Indian perspective of remdesivir: A promising COVID-19 drug

Sir,

Today, we are at war against an unprecedented pandemic of COVID-19, a highly contagious disease caused by a novel severe acute respiratory syndrome (SARS) coronavirus-2. It is a large family of RNA viruses that has already caused two similar diseases in the last two decades such as SARS pandemic in 2003 and outbreak in Middle East respiratory syndrome (MERS) in 2012.[1] According to the WHO, worldwide, there are more than 53 lakhs reported cases with more than 3.4 lakhs deaths as of May 25, 2020. In India, it has spread to all states with positive cases reaching to 1.45 lakhs with 4167 deaths.

Remdesivir, a nucleoside analog, is an investigational broad-spectrum antiviral drug. It was originally found by Gilead Sciences, a pharmaceutical company while targeting hepatitis-C, but remdesivir showed a potent activity against Ebola and MERS later. After COVID-19 outbreak, remdesivir was found to be effective against COVID-19 in vitro, but did not show significant clinical improvement in critically ill patients according to the study published in the lancet. Meanwhile, on May 1, remdesivir became the ray of hope when the US-Food and Drug Administration (FDA) granted emergency use authorization after preliminary results of NIAID sponsored clinical trial with remdesivir showed 31% faster recovery time (11 days vs. 15 days in placebo) and decrease in mortality.[2]

In India, despite all the proactive measures by central and state governments such as lockdown and social distancing, the COVID-19-positive cases continue to increase. Hence, with recent positive development with remdesivir, we need to be ready with measures to make sure the availability of remdesivir to such a huge population at affordable price.

Once the remdesivir gets necessary regulatory approval, the production and pricing becomes an important issue as Gilead Sciences hold the patent till 2035 in India. Further, according to Gilead Sciences, worldwide, they are capable of delivering maximum of 10 lakhs treatment courses by December 2020. However, as a sign of relief, last week, Gilead Sciences had entered into a nonexclusive license agreement with four Indian generic pharmaceuticals, including Cipla Ltd., Jubilant Life Sciences, Hetero Labs Ltd., and Mylan, thus enabling them to scale up production and also set their own prices.[3]

However, even after nonexclusive license, there are speculations that the price may not be affordable to a country like us. Hence, in such cases, according to Indian Patent Act 1970, regardless of the patent to Gilead Sciences, Government of India holds the power to issue compulsory license to other Indian pharmaceutical companies for production and sale of the drug.[4]

In India, remdesivir as a new drug must undergo clinical trial before getting marketing approval. However, if it gets approved by the US-FDA, according to the Clinical Trial Rules-2019, DCGI reserves the right to issue local clinical trial waiver in special circumstances with a close watch on its safety. Recently, two Indian pharmaceutical companies, Cipla and Hetero Labs Ltd., have sought clinical trial waiver from DCGI. However, the policy of compassionate use of drugs in India is also being developed. ICMR, AIIMS, CDSCO, and other stakeholders already had three rounds of brain storming sessions.

Since limited safety/toxicity data of remdesivir are available in COVID-19 patients, a robust pharmacovigilance will be mandatory. Pharmacokinetics of remdesivir has not been assessed in patients with renal, hepatic impairment and geriatric patients over 65 years with COVID-19. Further, transaminase elevation has been observed during clinical development with mechanism unknown. The FDA recommends determination of estimated glomerular filtration rate before dosing remdesivir, because sulfobutylether-β-cyclodextrin sodium used as an excipient accumulates in decreased renal function.[5] Suspected adverse drug reaction associated with remdesivir can be reported as usual by any health-care worker or the patient by calling at Pharmacovigilance Program of India toll free number 1800-180-3024.

To conclude, looking at the disease that killed more than 3 lakhs people and US-FDA has given emergency use authorization based on preliminary results showing it superior to placebo, remdesivir seems to be strong candidate. Further, results of ongoing trial will provide much needed clarity in near future. Meanwhile, India
Letter to the Editor

has to plan accordingly focusing on its availability, affordability, and safety for Indian population, till then we should use what best we have.

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