Safety, tolerability, pharmacokinetics and immunogenicity of a monoclonal antibody (SCTA01) targeting SARS-CoV-2 in healthy adults: A randomized, double-blind, placebo-controlled, phase I study

Running title: phase I study of SCTA01 for SARS-CoV-2

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Abstract

SCTA01 is a novel monoclonal antibody with promising prophylactic and therapeutic potential for COVID-19. This study aimed to evaluate the safety, tolerability, pharmacokinetics (PK) and immunogenicity of SCTA01 in healthy adults. This was a randomized, double-blind, placebo-controlled, dose-escalation phase I clinical trial. Healthy adults were randomly assigned into the following four cohorts, Cohort 1 (n=5, 3:2), Cohort 2 (n=8, 6:2), Cohort 3 and Cohort 4 (both n=10, 8:2), to receive SCTA01 (5, 15, 30 and 50 mg/kg, respectively) *versus* placebo. All participants were followed up for clinical, laboratory, PK and immunogenicity assessments for 84 days. The primary outcomes were the dose-limiting toxicity (DLT) and maximal tolerable dose (MTD), and the secondary outcomes included PK parameters, immunogenicity and adverse events (AE). Of the 33 participants, 18 experienced treatment-related AEs; the frequency was 52.0% (13/25) in participants receiving SCTA01 and 62.5% (5/8) in those receiving placebo. All AEs were mild. There was no serious AE or death. No DLT was reported, and MTD of SCTA01 was not reached. SCTA01 with a dose range 5-50mg/kg had nearly linear dose-proportional increases in C_{max} and AUC parameters. An anti-drug antibody response was detected in four (16.0%) participants receiving SCTA01, with low titers, between the baseline and day 28, but all became negative later. In conclusion, SCTA01 up to 50mg/kg was safe and well-tolerated in healthy participants. Its PK parameters were nearly linear dose-proportional.

Trial registration: ClinicalTrials.gov NCT04483375.

Keywords: COVID-19, SARS-Cov-2, monoclonal antibody, safety, pharmacokinetics

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and manifesting as respiratory tract infection with severe multiorgan dysfunction, has become a worldwide pandemic since the first reported case in December 2019 (1). The number of confirmed cases of COVID-19 has exceeded 103 million with over 2 million deaths as of February 1, 2020 (2). Remdesivir, a nucleotide prodrug of an adenosine analog, is currently the only drug approved for the treatment of COVID-19 (3), and efficacious therapeutic strategies for COVID-19 are still largely lacking.

Antibody-based passive immunotherapies including convalescent plasma and monoclonal antibodies are reported to be promising treatment options for COVID-19 as they neutralize SARS-CoV-2 by primarily targeting the receptor-binding domain (RBD) of the spike protein that mediates its entry into the host cells (4-13). Previous studies have shown that convalescent plasma is associated with improved viral load suppression, clinical symptoms and survival in the treatment of COVID-19 (6-13). However, the collection of sufficient plasma from infected COVID-19 patients is not always feasible and practical. Thus, monoclonal antibodies are highly expected to play a critical role in fighting against COVID-19. Currently, more than 20 anti-SARS-CoV-2 monoclonal antibodies are being investigated in the preclinical and clinical trials (14). Based on the clinical benefits and verified viral load decline in outpatient trials, an antibody cocktail consisting of casirivimab and imdevimab, and bamlanivimab as a monotherapy have been approved by the Food and Drug Administration of the United States of America in November 2020 for emergency use to treat patients with mild to moderate COVID-19 symptoms (5, 15, 16). Although bamlanivimab alone failed to demonstrate a clinical benefit for hospitalized COVID-19 patients without end-stage organ failure (17), a combination of bamlanivimab with etesevimab significantly

reduced hospitalizations and deaths among high-risk patients recently diagnosed with COVID-19 (18). Increasing evidence suggests that anti-SARS-CoV-2 monoclonal antibodies are efficacious in the prevention and treatment of COVID-19 (19).

SCTA01, also named HB27, is a newly developed monoclonal antibody of IgG1 subtype with functions similar to bamlanivimab, but possesses unique features (20). The Fc-mutated (LALA) modification of SCTA01 not only reduces antibody-dependent enhancement (ADE) and antibody-dependent cell cytotoxicity (ADCC), but also guarantees its high-affinity neutralizing responses (**Supplementary Figure 1**) (20). Our previous *in vitro* study validated the neutralizing activity of SCTA01 with a classical plaque reduction neutralization test value of 0.22nM (20). In addition, both prophylactic and therapeutic efficacies of SCTA01 were demonstrated in animal experiments (20). Specifically, a single dose of 20 mg/kg administered either before or 2 hours after SARS-CoV-2 exposure both resulted in >99.9% reduction of the viral RNA load 5 days post-infection in the lungs and trachea in the mice model, accompanied by alleviation of pulmonary pathological damage (20). In the rhesus monkey model, no obvious adverse events (AE) were observed when administrated with 10-fold of the effective dose of SCTA01 (500mg/kg) (20).

Based on these encouraging findings *in vitro* and in animal models, this randomized, double-blind, placebo-controlled phase I study was carried out to evaluate the safety, tolerability, pharmacokinetics (PK) and immunogenicity of SCTA01 targeting SARS-CoV-2 in healthy adults.

Results

Demographics and baseline characteristics of the participants

Overall, 33 participants (22 males and 11 females with an average age of 31.4±6.8 years) were randomized to receive SCTA01 (n=25) or placebo (n=8) between July 24, 2020 and August 21, 2020. The baseline demographic characteristics were balanced across cohorts (**Table 1**).

The average follow-up duration was 85.3 days for participants receiving SCTA01 and 84.5 days for those receiving the placebo. All participants completed the planned dose of SCTA01 or placebo (**Table 2**).

Safety and tolerability

Overall, 21 participants experienced 49 AEs; 18 participants had 34 AEs that were classified as TRAEs. The percentage of participants with TRAEs was lower with SCTA01 than placebo [13 (52.0%) *vs.* 5 (62.5%)]. All TRAEs were mild at grade 1 or 2, and no SAE or death was observed. Thus, there was no DLT, and MTD of SCTA01 was not reached in the present study. (**Table 3, Supplementary Table 1**).

Most TRAEs were experienced only by one participant receiving SCTA01. TRAEs occurring at a frequency greater than 10% included increased blood conjugated bilirubin (n=4, 16.0%) and unconjugated bilirubin (n=3, 12.0%) in participants receiving SCTA01, and increased blood unconjugated bilirubin (n=1, 12.5%), increased aspartate aminotransferase (n=1, 12.5%), decreased lymphocyte count (n=1, 12.5%), increased white blood cells in the urine (n=1, 12.5%) and decreased diastolic blood pressure (n=1, 12.5%) in participants receiving the placebo. The increased levels of blood bilirubin and alanine aminotransferase did not exceed 2 times the upper limit of normal (ULN). TRAEs were mostly self-recovered. Rash developed in a participant receiving 50mg/kg of SCTA01 was recovered after treatment with

loratadine combined with mometasone furoate cream, and epistaxis developed in another participant receiving 50mg/kg of SCAT01 was recovered after symptomatic medications (**Table 3**).

PK profiles

The mean SCTA01 serum concentrations *versus* time (linear and semi-logarithmic) displayed a dose-dependent manner (**Figure 1**).

The median T_{max} values were 1.32, 1.92, 2.83, and 3.16 h for SCTA01 doses of 5 mg/kg, 15 mg/kg, 30 mg/kg, and 50 mg/kg, respectively. C_{max}, AUC_{0-t}, $AUC_{0-\infty}$, and AUC_{0-28d} increased in a dose-dependent manner after SCTA01 infusion. The mean value of $t_{1/2}$ in each dose group was relatively close, between 25.8 and 30.2 days. In addition, similar CL and Vd values at different doses of SCTA01 were observed (**Table 4**).

The dose-proportional PK properties after SCTA01 administration are shown in **Supplementary Table 2**. Within the evaluated SCTA01 dose range (5-50 mg/kg), the slope β 1 of dose proportionality of main PK parameters (C_{max}, AUC_{0-t}, $AUC_{0-\infty}$ and AUC_{0-28d}) were close to 1, indicating that PK of SCTA01 was linear and dose-proportional in the dose range of 5-50 mg/kg (**Supplementary Figure 2**).

Immunogenicity

The incidences for a positive ADA and Nab response were 1/3, 1/6, 1/8, and 1/8, and 0/3, 1/6, 1/8 and 1/8, in the 5, 15, 30, and 50 mg/kg cohorts, respectively. Totally 4 out of 25 (4/25) and 3 out of 25 (3/25) participants had positive responses of ADA and Nab, respectively

(Table 5). One participant receiving 50mg/kg of SCTA01 had positive ADA and Nab responses at the baseline and on day 7. One participant receiving 15mg/kg of SCTA01 had a positive ADA response on days 7 and 28, and a positive Nab at day 28. One receiving 30mg/kg of SCTA01 had positive ADA and Nab responses on day 7. One in 5mg/kg of SCTA01 had a positive ADA but negative Nab on day 7. No correlation was found between the positive responses and SCTA01 doses, and all positive response titers were low. All participants became negative for ADA and Nab responses at the subsequent time points (**Table 5**).

Discussion

The ongoing COVID-19 pandemic underlines the urgent need to develop prophylactic and therapeutic agents. The novel monoclonal antibody SCTA01 for the treatment of COVID-19 was supported by our preclinical study which proved its nonclinical safety and antiviral activity (20). This phase I clinical trial demonstrated that SCTA01 appeared to be safe and tolerable at a single dose up to 50mg/kg in humans. All observed TRAEs were mild and most were self-recovered, and no SAE or death was observed. The dose-proportional PK characteristics of SCTA01 supported a single intravenous administration which may well cover the clinical disease course of COVID-19. In addition, a transient ADA response with low titers was observed in a small proportion of participants receiving SCTA01.

The present phase I trial in healthy volunteers exhibited a favorable safety in humans. During the 12-week observation period, no DLT was reported and hence no MTD of SCTA01 was established. No TRAE with severity greater than grade 3 was observed. An increased blood bilirubin level was the most common TRAE experienced in participants receiving the SCTA01 (n=7), but the level did not exceed 2 times the ULN. Protein in urine, sinus

bradycardia, prolonged QT interval and rash occurred in participants receiving SCTA01, but in none of those receiving the placebo. However, protein in urine presented in two participants receiving 5mg/kg and 15mg/kg, respectively, was mild (at grade 1), transient and self-recovered within one week after the completion of the SCTA01 administration. One participant receiving SCTA01 at 15mg/kg had a baseline sinus rhythm of 62 beats per minute experienced sinus bradycardia (47 beats per minute) on day 3 and recovered without intervention after 7 hours. Another one receiving the same dose of SCTA01 with a baseline QT interval close to the lower limit of normal (QTcB 449ms, QTcF 442ms) developed prolonged QT interval at grade 1 or 2 on days 3 (QTcB 460ms, QTcF 454ms), 14 (QTcB 451ms, QTcF 448ms), 42 (QTcB 458ms, QTcF 449ms) and 84 (QTcB 444ms, QTcF 449ms). However, no cardiac symptoms were reported, and the electrocardiogram findings were not considered clinically significant. Rash experienced in one participant receiving 50mg/kg of SCTA01 was successfully treated with loratadine and mometasone furoate cream. It is noticeable that previous clinical trials of other neutralizing antibodies, LY-CoV555 and REGAN-COV2, in outpatients reported symptoms such as nausea, diarrhea and dizziness, instead of laboratory abnormalities, as AEs (5, 15, 17). It is likely that it might be difficult to obtain regular laboratory results during the follow-up for trials conducted in outpatients with COVID-19 (5, 15). In the LY-CoV555 phase I trial, notable laboratory abnormalities including a decreased absolute neutrophil count and an increased hepatic enzyme level were reported, but they were declared to be drug-unrelated (5, 21). Considering the limited sample size in the present phase I study, the attribution of observed AEs to SCTA01 could not be fully determined and further investigation is warranted.

In the present trial, the highest dose of SCTA01 (50 mg/kg) used in healthy adults achieved a C_{max} of 1040 μg/mL and an $AUC_{0\text{-}28d}$ of 11900 d*μg/mL, which well reached the target goal.

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204 Based on our previous cell experiment and trials in animals of neutralization and efficacy
205 evaluation, SCTA01 at 20mg/kg remarkably reduced SARS-CoV-2 viral loads and alleviated
206 lung inflammation in mice and rhesus monkeys and SCTA01 at 500 mg/kg was related to the
207 efficacy and tolerable safety as reflected by normal laboratory results and organ functions in
208 rhesus monkeys (20). The starting dose in the present study in healthy participants was 100-
209 times lower than the maximum preclinical animal toxicity study dose of 500 mg/kg. Based on
210 dose conversion from animals to humans, 50 mg/kg SCTA01 is speculated to be sufficient in
211 the viral neutralization. In addition, antibody LY-CoV555 at 2800 mg dose in outpatients with
212 COVID-19 was proved to be efficient in viral clearance (5). We therefore speculate that a
213 single intravenous injection of SCTA01 at 50 mg/kg should be tried initially in the
214 subsequent human efficacy trials. In addition, unlike small molecules, monoclonal antibodies
215 do not depend on the kidney or liver for the clearance (22). Hence, corresponding organ
216 failures in severe or critical COVID-19 patients may have a minimal effect on the clearance
217 and metabolism of SCTA01 in the real clinical setting.
218
219 The PK profile of SCTA01 indicates that SCTA01 is active for a period that may exceed the
220 clinical course of COVID-19. Among patients with SARS-CoV-2 infection, mild or moderate
221 COVID-19 represents the majority while approximately one-fifth are categorized into severe
222 (14%) or critical (5%) cases requiring hospitalization or emergency intervention (23). The
223 median time from the onset of COVID-19 to the time experiencing dyspnea is 5-8 days and
224 the median time from the onset to acute respiratory distress syndrome is 8-12 days (24-27).
225 The median duration of viral shedding is 20.0 days in COVID-19 survivors (26). In the
226 present study, the maximum concentration of SCTA01 occurred at 1-3 h after infusion and
227 remained detectable for a long period with $t_{1/2}$ around 25.8-30.2 days. All these data indicate

the persistent antibody-viral responses by a single dose application of SCTA01. Of course, the real distribution of SCTA01 might be different in patients with SARS-CoV-2 infection due to multiple affecting factors. Further studies are necessary to confirm the PK profiles and investigate the pharmacodynamics of SCTA01in infected patients.

As a heterologous protein, SCTA01 may cause a positive ADA response which may alter the PK properties of the drug, affect its efficacy and eventually lead to clinical problems such as allergic reactions (28, 29). SCTA01 as a monoclonal antibody is considered to have low immunogenicity risk (30). Moreover, the target of SCTA01 is the spike protein of SARS-CoV-2, which is an exogenous target. In the present study, although four (16%) out of 25 healthy participants receiving SCTA01 presented with a positive ADA response, all responses were transient with low titers and turned negative during the follow-up. There was no correlation between positive ADA responses and SCTA01 doses. More importantly, there were no clinical allergic signs in these positive cases. Only one participant had a slightly elevation of alanine aminotransferase (grade 1) concurrent with a positive ADA response, which was recovered without medication. Furthermore, the baseline and PK characteristics in participants with a positive ADA response did not differ from that in those with negative responses. In our previous nonclinical study of SCTA01, no ADE response or ADCC phenomenon was detected (20). It is postulated that the Fc-mutated (LALA) modification of SCTA01 contributes to, at least partially, the reduction of ADE and ADCC. Therefore, a positive ADA response is thought to have limited clinically significant implications for SCTA01.

There are a couple of limitations in the present study. First, the sample size was relatively small, and as such the sample size was small in each cohort. Second, the study population

were healthy participants, instead of patients with COVID-19. Thus, multi-center, phase II/III trials with a larger sample size are ongoing to fully assess the efficacy and safety of SCTA01 in adult patients with COVID-19.

In conclusion, a single infusion of SCTA01 up to 50mg/kg is safe and well-tolerated in healthy participants at potentially therapeutic exposures. PK parameters were nearly linear dose-proportional and ADA incidence was acceptable with low titers.

Materials and Methods

Study design and participants

This was a double-blind, placebo-controlled, single-dose escalation, phase I randomized controlled trial. The inclusion criteria were as follows: 1) age ≥18 years, 2) body mass index (BMI) within 18.0-26.0 kg/m^2, 3) healthy status as evaluated by previous medical history, physical examination, 12 leads electrocardiogram, chest CT scan and laboratory tests, and 4) willingness to follow the study procedure, use contraceptive measures during the study period and within 6 months after the end of study. The exclusion criteria included: 1) allergy to humanized monoclonal antibodies and any ingredient of SCTA01, 2) suspected or verified SARS-CoV-2 infection, 3) a history of severe allergies, 4) infection or fever within 14 days before enrollment, 5) a history or presence of diseases, in the opinion of the investigator, which significantly affect the absorption, metabolism or elimination of drugs, 6) evidence of human immunodeficiency virus (HIV) infection and/or positive human HIV antibodies, 7) confirmed presence of hepatitis virus and syphilitic antibody, and 8) pregnancy or plan to be pregnant within 6 months after the study.

Written informed consent was obtained from all participants. The study protocol was

approved by the Institutional Review Board of Beijing Shijitan Hospital, Capital Medical University (approval number: 2020-38). The study was performed in accordance with the local requirements and International Conference on Harmonization-Good Clinical Practice (ICH-GCP) guidelines. This trial was registered at ClinicalTrials.gov (number NCT04483375).

Randomization and dose escalation

The random allocation sequence was generated using SAS v.9.4 (SAS Institute, Cary, NC) by an unblinded statistician. Randomization envelopes were used to randomly assign participants to receive a single dose of placebo or SCTA01 in one of four dose cohorts. Study participants and site investigators remained masked throughout the entire study. The dose-escalation rule was adopted. Totally, 33 participants were randomized into four cohorts as follows: 1) Cohort 1, five participants were randomly assigned 3:2 to SCTA01 5 mg/kg or placebo. A sentinel strategy was applied in the cohort. Initially, two participants (1:1) were recruited. Then three (2:1) were recruited as no safety issues were observed; 2) Cohort 2, eight participants were randomly assigned 6:2 to SCTA01 15 mg/kg or placebo; 3) Cohort 3, 10 participants were randomly assigned 8:2 to SCTA01 30 mg/kg or placebo; and 4) Cohort 4: 10 participants were randomly assigned 8:2 to SCTA01 50 mg/kg or placebo.

Drug administration and blood sample preparation

SCTA01 injection, which was manufactured by SCT Inc (China) and supplied in vials containing 25 mg/mL, was diluted with 0.9% normal saline to make a final concentration of 5 mg/mL for intravenous infusion. The participants recruited in the four cohorts were administered with SCTA01 at a dose of 5 mg/kg, 15 mg/kg, 30 mg/kg, and 50 mg/kg, respectively. The starting dose of 5 mg/kg was 100-times lower than the maximum

preclinical animal toxicity study dose of 500 mg/kg (20). The same volume of placebo formulated with excipients without SCTA01 was administered to participants in each cohort. Participants were administered under fasting conditions and remained fasting (without limit to water) for 4 h since administration. The intravenous infusion rate was controlled to be lower than 3.33 mL/h/kg.

Blood samples were obtained within 0.5 h before infusion (baseline), immediately after infusion (+5 min), at 1, 4 and 8 h (post-infusion), and on days 1, 3, 7, 14, 21, 28, 42, 63 and 84 for PK analysis. In addition, blood samples were obtained within 0.5 h before infusion (baseline), and on days 7, 14, 28, 42, 63 and 84 for immunogenicity analysis.

Determination of serum SCTA01 concentrations and immunogenicity

Serum SCTA01 concentrations were determined by enzyme-linked immunosorbent assay. Briefly, SARS-CoV-2 Spike protein was coated on a 96-well plate to capture SCTA01 in serum samples. Goat anti-human IgG-Fc secondary antibody was added, and streptavidin-conjugated with horseradish peroxidase and 3,3',5,5'-tetramethylbenzidine substrate were used for the reaction. The concentrations were detected at 450nm and 620 nm with a Molecular Devices Microplate reader (Molecular Devices, San Jose, CA, USA). The minimum required dilution of serum samples was 1:200. The serum SCTA01 concentrations were quantified by using a linear regression of a SCTA01 standard curve covering a range of 200–10,000 ng/mL.

Blood samples collected for immunogenicity analysis were assessed for anti-drug antibodies (ADA), and anti-SCTA01 neutralizing antibodies (Nab) on the basis of the Meso Scale Discovery electrochemiluminescence homogenous bridging assay (Meso Scale Discovery,

Rockville, MD, USA). After being separated from human serum by binding to SCTA01 in ELISA plate, anti-SCTA01 antibodies bind to both Ru-SCTA01 and Bio-SCTA01 molecules to form an antibody complex bridge, called "Biotinylated- SCTA01-ADA- SCTA01-ruthenylated", and then the complex bind to SA-MSD plate. With the addition of 2X MSD read buffer, ruthenium label produces a chemiluminescent signal which is proportional to the concentration of ADA (MESO QuickPlex SQ120, MSD). Determination of ADA consisted of 3 sequential steps as screening, confirmatory and titer assays as previously described (31). A titer cut point factor (TCPF) was set at 1.61 and positively confirmed samples with TCPF < 1.61 were reported with titer value of 1.

Determination of safety and tolerability of SCTA01

Safety profiles including clinical manifestations and abnormalities in electrocardiograms and laboratory tests were closely monitored on days 0, 1, 3, 7, 14, 21, 28, 42, 63 and 84. Any adverse events (AE) and serious AEs (SAE) experienced by the participants were recorded. A treatment-related AE (TRAE) was defined as any AE that was possibly, probably or definitely related to the study drug, as judged by the investigator, and the severity of a TRAE was determined based on the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1 (32).

The dose-limiting toxicity (DLT) was defined as TRAE of grade 3 or higher (32). If necessary, the unblinded statistician was requested to summarize the occurrence of DLTs in the SCTA01 group, and the investigator and the sponsor decided together whether or not to discontinue the dose escalation, to lower the dose, or to continue with the next dose group. The maximum tolerated dose (MTD) was defined as the highest dose of SCTA01 at which one out of three participants had DLT during the 84-day observation period (32).

353

354 ***Outcomes***

355 The primary endpoints were DLT and MTD of SCTA01. The secondary endpoints were the
356 PK parameters including the integral of the concentration-time curve from dosing to time-
357 point (AUC_{0-t}), the integral of the concentration-time curve from dosing to infinity ($AUC_{0-\infty}$),
358 half-life ($t_{1/2}$), the time taken to reach the maximum concentration (T_{max}), immunogenicity
359 indicated by the generation of ADA and safety reflected by the occurrence of AEs and SAEs.

360

361 ***Statistical analysis***

362 The sample size for this trial was based on the dose-escalation rule and not on any statistical
363 criteria.

364

365 The safety analysis included all randomized participants who received any dose of the study
366 drug. Participants receiving placebo in different cohorts were pooled together. All
367 participants who were randomized and received any dose of the SCTA01 or placebo were
368 included in the intention-to-treat analysis, whereas those who completed the study were
369 included in the per-protocol analysis. Categorical and continuous data including clinical
370 laboratory results, vital signs, and electrocardiographic features at each time-point were
371 summarized descriptively, as they were not appropriate for statistical analysis due to the
372 small sample size.

373

374 Participants who received SCTA01 and had at least one measurement of PK after the first
375 dose were included in PK analysis. The PK parameters including T_{max}, C_{max}, $AUC_{0-\infty}$, AUC_{0-t},
376 the integral of the concentration-time curve from dosing to day 28 (AUC_{0-28d}), $t_{1/2}$, Vd and
377 CL were calculated by a non-compartmental analysis with Certara Phoenix WinNonlin

software (version 8.3.1). The Power Model was used to analyze the dose-proportionality for 5-50mg/kg dose range. The SAS software (version 9.4, SAS Institute, Cary, North Carolina, USA) was used to perform statistical analysis.

Abbreviations

COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; RBD: receptor-binding domain; ADE: antibody-dependent enhancement; ADCC: antibody-dependent cell cytotoxicity; AE: adverse events; DLT: dose-limiting toxicity; MTD: maximal tolerable dose;

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Conflict of interest

Liangzhi Xie is the CEO of Sinocelltech Ltd., Beijing, China. Chunyun Sun, Shuping Xu, Lixin Yan, Weiqiu Chen, Xisheng Liu, Qing Liu are employees of Sinocelltech Ltd., Beijing, China. Other authors have no conflict of interest to declare.

Availability of data and material

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

403

404 **Authors' contributions**

405 XHW, LZX, SPX, CYS, WQC and LXY conceived and designed research; YJL, LQ, HHB,
406 YW, CYH, YL, CPL, LL, XQC, JL, YXT, MLS, XSL and QL collected data and conducted
407 research; YJL, LQ and HHB analyzed and interpreted data; YJL, LQ and HHB wrote the
408 initial paper; XHW and LZX revised the paper; XHW and LZX had primary responsibility
409 for final content. All authors read and approved the final manuscript.

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412 **References**

413 1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY,
414 Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Liu M, Tu W, Chen C, Jin L,
415 Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y,
416 Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JT, Gao GF, Cowling BJ, Yang B,
417 Leung GM, Feng Z. 2020. Early Transmission Dynamics in Wuhan, China, of Novel
418 Coronavirus-Infected Pneumonia. N Engl J Med 382:1199-1207.
419 2. Kurishima K, Watanabe H, Ishikawa H, Satoh H, Hizawa N. 2017. Survival of patients
420 with lung cancer and diabetes mellitus. Mol Clin Oncol 6:907-910.
421 3. Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, Fu S, Gao L, Cheng Z, Lu Q, Hu Y, Luo G,
422 Wang K, Lu Y, Li H, Wang S, Ruan S, Yang C, Mei C, Wang Y, Ding D, Wu F, Tang X,
423 Ye X, Ye Y, Liu B, Yang J, Yin W, Wang A, Fan G, Zhou F, Liu Z, Gu X, Xu J, Shang L,
424 Zhang Y, Cao L, Guo T, Wan Y, Qin H, Jiang Y, Jaki T, Hayden FG, Horby PW, Cao B,
425 Wang C. 2020. Remdesivir in adults with severe COVID-19: a randomised, double-blind,
426 placebo-controlled, multicentre trial. Lancet 395:1569-1578.
427 4. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S,
428 Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S.
429 2020. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a
430 Clinically Proven Protease Inhibitor. Cell 181:271-280.e278.
431 5. Chen P, Nirula A, Heller B, Gottlieb RL, Boscia J, Morris J, Huhn G, Cardona J,
432 Mocherla B, Stosor V, Shawa I, Adams AC, Van Naarden J, Custer KL, Shen L, Durante
433 M, Oakley G, Schade AE, Sabo J, Patel DR, Klekotka P, Skovronsky DM. 2021. SARS-
434 CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19. N Engl J Med
435 384:229-237.
436 6. Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, Zhou M, Chen L, Meng S, Hu Y, Peng C,

Yuan M, Huang J, Wang Z, Yu J, Gao X, Wang D, Yu X, Li L, Zhang J, Wu X, Li B, Xu Y, Chen W, Peng Y, Hu Y, Lin L, Liu X, Huang S, Zhou Z, Zhang L, Wang Y, Zhang Z, Deng K, Xia Z, Gong Q, Zhang W, Zheng X, Liu Y, Yang H, Zhou D, Yu D, Hou J, Shi Z, Chen S, Chen Z, Zhang X, Yang X. 2020. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci U S A 117:9490-9496.

7. Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, Wang F, Li D, Yang M, Xing L, Wei J, Xiao H, Yang Y, Qu J, Qing L, Chen L, Xu Z, Peng L, Li Y, Zheng H, Chen F, Huang K, Jiang Y, Liu D, Zhang Z, Liu Y, Liu L. 2020. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. Jama 323:1582-1589.

8. Abolghasemi H, Eshghi P, Cheraghali AM, Imani Fooladi AA, Bolouki Moghaddam F, Imanizadeh S, Moeini Maleki M, Ranjkesh M, Rezapour M, Bahramifar A, Einollahi B, Hosseini MJ, Jafari NJ, Nikpouraghdam M, Sadri N, Tazik M, Sali S, Okati S, Askari E, Tabarsi P, Aslani J, Sharifipour E, Jarahzadeh MH, Khodakarim N, Salesi M, Jafari R, Shahverdi S. 2020. Clinical efficacy of convalescent plasma for treatment of COVID-19 infections: Results of a multicenter clinical study. Transfus Apher Sci 59:102875.

9. Rasheed AM, Fatak DF, Hashim HA, Maulood MF, Kabah KK, Almusawi YA, Abdulamir AS. 2020. The therapeutic potential of convalescent plasma therapy on treating critically-ill COVID-19 patients residing in respiratory care units in hospitals in Baghdad, Iraq. Infez Med 28:357-366.

10. Salazar E, Christensen PA, Graviss EA, Nguyen DT, Castillo B, Chen J, Lopez BV, Eagar TN, Yi X, Zhao P, Rogers J, Shehabeldin A, Joseph D, Leveque C, Olsen RJ, Bernard DW, Gollihar J, Musser JM. 2020. Treatment of Coronavirus Disease 2019 Patients with Convalescent Plasma Reveals a Signal of Significantly Decreased Mortality. Am J Pathol 190:2290-2303.

11. Perotti C, Baldanti F, Bruno R, Del Fante C, Seminari E, Casari S, Percivalle E,

462 Glingani C, Musella V, Belliato M, Garuti M, Meloni F, Frigato M, Di Sabatino A,
463 Klersy C, De Donno G, Franchini M. 2020. Mortality reduction in 46 severe Covid-19
464 patients treated with hyperimmune plasma. A proof of concept single arm multicenter
465 trial. Haematologica.
466 12. Liu STH, Lin HM, Baine I, Wajnberg A, Gumprecht JP, Rahman F, Rodriguez D,
467 Tandon P, Bassily-Marcus A, Bander J, Sanky C, Dupper A, Zheng A, Nguyen FT,
468 Amanat F, Stadlbauer D, Altman DR, Chen BK, Krammer F, Mendu DR, Firpo-
469 Betancourt A, Levin MA, Bagiella E, Casadevall A, Cordon-Cardo C, Jhang JS,
470 Arinsburg SA, Reich DL, Aberg JA, Bouvier NM. 2020. Convalescent plasma treatment
471 of severe COVID-19: a propensity score-matched control study. Nat Med 26:1708-1713.
472 13. Hegerova L, Gooley TA, Sweerus KA, Maree C, Bailey N, Bailey M, Dunleavy V, Patel
473 K, Alcorn K, Haley R, Johnsen JM, Konkle BA, Lahti AC, Alexander ML, Goldman JD,
474 Lipke A, Lim SJ, Sullivan MD, Pauk JS, Pagel JM. 2020. Use of convalescent plasma in
475 hospitalized patients with COVID-19: case series. Blood 136:759-762.
476 14. Li L, Zhang W, Hu Y, Tong X, Zheng S, Yang J, Kong Y, Ren L, Wei Q, Mei H, Hu C,
477 Tao C, Yang R, Wang J, Yu Y, Guo Y, Wu X, Xu Z, Zeng L, Xiong N, Chen L, Wang J,
478 Man N, Liu Y, Xu H, Deng E, Zhang X, Li C, Wang C, Su S, Zhang L, Wang J, Wu Y,
479 Liu Z. 2020. Effect of Convalescent Plasma Therapy on Time to Clinical Improvement
480 in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial.
481 Jama 324:460-470.
482 15. Weinreich DM, Sivapalasingam S, Norton T, Ali S, Gao H, Bhore R, Musser BJ, Soo Y,
483 Rofail D, Im J, Perry C, Pan C, Hosain R, Mahmood A, Davis JD, Turner KC, Hooper
484 AT, Hamilton JD, Baum A, Kyratsous CA, Kim Y, Cook A, Kampman W, Kohli A,
485 Sachdeva Y, Graber X, Kowal B, DiCioccio T, Stahl N, Lipsich L, Braunstein N,
486 Herman G, Yancopoulos GD, Trial Investigators. 2021. REGN-COV2, a Neutralizing

Antibody Cocktail, in Outpatients with Covid-19. N Engl J Med 384:238-251.

16. Gottlieb RL, Nirula A, Chen P, Boscia J, Heller B, Morris J, Huhn G, Cardona J, Mocherla B, Stosor V, Shawa I, Kumar P, Adams AC, Van Naarden J, Custer KL, Durante M, Oakley G, Schade AE, Holzer TR, Ebert PJ, Higgs RE, Kallewaard NL, Sabo J, Patel DR, Klekotka P, Shen L, Skovronsky DM. 2021. Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19: A Randomized Clinical Trial. Jama.

17. ACTIV-3/TICO LY-CoV555 Study Group, Lundgren JD, Grund B, Barkauskas CE, Holland TL, Gottlieb RL, Sandkovsky U, Brown SM, Knowlton KU, Self WH, Files DC, Jain MK, Benfield T, Bowdish ME, Leshnower BG, Baker JV, Jensen JU, Gardner EM, Ginde AA, Harris ES, Johansen IS, Markowitz N, Matthay MA, Østergaard L, Chang CC, Davey VJ, Goodman A, Higgs ES, Murray DD, Murray TA, Paredes R, Parmar MKB, Phillips AN, Reilly C, Sharma S, Dewar RL, Teitelbaum M, Wentworth D, Cao H, Klekotka P, Babiker AG, Gelijns AC, Kan VL, Polizzotto MN, Thompson BT, Lane HC, Neaton JD. 2021. A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19. N Engl J Med 384:905-914.

18. Karlin NJ, Amin SB, Buras MR, Kosiorek HE, Verona PM, Cook CB. 2018. Patient outcomes from lung cancer and diabetes mellitus: a matched case-control study. Future Sci OA 4:Fso248.

19. Tuccori M, Ferraro S, Convertino I, Cappello E, Valdiserra G, Blandizzi C, Maggi F, Focosi D. 2020. Anti-SARS-CoV-2 neutralizing monoclonal antibodies: clinical pipeline. MAbs 12:1854149.

20. Zhu L, Deng YQ, Zhang RR, Cui Z, Sun CY, Fan CF, Xing XR, Huang WJ, Chen Q, Zhang NN. 2020. Double lock of a potent human therapeutic monoclonal antibody against SARS-CoV-2. National Science Review:nwaa297.

512 21. Jeong SS, Choi PJ, Yi JH, Yoon SS. 2017. Impact of Lifestyle Diseases on Postoperative
513 Complications and Survival in Elderly Patients with Stage I Non-Small Cell Lung
514 Cancer. Korean J Thorac Cardiovasc Surg 50:86-93.
515 22. Sivapalasingam S, Kamal M, Slim R, Hosain R, Shao W, Stoltz R, Yen J, Pologe LG,
516 Cao Y, Partridge M, Sumner G, Lipsich L. 2018. Safety, pharmacokinetics, and
517 immunogenicity of a co-formulated cocktail of three human monoclonal antibodies
518 targeting Ebola virus glycoprotein in healthy adults: a randomised, first-in-human phase
519 1 study. Lancet Infect Dis 18:884-893.
520 23. Wu Z, McGoogan JM. 2020. Characteristics of and Important Lessons From the
521 Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of
522 72 314 Cases From the Chinese Center for Disease Control and Prevention. Jama
523 323:1239-1242.
524 24. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z,
525 Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J,
526 Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. 2020. Clinical features of patients
527 infected with 2019 novel coronavirus in Wuhan, China. Lancet 395:497-506.
528 25. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y,
529 Zhao Y, Li Y, Wang X, Peng Z. 2020. Clinical Characteristics of 138 Hospitalized
530 Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. Jama
531 323:1061-1069.
532 26. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei
533 Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. 2020. Clinical course and risk
534 factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a
535 retrospective cohort study. Lancet 395:1054-1062.
536 27. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y,

Pan S, Zou X, Yuan S, Shang Y. 2020. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 8:475-481.

28. De Groot AS, Scott DW. 2007. Immunogenicity of protein therapeutics. Trends Immunol 28:482-490.

29. Hansel TT, Kropshofer H, Singer T, Mitchell JA, George AJ. 2010. The safety and side effects of monoclonal antibodies. Nat Rev Drug Discov 9:325-338.

30. Kernstock R, Sperinde G, Finco D, Davis R, Montgomery D. 2020. Clinical Immunogenicity Risk Assessment Strategy for a Low Risk Monoclonal Antibody. Aaps j 22:60.

31. Xue L, Clements-Egan A, Amaravadi L, Birchler M, Gorovits B, Liang M, Myler H, Purushothama S, Manning MS, Sung C. 2017. Recommendations for the Assessment and Management of Pre-existing Drug-Reactive Antibodies During Biotherapeutic Development. Aaps j 19:1576-1586.

32. van de Poll-Franse LV, Houterman S, Janssen-Heijnen ML, Dercksen MW, Coebergh JW, Haak HR. 2007. Less aggressive treatment and worse overall survival in cancer patients with diabetes: a large population based analysis. Int J Cancer 120:1986-1992.

555 **Figure legends**

556 **Figure 1.** Mean SCTA01 serum concentrations in different dose groups. (A) Mean SCTA01

557 serum concentrations *versus* time (linear scaled) in different dose groups; and (B) Semi-

558 logarithmic plot of concentration-time data in different dose groups.

559

560 **Table 1.** Baseline demographic characteristics of the participants

	SCTA01 dose				Total SCTA01 (n=25)	Placebo (n=8)
	5 mg/kg (n=3)	15 mg/kg (n=6)	30 mg/kg (n=8)	50 mg/kg (n=8)		
Age (years)						
Mean (SD)	28.0 (4.4)	31.8 (6.9)	30.9 (8.8)	33.4 (6.5)	31.6 (7.0)	30.8 (6.6)
Median (range)	26.0 (25-33)	34 (22-40)	29.5 (20-42)	34.5 (23-44)	33.0 (20-44)	28.5 (24-41)
Race						
Han	3 (100%)	6 (100%)	8 (100%)	8 (100%)	25 (100%)	8 (100%)
Other	0	0	0	0	0	0
Sex						
Male	1 (33.3%)	5 (83.3%)	5 (62.5%)	6 (75.0%)	17 (68.0%)	5 (62.5%)
Female	2 (66.7%)	1 (16.7%)	3 (37.5%)	2 (25.0%)	8 (32.0%)	3 (37.5%)
Height (cm)						
Mean (SD)	164.5 (4.1)	169.3 (3.1)	165.3 (9.4)	163.7 (8.0)	165.7 (7.3)	166.8 (7.3)
Median (range)	164.1 (160.6-168.8)	170.1 (164.8-172.9)	165.4 (153.8-179.2)	163.8 (151.6-174.0)	165.9 (151.6-179.2)	168.6 (154.6-175.6)
Body weight (kg)						
Mean (SD)	60.5 (2.5)	67.8 (2.4)	60.9 (6.2)	60.9 (7.8)	62.5 (6.3)	61.4 (5.8)
Median (range)	60.3 (58.2-63.1)	67.7 (65.1-70.9)	63.3 (50.2-67.8)	61.7 (49.6-70.5)	64.3 (49.6-70.9)	59.8 (54.1-71.9)
BMI (kg/m2)						
Mean (SD)	22.4 (0.3)	23.7 (0.5)	22.3 (1.9)	22.7 (1.7)	22.8 (1.5)	22.1 (2.1)
Median (range)	22.4 (22.1-22.6)	23.8 (23.4-24.0)	22.4 (20.8-23.3)	22.35 (21.5-24.0)	22.55 (20.2-24.0)	22.8 (21.8-23.9)

561 Data are presented as number of patients (%).

562 SD, standard deviation; BMI, body mass index.

563

564

565 **Table 2.** Administration of SCTA01 and placebo in the participants

	SCTA01 dose				Total SCTA01	Placebo
	5 mg/kg (n=3)	15 mg/kg (n=6)	30 mg/kg (n=8)	50 mg/kg (n=8)	(n=25)	(n=8)
Duration of observation (days)						
Mean (SD)	85.0 (0.0)	84.0 (0.0)	86.1 (4.5)	85.5 (1.4)	85.3 (2.7)	84.5 (0.5)
Median (range)	85.0 (85-85)	84.0 (84-84)	84.0 (84-97)	85.0 (85-89)	85.0 (84-97)	84.5 (84-85)
Actual total SCTA01 dose injected(mg)						
Mean (SD)	302.7 (12.3)	1016.3 (35.4)	1825.9 (185.3)	3043.8 (392.1)	1838.5 (1001.6)	/
Median (range)	301.5 (291-316)	1015.5 (977-1064)	1897.5 (1506-2034)	3082.5 (2480-3535)	1872.0 (291-3525)	/

566 The 33 participants were randomized into four cohorts as follows: 1) Cohort 1, 3:2 to SCTA01 5 mg/kg or placebo; 2) Cohort 2, 6:2 to SCTA01 15 mg/kg or
567 placebo; 3) Cohort 3, 8:2 to SCTA01 30 mg/kg or placebo; and 4) Cohort 4: 8:2 to SCTA01 50 mg/kg or placebo. Participants receiving placebo in the four
568 cohorts were pooled together.
569 SD, standard deviation.

570 **Table 3.** Number of participants with treatment-related adverse events within the 84 days

	SCTA01 dose				Total	
	5 mg/kg (N = 3)	15 mg/kg (N = 6)	30 mg/kg (N = 8)	50 mg/kg (N = 8)	**SCTA01** (N = 25)	**Placebo** (N = 8)
Any adverse event	1 (33.3)	2 (33.3)	5 (62.5)	5 (62.5)	13 (52.0)	5 (62.5)
Any adverse event of ≥ grade 3	0	0	0	0	0	0
Laboratory investigations	1 (33.3)	2 (33.3)	4 (50.0)	3 (37.5)	10 (40.0)	5 (62.5)
Increased conjugated bilirubin	1 (33.3)	0	2 (25.0)	1 (12.5)	4 (16.0)	0
Increased unconjugated bilirubin	1 (33.3)	0	1 (12.5)	1 (12.5)	3 (12.0)	1 (12.5)
Increased blood bilirubin	1 (33.3)	0	1 (12.5)	0	2 (8.0)	0
Increased alanine aminotransferase	0	1 (16.7)	0	0	1 (4.0)	0
Increased aspartate aminotransferase	0	0	0	0	0	1 (12.5)
Decreased neutrophil count	0	0	1 (12.5)	0	1 (4.0)	0
Decreased lymphocyte count	0	0	0	0	0	1 (12.5)
Increased fibrin D dimer	0	0	1 (12.5)	0	1 (4.0)	0
Increased platelet count	0	0	1 (12.5)	0	1 (4.0)	0
Decreased fibrinogen	0	0	1 (12.5)	0	1 (4.0)	0
Increased potassium	0	0	0	1 (12.5)	1 (4.0)	0
Increased white blood cell count in the urine	0	0	0	1 (12.5)	1 (4.0)	1 (12.5)
Protein in urine	1 (33.3)	1 (16.7)	0	0	2 (8.0)	0
Prolonged QT interval	0	1 (16.7)	0	0	1 (4.0)	0
Decreased diastolic blood pressure	0	0	0	0	0	1 (12.5)
Respiratory, thoracic and mediastinal disorders	0	0	0	1 (12.5)	1 (4.0)	0
Epistaxis	0	0	0	1 (12.5)	1 (4.0)	0
Cardiac disorders	0	1 (16.7)	0	0	1 (4.0)	0
Sinus bradycardia	0	1 (16.7)	0	0	1 (4.0)	0
Skin and subcutaneous tissue disorders	0	0	0	1 (12.5)	1 (4.0)	0
Rash	0	0	0	1 (12.5)	1 (4.0)	0
Renal and urinary disorders	0	0	1 (12.5)	0	1 (4.0)	0
Hematuria	0	0	1 (12.5)	0	1 (4.0)	0

571 Data are presented as the number (%) of participants with one or more TRAEs.

572

573 **Table 4.** Pharmacokinetic parameters of SCTA01

Parameters	SCTA01 dose			
	5 mg/kg (n=3)	15 mg/kg (n=6)	30 mg/kg (n=8)	50 mg/kg (n=8)
T_{max} (h)	1.32 (0.32-1.32)	1.92 (0.92-8.92)	2.83 (1.83-9.83)	3.16 (3.15-3.17)
C_{max} (μg/mL)	84.8	307	607	1040
$AUC_{0\text{-}28d}$ (d*μg/mL)	1120	3750	7700	11900
$AUC_{0\text{-}t}$ (d*μg/mL)	1940	6690	12700	19600
$AUC_{0\text{-}\infty}$ (d*μg/mL)	2270	7760	14400	21900
$t_{1/2}$ (d)	30.2	28.0	27.2	25.8
CL (L/h)	0.00563	0.00552	0.00538	0.00587
Vd (L)	5.82	5.31	5.00	5.16
$AUC_{0\text{-}inf}$/dose (d*μg/mL/mg)	7.49	7.62	7.93	7.34

574 Data are presented as median (range) or arithmetic mean.

575 T_{max}, the time taken to reach the maximum concentration; C_{max}, maximum concentration; AUC, the
576 area under the concentration-time curve; $AUC_{0\text{-}28d}$, the integral of the concentration-time curve from
577 dosing to day 28; $AUC_{0\text{-}t}$, the integral of the concentration-time curve from dosing to time-point;
578 $AUC_{0\text{-}\infty}$, the integral of the concentration-time curve from dosing to infinity; CL, clearance; Vd,
579 volume of distribution.
580
581

582 **Table 5.** Incidence of treatment emergent anti-drug antibody response after SCTA01
583 administration

Follow-up time	SCTA01 dose				Total
	5mg/kg (N = 3)	15mg/kg (N = 6)	30mg/kg (N = 8)	50mg/kg (N = 8)	SCTA01 (N = 25)
ADA					
Baseline	0	0	0	1	1
Day 7 (±1d)	1	1	1	1	4
Day 14 (±2d)	0	0	0	0	0
Day 28 (+3d)	0	1	0	0	1
Day 42 (±3d)	0	0	0	0	0
Day 63 (±3d)	0	0	0	0	0
Day 84 (±3d)	0	0	0	0	0
Overall	1	1	1	1	4
Nab					
Baseline	0	0	0	1	1
Day 7 (±1d)	0	0	1	1	2
Day 14 (±2d)	0	0	0	0	0
Day 28 (+3d)	0	1	0	0	1
Day 42 (±3d)	0	0	0	0	0
Day 63 (±3d)	0	0	0	0	0
Day 84 (±3d)	0	0	0	0	0
Overall	0	1	1	1	3

584 Data are presented as binary (1, number of participants with a positive response; 0, number of
585 participants with a negative response).
586 ADA, anti-drug antibody response; Nab, neutralizing antibodies