TITLE PAGE Title: Remdesivir could promote the occurrence of SARS-CoV-2 variants Author list: Philippe COLSON¹, Christian A. DEVAUX¹, Didier RAOULT¹* Affiliations: ¹ IHU Méditerranée Infection, Aix-Marseille Univ., Institut de Recherche pour le Développement (IRD), Assistance Publique - Hôpitaux de Marseille (AP-HM), Microbes Evolution Phylogeny and Infections (MEPHI), 19-21 boulevard Jean Moulin, 13005 Marseille, France. * Corresponding author: Didier RAOULT, IHU - Méditerranée Infection, 19-21 boulevard Jean Moulin, 13005 Marseille, France. Tel.: +33 413 732 401, Fax: +33 413 732 402; email: didier.raoult@gmail.com **Key words:** SARS-CoV-2; Covid-19; Remdesivir; variant; mutants Word counts: 175

TEXT

We read with interest Rubin et al.'s article that endorses Remdesivir approval by FDA. ¹ It
shortly follows a report on the occurrence of SARS-CoV-2 mutants in an immunosuppressed
patient who received four Remdesivir courses ² , which from our viewpoint should have
warranted two comments. The first is that this case is a quasi-experimental demonstration that
Remdesivir has no effect on viral carriage in immunosuppressed patients. The second
comment questions the direct role of Remdesivir in the rapidity of occurrence of mutations in
viral spike protein that binds the host cellular receptor and is a major target of host immune
response. There is at least another observation ³ that supports the hypothesis that Remdesivir
associated with convalescent plasma or monoclonal antibodies could promote the emergence
of viral variants with a mutated spike. Practically, it appears important to have a message
around Remdesivir, which efficacy was not recognized by the WHO
(https://www.who.int/news-room/feature-stories/detail/who-recommends-against-the-use-of-detail/who-recommends-agains-agai
remdesivir-in-covid-19-patients) and which potentially presents the risk of determining
SARS-CoV-2 mutations that could trigger new epidemics, as it could have been the case with
the VOC-202012/01 variant in England. ⁴

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