Dear Editor

ARCoV, which is developed by the Academy of Military Medical Sciences and Suzhou Abogen Biosciences in China, is a candidate mRNA vaccine encoding the receptor binding domain (RBD) of SARS-CoV-2 (Wuhan-Hu-1 strain). Its safety, tolerability, and immunogenicity profile have been confirmed in the phase 1 clinical trial in China. A multi-regional phase 3 clinical trial is currently underway to test the efficacy of ARCoV (NCT04847102). Here, we tested the cross-neutralization against SARS-CoV-2 variants of concern (VOCs) of a panel of serum samples from participants in the phase 1 clinical trial of ARCoV by pseudo- and authentic SARS-CoV-2. Our data suggest the immunity induced by the ARCoV vaccine reduced but still has significant neutralization against the Alpha and Delta variants. Moreover, ARCoV maintained activity against the Beta variant, despite of its obvious reduction in neutralizing titers. Our findings further support the solid protective neutralization activity against VOCs induced by ARCoV vaccine.

Herein, a set of sera of 11 participants in the phase 1 clinical trial of ARCoV was tested for neutralization of VOCs. All samples were collected on day 43 post initial immunization with 15 µg of ARCoV. The cross-neutralizing activity of these serum samples against all pseudo-SARS-CoV-2 VOCs except the Gamma and Omicron variants was assayed by a 50% neutralization assay. The VSV-based pseudovirus neutralization assay showed that all 11 serum samples still potently neutralized the Alpha variant with geometric mean titer (GMT) of 826.7 (1.7-fold reduction) in comparison with WT with GMT of 1440.9 (Figure 1a and Tables S1 and S2). We also observed 2.6-fold average reduction of the plasma neutralizing activity against the Delta (GMT: 548.9) variant. However, compared with the WT pseudovirus, the neutralization activity significantly reduced 2.4-fold for the Beta variant (GMT: 610.4) (Figure 1a, Tables S1 and S2, p < .05).

The continuous global circulation of SARS-CoV-2 has resulted in emergence of SARS-CoV-2 variants of concern (VOCs) including Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (B.1.617.2). In November 2021, a new VOC Omicron (B.1.1.529) emerged in South Africa with highly transmissibility. These VOCs contain multiple mutations in the spike protein of SARS-CoV-2, especially in neutralizing antibody binding sites (Table S1). These mutations have been reported to confer neutralization resistance to mAbs, a modest loss of susceptibility to convalescent plasma, and sera from vaccinated individuals in comparison with the wild-type Wuhan-01 bearing D614G.

Notably, our findings are consistent with the other recent reports assessing neutralization activity of two leading SARS-CoV-2 mRNA vaccines BNT162b2 and mRNA-1273 developed by Pfizer and Moderna, respectively. There is growing body of evidence that both humoral and cellular immune responses induced by SARS-CoV-2 mRNA vaccines play an important role in protection against VOCs. Therefore, the ARCoV-elicted cross-reactive T cell response is likely to be able to provide solid protection against the Beta variant despite of obvious reduction in neutralization activity. Of note, for Delta variant, the pseudovirus was less sensitive to neutralization of serum samples than that of authentic variant in comparison with WT. This discrepancy in
neurulation activity is possibly due to the absence of the G142D mutation in the S protein of the authentic virus (Table S2). Despite this, pseudovirus titers still represent a good prediction for the neutralization activity to the authentic viruses. A potential limitation of this study may be absent of data on neutralization activity to the authentic Omicron variant, which will be performed in the future study. Overall, our findings support the solid protective neutralization activity against VOCs induced by ARCoV vaccine, although the vaccine effectiveness against these variants must be validated by the undergoing phase 3 clinical trial.

Disclosure statement

C.F.Q. is an inventor on pending patent applications related to the ARCoV mRNA vaccine. All other authors declare no competing interests.

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