SUPPLEMENT

Additional data and Methods

Confidentiality is being maintained in accordance with Human Research Ethics Committee (HREC) requirements and Good Clinical Practice. All identifiable information on study participants is retained in password protected files inside locked cabinets and/or locked rooms at study sites. Access to this information is available only to immediate study staff, unless required by legislative or regulatory agencies and the HRECs. No identifying information will be included in study reports. Clinical specimens are being labelled with the participant ID number and corresponding laboratory numbers.

Nasopharyngeal bacteriology

Nasopharyngeal swabs are stored and processed as described previously. Batches will be thawed and cultured on selective media for *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and *Moraxella catarrhalis* with antibiotic susceptibility determined by the calibrated susceptibility disc diffusion method. The minimum inhibitory concentration for azithromycin will be determined by E-tests where non-susceptibility is identified using disk diffusion. The European Committee on Antimicrobial Susceptibility Testing criteria will be used to define non-susceptibility. When sputum is obtained, specimens will also be cultured for non-tuberculous mycobacteria, and stored for future studies on the respiratory microbiome, pending additional consent.

Primary ciliary dyskinesia Quality-of-life (PCD-QoL) scores

There are versions available of PCD-QoL scores that are age dependent (6-12 years, 13-18, >18-years) and there is also a parent proxy version. The adult version has 40-items and covers seven domains: physical function, emotional, treatment burden, respiratory and sinus symptoms, ears and hearing, social, and vitality and health perceptions. We are using the age-appropriate version.

Spirometry

Spirometry is performed by trained personnel in a seated position with a nose clip according to American Thoracic Society and European Respiratory Society guidelines. Measurements are valid when maximum inhalation is followed by a rapid forced exhalation until a volume plateau is achieved (>3s expiratory time when aged <10-years and >6s when ≥10-years). We are using an Easy on-PC spirometer (ndd Medizintechnik AG, Zurich, Switzerland), which is calibrated daily using a 3-litre syringe. In the presence of airway obstruction, post-bronchodilator spirometry is performed 10-minutes after 400 mcg of salbutamol is delivered through a spacer. The highest forced expiratory volume in 1-second and forced vital capacity values are reported after three valid measurements, post-salbutamol.

Mitigation methods used to reduce on impact of the pandemic on the trial

The SARs-COV-2 pandemic impacted upon our study in many ways, as outlined in the main text. During the study, we initiated several mitigations steps that included: (a) using e-consents (approved by all ethics committees); (b) posting trial medications to the participants home (instead of participants collecting trial medications from hospital pharmacies); and (c) undertaking on-line follow-up where possible and appropriate.

Adverse events

While erdosteine is a novel drug for the purpose we are examining in our randomised controlled trial (RCT), it is widely available over-the-counter (i.e. no prescription required) in over 40 countries worldwide. Nevertheless, we are collecting data on adverse events in our RCT as a secondary outcome. In light of the above, we do not anticipate any increase in clinically-important adverse events attributable to erdosteine.
References


