



Table 5a. Systemic Corticosteroids: Selected Clinical Trial Data

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The clinical trials described in this table do not represent all the trials that the Panel reviewed while developing the recommendations for systemic corticosteroids. The studies summarized below are those that have had the greatest impact on the Panel's recommendations. Unless stated otherwise, the clinical trials listed below only included participants aged ≥ 18 years.

Methods	Results	Limitations and Interpretation
RECOVERY: Open-Label RCT of Dexamethasone in Hospitalized Patients With COVID-19 in the United Kingdom¹		
<p>Key Inclusion Criterion</p> <ul style="list-style-type: none"> Hospitalized with suspected or laboratory-confirmed SARS-CoV-2 infection <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> Physician determination, based on patient's medical history, that risk of participation was too great An indication for corticosteroid therapy outside of the study <p>Interventions</p> <ul style="list-style-type: none"> DEX 6 mg IV or PO once daily plus SOC for up to 10 days or until discharge (n = 2,104) SOC alone (n = 4,321) <p>Primary Endpoint</p> <ul style="list-style-type: none"> All-cause mortality at 28 days 	<p>Participant Characteristics</p> <ul style="list-style-type: none"> Mean age 66 years; 64% men; 73% White 56% had ≥ 1 comorbidity; 24% with DM 89% had laboratory-confirmed SARS-CoV-2 infection Median of 7 days of DEX therapy At randomization: <ul style="list-style-type: none"> 16% received MV or ECMO 60% required supplemental oxygen but not MV 24% required no supplemental oxygen Received RDV: $< 1\%$ in both arms Received tocilizumab or sarilumab: 2% in DEX arm vs. 3% in SOC arm <p>Primary Outcome</p> <ul style="list-style-type: none"> All-cause mortality at 28 days in DEX arm vs. SOC arm: <ul style="list-style-type: none"> All patients: 23% vs. 26% (age-adjusted rate ratio 0.83; 95% CI, 0.75–0.93; $P < 0.001$) Patients who required MV or ECMO at randomization: 29% vs. 41% (rate ratio 0.64; 95% CI, 0.51–0.81) Patients who required supplemental oxygen but not MV at randomization: 23% vs. 26% (rate ratio 0.82; 95% CI, 0.72–0.94) Patients who did not require supplemental oxygen at randomization: 18% vs. 14% (rate ratio 1.19; 95% CI, 0.92–1.55) 	<p>Key Limitations</p> <ul style="list-style-type: none"> Open-label study Published data did not include results for key secondary endpoints (e.g., cause-specific mortality, need for renal replacement), AEs, and key subgroups (e.g., patients with comorbidities). Patients who required supplemental oxygen (but not MV) had variable severity of illness. It is unclear whether all patients in this group benefited from DEX or whether benefit was restricted to those requiring higher levels of supplemental oxygen. Patients aged > 80 years were preferentially assigned to receive supplemental oxygen therapy (and not MV). High mortality in this study may limit the generalizability of results to populations with lower baseline mortality. <p>Interpretation</p> <ul style="list-style-type: none"> In hospitalized patients with severe COVID-19 who required supplemental oxygen, DEX reduced mortality at 28 days. The greatest benefit was seen in those receiving MV at randomization. There was no survival benefit for DEX in patients who did not require supplemental oxygen at randomization.

Methods	Results	Limitations and Interpretation
CoDEX: Open-Label RCT of Dexamethasone in Patients With Moderate or Severe ARDS and COVID-19 in Brazil²		
<p>Key Inclusion Criteria</p> <ul style="list-style-type: none"> Confirmed or suspected SARS-CoV-2 infection Received MV within 48 hours of meeting criteria for moderate to severe ARDS (PaO₂/FiO₂ ≤200 mm Hg) <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> Received immunosuppressive drugs in past 21 days Death expected within 24 hours <p>Interventions</p> <ul style="list-style-type: none"> DEX 20 mg IV once daily for 5 days, then DEX 10 mg IV once daily for 5 days or until ICU discharge (n = 151) SOC alone (n = 148) <p>Primary Endpoint</p> <ul style="list-style-type: none"> Number of days alive and free from MV by Day 28 <p>Key Secondary Endpoints</p> <ul style="list-style-type: none"> All-cause mortality by Day 28 Number of ICU-free days by Day 28 Duration of MV by Day 28 Score on 6-point OS at Day 15 SOFA score at Day 7 	<p>Participant Characteristics</p> <ul style="list-style-type: none"> Mean age 61 years; 63% men Comorbidities in DEX arm vs. SOC arm: <ul style="list-style-type: none"> Obesity: 31% vs. 24% DM: 38% vs. 47% Vasopressor use: 66% in DEX arm vs. 68% in SOC arm Mean PaO₂/FiO₂: 131 mm Hg in DEX arm vs. 133 mm Hg in SOC arm Median of 10 days of DEX therapy No patients received RDV or tocilizumab 35% in SOC arm received corticosteroids for indications such as bronchospasm or septic shock <p>Primary Outcome</p> <ul style="list-style-type: none"> Mean number of days alive and free from MV by Day 28: 7 in DEX arm vs. 4 in SOC arm (<i>P</i> = 0.04) <p>Secondary Outcomes</p> <ul style="list-style-type: none"> No differences between arms by Day 28 in all-cause mortality (56% in DEX arm vs. 62% in SOC arm), number of ICU-free days, or duration of MV or at Day 15 in score on 6-point OS Mean SOFA score at Day 7: 6.1 in DEX arm vs. 7.5 in SOC arm (<i>P</i> = 0.004) <p>Other Outcome</p> <ul style="list-style-type: none"> Post hoc analysis of probability of death or MV by Day 15: 68% in DEX arm vs. 80% in SOC arm (OR 0.46) 	<p>Key Limitations</p> <ul style="list-style-type: none"> Open-label study Underpowered; enrollment stopped after release of data from the RECOVERY trial. Patients discharged before 28 days were not followed for rehospitalization or mortality. High mortality in this study may limit the generalizability of results to populations with a lower baseline mortality. More than one-third of those randomized to receive SOC also received corticosteroids. <p>Interpretation</p> <ul style="list-style-type: none"> Compared with SOC alone, DEX increased the number of days alive and free of MV over 28 days in patients with COVID-19 and moderate to severe ARDS.

Methods	Results	Limitations and Interpretation
Observational Cohort Study of Dexamethasone in Hospitalized Patients With COVID-19 Who Were Not on Intensive Respiratory Support in the United States³		
<p>Key Inclusion Criterion</p> <ul style="list-style-type: none"> • Within 14 days of a positive SARS-CoV-2 test result <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> • Recent receipt of corticosteroids • Receipt of IRS (defined as HFNC oxygen, NIV, or MV) within 48 hours • Hospital LOS <48 hours <p>Interventions</p> <ul style="list-style-type: none"> • Corticosteroids (95% received DEX) administered within 48 hours of admission (n = 7,507) • No corticosteroids administered (n = 7,433) <p>Primary Endpoint</p> <ul style="list-style-type: none"> • All-cause mortality at 90 days 	<p>Participant Characteristics</p> <ul style="list-style-type: none"> • Mean age 71 years; 95% men; 27% Black, 55% White • 77% did not receive IRS within 48 hours • 83% admitted within 1 day after positive SARS-CoV-2 test result • Median duration of DEX for patients who did not receive IRS: 5 days for those not on supplemental oxygen at baseline vs. 6 days for those on low-flow nasal cannula oxygen • Received RDV: 43% of those who received DEX vs. 13% of those who did not • Received anticoagulants: 46% of those who received DEX vs. 10% of those who did not <p>Primary Outcome</p> <ul style="list-style-type: none"> • Risk of all-cause mortality at 90 days higher in those who received DEX: <ul style="list-style-type: none"> • Combination of those not on supplemental oxygen and those on low-flow nasal cannula oxygen: HR 1.59; 95% CI, 1.39–1.81 • Those not on supplemental oxygen: HR 1.76; 95% CI, 1.47–2.12 • Those on low-flow nasal cannula oxygen: HR 1.08; 95% CI, 0.86–1.36 	<p>Key Limitations</p> <ul style="list-style-type: none"> • Retrospective observational study • Because nearly all patients on MV or HFNC oxygen received DEX, analysis was restricted to patients who did not receive IRS (i.e., those who received no supplemental oxygen or only low-flow nasal cannula oxygen). • There were differences between the arms in other therapies received. The investigators attempted to account for this using different approaches (e.g., propensity scoring, weighted analyses, subgroup/sensitivity analyses). <p>Interpretation</p> <ul style="list-style-type: none"> • In hospitalized patients with COVID-19, the use of DEX was not associated with a reduction in mortality among those who received low-flow nasal cannula oxygen during the first 48 hours after admission, but it was associated with increased mortality among those who received no supplemental oxygen during the first 48 hours after admission.

Methods	Results	Limitations and Interpretation
COVID STEROID 2: Blinded RCT of Dexamethasone 12 mg Versus 6 mg in Hospitalized Adults With COVID-19 and Severe Hypoxemia in Denmark, India, Sweden, and Switzerland^{4,5}		
<p>Key Inclusion Criteria</p> <ul style="list-style-type: none"> Confirmed SARS-CoV-2 infection Requiring oxygen ≥ 10 L/min, NIV, CPAP, or MV <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> Treated with DEX >6 mg (or equivalent) Treated with corticosteroid within past 5 days Invasive fungal infection or active TB <p>Interventions</p> <ul style="list-style-type: none"> DEX 12 mg IV once daily for up to 10 days (n = 497) DEX 6 mg IV once daily for up to 10 days (n = 485) <p>Primary Endpoint</p> <ul style="list-style-type: none"> Number of days alive without life support (MV, circulatory support, or kidney replacement therapy) at 28 days <p>Key Secondary Endpoints</p> <ul style="list-style-type: none"> Number of days alive without life support at 90 days Number of days alive and out of hospital at 90 days Mortality at 90 days Mortality at 28 days SAEs at 28 days 	<p>Participant Characteristics</p> <ul style="list-style-type: none"> Median age 65 years; 31% women DM: 27% in 12 mg arm vs. 34% in 6 mg arm Median of 7 days from symptom onset to hospitalization in both arms Received ICU care: 78% in 12 mg arm vs. 81% in 6 mg arm Oxygen requirements: <ul style="list-style-type: none"> 54% on oxygen via nasal cannula or face mask (median flow rate 23 L/min) 25% on NIV 21% on MV 63% received RDV; 12% received IL-6 inhibitors or JAK inhibitors Median of 7 days of DEX therapy in both arms <p>Primary Outcome</p> <ul style="list-style-type: none"> Median number of days alive without life support at 28 days: 22.0 in 12 mg arm vs. 20.5 in 6 mg arm (adjusted mean difference 1.3 days; 95% CI, 0.0–2.6; $P = 0.07$) <ul style="list-style-type: none"> 63.9% Bayesian probability of clinically important benefit and 0.3% Bayesian probability of clinically important harm for DEX 12 mg <p>Secondary Outcomes</p> <ul style="list-style-type: none"> At 90 days: <ul style="list-style-type: none"> Median number of days alive without life support: 84 in 12 mg arm vs. 80 in 6 mg arm ($P = 0.15$) Median number of days alive and out of hospital: 62 in 12 mg arm vs. 48 in 6 mg arm ($P = 0.09$) Mortality: 32% in 12 mg arm vs. 38% in 6 mg arm (adjusted relative risk 0.87; 99% CI, 0.70–1.07; $P = 0.09$) At 28 days: <ul style="list-style-type: none"> Mortality: 27% in 12 mg arm vs. 32% in 6 mg arm (adjusted relative risk 0.86; 99% CI, 0.68–1.08; $P = 0.10$) 	<p>Key Limitation</p> <ul style="list-style-type: none"> The randomized intervention period was <10 days for some patients because the trial allowed up to 4 days of DEX before enrollment. <p>Interpretation</p> <ul style="list-style-type: none"> Among patients with COVID-19 and severe hypoxemia, the use of DEX 12 mg once daily did not result in more days alive without life support at 28 days than DEX 6 mg once daily. A preplanned Bayesian analysis showed that DEX 12 mg had a higher probability of benefit and a lower probability of harm than DEX 6 mg.⁵

Methods	Results	Limitations and Interpretation
COVID STEROID 2: Blinded RCT of Dexamethasone 12 mg Versus 6 mg in Hospitalized Adults With COVID-19 and Severe Hypoxemia in Denmark, India, Sweden, and Switzerland^{4,5}, continued		
	<ul style="list-style-type: none"> • SAEs, including septic shock and invasive fungal infections: 11% in 12 mg arm vs. 13% in 6 mg arm (adjusted relative risk 0.83; 99% CI, 0.54–1.29; $P = 0.27$) 	
CAPE COVID: Double-Blind RCT of Hydrocortisone Among Critically Ill Patients With COVID-19 in France⁶		
<p>Key Inclusion Criteria</p> <ul style="list-style-type: none"> • Laboratory-confirmed SARS-CoV-2 infection or radiographically suspected COVID-19 with ≥ 1 of the following: <ul style="list-style-type: none"> • MV with PEEP ≥ 5 cm H₂O • PaO₂/FiO₂ <300 mm Hg and FiO₂ $\geq 50\%$ on HFNC • PaO₂/FiO₂ <300 mm Hg on reservoir mask oxygen • Pulmonary severity index score >130 <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> • Septic shock • Do-not-intubate orders <p>Interventions</p> <ul style="list-style-type: none"> • Continuous IV infusion of hydrocortisone 200 mg per day for 7 days, then 100 mg per day for 4 days, then 50 mg per day for 3 days; if patient improved by Day 4, then IV infusion of hydrocortisone 200 mg per day for 4 days, then 100 mg per day for 2 days, then 50 mg per day for 2 days (n = 76) • Placebo (n = 73) <p>Primary Endpoint</p> <ul style="list-style-type: none"> • Treatment failure (death or dependency on MV or high-flow oxygen) by Day 21 <p>Key Secondary Endpoints</p> <ul style="list-style-type: none"> • Need for intubation, prone positioning, ECMO, or inhaled nitric oxide • Nosocomial infection by Day 28 	<p>Participant Characteristics</p> <ul style="list-style-type: none"> • Mean age 62 years; 70% men; median BMI 28 • 96% had laboratory-confirmed SARS-CoV-2 infection • Median symptom duration of 9–10 days • 81% required MV at baseline • Received vasopressors: 24% in hydrocortisone arm vs. 18% in placebo arm • <5% received RDV or tocilizumab • Median duration of treatment with study drug: 11 days in hydrocortisone arm vs. 13 days in placebo arm ($P = 0.25$) <p>Primary Outcome</p> <ul style="list-style-type: none"> • Treatment failure by Day 21: 42% in hydrocortisone arm vs. 51% in placebo arm ($P = 0.29$) <p>Secondary Outcomes</p> <ul style="list-style-type: none"> • Need for intubation or prone positioning: no difference between arms (too few received ECMO or inhaled nitric oxide for comparison) • Need for intubation in those not on MV at baseline: 50% in hydrocortisone arm vs. 75% in placebo arm • Proportion of patients with nosocomial infection by Day 28: no difference between arms • Clinical status on Day 21: no difference between arms, but 15% died in hydrocortisone arm vs. 27% in placebo arm ($P = 0.06$) • Discharged from ICU by Day 21: 57% in hydrocortisone arm vs. 44% in placebo arm; 23% in both arms still required MV 	<p>Key Limitations</p> <ul style="list-style-type: none"> • Underpowered; enrollment stopped after release of data from the RECOVERY trial, resulting in limited power to detect differences between arms. • Limited information about comorbidities <p>Interpretation</p> <ul style="list-style-type: none"> • The use of hydrocortisone did not reduce the proportion of patients with COVID-19 and acute respiratory failure who experienced treatment failure by Day 21.

Methods	Results	Limitations and Interpretation
CAPE COVID: Double-Blind RCT of Hydrocortisone Among Critically Ill Patients With COVID-19 in France⁶, continued		
<ul style="list-style-type: none"> Clinical status on Day 21, as measured by a 5-item scale: <ul style="list-style-type: none"> Death In ICU and on MV Required high-flow oxygen therapy Required low-flow oxygen therapy Discharged from ICU 	<p>(<i>P</i> = 0.06)</p> <ul style="list-style-type: none"> Discharged from ICU by Day 21: 57% in hydrocortisone arm vs. 44% in placebo arm; 23% in both arms still required MV 	
REMAP-CAP: Randomized, Open-Label, Adaptive Trial of Hydrocortisone in Patients With Severe COVID-19⁷		
<p>Key Inclusion Criteria</p> <ul style="list-style-type: none"> Presumed or laboratory-confirmed SARS-CoV-2 infection ICU admission for respiratory or cardiovascular support <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> Presumed imminent death Systemic corticosteroid use >36 hours since ICU admission <p>Interventions</p> <ul style="list-style-type: none"> Hydrocortisone 50 mg IV every 6 hours for 7 days (n = 137) Shock-dependent hydrocortisone 50 mg IV every 6 hours for duration of shock for up to 28 days (n = 146) No hydrocortisone (n = 101) <p>Primary Endpoint</p> <ul style="list-style-type: none"> Number of days free of respiratory and cardiovascular organ support by Day 21 <p>Key Secondary Endpoint</p> <ul style="list-style-type: none"> In-hospital mortality 	<p>Participant Characteristics</p> <ul style="list-style-type: none"> Mean age 60 years; 71% men; 53% White Mean BMI range of 29.7–30.9 for the 3 arms 50% to 64% required MV <p>Primary Outcome</p> <ul style="list-style-type: none"> Median number of days free of organ support by Day 21: no difference between arms (0 in each arm) Median adjusted ORs for hydrocortisone arms vs. no hydrocortisone arm: <ul style="list-style-type: none"> OR 1.43 (95% CrI, 0.91–2.27) with 93% Bayesian probability of superiority for fixed-dose hydrocortisone arm OR 1.22 (95% CrI, 0.76–1.94) with 80% Bayesian probability of superiority for shock-dependent hydrocortisone arm <p>Key Secondary Outcome</p> <ul style="list-style-type: none"> In-hospital mortality: no difference between arms (30% in fixed-dose hydrocortisone arm vs. 26% in shock-dependent hydrocortisone arm vs. 33% in no hydrocortisone arm) 	<p>Key Limitations</p> <ul style="list-style-type: none"> Open-label study Enrollment stopped after release of data from the RECOVERY trial. <p>Interpretation</p> <ul style="list-style-type: none"> The use of hydrocortisone did not increase the median number of days free of organ support in either the fixed-dose or the shock-dependent hydrocortisone arms, although early termination limited the power to detect differences between the arms.

Methods	Results	Limitations and Interpretation
Single-Blind RCT of Methylprednisolone in Hospitalized Patients With COVID-19 Pneumonia in China⁸		
<p>Key Inclusion Criteria</p> <ul style="list-style-type: none"> Laboratory-confirmed SARS-CoV-2 infection Pneumonia confirmed by chest CT scan Hospitalized on general ward for <72 hours <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> Severe immunosuppression Corticosteroid use for other diseases <p>Interventions</p> <ul style="list-style-type: none"> Methylprednisolone 1 mg/kg per day IV for 7 days (n = 43) Saline (n = 43) <p>Primary Endpoint</p> <ul style="list-style-type: none"> Clinical deterioration at 14 days <p>Key Secondary Endpoints</p> <ul style="list-style-type: none"> Clinical cure at 14 days Time to clinical cure ICU admission In-hospital mortality Number of days hospitalized 	<p>Participant Characteristics</p> <ul style="list-style-type: none"> Mean age 56 years; 48% men Median of 8 days from symptom onset to randomization At randomization, 71% receiving oxygen via nasal cannula <p>Primary Outcome</p> <ul style="list-style-type: none"> Clinical deterioration at 14 days: 4.8% in both arms (OR 1.0; 95% CI, 0.134–7.442; <i>P</i> = 1.00) <p>Secondary Outcomes</p> <ul style="list-style-type: none"> No difference (all <i>P</i> > 0.05) between methylprednisolone arm and placebo arm for: <ul style="list-style-type: none"> Clinical cure at 14 days: 51% vs. 58% Median number of days to clinical cure: 14 vs. 12 ICU admission: 4.8% in both arms In-hospital mortality: 0% vs. 2.3% Median number of days hospitalized: 17 vs. 13 	<p>Key Limitations</p> <ul style="list-style-type: none"> Small sample size Terminated early because of decreasing incidence of COVID-19 pneumonia at study sites <p>Interpretation</p> <ul style="list-style-type: none"> The incidence of clinical deterioration did not differ between the methylprednisolone and placebo arms.

Methods	Results	Limitations and Interpretation
COVIDICUS: RCT of High-Dose Dexamethasone Versus Standard of Care Dexamethasone in Patients With COVID-19–Related Respiratory Failure in the ICU in France⁹		
<p>Key Inclusion Criteria</p> <ul style="list-style-type: none"> Laboratory-confirmed or suspected SARS-CoV-2 infection ICU admission in past 48 hours Respiratory failure (PaO₂ <70 mm Hg, SpO₂ <90% on room air, >30 breaths/min, labored breathing, respiratory distress, or need for oxygen ≥6 L/min) <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> Decision to limit life-sustaining treatment Therapy with ≥0.5 mg/kg per day of prednisone equivalent for ≥3 weeks Active and untreated bacterial, fungal, or parasitic infection <p>Interventions</p> <ul style="list-style-type: none"> High dose: DEX 20 mg IV once daily for 5 days, then DEX 10 mg IV once daily for 5 days (n = 270) SOC: DEX 6 mg IV once daily for 10 days (n = 239) or placebo (n = 37) <p>Primary Endpoint</p> <ul style="list-style-type: none"> All-cause mortality by Day 60 	<p>Participant Characteristics</p> <ul style="list-style-type: none"> Median age 67 years; 76% men Median of 9 days from symptom onset to randomization 81% with ≥1 comorbidity 17% received RDV; <1% received tocilizumab <p>Primary Outcome</p> <ul style="list-style-type: none"> All-cause mortality by Day 60: 26% in high-dose arm vs. 27% in SOC arm (HR 0.96; 95% CI, 0.69–1.33; <i>P</i> = 0.79) 	<p>Key Limitation</p> <ul style="list-style-type: none"> Comparator arm was initially a placebo but was changed to a standard dose of DEX after the RECOVERY trial results were released. <p>Interpretation</p> <ul style="list-style-type: none"> Among ICU patients with COVID-19–related respiratory failure, high-dose DEX did not significantly improve 60-day survival.

Methods	Results	Limitations and Interpretation
RECOVERY: Open-Label RCT of Two Doses of Dexamethasone in Hospitalized Patients With COVID-19 in the United Kingdom, Asia, and Africa¹⁰		
<p>Key Inclusion Criteria</p> <ul style="list-style-type: none"> Hospitalized with suspected or laboratory-confirmed SARS-CoV-2 infection SpO₂ <92% on room air <p>Key Exclusion Criteria</p> <ul style="list-style-type: none"> Physician determination, based on patient's medical history, that risk of participation was too great Contraindication to short-term corticosteroids Suspected or confirmed influenza Current use of ritonavir-boosted nirmatrelvir (Paxlovid), ritonavir, or other potent CYP3A inhibitor <p>Interventions</p> <ul style="list-style-type: none"> High-dose DEX 20 mg once daily plus SOC for 5 days followed by 10 mg once daily for 5 days or until discharge, whichever came first (n = 659) DEX 6 mg once daily plus SOC for 10 days or until discharge, whichever came first (n = 613) <p>Primary Endpoint</p> <ul style="list-style-type: none"> All-cause mortality at 28 days <p>Key Secondary Endpoints</p> <ul style="list-style-type: none"> Time to discharge from hospital Composite of MV (including ECMO) or death <p>Key Safety Endpoints</p> <ul style="list-style-type: none"> Infections other than COVID-19 Metabolic complications 	<p>Note</p> <ul style="list-style-type: none"> Enrollment for the subgroup of patients who received conventional oxygen or did not receive supplemental oxygen was stopped prematurely due to safety concerns. The results reported for this analysis only include patients from this subgroup. <p>Participant Characteristics</p> <ul style="list-style-type: none"> Mean age 61 years; 60% men; 54% Asian, 36% White 51% with ≥1 comorbidity; 19% with DM 53% received ≥1 COVID-19 vaccine dose 34% received RDV; 12% received tocilizumab or receipt of tocilizumab planned within 24 hours <p>Primary Outcome</p> <ul style="list-style-type: none"> All-cause mortality at 28 days: 19% in high-dose DEX arm vs. 12% in SOC arm (rate ratio 1.59; 95% CI, 1.20–2.10; P = 0.0012) <p>Secondary Outcomes</p> <ul style="list-style-type: none"> Time to discharge from hospital: 9 days in both arms Composite of MV or death: 20% in high-dose DEX arm vs. 13% in SOC arm (risk ratio 1.52; 95% CI, 1.18–1.97) <p>Safety Outcomes</p> <ul style="list-style-type: none"> Pneumonia not due to COVID-19: 10% in high-dose DEX arm vs. 6% in SOC arm (absolute difference 3.7%; 95% CI, 0.7–6.6) Hyperglycemia requiring new or increased insulin dose: 22% in high-dose DEX arm vs. 14% in SOC arm (absolute difference 7.4%; 95% CI, 3.2–11.5) 	<p>Key Limitations</p> <ul style="list-style-type: none"> Open-label study The larger RECOVERY trial stopped enrollment of patients in this subgroup (i.e., those who received conventional oxygen or did not receive supplemental oxygen) due to safety concerns. <p>Interpretation</p> <ul style="list-style-type: none"> In patients hospitalized with COVID-19 who had clinical hypoxemia (SpO₂ <92%) and did not require supplemental oxygen or required only conventional oxygen, use of high-dose DEX increased the risk of death and hyperglycemia when compared with the use of standard doses of corticosteroids.

Key: AE = adverse event; ARDS = acute respiratory distress syndrome; BMI = body mass index; CPAP = continuous positive airway pressure; CT = computed tomography; CYP = cytochrome P450; DEX = dexamethasone; DM = diabetes mellitus; ECMO = extracorporeal membrane oxygenation; FiO₂ = fraction of inspired oxygen; HFNC = high-flow nasal cannula; ICU = intensive care unit; IL = interleukin; IRS = intensive respiratory support; IV = intravenous; JAK = Janus kinase; LOS = length of stay; MV = mechanical ventilation; NIV = noninvasive ventilation; OS = ordinal scale; the Panel = the COVID-19 Treatment Guidelines Panel; PaO₂ = arterial partial pressure of oxygen; PEEP = positive end-expiratory pressure; PO = oral; RCT = randomized controlled trial; RDV = remdesivir; SAE = serious adverse event; SOC = standard of care; SOFA = sequential organ failure assessment; SpO₂ = oxygen saturation; TB = tuberculosis

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