Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Administration, US Department of Veterans Affairs. These data are available to approved individuals upon request after fulfilling specified requirements.

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Assessing the evidence on remdesivir

Remdesivir remains a controversial treatment for COVID-19.[1] ACTT-1 was an international study funded by the US National Institutes of Health that showed reduced time to recovery with remdesivir (its updated primary endpoint) and improvement on an eight-point ordinal scale (the original primary endpoint).[2] Mostly based on this trial, the US Food and Drug Administration (FDA) approved the emergency use of remdesivir for patients with COVID-19.[3] This decision was widely contested because of the paucity of clinically significant benefits on mortality. Afterwards, two additional, large clinical trials—WHO's Solidarity and the DisCoVeRy trial—showed a neutral effect on mortality without improvement in time to discharge.[1,4]

Hence, the question arises of which of these three trials we should listen to. Their study designs were essentially the same, but their circumstances were entirely different. The ACTT-1 preliminary report was published in May, 2020—before the RECOVERY trial reported that dexamethasone reduced mortality in patients hospitalised with COVID-19 in July, 2020.[2,5] Furthermore, it reported use of corticosteroids in only 23% of patients, with unknown indication.[2] By contrast, substantial parts of the study periods of the Solidarity and DisCoVeRy trials occurred after dexamethasone had become the standard of care. And although Solidarity mentions use of corticosteroids in almost 50% of participants (also without specification), DisCoVeRy mentions dexamethasone specifically and that almost 40% of participants received it.[1,4] Thus, it is reasonable to assume that a large proportion of the corticosteroids used in these trials were prescribed because of the results reported in RECOVERY, which was not the case for corticosteroid use in ACTT-1. Consequently, the standard of care was substantially different between ACTT-1 and Solidarity or DisCoVeRy. Because dexamethasone is now the standard of care, the treatment regimen of ACTT-1 is not compatible with the current treatment of patients admitted to hospital due to COVID-19.

In summary, the results of ACTT-1 are simply not applicable to present-day standard of care and Solidarity and DisCoVeRy should be given more weight when considering the addition of remdesivir to the treatment of patients in hospital due to COVID-19.

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We read with interest the Comment by Iwein Gyselinck and Wim Janssens concerning the recently published DisCoVeRy trial,[1,2] which concluded that given current evidence there is no reason to advocate remdesivir use outside clinical trials. Although we largely agree, the question remains whether there is still a need for additional trials, or whether already published and existing data are sufficient to conclude this.

At present, remdesivir has been tested in five large randomised trials in hospitalised patients.[1] With the exception of the ACTT-1 trial, which reported reduced time to recovery in patients with moderate COVID-19 and a median of 9 days between symptom onset and randomisation, most trials have failed to show significant benefit in mortality or disease progression.[1] Additionally, trials that evaluated viral endpoints did not find any effect on viral clearance with remdesivir.[2–4] Notably, median time from symptom onset to randomisation was relatively long in most published trials. Treatment initiation at the tail of the viral phase could explain the lack of effect on viral clearance, and possibly the limited clinical effect.[1]

Hence, testing remdesivir earlier in the disease course could be more relevant, and unpublished results from the PINETREE trial reported an 87% risk reduction for hospitalisation or death with a 3-day course of remdesivir compared with placebo.[5] However, with the encouraging preliminary results of oral molnupiravir from the MOVe-OUT trial (NCT04575597), oral antivirals might be the preferred treatment option for outpatients, making intravenous alternatives less attractive.

Remdesivir could also be a candidate drug for carefully selected hospitalised patients, since the RECOVERY trial showed a survival benefit of the monoclonal antibody cocktail REGN-COV2 in seronegative patients.[5] In seronegative individuals and immunocompromised patients in general, head-to-head comparisons between remdesivir and antiviral monoclonal antibodies could be an option. However, with emerging variants, testing combinations of monoclonal antibodies and other antivirals, including remdesivir, could be even more relevant, given the demonstrated effect of each compound.

Before moving ahead with new trials, it should be noted that the final report from the Solidarity trial is yet to be published. In our view, there is now an urgent need for an individual-level meta-analysis based on existing trials, including consolidated data from the Solidarity trial. Such a meta-analysis is planned and will hopefully clarify the role of remdesivir in hospitalised patients and help identify the potential need for additional trials.

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Clindamycin-resistant *Streptococcus pyogenes* in Chinese children

The Correspondence by Bryan White and Emily Siegrist[1] about clindamycin-resistant group A streptococcal infection attracted much attention in the USA. White and Siegrist argued that although the findings from some studies suggest a decrease in mortality from group A streptococcal infections in the USA, serious infections caused by clindamycin non-susceptible invasive group A streptococcus are increasing due to expansion of several *emm* types.[2] Therefore, we hope to provide some information about clindamycin-resistant group A streptococcus in China to compare its prevalence in different areas.

First, unlike in the USA and other countries and regions, the resurgence of group A streptococcal infection in China is mainly manifested in non-invasive group A streptococcal infections. Rheumatic fever rarely occurs. Next, in China, the resistance rate of group A streptococcus against clindamycin and macrolides in both adults and children has been very high since the 1990s but has varied by geographical location and time period (appendix). Chinese isolates mainly harbour the *ermB* resistance gene, with the constitutive macrolide, lincosamide, and streptogramin B ($cMLS_B$) resistance phenotypes. In China, clindamycin was not thought to be an appropriate medical intervention.

See **Online** for appendix

Finally, the high rate of resistance to clindamycin cannot be attributed to its clinical use because clindamycin was rarely used in paediatric patients in Western Pacific countries (including China).[3] Previous studies also suggested cross-resistance between clindamycin and erythromycin.[4] Cross-resistance to $cMLS_B$ antibiotics is mainly mediated by the *erm* genes, and various mechanisms are involved in streptogramin B resistance.[5]

In view of the existing data, there is high resistance to clindamycin and macrolides such as erythromycin; therefore, these treatments should not be recommended as an adjuvant treatment for children with β-lactam antibiotic allergy and group A streptococcal infection in China.

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