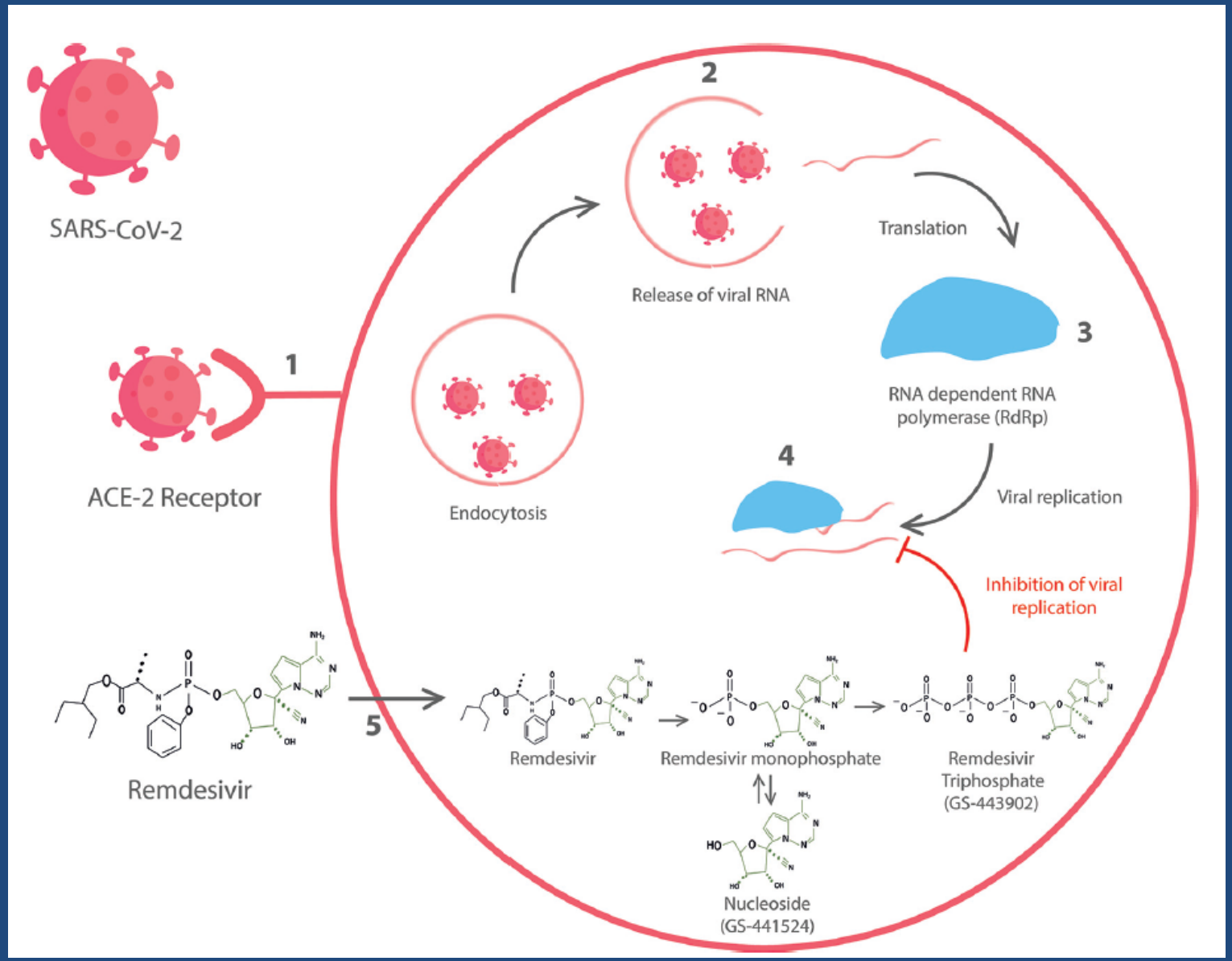
瑞德西韋使用時機及成效回顧

臺北榮民總醫院內科部感染科主治醫師
國立陽明交通大學急重症醫學研究所教授
林邑璁, M.D., Ph.D.

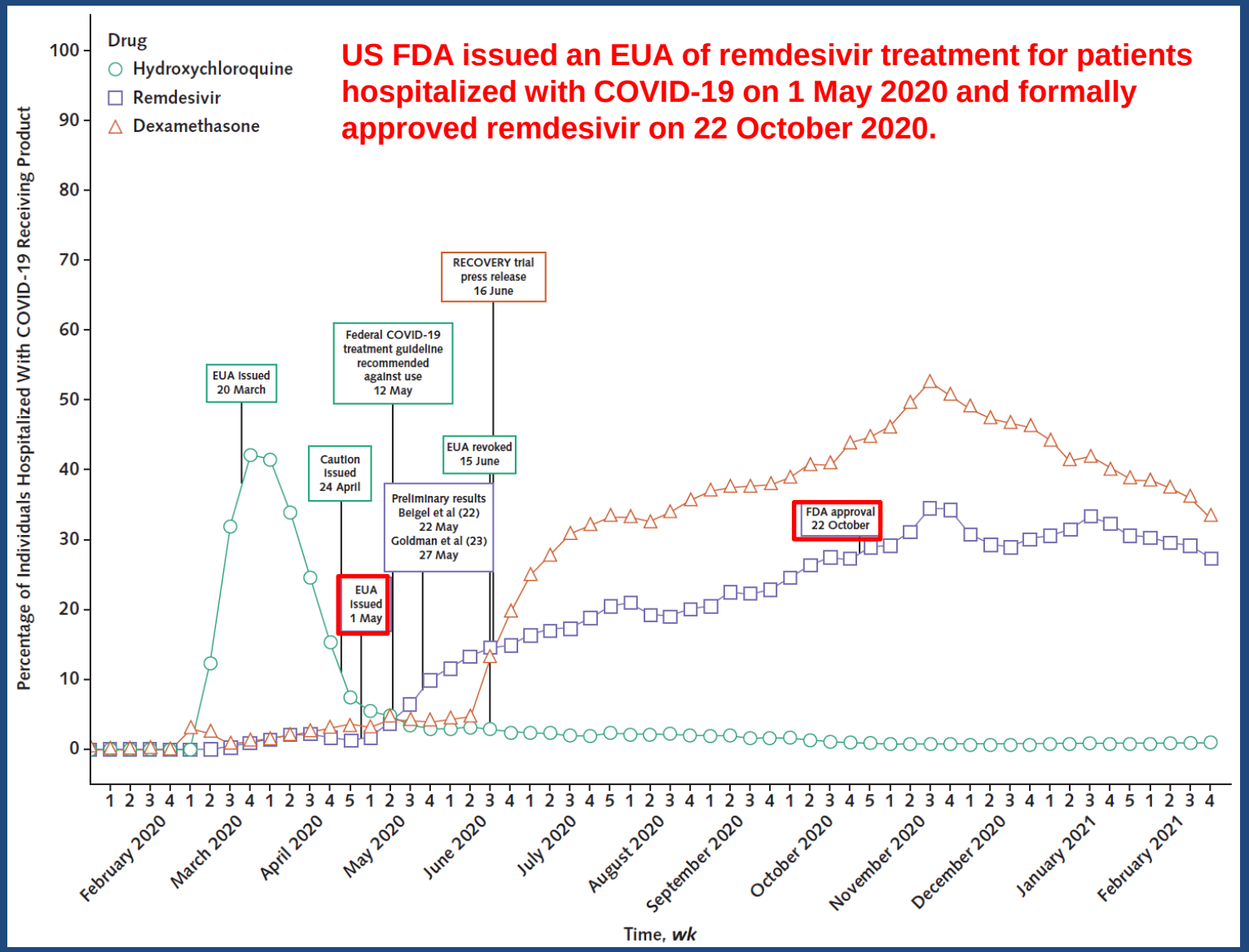
2021-08-28

Inhibition of viral replication by competing with endogenous ATP for incorporation into viral RNA via RNA-dependent RNA polymerase, leading to chain termination



Antimicrob Agents Chemother 2021;65(1):e01814-20

Use of hydroxychloroquine, remdesivir, and dexamethasone among individuals hospitalized with COVID-19, 1 February 2020 to 28 February 2021 (n= 137870) from the National COVID Cohort Collaborative in the United States.



It is unlikely that substantial new information comparing remdesivir with control will be published after the approval.

Ann Intern Med 2021 Aug 10. doi: 10.7326/M21-1991. Online ahead of print

新型冠狀病毒（SARS-CoV-2）感染臨床處置暫行指引

行政院衛生福利部疾病管制署 編

2021 年 7 月 13 日第十三版

表四、我國診治指引對 SARS-CoV-2 確診病患用藥建議彙整

我國診治指引對SARS-CoV-2確診病患用藥建議彙整

	不需用氧	需吸氧治療	高流量氧或NIV	插管
可降低死亡率，建議使用		Dexamethasone	Dexamethasone	Dexamethasone
		+Tocilizumab	+ Baricitinib或tocilizumab	+Tocilizumab
	Casirivimab+imdevimab或 Bamlanivimab+etesevimab			
加速臨床改善，考慮使用		+ Remdesivir		

- **Remdesivir (註 9)**

— 嚴重肺炎以上（未使用吸氧治療下的 SpO2 ≦ 94%、需使用吸氧治療、需使用高流量氧氣或非侵襲性呼吸器但未插管病患）。

— 成人劑量：200mg IVD D1，100mg IVD D2–5

— 孩童劑量：5mg/kg IVD D1，2.5mg/kg IVD D2–5

註 9：ACTT-1 試驗顯示，remdesivir 對需用氧氣但尚未插管病患，可加速臨床改善；對已使用呼吸器之病患則無法加速臨床改善或降低死亡率。

NIH COVID-19 Treatment Guidelines

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	The Panel **recommends against** the use of **dexamethasone (AIIa)** or other **corticosteroids (AIII)**.[a] There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients who are at high risk of disease progression, the use of remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use one of the following options: • **Remdesivir**[b,c] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone**[d] **plus remdesivir**[b,c] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)** • **Dexamethasone**[d] (when combination therapy with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone**[d] **(AI)** • **Dexamethasone**[d] **plus remdesivir**[b,c] **(BIII)** For patients who were recently hospitalized[e] with rapidly increasing oxygen needs and systemic inflammation: • Add either **baricitinib**[f,g] **(BIIa)** or **tocilizumab**[f,h] **(BIIa)** to one of the two options above
Hospitalized and Requires IMV or ECMO	For most patients: • **Dexamethasone**[d,i] **(AI)** For patients who are within 24 hours of admission to the ICU: • **Dexamethasone**[d,i] **plus tocilizumab**[f,h] **(BIIa)**

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19

- In patients with COVID-19 admitted to the hospital without the need for supplemental oxygen and oxygen saturation >94% on room air
  - **against the routine use of remdesivir** (Conditional recommendation, Very low certainty of evidence)
- In hospitalized patients with severe COVID-19 (SpO2 ≤94% on room air)
  - **remdesivir over no antiviral treatment** (Conditional recommendation, Moderate certainty of evidence)
- In patients on supplemental oxygen but not on mechanical ventilation or ECMO
  - **5 days of remdesivir rather than 10 days of remdesivir** (Conditional recommendation, Low certainty of evidence)
- In patients with COVID-19 on invasive ventilation and/or ECMO,
  - **against the routine initiation of remdesivir** (Conditional recommendation, Very low certainty of evidence)

Surviving Sepsis Campaign Guidelines on the Management of Adults With Coronavirus Disease 2019 (COVID-19) in the ICU: First Update

Recommendation/Statement	Justification
6. For adults with severe COVID-19 who do not require mechanical ventilation, we suggest using IV remdesivir over not using it (weak recommendation). *Remark*: Remdesivir should *ideally* be started within 72 hours of positive severe acute respiratory syndrome coronavirus 2 polymerase chain reaction or antigen testing. **ACTT-1 trial randomized patients within 72 hours of positive testing for SARS-CoV-2**	• The result of a placebo-controlled trial showed large reduction in time to recovery and hospital stay • Subgroup analysis from the three trials showed a discordant effect on mortality, suggesting a possible reduction in death in patients who are not invasively ventilated • Despite cost and limited availability, we believe that many patients, if presented with data, would prefer to receive remdesivir
7. For adults undergoing mechanical ventilation for critical COVID-19, we suggest against starting IV remdesivir (weak recommendation).	• Limited data on the effect of remdesivir on outcomes of mechanically ventilated patients • Until more data is available, current costs and limited drug availability favor a weak recommendation against its use in this population

BMJ 2020;370:m3379

RAPID RECOMMENDATIONS

A living WHO guideline on drugs for covid-19

We suggest against administering remdesivir in addition to usual care for the treatment of patients hospitalized with covid-19, regardless of disease severity (weak or conditional recommendation).

This recommendation seems to prioritize resources and equity rather than the discordant effect of remdesivir by disease severity.

Considerations in patients with renal insufficiency

- Because remdesivir formulations contain sulfobutylether-β-cyclodextrin (SBECD), patients with an estimated glomerular filtration rate (eGFR) of <50 mL/min were excluded from some clinical trials of remdesivir; other trials had an eGFR cutoff of <30 mL/min.
- Remdesivir is not recommended for patients with an eGFR <30 mL/min due to lack of data.
- In two observational studies that evaluated the use of remdesivir in hospitalized patients with COVID-19, no significant differences were reported in the incidences of adverse effects or acute kidney injury between patients with an estimated creatinine clearance (CrCl) <30 mL/min and those with an estimated CrCl ≥30 mL/min.

Clin Infect Dis. 2020 Dec 14:ciaa1851.
Antimicrob Agents Chemother. 2021 Jun 17;65(7):e0094321

Considerations in Pregnancy

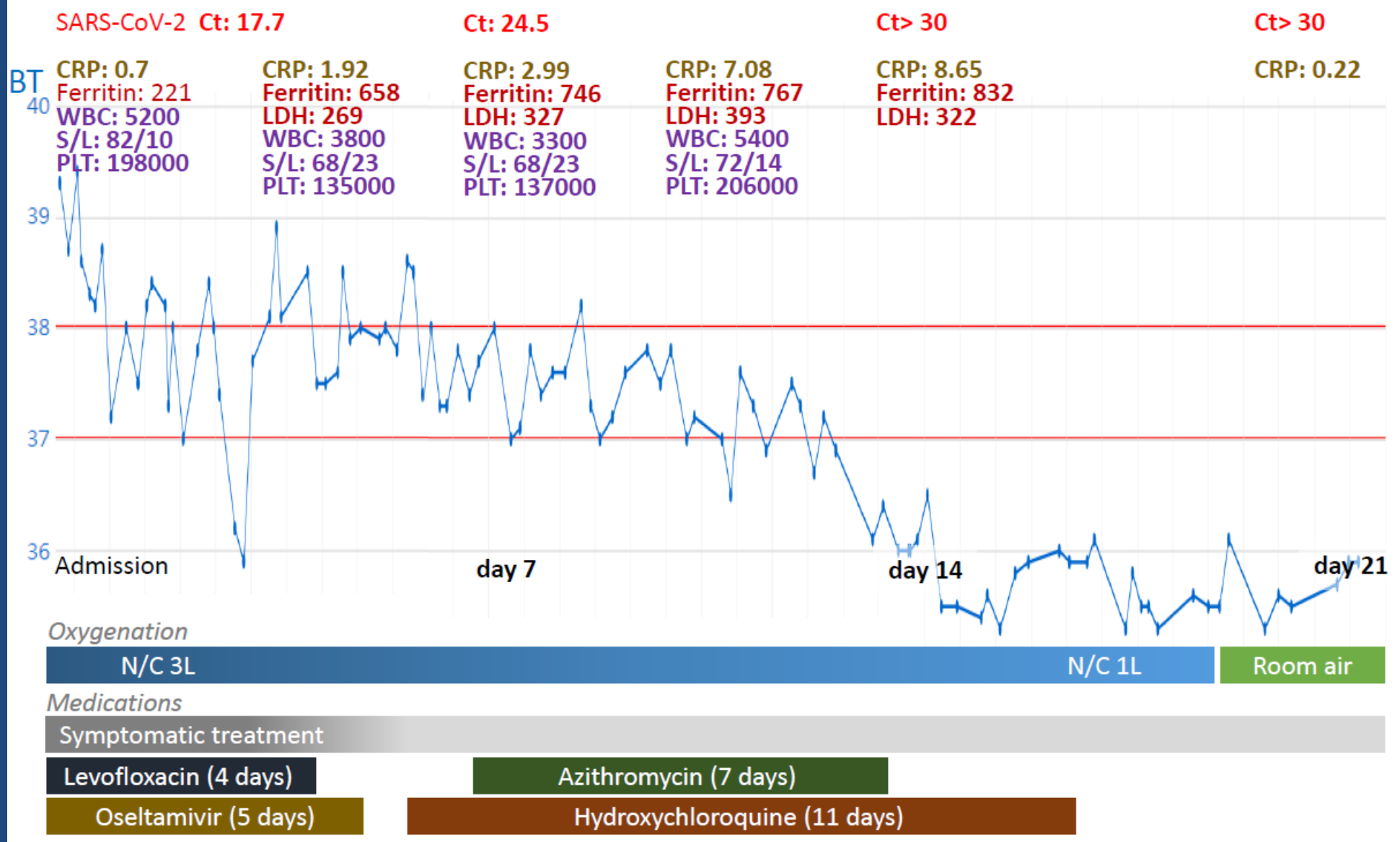
- Pregnant people have an elevated risk of severe COVID-19-related complications
- Pregnant patients were excluded from the clinical trials
- Data are accumulating from post-marketing registries, compassionate use programmes and case series/reports
- NIH panel: remdesivir should not be withheld from pregnant patients if it is otherwise indicated.
- Knowledge gaps to help inform clinical decision

Clin Infect Dis. 2020 Oct 8;ciaa1466
J Antimicrob Chemother, dkab311

59-year-old male, admitted on 2020/3/17

Past history: CAD, HTN

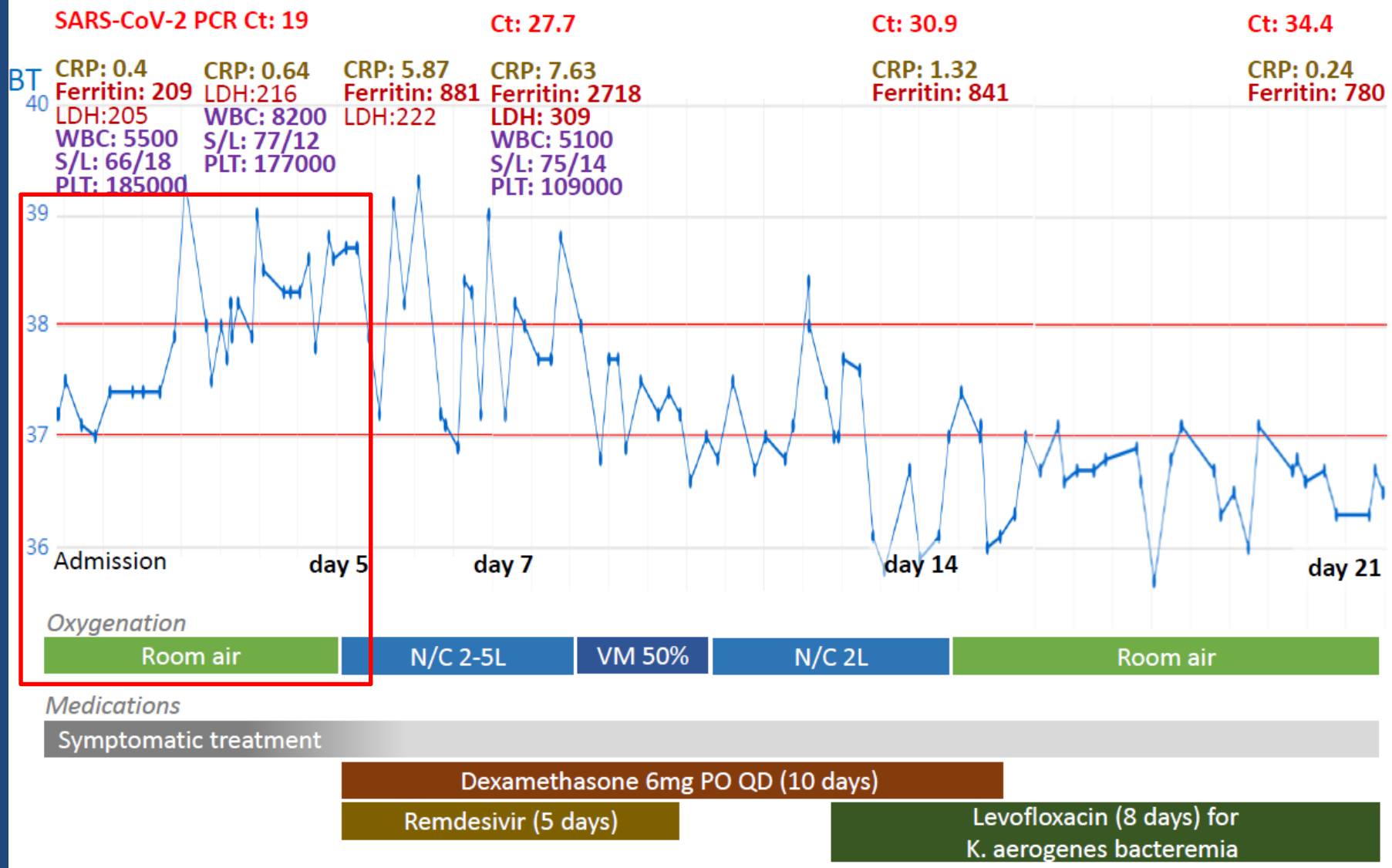
Symptoms: fever, cough, sore throat (3 days), Diagnosis: COVID-19, pneumonia, severe disease



62-year-old male, admitted on 2021/5/25

Past history: Type 2 DM, HTN, HBV carrier

Symptoms: fever, cough, sore throat (2 days), Diagnosis: COVID-19, pneumonia, severe disease



We do not think that waiting for clinical deterioration before deciding on antiviral treatment is a prudent or practical approach.

Antimicrob Agents Chemother 2021;65(1):e01814-20

IDSA
Infectious Diseases Society of America

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19

- There is a need for more rigorous trials to assess the benefits and harms of remdesivir in patients with moderate COVID-19 (oxygen saturation >94%).
- The panel recognized a knowledge gap when assessing whether greater benefit could be attained for patients with oxygen saturation >94% and no supplemental oxygen.

IDSA
Infectious Diseases Society of America

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19

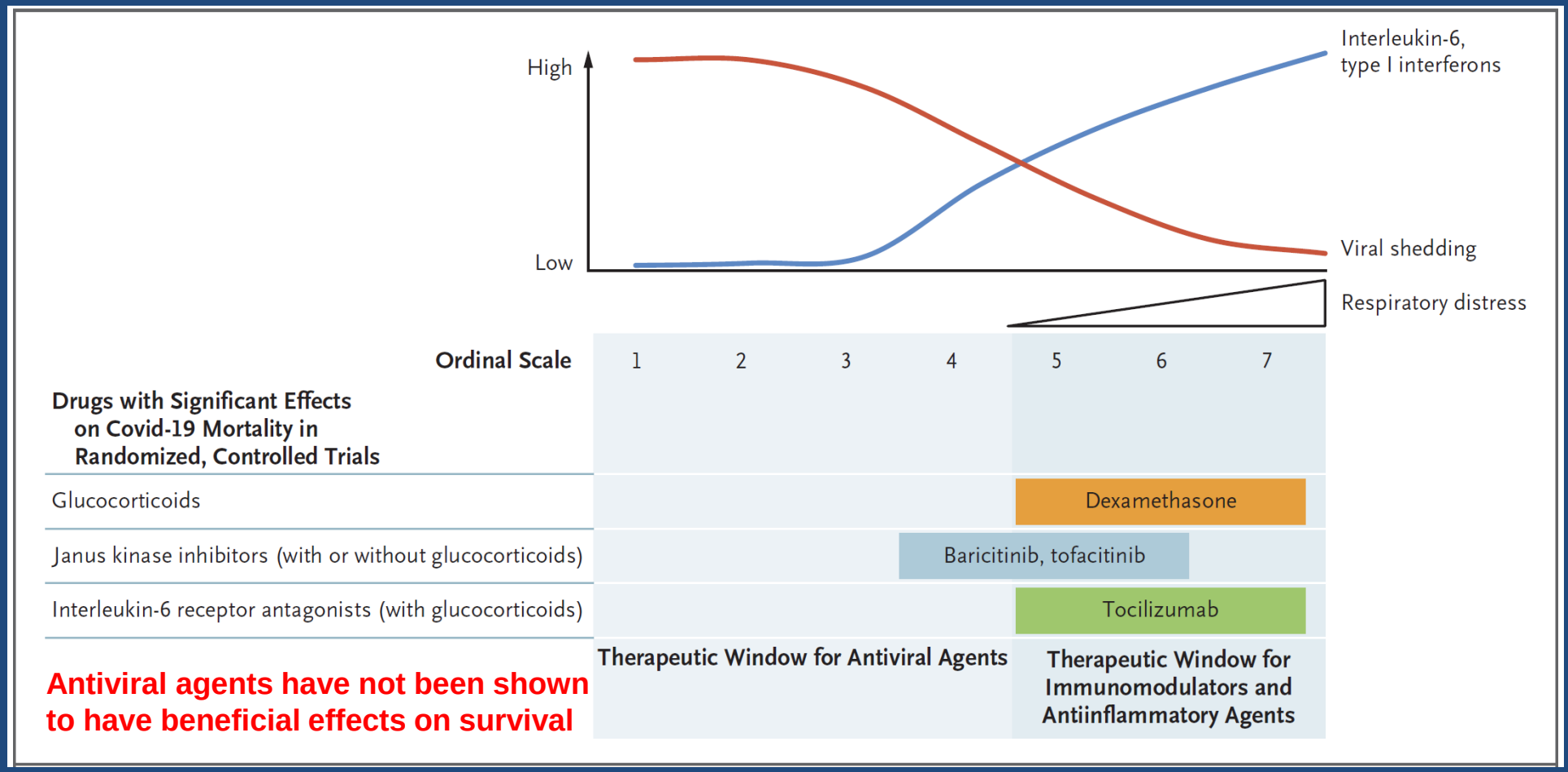
- Immunocompromised patients who are unable to control viral replication may still benefit from remdesivir despite SpO2 that exceeds 94% on room air or a requirement for mechanical ventilation.
- Management of immunocompromised patients with uncontrolled viral replication is a knowledge gap and additional research into such populations is needed.

NIH | COVID-19 Treatment Guidelines

There is insufficient evidence to recommend either for or against the use of Remdesivir in patients who do not require supplemental oxygen

- The NIH Panel recognizes that there may be situations in which a clinician judges that remdesivir is an appropriate treatment for a hospitalized patient with moderate disease
  - e.g., in cases where a person is at a particularly high risk for clinical deterioration

N Engl J Med. 2021 Jul 29;385(5):463-465



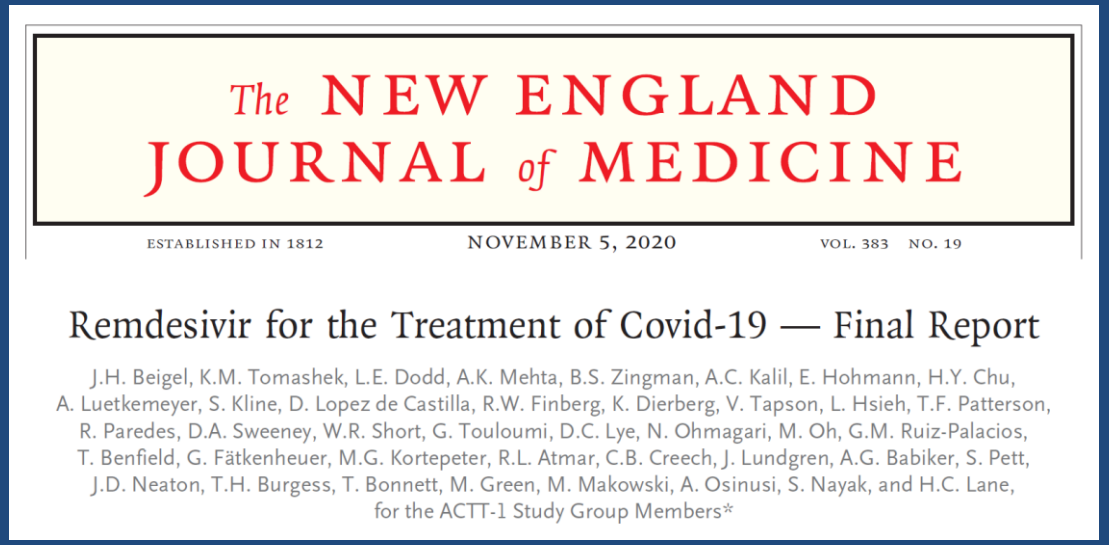
1	Not hospitalized, with no limitations on activities.
2	Not hospitalized, limitation on activities and/or requiring home oxygen.
3	Hospitalized, not requiring supplemental oxygen – no longer requires ongoing medical care.
4	Hospitalized, not requiring supplemental oxygen, requiring ongoing medical care (Covid-19-related or otherwise)
5	Hospitalized, requiring supplemental oxygen by low-flow devices
6	Hospitalized, on non-invasive ventilation or on high-flow oxygen devices
7	Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation
8	Death

Antiviral agents are likely to be most effective in early stages of infection during the first week after symptom onset when disease is still mild to moderate.

未確立的問題

- 是否有其他危險因子(需氧量以外)來決定remdesivir的使用
- remdesivir是否要更早使用
- remdesivir和其他藥物併用的效果
- remdesivir是否應根據病毒量來使用

Adaptive COVID-19 Treatment Trial (ACTT-1)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 5, 2020 VOL. 383 NO. 19

Remdesivir for the Treatment of Covid-19 — Final Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil, E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de Castilla, R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R. Paredes, D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari, M. Oh, G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter, R.L. Atmar, C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H. Burgess, T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H.C. Lane, for the ACTT-1 Study Group Members*

Key Inclusion Criteria:

- Aged ≥18 years
- Laboratory-confirmed SARS-CoV-2 infection
- At least 1 of the following conditions:
  - Pulmonary infiltrates, as determined by radiographic imaging
  - SpO_2 ≤94% on room air
  - Required supplemental oxygen
  - Required mechanical ventilation
  - Required ECMO

Interventions:

- IV RDV 200 mg on Day 1, then 100 mg daily for up to 9 more days
- Placebo for 10 days

Number of Participants:

- RDV (n = 541) and placebo (n = 521)

Participant Characteristics:

- Median time from symptom onset to randomization was 9 days (IQR 6–12 days).

2020/2/21—2020/4/19

Outcomes

Overall Results:

- RDV reduced time to recovery compared to placebo (10 days vs. 15 days; RRR 1.29; 95% CI, 1.12–1.49; $P < 0.001$).
- Clinical improvement based on ordinal scale was higher at Day 15 in RDV arm (OR 1.5; 95% CI, 1.2–1.9; $P < 0.001$).
- No statistically significant difference in mortality by Day 29 between RDV and placebo arms (HR 0.73; 95% CI, 0.52–1.03; $P = 0.07$).
- Benefit of RDV was greatest in patients randomized during the first 10 days after symptom onset.

- No observed difference in time to recovery between arms in patients on high-flow oxygen or noninvasive ventilation at enrollment (RRR 1.09; 95% CI, 0.76–1.57). No evidence that RDV affected mortality rate in this subgroup (HR 1.02; 95% CI, 0.54–1.91).
- No observed difference in time to recovery between arms in patients on mechanical ventilation or ECMO at enrollment (RRR 0.98; 95% CI, 0.70–1.36). No evidence that RDV affected mortality rate in this subgroup (HR 1.13; 95% CI, 0.67–1.89).

Recovery: either discharge from the hospital or hospitalization for infection-control purposes only.

- Benefit of RDV for reducing time to recovery was clearest in patients who **required supplemental oxygenation at enrollment** (n = 435; RRR 1.45; 95% CI, 1.18–1.79), and RDV appeared to confer **a survival benefit in this subgroup** (HR for death by Day 29 **0.30; 95% CI, 0.14–0.64**).

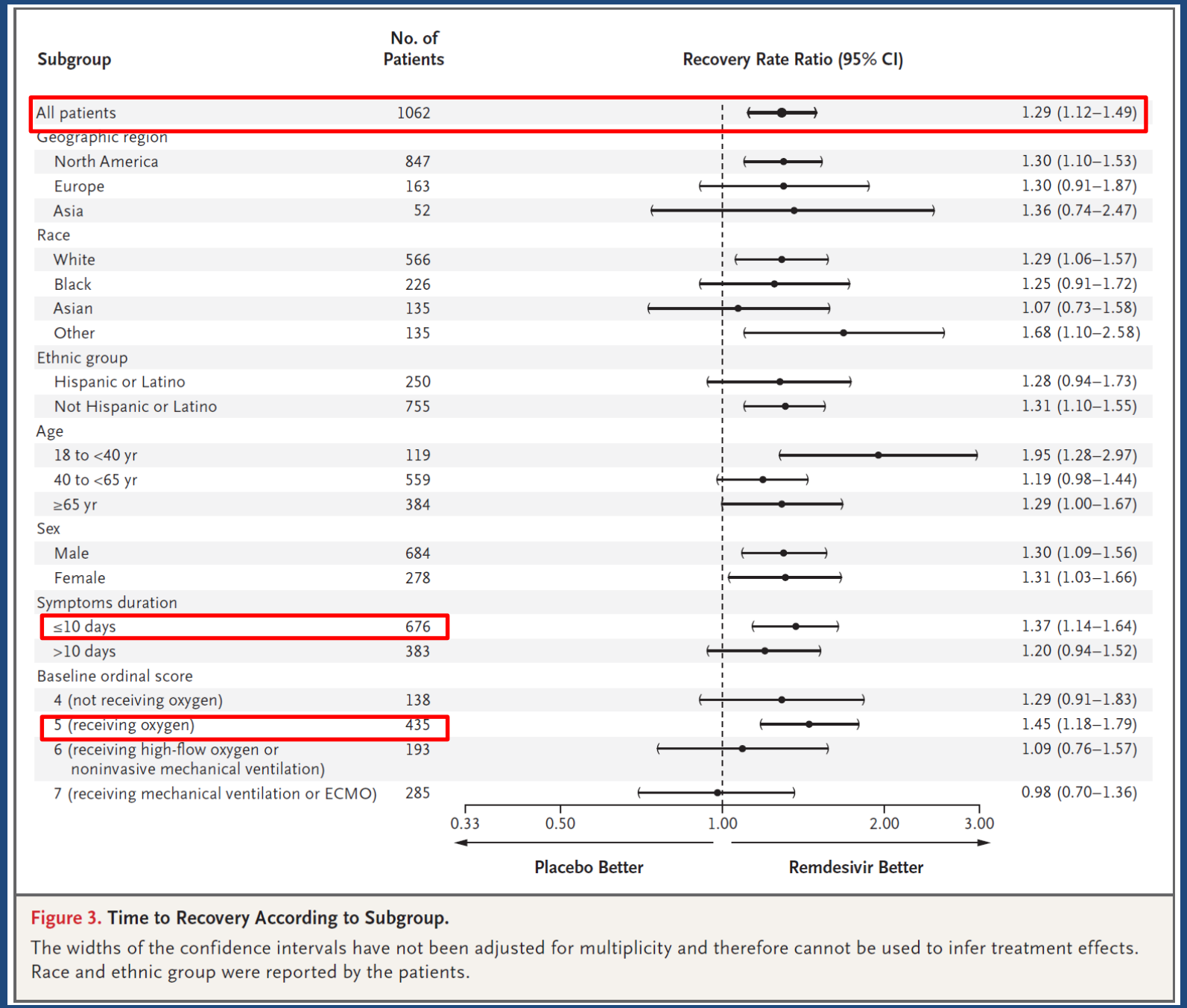


Figure 3. Time to Recovery According to Subgroup.

The widths of the confidence intervals have not been adjusted for multiplicity and therefore cannot be used to infer treatment effects. Race and ethnic group were reported by the patients.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 11, 2021 VOL. 384 NO. 6

Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results

WHO Solidarity Trial Consortium*

BACKGROUND

World Health Organization expert groups recommended mortality trials of four repurposed antiviral drugs — remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a — in patients hospitalized with coronavirus disease 2019 (Covid-19).

Key Inclusion Criteria:

- Aged ≥18 years
- Not known to have received any study drug
- Not expected to be transferred elsewhere within 72 hours
- Physician reported no contraindications to study drugs

Interventions:

- IV RDV 200 mg on Day 0, then 100 mg daily on Days 1–9
- Local SOC

Number of Participants:

- ITT analysis: RDV (n = 2,743) and SOC (n = 2,708)

2020/3/22—2020/10/4

No data on time from symptom onset to enrollment !!

Primary Outcomes:

- In-hospital mortality: 301 deaths (11.0%) in RDV arm, 303 deaths (11.2%) in SOC arm
- Rate ratios for in-hospital death:
  - Overall: 0.95 (95% CI, 0.81–1.11)
  - No mechanical ventilation at entry: 0.86 (99% CI, 0.67–1.11)
  - Mechanical ventilation at entry: 1.20 (99% CI, 0.80–1.80)

Secondary Outcomes:

- Initiation of mechanical ventilation: 295 patients (10.8%) in RDV arm, 284 patients (10.5%) in SOC arm

Baseline oxygen status, other than mechanical ventilation, was not described in the Solidarity study.

Remdesivir Versus Placebo for Severe COVID-19 in China

Lancet 2020; 395: 1569–78

Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial

Yeming Wang, Dingyu Zhang*, Guanhua Du*, Ronghui Du*, Jianping Zhao*, Yang Jin*, Shouzhi Fu*, Ling Gao*, Zhenshun Cheng*, Qiaofa Lu*, Yi Hu*, Guangwei Luo*, Ke Wang, Yang Lu, Huadong Li, Shuzhen Wang, Shunan Ruan, Chengqing Yang, Chunlin Mei, Yi Wang, Dan Ding, Feng Wu, Xin Tang, Xianzhi Ye, Yingchun Ye, Bing Liu, Jie Yang, Wen Yin, Aili Wang, Guohui Fan, Fei Zhou, Zhibo Liu, Xiaoying Gu, Jiuyang Xu, Lianhan Shang, Yi Zhang, Lianjun Cao, Tingting Guo, Yan Wan, Hong Qin, Yushen Jiang, Thomas Jaki, Frederick G Hayden, Peter W Horby, Bin Cao, Chen Wang*

Key Inclusion Criteria:

- Aged ≥18 years
- Laboratory-confirmed SARS-CoV-2 infection
- Time from symptom onset to randomization <12 days
- SpO_2 ≤94% on room air or PaO_2/FiO_2 <300 mm Hg
- Radiographically confirmed pneumonia

2020/2/6---2020/3/12

Number of Participants:

- ITT analysis: RDV (n = 158) and placebo (n = 78)
- Study stopped before reaching target enrollment of 453 patients due to control of the COVID-19 outbreak in China.

Interventions:

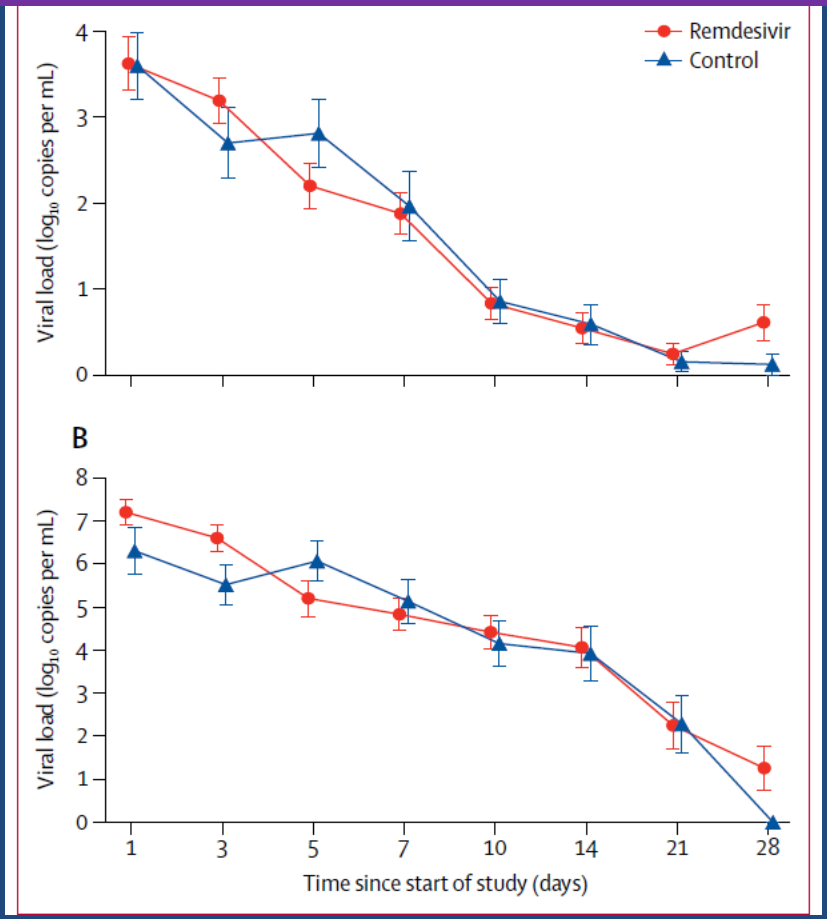
- IV RDV 200 mg on Day 1, then 100 mg daily for 9 days
- Saline placebo for 10 days

Clinical improvement was defined as a 2-point reduction in patients' admission status on a six-point ordinal scale, or live discharge from the hospital, whichever came first.

Outcomes:

- No difference in time to clinical improvement between RDV and placebo arms (median time 21 days vs. 23 days; HR 1.23; 95% CI, 0.87–1.75).
- For patients who started RDV or placebo within 10 days of symptom onset, faster time to clinical improvement was seen with RDV (median time 18 days vs. 23 days; HR 1.52; 95% CI, 0.95–2.43); however, this was not statistically significant.
- 28-day mortality was similar between arms (14% of patients in RDV arm, 13% in placebo arm).
- No difference between arms in SARS-CoV-2 viral load at baseline, and rate of decline over time was similar.

In the subset of patients from whom expectorated sputa could be obtained (103 patients), the mean viral RNA load at enrolment was nearly 1-log higher in the remdesivir group than the placebo group at enrolment (figure 3B). When adjusted for baseline sputum viral load at enrolment, **the remdesivir group showed no significant difference at day 5 from placebo, but a slightly more rapid decline in load (p=0·0672).**



Remdesivir versus standard of care in hospitalized patients with moderate COVID-19

JAMA. 2020;324(11):1048-1057.

JAMA | Original Investigation

Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19

A Randomized Clinical Trial

Key Inclusion Criteria:

- Laboratory-confirmed SARS-CoV-2 infection
- Moderate pneumonia, defined as radiographic evidence of pulmonary infiltrates and SpO_2 >94% on room air

Interventions:

- IV RDV 200 mg on Day 1, then 100 mg daily for 9 days
- IV RDV 200 mg on Day 1, then 100 mg daily for 4 days
- Local SOC

Number of Participants:

- 584 patients began treatment: 10-day RDV (n = 193), 5-day RDV (n = 191), and SOC (n = 200)

2020/3/15—2020/4/18

Outcomes:

- 5-day RDV had significantly higher odds of better clinical status distribution on Day 11 than SOC (OR 1.65; 95% CI, 1.09–2.48; $P = 0.02$).
- Clinical status distribution on Day 11 was not significantly different between the 10-day RDV and SOC arms ($P = 0.18$).
- By Day 28, there were more hospital discharges among patients who received RDV (89% in 5-day arm and 90% in 10-day arm) than those who received SOC (83%).
- Mortality was low in all arms (1% to 2%).

1: Death
2: Hospitalized, requiring invasive mechanical ventilation or extracorporeal membrane oxygenation
3: Hospitalized, requiring noninvasive ventilation or high-flow oxygen
4: Hospitalized, requiring low-flow supplemental oxygen
5: Hospitalized, not requiring supplemental oxygen but requiring ongoing medical care
6: Hospitalized, not requiring supplemental oxygen or medical care
7: Not hospitalized

Different durations of remdesivir treatment in hospitalized patients

After adjusting for imbalances in baseline clinical status, Day 14 distribution in clinical status on the ordinal scale was similar between arms (P = 0.14).

Remdesivir for 5 or 10 Days in Patients with Severe Covid-19

Key Inclusion Criteria:

- Aged ≥12 years
- Laboratory-confirmed SARS-CoV-2 infection
- Radiographic evidence of pulmonary infiltrates
- SpO_2 ≤94% on room air or receipt of supplemental oxygen

Key Exclusion Criteria:

- Receipt of mechanical ventilation or ECMO
- Multiorgan failure

Interventions:

- IV RDV 200 mg on Day 1, then 100 mg daily for 4 days
- IV RDV 200 mg on Day 1, then 100 mg daily for 9 days

Number of Participants:

- 397 participants began treatment: 5-day RDV (n = 200) and 10-day RDV (n = 197)

2020/3/6—2020/3/26

IDSA
Infectious Diseases Society of America

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19

- The panel recognized the benefit of a shorter course of treatment, if providing similar or greater efficacy, on the availability of remdesivir.
- However, in a subgroup analysis of mechanically ventilated patients, the duration of treatment was 10 days in ACTT-1 trial.
  - The panel recognized that a longer course of treatment could be desirable in this population.

NIH COVID-19 Treatment Guidelines

DISEASE SEVERITY	PANEL'S RECOMMENDATIONS
Hospitalized but Does Not Require Supplemental Oxygen	The Panel **recommends against** the use of **dexamethasone (AIIa)** or other **corticosteroids (AIII)**.[a] There is insufficient evidence to recommend either for or against the routine use of remdesivir. For patients who are at high risk of disease progression, the use of remdesivir may be appropriate.
Hospitalized and Requires Supplemental Oxygen	Use one of the following options: • **Remdesivir**[b,c] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone**[d] **plus remdesivir**[b,c] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)** • **Dexamethasone**[d] (when combination therapy with remdesivir cannot be used or is not available) **(BI)**
Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation	Use one of the following options: • **Dexamethasone**[d] **(AI)** • **Dexamethasone**[d] **plus remdesivir**[b,c] **(BIII)** For patients who were recently hospitalized[e] with rapidly increasing oxygen needs and systemic inflammation: • Add either **baricitinib**[f,g] **(BIIa)** or **tocilizumab**[f,h] **(BIIa)** to one of the two options above
Hospitalized and Requires IMV or ECMO	For most patients: • **Dexamethasone**[d,i] **(AI)** For patients who are within 24 hours of admission to the ICU: • **Dexamethasone**[d,i] **plus tocilizumab**[f,h] **(BIIa)**

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

Remdesivir plus Dexamethasone

- The combination of remdesivir plus dexamethasone has not been rigorously studied in clinical trials.
- Some studies have suggested that corticosteroids slow SARS-CoV-2 clearance, but the results to date are inconclusive.
- Despite the lack of clinical trial data, there is a theoretical rationale for combining remdesivir and dexamethasone.

NIH guideline

Clin Infect Dis. 2021 Jun 10;ciab536.

Clinical Infectious Diseases

MAJOR ARTICLE

Improved Survival Among Hospitalized Patients With Coronavirus Disease 2019 (COVID-19) Treated With Remdesivir and Dexamethasone. A Nationwide Population-Based Cohort Study

Two Danish population-based nationwide cohorts of individuals hospitalized with COVID-19 during February through December 2020 were studied.

standard of care (SOC) **SOC with remdesivir and dexamethasone** **possible differences in SOC??**

- The 30-days mortality rate of 1694 individuals treated with remdesivir and dexamethasone in addition to SOC was 12.6% compared to 19.7% for 1053 individuals receiving SOC alone.
- **A weighted OR of 30-day mortality of 0.47 (95% CI: .38–.57)** for patients treated with remdesivir and dexamethasone compared to patients receiving SOC alone.
- **Progression to MV was reduced (OR 0.36; 95% CI: .29–.46).**

	February–May n = 1053	June–December n = 1694	*P* value	SMD	SMD After IPTW
Other, no. (%)	360 (35.9%)	808 (47.7%)	<.001	0.240	0.015
Symptom duration, days	7 (3–10)	6 (3–9)	<.001	…	…
Radiographic evidence of pneumonic infiltration, no. (%)	810 (80.8%)	1566 (92.4%)	<.001	0.346	0.005
Supplemental oxygen, no. (%)	464 (44.6%)	1610 (95.0%)	<.001	1.315	0.003
Duration of hospitalization before first dose of remdesivir, days	…	1 (0–1)	…	…	…
Duration of symptoms before first dose of remdesivir, days	…	7 (4–10)	…	…	…
Duration of hospitalization before first dose of dexamethasone, days	…	1 (0–1)	…	…	…

J Antimicrob Chemother. 2021 Aug 9;dkab256. Online ahead of print.

J Antimicrob Chemother
doi:10.1093/jac/dkab256

Journal of Antimicrobial Chemotherapy

The association of remdesivir and in-hospital outcomes for COVID-19 patients treated with steroids

Toshiki Kuno [1]*, Yoshihisa Miyamoto[2], Masao Iwagami[3], Miho Ishimaru[3], Mai Takahashi[1] and Natalia N. Egorova[4]

- Retrospective study
- 9965 hospitalized patients who were discharged between **1 March 2020 and 30 March 2021**,with COVID-19 in the Mount Sinai Health System.

- We aimed to investigate whether remdesivir reduces in-hospital mortality among patients with COVID-19 treated with steroids.
- The final cohort included 3372 COVID-19 patients treated with steroids (within 2 days of admission), and 1336 (39.6%) received remdesivir.
- 1:1 propensity score matching (N= 999 pairs)

- **Median time from admission to the time when remdesivir was given was 23.0 h [IQR 16.1, 35.8].**
- **Among patients on remdesivir, remdesivir course was: 1–4 days, n = 343 (25.7%); 5 days, n = 973 (72.8%); and 6–10 days, n=20 (1.5%).**

Table 2. Treatment by remdesivir and in-hospital outcomes

	Before propensity score matching			After propensity score matching		
	patients without remdesivir, *N* = 2036	patients with remdesivir, *N* = 1336	*P* value	patients without remdesivir, *N* = 999	patients with remdesivir, *N* = 999	*P* value
In-hospital mortality	573 (28.1)	285 (21.3)	<0.001	216 (21.6)	214 (21.4)	0.96
ICU admission	576 (28.3)	363 (27.2)	0.50	222 (22.2)	260 (26.0)	0.053
Endotracheal intubation	375 (18.4)	196 (14.7)	0.005	140 (14.0)	140 (14.0)	>0.999
AKI			<0.001			0.001
no AKI	1335 (65.6)	1096 (82.0)		765 (76.6)	824 (82.5)	
Stage 1	200 (9.8)	102 (7.6)		81 (8.1)	72 (7.2)	

- Remdesivir was not significantly associated with in hospital mortality (OR [95% CI] 0.93 [0.74–1.16], P=0.20) after multiple imputation. The IPTW analysis also showed the similar results (OR [95% CI] 0.87 [0.71–1.06], P = 0.17).
- The incidence of AKI was significantly lower in patients with remdesivir compared with those without after propensity score matching (17.5% versus 23.4%, respectively, P=0.001). IPTW analysis showed the similar result (OR [95% CI] 0.60 [0.48–0.76], P<0.001).

Table 3. In-hospital mortality for subgroups of patients stratified by endotracheal intubation, antibody and study period

	Before propensity score matching in each subgroup			After matching by propensity score in each subgroup		
	patients without remdesivir, *N* (%)	patients with remdesivir, *N* (%)	*P* value	patients without remdesivir, *N* (%)	patients with remdesivir, *N* (%)	*P* value
Patients without endotracheal intubation	*N* = 1661, 292 (17.6)	*N* = 1140, 121 (10.6)	<0.001	*N* = 862, 110 (12.8)	*N* = 862, 94 (10.9)	0.26
Patients with endotracheal intubation	*N* = 375, 281 (74.9)	*N* = 196, 164 (83.7)	0.022	*N* = 130, 108 (83.1)	*N* = 130, 108 (83.1)	>0.999
Patients with COVID-19 antibody-positive	*N* = 515, 123 (23.9)	*N* = 660, 162 (24.5)	0.85	*N* = 377, 79 (21.0)	*N* = 377, 89 (23.6)	0.43
Patients with COVID-19 antibody-negative	*N* = 472, 103 (21.8)	*N* = 246, 40 (16.3)	0.094	*N* = 223, 42 (18.8)	*N* = 223, 36 (16.1)	0.53
Patients who were discharged after 17 February 2021	*N* = 673, 148 (22.0)	*N* = 648, 160 (24.7)	0.27	*N* = 425, 81 (19.1)	*N* = 425, 98 (23.1)	0.18

The in-hospital mortality was not different among patients who were given remdesivir within 24 h (n = 705) and those who were given remdesivir between 24 and 72 h (n = 516) after matching patients by propensity score (439 pairs: 19.8% versus 21.6%, respectively, P=0.56).

JAMA Network Open. 2021;4(3):e213071. doi:10.1001/jamanetworkopen.2021.3071

JAMA Network | Open

Original Investigation | Infectious Diseases

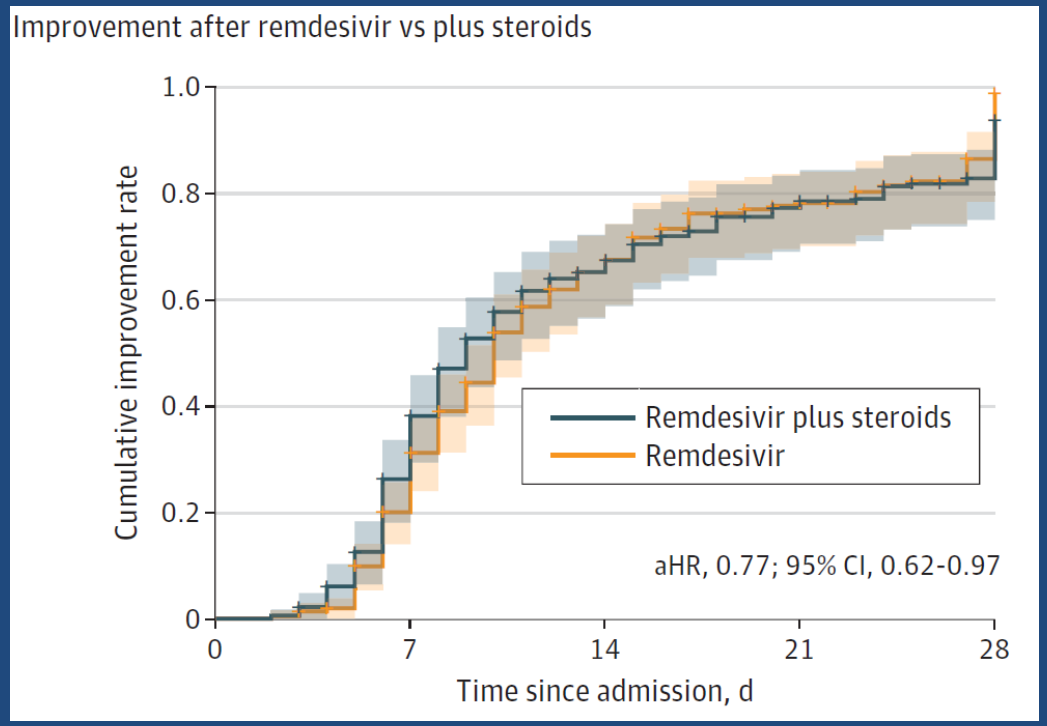
Comparison of Time to Clinical Improvement With vs Without Remdesivir Treatment in Hospitalized Patients With COVID-19

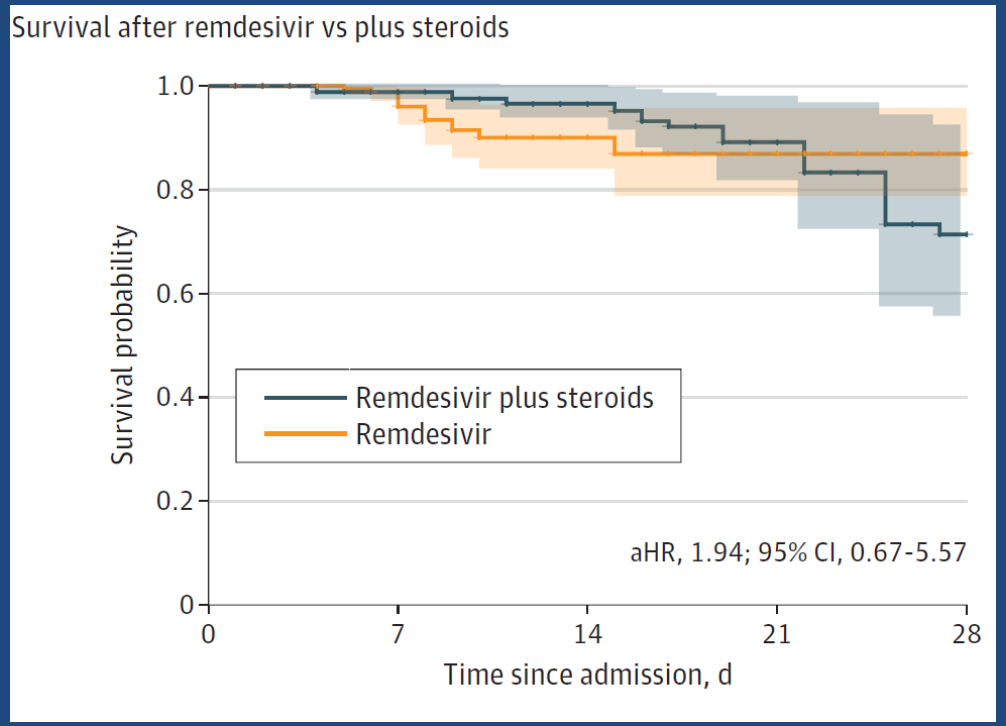
This retrospective comparative effectiveness research study was conducted from March 4 to August 29, 2020, in a 5-hospital health system in the Baltimore, Maryland, and Washington, DC, area.

- Of 2483 individuals with confirmed SARS CoV-2 infection assessed by PCR, those who received remdesivir were matched to infected individuals who did not receive remdesivir using time invariant covariates and time-dependent covariates.
- Approximately 80% of patients in our cohort were non-white individuals compared with 30% to 47% in clinical trials.
- 303 patients (88.6%) received a 5-day course.
- **The median time from admission to treatment initiation was 1.1 days (IQR, 0.8-2.4 days).**

- Remdesivir recipients had a shorter time to clinical improvement than matched controls without remdesivir treatment **(median, 5.0 days [IQR, 4.0-8.0 days] vs 7.0 days [IQR, 4.0-10.0 days]; adjusted HR, 1.47 [95%CI, 1.22-1.79])**.

- Remdesivir recipients had a 28-day mortality rate of 7.7% (22 deaths) compared with 14.0% (40 deaths) among matched controls, **but this difference was not statistically significant in the time-to-death analysis (adjusted HR, 0.70; 95%CI, 0.38-1.28).**





- **We compared 184 patients who received remdesivir plus corticosteroids with 158 patients who received remdesivir alone.**
- 68 individuals (37%) in the remdesivir and corticosteroid group had severe disease (requiring high-flow nasal cannula, noninvasive ventilation, mechanical ventilation, extracorporeal membrane oxygenation, or vasopressors) compared with 41 individuals (26%) in the remdesivir group. The sample sizes were too small to evaluate the benefits for patients with severe disease.

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A shorter symptom onset to remdesivir treatment (SORT) interval is associated with a lower mortality in moderate-to-severe COVID-19: A real-world analysis

Ravindra M. Mehta*, Sameer Bansal, Suhitha Bysani, Hariprasad Kalpakam

Apollo Super Specialty Hospital, Jayanagar 3rd Block, Bangalore 560011, Karnataka, India

- This single-center retrospective study was conducted between June 25, 2020 and October 3, 2020 at a tertiary dedicated COVID care hospital in adult patients with moderate-to-severe COVID-19 in Bangalore, India.
- **Patients with moderate-to-severe COVID-19 (moderate: SpO2 <94%; severe: SpO2 <90%) were included.**
- **Remdesivir: 5-10 days**
- The main outcome was impact of **symptom onset to remdesivir treatment (SORT) interval** on in-hospital all cause mortality.
- Subgroups were formed and analyzed based on SORT interval.

Characteristics and outcomes of the overall study population[a] and comparison of outcomes in patients with COVID-19 with SORT interval ≤9 and >9 days.

	Total (N = 346)	SORT interval ≤9 days (n = 260)	SORT interval >9 days (n = 86)	p-Value[b]
Age (years), median (IQR)	60 (49.3–69)	60 (49.8–69)	59 (49.3–68)	0.96
Sex, n (%)				
Male	270 (78.0)	202 (77.7)	68 (79.1)	0.91
Female	76 (22.0)	58 (22.3)	18 (20.9)	
Comorbidities, n (%)				
DM	173 (50.0)	133 (51.2)	40 (46.5)	0.17
HTN	163 (47.1)	119 (45.8)	44 (51.2)	
CHD	54 (15.6)	41 (15.8)	13 (15.1)	
CKD	18 (5.2)	9 (3.5)	9 (10.5)	
Chronic respiratory diseases (asthma, COPD), n (%)	12 (3.5)	8 (3.1)	4 (4.7)	
Ancillary therapies, n (%)				
Corticosteroids	346 (100.0)	260 (100.0)	86 (100.0)	0.73
Convalescent plasma	131 (37.9)	103 (39.6)	28 (32.6)	
Tocilizumab	37 (10.7)	28 (10.8)	9 (10.5)	
SORT (days), median (IQR)	6 (4–9)	5 (4–7)	11 (10–12)	<0.001
Disease (COVID-19) severity, n (%)				
Moderate	109 (31.5)	86 (33.1)	23 (26.7)	0.34
Severe	237 (68.5)	174 (66.9)	63 (73.3)	
Outcomes (overall), n (%)				
Discharged	270 (78.0)	213 (81.9)	57 (66.3)	0.004
Death	76 (22.0)	47 (18.1)	29 (33.7)[c]	
LOHS (days), median (IQR)	11 (7–16)	10 (7–16)	12 (7–17)	0.34
Mortality (disease severity), n (%)				
Moderate	3 (0.9)[d]	3 (1.2)	0 (0.0)	0.004
Severe	73 (21.1)[d]	44 (16.9)	29 (33.7)	

- **All-cause mortality was significantly lower in patients with SORT interval </=9 days vs SORT interval >9 days (18.1% vs 33.7%; p =0.004).**
- **The odds of death were significantly lower in patients with SORT interval </=9 days vs >9 days (odds ratio = 0.43; 95% CI, 0.25–0.75; p = 0.003).**

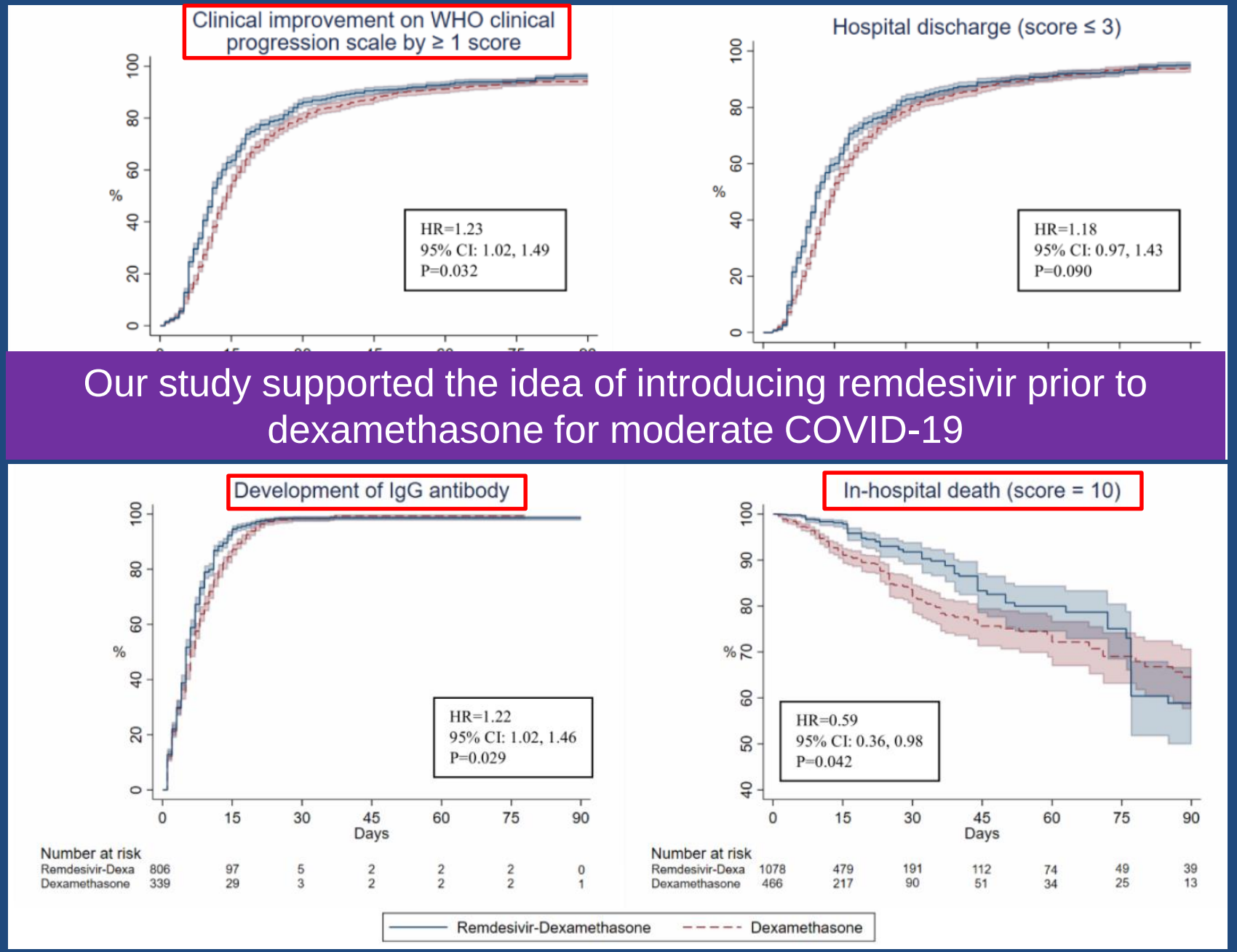
Optimal timing of remdesivir initiation in hospitalized COVID-19 patients administered with dexamethasone

Dexamethasone of 6mg once daily for up to 10 days was recommended for hospitalized patients with pneumonia, and those who required supplemental oxygen or invasive mechanical ventilation.

A territory-wide cohort of **10,445** COVID-19 patients from Hong Kong who were hospitalized between 21st January 2020 and 31st January 2021

- **1544 patients had received dexamethasone during hospitalization**
- **Exposure group**: patients who had initiated **remdesivir prior to dexamethasone (n=93), or co-initiated the two drugs simultaneously (n=373)**
- **Non-exposure group**: patients who were given **remdesivir after dexamethasone (n=149), or those without remdesivir use (n=929).** The median of delay of remdesivir initiation following dexamethasone was 2 (interquartile range: 1-4) days.

	Remdesivir Dexamethasone (n=466)	Dexamethasone (n=1,078)
No oxygen therapy	72 %	67 %
Supplemental oxygen without ventilation	23 %	31 %
Mechanical ventilation	4 %	2 %


Clinical improvement on WHO clinical progression scale by ≥ 1 score
HR=1.23
95% CI: 1.02, 1.49
P=0.032
Hospital discharge (score ≤ 3)
HR=1.18
95% CI: 0.97, 1.43
P=0.090
Our study supported the idea of introducing remdesivir prior to dexamethasone for moderate COVID-19
Development of IgG antibody
HR=1.22
95% CI: 1.02, 1.46
P=0.029
Days
Number at risk
Remdesivir-Dexa 806 97 5 2 2 2 0
Dexamethasone 339 29 3 2 2 2 1
In-hospital death (score = 10)
HR=0.59
95% CI: 0.36, 0.98
P=0.042
Days
Number at risk
Remdesivir-Dexa 1078 479 191 112 74 49 39
Dexamethasone 466 217 90 51 34 25 13
Remdesivir-Dexamethasone
Dexamethasone

ACTT-2 trial

- **A double-blind, randomized, placebo-controlled trial evaluating baricitinib plus remdesivir in hospitalized adults with Covid-19.**
- **All the patients received remdesivir (≤10 days) and either baricitinib (≤14 days) or placebo (control).**

- Baricitinib: Janus kinase 1 and 2 inhibitor
- A total of 1033 patients underwent randomization (with 515 assigned to combination treatment and 518 to control) during May 8, 2020 and July 1, 2020.
- Patients who were using a medication off-label as a specific treatment for COVID-19, including corticosteroids, at study entry were excluded from the trial.

- Patients receiving baricitinib had a median time to recovery of 7 days (95% CI, 6 to 8), as compared with 8 days (95% CI, 7 to 9) with control (RR for recovery, 1.16; 95% CI, 1.01 to 1.32; P = 0.03), and a 30% higher odds of improvement in clinical status at day 15 (OR, 1.3; 95% CI, 1.0 to 1.6).
- Patients receiving high-flow oxygen or noninvasive ventilation at enrollment had a time to recovery of 10 days with combination treatment and 18 days with control (rate ratio for recovery, 1.51; 95% CI, 1.10 to 2.08).
- The 28-day mortality was 5.1% in the combination group and 7.8% in the control group (HR for death, 0.65; 95% CI, 0.39 to 1.09).

Ongoing trial: Adaptive COVID-19 Treatment Trial 4 (ACTT-4)

- Randomized double-blind placebo-controlled trial.
- A multicenter trial (approximately 100 sites globally).
- ACTT-4 will evaluate the combination of baricitinib and remdesivir compared to dexamethasone and remdesivir.
- The primary objective is to evaluate the clinical efficacy of baricitinib + remdesivir versus dexamethasone + remdesivir as assessed by the mechanical ventilation free survival by Day 29.
- The key secondary objective is to evaluate the clinical efficacy of baricitinib + remdesivir versus dexamethasone + remdesivir according to clinical status (8-point ordinal scale) at Day 15.

Clin Infect Dis. 2021 Aug 19: ciab712 Online ahead of print

Deconstructing the Treatment Effect of Remdesivir in the Adaptive COVID-19 Treatment Trial-1: Implications for Critical Care Resource Utilization

Remdesivir reduced time to recovery compared to placebo (10 days vs. 15 days; RRR 1.29; 95% CI, 1.12–1.49; P < 0.001).

We investigated how the dynamics of clinical progression changed along 4 pathways: recovery, improvement in respiratory therapy requirement, deterioration in respiratory therapy requirement, and death.

- Competing risks analysis: remdesivir reduced clinical deterioration (hazard ratio, 0.73; 95% CI, 0.59-0.91) and increased clinical improvement (hazard ratio, 1.22; 95% CI, 1.08, 1.39) relative to baseline.
- Multistate models: remdesivir inhibits worsening to ordinal scores of greater clinical severity among patients **on room air or low-flow oxygen (HR, 0.74; 95% CI, 0.57-0.94)** and **among patients receiving mechanical ventilation or high-flow oxygen/ noninvasive positive-pressure ventilation (HR, 0.73; 95% CI, 0.53-1.00) at baseline**.

Clin Infect Dis. 2021 Aug 11:ciab695. Online ahead of print

Title: Remdesivir for the prevention of invasive mechanical ventilation or death in COVID-19 - A post-hoc analysis of the Adaptive COVID-19 Treatment Trial-1 Cohort Data

- **ACTT-1 was not designed to evaluate remdesivir's impact on progression to invasive mechanical ventilation or death.**
- We retrospectively explore RDV's treatment effect within the dataset as a whole and by defining a new risk profile for disease progression, not solely dependent upon baseline oxygen requirement.

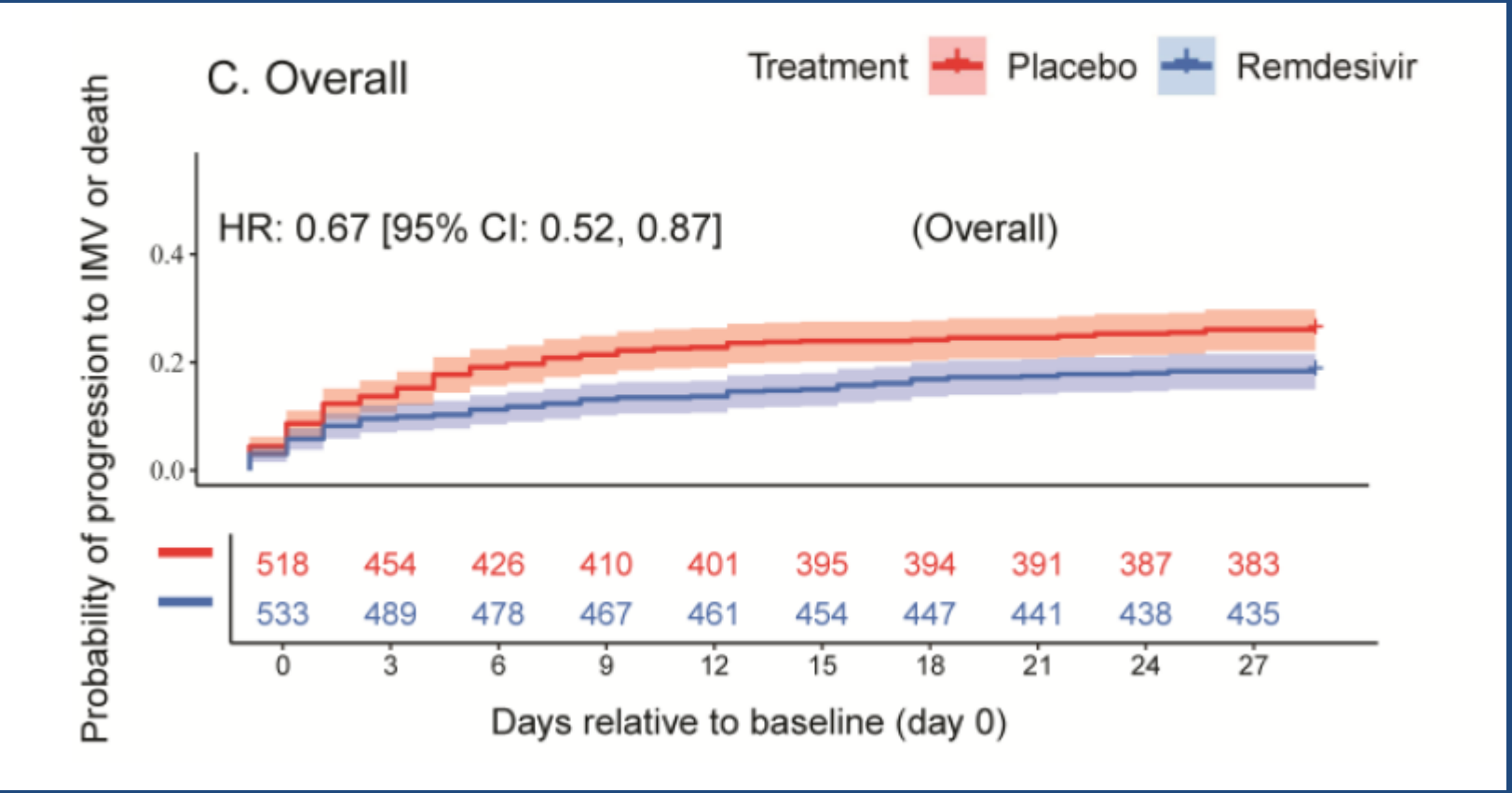
Ordinal scale:
1, not hospitalized and no limitations of activities
2, not hospitalized, with limitation of activities, home oxygen requirement, or both
3, hospitalized, not requiring supplemental oxygen and no longer requiring ongoing medical care
4, hospitalized, not requiring supplemental oxygen but requiring ongoing medical care
5, hospitalized, requiring any supplemental oxygen
6, hospitalized, requiring noninvasive ventilation or use of high-flow oxygen devices
7, hospitalized, receiving invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO)
8, death.

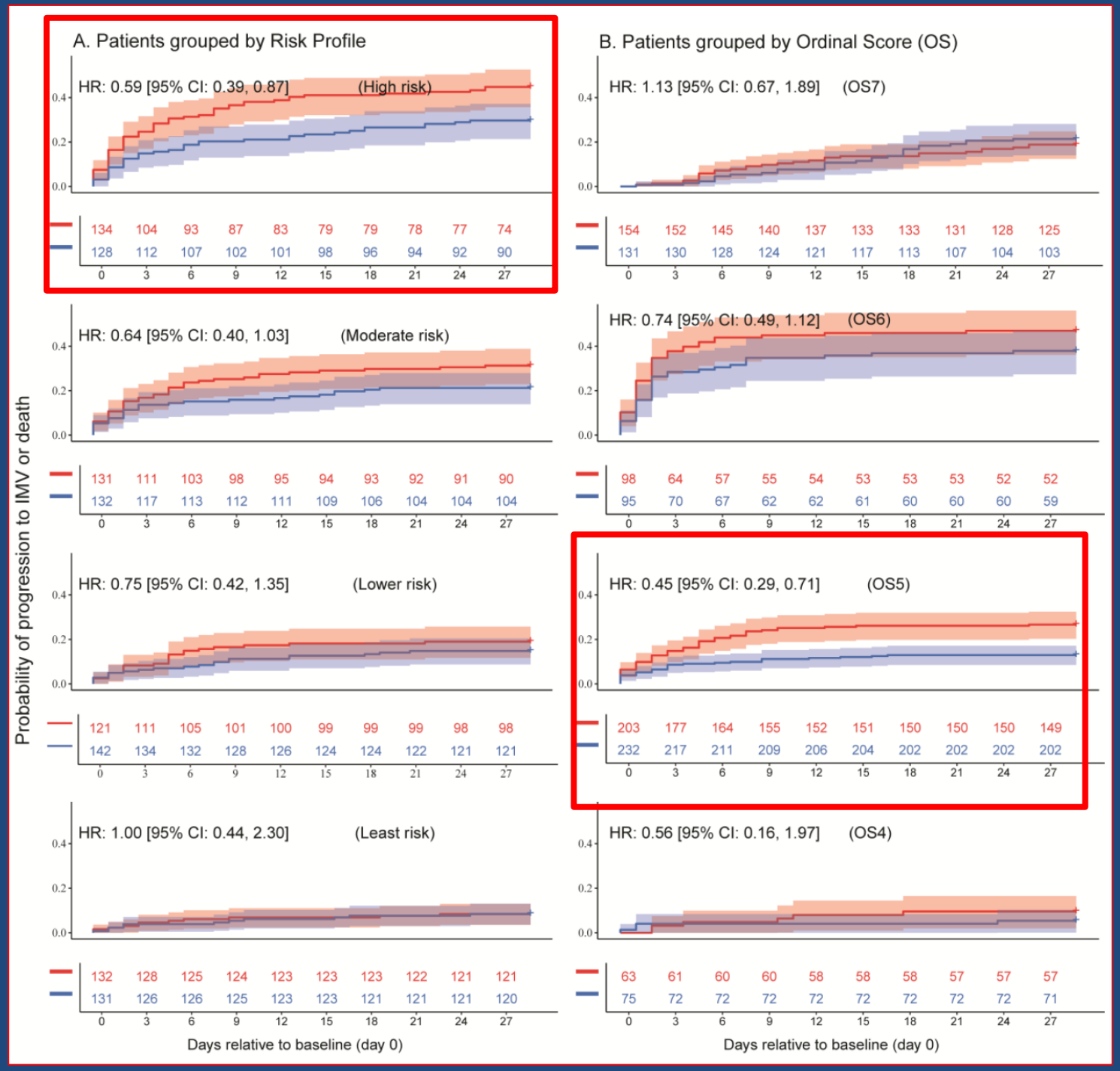
- The risk profile included 4 baseline variables: (1) platelet count, (2) absolute lymphocyte count (ALC), (3) absolute neutrophil count (ANC) and (4) oxygen requirement.
- Independently, lower platelet count, lower ALC, and higher ANC were associated with greater risk of progression to IMV or death

Each risk quartile included participants with a range of baseline oxygen requirements

Variable	Risk Profile : High Risk (N=262)	Risk Profile: Moderate Risk (N=263)	Risk Profile: Lower Risk (N=263)	Risk Profile: Least Risk (N=263)	OS7 (N=285)	OS6 (N=193)	OS5 (N = 435)	OS4 (N=138)
Progression to IMV or death--n (% events per group)	98 (37.4 %)	69 (26.2%)	44 (16.7%)	22 (8.3%)	57 (20.0%)	82 (42.5%)	84 (19.3%)	10 (7.2%)
Death--n (% all deaths)	62 (45.6 %)	37 (27.2%)	22 (16.2%)	15 (11%)	57 (41.9%)	39 (28.7%)	34 (25%)	6 (4.4%)
Recovery --n (% all recoveries)	145 (19.3 %)	180 (24%)	200 (26.6%)	226 (30.1%)	140 (18.6%)	118 (15.7%)	362 (48.2%)	131 (17.4%)
Baseline Oxygen Requirement n OS7;OS6;OS5;OS4 (%)	89;49;100;24 (34.0, 18.7, 38.2, 9.2)%	73;56;102;32 (27.8, 21.3, 38.8, 12.2)%	67;48;105;43 (25.5, 18.3, 39.9, 16.3)%	56;40;128; 39 (21.3, 15.2, 48.7, 14.8)%	-	-	-	-
ANC--median (25th,75th percentile)	8.1 (6-10.9)	5.5 (4.1-7.4)	4.8 (3.5-6)	3.5 (2.5-4.8)	7.1 (5.1-9.7)	5.7 (3.7-8)	4.5 (3.3-6.3)	3.7 (2.5-4.9)
ALC--median (25th,75th percentile)	0.6 (0.4-0.8)	0.9 (0.7-1.1)	1.1 (0.9-1.3)	1.4 (1.1-1.8)	0.9 (0.6-1.2)	0.8 (0.6-1.2)	1.0 (0.8-1.4)	1.0 (0.8-1.4)
Platelets--median (25th,75th percentile)	192.5 (152.2 - 251.0)	215.0 (159.5-274.0)	226.0 (171.0-283.5.0)	254.0 (194.0-352.0)	235.0 (181.0-295.0)	229.0 (173.0-294.0)	218.0 (166.5-283.0)	183.0 (142.2-260.6)

Treatment with RDV was associated with fewer progressions to IMV or death across the entire cohort





This post-hoc analysis suggests that baseline oxygen requirements may be too blunt of an instrument to assess an individual's risk of progression to IMV or death and response to RDV treatment.

Including other patient-specific variables may be a better metric for RDV use.

Ann Intern Med. doi:10.7326/M21-0653

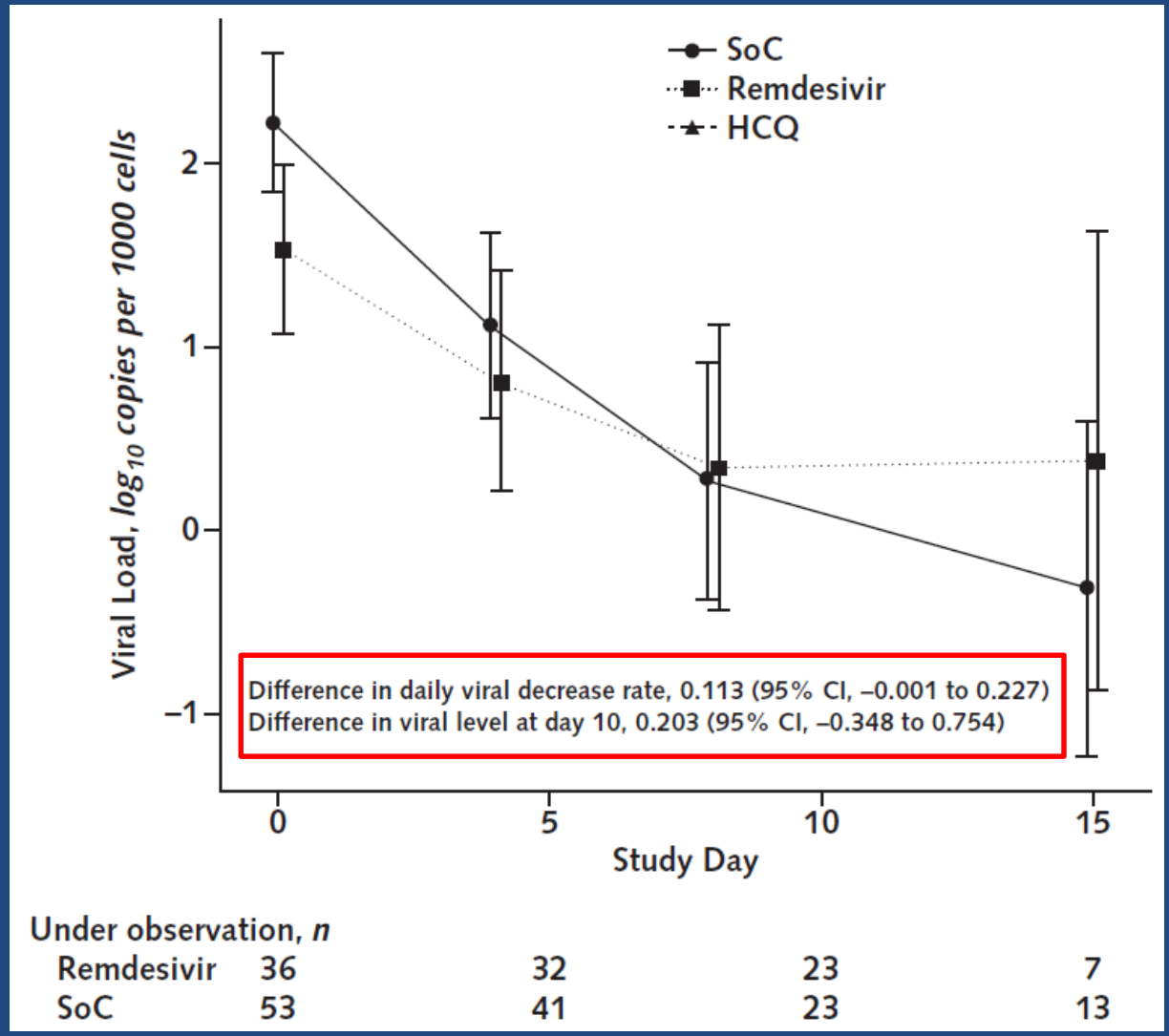
This article was published at Annals.org on 13 July 2021.

Annals of Internal Medicine ORIGINAL RESEARCH

Evaluation of the Effects of Remdesivir and Hydroxychloroquine on Viral Clearance in COVID-19

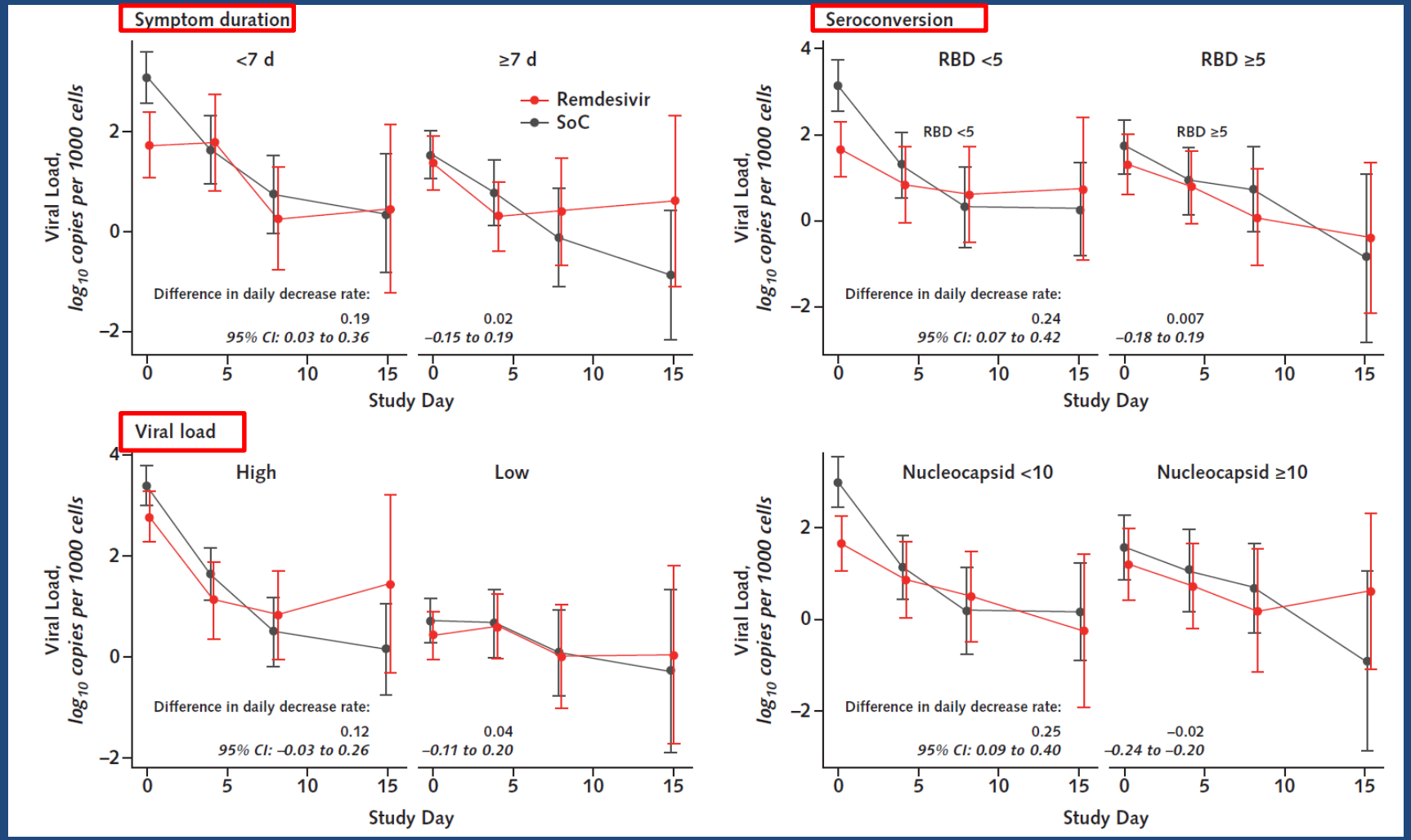
A Randomized Trial

- **The WHO Solidarity trial showed no effect of remdesivir or hydroxychloroquine on mortality, but the antiviral effects of these drugs are not known.**
- NOR-Solidarity is an independent, add-on, randomized controlled trial to the WHO Solidarity trial that included biobanking and 3 months of clinical follow-up (ClinicalTrials. gov: NCT04321616)
- Between 28 March and 4 October 2020, a total of 185 patients were randomly assigned and 181 were included in the full analysis set in 23 hospitals in Norway.
- Patients received remdesivir (n= 42), HCQ (n = 52), or standard of care (SoC) (n = 87).



The findings question the antiviral potential of these drugs in hospitalized patients with COVID-19.

Viral load is given as the log value in 1000 cells. Viral clearance is expressed as an average decrease rate during the first week after randomization. Treatment effects are given as estimated differences in daily viral decrease rates between the remdesivir or HCQ group and its respective SoC during the first week, and in differences in viral load at day 10.



- The effect of remdesivir on viral load would be dependent on symptom duration before hospitalization (≥7 vs. <7 days), the presence of SARS-CoV-2 antibodies, or high or low viral load at hospital admission.
- **In these subgroup analyses, remdesivir did not exert any increased oropharyngeal viral clearance compared with SoC**

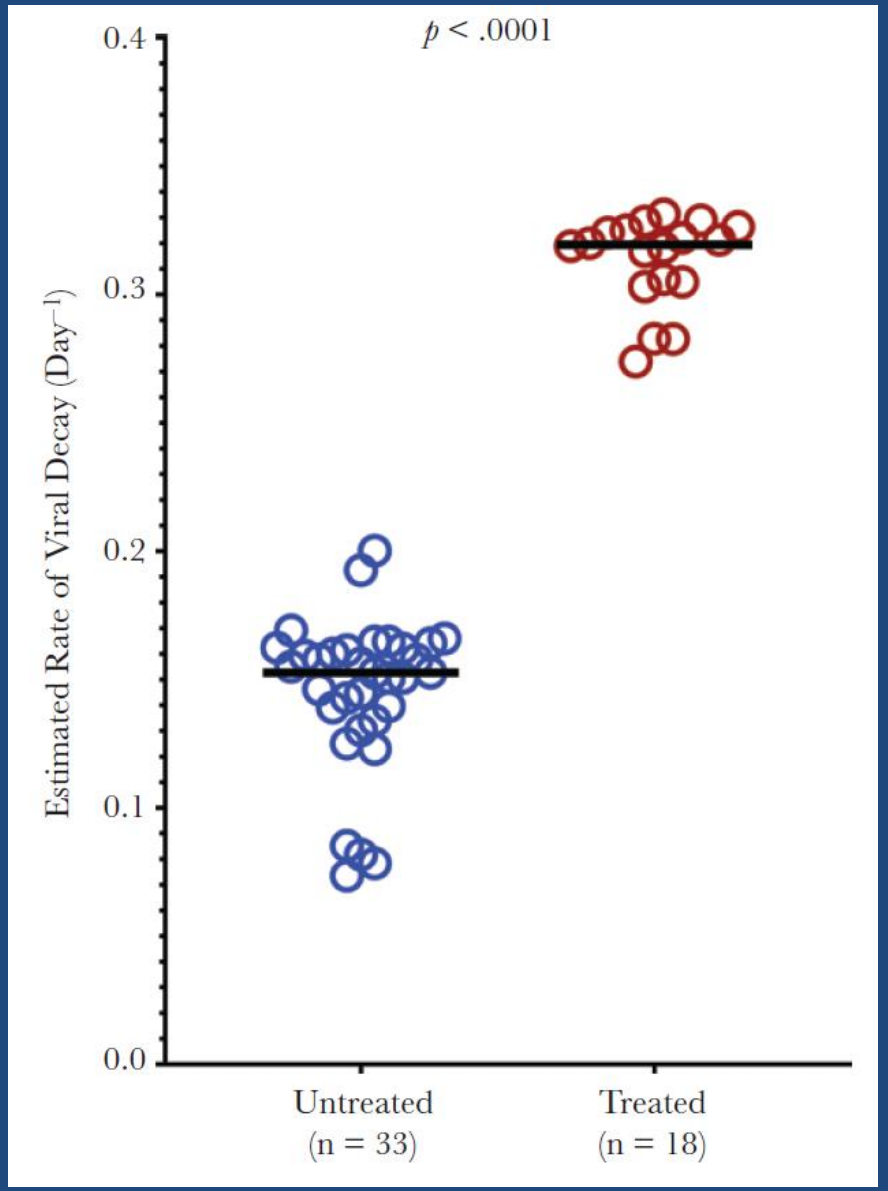
Open Forum Infect Dis. 2021; 8(8):ofab153.

Open Forum Infectious Diseases

BRIEF REPORT

Viral Load Kinetics of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospitalized Individuals With Coronavirus Disease 2019

In this model, we found higher median viral decay rates in remdesivir-treated participants (untreated vs treated: r = 0.15 vs 0.31, P < .0001)



Clin Infect Dis. 2021 Aug 19: ciab698 Online ahead of print

Remdesivir and Mortality in Patients with COVID-19

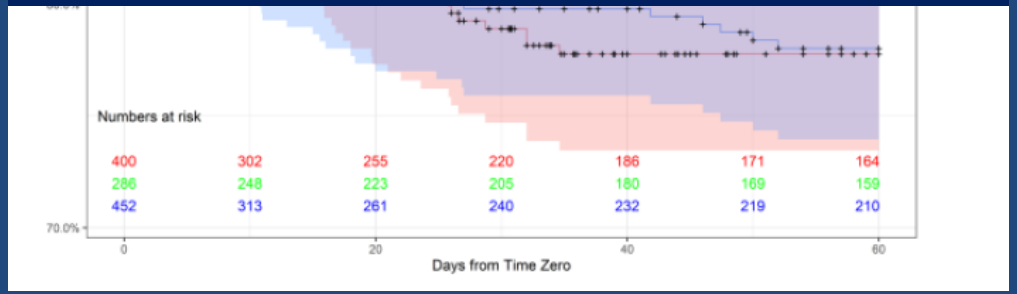
The impact of remdesivir (RDV) on COVID-19 mortality is controversial, and the mortality effect in sub-groups of baseline disease severity has been incompletely explored.

30-day survival: 89.8% (RDV), 78.9% (HCQ), 79.8% (BSC)
60-day survival: 87.3% (RDV), 77.8% (HCQ), 78.0% (BSC)

- Providence St. Joseph Health consists of 51 hospitals
- 2020/2/28—2020/5/29
- COVID-19 pneumonia, and hypoxia requiring supplemental oxygen or SpO2 ≤ 94% on room air.
- 1,138 patients were enrolled including 286 who received RDV, and 852 treated with best supportive care (BSC), 400 of whom received hydroxychloroquine.
- Corticosteroids were used in 20.4% of the cohort (12.6% in RDV and 23% in BSC).
- 30-day mortality: 16.0 %
- **Duration of symptoms before treatment initiation was not assessed**

In persons receiving RDV compared to those receiving BSC the HR (95%CI) for death was 0.60 (0.40–0.90) in the risk-adjusted model, p=0.014.

In the sub-group of persons with baseline use of low-flow oxygen, the HR (95%CI) for death in RDV compared to BSC was 0.63 (0.39 – 1.00), p=0.049.



Open Forum Infect Dis. 2021; 8(7):ofab278

Open Forum Infectious Diseases

MAJOR ARTICLE

Remdesivir Versus Standard-of-Care for Severe Coronavirus Disease 2019 Infection: An Analysis of 28-Day Mortality

remdesivir cohort

The prospective Study 5773 (Clinical trial: NCT04292899/GS-US-540-5773) is a phase 3, randomized, open-label study conducted at 55 sites in the United States, Europe, and Asia (March 6, 2020 to April 27, 2020).

nonremdesivir cohort

The retrospective Study 5807 (Clinical trial: EUPAS34303/GS-US-540-5807) was a real-world longitudinal cohort study conducted at 32 sites in the United States, Europe, and Asia (February 6, 2020 to May 15, 2020).

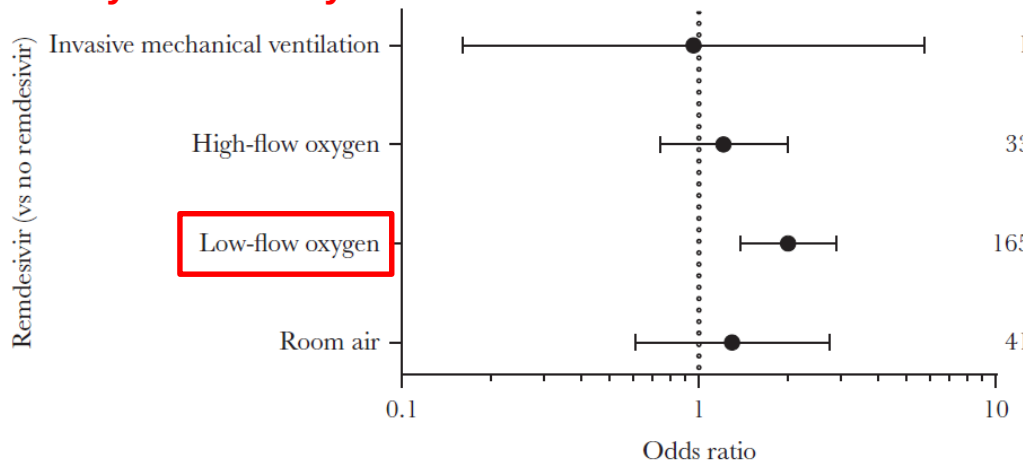
- Both studies enrolled severe COVID-19: patients had oxygen saturation ≤94% on room air or required supplemental oxygen and with radiographically confirmed pulmonary infiltrates.
- Propensity score matching (up to 1:10 ratio) was used to ensure comparable populations

Table 2. Baseline Factors Included in the Propensity Score Model[a]

Duration of symptoms before baseline
Clinical status using the 7-point ordinal scale score
Age (<40 years, 40–64 years, and ≥65 years)
Sex
Race (Asian, black, other, and white)
Country of enrollment (Italy, Spain, United States, other)
Obesity
Comorbidities (hypertension, cardiovascular disease, diabetes mellitus, COPD, asthma)
Investigational COVID-19 medications at the time of study design (azithromycin, biologics, HIV protease inhibitors, hydroxychloroquine, ribavirin[b]) taken at/before baseline

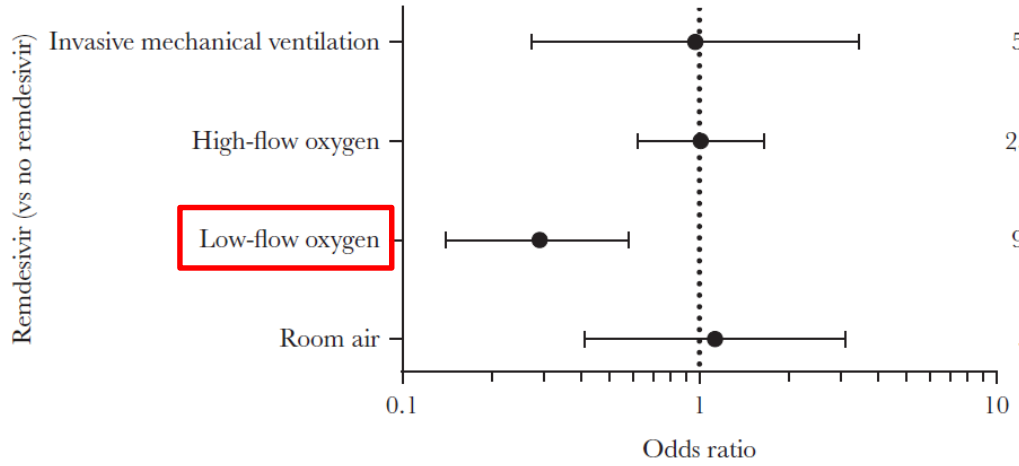
- A total of 368 (remdesivir) and 1399 (nonremdesivir) patients were included in the matched analysis.
- The day 14 clinical recovery rate was significantly higher among the remdesivir versus the nonremdesivir cohort (65.2% vs 57.1%; odds ratio [OR], 1.49; 95% confidence interval [CI], 1.16–1.90; P = 0.002).
- The day 28 mortality rate was significantly lower in the remdesivir cohort versus the nonremdesivir cohort (12.0% vs 16.2%; OR, 0.67; 95% CI, 0.47–.95; P = .03).

A **day 14 recovery**



	Remdesivir *n*/*N* (%)	Nonremdesivir *n*/*N* (%)	Odds ratio of recovery (95% CI)	*P* value
Invasive mechanical ventilation	1/12 (8.3)	9/48 (18.2)	0.96 (0.16–5.76)	*P* = .96
High-flow oxygen	33/94 (35.1)	110/351 (31.4)	1.21 (0.74–1.99)	*P* = .45
Low-flow oxygen	165/210 (78.6)	527/803 (65.7)	2.00 (1.38–2.90)	*P* = .0002
Room air	41/52 (78.9)	151/196 (77.1)	1.29 (0.61–2.75)	*P* = .50

B **day 28 all-cause mortality**



	Remdesivir *n*/*N* (%)	Nonremdesivir *n*/*N* (%)	Odds ratio of death (95% CI)	*P* value
Invasive mechanical ventilation	5/12 (41.7)	16/48 (33.5)	0.97 (0.27–3.44)	*P* = .96
High-flow oxygen	25/94 (26.6)	98/351 (28.0)	1.01 (0.62–1.65)	*P* = .96
Low-flow oxygen	9/210 (4.3)	101/803 (12.5)	0.29 (0.14–0.58)	*P* = .0005
Room air	5/52 (9.6)	11/197 (5.5)	1.13 (0.41–3.09)	*P* = .82

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Pre-Hospital Administration of Remdesivir during a SARS-CoV-2 Outbreak in a Skilled Nursing Facility

This off-label use was undertaken in the context of a large-scale outbreak in a high-prevalence region.

- Idaho State Veteran's Home-Boise is a state-owned, 124-bed SNF
- Beginning on October 31, 2020, all patients with a SARS-CoV-2 diagnosis within the preceding 10 days were offered a 5-day course of remdesivir.
- 54 patients, 9 died (16.6 %)
- 34 patients received remdesivir

		Died (N=9)	Survived (N=45)	Total (N=54)
Category	**Characteristic**	**n (%)**	**n (%)**	**n**
Antiviral Treatment	Received any RDV	5 (55.6)	34 (75.6)	39
	Days on RDV, mean ± SD	1.60 ± 2.07	3.70 ± 2.16	--
	Started RDV within 48hr of diagnosis	1 (11.1)	23 (51.1)	24
	Days from diagnosis to RDV, mean ± SD	4.40 ± 1.95	2.10 ± 2.55	--
	Completed 5-day course of RDV	2 (22.2)	32 (71.1)	34

Table 2: Predictors of Mortality

Category	Variable	p value
Antiviral	Received any RDV	0.2306
Treatment	Started RDV within 48hr of diagnosis	0.0539*
	Completed 5-day course of RDV	**0.0130***,†
	Days on RDV	**0.0160***
Demographics	Age	0.0811*
	BMI	0.2957
	Overweight or Obese BMI	0.2465
	Obese BMI	0.1713*
Concomitant	Dexamethasone	0.1578*
Therapy	Days on Dexamethasone	0.9690
	Apixaban	1.0000
	Baseline Supplemental Oxygen	**0.0397***
Co-existing	Smoking	0.6843
Conditions	Hypertension	0.7335
	Cardiovascular Disease	0.2222
	Respiratory Disease	0.5261
	Cancer	0.4603
	Dementia	0.1578*
	Chronic Kidney Disease	0.8800
	Diabetes mellitus	0.0847*,†

* indicates variable was entered in stepwise logistic regression; † indicates variable was included in final stepwise regression model. The model did not converge for race, BMI category, baseline liver disease, and code status.

Subsequent stepwise logistic regression modeling revealed two variables significantly predictive of survival when independent variables were considered simultaneously: completion of a **5-day remdesivir course (adjusted OR=16.9, 95% CI=2.4, 118.5, p=0.0044)** and **diabetes mellitus (adjusted OR=0.1, 95% CI=0.014, 0.719, p=0.0221),**

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Clinical improvement, outcomes, antiviral activity, and costs associated with early treatment with remdesivir for patients with COVID-19

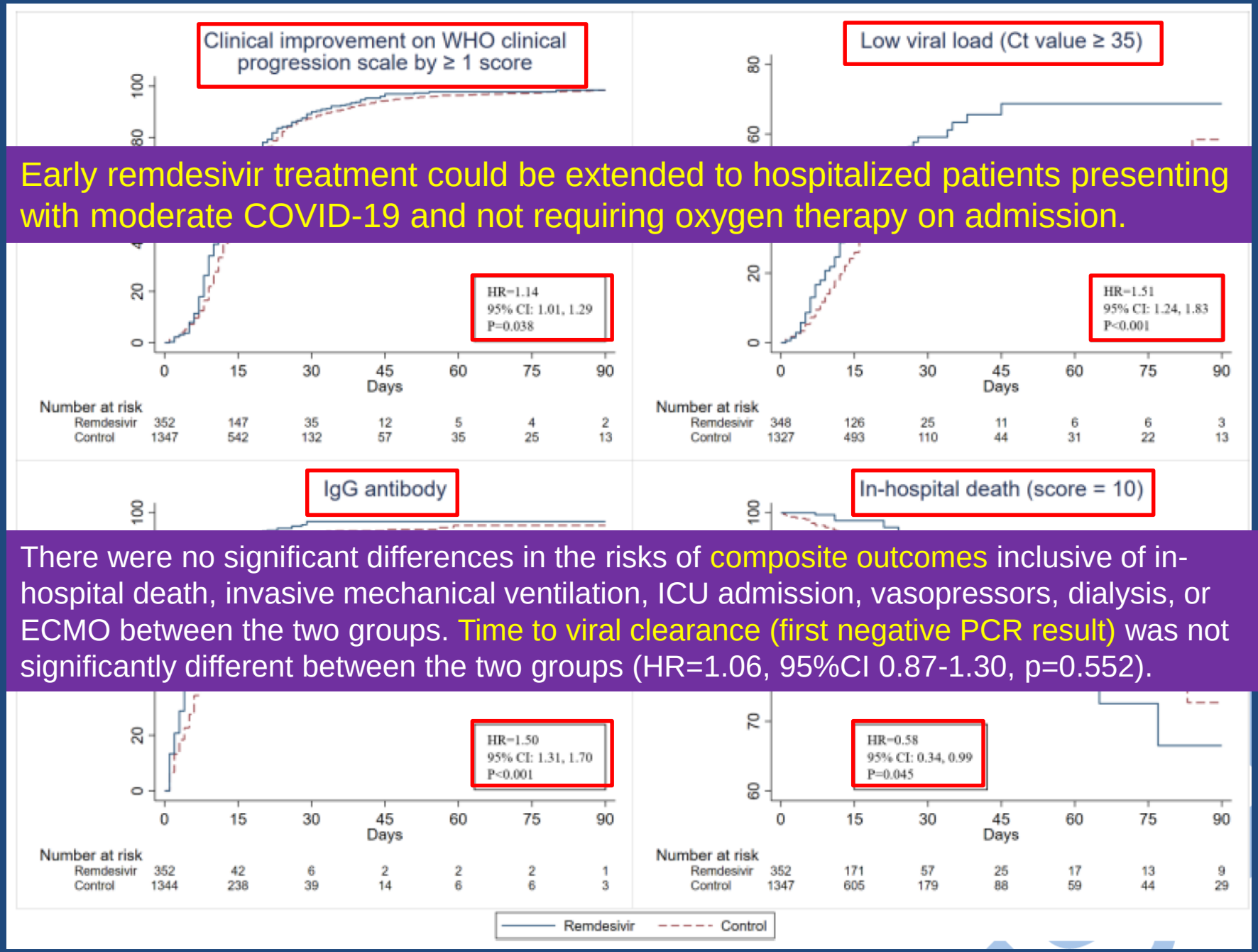
Carlos K.H. Wong[1,2] PhD, Kristy T.K. Lau[1] MSc, Ivan C.H. Au[2] BSc, Xi Xiong[1] MSc, Eric H. Y. Lau[3,4] PhD, Benjamin J. Cowling[3,4] PhD

A territory-wide retrospective cohort of 10,419 patients with COVID-19 hospitalized from 2020/1/21 to 2021/1/31 in Hong Kong

- Early remdesivir users were matched with controls using propensity-score matching in a ratio of up to 1:4.
- Early treatment with remdesivir : **remdesivir within the first 2 days of admission.**
- **411 had received early remdesivir treatment**
- **10,008 patients received remdesivir after the first 2 days of admission (n=450) or had not received any remdesivir (n=9,558).**
- **No information about the proportion of steroid use.**

	Remdesivir (n=352)	Control (n=1,347)
No oxygen therapy	279 (79.3%)	1122 (83.3%)
Supplemental oxygen without ventilation	68 (19.3%)	215 (16.0%)
Mechanical ventilation	5 (1.4%)	10 (0.7%)

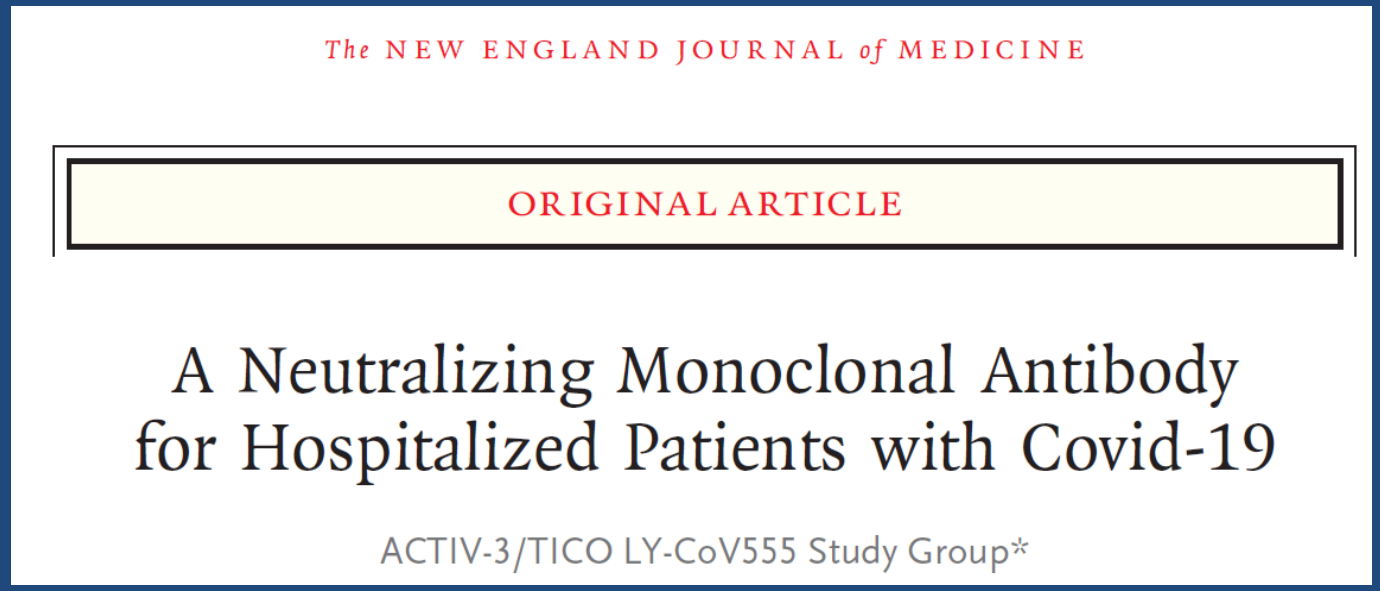
The median duration of remdesivir treatment was 5 days with a cumulative dosage of 600mg



Early remdesivir treatment could be extended to hospitalized patients presenting with moderate COVID-19 and not requiring oxygen therapy on admission.

There were no significant differences in the risks of composite outcomes inclusive of in-hospital death, invasive mechanical ventilation, ICU admission, vasopressors, dialysis, or ECMO between the two groups. Time to viral clearance (first negative PCR result) was not significantly different between the two groups (HR=1.06, 95%CI 0.87-1.30, p=0.552).

N Engl J Med 2021;384:905-14.



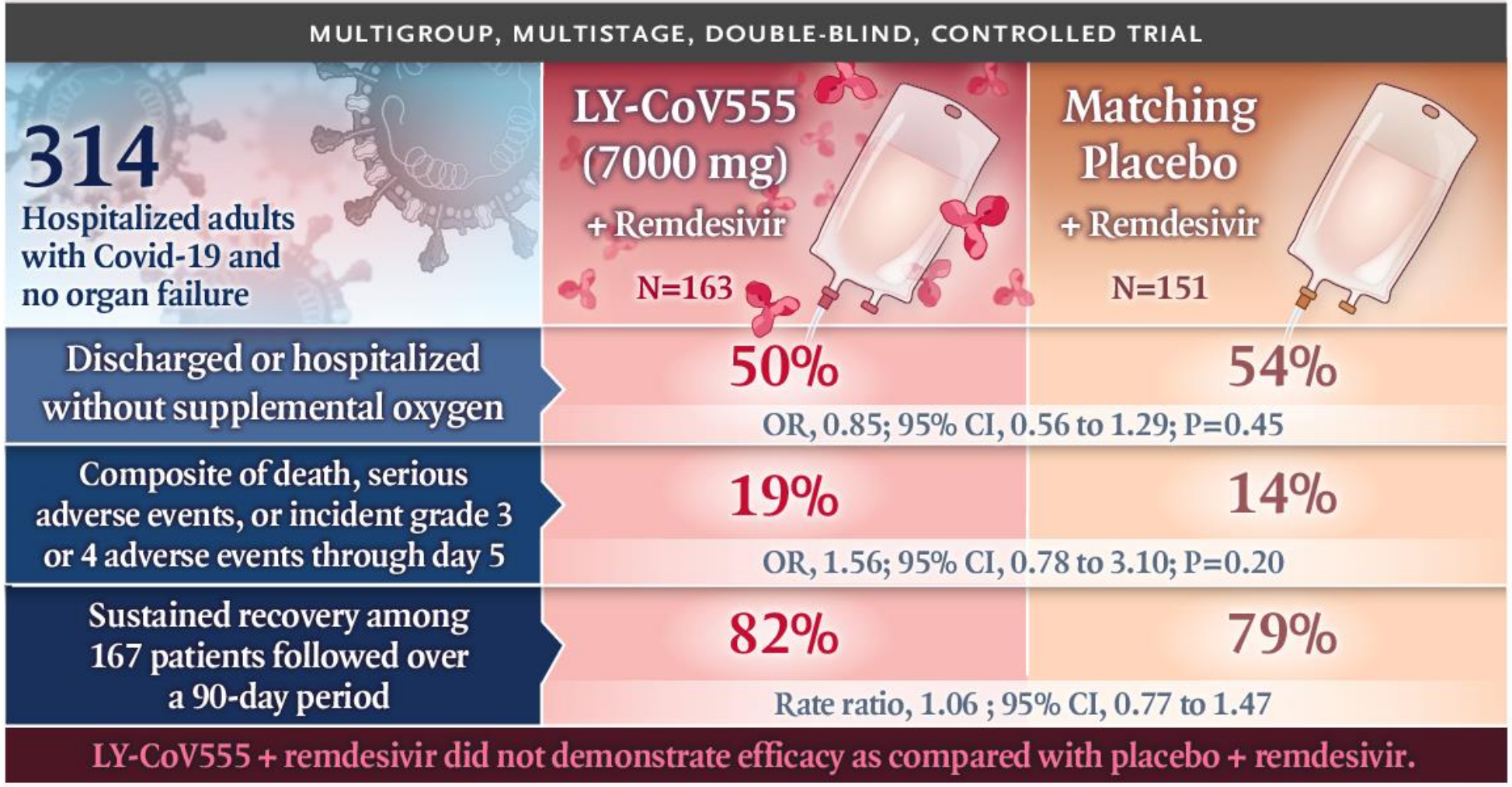
Aim: the possible role of neutralizing monoclonal antibodies and other antiviral interventions in patients who are hospitalized with Covid-19

- **The median interval since the onset of symptoms was 7 days (IQR, 5 to 9).**
- On October 26, 2020, the data and safety monitoring board recommended stopping enrollment for futility after 314 patients (163 in the **bamlanivimab** group and 151 in the placebo group) had undergone randomization and infusion.

- Hospitalized patients who had Covid-19 without end-organ failure was randomized in a 1:1 ratio to receive either **bamlanivimab** or matching placebo.

- **All the patients received high-quality supportive care as background therapy, including the antiviral drug remdesivir and, when indicated, supplemental oxygen and glucocorticoids.**

A total of 298 patients (95%) had begun to receive remdesivir before or on the day of randomization



ACTIV-3/TICO LY-CoV555 Study Group 10.1056/NEJMoa2033130

從最近的觀察性研究的發現

- 是否有其他危險因子(需氧量以外)來決定remdesivir的使用: 越來越多證據顯示氧氣的需求不是唯一標準
- remdesivir是否要更早使用: 盡可能提早使用
- remdesivir和其他藥物併用的效果: 指引支持的常見作法,文獻上也是支持remdesivir盡早使用
- remdesivir是否應根據病毒量來使用: 沒有相關文獻

Thanks For Your Attention