Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo controlled, phase 2 trial

Phillip D Monk, Richard J Marsden, Victoria J Tear, Jody Brookes, Toby N Batten, Marcin Mankowski, Felicity J Gabbay, Donna E Davies, Stephen T Holgate, Ling-Pei Ho, Tristan Clark, Ratko Djukanovic, Tom M A Wilkinson, on behalf of the Inhaled Interferon Beta COVID-19 Study Group

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Article summary

This randomised, double-blind, placebo-controlled, phase 2 pilot trial sought to evaluate the safety and efficacy of inhaled nebulised interferon beta-1a in patients hospitalised with COVID-19. The activity of interferon beta, a cytokine critical to antiviral immunity, is now known to be impaired in SARS-CoV-2 infection 1-3 . Previous studies suggest that SNG001, an inhaled formulation of interferon beta-1a, enhances local immune responses to respiratory viruses 4-6 . 101 participants, hospitalised with confirmed COVID-19 at nine UK sites, were randomised 1:1 to receive SNG001 or placebo once daily by nebuliser for up to 14 days. The primary outcome was change in illness severity, as measured by the WHO Ordinal Scale for Clinical Improvement (OSCI) 7 . SNG001 tolerability was a notable secondary outcome. Outcomes were assessed throughout the treatment period and the subsequent 14-day follow-up period.

The intention-to-treat analysis ultimately compared 48 participants who received SNG001 and 50 who received placebo. The odds of clinical improvement for the SNG001 group, as indicated by change on the OSCI, were more than two-fold greater than the placebo group at day 15 or 16 (odds ratio 2.32 [95% CI 1.07-5.04]; p=0.033) and more than three-fold greater at day 28 (3.15 [1.39-7.14]; p=0.006). Similarly, patients who received SNG001 were twice as likely to recover to an OSCI score of 1 (no limitation of activities) during the treatment period (44% vs 22%; hazard ratio 2.19 [95% CI 1.03-4.69]; p=0.043), with three-fold greater odds of recovery at day 28 (OR 3.58; [95% CI 1.41-9.04]; p=0.007). There were no significant differences between groups in the odds of hospital discharge or time to hospital discharge. SNG001 was well tolerated; headache was the most common adverse event, affecting 15% of patients in the SNG001 group and 10% in the placebo group.

Critical appraisal

This study had many strengths; namely multi-centre design, randomisation, placebo-control, and double-blinding. Naturally however, as this was an early-phase trial the sample size was small. This limits the generalisability of findings and manifested in treatment group imbalances following randomisation. Although both groups were well-matched for age, gender and overall comorbidities, they were less well-matched for baseline disease severity and specific comorbidities such as cardiovascular disease, diabetes and hypertension.
The OSCI, developed by the WHO to standardize trials of investigational COVID-19 treatments, is relatively new and remains largely unvalidated in this context. Furthermore, ventilated patients, who represent the greatest burden of COVID-19 and the most in need of effective treatments, were not included in this trial due to incompatibility with the study

nebuliser.

Reflection

There continues to be a critical deficit of effective treatments for COVID-19. Current evidence-based interventions are limited to dexamethasone 8 and remdesivir 9 . Inhaled interferon beta-based therapies such as SNG001 remain in the early stages of development and these findings, while positive, will not change clinical practice. Given the current need however, investigational therapies with encouraging early-phase results are likely to be fast-tracked. Inhaled interferon beta therapies represent a rational avenue for new drug development, informed by an existing 'pre-pandemic' evidence base and a growing understanding of the pathophysiology underlying COVID-19. The promising results associated with SNG001, as reported in this trial, provide strong justification for future studies with larger, more diverse populations.

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