[Baricitinib] for [COVID-19]

Review information

Authors

[Empty name][1]

[1][Empty affiliation]

Citation example: [Empty name]. [Baricitinib] for [COVID-19]. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Ely 2021

Methods	
Participants	
Interventions	
Outcomes	
Identification	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Risk of bias in selection of the reported result	Unclear risk	
Overall risk of bias	Unclear risk	
Risk of bias arising from the randomization process	Unclear risk	
Risk of bias in measurement of the outcome	Unclear risk	
Risk of bias due to deviations from the intended interventions	Unclear risk	
Missing outcome data	Unclear risk	

Kalil 2020

Methods	**Study design:** Randomized controlled trial **Study grouping:**
Participants	**Baseline Characteristics** Baricitinib plus remdesivir ● *No. randomised (N)*: 515 ● *Participants with laboratory confirmed COVID-19 (%)*: 100 ● *Participants with moderate illness (%)*: 69.5 ● *Participants with severe illness (%)*: 30.5 ● *Age (mean [range])*: 55.8 [16.0] ● *Female participants (%)*: 38.1 ● *Participants with hypertension (%)*: 51 ● *Participants with diabetes (%)*: 39 Remdesivir ● *No. randomised (N)*: 518 ● *Participants with laboratory confirmed COVID-19 (%)*: 100 ● *Participants with moderate illness (%)*: 67.2 ● *Participants with severe illness (%)*: 32.8 ● *Age (mean [range])*: 55.0 [15.4] ● *Female participants (%)*: 35.7 ● *Participants with hypertension (%)*: 52 ● *Participants with diabetes (%)*: 35 Overall ● *No. randomised (N)*: 1033 ● *Participants with moderate illness (%)*: 68.3 ● *Participants with severe illness (%)*: 31.7 ● *Age (mean [range])*: 55.4 [15.7] ● *Female participants (%)*: 36.9 ● *Participants with hypertension (%)*: 52 ● *Participants with diabetes (%)*: 37 **Included criteria:** 1. Admitted to a hospital with symptoms suggestive of COVID-19.2. Subject (or legally authorized representative) provides informed consent prior toinitiation of any study procedures.3. Subject (or legally authorized representative) understands and agrees to comply withplanned study procedures.4. Male or non-pregnant female adult ≥18 years of age at time of enrollment.5. Has laboratory-confirmed SARS-CoV-2 infection as determined by PCR or othercommercial or public health assay in any specimen6. Illness of any duration, and at least one of the following:● Radiographic infiltrates by imaging (chest x-ray, CT scan, etc.), OR● SpO2 ≤ 94% on room air, OR● Requiring supplemental oxygen, OR● Requiring mechanical ventilation.7. Women of childbearing potential must agree to either abstinence or use at least oneprimary form of contraception not including hormonal contraception from the time ofscreening through Day 29.8. Agrees to not participate in another clinical trial for the treatment of COVID-19 orSARS-CoV-2 through Day 29. **Excluded criteria:** ALT or AST > 5 times the upper limit of normal.2. Estimated glomerular filtration rate (eGFR) < 30 ml/min (including patients

	receivinghemodialysis or hemofiltration).3. Pregnancy or breastfeeding.4. Anticipated discharge from the hospital or transfer to another hospital which is not astudy site within 72 hours.5. Allergy to any study medication. **Pretreatment:**
Interventions	**Intervention Characteristics** Baricitinib plus remdesivir ● *Intervention (including dosage, route of administration, loading and maintenance phases)*: Baricitinib was administeredas a 4-mg daily dose (either orally [two 2-mg tablets]or through a nasogastric tube) for 14 days oruntil hospital discharge. Patients with an estimatedglomerular filtration rate of less than 60 ml perminute received baricitinib at a dose of 2 mgonce daily. ● *Co-intervention (including description of standard care)*: Patients received remdesivir intravenouslyas a 200-mg loading dose on day 1, followedby a 100-mg maintenance dose administered daily on days 2 through 10 or until hospitaldischarge or death ● *Duration of treatment (days)*: 14 days or hospital discharge ● *Follow up after randomisation (days)*: 29 days Remdesivir ● *Intervention (including dosage, route of administration, loading and maintenance phases)*: Matched placebo ● *Co-intervention (including description of standard care)*: Patients received remdesivir intravenouslyas a 200-mg loading dose on day 1, followedby a 100-mg maintenance dose administereddaily on days 2 through 10 or until hospitaldischarge or death ● *Duration of treatment (days)*: 14 days or hospital discharge ● *Follow up after randomisation (days)*: 29 days
Outcomes	*All-cause mortality (Day 28)* ● **Outcome type**: DichotomousOutcome *All-cause mortality (Day 14)* ● **Outcome type**: DichotomousOutcome *Invasive mechanical ventilation* ● **Outcome type**: DichotomousOutcome *NIV / HFNO* ● **Outcome type**: DichotomousOutcome *Serious adverse events* ● **Outcome type**: DichotomousOutcome *Adverse events* ● **Outcome type**: DichotomousOutcome *Clinical recovery* ● **Outcome type**: DichotomousOutcome
Identification	**Sponsorship source:** Division of Microbiology and Infectious Diseases (DMID),National Institute of Allergy and Infectious Diseases,National Institutes of Health **Country:** United States of America

	Setting: Hospital **Comments:** **Authors name:** A.C. Kalil **Institution:** University of Nebraska Medical Center **Email:** akalil@unmc.edu **Address:** University of Nebraska MedicalCenter, 985400 Nebraska Medicine,Omaha, NE 68198-5400 **Clinical trial identifier:** ClinicalTrials.gov number,NCT04421027 **Preprint or peer reviewed:** Peer reviewed **Single centre or multi-centre (no. of centres):** Multi-centre 67 trial sites in 8 countries:the United States (55 sites), Singapore (4),South Korea (2), Mexico (2), Japan (1), Spain (1),the United Kingdom (1), and Denmark (1).
Notes	**Included** Median duration of initial hospitalization (IQR) — days Bricitinib 8 (5 to 15) vs placebo 8 (5 to 20)Median time to recovery (95% CI) — days Bricitinib 7 (6–8) vs placebo 8 (7–9) **Included** New use of Mechanical ventilation No. of patients/total no. Baricitinib+RDV 46/461 vs Placebo+RDV 70/461. We have used version 2 of the Cochrane risk-of-bias tool for randomised trials (RoB 2) to assess the risk of bias for this study. Refer to Main text > Published notes for more details.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Risk of bias in selection of the reported result	Low risk	"Randomisation was stratified by study site and disease severity at enrollment and was performed using a web-based Internet Data Entry System, Advantage eClinical".
Overall risk of bias	Low risk	Allocation sequence concealed
Risk of bias arising from the randomization process	Low risk	Randomisation performed using a web-based internet data entry system, Advantage eClinical.
Risk of bias in measurement of the outcome	Low risk	"The trial team was unaware of the trial-group assignments until after all data queries were resolved and the database was locked."
Risk of bias due to deviations from the intended interventions	Low risk	The majority of patients received intended intervention.
Missing outcome data	Low risk	Results reported for intention to treat population.

Marconi 2021

Methods	
Participants	
Interventions	
Outcomes	
Identification	
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Risk of bias in selection of the reported result	Unclear risk	
Overall risk of bias	Unclear risk	
Risk of bias arising from the randomization process	Unclear risk	
Risk of bias in measurement of the outcome	Unclear risk	
Risk of bias due to deviations from the intended interventions	Unclear risk	
Missing outcome data	Unclear risk	

Footnotes

Characteristics of excluded studies

Footnotes

References to studies

Included studies

Ely 2021

[Empty]

Kalil 2020

Kalil AC; Patterson TF; Mehta AK; Tomashek KM; Wolfe CR; Ghazaryan V; Marconi VC; Ruiz-Palacios GM; Hsieh L; Kline S; Tapson V; Iovine NM; Jain MK; Sweeney DA; El Sahly HM; Branche AR; Regalado Pineda J; Lye DC; Sandkovsky U; Luetkemeyer AF; Cohen SH; Finberg RW; Jackson PEH; Taiwo B; Paules CI; Arguinchona H; Goepfert P; Ahuja N; Frank M; Oh MD; Kim ES; Tan SY; Mularski RA; Nielsen H; Ponce PO; Taylor BS; Larson L; Rouphael NG; Saklawi Y; Cantos VD; Ko ER; Engemann JJ; Amin AN; Watanabe M; Billings J; Elie MC; Davey RT; Burgess TH; Ferreira J; Green M; Makowski M; Cardoso A; de Bono S; Bonnett T; Proschan M; Deye GA; Dempsey W; Nayak SU; Dodd LE; Beigel JH. Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19.. N Engl J Med 2020. [DOI: 10.1056/NEJMoa2031994]

Marconi 2021

[Empty]

Excluded studies

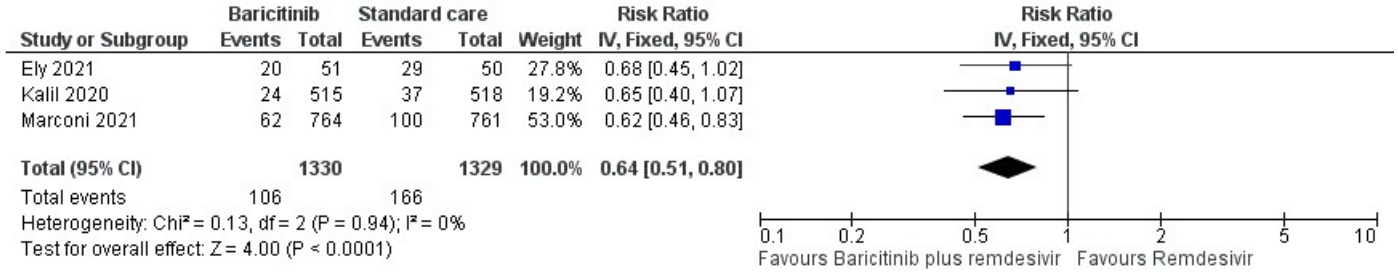
Data and analyses

1 Baricitinib vs standard care

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Discontinuation due to adverse event	1	1502	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.57, 1.12]
1.2 Duration of hospitalisation	0	0	Mean Difference (IV, Random, 95% CI)	Not estimable
1.8 All-cause mortality (Day 28)	3	2659	Risk Ratio (IV, Fixed, 95% CI)	0.64 [0.51, 0.80]
1.9 All-cause mortality (Day 14)	1	1033	Risk Ratio (IV, Fixed, 95% CI)	0.54 [0.23, 1.25]
1.12 Invasive mechanical ventilation	1	922	Risk Ratio (IV, Fixed, 95% CI)	0.66 [0.46, 0.93]
1.13 NIV / HFNO	1	706	Risk Ratio (IV, Fixed, 95% CI)	0.83 [0.63, 1.10]
1.16 Serious adverse events	3	2617	Risk Ratio (IV, Fixed, 95% CI)	0.77 [0.66, 0.90]
1.17 Adverse events	3	2634	Risk Ratio (IV, Fixed, 95% CI)	0.94 [0.87, 1.01]
1.24 Clinical recovery	2	1134	Risk Ratio (IV, Fixed, 95% CI)	1.08 [1.01, 1.14]

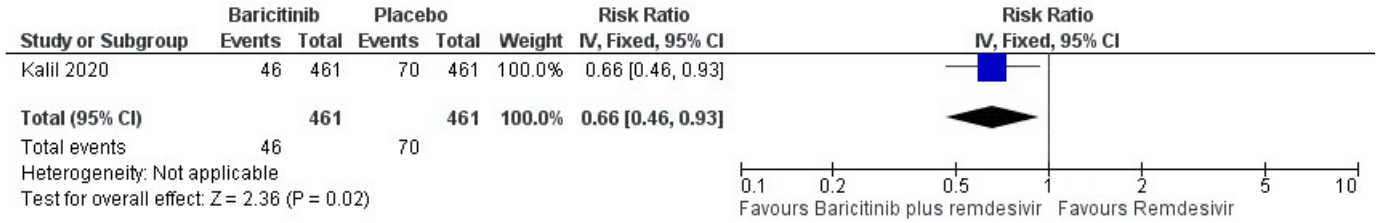
Figures

Figure 1 (Analysis 1.8)



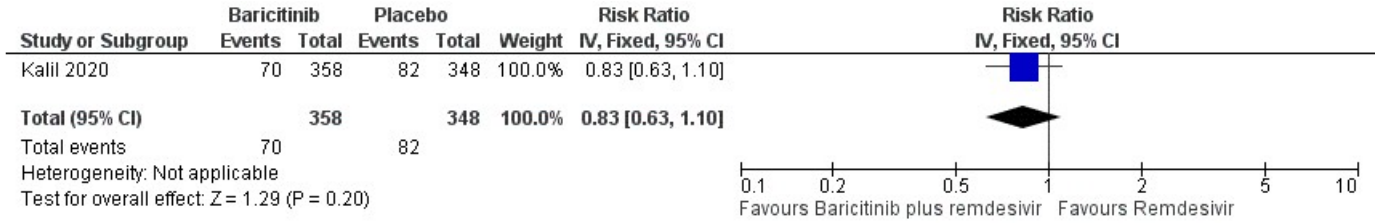
Forest plot of comparison: 1 Baricitinib vs standard care, outcome: 1.8 All-cause mortality (Day 28).

Figure 2 (Analysis 1.12)



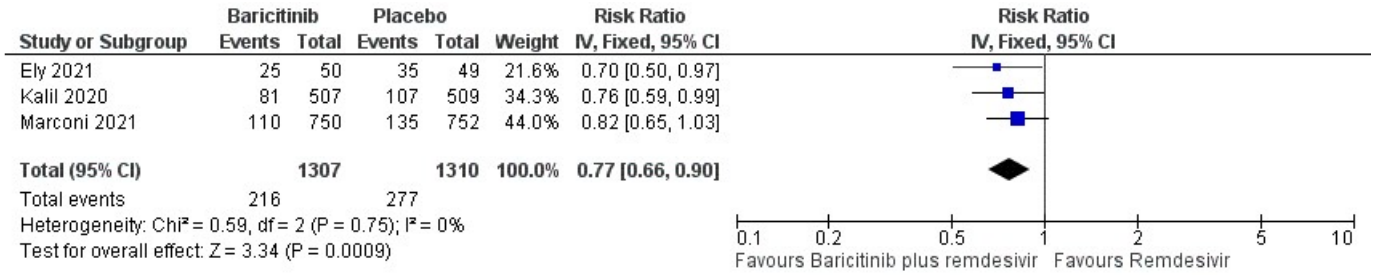
Forest plot of comparison: 1 Baricitinib vs standard care, outcome: 1.12 Invasive mechanical ventilation.

Figure 3 (Analysis 1.13)



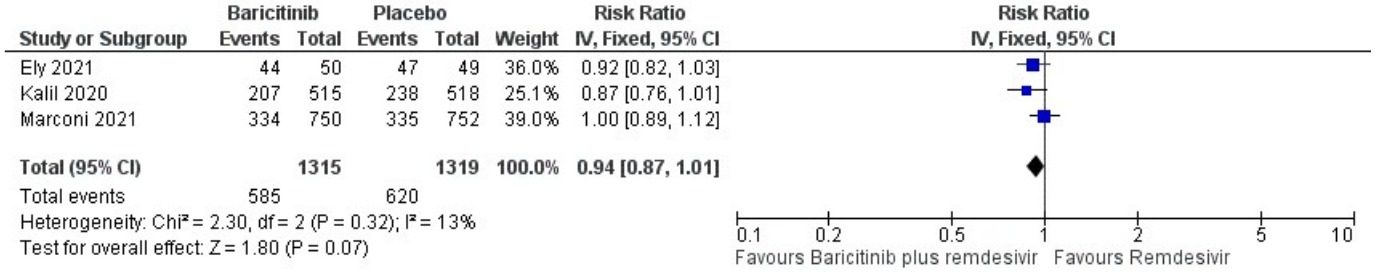
Forest plot of comparison: 1 Baricitinib vs standard care, outcome: 1.13 NIV / HFNO.

Figure 4 (Analysis 1.16)



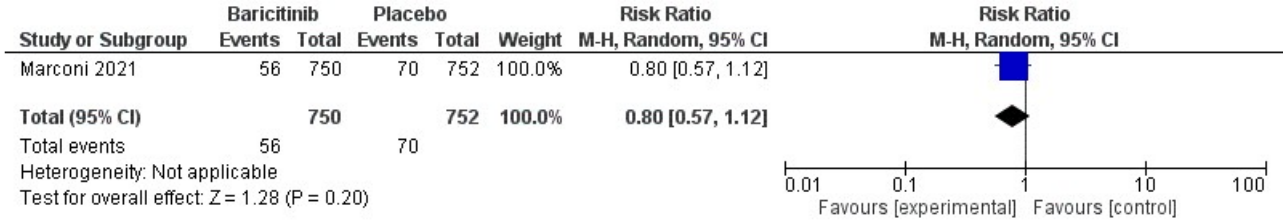
Forest plot of comparison: 1 Baricitinib vs standard care, outcome: 1.16 Serious adverse events.

Figure 5 (Analysis 1.17)



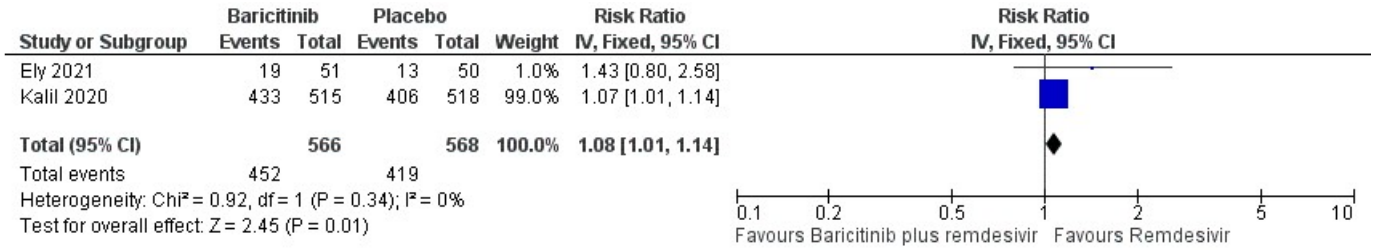
Forest plot of comparison: 1 Baricitinib vs standard care, outcome: 1.17 Adverse events.

Figure 6 (Analysis 1.1)



Forest plot of comparison: 1 Baricitinib vs standard care, outcome: 1.1 Discontinuation due to adverse event.

Figure 7 (Analysis 1.24)



Forest plot of comparison: 1 Baricitinib vs standard care, outcome: 1.24 Clinical recovery.