ASHP/SCCM COVID-19
Pharmacology Debates: Steroid and Antiviral Use

COVID-19 Resources

Audience Participation

Control Panel
This webcast is being recorded. The recording will be available in early August.

To access go to: covid19.sccm.org/webcast or https://www.ashp.org/COVID-19

The Society of Critical Care Medicine (SCCM) and the American Society of Health-System Pharmacists (ASHP) partnered to produce this webinar on COVID-19.
Today’s Moderator

Moderator:
Mojdeh Heavner, Pharm.D., BCPS, BCCCP, FCCM
Associate Professor and Vice Chair of Clinical Services
Department of Pharmacy Practice and Science
University of Maryland School of Pharmacy
Baltimore, Maryland, USA
No disclosures

ASHP/SCCM COVID-19 Pharmacology Debates: Antiviral Use

COVID-19 Resources
Polling Question:
If you were to utilize remdesivir in a patient with COVID-19, who do you feel is the most appropriate patient?

A. All patients with COVID-19 should receive remdesivir at any time point after diagnosis
B. Only patients on supplemental O₂ should receive remdesivir within 10-14 days of diagnosis
C. Only patients requiring mechanical ventilation should receive remdesivir within 10-14 days of diagnosis
D. I would not give remdesivir to any patient with COVID-19 at any time point after diagnosis

Debate 1- Antiviral Use in COVID-19 Patients

Gretchen Sacha, Pharm.D., BCCCP
Critical Care Pharmacy Specialist
Cleveland Clinic
Cleveland, Ohio, USA

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Infectious Diseases/Antimicrobial Stewardship Residency Program Director
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Medical University of South Carolina (MUSC)
College of Pharmacy
MUSC Health

Disclosure: Speakers Bureau for Cepheid
Pro: Remdesivir Use In COVID-19 Patients

Gretchen Sacha, Pharm.D.
Critical Care Clinical Pharmacy Specialist
Cleveland Clinic
Cleveland, Ohio, USA

COVID-19 Resources

Antivirals in COVID-19

- Hydroxychloroquine (Plaquenil®) / Chloroquine
- Lopinavir/Ritonavir (Kaletra®)
- Favipiravir (Avigan®)
- Baloxavir
- Umifenovir (Arbidol®)
- Remdesivir

COVID-19 Resources
Remdesivir

• Broad spectrum anti-viral agent
• Adenosine analogue – inhibits viral RNA polymerase
• In vitro and in vivo activity against Ebola, SARS-CoV, and MERS-CoV
• Demonstrated in vitro and in vivo activity against SARS-CoV-2 in Vero E6 cells and Rhesus macaques
• Compassionate use: 68% of patients experienced improvement in oxygen-support class after remdesivir initiation


Remdesivir – Clinical Efficacy

• April 29th 2020: Publication of placebo-controlled RCT – Hubei, China
• Adults, 12 days of sx onset, SpO₂ ≤94% on RA or P/F <300 mmHg
• Remdesivir IV 200 mg x 1 then 100 mg daily x 10 days total

<table>
<thead>
<tr>
<th></th>
<th>Remdesivir n=158</th>
<th>Placebo n=78</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to clinical improvement, days</td>
<td>21.0 (13.0-28.0)</td>
<td>23.0 (15.0-28.0)</td>
<td>HR 1.23 (95% CI 0.87-1.75)</td>
</tr>
<tr>
<td>28 day mortality, n (%)</td>
<td>22 (14%)</td>
<td>10 (13%)</td>
<td>1.1% (95% CI -8.1 to 19.3)</td>
</tr>
</tbody>
</table>

**Remdesivir – ACTT-1 Trial**

- May 22nd 2020
- Adults, 72 hours from diagnosis, radiographic infiltrates OR clinical assessment AND SpO₂ ≤94% on RA OR supplemental O₂
- Remdesivir x 10 days

<table>
<thead>
<tr>
<th>Patient status, n (%)</th>
<th>Remdesivir n=541</th>
<th>Placebo n=522</th>
</tr>
</thead>
<tbody>
<tr>
<td>No supplemental O₂</td>
<td>67 (12.4)</td>
<td>60 (11.5)</td>
</tr>
<tr>
<td>Supplemental O₂</td>
<td>222 (41.0)</td>
<td>199 (38.1)</td>
</tr>
<tr>
<td>NIPPV or HF</td>
<td>98 (18.1)</td>
<td>99 (19.0)</td>
</tr>
<tr>
<td>IPPV or ECMO</td>
<td>125 (23.1)</td>
<td>147 (28.2)</td>
</tr>
</tbody>
</table>

**Clinical Outcomes**

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Remdesivir n=541</th>
<th>Placebo n=522</th>
<th>RR or HR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of recoveries, n (%)</td>
<td>334 (62.1)</td>
<td>273 (52.4)</td>
<td>-</td>
</tr>
<tr>
<td>Time to recovery, days</td>
<td>11 (9-12)</td>
<td>15 (13-19)</td>
<td>RR: 1.32 (1.12-1.55)</td>
</tr>
<tr>
<td>Supplemental O₂ (n=421)</td>
<td>7 (6-8)</td>
<td>9 (7-11)</td>
<td>RR: 1.47 (1.17-1.84)</td>
</tr>
<tr>
<td>NIPPV or HF (n=197)</td>
<td>16 (NE-10)</td>
<td>22 (NE-12)</td>
<td>RR: 1.20 (0.79-1.81)</td>
</tr>
<tr>
<td>MV or ECMO (n=272)</td>
<td>-</td>
<td>28 (NE-22)</td>
<td>RR: 0.95 (0.64-1.42)</td>
</tr>
<tr>
<td>14 day mortality, n (%)</td>
<td>32 (5.9)</td>
<td>54 (10.4)</td>
<td>HR: 0.70 (0.47-1.04)</td>
</tr>
<tr>
<td>Supplemental O₂ (n=421)</td>
<td>4 (1.8)</td>
<td>19 (9.5)</td>
<td>HR: 0.22 (0.08-0.58)</td>
</tr>
<tr>
<td>NIPPV or HF (n=197)</td>
<td>13 (13.3)</td>
<td>13 (13.1)</td>
<td>HR: 1.12 (0.53-2.38)</td>
</tr>
<tr>
<td>MV or ECMO (n=272)</td>
<td>13 (10.4)</td>
<td>19 (12.9)</td>
<td>HR: 1.06 (0.59-1.92)</td>
</tr>
</tbody>
</table>

*Recovery rate ratio or hazard ratio based on Cox model for time to event.

**Remdesivir – Clinical Efficacy**

- SIMPLE-Severe study: no difference 5 days vs. 10 days remdesivir

<table>
<thead>
<tr>
<th>June 1, 2020 – SIMPLE-Moderate Study Press Release</th>
<th>Remdesivir x5d n=191</th>
<th>Remdesivir x 10d n=193</th>
<th>Standard of Care n=200</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 point improvement in ordinal scale, n (%)</td>
<td>134 (70)</td>
<td>126 (65)</td>
<td>121 (61)</td>
</tr>
<tr>
<td>≥1 point improvement in ordinal scale, n (%)</td>
<td>146 (76)</td>
<td>135 (70)</td>
<td>132 (66)</td>
</tr>
<tr>
<td>Death, n (%)</td>
<td>0 (0)</td>
<td>2 (1)</td>
<td>4 (2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>July 24, 2020 – SIMPLE-Severe vs Retrospective Cohort – IPTW Matching</th>
<th>Remdesivir (SIMPLE-Severe) n=312</th>
<th>Standard of Care (Retrospective) n=818</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical recovery by day 14</td>
<td>74.4%</td>
<td>59.0%</td>
<td>aOR 2.03 (1.34-3.08)</td>
</tr>
<tr>
<td>14 day mortality</td>
<td>7.6%</td>
<td>12.5%</td>
<td>aOR 0.38 (0.22-0.68)</td>
</tr>
</tbody>
</table>
Clinical Recommendations

- Not currently FDA approved
  - Approved in Japan, Taiwan, India, Singapore, UAE – Veklury®
  - Conditional marketing authorization in Europe Union
- Available through FDA Emergency Use Authorization
  - Requirements: SpO₂ ≤94% on RA, supplemental O₂, mech vent, or ECMO
- NIH COVID-19 treatment guidelines recommend remdesivir
- Remdesivir should be considered in patients hospitalized for COVID-19 requiring with SpO₂ ≤94% on RA or supplemental oxygen
  - 200 mg IV once followed by 100 mg IV x 5 -10 days (10d if intubated)
Notable Data

- Compassionate Use RDV
- RDV in severe COVID-19
- Concomitant use of LPV/r, interferons, corticosteroids
- Adaptive COVID-19 Treatment Trial
- NIH-sponsored
- Multinational, randomized, placebo-controlled trial
- Manufacturer-sponsored
- Multinational, randomized, open-label

Grein et al
Wang et al
ACTT-1
SIMPLE-1

Baseline Score: 4 (Room-Air)

Clinical outcomes on day 14 or 15 by baseline clinical status

- ACTT-1: improved ordinal score at day 15 (OR 1.51; 95% CI 0.76–3.00) vs. placebo
  - ↑ # of pts discharged or able to be discharged (90% vs. 78%)
  - ↓ # of pts with severity of disease progression (8% vs. 16%)
- SIMPLE-1: 25% of pts with disease progression (n=52)
- SIMPLE-2: modest benefit in improvement in d11 status
- Small benefit in clinical improvement, no difference in progression of disease severity/death
  - Low incidence of end points in mild-moderate illness

LPV/r: lopinavir/ritonavir

Baseline Score: 5 (Low-flow $O_2$)

- ACTT-1: mortality benefit (HR 0.22 [95% CI 0.08–0.58]) vs. placebo
  - ↓ time to recovery (RR 1.47 [95% CI 1.17–1.84])
- SIMPLE-1: rate of discharge (70.2%), disease progression (12.9%), and death (3.3%)
- Wang et al: NO benefit in this pt population (majority)
- Benefit in mortality, clinical improvement, and disease progression

Clinical outcomes on day 14 or 15 by baseline clinical status

Baseline Score: 6 (High-flow/NIMV)

- ACTT-1: recovery rate ratio of 1.20 (0.79-1.81) vs. placebo
  - ↑ proportion of pts discharged (58% vs 44%) and ↓ rate of progression (25% vs 34%) at d15
- SIMPLE-1: 32% discharged and 43% progressed to MV or death
  - Subgroup: no improvement with additional 5d of therapy at d14
  - Similar death rates to placebo
  - No clinically meaningful benefit in mortality, clinical improvement, and disease progression

NIMV: non-invasive mechanical ventilation
Baseline Score: 7 (Invasive MV)

Clinical outcomes on day 14 or 15 by baseline clinical status

- ACTT-1: recovery rate ratio of 0.95 (0.64-1.42) vs. placebo
  - NO reduction in mortality (11.3% vs. 14.1%; HR 1.06 [95% CI 0.59–1.92])
- SIMPLE-1: ↓mortality rate with additional 5 days of therapy
  - ↑mortality vs. placebo group in ACTT-1 (41.7% vs. 16.5%)
  - ↓discharge vs. placebo group in ACTT-1 (8.3% vs. 15.7%) by d14 or d15
- Numerical mortality benefit in SIMPLE-1, but NO benefit over placebo at d15 in ACTT-1. No clinically meaningful benefit in mortality, clinical improvement, and disease progression


Allocation Timeline

Jan 25th 2020
Compassionate Use

June 29th, 2020
DHHS secures 500K
EUA commercial
courses

May 1st, 2020
EUA donated supply

July 13th, 2020 EUA Commercial product via Amerisource Bergen

September 2020 ?!

https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/factsheet.aspx
### Allocation Process

- Non-standardized allocation practices between states
- Centralized vs. lottery vs. hospital status
- Leftover donated supply and geographic distribution
- “First-wave” supply

### Payment and Reimbursement

#### Payment
- Wholesale acquisition cost (WAC) of ~$520 per 100mg vial
- Discounted price for federal facilities
- Typical 5-day course of remdesivir (total of 6 vials) → $3,120 per course

#### Reimbursement
- CARES Act Provider Relief Fund to reimburse for uninsured patients
- Private Insurers
  - Committed to wave cost-sharing payments for members
#FiveForFive – A Stewardship Mantra

Limited Resource → Category 5 – on low-flow supplemental O₂ → Duration – 5 days → *10-14d from PCR-positivity**

Looking ahead....

Special populations
- Pregnancy
- Pediatrics
- Renal and liver dysfunction
- Mechanical ventilation and ECMO

Trials
- ACTT-1 d28
- ACTT-2
- SIMPLE-2
- SOLIDARITY
- DisCoVeRy
- Case Series
Polling Question:
If you were to utilize remdesivir in a patient with COVID-19, who do you feel is the most appropriate patient?

A. All patients with COVID-19 should receive remdesivir at any time point after diagnosis
B. Only patients on supplemental O2 should receive remdesivir within 10-14 days of diagnosis
C. Only patients requiring mechanical ventilation should receive remdesivir within 10-14 days of diagnosis
D. I would not give remdesivir to any patient with COVID-19 at any time point after diagnosis

Question and Answer

Speaker: Gretchen Sacha
Pharm.D., BCCCP

Speaker: Krutika N. Mediwalu
Pharm.D., BCPS, BCIDP

Moderator: Mojdeh Heavner
Pharm.D., BCPS, BCCCP, FCCM
Polling Question:
Do you recommend the use of corticosteroids for the treatment of all hospitalized patients with COVID-19?

A. Yes  
B. No  
C. Unsure/Undecided
Polling Question:
In which group of hospitalized patients with COVID-19 do you recommend the use of corticosteroids?

A. Receiving invasive mechanical ventilation only
B. Receiving supplemental oxygen (not mechanically ventilated) only
C. Receiving any supplemental oxygen (invasive and non-invasive ventilation)
D. On room air (no supplemental oxygen)
E. All of the above
F. Unsure/Undecided

Debate 2- Steroid Use in COVID-19 Patients

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Disclosures: No relevant disclosures
Pro: Steroid Use for COVID-19

Mitchell Buckley, PharmD, FASHP, FCCM, FCCP, BCPS, BCCCP

COVID-19 Resources

Objectives

• Evaluate clinical data on corticosteroid use in COVID-19

• Review clinical practice guideline recommendations

• Recommend an evidence-based strategy employing the use of corticosteroids in COVID-19 patients
Disclosure

• No relevant conflict of interest related to the content of the presentation

Results From June 24th PRO/CON Debate on Immunomodulator Use

Do you recommend the use of corticosteroids for the treatment of patients with COVID-19?

<table>
<thead>
<tr>
<th></th>
<th>Pre-debate</th>
<th>Post-debate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>27</td>
<td>39</td>
</tr>
<tr>
<td>No</td>
<td>52</td>
<td>47</td>
</tr>
<tr>
<td>Unsure/Undecided</td>
<td>21</td>
<td>14</td>
</tr>
</tbody>
</table>
Severity of Illness

Time

Viral response phase
Hyperinflammatory Phase

Early Infection
Pulmonary Phase

Reduce immunosuppression
Careful use of immunomodulators

Randomized Clinical Trials

Adapted from Siddiqi HK. J Heart and Lung Transplant. 2020;39(5):405-407.

COVID-19 Resources
GLUCOCOVID Trial

**Patient Eligibility**
- Symptom duration ≥ 7 days
- Radiologic evidence lung disease
- Moderate-Severe disease
- Laboratory evidence of hyper-inflammation

**Methylprednisolone Regimen**
- 40mg IV q12h x 3 days, then
- 20mg IV q12h x 3 days

**Primary Composite Endpoint**
- In-hospital all-cause mortality
- Higher level of care (ICU admission)
- Progression of respiratory failure that required NIV

<table>
<thead>
<tr>
<th>Study Analysis Groups</th>
<th>Methylprednisolone (n=56)</th>
<th>Control (n=29)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (ITT)</td>
<td>34%</td>
<td>48%</td>
<td>0.70 (0.41-1.18)</td>
</tr>
<tr>
<td>≤72 years (ITT)</td>
<td>16%</td>
<td>40%</td>
<td>0.40 (0.14-1.14)</td>
</tr>
<tr>
<td>&gt;72 years (ITT)</td>
<td>48%</td>
<td>67%</td>
<td>0.66 (0.66-1.11)</td>
</tr>
<tr>
<td>All patients (Per-Protocol)</td>
<td>24%</td>
<td>48%</td>
<td>0.50 (0.27-0.94)</td>
</tr>
</tbody>
</table>
RECOVERY Trial – Preliminary Report

6425 patients randomized
Dexamethasone 6mg PO/IV daily (n=2104) – up to 10 days
vs. usual care alone (n=4321)

Table 2. Primary and Secondary Outcomes.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dexamethasone (N = 2104)</th>
<th>Usual Care (N = 4321)</th>
<th>Rate or Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality at 28 days</td>
<td>482/2104 (22.9)</td>
<td>1110/4321 (25.7)</td>
<td>0.83 (0.75–0.93)</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharged from hospital within 28 days</td>
<td>1413/2104 (67.2)</td>
<td>2745/4321 (63.5)</td>
<td>1.10 (1.03–1.17)</td>
</tr>
<tr>
<td>Invasive mechanical ventilation or death†</td>
<td>456/1780 (25.6)</td>
<td>994/3638 (27.3)</td>
<td>0.92 (0.84–1.01)</td>
</tr>
<tr>
<td>Invasive mechanical ventilation</td>
<td>102/1780 (5.7)</td>
<td>285/3638 (7.8)</td>
<td>0.77 (0.62–0.95)</td>
</tr>
<tr>
<td>Death</td>
<td>387/1780 (21.7)</td>
<td>827/3638 (22.7)</td>
<td>0.93 (0.84–1.03)</td>
</tr>
</tbody>
</table>

### RECOVERY Trial – Preliminary Report

#### C Oxygen Only (N=3883)

<table>
<thead>
<tr>
<th></th>
<th>Usual care</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at Risk</td>
<td>2604</td>
<td>1279</td>
</tr>
<tr>
<td>Days since Randomization</td>
<td>2195</td>
<td>1135</td>
</tr>
<tr>
<td></td>
<td>2018</td>
<td>1036</td>
</tr>
<tr>
<td></td>
<td>1950</td>
<td>1006</td>
</tr>
<tr>
<td></td>
<td>1916</td>
<td>981</td>
</tr>
</tbody>
</table>

**Rate ratio, 0.82 (95% CI, 0.72–0.94)**

#### B Invasive Mechanical Ventilation (N=1007)

<table>
<thead>
<tr>
<th></th>
<th>Usual care</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. at Risk</td>
<td>683</td>
<td>324</td>
</tr>
<tr>
<td>Days since Randomization</td>
<td>572</td>
<td>290</td>
</tr>
<tr>
<td></td>
<td>481</td>
<td>248</td>
</tr>
<tr>
<td></td>
<td>424</td>
<td>232</td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>228</td>
</tr>
</tbody>
</table>

**Rate ratio, 0.64 (95% CI, 0.51–0.81)**

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### RECOVERY Trial – Preliminary Report

#### Respiratory Support at Randomization

<table>
<thead>
<tr>
<th>Supporting Method</th>
<th>Dexamethasone</th>
<th>Usual Care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of events</td>
<td>total no.</td>
</tr>
<tr>
<td></td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>Invasive mechanical</td>
<td>95/324</td>
<td>283/683</td>
</tr>
<tr>
<td>ventilation</td>
<td>29.3</td>
<td>41.4</td>
</tr>
<tr>
<td>Oxygen only</td>
<td>298/1279</td>
<td>682/2604</td>
</tr>
<tr>
<td>No oxygen received</td>
<td>89/501</td>
<td>145/1034</td>
</tr>
<tr>
<td>All Patients</td>
<td>482/2104</td>
<td>1110/4321</td>
</tr>
</tbody>
</table>

**Rate Ratio (95% CI)**

- **Invasive mechanical ventilation**: 0.64 (0.51–0.81)
- **Oxygen only**: 0.82 (0.72–0.94)
- **No oxygen received**: 1.19 (0.91–1.55)
- **All Patients**: 0.83 (0.75–0.93)

Chi-square trend across three categories: 11.5 (P<0.001)

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### RECOVERY Trial – Preliminary Report

#### Treatment allocation

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dexamethasone (n=2104)</th>
<th>Usual care (n=4321)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up forms received</td>
<td>2079</td>
<td>4278</td>
</tr>
<tr>
<td>Treatments given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>1975 (95%)</td>
<td>336 (8%)</td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>2 (&lt;0.5%)</td>
<td>4 (&lt;0.5%)</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>17 (1%)</td>
<td>22 (1%)</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>499 (24%)</td>
<td>1082 (25%)</td>
</tr>
<tr>
<td>Tocilizumab or sarilumab</td>
<td>43 (2%)</td>
<td>128 (3%)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>7 (&lt;0.5%)</td>
<td>12 (&lt;0.5%)</td>
</tr>
</tbody>
</table>

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### COVID-19 Resources

**Clinical Practice Guidelines**
Guideline Recommendations

<table>
<thead>
<tr>
<th>Source</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH (updated July 17, 2020)</td>
<td>• <strong>Recommends</strong> using dexamethasone 6 mg / day for up to 10 days... in patients who are...   \</td>
</tr>
<tr>
<td></td>
<td>• Mechanically ventilated (AI)</td>
</tr>
<tr>
<td></td>
<td>• Requiring supplemental oxygen but who are not mechanically ventilated (BI)</td>
</tr>
<tr>
<td></td>
<td>• <strong>Recommends against</strong> using dexamethasone in patients who DO NOT require supplemental oxygen (AI).</td>
</tr>
<tr>
<td>IDSA (updated June 25, 2020)</td>
<td>• Among hospitalized patients with severe* COVID-19, the IDSA guideline panel <strong>suggests</strong> glucocorticoids rather than no glucocorticoids. (Conditional recommendation, Moderate certainty of evidence)</td>
</tr>
<tr>
<td></td>
<td>• Among hospitalized patients with COVID-19 without hypoxemia requiring supplemental oxygen, the IDSA guideline panel <strong>suggests against</strong> the use of glucocorticoids. (Conditional recommendation, Low certainty of evidence)</td>
</tr>
<tr>
<td>Surviving Sepsis Campaign</td>
<td>• In mechanically ventilated adults with COVID-19 and ARDS, we <strong>suggest</strong> using systemic corticosteroids, over not using corticosteroids.</td>
</tr>
<tr>
<td>(updated March 20, 2020)</td>
<td>• In mechanically ventilated adults with COVID-19 and respiratory failure (without ARDS), we <strong>suggest against</strong> the routine use of systemic corticosteroids.</td>
</tr>
</tbody>
</table>

Supporting Evidence for Steroids

✓ COVID-19 associated with pro-inflammatory response

✓ RECOVERY Trial
  • Strength in numbers…. large sample size
  • Survival benefit

✓ Previous corticosteroid ARDS trials ≠ COVID-19 ARDS
  • DEXA-ARDS trial
  • Single pathogen → disease state
Con: Steroid Use for COVID-19

Amy L. Dzierba, PharmD, FCCM, FCCP, BCCCP

COVID-19 Resources

Guideline Recommendations

• In mechanically ventilated adults with COVID-19 and respiratory distress syndrome (ARDS), we suggest against the routine use of systemic corticosteroids.
• In mechanically ventilated adults with COVID-19 and ARDS, we suggest using systemic corticosteroids, over not using corticosteroids.
• Among hospitalized patients with COVID-19 pneumonia, the IDSA guideline panel suggests against the use of corticosteroids.
• Among hospitalized patients with ARDS due to COVID-19, the IDSA guideline panel recommends the use of corticosteroids in the context of a clinical trial.
• Recommends against the routine use of systemic corticosteroids for the treatment of mechanically ventilated patients with COVID-19 without ARDS.
• In mechanically ventilated adults with COVID-19 and ARDS, there are insufficient data to recommend either for or against corticosteroid therapy in the absence of another indication.

All Roads Lead to RECOVERY...

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dexamethasone (N=2104)</th>
<th>Usual Care (N=4321)</th>
<th>Rate or Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality at 28 days</td>
<td>482/2104 (22.9)</td>
<td>1110/4321 (25.7)</td>
<td>0.83 (0.75–0.93)</td>
</tr>
</tbody>
</table>

Should corticosteroids be used in all hospitalized patients with COVID-19?

Adapted from Siddiqi HK and Mehra MR. J Heart Lung Transplant. 2020;39:405-407.
Patients Requiring Invasive Mechanical Ventilation

- Viral response phase
- Host inflammatory response phase
- Early Infection
- Pulmonary Phase
- Hyperinflammatory Phase

Adapted from Siddiqi HK and Mehra MR. J Heart Lung Transplant. 2020;39:405-407.

Patients Requiring Oxygen Support (not mechanical ventilation)

- 32-year-old woman requiring 3 liters/min nasal cannula
- 65-year-old woman with diabetes mellitus requiring 5 liters/min nasal cannula
- 55-year-old obese man with diabetes requiring high flow nasal cannula at 60 liters/min on 100% FiO₂

Should corticosteroids be used in all hospitalized patients with COVID-19 requiring oxygen support (not mechanical ventilation)?

- **Right Time**
  - Balance between preventing collateral damage from immune response and interrupting the immune system

- **Right Patient**
  - 17% of RECOVERY patients were not deemed eligible
  - Concomitant medications
  - SARS-CoV-2 versus COVID-19

- **Right Drug/Dose/Duration**
  - Dexamethasone 6 mg daily up to 10 days or clinical improvement

__COVID-19 Resources__


Guideline Recommendations

- Among hospitalized patients with COVID-19 without hypoxemia requiring supplemental oxygen, the IDSA guideline panel suggests against the use of glucocorticoids.
- Among hospitalized patients with severe* COVID-19, the IDSA guideline panel suggests glucocorticoids rather than no glucocorticoids.

- **Recommends** using dexamethasone 6 mg / day for up to 10 days in patients who are
  - Mechanically ventilated (AI)
  - Requiring supplemental oxygen but who are not mechanically ventilated (BI)
- **Recommends against** using dexamethasone in patients who DO NOT require supplemental oxygen.

*Severe illness is defined as patients with $\text{SpO}_2 \leq 94\%$ on room air, and those who require supplemental oxygen, mechanical ventilation, or ECMO.


Supporting Evidence Against Routine Corticosteroid Use

✓ COVID-19 associated with pro-inflammatory response
  ❌ All patients will not have the same dysregulated response

✓ RECOVERY Trial
  ❌ Not all patient populations may benefit

Polling Question:
Do you recommend the use of corticosteroids for the treatment of all hospitalized patients with COVID-19?

A. Yes
B. No
C. Unsure/Uncertain
Polling Question:
In which group of hospitalized patients with COVID-19 do you recommend the use of corticosteroids?

A. Receiving invasive mechanical ventilation only
B. Receiving supplemental oxygen (not mechanically ventilated) only
C. Receiving any supplemental oxygen (invasive and non-invasive ventilation)
D. On room air (no supplemental oxygen)
E. All of the above
F. Unsure/Undecided

Question and Answer

Speaker: Mitchell Buckley
Pharm.D., FASHP, FCCM, FCCP, BCCCP, BCPS

Speaker: Amy L. Dzierba, Pharm.D.
FCCM, FCCP, BCCCP

Moderator: Mojdeh Heavner
Pharm.D., BCPS, BCCCP, FCCM
Thank You for Attending

• The recording of this webcast will be available in August 2020, to access go to: covid19.sccm.org/webcast or https://www.ashp.org/COVID-19

• To register for additional COVID-19 related webcasts, visit: sccm.org/disaster or www.ashp.org/COVID-19

• To sign up for additional webinars on COVID-19 visit ashp.org/COVID-19/Stay-Informed

• Visit sccm.org/COVID19RapidResources for more resources

• For more information on ASHP’s COVID-19 resources visit ASHP.org/COVID-19