dysphagia. Of these patients only 2.4% (n=2) were found to have oropharyngeal dysphagia on clinical assessment.

This preliminary study emphasises the importance of the SLT role within the Multi-Disciplinary Team; to identify whether these symptoms warrant further assessment. This study also highlights the benefits of access to instrumental assessment to prevent patient morbidity and inform diagnostic management.

Further prospective studies with larger patient cohorts may help to understand patient-reported symptoms of dysphagia further, and continue to inform clinical decision-making.

Developing treatments for COVID-19

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LENZILUMAB EFFICACY AND SAFETY IN NEWLY HOSPITALIZED COVID-19 SUBJECTS: RESULTS FROM THE LIVE-AIR PHASE 3 RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Background Severe COVID-19 pneumonia results from a hyperinflammatory immune response (cytokine storm, CS), characterized by GM-CSF mediated activation and trafficking of myeloid cells, leading to elevations of downstream inflammatory chemokines (MCP-1, IL-8, IP-10) and cytokines (IL-6, IL-1). CS leads to fever, hypotension, coagulopathy, respiratory failure, ARDS, and death. Lenzilumab is a novel Humaneered[®] anti-human GM-CSF monoclonal antibody that binds GM-CSF and prevents signaling through its receptor. The LIVE-AIR Phase 3 randomized, double-blind, placebo-controlled trial investigated the efficacy and safety of lenzilumab to improve the likelihood of ventilator-free survival (referred to herein as survival without ventilation, SWOV), beyond standard supportive care, in hospitalized subjects with severe COVID-19.

Methods Subjects with COVID-19 (n=520), ≥18 years, and ≤94% oxygen saturation on room air and/or requiring supplemental oxygen, but not invasive mechanical ventilation, were randomized to receive lenzilumab (600 mg, n=261) or placebo (n=259) via three intravenous infusions administered 8 hours apart. Subjects were followed through Day 28 following treatment.

Results Baseline demographics were comparable between the two treatment groups: male, 64.7%; mean age, 60.5 years; mean BMI, 32.5 kg/m²; median CRP, 79 mg/L; CRP was <150 mg/L in 78% of subjects. The most common comorbidities were hypertension (65.6%), obesity (55.1%), diabetes (53.4%), chronic kidney disease (14.0%), and coronary artery disease (13.6%). Subjects received steroids (93.7%), remdesivir (72.4%), or both (69.1%). Lenzilumab improved the likelihood of SWOV by 54% in the mITT population (HR: 1.54; 95%CI: 1.02–2.32, p=0.0403). SWOV also relatively improved by 92% in the predefined subgroup of subjects who

received both corticosteroids and remdesivir (1.92; 1.20–3.07; nominal p=0.0067). A key secondary endpoint of incidence of IMV, ECMO or death was also improved in patients receiving remdesivir (p=0.020) or remdesivir and corticosteroids (p=0.0180). Serious adverse events were reported in 24.7% and 29.6% of the lenzilumab and placebo patients, respectively. Compared with placebo, lenzilumab produced no infusion-related reactions, and no attributable serious adverse events; including, hematologic or liver enzyme abnormalities, pulmonary alveolar proteinosis, or increased incidence of infection.

Conclusion Lenzilumab significantly improved SWOV in hypoxic COVID-19 patients upon hospitalization, with the greatest benefit observed in patients receiving treatment with remdesivir and corticosteroids. NCT04351152

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C-REACTIVE PROTEIN AS A BIOMARKER FOR IMPROVED EFFICACY OF LENZILUMAB IN COVID-19 PATIENTS: RESULTS FROM THE LIVE-AIR TRIAL

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Background The hyperinflammatory cytokine storm (CS) of COVID-19 is mediated by GM-CSF leading to release of downstream inflammatory chemokines, cytokines, and markers of systemic inflammation (C-reactive protein, CRP). The LIVE-AIR study demonstrated that lenzilumab, an anti-GM-CSF monoclonal antibody in patients hospitalized with COVID-19, safely improved the likelihood of achieving the primary endpoint, survival without ventilation (SWOV) by 1.54-fold (HR: 1.54; 95%CI: 1.02–2.32, p=0.0403) compared with placebo. An exploratory analysis in patients with CRP<150 mg/L and age<85 years was conducted to determine lenzilumab efficacy when administered prior to advanced inflammation.

Methods LIVE-AIR was a phase 3 randomized, double-blind, placebo-controlled trial. Patients with COVID-19 (n=520), ≥18 years, and ≤94% oxygen saturation on room air and/or requiring supplemental oxygen, but not invasive mechanical ventilation (IMV), were randomized to receive lenzilumab (600 mg, n=261) or placebo (n=259) via three intravenous infusions administered 8 hours apart. Participants were followed through Day 28 following treatment.

Results Overall, baseline demographics were comparable between treatment groups: male, 64.7%; mean age, 60.5 years; mean BMI, 32.5 kg/m²; median CRP, 79 mg/L; CRP was <150 mg/L in 78% of participants. Participants received steroids (93.7%), remdesivir (72.4%), or both (69.1%). Lenzilumab (n=159) improved the likelihood of SWOV by 3.04-fold in participants with CRP<150 mg/L and age<85 years (3.04; 1.68–5.51, nominal p=0.0003) compared with placebo (n=178). Response to lenzilumab was observed in the first through third quartiles of baseline CRP (<41 mg/L, HR:8.33;

41<79 mg/L, HR:1.60; 79<137 mg/L, HR: 2.12; >137 mg/L, HR: 1.17). The incidence of IMV, ECMO, or death was reduced (OR: 0.31; 95%CI: 0.15–0.63, $p=0.002$) and mortality was improved by 2.22-fold (OR: 2.22; 95%CI: 1.07–4.67, $p=0.034$). In these participants, lenzilumab decreased CRP as early as Day 2 following treatment, compared with placebo which was further decreased by 38% on Day 28 compared with placebo (24.4 ± 3.4 mg/L vs 39.1 ± 4.9 mg/L).

Conclusion Lenzilumab significantly improved SWOV in hospitalized, hypoxic participants with COVID-19 pneumonia with the greatest benefits in SWOV and survival in patients with CRP<150 mg/L and age <85 years. Inhibition of GM-CSF, an orchestrator of CS, early in the hyperinflammatory response improved outcomes in COVID-19. NCT04351152

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A RANDOMISED CLINICAL TRIAL OF AZITHROMYCIN VERSUS STANDARD CARE IN AMBULATORY COVID-19 – THE ATOMIC2 TRIAL

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Background The antibacterial, anti-inflammatory and antiviral properties of azithromycin suggest therapeutic potential against COVID-19. Randomised data in mild-moderate disease are lacking. We assessed whether azithromycin is effective in reducing hospitalisation in patients with mild-moderate COVID-19.

Methods This open-label, randomised superiority clinical trial at 19 centres in the United Kingdom enrolled adults, ≥ 18 years, presenting to hospitals with clinically-diagnosed highly-probable or confirmed COVID-19 infection, with <14 days symptoms, considered suitable for initial ambulatory management. Patients were randomised (1:1) to azithromycin (500 mg daily orally for 14 days) or to standard care without macrolides. The primary outcome was the difference in proportion of participants with death or hospital admission from any

Abstract S50 Figure 1 Kaplan-Meier plot of time to hospitalisation in the ITT +ve population

cause over the 28 days from randomisation, assessed according to intention-to-treat (ITT). Trial registration: ClinicalTrials.gov, NCT04381962, Study closed.

Results 298 participants were enrolled from 3rd June 2020 to 29th January 2021. The primary outcome was assessed in 292 participants. The primary endpoint was not significantly different between the azithromycin and control groups (Adjusted OR 0.91 [95% CI 0.43–1.92], $p=0.80$).

Conclusions In patients with mild-moderate COVID-19 managed without hospital admission, adding azithromycin to standard care treatment did not reduce the risk of subsequent hospitalisation or death. Our findings do not support the use of azithromycin in patients with mild-moderate COVID-19.

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EVALUATION OF TREATMENT APPROACHES FOR HOSPITALIZED COVID-19 PATIENTS

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Background COVID-19 has driven innovation leading to emergency use authorization of treatments that address its urgent healthcare needs. However, physicians, payers and healthcare systems are challenged to select among these novel treatments for both effectiveness and value. Reliance on change in relative, rather than absolute, risk often makes discrimination of treatment effects between medications impractical, with potentially misleading conclusions. Number Needed to Treat (NNT), the reciprocal of the Absolute Risk Reduction, can be a valuable alternative in assessing benefit:risk. The objective of the current analysis was to calculate NNT for reported endpoints of COVID-19 treatments.

Methods Clinical information was captured from published literature and pre-prints from investigations of COVID-19 treatments. NNTs were calculated for reported endpoints. Outpatient treatments to reduce viral load included neutralizing antibody ‘cocktails’ REGN-COV2¹ and bamlanivimab/etesevimab.² Inpatient treatments included the anti-viral: remdesivir^{3,4}; and immune modulators: baricitinib⁵, and lenzilumab.⁶

Results REGN-COV2 reduced the number of medically attended visits with NNT of 33.3. The NNT for hospitalization or death was 20 for bamlanivimab/etesevimab. NNTs for 28-day mortality with inpatient treatment were 37 for baricitinib, 26.3 for remdesivir alone, and 22.7 for lenzilumab. Additional analyses of lenzilumab resulted in NNT of 14.7 when combined with remdesivir and corticosteroids, 15.4 when combined with remdesivir, and 13.9 in patients with baseline CRP<150mg/L and age<85 years. The NNT for lenzilumab to prevent survival without ventilation (SWOV) was 15.4 which, decreased to 6.4 in patients with baseline CRP<150mg/L and age<85 years. The number needed to prevent a serious adverse event was 20 for baricitinib, 15 for remdesivir, and 20.4 for lenzilumab.

Conclusion The NNT for COVID-19 treatments varied with setting, endpoint, and mechanism. The NNT for lenzilumab improved with refinement of concomitant medications and patient phenotype. NNT provides a simple measure for comparative analyses that helps inform clinical decision-making and resource allocation.

REFERENCES

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