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Evaluation of the efficacy of sofosbuvir plus daclatasvir in combination with ribavirin for hospitalized COVID-19 patients with moderate disease compared with standard care: a single-centre, randomized controlled trial

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Background: New therapeutic options are urgently needed to tackle the novel coronavirus disease 2019 (COVID-19). Repurposing existing pharmaceuticals provides an immediate treatment opportunity. We assessed the efficacy of sofosbuvir and daclatasvir with ribavirin for treating patients with COVID-19.

Methods: This was a single-centre, randomized controlled trial in adults with moderate COVID-19 admitted to the Ghaem Shahr Razi Hospital in Mazandaran Province, Iran. Patients were randomly assigned to 400 mg sofosbuvir, 60 mg daclatasvir and 1200 mg ribavirin (intervention group) or to standard care (control group). The primary endpoint of this study was length of hospital stay. This study is registered by IRCT.ir under the ID: IRCT20200328046886N1.

Results: Between 20 March 2020 and 8 April 2020, 48 patients were recruited; 24 patients were randomly assigned to the intervention group and 24 to the control group. The median duration of hospital stay was 6 days in both groups ($P = 0.398$). The number of ICU admissions in the sofosbuvir/daclatasvir/ribavirin group was not significantly lower than the control group (0 versus 4, $P = 0.109$). There was no difference in the number of deaths between the groups (0 versus 3, $P = 0.234$). The cumulative incidence of recovery was higher in the sofosbuvir/daclatasvir/ribavirin arm (Gray's $P = 0.033$).

Conclusions: This randomized trial was too small to make definitive conclusions. There were trends in favour of the sofosbuvir/daclatasvir/ribavirin arm for recovery and lower death rates. However, there was an imbalance in the baseline characteristics between the arms. Larger randomized trials should be conducted to investigate this treatment further.

Introduction

The novel coronavirus (COVID-19) epidemic, which began in early December 2019 in Wuhan, China,[1,2] has spread to most countries in the world and has led to a catastrophic burden on healthcare systems. The first confirmed case of the disease in Iran was reported from Qom city on 19 February 2020[3] and the disease has now been confirmed in all provinces of the country. According to the WHO, confirmed cases to date (29 May 2020) exceeded

146 000 in Iran, with more than 7600 deaths.[4] Unfortunately, therapeutic options thought to be effective have been proven otherwise one by one.[5–8] New options are needed urgently, but require time to develop. Repurposing existing pharmaceuticals provides an immediate treatment opportunity. Current trials include remdesivir, hydroxychloroquine, chloroquine, favipiravir, lopinavir/ritonavir and nitazoxanide;[9] however, with the possible exception of remdesivir,[8,10] these drugs have not shown efficacy in treating patients with COVID-19.

The once-daily combination of sofosbuvir and daclatasvir has demonstrated success as treatment for HCV.[11,12] The combination has since been added to the Essential Medicines List in 2015 and has been made accessible worldwide in generic formulations.[13] A generic fixed dose combination of sofosbuvir and daclatasvir (400/60 mg, respectively) is used to treat HCV in Iran and therefore is a pragmatic candidate for trial against COVID-19.

Sofosbuvir has a broad antiviral spectrum including other members of the Flaviviridae and Togaviridae families including yellow fever,[14] Zika,[15] dengue[16] and chikungunya viruses.[17]COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a positive-sense RNA virus. SARS-CoV-2 shares a similar replication mechanism with other RNA viruses, requiring enzymes including RNA-dependent polymerase (RdRp), main protease (M^{pro}), helicase and other non-structural proteins, which therefore act as attractive targets to model antiviral drugs against.[18] *In silico* studies have predicted that sofosbuvir, daclatasvir and ribavirin may bind with high energy to the SARS-CoV-2 RdRp enzyme and M^{pro} and inhibit their function.[19–25] Some *in vitro* studies did not find sofosbuvir or ribavirin to be effective at reducing SARS-CoV-2-induced cellular death at feasible concentrations.[24,26] However, in a more recent *in vitro* study, the effects of sofosbuvir, daclatasvir and ribavirin in inhibiting replication of infectious SARS-CoV-2 virus particles were studied in three different cell lines. Daclatasvir was consistently able to inhibit the virus in all tested cell lines whilst sofosbuvir and ribavirin were less effective and only worked in certain cell lines.[25]

Sofosbuvir and daclatasvir have demonstrated good safety profiles with minimal drug interactions[27,28] and may be an affordable and widely available treatment option for COVID-19.[29] We therefore conducted a randomized controlled trial in adult patients hospitalized with COVID-19 in Ghaem Shahr Razi Hospital to evaluate the efficacy and safety of sofosbuvir and daclatasvir in combination with ribavirin compared with standard care.

Methods

Study design and participants

This study was a single-centre, randomized clinical trial to evaluate the effectiveness of sofosbuvir/daclatasvir with ribavirin against controls who received standard of care for COVID-19 at the time of the study. The study population were patients suspected of having COVID-19 who were referred to Ghaem Shahr Razi Hospital in Mazandaran Province between 20 March 2020 and 8 April 2020. Patients with initial symptoms of fever (oral temperature $\geq$37.8°C at least once before enrolment) and/or cough, shortness of breath and gastrointestinal symptoms were considered to be suspected of having COVID-19. To confirm COVID-19 infection, a positive qualitative RT–PCR for SARS-CoV-2 and/or features consistent with COVID-19 on a chest CT scan was required.[30] Cases of confirmed COVID-19 in the age group of 18–80 years were included. Only patients with moderate disease on admission were included, which was defined as respiratory rate of <24/min, arterial O_2 saturation of >94% and symptom onset $\leq$8 days prior to admission, together with compatible findings in a chest CT scan.[30]

Patients with multiorgan failure, active cancer, renal insufficiency (creatine clearance less than 50 mL/min/1.73 m^2), anaemia (haemoglobin less than 9 g/dL), pregnant women or men with a pregnant wife, and patients treated with amiodarone, phenytoin, phenobarbital, rifabutin or carbamazepine were excluded. All patients were required to provide written informed consent prior to participation in the study.

Randomization and masking

Once patients fulfilled inclusion and exclusion criteria and signed the consent form, they were randomly assigned to each treatment arm in a 1:1 ratio by block randomization and a block size of 4. Sealed envelope online software was used to randomize patients to the intervention and control groups. The study was open label and patients and managing physicians were not blind to patient allocation.

Procedures

After randomization, the intervention group received the combined single-pill once-daily regimen of sofosbuvir/daclatasvir at a dose of 400/60 mg (Sovodak, Fanavaran Rojan Mohaghegh Daru Co, Tehran, Iran) and ribavirin 600 mg twice daily. The control group received hydroxychloroquine (400 mg single dose) and lopinavir/ritonavir (400/100 mg twice daily), with or without ribavirin (600 mg twice daily), according to the national recommendation at the time of the study.

Clinical and laboratory monitoring

Demographic, clinical, radiological and laboratory data of patients were collected at baseline.

Outcomes

The primary outcome of the study was length of hospital stay. Secondary outcomes included the frequency of ICU admission, invasive mechanical ventilation, duration of ICU admission, mechanical ventilation and, finally, the frequency and time to recovery, defined as hospital discharge alive.

Statistical analysis

Reducing the length of hospital stay by 4 days was considered to be the desired outcome of this study. At 90% power and a 4 day difference in hospitalization length between the two groups, the calculated sample size equalled 24 in each group (corrected for 10% attrition rate). The outcomes of this study were analysed in the ITT population of randomized patients.

Comparison between the two groups was performed by a Mann–Whitney *U*-test for continuous outcomes and Fisher's exact test for categorical outcomes. Time to recovery was compared by graphically plotting the cause-specific cumulative incidence functions (CIFs) by treatment group; difference between groups was evaluated by Gray's test for the equality of CIFs. Adjustment for baseline characteristics was carried out using Cox Proportional Hazards and competing risks regression models [see Table S1 (available as Supplementary data at *JAC* Online)]. A *P* value was considered statistically significant at the $P < 0.05$ threshold. Statistical analysis was performed using STATA (version 16.0; StataCorp) and R software (version 3.6.3; R Foundation).

Ethics approval

The study protocol was approved by the institutional review board and ethics committee of Mazandaran University of Medical Sciences (approval

number: IR.MAZUMS.REC.1399.019). This study is registered by IRCT.ir (ID: IRCT20200328046886N1), accessible at https://www.irct.ir/trial/46885.

Results

Between 20 March 2020 and 8 April 2020, 195 patients were screened and 48 patients met the enrolment criteria and were recruited and randomized to the intervention arm ($n = 24$) or the control arm ($n = 24$, Figure 1). The median age (years) of participants in the sofosbuvir/daclatasvir group was 45 (IQR 38–69) and in the control group was 60 (IQR 48–69). A total of 18 patients were men (38%) versus 30 (63%) women (Table 1). Overall, 30 patients (63%) had existing comorbidities, which were most commonly diabetes and hypertension. The median time to admission from symptom onset was 5 days for both groups (IQR 4–5). The age, sex and baseline characteristics were generally similar between the two groups (Table 1); however, the control arm was on average 15 years older ($P = 0.158$) and had higher rates of diabetes ($P = 0.006$) and slightly higher rates of hypertension ($P = 0.547$). Two of the control subjects received hydroxychloroquine alone; the others received lopinavir/ritonavir either alone or in combination with hydroxychloroquine and, in one case, ribavirin.

The median length of hospitalization in the intervention group and control group was the same (6 days). No patients in the intervention group were admitted to ICU or required invasive mechanical ventilation compared with four individuals in the control group. No patients in the intervention group died compared with three in the control group; however, these differences were not significant (Table 2). The CIF for recovery by treatment arm is shown in Figure 2. Median time to recovery was 6 days in both groups; however, the difference between the groups was significant (Gray's test $P = 0.033$). After adjustment for potential baseline confounders, the association between treatment group and time to recovery was not significant (Table S1).

Discussion

This randomized trial found that the combination of sofosbuvir/daclatasvir/ribavirin compared with standard care showed limited clinical improvement in moderate COVID-19 patients.

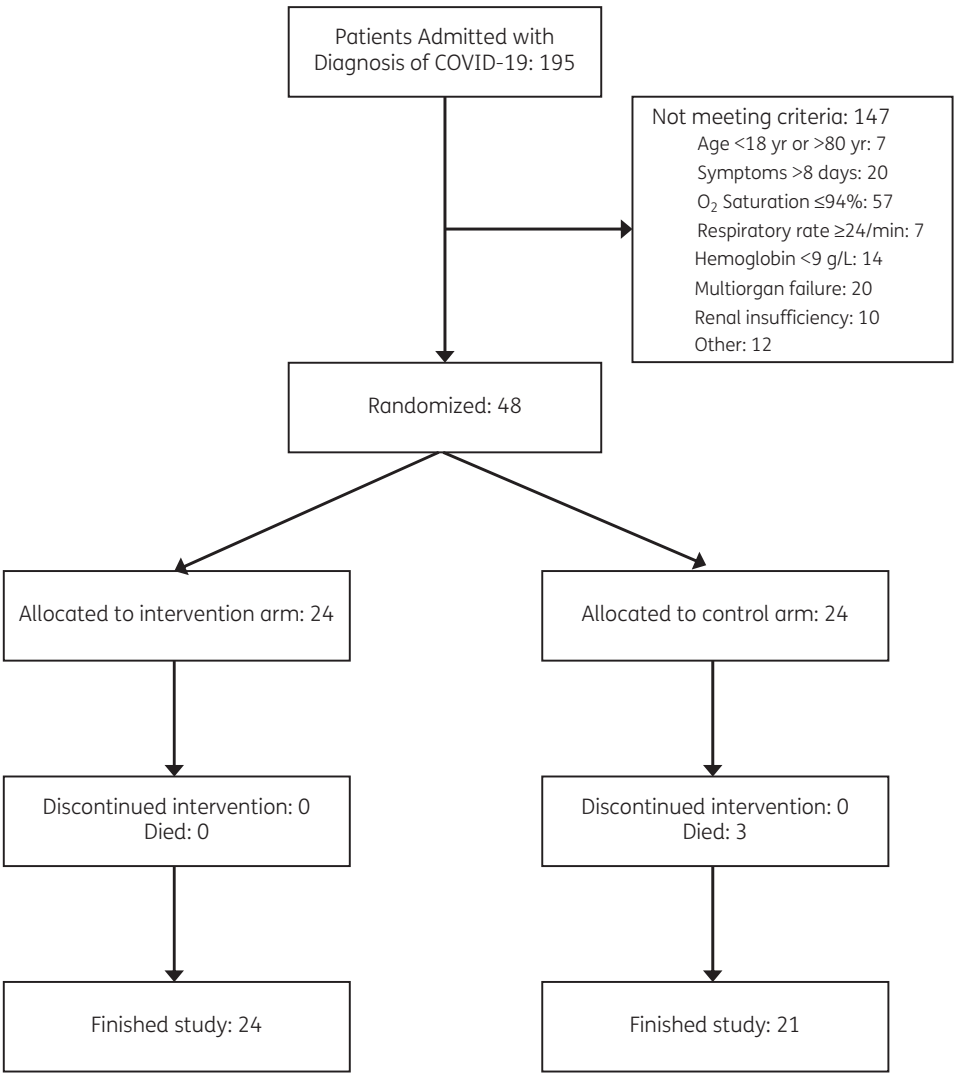

Figure 1. Trial profile.

Table 1. Baseline characteristics of patients

	SOF/DCV/RBV (*n* = 24)	Control (*n* = 24)	*P* value
Male, *n* (%)	11 (46)	7 (29)	0.371
Age (years), median (IQR)	45 (38–69)	60 (47.5–68.5)	0.158
Time from symptom onset (days), median (IQR)	5 (3–5)	5 (4–7)	0.457
Respiratory rate (/min), median (IQR)	20 (18–22)	20 (18–22)	0.925
Temperature (°C), median (IQR)	37.0 (36.6–37.5)	37.5 (36.9–37.8)	0.139
Comorbidities, *n* (%)			
any	13 (54)	17 (71)	0.371
diabetes	4 (17)	14 (58)	0.006
hypertension	7 (29)	10 (42)	0.547
ischaemic heart disease	4 (17)	7 (29)	0.494
COPD	1 (4)	0 (0)	1.000
Laboratory findings on admission, median (IQR)			
arterial O_2 saturation (%)	95 (95–95)	95 (95–96)	0.269
haemoglobin (g/dL)	12 (11–13)	12 (11–13)	0.765
WBCs ($\times 10^9$/L)	6.4 (5.2–7.7)	6.2 (5.9–9.2)	0.602
AST (U/L)	26 (16–36)	26 (19–35)	0.898
ALT (U/L)	21 (15–39)	24 (15–35)	0.840
creatinine (mg/dL)	0.9 (0.8–0.9)	0.9 (0.8–1.1)	0.522
ESR (mm/h)	47 (27–67)	61 (37–120)	0.099
BUN (mg/dL)	29 (20–37)	26 (19–35)	0.339
INR	1.3 (1.2–1.4)	1.3 (1.2–1.6)	0.567

SOF/DCV/RBV, sofosbuvir/daclatasvir/ribavirin; ESR, Erythrocyte Sedimentation Rate; BUN, Blood Urea Nitrogen; INR, International Normalized Ratio.
Percentages are calculated from non-missing values.
P values are calculated using Fisher's exact test for categorical outcomes and Mann–Whitney *U*-test for continuous outcomes.

Table 2. Clinical outcomes comparison between the two groups

	SOF/DCV/RBV (*n* = 24)	Control (*n* = 24)	*P* value
Duration of hospitalization (days), median (IQR)	6 (5–7)	6 (5.5–7.5)	0.398
Final outcome, *n* (%)			
recovery	24 (100)	21 (88)	0.234
death	0 (0)	3 (13)	
Time to recovery (days), median (IQR)[a]	6 (5–7)	6 (6–8)	0.033
Other outcomes			
ICU admission, *n* (%)	0 (0)	4 (17)	0.109
duration (days), median (IQR)	—	2.5 (1.5–7)	
invasive mechanical ventilation, *n* (%)	0 (0)	4 (17)	0.109
duration (days), median (IQR)	—	2.5 (1.5–7)	

SOF/DCV/RBV, sofosbuvir/daclatasvir/ribavirin.
P values are calculated using Fisher's exact test for categorical outcomes and Mann–Whitney *U*-test for continuous outcomes.
[a]Estimated from the CIF, accounting for death as a competing risk; *P* value is for Gray's test for the equality of CIFs.

Sofosbuvir/daclatasvir/ribavirin did not reduce the duration of hospitalization, but cumulative incidence of recovery was higher in the sofosbuvir/daclatasvir/ribavirin group compared with the control group. Fewer ICU admissions and deaths were observed in the sofosbuvir/daclatasvir/ribavirin arm; however, these differences were not significant.

To our knowledge, this is the first clinical trial of sofosbuvir/daclatasvir/ribavirin in COVID-19 patients; however, there are limitations to our study. The median age was higher in the control arm and there were more patients with diabetes in the control arm. In a sensitivity analysis, we adjusted our results for observed baseline imbalance; however, the interpretation of these models is limited due to the small sample size and possible error margin. Most importantly, the number of patients was not high enough to identify probable beneficial effects on survival. A larger study would be required in order to prove such an effect. We also

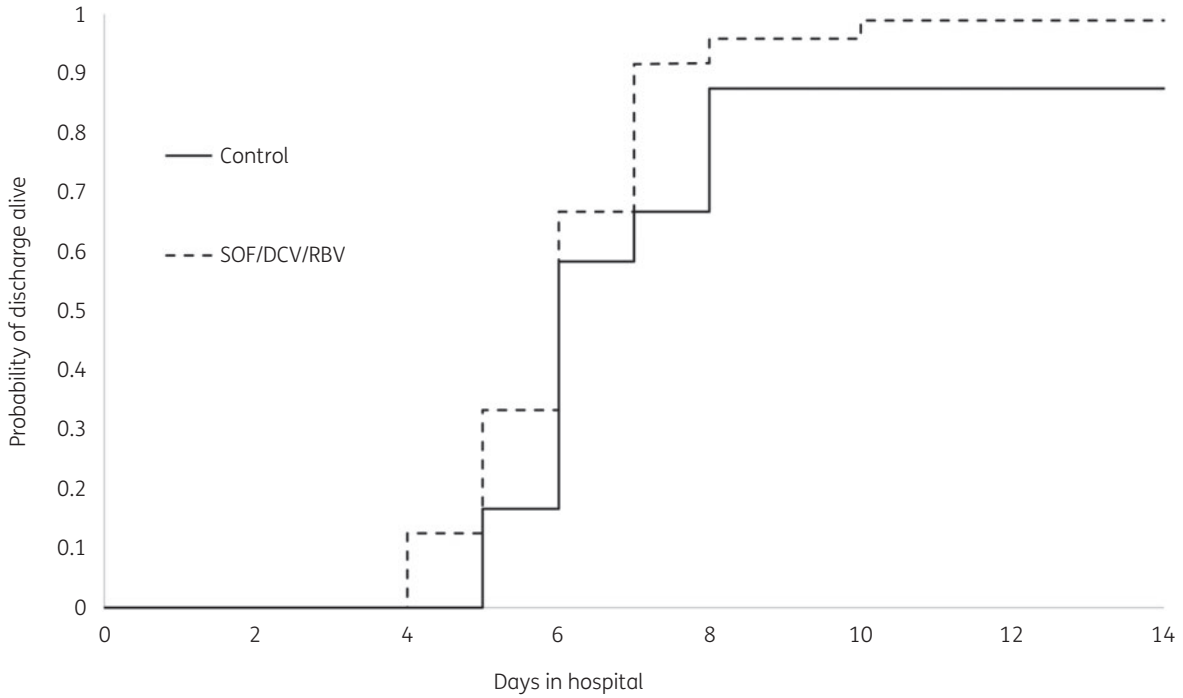

Figure 2. Cumulative incidence of recovery by treatment arm. SOF/DCV/RBV, sofosbuvir/daclatasvir/ribavirin.

excluded elderly subjects, who have higher mortality and might have benefited more from sofosbuvir/daclatasvir/ribavirin. It would be interesting to see the effects of sofosbuvir/daclatasvir plus/minus ribavirin in more advanced cases and in elderly patients.

Another limitation of our study is lack of blinding. Unfortunately, due to the urgent situation imposed by COVID-19, it was not possible to prepare a suitable placebo in time. Whilst we found clinical improvement benefits, we were not able to analyse biological markers of improvement as we did not measure viral decay nor serological inflammatory markers over time, which would both be helpful data to demonstrate effective antiviral therapy.

In this trial of 24 patients per arm, there was no statistically significant difference in length of hospital stay between the arms. However, the sample size could be too small to make reliable conclusions. We are also not able to clearly identify from this study whether the benefits found in terms of clinical improvement and cumulative incidence of recovery were directly from the effects of sofosbuvir or daclatasvir or ribavirin or due to a synergistic effect of the combination of all three antivirals. *In vitro* models have shown a synergistic effect when combining other antivirals against COVID-19.[24] Another study in China has shown that the combination of ribavirin with lopinavir/ritonavir and interferon β-1 together is superior to lopinavir/ritonavir alone in COVID-19.[31]

There are seven more trials registered in https://www.irct.ir/ working on sofosbuvir-containing regimens in COVID-19 and various others studies around the world include ribavirin-containing regimens. We are aware that in at least five of these sofosbuvir-containing trials in Iran, data collection has finished. If the cumulative results of these trials indicate beneficial effect, it is well advised that a larger trial be performed on this subject. A large trial could identify the effects on mild, moderate and severe cases in elderly patients and the effects on survival and hospital stay.

If sofosbuvir/daclatasvir is proven to be effective against COVID-19, given that both are widely available in generic formulations, costing an estimated $5 per 14 day course or only $0.39 per day as a combination, sofosbuvir/daclatasvir may be an affordable and accessible treatment option for COVID-19.[29] The promising results of this small sample warrant further trials into the effectiveness of sofosbuvir and daclatasvir for the treatment of COVID-19.

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Transparency declarations

S. Merat has received travel grants from and is a stockholder of Fanavaran Rojan Mohaghegh Daru Co. All other authors: none to declare.

Author contributions

H.A.K. and H.T.F. designed the study. F.B., A.R.D.B., L.D., A.H.O., A.A. and M.S. helped with patient management and care. S. Moradi, A.M.S., H.W., B.S. and A.H. worked on the statistical analysis. S. Merat, A.M.S., J.L. and A.G. helped with the preparation of the manuscript. All authors critically revised and approved the final published version.

Supplementary data

Table S1 is available as Supplementary data at *JAC* Online.

References

1 Huang C, Wang Y, Li X *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497–506.

2 Park M, Cook AR, Lim JT *et al*. A systematic review of COVID-19 epidemiology based on current evidence. *J Clin Med* 2020; **9**: 967.

3 Abdi M. Coronavirus disease 2019 (COVID-19) outbreak in Iran: actions and problems. *Infect Control Hosp Epidemiol* 2020; **41**: 754–5.

4 WHO. WHO COVID-19 Data Explorer. https://covid19.who.int/explorer.

5 Geleris J, Sun Y, Platt J *et al*. Observational study of hydroxychloroquine in hospitalized patients with Covid-19. *N Engl J Med* 2020; **382**: 2411–8.

6 Cao B, Wang Y, Wen D *et al*. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med* 2020; **382**: 1787–99.

7 Tang W, Cao Z, Han M *et al*. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. *BMJ* 2020; **369**: m1849.

8 Wang Y, Zhang D, Du G *et al*. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet* 2020; **395**: 1569–78.

9 Sanders JM, Monogue ML, Jodlowski TZ *et al*. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. *JAMA* 2020; doi: 10.1001/jama.2020.6019.

10 Beigel JH, Tomashek KM, Dodd LE *et al*. Remdesivir for the treatment of COVID-19—preliminary report. *N Engl J Med* 2020; doi:10.1056/NEJMoa2007764.

11 AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. *Hepatology* 2015; **62**: 932–54.

12 Merat S; SD1000 Research Team. SD1000: high sustained viral response rate in 1361 patients with hepatitis C genotypes 1, 2, 3, and 4 using a low-cost, fixed-dose combination tablet of generic sofosbuvir and daclatasvir: a multicenter, Phase III clinical trial. *Clin Infect Dis* 2020; **70**: 2206–12.

13 WHO. Annex 1: 19th WHO Model List of Essential Medicines (April 2015). https://www.who.int/medicines/publications/essentialmedicines/en/.

14 de Freitas CS, Higa LM, Sacramento CQ *et al*. Yellow fever virus is susceptible to sofosbuvir both in vitro and in vivo. *PLoS Negl Trop Dis* 2019; **13**: e0007072.

15 Bullard-Feibelman KM, Govero J, Zhu Z *et al*. The FDA-approved drug sofosbuvir inhibits Zika virus infection. *Antiviral Res* 2017; **137**: 134–40.

16 Gan CS, Lim SK, Chee CF *et al*. Sofosbuvir as treatment against dengue? *Chem Biol Drug Des* 2018; **91**: 448–55.

17 Ferreira AC, Reis PA, de Freitas CS *et al*. Beyond members of the Flaviviridae family, sofosbuvir also inhibits chikungunya virus replication. *Antimicrob Agents Chemother* 2019; **63**: e01389–18.

18 Chen Y, Liu Q, Guo D. Emerging coronaviruses: genome structure, replication, and pathogenesis. *J Med Virol* 2020; **92**: 418–23.

19 Chien M, Anderson TK, Jockusch S *et al*. Nucleotide analogues as inhibitors of SARS-CoV-2 polymerase. *bioRxiv* 2020; doi:10.1101/2020.03.18.997585.

20 Elfiky AA, Mahdy SM, Elshemey WM. Quantitative structure-activity relationship and molecular docking revealed a potency of anti-hepatitis C virus drugs against human corona viruses. *J Med Virol* 2017; **89**: 1040–7.

21 Kim J, Zhang J, Cha Y *et al*. Advanced bioinformatics rapidly identifies existing therapeutics for patients with coronavirus disease-2019 (COVID-19). *J Transl Med* 2020; **18**: 257.

22 Elfiky AA. Ribavirin, remdesivir, sofosbuvir, galidesivir, and tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): a molecular docking study. *Life Sci* 2020; **253**: 117592.

23 Alabboud M, Javadmanesh A. In silico study of various antiviral drugs, vitamins, and natural substances as potential binding compounds with SARS-CoV-2 main protease. *DLS* 2020; **1**: 44–63.

24 Lo HS, Hui KPY, Lai H-M *et al*. Simeprevir suppresses SARS-CoV-2 replication and synergizes with remdesivir. *bioRxiv* 2020; doi:10.1101/2020.05.26.116020.

25 Sacramento CQ, Fintelman-Rodrigues N, Temerozo JR *et al*. The in vitro antiviral activity of the anti-hepatitis C virus (HCV) drugs daclatasvir and sofosbuvir against SARS-CoV-2. *bioRxiv* 2020; doi:10.1101/2020.06.15.153411.

26 Liu S, Lien CZ, Selvaraj P *et al*. Evaluation of 19 antiviral drugs against SARS-CoV-2 infection. *bioRxiv* 2020; doi:10.1101/2020.04.29.067983.

27 FDA. SOVALDI® (Sofosbuvir) Tablets, for Oral Use. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/204671s004lbl.pdf. 2015.

28 FDA. DAKLINZA® (Daclatasvir) Tablets, for Oral Use. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/206843s006lbl.pdf. 2015.

29 Hill A, Wang J, Levi J *et al*. Minimum costs to manufacture new treatments for COVID-19. *J Virus Erad* 2020; **6**: 61–9.

30 Mahdavi A, Khalili N, Davarpanah AH *et al*. Radiologic management of COVID-19: preliminary experience of the Iranian Society of Radiology COVID-19 Consultant Group (ISRCC). *Iran J Radiol* 2020; **17**: e102324.

31 Hung IF, Lung KC, Tso EY *et al*. Triple combination of interferon β-1b, lopinavir-ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial. *Lancet* 2020; **395**: 1695–704.