Appendix 3 - Included, excluded and ongoing studies - Remdesivir for COVID-19: A living systematic review

Included randomized trials

ACTT-1 (1-4)	Details or comments
REFERENCES	**Publication thread for ACTT-1 (Adaptive COVID-19 Treatment Trial)** Epistemonikos
Beigel et al (1)	Type: Journal article Epistemonikos
ISRCTN13035264 (2)	Type:Trial registry Epistemonikos
NCT04280705 (3)	Type:Trial registry Epistemonikos
National Institutes of Health (4)	Type: Press release Epistemonikos
STUDY DESIGN ☑ Randomized trial ☐ Comparative, non-randomized ☐ Non-comparative study	QUOTE: Multicenter, Adaptive, Randomized Blinded Controlled Trial Eligible patients were randomly assigned in a 1:1 ratio to receive either remdesivir or placebo. Randomization was stratified by study site and disease severity at enrollment
POPULATION: INCLUSION CRITERIA	QUOTE: Participants 18 years of age or older who were hospitalized with

☐COVID-19 ☑COVID-19 pneumonia ☐Severe COVID-19 pneumonia	symptoms suggestive of COVID-19 were assessed for eligibility. Participants had to meet one of the following criteria suggestive of lower respiratory tract infection at the time of enrollment: radiographic infiltrates by imaging study, peripheral oxygen saturation (SpO2) ≤94% on room air, or requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). There was no limit to the duration of symptoms prior to enrollment. Participants had to have a laboratory-confirmed SARS-CoV-2 infection as determined by a positive reverse transcription, polymerase-chain-reaction (RT-PCR) assay result from any respiratory specimen collected <72 hours prior to randomization. During the study, this criterion was modified due to limitations in testing capacity to also allow a RT-PCR positive specimen that was collected ≥72 hours prior to randomization if the site was unable to obtain a repeat sample and if the participant had progressive disease consistent with ongoing SARS-CoV-2 infection. Other inclusion criteria included agreeing not to participate in another COVID-19 treatment clinical trial through Day 29 and practicing heterosexual abstinence or using study-specified contraception through Day 29 for women of childbearing potential. Exclusion criteria included having either an alanine aminotransferase (ALT) or an aspartate aminotransferase (AST) > 5 times the upper limit of the normal range; impaired renal function as determined by calculating an estimated glomerular filtration rate (eGFR), or need for hemodialysis or hemofiltration; allergy to study product; pregnancy or breast-feeding; and anticipated discharge from the hospital or transfer to another hospital within 72 hours of enrollment.
INTERVENTION ☑Remdesivir	QUOTE: 200 mg of Remdesivir administered intravenously on day 1, followed by a 100 mg once-daily maintenance dose of Remdesivir while hospitalized

	for up to a 10 days total course.
COMPARISON ☑ Placebo (plus standard care) ☐ No treatment (standard care)	QUOTE: A matching placebo was administered according to the same schedule and in the same volume as the active drug. A normal saline placebo was used at the European sites and at some non-European sites owing to a shortage of matching placebo; the infusions were masked with an opaque bag and tubing covers to maintain blinding. All patients received supportive care according to the standard of care for the trial site hospital. If a hospital had a written policy or guideline for use of other treatments for Covid-19, patients could receive those treatments. In the absence of a written policy or guideline, other experimental treatment or off-label use of marketed medications intended as specific treatment for Covid-19 were prohibited from day 1 through day 29 (though such medications could have been used before enrollment in this trial)..
OUTCOMES ☑ All-cause mortality ☑ Invasive mechanical ventilation ☑ Adverse effects leading to discontinuation ☐ Time to viral clearance ☐ Length of hospital stay	All-cause mortality: This outcome was measured at 14 and 28 days of follow up. Mechanical ventilation: This outcome was measured together with other outcomes in an ordinal scale of clinical improvement. The result of the first follow-up was considered. Adverse effects leading to discontinuation: All serious adverse events and grade 3 or 4 adverse events that represented an increase in severity from day 1 and any grade 2 or higher suspected drug-related hypersensitivity reactions were recorded. Time to viral clearance: This outcome was not reported.

☐Extracorporeal membrane oxygenation ☑Serious adverse effects	Length of hospital stay: This outcome was not reported. Extracorporeal membrane oxygenation: This outcome was measured together with other outcomes in an ordinal scale of clinical improvement. This information was not considered for data extraction. . Serious adverse events: This outcome was measured after randomization through day 28 (longer follow-up).
RISK OF BIAS	
Risk of bias arising from the randomization process	**Low risk for all outcomes.** Eligible patients were randomly assigned in a 1:1 ratio to receive either remdesivir or placebo. Randomization was stratified by study site and disease severity at enrollment Randomization was stratified by study site and disease severity at enrollment and was performed using a web-based Internet Data Entry System, Advantage eClinical
Risk of bias due to deviations from intended interventions	**Some concern for all outcomes.** All patients received supportive care according to the standard of care for the trial site hospital. If a hospital had a written policy or guideline for use of other treatments for Covid-19, patients could receive those treatments. In the absence of a written policy or guideline, other experimental treatment or off-label use of marketed medications intended as specific treatment for Covid-19 were prohibited from day 1 through day 29 (though such medications could have been used before enrollment in this trial). No specific information was reported on possible treatments or co-

	interventions received by patients in the different centers.
Risk of bias due to missing outcome data	**High risk for all outcomes.** There are important missing results (outcome data) as these are preliminary results and the follow-up is still ongoing
Risk of bias in measurement of outcomes	**Low risk of bias for all outcomes.** All follow-up safety and efficacy evaluations will be performed by blinded clinic staff.
Risk of bias in selection of reported results	**Low risk of bias** All outcomes were listed as pre-planned outcomes and were analyzed in accordance with a pre-specified analysis plan.

CAP-China remdesivir 2 (4-6)	Details or comments
REFERENCES	**Publication thread for CAP-China remdesivir 2** Epistemonikos
Wang et al (4)	Type: Journal article Epistemonikos
Wang et al (5)	Type: Protocol article Epistemonikos
NCT04257656 (6)	Type:Trial registry Epistemonikos

STUDY DESIGN ☑ Randomized trial ☐ Comparative, non-randomized ☐ Non-comparative study	QUOTE: Phase 3, parallel group, randomized, doubleblind, placebo-controlled, superiority, multicentre trial. Allocation ratio is 2:1 in favour of remdesivir
POPULATION: **INCLUSION CRITERIA** ☐ COVID-19 ☑ COVID-19 pneumonia ☐ Severe COVID-19 pneumonia	QUOTE: Men and non-pregnant women with COVID-19 who were aged at least 18 years and were RT-PCR positive for SARS-CoV-2, had pneumonia confirmed by chest imaging, had oxygen saturation of 94% or lower on room air or a ratio of arterial oxygen partial pressure to fractional inspired oxygen of 300 mm Hg or less, and were within 12 days of symptom onset.
INTERVENTION ☑ Remdesivir	QUOTE: Patients received either intravenous remdesivir (200 mg on day 1 followed by 100 mg on days 2–10 in single daily infusions) or the same volume of placebo infusions for a total of 10 days.
COMPARISON ☑ Placebo (plus standard care) ☐ No treatment (standard care)	QUOTE: Placebo in 350 ml normal saline (0.9% sodium chloride) single daily dose infused intravenously over approximately 30–60 min (with a target time of 30 min) for 1 day (b) Maintenance dose: Placebo in 250 ml normal saline (0.9% sodium chloride) single daily dose infused intravenously over approximately 30–60 min (with a target time of 30 min) for 9 days. No standard treatment was reported. Patients were permitted concomitant use of lopinavir–ritonavir, interferons, and corticosteroids
OUTCOMES	All-cause mortality: This outcome was measured after

☑All-cause mortality ☑Invasive mechanical ventilation ☑Adverse effects leading to discontinuation ☐Time to viral clearance ☑Length of hospital stay ☐Extracorporeal membrane oxygenation ☑Serious adverse effects	randomization through day 21 (longer follow-up). Mechanical ventilation: This outcome was measured together with other outcomes in an ordinal scale of clinical improvement. The result of the first follow-up was considered. Adverse effects leading to discontinuation: The safety assessment included daily monitoring for adverse events. Safety outcomes included treatment-emergent adverse events, serious adverse events, and premature discontinuations of study drug. Time to viral clearance: This outcome was not reported. Length of hospital stay: This outcome was reported. Extracorporeal membrane oxygenation: This outcome was measured together with other outcomes in an ordinal scale of clinical improvement. This information was not considered for data extraction. Serious adverse events: This outcome was measured after randomization through day 28 (longer follow-up).
RISK OF BIAS	
Risk of bias arising from the randomization process	**Some concern risk for all outcomes.** Some imbalances existed at enrollment between the groups, including more patients with hypertension, diabetes, or coronary artery disease in the remdesivir group than the placebo group. More patients in the control group than in the

	remdesivir group had been symptomatic for 10 days or less at the time of starting remdesivir or placebo treatment, and a higher proportion of remdesivir recipients had a respiratory rate of more than 24 breaths per min. No other major differences in symptoms, signs, laboratory results, disease severity, or treatments were observed between groups at baseline.
Risk of bias due to deviations from intended interventions	**Low risk for all outcomes** The study was blinded to clinicians and research staff.
Risk of bias due to missing outcome data	**Low risk of bias** All randomized patients completed the study.
Risk of bias in measurement of outcomes	**Low risk of bias for all reported outcomes.** The study was blind to participants. Outcomes are unlikely to be influenced by the assigned intervention.
Risk of bias in selection of reported results	**Low risk of bias** All outcomes were listed as pre-planned outcomes and were analyzed in accordance with a pre-specified analysis plan.

SIMPLE 2 (8-11)	Details or comments
REFERENCES	**Publication thread for SIMPLE 2** Epistemonikos
Spinner et al (8)	Type: Journal article Epistemonikos

NCT04292730 (9)	Type:Trial registry Epistemonikos
Gilead Sciences (10)	Type: Press release Epistemonikos
Maffei D et al (11)	Type: Press release Epistemonikos
STUDY DESIGN ☑ Randomized trial ☐ Comparative, non-randomized ☐ Non-comparative study	QUOTE: Randomized, open-label trial of hospitalized patients. Patients were enrolled at 105 hospitals in the United States, Europe, and Asia between 15 March, 2020, and 18 April, 2020, and randomly assigned in a 1:1:1 ratio to receive up to a 5-day course of remdesivir, up to a 10-day course of remdesivir, or standard care. Randomization was not stratified.
POPULATION: INCLUSION CRITERIA ☐ COVID-19 ☑ COVID-19 pneumonia ☐ Severe COVID-19 pneumonia	QUOTE: Eligibility Criteria A. Inclusion Criteria Patients must meet all of the following inclusion criteria to be eligible for participation in this study: 1. Willing and able to provide written informed consent (participants ≥ 18 years of age) or assent (participants ≥ 12 and < 18 years of age) prior to performing study procedures. For participants ≥ 12 and < 18 years of age, a parent or legal guardian willing and able to provide written informed consent prior to performing study procedures 2. Aged ≥ 18 years (at all sites), or aged ≥ 12 and < 18 years of age weighing ≥ 40 kg (where permitted according to local law and approved nationally and by the relevant institutional review board [IRB] or

	independent ethics committee [IEC]) 3. SARS-CoV-2 infection confirmed by PCR ≤ 4 days before randomization 4. Currently hospitalized and requiring medical care for COVID-19 5. SpO2 > 94% on room air at screening 6. Radiographic evidence of pulmonary infiltrates 7. Men and women of childbearing potential who engage in heterosexual intercourse must agree to use protocol specified method(s) of contraception.
INTERVENTION ☑ Remdesivir	QUOTE: 200 mg of remdesivir intravenously on day 1, followed by 100 mg of remdesivir once daily for the subsequent days, infused over 30 to 60 minutes. 5-day course of remdesivir, up to a 10-day course of remdesivir
COMPARISON ☐ Placebo (plus standard care) ☑ No treatment (standard care)	QUOTE: Treatment with standard of care according to local guidelines. The original protocol allowed use of other agents with presumptive activity against SARS-CoV-2 if such use was local standard care. This exception was disallowed in a subsequent amendment.
OUTCOMES ☑ All-cause mortality ☑ Invasive mechanical ventilation ☐ Adverse effects leading to discontinuation ☐ Time to viral clearance	All-cause mortality: This outcome was measured at 7, 14 and 28 days of follow up. Mechanical ventilation: This outcome was measured together with other outcomes in an ordinal scale of clinical improvement. The result of the first follow-up was considered. Adverse effects leading to discontinuation: Reported, but not usable in a meta-analysis Time to viral clearance: This outcome was not reported.

☐Length of hospital stay ☐Extracorporeal membrane oxygenation ☑Serious adverse effects	Length of hospital stay: Reported, but not usable in a meta-analysis. Extracorporeal membrane oxygenation: This outcome was measured together with other outcomes in an ordinal scale of clinical improvement. This information was not considered for data extraction. Serious adverse events: This outcome was measured after randomization through day 28 (longer follow-up).
RISK OF BIAS	
Risk of bias arising from the randomization process	**Low risk for all outcomes.** The allocation sequence was adequately concealed. Any baseline differences observed between intervention groups appear to be compatible with chance. Patients were enrolled at 105 hospitals in the United States, Europe, and Asia between 15 March, 2020, and 18 April, 2020, and randomly assigned in a 1:1:1 ratio to receive up to a 5-day course of remdesivir, up to a 10-day course of remdesivir, or standard care. Randomization was not stratified. The randomization list was created and validated by the interactive web response system (IWRS) vendor. A dummy randomization list was provided in Microsoft Excel format to the biostatistician employed by the study sponsor for review. A separate list of sequential patient numbers within each treatment group was generated by the IWRS vendor. The randomization had a block size of 6. Based on the treatment from the randomization list, the IWRS provided the next sequential patient number to the site along with the treatment group assignment. The appropriate number of vials of open-label study

	drug were assigned to the patient. Sites did not have access to the randomization list and could not know the sequence of treatments.
Risk of bias due to deviations from intended interventions	**Some concern for all outcomes.** A small proportion of patients allocated to remdesivir did not start treatment; there may be some chances that some disclosed reasons could be conditioned by the clinicians knowledge of patients' condition Also, there were critical differences in concomitant medication received between groups because of the trial context. Other cointerventions. It is possible that trial personnel (carers and people delivering the interventions) undermine the trial comparisons by implementing non-protocol interventions or failing to implement the protocol interventions. Treatment was open label because the sponsor had an insufficient number of placebo-containing vials to support this trial. The original protocol allowed use of other agents with presumptive activity against SARS-CoV-2 if such use was local standard care. Although this exception was disallowed in a subsequent amendment, some patients had already received other concurrent therapies.
Risk of bias due to missing outcome data	**Low risk for all outcomes.** Outcome data were available for all, or nearly all, randomized participants Of 612 patients who consented and were assessed for eligibility, 596 underwent randomization and 584 began the study: 193 began a 10-day

	course of remdesivir, 191 patients began a 5-day course of remdesivir, and 200 continued standard care. Of the 16 patients who were not randomized, 13 did not meet eligibility criteria and 3 withdrew consent. Twelve randomized patients did not receive treatment: 8 withdrew consent, 3 had protocol violations, and 1 was withdrawn by investigator discretion.
Risk of bias in measurement of outcomes	**Low risk of bias for all outcomes.** The measurement or ascertainment of the outcome did not differ between intervention groups and the assessment of the outcome could not have been influenced by knowledge of the intervention received.
Risk of bias in selection of reported results	**Low risk of bias** All outcomes were listed as pre-planned outcomes and were analyzed in accordance with a pre-specified analysis plan.

References to included randomized trials

1. Beigel JH, Tomashek KM, Dodd LE, Mehta AK, Zingman BS, Kalil AC, Hohmann E, Chu HY, Luetkemeyer A, Kline S, Lopez de Castilla D, Finberg RW, Dierberg K, Tapson V, Hsieh L, Patterson TF, Paredes R, Sweeney DA, Short WR, Touloumi G, Lye DC, Ohmagari N, Oh MD, Ruiz-Palacios GM, Benfield T, Fätkenheuer G, Kortepeter MG, Atmar RL, Creech CB, Lundgren J, Babiker AG, Pett S, Neaton JD, Burgess TH, Bonnett T, Green M, Makowski M, Osinusi A, Nayak S, Lane HC, ACTT-1 Study Group Members. Remdesivir for the Treatment of Covid-19 - Preliminary Report. The New England journal of medicine. 2020;
2. University of Minnesota. Adaptive COVID-19 treatment trial in the EU & UK. isrctn.com. 2020;
3. National Institute of Allergy and Infectious Diseases (NIAID). Adaptive COVID-19 Treatment Trial. clinicaltrials.gov. 2020;
4. NIH. NIH clinical trial shows Remdesivir accelerates recovery from advanced COVID-19. News releases - National Institutes of Health (NIH). 2020;
5. Wang, Yeming, Zhang, Dingyu, Du, Guanhua, Du, Ronghui, Zhao, Jianping, Jin, Yang, Fu, Shouzhi, Gao, Ling, Cheng, Zhenshun, Lu, Qiaofa, Hu, Yi, Luo, Guangwei, Wang, Ke, Lu, Yang, Li, Huadong, Wang, Shuzhen, Ruan,

Shunan, Yang, Chengqing, Mei, Chunlin, Wang, Yi, Ding, Dan, Wu, Feng, Tang, Xin, Ye, Xianzhi, Ye, Yingchun, Liu, Bing, Yang, Jie, Yin, Wen, Wang, Aili, Fan, Guohui, Zhou, Fei, Liu, Zhibo, Gu, Xiaoying, Xu, Jiuyang, Shang, Lianhan, Zhang, Yi, Cao, Lianjun, Guo, Tingting, Wan, Yan, Qin, Hong, Jiang, Yushen, Jaki, Thomas, Hayden, Frederick G, Horby, Peter W, Cao, Bin, Wang, Chen. Remdesivir in adults with severe COVID-19: a randomized, double-blind, placebo-controlled, multicentre trial. The Lancet. 2020;395(10236):1569-1578.

6. Wang Y, Zhou F, Zhang D, Zhao J, Du R, Hu Y, Cheng Z, Gao L, Jin Y, Luo G, Fu S, Lu Q, Du G, Wang K, Lu Y, Fan G, Zhang Y, Liu Y, Ruan S, Liu W, Jaki T, Hayden FG, Horby PW, Cao B, Wang C. Evaluation of the efficacy and safety of intravenous remdesivir in adult patients with severe COVID-19: study protocol for a phase 3 randomized, double-blind, placebo-controlled, multicentre trial. Trials. 2020;21(1):422.
7. Capital Medical University. Severe 2019-nCoV Remdesivir RCT. clinicaltrials.gov. 2020;
8. Spinner CD, Gottlieb RL, Criner GJ, Arribas López JR, Cattelan AM, Soriano Viladomiu A, Ogbuagu O, Malhotra P, Mullane KM, Castagna A, Chai LYA, Roestenberg M, Tsang OTY, Bernasconi E, Le Turnier P, Chang SC, SenGupta D, Hyland RH, Osinusi AO, Cao H, Blair C, Wang H, Gaggar A, Brainard DM, McPhail MJ, Bhagani S, Ahn MY, Sanyal AJ, Huhn G, Marty FM, GS-US-540-5774 Investigators. Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. JAMA. 2020;
9. Gilead Sciences. Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-5734™) in Participants With Moderate Coronavirus Disease (COVID-19) Compared to Standard of Care Treatment. clinicaltrials.gov. 2020;
10. Gilead Sciences, Inc.. Gilead Announces Results From Phase 3 Trial of Remdesivir in Patients With Moderate COVID-19. Press Release. 2020;
11. Maffei D, Sonia C. Gilead Announces Results From Phase 3 Trial of Remdesivir in Patients With Moderate COVID-19. Business Wire. 2020;

Excluded studies

Study name	Reason for exclusion
SIMPLE Goldman et al (12) NCT04292899 (13) Press release (14)	Wrong comparison
Humeniuk R et al Humeniuk R et al (15)	Wrong population

References to excluded randomized trials

12. Goldman JD, Lye DCB, Hui DS, Marks KM, Bruno R, Montejano R, Spinner CD, Galli M, Ahn MY, Nahass RG, Chen YS, SenGupta D, Hyland RH, Osinusi AO, Cao H, Blair C, Wei X, Gaggar A, Brainard DM, Towner WJ, Muñoz J, Mullane KM, Marty FM, Tashima KT, Diaz G, Subramanian A, GS-US-540-5773 Investigators. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. The New England journal of medicine. 2020;
13. Gilead Sciences. Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-5734™) in Participants With Severe Coronavirus Disease (COVID-19). clinicaltrials.gov. 2020;
14. Gilead Sciences, Inc.. Gilead announces results from phase 3 trial of investigational antiviral remdesivir in patients with severe COVID-19. Press release - Gilead Science. 2020;
15. Humeniuk R, Mathias A, Cao H, Osinusi A, Shen G, Chng E, Ling J, Vu A, German P. Safety, Tolerability, and Pharmacokinetics of Remdesivir, an Antiviral for Treatment of COVID-19, in Healthy Subjects. Clinical and translational science. 2020;

References to excluded non- randomized trials

1. Ahluwalia M, Givertz MM, Mehra MR. A Proposed Strategy for Management of Immunosuppression in Heart Transplant Patients with COVID-19. Clinical transplantation. 2020;:e14032.
2. Akinosoglou K, Velissaris D, Ziazias D, Davoulos C, Tousis A, Tsiotsios K, Kalogeropoulou C, Spyridonidis A,

Marangos M, Fligkou F, Gogos C. Remdesivir and Tocilizumab: Mix or Match. Journal of medical virology. 2020;

3. Anderson J, Schauer J, Bryant S, Graves CR. The use of convalescent plasma therapy and remdesivir in the successful management of a critically ill obstetric patient with novel coronavirus 2019 infection: A case report. Case reports in women's health. 2020;27:e00221.
4. Antinori S, Cossu MV, Ridolfo AL, Rech R, Bonazzetti C, Pagani G, Gubertini G, Coen M, Magni C, Castelli A, Borghi B, Colombo R, Giorgi R, Angeli E, Mileto D, Milazzo L, Vimercati S, Pellicciotta M, Corbellino M, Torre A, Rusconi S, Oreni L, Gismondo MR, Giacomelli A, Meroni L, Rizzardini G, Galli M. Compassionate remdesivir treatment of severe Covid-19 pneumonia in intensive care unit (ICU) and Non-ICU patients: Clinical outcome and differences in post_treatment hospitalisation status. Pharmacological research. 2020;158:104899.
5. Boyarsky BJ, Chiang TP, Werbel WA, Durand CM, Avery RK, Getsin SN, Jackson KR, Kernodle AB, Van Pilsum Rasmussen SE, Massie AB, Segev DL, Garonzik-Wang JM. Early Impact of COVID-19 on Transplant Center Practices and Policies in the United States. American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons. 2020;20(7):1809-1818.
6. Brooke E Nichols, Lise Jamieson, Sabrina RC Zhang, Sheetal Silal, Juliet Pulliam, Ian Sanne, Gesine Meyer-Rath. The role of remdesivir in South Africa: preventing COVID-19 deaths through increasing ICU capacity. medRxiv. 2020;
7. Byrd KM, Beckwith CG, Garland JM, Johnson JE, Aung S, Cu-Uvin S, Farmakiotis D, Flanigan T, Gillani FS, Macias-Gil R, Mileno M, Ramratnam B, Rybak NR, Sanchez M, Tashima K, Mylonakis E, Kantor R. SARS-CoV-2 and HIV coinfection: clinical experience from Rhode Island, United States. Journal of the International AIDS Society. 2020;23(7):e25573.
8. Chao JY, Derespina KR, Herold BC, Goldman DL, Aldrich M, Weingarten J, Ushay HM, Cabana MD, Medar SS. Clinical Characteristics and Outcomes of Hospitalized and Critically Ill Children and Adolescents with Coronavirus Disease 2019 (COVID-19) at a Tertiary Care Medical Center in New York City. The Journal of pediatrics. 2020;223:14-19.e2.
9. Chen-Yang Hsu, Chao-Chih Lai, Amy Ming-Fang Yen, Sam Li-She Chen, Hsiu-Hsi Chen. Efficacy of remdesivir in COVID-19 patients with a simulated two-arm controlled study. medRxiv. 2020;
10. Daunt A, Perez-Guzman PN, Liew F, Hauck K, Costelloe CE, Thursz MR, Cooke G, Nayagam S. Validity of the UK Early Access to Medicines Scheme Criteria for Remdesivir use in patients with COVID-19 disease. The Journal of infection. 2020;
11. David Grimaldi, Nadia Aissaoui, Gauthier Blonz, Giuseppe Carbutti, Romain Courcelle, Stephane Gaudry, Julien Higny, Geoffrey Horlait, Sami Hraiech, Laurent Lefebvre, Francois Lejeune, Andre Ly, Michael Piagnerelli,

Bertrand Sauneuf, Nicolas Serck, Thibaud Soumagne, Piotr Szychowiak, Julien Textoris, Benoit Vandenbunder, Christophe Vinsonneau, Jean Baptiste Lascarrou. Characteristics and outcomes of Acute Respiratory Distress Syndrome related to COVID-19 in Belgian and French Intensive Care Units according to antiviral strategies. The COVADIS multicenter observational study. medRxiv. 2020;

12. Derespina KR, Kaushik S, Plichta A, Conway EE, Bercow A, Choi J, Eisenberg R, Gillen J, Sen AI, Hennigan CM, Zerihun LM, Doymaz S, Keenaghan MA, Jarrin S, Oulds F, Gupta M, Pierre L, Grageda M, Ushay HM, Nadkarni VM, Agus MSD, Medar SS. Clinical Manifestations and Outcomes of Critically Ill Children and Adolescents with COVID-19 in New York City. The Journal of pediatrics. 2020;
13. Dubert M, Visseaux B, Isernia V, Bouadma L, Deconinck L, Patrier J, Wicky PH, Le Pluart D, Kramer L, Rioux C, Le Hingrat Q, Houhou-Fidouh N, Yazdanpanah Y, Ghosn J, Lescure FX. Case reports study of the first five patients COVID-19 treated with remdesivir in France. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2020;98:290-293.
14. Durante-Mangoni E, Andini R, Bertolino L, Mele F, Florio LL, Murino P, Corcione A, Zampino R. Early experience with remdesivir in SARS-CoV-2 pneumonia. Infection. 2020;
15. Easterlin M.C., De Beritto T., Yeh A.M., Wertheimer F.B., Ramanathan R.. Extremely Preterm Infant Born to a Mother With Severe COVID-19 Pneumonia. Journal of Investigative Medicine High Impact Case Reports. 2020;8.
16. Firstenberg MS, Stahel PF, Hanna J, Kotaru C, Crossno J, Forrester J. Successful COVID-19 rescue therapy by extra-corporeal membrane oxygenation (ECMO) for respiratory failure: a case report. Patient safety in surgery. 2020;14(1):20.
17. Franzetti M, Pozzetti U, Carugati M, Pandolfo A, Molteni C, Faccioli P, Castaldo G, Longoni E, Ormas V, Iemoli E, Piconi S. Interleukin-1 receptor antagonist anakinra in association with remdesivir in severe Coronavirus disease 2019: A case report. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases. 2020;97:215-218.
18. Frauenfelder C, Brierley J, Whittaker E, Perucca G, Bamford A. Infant With SARS-CoV-2 Infection Causing Severe Lung Disease Treated With Remdesivir. Pediatrics. 2020;
19. Grein J, Ohmagari N, Shin D, Diaz G, Asperges E et al. Compassionate Use of Remdesivir for Patients with Severe Covid-19. The New England journal of medicine. 2020;382(24):2327-2336.
20. Götzinger F, Santiago-García B, Noguera-Julián A, Lanaspa M, Lancella L, Calò Carducci FI, Gabrovska N, Velizarova S, Prunk P, Osterman V, Krivec U, Lo Vecchio A, Shingadia D, Soriano-Arandes A, Melendo S, Lanari M, Pierantoni L, Wagner N, L'Huillier AG, Heininger U, Ritz N, Bandi S, Krajcar N, Roglić S, Santos M, Christiaens C, Creuven M, Buonsenso D, Welch SB, Bogyi M, Brinkmann F, Tebruegge M, ptbnet COVID-19 Study Group.

COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. The Lancet. Child & adolescent health. 2020;

21. Helleberg M, Niemann CU, Moestrup K, Kirk O, Lebech AM, Lane C, Lundgren J. Persistent COVID-19 in an Immunocompromised Patient Temporarily Responsive to Two Courses of Remdesivir Therapy. The Journal of infectious diseases. 2020;
22. Hill A, Wang J, Levi J, Heath K, Fortunak J. Minimum costs to manufacture new treatments for COVID-19. Journal of virus eradication. 2020;6(2):61-69.
23. Hillaker E, Belfer JJ, Bondici A, Murad H, Dumkow LE. Delayed Initiation of Remdesivir in a COVID-19 Positive Patient. Pharmacotherapy. 2020;40(6):592-598.
24. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, Spitters C, Ericson K, Wilkerson S, Tural A, Diaz G, Cohn A, Fox L, Patel A, Gerber SI, Kim L, Tong S, Lu X, Lindstrom S, Pallansch MA, Weldon WC, Biggs HM, Uyeki TM, Pillai SK, Washington State 2019-nCoV Case Investigation Team. First Case of 2019 Novel Coronavirus in the United States. The New England journal of medicine. 2020;382(10):929-936.
25. Hundt MA, Deng Y, Ciarleglio MM, Nathanson MH, Lim JK. Abnormal Liver Tests in COVID-19: A Retrospective Observational Cohort Study of 1827 Patients in a Major U.S. Hospital Network. Hepatology (Baltimore, Md.). 2020;
26. Hussain H, Fadel A, Alwaeli H, Guardiola V. Coronavirus (COVID-19) Fulminant Myopericarditis and Acute Respiratory Distress Syndrome (ARDS) in a Middle-Aged Male Patient. Cureus. 2020;12(6):e8808.
27. Igbinosa I, Miller S, Bianco K, Nelson J, Kappagoda S, Blackburn BG, Grant P, Subramanian A, Lyell D, El-Sayed Y, Aziz N. Use of Remdesivir for Pregnant Patients with Severe Novel 2019 Coronavirus Disease. American journal of obstetrics and gynecology. 2020;
28. Jiandong Zhou, Gary Tse, Sharen Lee, Tong Liu, William KK Wu, zhidong cao, Dajun Zeng, Ian CK Wong, Qingpeng Zhang, Bernard MY Cheung. Identifying main and interaction effects of risk factors to predict intensive care admission in patients hospitalized with COVID-19: a retrospective cohort study in Hong Kong. medRxiv. 2020;
29. Kaushik S, Aydin SI, Derespina KR, Bansal PB, Kowalsky S, Trachtman R, Gillen JK, Perez MM, Soshnick SH, Conway EE, Bercow A, Seiden HS, Pass RH, Ushay HM, Ofori-Amanfo G, Medar SS. Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 Infection: A Multi-institutional Study from New York City. The Journal of pediatrics. 2020;
30. Lanlan Zhou, Kelsey Huntington, Shengliang Zhang, Lindsey Carlsen, Eui-Young So, Cassandra Parker, Ilyas Sahin, Howard Safran, Suchitra Kamle, Chang-Min Lee, Chun-Geun Lee, Jack A. Elias, Kerry S. Campbell, Mandar T. Naik, Walter J. Atwood, Emile Youssef, Jonathan A. Pachter, Arunasalam Navaraj, Attila A. Seyhan, Olin Liang, Wafik El-

Deiry. Natural Killer cell activation, reduced ACE2, TMPRSS2, cytokines G-CSF, M-CSF and SARS-CoV-2-S pseudovirus infectivity by MEK inhibitor treatment of human cells. bioRxiv. 2020;

31. Lee C, Ahn MY, Byeon K, Choi JP, Hahm C, Kim H, Kim S, Kim TH, Oh J, Oh DH. Clinical Experience with Use of Remdesivir in the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2: a Case Series. Infection & chemotherapy. 2020;
32. Leegwater E, Strik A, Wilms EB, Bosma LBE, Burger DM, Ottens TH, van Nieuwkoop C. Drug-induced liver injury in a COVID-19 patient: potential interaction of remdesivir with P-glycoprotein inhibitors. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020;
33. Maharaj AR, Wu H, Hornik CP, Balevic SJ, Hornik CD, Smith PB, Gonzalez D, Zimmerman KO, Benjamin DK, Cohen-Wolkowiez M, Best Pharmaceuticals for Children Act–Pediatric Trials Network Steering Committee. Simulated Assessment of Pharmacokinetically Guided Dosing for Investigational Treatments of Pediatric Patients With Coronavirus Disease 2019. JAMA pediatrics. 2020;:e202422.
34. McCoy J.A., Short W.R., Srinivas S.K., Levine L.D., Hirshberg A.. Compassionate use of remdesivir for treatment of severe coronavirus disease 2019 in pregnant women at a United States academic center. American J. Obstet. Gynecol. MFM. 2020;
35. Montastruc F, Thuriot S, Durrieu G. Hepatic disorders with the use of remdesivir for coronavirus 2019 (COVID-19). Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2020;
36. Naqvi M, Zakowski P, Glucksman L, Smithson S, Burwick RM. Tocilizumab and Remdesivir in a Pregnant Patient With Coronavirus Disease 2019 (COVID-19). Obstetrics and gynecology. 2020;
37. Nathaniel James Rhodes, Atheer Dairem, William Moore, Anooj Shah, Michael J Postelnick, Melissa E. Badowski, Sarah M Michienzi, Jaime L Borkowski, Radhika S Polisetty, Karen Fong, Emily S Spivek, James R Beardsley, Cory M Hale, Andrea M Pallotta, Pavithra Srinivas, Lucas T Schulz. Multicenter point-prevalence evaluation of the utilization and safety of drug therapies for COVID-19. medRxiv. 2020;
38. Nichols BE, Jamieson L, Zhang SRC, Rao GA, Silal S, Pulliam JRC, Sanne I, Meyer-Rath G. The role of remdesivir in South Africa: preventing COVID-19 deaths through increasing ICU capacity. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020;
39. Olender SA, Perez KK, Go AS, Balani B, Price-Haywood EG, Shah NS, Wang S, Walunas TL, Swaminathan S, Slim J, Chin B, De Wit S, Ali SM, Soriano Viladomiu A, Robinson P, Gottlieb RL, Tsang TYO, Lee IH, Haubrich RH, Chokkalingam AP, Lin L, Zhong L, Bekele BN, Mera-Giler R, Gallant J, Smith LE, Osinusi AO, Brainard DM, Hu H, Phulpin C, Edgar H, Diaz-Cuervo H, Bernardino JI. Remdesivir for Severe COVID-19 versus a Cohort Receiving

Standard of Care. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020;

40. Olga Vasylyeva, Tara Chen, John Hanna. Remdesivir for COVID-19: match-population analysis with compassionate use of Remdesivir for severe COVID-19. medRxiv. 2020;
41. Orf K, Rogosic S, Dexter D, Ancliff P, Badle S, Brierley J, Cheng D, Dalton C, Dixon G, Du Pré P, Grandjean L, Ghorashian S, Mittal P, O'Connor D, Pavasovic V, Rao A, Samarasinghe S, Vora A, Bamford A, Bartram J. Remdesivir during induction chemotherapy for newly diagnosed paediatric acute lymphoblastic leukaemia with concomitant SARS-CoV-2 infection. British journal of haematology. 2020;
42. Pierce-Williams RAM, Burd J, Felder L, Khoury R, Bernstein PS, Avila K, Penfield CA, Roman AS, DeBolt CA, Stone JL, Bianco A, Kern-Goldberger AR, Hirshberg A, Srinivas SK, Jayakumaran JS, Brandt JS, Anastasio H, Birsner M, O'Brien DS, Sedev HM, Dolin CD, Schnettler WT, Suhag A, Ahluwalia S, Navathe RS, Khalifeh A, Anderson K, Berghella V. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. American journal of obstetrics & gynecology MFM. 2020;:100134.
43. Rivera DR, Peters S, Panagiotou OA, Shah DP, Kuderer NM, Hsu CY, Rubinstein SM, Lee BJ, Choueiri TK, de Lima Lopes G, Grivas P, Painter CA, Rini BI, Thompson MA, Arcobello J, Bakouny Z, Doroshow DB, Egan PC, Farmakiotis D, Fecher LA, Friese CR, Galsky MD, Goel S, Gupta S, Halfdanarson TR, Halmos B, Hawley JE, Khaki AR, Lemmon CA, Mishra S, Olszewski AJ, Pennell NA, Puc MM, Revankar SG, Schapira L, Schmidt A, Schwartz GK, Shah SA, Wu JT, Xie Z, Yeh AC, Zhu H, Shyr Y, Lyman GH, Warner JL. Utilization of COVID-19 treatments and clinical outcomes among patients with cancer: A COVID-19 and Cancer Consortium (CCC19) cohort study. Cancer discovery. 2020;
44. Segar S, Bouland D, Torriani F, Kwak K, Asudani D, Taplitz R, Gupta V. Flight of the COVID-19 patient: experience with a Wuhan evacuee: a case report. Journal of medical case reports. 2020;14(1):66.
45. Sodani P, Mucci L, Girolimetti R, Tedesco S, Monaco F, Campanozzi D, Brunori M, Maltoni S, Bedetta S, Di Carlo AM, Candoli P, Mancini M, Rebonato A, D'Adamo F, Capalbo M, Frausini G. Successful recovery from COVID-19 pneumonia after receiving baricitinib, tocilizumab, and remdesivir. A case report: Review of treatments and clinical role of computed tomography analysis. Respiratory medicine case reports. 2020;31:101115.
46. Kujawski, Wong, Collins et al. First 12 patients with coronavirus disease 2019 (COVID-19) in the United States. medRxiv. 2020;
47. Tempestilli M, Caputi P, Avataneo V, Notari S, Forini O, Scorzolini L, Marchioni L, Ascoli Bartoli T, Castilletti C, Lalle E, Capobianchi MR, Nicastri E, D'Avolio A, Ippolito G, Agrati C. Pharmacokinetics of remdesivir and GS-441524 in two critically ill patients who recovered from COVID-19. The Journal of antimicrobial chemotherapy. 2020;

48. Ting-Yu Lin, Wei-Jung Chang, Chen-Yang Hsu, Chao-Chih Lai, Amy Ming-Fang Yen, Sam Li-Sheng Chen, Hsiu-Hsi Chen. Impacts of remdesivir on dynamics and efficacy stratified by the severity of COVID-19: a simulated two-arm controlled study. medRxiv. 2020;
49. Tymor Carpenter Hamamsy, Richard Bonneau. Twitter activity about treatments during the COVID-19 pandemic: case studies of remdesivir, hydroxychloroquine, and convalescent plasma. medRxiv. 2020;
50. Zampino R, Mele F, Florio LL, Bertolino L, Andini R, Galdo M, De Rosa R, Corcione A, Durante-Mangoni E. Liver injury in remdesivir-treated COVID-19 patients. Hepatology international. 2020;
51. Pasquini Z, Montalti R, Temperoni C, Canovari B, Mancini M, Tempesta M, Pimpini D, Zallocco N, Barchiesi F. Effectiveness of remdesivir in patients with COVID-19 under mechanical ventilation in an Italian ICU. The Journal of antimicrobial chemotherapy. 2020;

Ongoing studies

References to ongoing randomized trials

1. Capital Medical University. Mild/Moderate 2019-nCoV Remdesivir RCT. clinicaltrials.gov. 2020;
2. FIB-HCSC. An international randomized trial of additional treatments for COVID-19 in hospitalized patients who are all receiving the local standard of care. EU Clinical Trials Register. 2020;
3. Gilead Sciences, Inc.. A Phase 3 Randomized Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-5734™) in Participants with Severe COVID-19. EU Clinical Trials Register. 2020;
4. Gilead Sciences. Study to Evaluate the Efficacy and Safety of Remdesivir (GS-5734™) Treatment of Coronavirus Disease 2019 (COVID-19) in an Outpatient Setting. clinicaltrials.gov. 2020;
5. Gilead Sciences. Study to Evaluate the Safety and Antiviral Activity of Remdesivir (GS-5734™) in Participants With Moderate Coronavirus Disease (COVID-19) Compared to Standard of Care Treatment. clinicaltrials.gov. 2020;
6. Hoffmann-La Roche. A Study to Evaluate the Efficacy and Safety of Remdesivir Plus Tocilizumab Compared With Remdesivir Plus Placebo in Hospitalized Participants With Severe COVID-19 Pneumonia. clinicaltrials.gov. 2020;
7. INSERM. Multi-centre, adaptive, randomized trial of the safety and efficacy of treatments of COVID-19 in hospitalized adults. EU Clinical Trials Register. 2020;
8. Institut National de la Santé Et de la Recherche Médicale, France. Trial of Treatments for COVID-19 in Hospitalized Adults. clinicaltrials.gov. 2020;

9. National Institute of Allergy and Infectious Diseases (NIAID). Adaptive COVID-19 Treatment Trial 2 (ACTT-II). clinicaltrials.gov. 2020;
10. National Institute of Allergy and Infectious Diseases (NIAID). Adaptive COVID-19 Treatment Trial 3 (ACTT-3). clinicaltrials.gov. 2020;
11. National Institute of Allergy and Infectious Diseases (NIAID). Therapeutics for Inpatients With COVID-19. clinicaltrials.gov. 2020;
12. Oslo University Hospital. The Efficacy of Different Antiviral Drugs in (Severe Acute Respiratory Syndrome-Corona Virus-2) SARS-CoV-2. clinicaltrials.gov. 2020;
13. QuantumLeap Healthcare Collaborative. I-SPY COVID-19 TRIAL: An Adaptive Platform Trial for Critically Ill Patients. clinicaltrials.gov. 2020;
14. Regents of the University of Minnesota. A Multicenter, Adaptive, Randomised Blinded Controlled Trial of the Safety and Efficacy of Investigational Therapeutics for the Treatment of COVID-19 in Hospitalized Adults - Version for European U... EU Clinical Trials Register. 2020;
15. ViralClear Pharmaceuticals, Inc.. Study of Merimepodib in Combination With Remdesivir in Adult Patients With Advanced COVID-19. clinicaltrials.gov. 2020;
16. World Health Organization. Public health emergency SOLIDARITY trial of treatments for COVID-19 infection in hospitalized patients. isrctn.com. 2020;

References to other ongoing studies (not randomized)

1. Assistance Publique - Hôpitaux de Paris. Multicenter, Retrospective Study of the Effects of Remdesivir in the Treatment of Severe Covid-19 Infections. clinicaltrials.gov. 2020;
2. Gilead Sciences Inc.. Phase 2/3 study of Remdesivir in patients from birth to <18 years old with COVID-19. EU Clinical Trials Register. 2020;
3. Gilead Sciences, Inc.. Expanded Access Treatment Protocol: Remdesivir (RDV;GS-5734) for the Treatment of SARS-CoV2 (CoV) Infection- COVID-19. EU Clinical Trials Register. 2020;
4. Gilead Sciences. Expanded Access Treatment Protocol: Remdesivir (RDV; GS-5734) for the Treatment of SARS-CoV2 (CoV) Infection. clinicaltrials.gov. 2020;
5. Gilead Sciences. Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of Remdesivir (GS-5734™) in Participants From Birth to < 18 Years of Age With Coronavirus Disease 2019 (COVID-19). clinicaltrials.gov. 2020;

6. Groupe Hospitalier Pitie-Salpetriere. Adverse Events Related to Treatments Used Against Coronavirus Disease 2019. clinicaltrials.gov. 2020;
7. Groupe Hospitalier Pitie-Salpetriere. Effect of Treatments in Patients Hospitalized for Severe COVID-19 Pneumonia: a Multicenter Cohort Study. clinicaltrials.gov. 2020;
8. Tehran University of Medical Sciences. A single-arm multicenter clinical trial to evaluate the safety and efficacy of Remdesivir in COVID-19 patients with progressive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Iranian Registry of Clinical Trials. 2020;
9. US Army Medical Research and Development Command. Expanded Access Remdesivir (RDV; GS-5734™). clinicaltrials.gov. 2020;
10. UNICEF. Investigational Treatments for COVID-19 in Tertiary Care Hospital of Pakistan. clinicaltrials.gov. 2020;