nucleotide variants were found in the spike receptor-binding domain (RBD) and N-terminal domain (NTD), regions that have been associated with immune escape.[4] In contrast, no RBD or NTD mutations were found in Patient 1, who did not receive antibodies, or in Patients 4 and 5, who received convalescent plasma and had intact T-cell responses to SARS-CoV-2.

To assess whether viruses obtained from Patients 1, 2, and 3 had been neutralized by autologous serum, we constructed infectious pseudoviruses expressing variant spikes (Fig. S10). Serum from Patients 1, 2, and 3 did not neutralize pseudoviruses with variant spikes, even though serum from Patients 2 and 3 neutralized the reference pseudovirus (Fig. S11). Thus, spike mutations in Patients 2 and 3 conferred neutralization resistance to bamlanivimab.

Our results underscore the potential importance of selective pressures such as the use of monoclonal antibodies — in combination with the lack of an effective endogenous immune response — in promoting the emergence of SARS-CoV-2 escape mutations. These findings highlight the need to better understand the ramifications of different therapies in immunocompromised patients. Our results also corroborate the findings of previous studies in which patients with B-cell deficiencies were found to elicit effector T cells,[5] an outcome that may signal an important role for T cells in controlling infection.

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Shorter Treatment for Tuberculosis in Children

TO THE EDITOR: In the SHINE trial, Turkova and colleagues (March 10 issue)[1] report important findings about a shorter treatment regimen for nonsevere tuberculosis in African and Indian children under the age of 16 years. However, radiographs of the chest had 37% discordant interpretations at baseline, which suggests that many patients had atypical findings of nonsevere tuberculosis. Such atypical results may reflect the presence of other pathogens in addition to *Mycobacterium tuberculosis*. If this was the case, we need to consider the effect of these factors on the conclusions of this clinical trial. Of note, 75% of the patients in this trial were younger than 7 years old, so more data are needed with respect to older children.

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TO THE EDITOR: The article by Turkova et al. provides evidence for decreasing the duration of antituberculosis treatment in children with nonsevere tuberculosis. All the children initially received 2 months of standard therapy with isoniazid, rifampin, and pyrazinamide, with or without ethambutol according to local guidelines, during the intensive phase. This treatment was followed by standard therapy with isoniazid and rifampin in the continuation phase for either 2 months in the 4-month group (intervention) or 4 months in the 6-month group (control). Ethambutol was not administered during the continuation phase. In the Indian national program, the continuation phase includes ethambutol to prevent amplification of rifampin resistance in case of initial isoniazid resistance, which has been shown to occur in approximately 11% of newly diagnosed cases of tuberculosis and 25% of retreatment cases in India.[1] Before ethambutol is removed from the continuation phase, baseline information regarding isoniazid resistance as determined by line-probe assay is desirable. In the SHINE trial, 32% of the children had peripheral lymph-node tuberculosis, which should be monitored after treatment completion. Because the continuation phase aims to reduce the risk of relapse, a 2-year follow-up of the patients who received the shorter treatment regimen would be important for detecting relapse.

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THE AUTHORS REPLY: Chen suggests that discordant interpretation of chest radiography implies possible misdiagnosis of tuberculosis. In our trial, chest radiographs were centrally read by independent experts who had similar levels of expertise and experience and who did not have access to clinical data. Discordant imaging findings in pediatric tuberculosis are expected owing to a high variability in interpretation among readers, a well-recognized limitation.[1] Furthermore, the radiologic spectrum in pediatric tuberculosis is wide and includes normal chest radiographic findings and changes that are not typical for tuberculosis, even in microbiologically confirmed cases in which the diagnosis is certain.[2] The final adjudication of tuberculosis status in our trial was based on standard case definitions, with the use of the results of chest radiography along with contact history, clinical and microbiologic information, and response to treatment.[3]

Mishra and Mulani comment that a regimen for tuberculous lymphadenitis should include ethambutol in the continuation phase in settings with high isoniazid resistance. In our trial, unfavorable outcomes were infrequent in children with tuberculous lymphadenitis who received no ethambutol during the continuation phase. Furthermore, we found no evidence that ethambutol improved efficacy: an exploratory analysis showed similar proportions of unfavorable outcomes with and without ethambutol. In addition, in a pharmacokinetic substudy of the SHINE trial, we found low ethambutol levels across all weight categories.[4] The correspondents also suggest that 2-year follow-up is required to pick up late relapses of tuberculous lymphadenitis. Microbiologically confirmed relapses are rare in children with tuberculous lymphadenitis, and most cases of apparent worsening are related to a paradoxical reaction.[5] In our trial, of the 372 children with tuberculous lymphadenitis, 11 (3%) had an unfavorable outcome (5 in the 4-month group and 6 in the 6-month group), with no evidence of a between-group difference. We suggest that rather than extending follow-up, resources would be better invested in the education of patients and their caregivers to seek prompt medical review if tuberculosis symptoms recur, as outlined in the current World Health Organization guidelines.

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Since publication of their article, the authors report no further potential conflict of interest.

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Endovascular Therapy for Large Acute Strokes

TO THE EDITOR: Yoshimura et al. (April 7 issue)[1] report the results of a major trial investigating endovascular thrombectomy in patients with extensive strokes. The authors found a substantial treatment effect among patients who received endovascular therapy as compared with those who received medical care in this population (absolute difference of 18 percentage points in the percentage of patients with a modified Rankin scale score 0 through 3 [on a scale from 0 to 6, with higher scores indicating greater disability], with the results favoring endovascular treatment). In the trial, 86% of the patients were selected on the basis of findings on magnetic resonance imaging (MRI) (see Table 1 in the article). Moreover, only 28% of the patients received low-dose intravenous recombinant tissue plasminogen activator, even though 66% of patients arrived within 4.5 hours after symptom onset. This low ratio is not necessarily typical in other health care environments.[2] In addition, since the selection of patients for the treatment of acute stroke on the basis of findings on MRI is not standard in many stroke centers, it remains unclear how the results should be generalized into daily practice in other regions of the world. The size of the treatment effect is similar to that reported in the meta-analysis conducted by the HERMES (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials) trial group[3] and might influence the further progress of ongoing trials that are still based on clinical equipoise.[4,5]

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THE AUTHORS REPLY: The therapeutic doses of medications used in different countries, ethnic groups, and age groups often differ. Nevertheless, as Meyer and Broocks comment, the effect size observed in our trial was similar to the pooled effects of meta-analyses from Western countries. MRI is prioritized for the initial assessment of stroke in Japan because it allows for the evaluation of cerebral vessel occlusions without the use of contrast material and provides a fairly accurate demonstration of the size of an ischemic or infarcted area.[1] Although it is possible that with higher doses or higher rates of use of thrombolytic agents, cerebral arteries might have recanalized more effectively, it is also possible that an increase in the incidence of symptomatic intracranial hemorrhages might have been anticipated, leading to poor functional outcomes overall.[2] To clarify these issues, we are eager to see the results of ongoing trials that