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.

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 10^7 EID50/ dose in 0.2mL and the high-dose vaccine composed of 1x $10^{7.7}$ 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.