Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Virological cure, clinical efficacy and safety of Remdesivir supplementation against SARS-CoV 2 infection; evidence from human studies

Cure virologique, efficacité clinique et sécurité de la supplémentation en Remdesivir contre l'infection par le SRAS-CoV 2 ; preuves issues d'études sur l'homme

Dear Editor,

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV 2) is a novel beta-coronavirus which emerged in December 2019 in Wuhan, Hubei Province, China [1]. The Chinese health community confirmed that the novel coronavirus was the causative agents of a severe form of viral pneumonia, named 2019-nCoV in January 2020 [1,2]. In recent months, cases of COVID-19 (coronavirus disease 2019) were reported in at least 21 countries. Therefore, the WHO declared a pandemic in March 2020 [1,3]. The majority of humans infected with COVID-19 have respiratory illness which, in 5% of cases, develops into critical illness due to acute respiratory distress syndrome and respiratory failure [4].

There is no selective treatment for COVID-19, while the number of cases has reached 11,000,000 worldwide [5]. Remdesivir

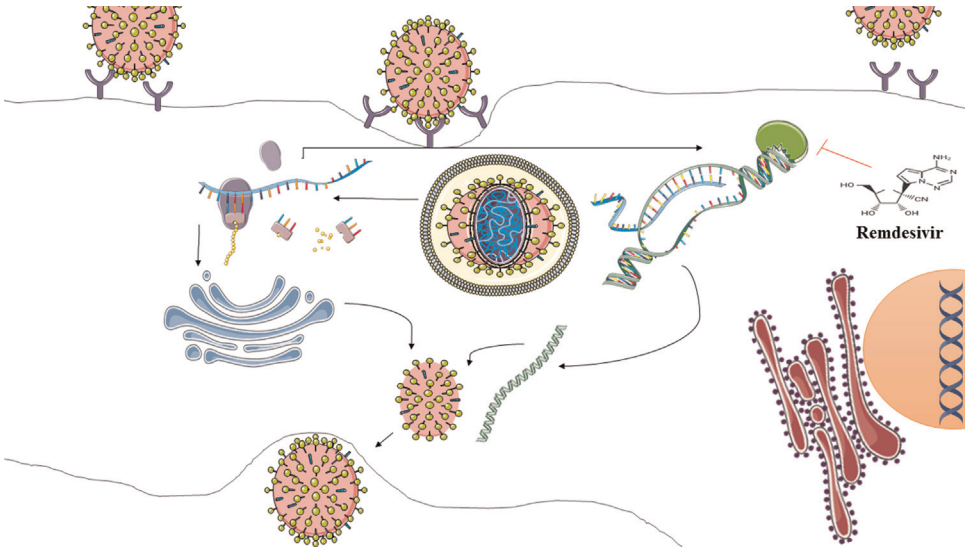

FIGURE 1

Remdesivir mechanism of action against SARS-CoV 2Mécanisme d'action du Remdesivir contre le SRAS-CoV 2

TABLE I

Characteristic of studies included.

Caractéristiques des études incluses.

First author	Location	Sample size	Mean age	Dosages of remdesivir	Weaning mechanical ventilation (%)	Death	Adverse event	Ref
Holshue et al.	USA	1	35	NR dosage for 7 days	100%	0	0	17
Kujawski et al.	USA	12	53	NR	100%	0	NA	18
Lescure et al.	France	5	53	200 mg of on da y 1 followed by 100 mg daily for 9 days	33.3%	0	30%	19
Hillaketer et al.	USA	1	40	200 mg of on day 1 followed by 100 mg daily for 9 days	100%	0	0	20
Grien et al.	USA	53	64	200 mg of on day 1 followed by 100 mg daily for 9 days	67.92%	7	60%	16
Wang et al.	China	236	65	200 mg of on day 1 followed by 100 mg daily for 9 days	65% in cases 58% in controls	15 in cases 7 in control	17%	15
Biegel et al.	Worldwide	1069	58.9	200 mg of on day 1 followed by 100 mg daily for 9 days	NR	32 in cases 54 in controls	48.1%	21
Goldman et al.	Worldwide	397	61.5	200 mg of on day 1 followed by 100 mg daily for 9/4 days	64% in cases 54% in controls	16 in cases 21 in controls	14%	22

NR: not reported.

(GS-5734) is a monophosphoramidate prodrug which is a nucleoside analogue of adenosine triphosphate, initially developed to treat Ebola (filovirus) infection, but which shows, both in vitro and in vivo, inhibitory efficacy against paramyxoviruses, pneumoviruses and beta-coronaviruses (SARS-CoV 1 and MERS-CoV) [6–9]. In addition, Pizzorno et al. showed that Remdesivir has inhibitory effects on SARS-CoV-2 replication in human nasal and bronchial epithelial cells [10], and Williamson et al. confirmed potential inhibitory effects of SARS-CoV 2 in a rhesus macaque model (*figure 1*) [11].

Numerous studies investigated the therapeutic effects of Remdesivir against SARS-CoV 2 [12–14]. The FDA confirmed efficacy in the US [13,14], but clinical findings are controversial [15,16].

The aim of the present study was to assess the clinical efficacy and safety of Remdesivir in the treatment of COVID-19 patients, using human studies.

We performed a search of the PubMed, Scopus, Cochrane library, Google Scholar, medRxiv and bioRxiv databases to obtain articles on the efficacy of Remdesivir in COVID-19. A systematic search was conducted up to July 2020 using MeSH terms such as "2019 novel coronavirus", "2019-nCoV", "COVID-19", "coronavirus disease 2019", and "Remdesivir". The title and abstract of retrieved articles were evaluated for relevance, and potentially relevant articles were reviewed in full-text to extract information on (1) first author, (2) country, (3) sample size, (4) mean age, (5) mortality, (6) number of adverse events, (7) Remdesivir doses, (8) the percentage of mechanically ventilated patients, and (9) number of references (*Table I*).

Data on virological cure (virus clearance on RT-PCR), improvement, hospital discharge, adverse events and death were used to measure event rates with 95% confidence intervals. We also calculated recovery time and the clinical efficacy of Remdesivir from randomized clinical trial documents using Comprehensive Meta-Analysis (CMA) software version 2.2 (Biostat, Englewood, NJ, USA). For pooled data, odds ratios were calculated by a random effects model, based on the Dersimonian and Laird method for high heterogeneity between studies, including I^2 index > 25% and Cochran Q test *P*-value > 0.05. A fixed-effects model was used for low heterogeneity cases. In addition, Egger's regression model and Begg and Mazumdar rank correlation were used to determine publication bias [17].

We screened 76 records identified in the databases. After excluding 68 inappropriate articles, 8 articles, for 1774 patients, were included for analysis [18–22]. The efficacy of Remdesivir supplementation on oxygen saturation in COVID-19 patients and discharged patients was 55.3% (95% CI, 51.3–59.3%; *P*-value: 0.01; *Q*-value: 23.64; I^2: 78.85; Beggs *P*-value: 0.50; Eggers *P*-value: 0.32) and 59.1% (95% CI, 56–62.2%; *P*-value: 0.01; *Q*-value: 12.08; I^2: 58.61; Beggs *P*-value:0.35; Eggers *P*-value: 0.23) respectively. Adverse event and mortality rates in COVID-19 patients treated by Remdesivir were 46.3% (95% CI, 43.2–49.4%; *p*-value: 0.02; *Q*-value: 257.95; I^2: 97.64; Beggs *P*-value: 0.50; Eggers *P*-value: 0.46) and 8.2% (95% CI, 6.7–9.9%; *P*-value: 0.001; *Q*-value: 7.00; I^2: 14.30; Beggs *P*-value: 0.50; Eggers *P*-value: 0.28). Remdesivir supplementation was associated with a high rate of virological cure (viral clearance from sterile samples) of 90.9% (95% CI, 64.6–98.2%; *P*-value: 0.008; *Q*-value: 0.69; I^2: 0.00; Beggs *P*-value: 0.14; Eggers *P*-value: 0.046). It thus seemed that Remdesivir is an appropriate therapeutic agent for the treatment of COVID-19 patients.

In the next step, we evaluated the clinical efficacy and safety of Remdesivir in human clinical trials. A total of 1295 patients were included: 696 receiving Remdesivir and 599 placebo (control). Remdesivir significantly improved COVID-19 patients compared to placebo (odds ratio: 1.85; 95% CI, 1.47–2.31; *P*-value: 0.001; *Q*-value: 1.32; I^2: 24.50). Time to recovery was significantly shorter (OR: 1.14; 95% CI, 1.01–1.30; *P*-value: 0.034; *Q*-value: 11.42; I^2: 82.49; Beggs *P*-value: 0.50; and Eggers *P*-value: 0.034). There was no significant difference in adverse event rate (OR: 0.77; 95% CI, 0.60–0.99; *P*-value: 0.049; *Q*-value: 1.12; I^2: 10.84) or mortality (OR: 0.62; 95% CI, 0.41–0.93; *P*-value: 0.02; *Q*-value: 1.55; I^2: 35.75).

Overall, we showed that Remdesivir was an efficient therapeutic agent against SARS-CoV 2; particularly, time to recovery was reduced compared placebo. Recently, after the first trials on 1,061 COVID-19 patients treated by Remdesivir, the NIH concluded that Remdesivir has clinical benefit for treatment and shortens time to recovery in SARS-CoV2 patients [23]. However, there remain 30 trials registered in the ClinicalTrials.gov database which need to enroll patients. In addition, there is bias in the current completed trials on the efficacy of Remdesivir against COVID-19; for example, Chinese trials investigated more severe COVID-19 patients; there is diversity in patient enrolment and in end-points; there are no control groups in case reports which investigated the efficacy of Remdesivir for COVID-19; and some trials showed no significant difference between Remdesivir and placebo groups [15,16,24].

The present analysis confirmed the clinical benefit of Remdesivir in COVID-19 patients. Several other studies led to a green light: (1) the FDA recommended the use of Remdesivir on May 2 following the open-label multicenter study in 53 patient by Grein et al. [16]; (2) the FDA gave a green light for Remdesivir following the randomized controlled study of more than 1000 hospitalized patients by Beigel et al. [25]; (3) the European Medicines Agency gave market authorization for Remdesivir on June 25; and (4) the French ANSM drug safety agency granted Remdesivir a temporary use authorization (ATU) on July 2 for adults and children over 12 years old. Nevertheless, there were several limitations in the current analysis: (1) a small number of studies, (2) small sample size, (3) patient enrollment issues, and (4) heterogeneity between studies impairing reliability. The present study showed the efficacy of Remdesivir for the treatment of COVID-19 in terms of shortening time to recovery. However, there are few studies, and randomized clinical trials take time; there is finally no convincing evidence of beneficial results of Remdesivir for the treatment of COVID-19 patients, and more trials with a greater number of patients are needed to confirm the present findings and suggestions.

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Masoud Keikha: supervision, data analysis, revising and editing manuscript.

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Can Curcumin be used as a therapeutic agent to eradicate *Helicobacter pylori* infection? Evidence from human clinical trials

La curcumine peut-elle être utilisée comme agent thérapeutique pour éradiquer une infection à Helicobacter pylori ? Preuves issues d'essais cliniques sur l'homme

Helicobacter pylori (*H. pylori*) is a gram-negative, microaerophilic, and spiral form bacterium that colonizes in the gastric sub-mucus of about half of the world's population, such that they are infected with this bacterium at childhood in the developing countries, and nearly 100% of the population in these regions is infected with *H. pylori* [1,2]. The *H. pylori*-infected populations often remain asymptomatic, while *H. pylori*-related gastrointestinal diseases i.e. peptic ulcer and gastric adenocarcinoma are seen in 10-15% of people [2,3]. Therefore, eradication of *H. pylori* infection is an important strategy for the prevention of peptic ulcer and gastric cancer (GC) [4]. However, the eradication of *H. pylori* infection has been a major challenge in recent years due to the spread of antibiotic resistance, and also the misuse, side effects, high cost of antibiotics, as well as the lack of vaccines [4–6]. Herbal