



Severe sinus bradycardia associated with remdesivir in a child with severe SARS-COV-2 infection—reply

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Dear Editor:

We would like to thank Sanchez-Codez et al. for their comments regarding our article. The authors report the development of a mild sinus bradycardia in a child on remdesivir therapy (RDV), assumed to be an adverse effect of the drug.

As discussed previously in our article [1], clinical trials for children with COVID-19 are urgently needed to assess the drug's safety. About 2119 patients have currently received the drug in large controlled clinical trials [2–5], with detailed reporting of adverse effects. However, none of these trials included young children. Sinus bradycardia was reported in one patient (0.04%) [2–4]. Wang et al. reported cardiac side effects significantly less often in patients receiving RDV (9/155; 5.8%) than in patients under placebo (11/78; 14.8%) [2]. Berger et al. reported a similar rate of cardiac adverse effects in the RDV group and in the control group, respectively [3]. Kalil et al. treated up to 1033 patients with RDV, observing cardiac side effects in 24 patients (2.3%) [4]. However, a considerable number of patients presented with

underlying cardiovascular diseases received concomitant medications and/or presented other comorbidities [2–5]. In addition, SARS-CoV-2 may directly cause myocardial damage by entering cardiomyocytes via the ACE2 receptor, due to cytokine storm, or as a result of hypoxemia [6].

Limited data are available regarding the occurrence of arrhythmias in children with COVID-19. Some small series have reported arrhythmias in up to 16% of children admitted with SARS-COV-2, almost all of them not treated with RDV. These arrhythmias were mild or less harmful than the ones reported in adults [6]. For these reasons, establishing RDV as the certain/probable cause of the reported bradycardia cannot be concluded.

Sporadic case reports or small series of children with COVID-19 and underlying cardiac disease have been published previously [6, 7]. Four out of the 28 reported children died (14%), and many presented with acute decompensation of their underlying condition [6, 7].

Electrocardiographic monitoring should be performed in all admitted children with COVID-19, especially if they are receiving compassionate treatments or have a cardiac underlying condition, until more data become available.

Author contributions Ana Mendez Echevarria and Kinga Amalia Sandor-Bajusz wrote the initial reply, and Cristina Calvo reviewed the definitive manuscript. KingaAmalia Sandor-Bajusz reviewed the english language.

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Compliance with ethical standards

Conflict of interest The corresponding author (Ana Mendez-Echevarria) is the principal investigator in La Paz Hospital of the Clinical Trial GS-US-540-5823 (Promoter: GILEAD®). The corresponding author has been part of the Advisory Board COVID-19 of GILEAD®. The rest of the authors (Kinga-Amalia Sándor-Bajusz and Cristina Calvo) have no conflict of interest to declare.

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