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.

We declare no competing interests.

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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]