Remdesivir in COVID-19 Patients with Impaired Renal Function

In their perspective, Adamsick et al. argue that, on the basis of its known pharmacokinetics, a 5-day course of remdesivir in patients with an eGFR of <30 ml/min per 1.73 m² should be considered safe. Therefore, in their opinion, patients with coronavirus disease 2019 (COVID-19) who have impaired renal function should be offered remdesivir treatment, because this is a potentially life-saving treatment for such a vulnerable population.

We agree with the authors that accumulation of the carrier sulfobutylether-β-cyclodextrin is likely to be of no concern because there is clinical experience with other agents, such as voriconazole. However, with respect to remdesivir and its metabolite GS-441524, to our knowledge, there are no human data to claim its safety in people with impaired renal function because they were excluded from the clinical trials. It should be emphasized that, in repeat-dose toxicity studies in rats and monkeys, the kidney (i.e., tubular epithelium) was identified as the primary target organ of remdesivir toxicity. Furthermore, although remdesivir exhibits low renal excretion as an intact drug (<10% of the administered dose), 49% was recovered as GS-441524, and a total of 74% of a radiolabeled dose was recovered in urine. Not surprisingly, a recent pharmacokinetic study showed higher GS-441524 levels in a patient with renal dysfunction. Apparently, because GS-441524 will be removed by hemodialysis, toxicity of remdesivir or its metabolite will not be an issue in patients who are already on hemodialysis. In contrast, in patients with COVID-19 and CKD, it cannot be excluded that remdesivir treatment might lead to an urgent need for RRT, and that remdesivir in this patient population might even have a negative risk-benefit ratio. The recent signal on potential renal side effects of remdesivir also holds concern about its use in patients with CKD.

Therefore, we would like to discourage remdesivir as routine treatment in patients with COVID-19 and CKD (eGFR of <30 ml/min per 1.73 m²). Its use should be reserved to the context of clinical trials to improve our knowledge on safety and efficacy.

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REFERENCES


See related reply, “Authors’ Reply,” on pages xxx-xxx, and original perspective article, “Remdesivir in Patients with Acute or Chronic Kidney,” in Vol. 31, Iss. 7, on pages xxx-xxx.

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