To the Editor: Temesgen et al care-
fully depicted the clinical benefit pro-
vided by lenzilumab in cases of coronavirus disease 2019, sustained by the novel severe acute respiratory coronavirus 2 (SARS-CoV-2), where cytokine storm may lead to fatal multi-
organ failure. Lymphopenia is a typical finding occurring at early onset of the disease and lenzilumab administration showed a significant improvement in terms of lymphocyte count, which has not been fully understood by the investigators, suggesting that granulocyte-monocyte colony-stimu-
lating factor might have a direct impact on T cells.

SARS-CoV-2—related hyperin-
flammatory pattern resembles the cytokine release syndrome occurring in chimeric antigen receptor T cell therapy, where the host monocyte-
macrophage system is the major source of cytokine production (eg, interleukins 1 and 6). In this setting, lenzilumab was shown to be effective in reducing chimeric antigen recep-
tor T-cell—mediated cytokine release syndrome and neuroinflammation at the same time, enhancing adoptive T cell therapy as well.3

Previous preclinical data in SARS-
CoV—infected mice showed that in-
flammatory monocyte-macrophage response, secondary to dysregulated type-I interferon activity during SARS-CoV infection, results in lethal pneumonia and cytokine-induced apoptosis of T cells (specifically medi-
ated by tumor necrosis factor alpha).4

As already known, granulocyte-
monocyte colony-stimulating factor inhibition turned out to broadly modulate monocyte-macrophage ac-
tivity by simultaneously reducing a spectrum of inflammatory cytokines, including tumor necrosis factor alpha. We therefore suggest that the direct regulation of monocyte-
macrophage activity by lenzilumab, with subsequent broad cytokines shut-
down, could provide a more favorable micro-environment where effector T cells could also be protected from cytokine-induced apoptosis. This would preserve a non-exhausted T-cell phenotype, being more effective against infections and performing more potently T-cell specific antiviral immunity to achieve viral clearance.

Aware of the good safety profile of lenzilumab in this current study and previous analysis,1,3 the treatment is feasible and safe and the ongoing randomized phase III trial (NCT04351152) will extensively confirm the lymphocyte recovery in SARS-CoV-2 infection and the impact of the drug on the coronavirus disease 2019 clinical improvement.

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1. Temesgen Z, Assi M, Shweta FNU, et al. GM-CSF neutralization with lenzilumab in severe COVID-


2. Agrawal S, June CH. Harnessing CAR T-cell insights to develop treatments for hyperinflammatory re-


3. Sterner RM, Sakemura R, Cox JC, et al. GM-CSF inhibi-
tion reduces cytokine release syndrome and neuroinflammation but enhances CAR-T cell func-


SARS-CoV infection, results in lethal pneumonia in SARS-CoV—infected Mice. Cell Host Microbe.

5. Patriak MM, Salman DA, Manganikar AA, et al. Phase I study of lenzilumab, a recombinant anti-
human GM-CSF antibody, for chronic myelomonocy-


In Reply — Clinical Benefit of Lenzilumab in Cases of Coronavirus Disease 2019

To The Editor: We thank Dr Aroldi and colleagues for their letter in response to our manuscript “GM-
CSF Neutralization with Lenzilumab in Severe COVID-19 Pneumonia: A Case-Cohort Study.”1

We agree that lenzilumab may benefit patients with severe acute respira-

tory syndrome coronavirus 2 through modulation of monocyte-macrophage activity by reducing a spectrum of hyperinflammatory cytokines. We are also intrigued by the observation that lenzilumab may improve lymphocyte counts. Although the mechanism re-

mains to be elucidated in full, we have observed improved lymphocyte prolif-
eration and lymphocyte effector function in preclinical models with lenzilumab.2,3 We agree that modulation of the monocyte-macrophage ac-
tivity may provide a more favorable micro-environment for T cells resulting in reduced apoptosis.

We look forward to replicating the positive signal in clinical and labora-
tory markers as well as the excellent

Regulatory Information

Product Name: Lenzilumab

NCT04351152

ClinicalTrials.gov Identifier: NCT04351152

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safety profile of lenzilumab that we noted in our study in the ongoing randomized phase 3 clinical trial (NCT04351152). This phase 3 trial is now 80% enrolled and a recent interim analysis was favorable with lenzilumab showing clinical benefit over and above concomitant dexamethasone and remdesivir.4

We also look forward to results from the ACTIV-5/Big Effect Trial sponsored by the National Institutes of Health which will determine if the combination of lenzilumab and remdesivir is superior to remdesivir alone (NCT04583969). This trial is now actively enrolling patients.

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Neutralization of Fecal Aerosol-Laden SARS-CoV-2: Public Health Implications

To the Editor: The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents an unprecedented challenge to global health.1 The looming threat of socioeconomic collapse, livelihood, and human security needs to be intervened.2 Action taken to disrupt the pathways of viral transmission can have positive outcomes on the coronavirus disease 2019 disease burden.

The primary transmission route of the virion through respiratory aerosols is well documented.3 There is an emerging recognition of potential transmission of SARS-CoV-2 through aerosolization of virus-laden stools.4 Air sampling for SARS-CoV-2 in hospital toilets used by patients has yielded positive results.5,6 Recent studies reported the presence of SARS-CoV-2 viral RNA in fecal samples that were detected even after 22.3±29.8 (mean ± SD) days from diagnosis.7,8 Another review suggested that SARS-CoV-2 can be excreted in urine in addition to stool.9

The phylogenetically related severe acute respiratory syndrome coronavirus 1 transmission through fecal bioaerosols was well highlighted in the Amoy Garden residential complex incident in Hong Kong in 2003.10 This outbreak led to more than 300 confirmed cases and 50 fatalities.10,11 Clusters of fecal transmissions of SARS-CoV-2 are being reported in hospitals and high-rise apartments in China. Epidemiological investigations using tracer studies point toward passage of virus-laden fecal bioaerosols through exhaust fans and faulty sewage systems.12

With the exponential rise in world infection rates, such a transmission modality poses a potential risk for countries with high population densities. The lesser spatial separation of living spaces in concentrated areas presents a major risk for fecal aerosol infiltration. As evidence of transmission through lesser known pathways accumulates, innovative approaches may be needed.

In the November issue of Mayo Clinic Proceedings, McDermott et al13 suggested shutting the toilet lid while flushing, closing lavatory doors, staff education, adequate ventilation, better plumbing, and UV irradiation of circulating air for hospital infection control.14 These recommendations are salutary and can add to the efficacy of hospital infection control. We suggest an additional universally affordable option that could disinfect aerosols at its source, in the clinical as well as community settings.

Adding a household disinfectant (5% sodium hypochlorite [NaOCl]) in the water cistern of the flush tank could be useful. This step can be achieved by treating with sustained-release NaOCl tablets in addition to liquid bleach. Such treated water (reaching 1% NaOCl concentration) could lower the quantum of viable viral particles in the fecal aerosol generated during flushing. Sodium hypochlorite releasing free chlorine is suggested for inactivation of SARS-CoV-2 in residential and hospital wastewater treatment plants.15 Further studies are needed to test