



July 1, 2020

## Dexamethasone for COVID-19 = Randomized Evaluation of COVID-19 Therapy (RECOVERY trial) =

### Background:<sup>1,2,3,4</sup>

COVID-19 is a novel illness with high morbidity and mortality for which there is a lack of approved treatments. Remdesivir, currently available under an FDA Emergency Use Authorization, has been shown to reduce time to recovery among inpatients with COVID-19 (11 vs 15 days,  $p < 0.001$ ). According to RCT data from the RECOVERY Trial (published in preprint), **dexamethasone for the treatment of inpatients with severe COVID-19 has been demonstrated to improve survival**. The IDSA Guidelines currently recommend glucocorticoids for hospitalized patients with severe COVID-19 (SpO<sub>2</sub>  $\leq 94\%$  on room air, and those who require supplemental oxygen, mechanical ventilation, or ECMO).

### Methods<sup>5</sup>:

- The RECOVERY study is a randomized, controlled, open-label, adaptive platform clinical trial comparing numerous potential COVID-19 treatments to usual care (placebo) in hospitalized patients with confirmed COVID-19.
- 11,320 patients were enrolled at 176 hospitals across the United Kingdom. Active arm participants were given dexamethasone 6mg daily, either orally or IV for ten days or until discharge. A 2:1 ratio of usual care (N= 4,321) to dexamethasone patients (N=2,104) was used. The study began in March 2020 and was halted on June 8, 2020.
- Mean age of participants was 66.1 years, and 36% were female. A history of diabetes was present in 24% of patients, heart disease in 27%, and chronic lung disease in 21%. Fifty-six percent of participants had at least one major comorbidity. The primary efficacy outcome was 28-day mortality.

### Results<sup>5</sup>:

- In total, 28-day mortality occurred in 24.6% (1065/4321) of usual care patients and 21.6% (454/2104) in patients receiving dexamethasone (Rate Ratio 0.83; 95% CI 0.74-0.92,  $p < 0.001$ ). In a subgroup analysis, researchers reported the following outcomes data in various patient characteristic groups:

	Deaths in Usual Care	Deaths in Dexamethasone	Results / Confidence Interval
In ventilated patients	278 of 683 (40.7%)	94 of 324 (29.0%)	<b>RR: 0.65; 95% CI: 0.51-0.82, <math>p &lt; 0.001</math></b>
In oxygenated patients	650 of 2604 (25.0%)	275 of 1279 (21.5%)	<b>RR: 0.80; 95% CI: 0.70-0.92; <math>p &lt; 0.002</math></b>
No respiratory support	137 of 1034 (17.0%)	85 of 501 (13.2%)	RR: 1.22; 95% CI: 0.93-1.61; $p = 0.14$

- In ventilated patients, dexamethasone reduced 28-day mortality by a statistically significant 35% vs. usual care.
  - 1 death would be prevented for every 8 ventilated patients who received dexamethasone
- In patients on supplemental oxygen, 28-day mortality was statistically significantly reduced by 20% in patients receiving dexamethasone.
  - 1 death would be prevented for every 25 patients who received supplemental oxygen and dexamethasone
- In patients who received no oxygen (moderately ill), no difference was noted with dexamethasone vs. usual care.

### Impact and Points to Consider<sup>5,6</sup>:

- Dexamethasone is the first medication to demonstrate a reduction in mortality due to COVID-19.
- Methodologically well-designed trial (multi-site, randomized, placebo comparator, blinded) with large effect size.
- Drug characteristics are well known (inexpensive, low dose) with a history of safety/use in various populations.
- Study limitations include:
  - Reporting of subgroup analyses (e.g. ventilated patients) that were not pre-specified and may be misleading;
  - Final outcome was unknown in 28% of enrolled patients; 1807 patients remained hospitalized at end of trial;
  - Reporting of dexamethasone patients >28 days could identify if harm occurred with mild-moderate illness.

### References:

1. U.S. Food and Drug Administration. Fact Sheet for Health Care Providers. [Emergency Use Authorization of Remdesivir. \(GS-5734\)](#).
2. IHS National Pharmacy and Therapeutics Committee. [Emerging Treatments Update: Remdesivir](#). Available online. Accessed May 14, 2020.
3. Beigel J, et al. [Remdesivir for the Treatment of COVID-19 – Preliminary Report](#). NEJM 2020, May 22. DOI: 10.1056/NEJMoa2007764.
4. IDSA. [Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19](#). Accessed June 30, 2020.
5. The RECOVERY Collaborative Group. [Effect of dexamethasone in hospitalized patients with COVID-19—preliminary report](#). 22 Jun 2020 (preprint).
6. Mahase E. [Covid-19: Low dose steroid cuts death in ventilated patients by one third, trial finds](#). BMJ 2020;369:m2422. doi: 10.1136/bmj.m2422 pmid: 32546467