Slide 1

COVID-19: Therapeutic and Vaccine Prospects

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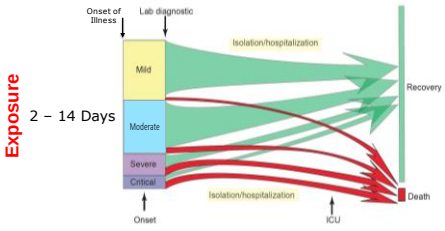
Therapeutics for SARS CoV2

Clinical Course

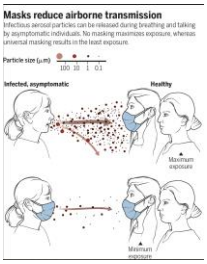


Zunyou Wu, CROI 2020, Boston, March 8 – 11,2020

Aylward B et al, WHO-China Mission, 2020

Determinants of Clinical Course

- Comorbid conditions
  - Age, cardiovascular disease, pulmonary disease, renal dysfunction, liver disease, obesity
- Inoculum size
- Unique aspects of viral pathogenesis



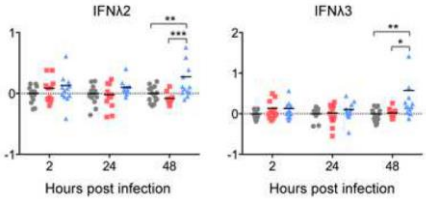
Prather KA, Wang CC, Schooley RT. Reducing transmission of SARS-CoV-2 [published online ahead of print, 2020 May 27]. *Science*. 2020;eabc6197. doi:10.1126/science.abc6197

Masking Rationale

Reduces personal exposure load
Lower likelihood of infection
Less severe infection

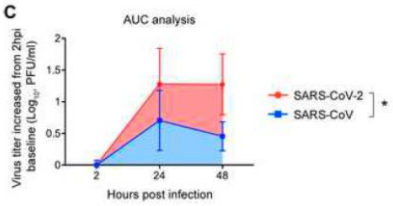
Reduces aerosols in the environment

SARS CoV-2 Evades Innate Immunity



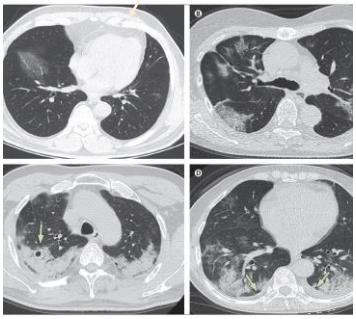
Yuen, Clin Inferct Dis,

SARS CoV-2 Replicates 3.5-fold more Rapidly in Human Lung Explants

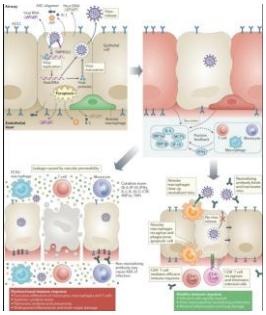


Yuen, Clin Inferct Dis

Chest CT Findings

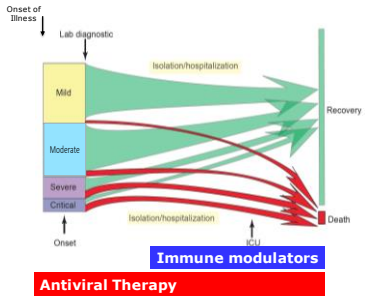


Pathogenesis of SARS CoV-2 Infection



Tay, Nat Med 2020

Treatment of SARS CoV-2 Infection



Immune modulators

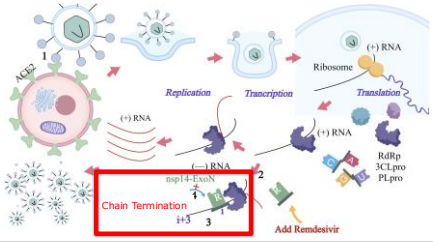
Antiviral Therapy

Zunyou Wu, CROI 2020, Boston, March 8 – 11,2020 Aylward B et al, WHO-China Mission, 2020

Putative Antiviral Agents: An Abbreviated Summary

- X Hydroxychloroquine (with or without azithromycin)
- X Maraviroc
- X Lopinavir-ritonavir
- X Ivermectin
- X Convalescent plasma (clinical trials in progress)
- Neutralizing monoclonals
- Remdesivir

Remdesivir and the SARS-CoV-2 Replicative Cycle



- SARS-CoV-2 enters target cells by binding to the ACE2 receptor on the cell surface
- Releases its RNA, translates RNA-dependent RNA polymerase (RdRp) or RNA replicase
- Remdesivir is an RNA-dependent RNA polymerase inhibitor

Remdesivir

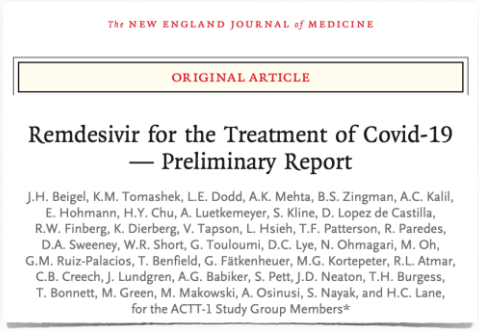
- Remdesivir is a broad acting nucleoside analog RNA polymerase inhibitor
  - EC_{50} of 0.137 – 0.77 µM against SARS-CoV-2 in Vero cells; nanomolar activity in human airway epithelial cells
- RDV has broad spectrum activity against filoviruses (Ebola, Marburg, SARS-CoV, MERS-CoV) and paramyxoviruses (RSV, Nipah, and Hendra)
  - Clinical and virologic efficacy against SARS-CoV-1 and SARS-CoV-2 in mouse and primate models
    - Reduces lung viral loads, lung pathology, and clinical signs of pulmonary dysfunction

De Wit, et al. PNAS 2020; Sheahan et al., Nature Comm 2020; Pizzorno A, et al. (https://www.biorxiv.org/content/10.1101/2020.03.31.017889v1); Williamson BN, et al. (https://www.biorxiv.org/ content/ 10.1101/ 2020.04.15.043166v2); Wang M, et al. *Cell Research* 2020

Remdesivir

- Generally favorable safety profile based on previous studies of > 500 treated pts (healthy volunteers in phase 1 studies and pts with acute Ebola disease)
  - Treatment emergent AEs→ elevations in ALT, AST
- PK profile indicates high and persistent levels of active nucleoside triphosphate metabolites in PBMCs → allows once daily dosing
  - $t_{1/2}$ of active metabolite in PBMCs 32-48h with C_{max} > 10 µM
  - Plasma $t_{1/2}$ 0.66-1h after infusion
- Renally excreted; CYP3A4 inhibitor but significant DDIs unlikely due to rapid clearance after IV administration; no induction of enzymes or transporters

Gilead Investigator's Brochure; 2020



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary 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*

DMID 20-0006: Adaptive COVID-19 Treatment Trial (ACTT-1)

- Study design: Stage 1 adaptive design → randomized, double-blind, placebo-controlled multicenter trial comparing remdesivir (IV) vs placebo
- Inclusion
  - Hospitalized participants confirmed PCR positive for SARS-CoV-2
  - At least **one** of the following:
    - Radiographic infiltrates
    - RA $SpO_2 \leq 94\%$
    - Requiring supplemental oxygen or mechanical ventilation
- Exclusion
  - ALT or AST > 5x ULN; estimated GFR < 30 ml/min; pregnancy or breast feeding; anticipated discharge within 72h

DMID 20-0006 Study Sites and Treatment Regimen

- Multicenter trial conducted at 99 sites
  - United States had 60 trial sites and 13 subsites
  - 8 sites in California
- Enrollment period: 21 Feb to 19 Apr 2020 (58 days)
- Eligible participants were randomized 1:1 to receive:
  - Remdesivir 200mg IV loading dose day 1 then 100mg/d days 2-10
  - Placebo IV days 1-10
- Randomization was stratified by disease severity at time of enrollment

DMID 20-0006: Primary and Secondary Outcomes

Primary Endpoint

- Time to recovery, defined as the first day, during the 28 days after enrollment, on which a patient satisfied categories 1, 2, or 3

Key secondary endpoints

- Mortality at day 14 and day 28
- Safety

Ordinal Scale

1. Not hospitalized, no limitations
2. Not hospitalized, limitation of activities, requiring home O2 or both
3. Hospitalized, not requiring supplemental O2 and no longer requiring ongoing medical care (inpatient for infection control reasons)

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4. Hospitalized, not requiring supplemental O2, requiring ongoing medical care (COVID-19 or otherwise)
5. Hospitalized, supplemental O2
6. Hospitalized, receiving noninvasive ventilation or high-flow O2 devices
7. Hospitalized, receiving invasive mechanical ventilation or ECMO
8. Death

DMID 20-0006 Enrollment

- 1107 participants were screened; 1063 were randomized
- At the time of the analysis (based on data through April 28, 2020), 731 pts had completed the trial, recovered or died
  - 541 pts were randomized to remdesivir
    - 531 received remdesivir as assigned (98.2%); 391 completed followup through day 29 or died
    - **132 had not yet recovered or completed followup**
  - 522 pts were randomized to placebo
    - 518 received placebo as assigned (99.2%); 340 pts completed followup through day 29 or died
    - **169 had not yet recovered or completed followup**

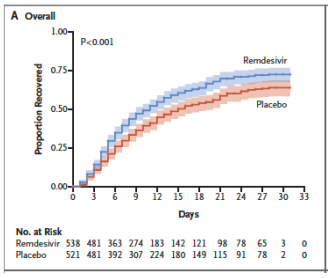
Baseline Characteristics

Table 1. Demographic and Clinical Characteristics at Baseline.*

Characteristic	All (N=1063)	Remdesivir (N=541)	Placebo (N=522)
Age — yr	58.9±15.0	58.6±14.6	59.2±15.4
Male sex — no. (%)	684 (64.3)	352 (65.1)	332 (63.6)
Race or ethnic group — no. (%)†			
American Indian or Alaska Native	7 (0.7)	4 (0.7)	3 (0.6)
Asian	134 (12.6)	77 (14.2)	57 (10.9)
Black or African American	219 (20.6)	108 (20.0)	111 (21.3)
White	565 (53.2)	279 (51.6)	286 (54.8)
Hispanic or Latino — no. (%)	249 (23.4)	132 (24.4)	117 (22.4)
Median time (IQR) from symptom onset to randomization — days‡	9 (6–12)	9 (6–12)	9 (7–13)
No. of coexisting conditions — no. /total no. (%)‡			
None	193/920 (21.0)	91/467 (19.5)	102/453 (22.5)
One	248/920 (27.0)	131/467 (28.1)	117/453 (25.8)
Two or more	479/920 (52.1)	245/467 (52.5)	234/453 (51.7)
Coexisting conditions — no./total no. (%)			
Hypertension	460/928 (49.6)	231/469 (49.3)	229/459 (49.9)
Obesity	342/925 (37.0)	177/469 (37.7)	165/456 (36.2)
Type 2 diabetes	275/927 (29.7)	144/470 (30.6)	131/457 (28.7)
Score on ordinal scale — no. (%)			
4. Hospitalized, not requiring supplemental oxygen, requiring ongoing medical care (Covid-19–related or otherwise)	127 (11.9)	67 (12.4)	60 (11.5)
5. Hospitalized, requiring supplemental oxygen	421 (39.6)	222 (41.0)	199 (38.1)
6. Hospitalized, receiving noninvasive ventilation or high-flow oxygen devices	197 (18.5)	98 (18.1)	99 (19.0)
7. Hospitalized, receiving invasive mechanical ventilation or ECMO	272 (25.6)	125 (23.1)	147 (28.2)
Baseline score missing	46 (4.3)	29 (5.4)	17 (3.3)

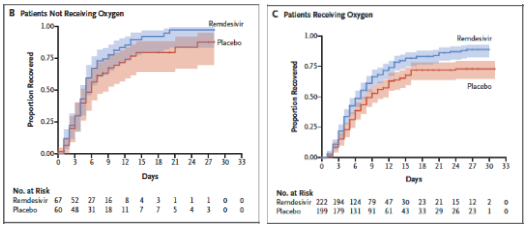
Results: Primary Outcome

- Shorter time to recovery in the remdesivir group vs placebo
  - 11 vs 15 days
  - Rate ratio for recovery 1.32, 95% CI, 1.13 to 1.55; p<0.001
- Outcomes similar for those with a duration of symptoms at time of randomization of ≤ 10 days vs > 10 days



Beigel JH, et al. NEJM 2020

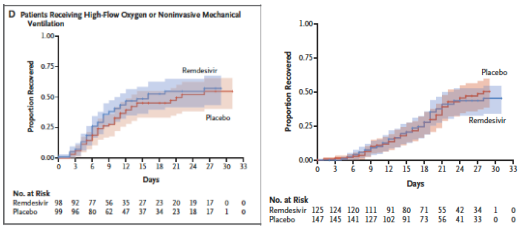
Results: Primary Outcome



Among pts with baseline ordinal score of 4, RR for recovery was 1.38

For pts with baseline ordinal score of 5, RR for recovery was 1.47

Results: Primary Outcome



Among pts with baseline ordinal score of 6, RR for recovery was 1.20

Among pts with baseline ordinal score of 7, RR for recovery was 0.95

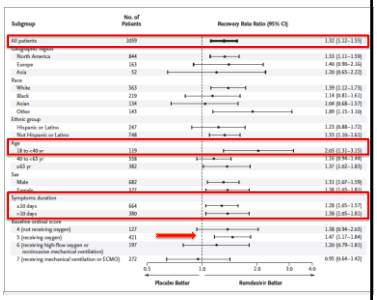
Secondary Outcomes: Mortality and Day 15 Improvement in Ordinal Score

Table 2. Outcomes Overall and According to Score on the Ordinal Scale in the Intention-to-Treat Population.*

	Overall*		Ordinal Score at Baseline							
			4		5		6		7	
	Remdesivir (N=538)	Placebo (N=521)	Remdesivir (N=67)	Placebo (N=60)	Remdesivir (N=222)	Placebo (N=199)	Remdesivir (N=98)	Placebo (N=99)	Remdesivir (N=125)	Placebo (N=147)
Recovery										
No. of recoveries	334	273	61	47	177	128	47	43	45	51
Median time to recovery (95% CI) — days	11 (9–12)	15 (13–19)	5 (4–6)	6 (4–8)	7 (6–8)	9 (7–11)	16 (NE–16)	22 (NE–12)	NE–NE	28 (NE–22)
Rate ratio (95% CI)†	1.32 (1.12–1.55 [P<0.001])		1.38 (0.94–2.03)		1.47 (1.17–1.84)		1.20 (0.79–1.81)		0.95 (0.64–1.42)	
Mortality										
Hazard ratio (95% CI)	0.70 (0.47–1.04)		0.46 (0.04–5.08)		0.22 (0.08–0.58)		1.12 (0.53–2.38)		1.06 (0.59–1.92)	
No. of deaths by day 14	32	54	1	1	4	19	13	13	13	19
Kaplan–Meier estimate — % (95% CI)	7.1 (5.0–9.9)	11.9 (9.2–15.4)	1.5 (0.2–10.1)	2.5 (0.4–16.5)	2.4 (0.9–6.4)	10.9 (7.1–16.7)	15.2 (9.0–25.0)	14.7 (8.7–24.3)	11.3 (6.7–18.8)	14.1 (9.2–21.2)
Ordinal score at day 15 (±2 days) — no. (%)‡										
Patients with baseline and day 15 score data — no.	434	410	60	51	196	161	71	77	101	115
1	99 (22.8)	76 (18.5)	22 (36.7)	15 (29.4)	54 (27.6)	45 (28.0)	13 (18.3)	7 (9.1)	10 (9.9)	8 (7.0)
2	158 (36.4)	127 (31.0)	25 (41.7)	21 (41.2)	95 (48.5)	66 (41.0)	28 (39.4)	27 (35.1)	6 (5.9)	10 (8.7)
3	11 (2.5)	6 (1.5)	7 (11.7)	4 (7.8)	4 (2.0)	2 (1.2)	0	0	0	0
4	23 (5.3)	20 (4.9)	1 (1.7)	3 (5.9)	12 (6.1)	7 (4.3)	4 (5.6)	4 (5.2)	6 (5.9)	6 (5.2)
5	34 (7.8)	40 (9.8)	3 (5.0)	5 (9.8)	14 (7.1)	6 (3.7)	2 (2.8)	7 (9.1)	15 (14.9)	22 (19.1)
6	16 (3.7)	14 (3.4)	1 (1.7)	0 (0)	1 (0.5)	3 (1.9)	6 (8.5)	6 (7.8)	7 (6.9)	5 (4.3)
7	93 (21.4)	93 (22.6)	0 (0)	2 (3.9)	12 (6.1)	12 (7.5)	5 (7.0)	13 (16.9)	43 (42.6)	45 (39.1)
8	33 (7.6)	55 (13.4)	1 (1.7)	1 (2.0)	4 (2.0)	20 (12.4)	13 (18.3)	13 (16.9)	14 (13.9)	19 (16.5)
Odds ratio (95% CI)	1.50 (1.18–1.91 [P=0.001])		1.51 (0.76–3.00)		1.31 (0.89–1.92)		1.60 (0.89–2.86)		1.04 (0.64–1.68)	

Results: Key Subgroup Outcomes

- Recovery rate ratio was improved for remdesivir-treated pts overall and regardless of duration of symptoms prior to randomization
- Except for baseline ordinal score 5 subgroup, 95% CI overlapped for all other subgroups
- Confounding for indication or insufficient statistical power for higher and lower score subgroups?



Beigel JH, et al. NEJM 2020

Safety Outcomes

- Fewer serious adverse events occurred in pts receiving remdesivir compared to placebo (21.1% vs. 27%)
  - Most common SAEs were respiratory failure, hypotension, viral pneumonia, AKI
- Grade 3 or 4 adverse events occurred less frequently in the remdesivir group than placebo (28.8% vs. 33%)
  - Most common AEs were anemia/decreased Hgb, AKI, decreased eGRF/Cr clearance, increased Cr, hyperglycemia, increased aminotransferases
  - DVTs and PEs were relatively uncommon, occurring in 1.4% and 0.6%, respectively
- No deaths were attributed to study medications

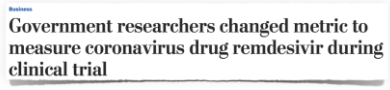
Conclusions

- Remdesivir-treated patients had a significantly shorter time to recovery (11d vs. 15d) compared to placebo
  - The effect was similar regardless of duration of symptoms prior to randomization
- 15d mortality was lower in the remdesivir arm vs. placebo (7.1% vs. 11.9%; HR 0.70; 95% CI 0.47-1.04) but did not reach statistical significance (p=0.07)
- Remdesivir was associated with fewer AEs than placebo

Limitations and Controversies

- Preliminary results; 301 pts had not recovered or completed followup through day 29
  - "To ensure the accuracy of the reported findings, we evaluated the primary outcome, key secondary outcomes, and mortality results based on current data through May 18, 2020. The results were similar to those reported in the Results section of this article."

Limitations and Controversies


Business

Government researchers changed metric to measure coronavirus drug remdesivir during clinical trial

- Original primary outcome/endpoint: "difference in clinical status by day 15 based on 8-category ordinal score"
  - Changed due to observations about the protracted course of COVID-19 disease
  - Change occurred after 72 pts enrolled; not based on interim review of study data
- The original primary outcome was made a key secondary outcome
  - Odds ratio for improvement in clinical status by day 15 based on the 8-point ordinal score was significantly better for remdesivir than placebo

Other Remdesivir Trials

Putting them into context

Remdesivir vs. Placebo in China

- Randomized, double-blind, placebo-controlled multicenter trial
- 237 pts enrolled with 2:1 randomization to remdesivir vs placebo
- Terminated early due to predetermined criteria; outbreak was controlled
- Statistically underpowered for the primary endpoint of clinical improvement

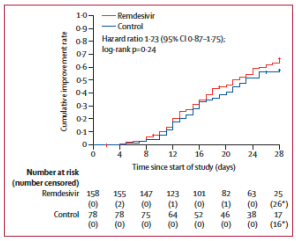
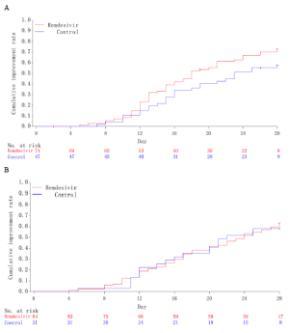


Figure 2: Time to clinical improvement in the intention-to-treat population

Wang Y, et al. Lancet 2020

Remdesivir vs. Placebo in China

- Symptoms ≤ 10d → median time to recovery was 18d for remdesivir vs 23d for placebo
  - HR 1.52; 95% CI 0.9 to 2.43
- Symptoms > 10d → median time to recovery was 23d vs 24d
  - HR 1.07; 95% CI 0.63 to 1.83



Wang Y, et al. Lancet 2020

Remdesivir for 5 vs 10 Days Duration for Severe COVID-19

- Randomized, open-label, phase 3 trial in 397 hospitalized pts with SARS-CoV-2 pneumonia, RA O_2 sat ≤ 94%
  - Pts randomized to 10d significantly worse baseline clinical status (p=0.02)
- Clinical improvement of ≥ 2 points on the ordinal scale in 64% in 5d group vs 54% in 10d group (p=0.14)

Goldman JD, et al. NEJM 2020

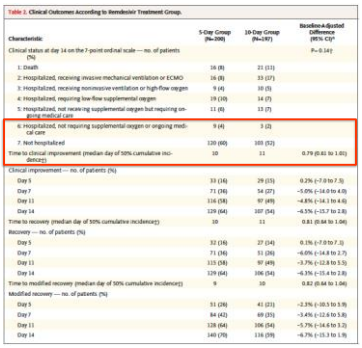


Table 3. Clinical Outcomes According to Remdesivir Treatment Group.

Characteristic	5-Day Group (N=200)	10-Day Group (N=197)	Baseline-Adjusted Difference (95% CI)*
Clinical status at day 14 on the 7-point ordinal scale — no. of patients (%)			P=0.14†
1: Death	16 (8)	21 (11)	
2: Hospitalized, receiving invasive mechanical ventilation or ECMO	16 (8)	33 (17)	
3: Hospitalized, receiving noninvasive ventilation or high-flow oxygen	9 (4)	10 (5)	
4: Hospitalized, requiring low-flow supplemental oxygen	19 (10)	14 (7)	
5: Hospitalized, not receiving supplemental oxygen but requiring ongoing medical care	11 (6)	13 (7)	
6: Hospitalized, not requiring supplemental oxygen or ongoing medical care	9 (4)	3 (2)	
7: Not hospitalized	120 (60)	103 (52)	
Time to clinical improvement (median day of 50% cumulative incidence)	10	11	0.79 (0.61 to 1.01)
Clinical improvement — no. of patients (%)			
Day 5	33 (16)	29 (15)	0.2% (−7.0 to 7.3)
Day 7	71 (36)	54 (27)	−5.0% (−14.0 to 4.0)
Day 11	116 (58)	97 (49)	−4.8% (−14.1 to 4.6)
Day 14	129 (64)	107 (54)	−6.5% (−15.7 to 2.8)
Time to recovery (median day of 50% cumulative incidence)	10	11	0.81 (0.64 to 1.04)
Recovery — no. of patients (%)			
Day 5	32 (16)	27 (14)	0.1% (−7.0 to 7.1)
Day 7	71 (36)	51 (26)	−6.0% (−14.8 to 2.7)
Day 11	115 (58)	97 (49)	−3.7% (−12.8 to 5.5)
Day 14	129 (64)	106 (54)	−6.3% (−15.4 to 2.8)
Time to modified recovery (median day of 50% cumulative incidence)	9	10	0.82 (0.64 to 1.04)
Modified recovery — no. of patients (%)			
Day 5	51 (26)	41 (21)	−2.3% (−10.5 to 5.9)
Day 7	84 (42)	69 (35)	−3.4% (−12.6 to 5.8)
Day 11	128 (64)	106 (54)	−5.7% (−14.6 to 3.2)
Day 14	140 (70)	116 (59)	−6.7% (−15.3 to 1.9)

Putative Immunomodulatory Agents: An Abbreviated Summary

- ✘ IL-6 Blockers
  - Tocilizumab, Sarilumab
- ✘ Janus-Associated Kinase (JAK) Inhibitors
  - Baricitinib, ruxolinitimib
- ✘ Leronlimab
- Corticosteroids
  - dexamethasone

RECOVERY Trial: Dexamethasone Results

- Study Design: Randomized, open-label, adaptive platform trial comparing different possible treatments with "usual care" in hospitalized pts with Covid-19
  - 176 National Health Service hospitals in UK
  - Eligibility: Clinically suspected or lab confirmed SARS-CoV-2 infection
  - Treatment: 2,104 pts randomly allocated to dexamethasone 6 mg/d for up to 10d vs. 4,321 concurrently allocated to usual care
  - Primary endpoint: 28d mortality

medRxiv preprint doi: https://doi.org/10.1101/2020.06.22.20137273; June 22, 2020

RECOVERY: Randomization and Procedures

- 2:1 randomization
- Web-based CRF
  - Entry: demographics, level of respiratory support, major comorbidities, treatment available at each site
  - Single on-line followup form at discharge, death or day 28 (adherence to allocated treatment, receipt of other treatment, duration of adm, respiratory or renal support status, vital status)
  - Primary endpoint → all-cause mortality within 28d
  - Secondary outcomes → time to discharge, receipt of mechanical ventilation, ECMO, duration of ventilation, cause-specific mortality

RECOVERY: Results

- Mean age 66.1 yrs; 36% women
  - DM 24%
  - CVD 27%
  - Chronic lung disease 21%
  - At randomization 56% had ≥ 1 comorbidity; 82% confirmed SARS-CoV-2, 16% on MV/ECMO, 60% on O_2
- Median duration of dexamethasone 6d (7% of the usual care group also received dexamethasone)
  - Few pts in this group received HCQ, LPV/r, IL-6 antagonists or remdesivir (data not available; unclear what proportion of pts in this group received other corticosteroids)

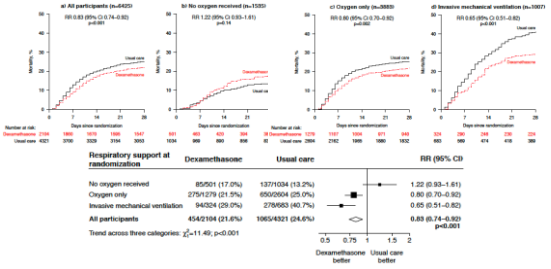
RECOVERY: Primary Outcome Results

- 28d mortality 21.6% in dexamethasone arm vs. 24.6% usual care (RR 0.83; 95% CI, 0.74-0.92; P < 0.001)
- Greatest benefit among those receiving mechanical ventilation at randomization

Table 2: Effect of allocation to dexamethasone on main study outcomes

	Treatment allocation			
	Dexamethasone (n=2104)	Usual care (n=4321)	RR (95% CI)	p-value
Primary outcome:				
28-day mortality	454 (21.6%)	1065 (24.6%)	0.83 (0.74-0.92)	<0.001
Secondary outcomes:				
Discharged from hospital within 28 days	1360 (64.6%)	2639 (61.1%)	1.11 (1.04-1.19)	0.002
Receipt of invasive mechanical ventilation or death*	425/1780 (23.9%)	939/3638 (25.8%)	0.91 (0.82-1.00)	0.049
Invasive mechanical ventilation	92/1780 (5.2%)	258/3638 (7.1%)	0.76 (0.61-0.96)	0.021
Death	360/1780 (20.2%)	787/3638 (21.6%)	0.91 (0.82-1.01)	0.07

RECOVERY: Results by Subgroup



Dexamethasone reduced 28d mortality by ~33% in those on MV; ~20% for those on O_2 without MV; benefit primarily observed in pts more than 7d after symptom onset; no benefit and possible harm in those not receiving O_2

28-Day Mortality: ACTT-1 vs RECOVERY

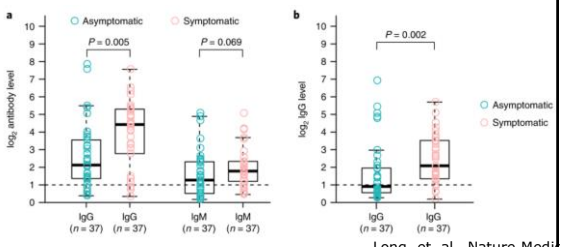
	ACTT-1 RDV	ACTT-1 Placebo	RECOVERY Control	RECOVERY Dex
No oxygen requirement (ordinal score 4)	4.6%	5.6%	10%	13%
			mortality rate ratio 1.22 [0.86 , 1.75]; p=0.14	
Oxygen requirement (ordinal score 4)	4.3%	13.0%	25%	20%
			mortality rate ratio 0.80 [0.67,0.96]; p=0.0021	
High Flow Oxygen (ordinal score 6)	23.3%	22.2%		
Vent or ECMO	22.7%	20.3%	41%	27%
			mortality rate ratio 0.65 [0.48, 0.88]; p=0.0003	
Overall	12.0	15.2		
Mortality ratio	0.79		0.83	

Vaccines for SARS CoV-2

Vaccines: Opportunities and Challenges

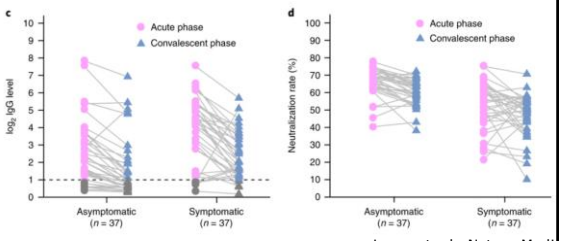
- Multiple vaccine platforms
  - Protein, mRNA, DNA, chimeric viruses, attenuated viruses, non-replicating viral vectors
- Clear demonstration of immunogenicity in man in Phase 2 studies
- Challenges:
  - What are the correlates of immunity?
  - Will vaccines induce durable immunity?
  - Will they be immunogenic in the most vulnerable populations

Symptomatic People Make More Vigorous Immune Responses



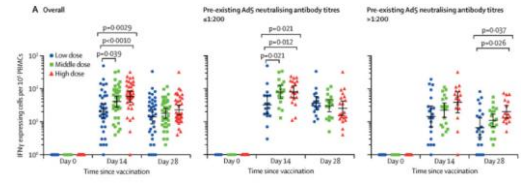
Long, et. al., Nature Medic

Coronavirus Immunity is Fleeting



Long, et. al., Nature Medic

Coronavirus Vaccine Immunity is Also Fleeting



Zhu, et. al. Lancet VOLUME 395, ISSUE 10240, P18

Conclusions

- Remdesivir is effective in reducing time to recovery and improving survival in select subgroups and should be considered in those with moderate to severe Covid-19 ($SpO_2 \leq 94\%$ on RA or requiring oxygen)
- Dexamethasone appears to improve survival for those with severe Covid-19 disease (mechanical ventilation or requiring O_2)
- Multiple vaccines are under active development
  - As in HIV-1, the pathway to an effective coronavirus vaccine is highly likely to be a long and winding road

Slide 48

Thank You!