CASE STUDIES IN ETHICAL CHALLENGES DURING COVID-19: VACCINE CHALLENGE TRIALS

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OUTLINES

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- Covid-19 vaccines Studies Statistics
- Case Study I
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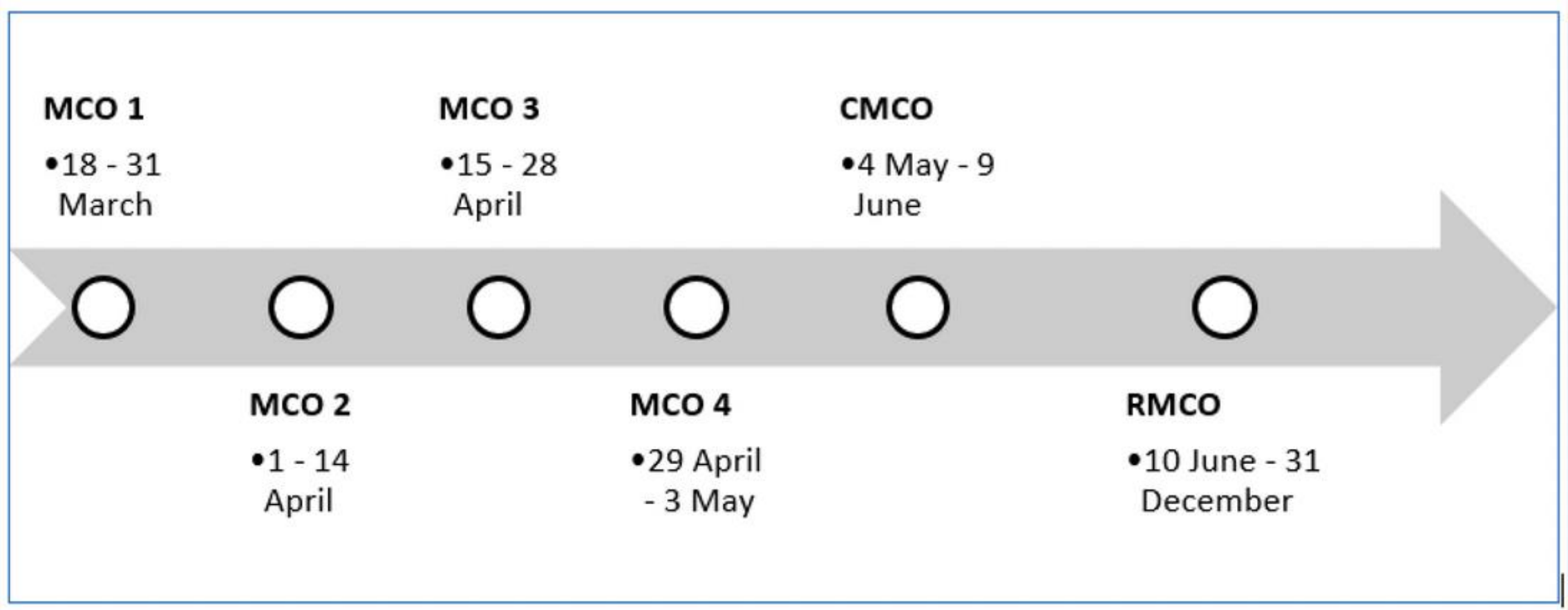
FIRST CASE OF COVID IN MALAYSIA – 25/1/2020

First case of Malaysian positive for coronavirus

04/02/2020 05:31 PM

KUALA LUMPUR, Feb 4 -- A 41-year-old man is the first Malaysian who has tested positive for the novel coronavirus 2019 (2019-nCoV).

MOVEMENT CONTROL ORDER



FIRST VACCINATION ON THE 24 FEBRUARY 2021

Malaysia launches COVID-19 vaccination drive as PM gets first shot

By **Joseph Sipalan**

February 24, 2021 3:57 PM GMT+8 · Updated 3 years ago

Aa

Malaysia to ease COVID curbs for fully vaccinated in eight states

Reuters

August 8, 2021 7:02 PM GMT+8 · Updated 2 years ago

KUALA LUMPUR, Aug 8 (Reuters) - Malaysia will relax some COVID-19 restrictions for fully vaccinated people in eight states that have met criteria such as reduced case numbers and higher vaccination rates, Prime Minister Muhyiddin Yassin said on Sunday.

The measures, which will allow dining in at restaurants, outdoor individual sports and interstate tourism, will take effect on Tuesday, Muhyiddin said in a televised address.

"I understand, many are tired of the pandemic or are dealing with pandemic fatigue," he said.

MY SEJAHTERA APP

Report: MySejahtera ranked among top Covid-19 apps worldwide in 2021

By **ANGELIN YEOH**

MOBILE APPS

Thursday, 13 Jan 2022

4:20 PM MYT

Related News

BACKGROUND

- With the MCO, Medical Research & Ethics Committee (MREC), Ministry of Health Malaysia -the method of meeting to virtual meeting to ensure the continuity of its functions.
- Ad-hoc meeting with quorum held virtually

MREC
Medical Research and Ethics Commitee

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COVID-19 VACCINES STATISTICS

- 12 applications for COVID-19 vaccines
- 6 approved via full board review
- 6 have incomplete submission

CASE STUDY 1: SARS-COV-2 VACCINE, INACTIVATED

- **Overview of the Trial**
  - Efficacy study: A randomized, double-blinded and placebo-controlled design involving 32,820 healthy subjects aged 18 years and above
  - 1:1 ratio - randomly inoculated with two doses of investigational vaccine or placebo following Day 0-Day 14 immunization schedule
  - collect symptomatic and laboratory-confirmed COVID-19 cases

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ETHICAL REVIEW AND DECISION ON THE TRIAL

- Nov 2020
- Ethical review
- The expertise and experience of the study team
- The study site has the appropriate facilities – cold chain of the vaccine is maintained and facilities required to conduct vaccine trial.
- Approved in Dec 2020

WHAT HAPPENED AFTER THAT?

- National Vaccination Programme for COVID-19 virus on 24 Feb 2021 (2 months after the study is approved)
- Restricted social activities are allowed for those completed 2 doses of vaccination on 8 Aug 2021

THIS LED TO ….

- **high withdrawal** as participants no longer willing to stay in the study as they had limitation in social activities.
- **high protocol deviations** in which study participants had deviated from protocol and obtained other vaccines from National Vaccination Programme.

- Study participants were **unblinded** and updated their vaccination status to allow them to involve in the social activities.
- Placebo arm was given vaccines
- Study design was amended to cross over.

HOWEVER THE STUDY WAS TERMINATED

- Introduction of booster shot in February 2022 to maintain the “fully vaccinated” status and enjoy the privilege of mobility.
- The inactivated vaccine platform seems to show lower protection level even with a booster dose.
- The study vaccine may not be able to confer sufficient protection efficacy against Omicron VOC infection

CASE STUDY 2: PHASE III STUDY OF SARS-COV-2 VACCINE INACTIVATED FROM INSTITUTE OF MEDICAL BIOLOGY

- a multi-national, endpoint-driven, randomized, double-blind, placebo-controlled, adaptive study in which participating adults will be randomized 1:1 to receive 2 doses of either candidate vaccine or placebo on Day 0 and 28.

ETHICAL REVIEW

- National immunization program of COVID-19 leading to subjects in this study excluded from the vaccination program
- Clearly state regarding the risk of exclusion from national vaccination program in the Patient Informed Consent
- Following satisfactory feedback from the PI on 15 Apr 2021, study was approved on 23 Apr 2021.

CASE STUDY 2

- Low recruitment rate
- Report that the study was done at the sites not approved by MREC
- Had an audit compliance review to the study sites
- One of the study sites had extended the vaccination outside the facility
- Informed consent documentation insufficiency
- Use of unapproved patient facing materials by the study teams.

- Corrective actions and preventive actions had been done accordingly.
- However, this study was terminated due to unable to enroll sufficient study participants following the change of national policy for COVID-19.

PLACEBO CONTROLLED ?

- Maybe there is a better drug with less side effects?
- Depriving the patient of getting effective treatment ?

- Uses of placebo if

- There is no proven effective intervention

- Not to treat poses negligible risks of participation
- Compelling methodological reasons for using placebo and not to treat does not imply in risk of serious harm to participant

Contoso

LESSONS LEARNT

- Timely Risk Communication to trial participants are crucial to ensure right, safety and well-being of trial participants.
- State clearly in the informed consent
- Patient understood the risks in the study

LESSONS LEARNT

- COVID-19 virus pandemic are dynamic, clinical trial protocol must be able to adapt to the national response system as well.
- Variants of COVID-19- whether the study is still relevant to be continued or modifications are required to ensure its scientific validity.
- Communications to study participants - clear and updated from time to time to ensure retention without need to compromise their daily activities due to their involvement in COVID-19 vaccines trial.

LESSONS LEARNT

- Study team must be aware and ready to terminate a study when recruitment is below their expectation.
- Compliance review is important to ensure safety and well being of trial participants.

CONCLUSION

- Covid 19 pandemic gave opportunity of different design and methodology in conducting clinical trials
- Each study is different and managing the challenges should be individualized
- Importantly the safety and wellbeing of the patient is the utmost priority

THANK YOU!

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