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A randomised trial of anti-GM-CSF otilimab in severe COVID-19 pneumonia (OSCAR)

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Therapeutic blocking of GM-CSF with otilimab did not significantly improve clinical status in patients with severe COVID-19; however, otilimab demonstrated an acceptable safety profile and reduced markers of inflammation https://bit.ly/3QquyYP

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Abstract

Background Granulocyte–macrophage colony-stimulating factor (GM-CSF) and dysregulated myeloid cell responses are implicated in the pathophysiology and severity of COVID-19.

Methods In this randomised, sequential, multicentre, placebo-controlled, double-blind study, adults aged 18–79 years (Part 1) or ⩾70 years (Part 2) with severe COVID-19, respiratory failure and systemic inflammation (elevated C-reactive protein/ferritin) received a single intravenous infusion of otilimab 90 mg (human anti-GM-CSF monoclonal antibody) plus standard care (NCT04376684). The primary outcome was the proportion of patients alive and free of respiratory failure at Day 28.

Results In Part 1 (n=806 randomised 1:1 otilimab:placebo), 71% of otilimab-treated patients were alive and free of respiratory failure at Day 28 *versus* 67% who received placebo; the model-adjusted difference of 5.3%

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was not statistically significant (95% CI −0.8–11.4%, p=0.09). A nominally significant model-adjusted difference of 19.1% (95% CI 5.2–33.1%, p=0.009) was observed in the predefined 70–79 years subgroup, but this was not confirmed in Part 2 (n=350 randomised) where the model-adjusted difference was 0.9% (95% CI −9.3–11.2%, p=0.86). Compared with placebo, otilimab resulted in lower serum concentrations of key inflammatory markers, including the putative pharmacodynamic biomarker CC chemokine ligand 17, indicative of GM-CSF pathway blockade. Adverse events were comparable between groups and consistent with severe COVID-19.

Conclusions There was no significant difference in the proportion of patients alive and free of respiratory failure at Day 28. However, despite the lack of clinical benefit, a reduction in inflammatory markers was observed with otilimab, in addition to an acceptable safety profile.