Parallel Session 1: Combating COVID-19

T1a - Comparing Immunogenicity against SARS-CoV-2 in Covid-19 Vaccinees and Convalescent Patients

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Background: Vaccinating COVID-19 recovered patients with mRNA vaccines boosts their immune response against wild type viruses (WT), in view of increasing prevalence of virus variants, we aimed to investigate whether vaccine platform and time of vaccination affects the immunogenicity against SARS-CoV-2 wild type and delta variant strains.

Methods: Convalescent COVID-19 patients aged above 18 years were recruited and blood samples were taken at after discharged, one month, three months, six months post-recovery. Then, COVID-19 recovered subjects received one dose of BNT162b2 (PC-B) or CoronaVac (PC-C) vaccines, and their sera samples were collected before vaccination as baseline and at day 28 post-vaccination. Furthermore, SARS-naïve volunteers were administrated two doses of BNT162b2 (CN-B) or CoronaVac (CN-C) vaccines and taken blood at baseline, day 21 (CN-B) or day 28 (CN-C), and day 56 post-primer dose. The neutralizing antibody in sera against SARS-CoV-2 HKU-001a (WT) and B.1.617.2 (delta variant, DV) was determined with live virus neutralization assay (vMN).

Findings: vMN geometric mean titre (GMT) against WT in COVID-19 recovered individuals decreased to 26·9 [95% confidence interval (CI), 22·9-31·5] from 73·6 (95%CI, 63·8-84·8) at 6 months post-recovery. After receiving one dose of BNT162b2, subjects in PC-B group, one dose of BNT162b2 enhanced antibody response against WT with 22·3 folds increase, and induced 20·4 folds increase of GMT against DV which was significantly higher than that after a booster vaccination in CN-B group (11·1 folds) (p=0·007). Similarly, recovered subjects in PC-C group showed significant increase of GMT against DV after primer vaccination than SARS-CoV-2 naïve subjects in CN-C group after booster vaccination (2·2 vs 1·3) (p=0·029). In both PC-B and PC-C groups, there was no difference between GMT against WT and DV after vaccination. Subjected showed inferior GMT against delta variant compared to GMT against wild type in CN-C and CN-B groups on day 56.

Interpretation: One dose of COVID-19 vaccines enhanced the pre-existing neutralizing activity in recovered subjects. The antibody response to DV was non-inferior to that against wild type in recovered subjects after vaccination, while SARS-naïve subjects showed a significantly lower antibody activity against DV than against WT. Long term follow-up should be performed to determine the duration of antibody response in COVID-19 recovered people after vaccination.

Project Number: COVID1903010 – Project 2

Parallel Session 1: Combating COVID-19

T1a - Clinical Study of Flu-based and PD1-based Vaccines for the SARS-CoV2 [Title of presentation: A Phase 1, Randomized, Double-blinded, Placebo-controlled, Dose-escalation and Dose-expansion Study to Evaluate the Safety and Immunogenicity of DelNS1-nCoV-RBD LAIV for COVID-19 in Healthy Adults]

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Background: In response to the outbreak of SARS-CoV-2 in late-2019, a panel of DelNS1-based RBD vaccines composed of H1N1 subtype (HA and NA derived from strain of 2009) – namely DelNS1-nCoV-RBD LAIV – have been made. The vaccine is delivered intranasally. The purpose of this study is to evaluate the safety and immunogenicity of DelNS1-nCoV-RBD LAIV for COVID-19 in healthy adults.

Methods: We conducted a phase 1 randomized, double-blinded, placebo-controlled study on healthy subjects between the age of 18 to 55 and COVID-19 vaccines naïve, between March 2021 to September 2021. Subjects were enrolled and randomly assigned (4:1) into DelNS1-nCoV-RBD LAIV (low/ high dose) or placebo group. The low-dose vaccine composed of 1x 107 EID50/ dose in 0.2mL and the high-dose vaccine composed of 1x 107.7 EID50/ dose in 0.2mL and the placebo vaccine composed of 0.9% normal saline/dose in 0.2mL. Recruited subjects were administered the vaccine intranasally on day 1 and day 29. All recruited subjects were monitored from day 1 to day 56. The primary end-point was the safety of the vaccine and the secondary end-points included the mucosal total Ig in saliva against the SARS-CoV-2 RBD, microneutralization neutralization against the live SARS-CoV-2, anti SARS-CoV-2 RBD IgG and the T-cell responses against the SARS-CoV-2 spike peptide.

Findings: Twenty-nine healthy Chinese subjects were recruited of which 11 subjects were recruited into the low-dose group, 12 subjects were recruited into the high-dose group and 6 subjects recruited into the placebo group. Twenty subjects (69%) were male. No subject was discontinued due to an adverse event. No adverse events of special interest or severe adverse events were reported within 56 days after the first vaccination in all three groups. There was no significant difference in the incidence of any reactogenicities (p=0.595) or unsolicited adverse events (p=0.620) within 56 days after the first vaccination among all the groups. Although statistically not significant, there was a trend that the total mucosal Ig fold increase after the first dose at day 4 were higher in the high-dose group when compared to the low-dose and placebo groups (day 4: 5.2 vs. 3.3 vs. 3.6; p=0.64), and after the second dose at day 32 in both the low-dose and the high-dose group when compared to the placebo group (day 32: 3.1 vs. 4.5 vs. 1.58; p=0.52). The T-cell response was also higher in the high-dose group than the low-dose and placebo groups on day 15 and day 43 after the first vaccination (day 15: 15 vs. 1 vs. 1; p=0.24 and day 43: 12.5 vs.1 vs. 5; p=0.55).

Conclusion: The intranasal DelNS1-nCoV-RBD LAIV is safe and immunogenic. A phase-2 clinical trial with larger sample size is warranted.

Project Number: COVID190123

Parallel Session 1: Combating COVID-19

T1b - To Compare the Reactogenicity and Immunogenicity of the Recommended COVID-19 Vaccines in Young Adolescents in Hong Kong

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Introduction and Project Objectives: Adolescents remain at risk of severe COVID-19 and atypical presentations such as multisystem inflammatory syndrome in children (MIS-C). Safety and immunogenicity of mRNA and inactivated COVID-19 vaccination need to be understood, including in healthy adolescents and those with severe immune compromise, which may alter the safety profile and immune response of the vaccines.

Methods: Healthy adolescents are recruited for vaccination with 2 doses of CoronaVac or BNT162b2, with antibody and T cell response assessment for 3 years, and compared against their parents. Reactogenicity is solicited for 7 days and severe adverse events are monitored for 3 years. Patients with primary (monogenic) and secondary immune compromise are also recruited and compared against healthy adolescents.

Results: Both CoronaVac and BNT162b2 are associated with favourable reactogenicity profile. No severe adverse events were recorded in adolescent participants with good past health or allergic history to PEG-containing drugs and first dose of BNT162b2 during the data observation period. Anti-Spike-RBD and surrogate neutralizing antibody responses and T cell responses are non-inferior in healthy adolescents compared with adults for either vaccines. Both vaccines induced antibody response and helper and cytotoxic T cell response in healthy adolescents. Patients with severe immune compromise have attenuated responses to vaccination.

Conclusion and Discussion: Both vaccines appear safe and immunogenic in healthy adolescents. Three doses of vaccine may be beneficial in those receiving CoronaVac and those with immune compromise. Vaccination is safe in those with PEG-containing drug allergies or hypersensitivity reactions to first dose of BNT162b2.

Project Number: COVID19F02

Parallel Session 1: Combating COVID-19

T1c - Long-term Longitudinal Comparisons of Health Status and Immune Responses in Convalescent COVID-19 and Vaccinated Cohorts in Hong Kong

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Objectives: 1. To examine the health status and immune responses of COVID-19 patients who have recovered from different levels of disease severity. 2a. To investigate the SARS-CoV-2 specific cellular and humoral immune responses and 2b. To identify the early signatures associate to these responses from community subjects who have received different types of COVID-19 vaccines. 3. A booster study also conducted for subjects who have had poor antibody response despite having received 2 doses of CoronaVac.

Methodology: The health conditions of adults (N=400) who recovered from varying severity of COVID-19 are being assessed and their blood are collected at 6, 12, 24 and 36 months after discharge. The assessment package includes: lung function tests, 6-min walk distance (6MWD), chest radiographs/CT, and SF36 questionnaire. Blood samples from community cohorts are collected from before and serially up to 36 months after receiving one of the 2 COVID-19 vaccines (N=350 in each group of Biontech vs CoronaVac). The kinetics of SARS-CoV-2 specific humoral and cellular immune responses from both convalescent and vaccinated cohorts are determined by neutralization assay and by measuring specific T cell responses upon stimulation of SARS-CoV-2 specific peptide library respectively. The antiviral level of the human plasma with various neutralization titer collected from different vaccinated cohorts will be tested in mouse model and ADCC assay.

Results:

a) The majority of patients have normal spirometry but their 6MWD and SF 36 response were lower than the general population. Because the rate of antibody waning slows with time, we fitted lines of decay to 115 sera from 62 convalescent patients collected beyond 90 days after symptom onset and estimate that PRNT50 antibody will remain detectable for around 1,717 days after symptom onset and that levels conferring 50% protection will be maintained for around 990 days post-symptom onset, in symptomatic patients (Lau E, et al. EClinicalMed 2021).
b) Through the head-to-head comparison, vaccination with BNT162b2 (n=49) induces significantly higher levels of SARS-CoV-2 specific binding and neutralizing antibody responses when compared to CoronaVac (n=49) at 1 month post second dose. CoronaVac induces higher CD4+ and CD8+ T cell responses to the structural protein than BNT162b2 (Mok C, et al. Respirology 2021).
c) Our RCT study has shown that BNT162b2 booster dose (n=40) for 80 community subjects who have poorly responded to 2 doses of CoronaVac is significantly more immunogenic than a CoronaVac booster (n=40). BNT162b2 also elicits high level of SARS-CoV-2 specific neutralizing antibody to different variants of concern. The adverse reactions were only mild and short-lived (to be submitted).

Project Number: COVID1903003

Parallel Session 1: Combating COVID-19

T1d - Comparison of Inactivated and mRNA Vaccines for COVID-19

Project 1: Comprehensive assessment of longitudinal vaccine-induced immune responses, safety and potential effectiveness of COVID-19 vaccines
Project 2: Randomized trial of COVID-19 booster vaccinations (Cobovax trial)

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Introduction: In early 2020, Hong Kong was one of the first-affected locations by the COVID-19 pandemic outside of mainland China. However, timely public health measures have successfully controlled a number of surges in daily case numbers, and fewer than 12,000 confirmed cases were recorded in the first 18 months of the pandemic. The objective of these studies is to assess the immune responses to COVID-19 vaccines and inform vaccination strategies.

Methods: In COVID1903001, two observational cohorts have been established to study immune responses to COVID-19 vaccines in Hong Kong. The first cohort includes up to 1500 individuals of all ages, followed for up to 4 years after receiving a first dose of COVID-19 vaccination. The second cohort includes up to 1000 older adults, followed for up to 4 years from April 2021. In both cohorts blood samples are collected every 6 months, and the first cohort includes additional blood draws after any dose of vaccination. In COVID19F01, 400 adults who have received two doses of COVID-19 vaccine will be randomly allocated to receive a third dose of either inactivated or mRNA vaccine, with blood samples collected at 1, 6 and 12 months after the 3rd dose. In both studies samples will be tested for antibodies and cellular responses against SARS-CoV-2 to allow quantification of the strength and duration of immune responses to vaccination.

Results: Antibody responses to two doses of mRNA vaccines were on average 10 times higher than antibody responses to two doses of inactivated vaccine. Immediate reactions to inactivated vaccine were milder. Antibody levels declined faster in recipients of the inactivated vaccine, to low levels by 3-6 months.

Conclusion: mRNA vaccines conferred higher antibody titers than inactivated vaccines, but both vaccine technologies improved immunity against COVID-19. Vaccination provides a pathway back to a new normal, by replacing the public health and social measures that have so far prevented large epidemics. However any relaxation of public health measures will only be safe once we can achieve a high level of population immunity, and third doses will likely be required within the next 6 months particularly in individuals who initially received two doses of inactivated vaccine.

Project Number: COVID1903001
Project Number: COVID19F01

Parallel Session 1: Combating COVID-19

T1e - COVID-19 Vaccines Adverse Events Response and Evaluation (CARE) Programme [Title of presentation: Bell's palsy following Vaccination with mRNA (BNT162b2) and Inactivated (CoronaVac) SARS-CoV-2 vaccines: a Case Series and Nested Case-control Study.]

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Lo Shiu Kwan Kan Po Ling Professor in Pharmacy, Head of Department of Pharmacology and Pharmacy, The University of Hong Kong, Hong Kong SAR, China

Background: Bell's palsy is a rare adverse event reported in clinical trials of COVID-19 vaccines. However, to our knowledge no population-based study has assessed the association between the inactivated SARS-CoV-2 vaccines and Bell's palsy. The aim of this study was to evaluate the risk of Bell's palsy after BNT162b2 and CoronaVac vaccination.

Methods: In this case series and nested case-control study done in Hong Kong, we assessed the risk of Bell's palsy following vaccination with BNT162b2 (Fosun-BioNTech [equivalent to Pfizer-BioNTech]) or CoronaVac (from Sinovac Biotech, Hong Kong) using data from the Department of Health and Hospital Authority's territory-wide electronic health records (the Clinical Data Analysis and Reporting System -CDARS). We described reported cases of Bell's palsy among vaccine recipients. We compared the estimated age-standardised incidence of clinically confirmed cases among individuals who had received the CoronaVac or BNT162b2 vaccination (up to 42 days before presentation) with the background incidence in the population. A nested case-control study was also done using conditional logistic regression to estimate the odds ratio (OR) for risk of Bell's palsy and vaccination. Cases and controls were matched (1:4) by age, sex, admission setting, and admission date.

Results: Between February 23 and May 4, 2021, 451 939 individuals received the first dose of CoronaVac and 537 205 individuals received the first dose of BNT162b2. 28 clinically confirmed cases of Bell's palsy were reported following CoronaVac and 16 cases were reported following BNT162b2. The age-standardised incidence of clinically confirmed Bell's palsy was 66·9 cases per 100 000 person-years (95% CI 37·2 to 96·6) following CoronaVac vaccination and 42·8 per 100 000 person-years (19·4 to 66·1) for BNT162b2 vaccination. The age-standardised difference for the incidence compared with the background population was 41·5 (95% CI 11·7 to 71·4) for CoronaVac and 17·0 (-6·6 to 40·6) for BNT162b2, equivalent to an additional 4·8 cases per 100 000 people vaccinated for CoronaVac and 2·0 cases per 100 000 people vaccinated for BNT162b2. In the nested case-control analysis, 298 cases were matched to 1181 controls, and the adjusted ORs were 2·385 (95% CI 1·415 to 4·022) for CoronaVac and 1·755 (0·886 to 3·477) for BNT162b2.

Conclusion: Our findings suggest an overall increased risk of Bell's palsy after CoronaVac vaccination. However, the beneficial and protective effects of the inactivated COVID-19 vaccine far outweigh the risk of this generally self-limiting adverse event. Additional studies are needed in other regions to confirm our findings. (Lancet Infect Dis. 2021 Aug 16;S1473-3099(21)00451-5.)

Project Number: COVID19F01