2. SYNOPSIS

Study centre

This was a single centre study conducted in China. The Principal Investigator was PPD , China.

Publications

None at the time of writing this report.

Objectives and criteria for evaluation

Table S1 Objectives and Endpoints

Type	Objectives	Endpoints
Primary		
PK	• To evaluate serum concentrations of nirsevimab	• Summary of nirsevimab serum concentrations and estimated PK parameters (C_{max}, T_{max}, AUC_{0-150}, and others if data permit)
Secondary		
ADA	• To evaluate ADA responses to nirsevimab in serum	• Incidence of ADA to nirsevimab in serum
Safety	• To evaluate the safety and tolerability of nirsevimab when administered as a single fixed IM dose of 300 mg to healthy Chinese adult subjects	• Occurrence of all TEAEs, TESAEs, AESIs, and NOCDs • Clinical laboratory assessments, vital signs

ADA = antidrug antibody; AESI = adverse event of special interest; AUC_{0-150} = area under the concentration-time curve from time 0 to 150 days; C_{max} = maximum observed concentration; IM = intramuscular; NOCD = new onset chronic disease; PK = pharmacokinetics; TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event; T_{max} = time to maximum observed concentration.

Study design

This was a Phase 1, randomised, double-blind, placebo-controlled study to evaluate the pharmacokinetics (PK), safety, and tolerability of nirsevimab compared to placebo when administered as a single fixed intramuscular (IM) dose of 300 mg to healthy Chinese adult subjects. Enrolment was planned at a single study centre in China.

Approximately 24 subjects were planned to be randomly assigned in a 3:1 ratio to receive nirsevimab (n = 18) or placebo (n = 6). All subjects were followed for approximately 150 days after dosing to assess safety, PK, and ADA response.

Target population and sample size

The target population of the study was healthy adult Chinese subjects.

This study planned to randomise approximately 24 subjects, of whom 18 were to receive nirsevimab and 6 were to receive placebo. All analyses were descriptive in nature and no hypothesis was tested statistically, therefore no formal sample size calculation was performed.

Current sample size and sampling scheme were selected to facilitate estimation and numerical comparison of maximum observed concentration (C_{max}), time to maximum observed concentration (T_{max}), and area under the concentration-time curve from time 0 to 150 days (AUC_{0-150}) between adult Chinese subjects from this study and non-Chinese adult subjects from the global Phase 1a Study D5290C00001. This PK comparison was presented separately from the clinical study report (CSR).

Investigational product and comparator(s): dosage, mode of administration and batch numbers

Nirsevimab: Supplied as 50 mg (nominal) per vial solution. The solution contains 100 mg/mL nirsevimab, CCI histidine/histidine - hydrochloride (HCl), CCI arginine-HCl, CCI sucrose, CCI polysorbate 80, pH 6.0. The nominal fill volume is 0.5 mL.

Route: Intramuscular (IM) injection.

Batch number: P65706LA.

Placebo: Commercially available 0.9% (w/v) saline (sterile for human use) provided by the study site.

Route: IM injection.

Batch number: Not applicable.

Duration of treatment

Single IM dose.

Statistical methods

Study population

PK population: The PK population included all subjects who received any dose of IP and had at least one measurable post-dose serum PK observation and for whom PK blood samples were assumed not to be affected by factors such as important protocol deviations (if any, determined prior to unblinding). Pharmacokinetic analyses were based on the PK population. Subjects who received placebo were not part of the PK population.

As-treated Population: All subjects who were randomised into the study and received any amount of IP were included in the As-treated Population. All safety summaries were based on this analysis set and all subjects were analysed according to the actual treatment received.

Statistical methods

Tabular summaries were presented by treatment group. Categorical data were summarised by the number and percentage of subjects in each category

Pharmacokinetic data, from the PK population, as well as other data including immunogenicity and safety data were analysed and summarised descriptively. Serum concentrations of nirsevimab at selected time points were evaluated to confirm that adequate exposures are maintained after dosing. Nirsevimab serum concentration data were presented in descriptive statistics. Serum PK parameters such as C_{max}, T_{max}, and AUC_{0-150} were estimated using non-compartmental analysis and summarised with descriptive statistics.

No statistical hypotheses were evaluated based on formal statistical tests.

Results

Summary of study population

Of the 123 subjects screened for the study, a total of 24 subjects were randomised and received study treatment (18 subjects in the nirsevimab group and 6 subjects in the placebo group). The majority of the subjects were male (70.8%), and all were Asian, with a mean age of 29.3 years PPD . All 24 subjects completed the study.

Summary of pharmacokinetic results

Following the administration of study treatment, serum nirsevimab concentrations increased until a geometric mean C_{max} of 46.882 µg/mL was reached at a median T_{max} of approximately 7 days.

The individual serum concentration-time profiles show that the between subject variability was low, which was reflected in the geometric coefficient of variation of the C_{max} (21.7%) and AUC_{0-150} (13.6%).

Summary of immunogenicity results

No subjects had detectable levels of ADAs during the course of the study.

Summary of safety results

All 24 subjects received the complete dose of study treatment. Overall, 5 subjects (27.8%) in the nirsevimab group and 2 subjects (33.3%) in the placebo group reported TEAEs. All TEAEs reported were of CTCAE Grade 1 or 2.

One subject (5.6%) in the nirsevimab group reported TEAEs related to the IP (blood creatinine increased, complement factor decreased, and platelet count decreased). The AE of platelet count decreased was reported as an AESI.

There were no TESAEs, TESAEs with the outcome of death, NOCDs, AEs that led to interruption of the study treatment reported, or Coronavirus disease 2019 (COVID-19) related AEs.

Overall, clinical laboratory and other safety assessments were in line with the reported safety profile of nirsevimab and there were no new safety concerns.

Conclusions

- Subject disposition and baseline characteristics were well balanced between treatment groups and in alignment with the expectations for the population being studied. All subjects received the assigned study treatment and completed the study.
- Following the administration of study treatment, serum nirsevimab concentrations increased until a geometric mean C_{max} of 46.882 μg/mL was reached at a median T_{max} of approximately 7 days.
- The individual serum concentration time profiles show that the between subject variability was low, which was reflected in the coefficient of variation of the C_{max} (21.7%) and AUC_{0-150} (13.6%).
- No subjects had detectable levels of ADAs during the course of the study.
- Overall, nirsevimab was safe and well tolerated in healthy Chinese adult subjects. No new safety findings were observed in the study.