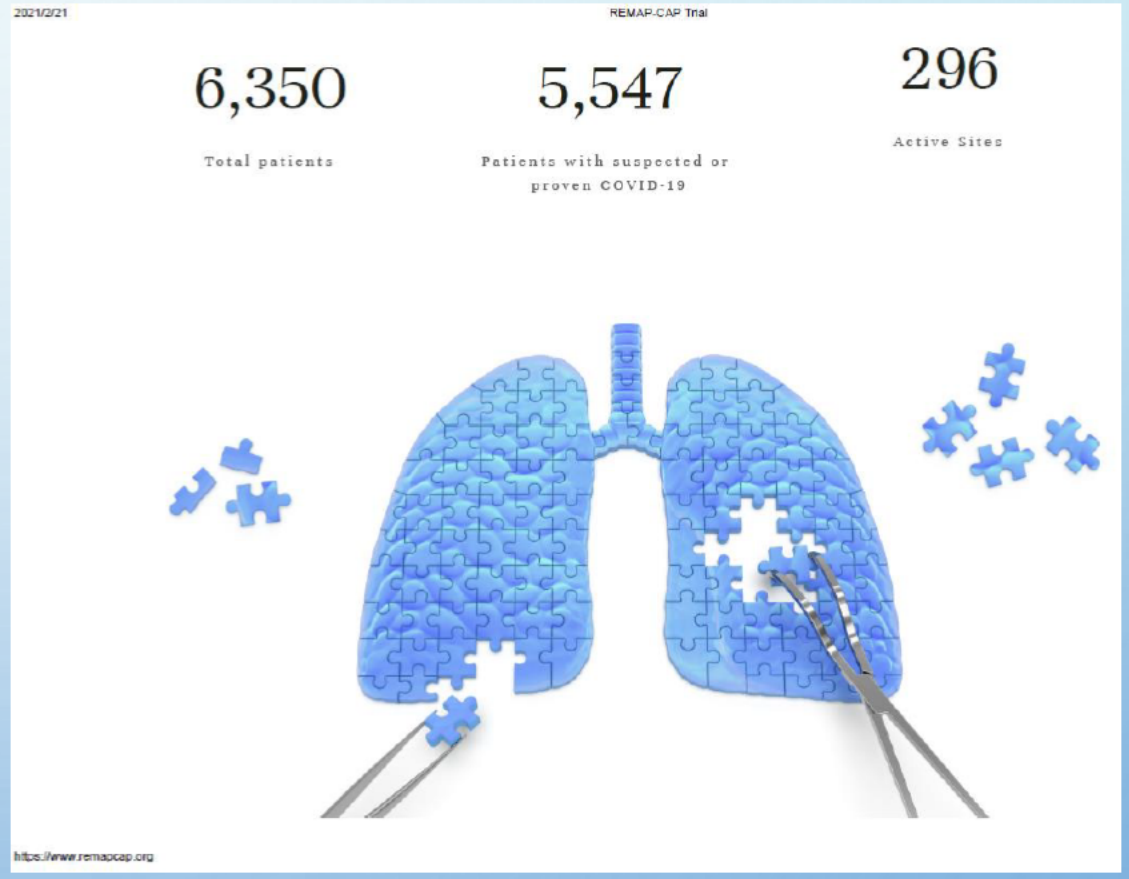
As the threat of the COVID-19 pandemic developed in early 2020, the P
protocol was updated to be more applicable to this new disease. These
defined in the Pandemic Appendix to Core (PAtC) protocol. Version 1.0 was completed on 31st January 2020 and updated to version 1.1 on 12th February 2020. The first participant with COVID-19 recruited to the trial was on 9th March 2020.

https://www.remapcap.org/

# REMAP-CAP: accumulation status as of **Feb. 21, 2021**

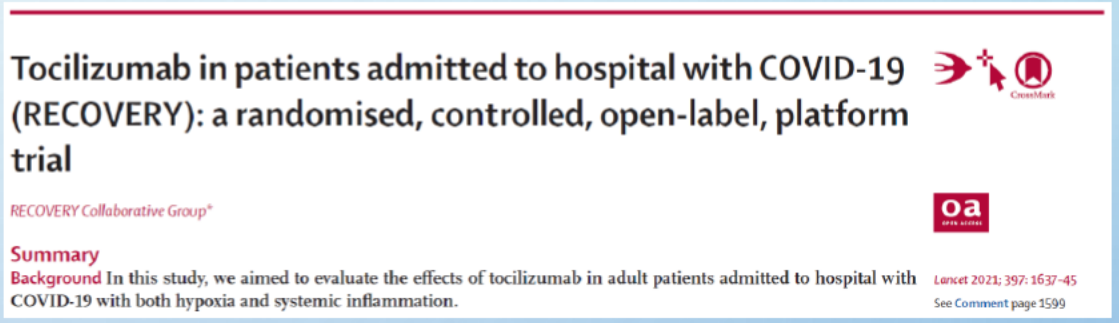



**Patient Randomizations**



# Other platform trials

- RECOVERY trial: Tocilizumab
  - Included in application data package
- ACTT-1 Study: Remdesivir
  - Included in application data package
  - Special approval in **May 2020**



Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial

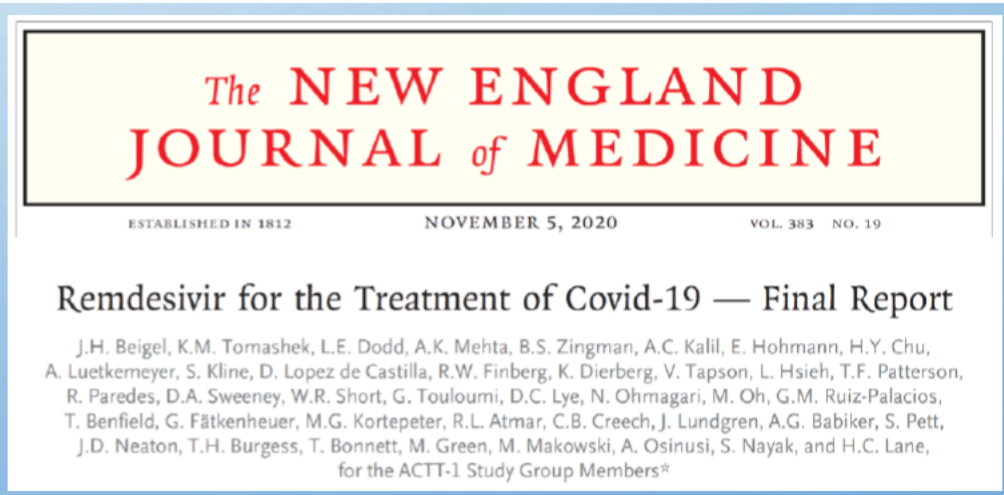
RECOVERY Collaborative Group*

Summary

Background In this study, we aimed to evaluate the effects of tocilizumab in adult patients admitted to hospital with COVID-19 with both hypoxia and systemic inflammation.

Lancet 2021; 397: 1637–45

See Comment page 1599



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Remdesivir for the Treatment of Covid-19 — Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

# These **speedy large-scale** platform evidence

- Different in nature from a normal confirmatory study
  - ◆But provided **valuable evidence** that will surely save mankind
- Now that the Corona Disaster has accelerated the **experience of innovative trials**
  - ◆We would like to invite those who were at the **center of the experience** to discuss the **future of platform** trials
  - ◆In Japan, utilization of **real world evidence** is intensively discussed
  - ◆We sould focus on the improvement in **data quality** and **efficiency** that **infrastructure sharing** and **trial design** can bring

# Program

- 13:15-13:45 Construction of adaptive platform clinical trial：as an example of REMAP-CAP（Univ. Tokyo, Dr. Ichihara）
- 13:45-14:25 Statistical issues of platform trial（Dr. Nomura, Dr. Uemura）
- 14:25-14:55 Platform trial：based on the experience（PMDA Dr. Asano）

<10 minutes break>

- 15:05-16:00 Not all platform trials are created equal: lessons learned from clinical trials in outbreak settings（NIAID, Dr. Lori E. Dodd）

<15 minutes break>

- 16:15-17:15 Panel Discussion: All speakers + St. Marianna Univ. , Dr. Fujitani(Principal Investigator of REMAP-CAP Japan)