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AASLD COVID-19 Working Group Presents

Clinical Insights: COVID-19 and the Liver – Case Studies and Updates

April 16, 2020
5-6 pm ET

Presenters:
Ryan M. Kwok, MD
Michael L. Schilsky, MD, FAASLD

Moderator:
Elizabeth C. Verna, MD, MS

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NEW: Includes Spanish and Portuguese versions of the Clinical Insights documents

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Released Today: Clinical Best Practice Advice for Hepatology and Liver Transplant Providers During the COVID-19 Pandemic: AASLD Expert Panel Consensus Statement

Now available online via *HEPATOLOGY*: view the AASLD expert panel consensus statement regarding clinical best practice advice for providers during the COVID-19 pandemic.

This document provides data on what is currently known about COVID-19, and how it may impact hepatologists and liver transplant providers and their patients. The aim is to provide a template for the development of clinical recommendations and policies to mitigate the impact of the COVID-19 pandemic on liver patients and healthcare providers.

For resources and updates on COVID-19 and the liver, visit aasld.org/COVID19

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Upcoming COVID-19 Webinar

Thursday, April 30, 2020

5-6pm Eastern

Clinical Insights: COVID-19 and the Liver – Case Studies and Updates

Registration Now Open: http://www.aasld.org/COVID19

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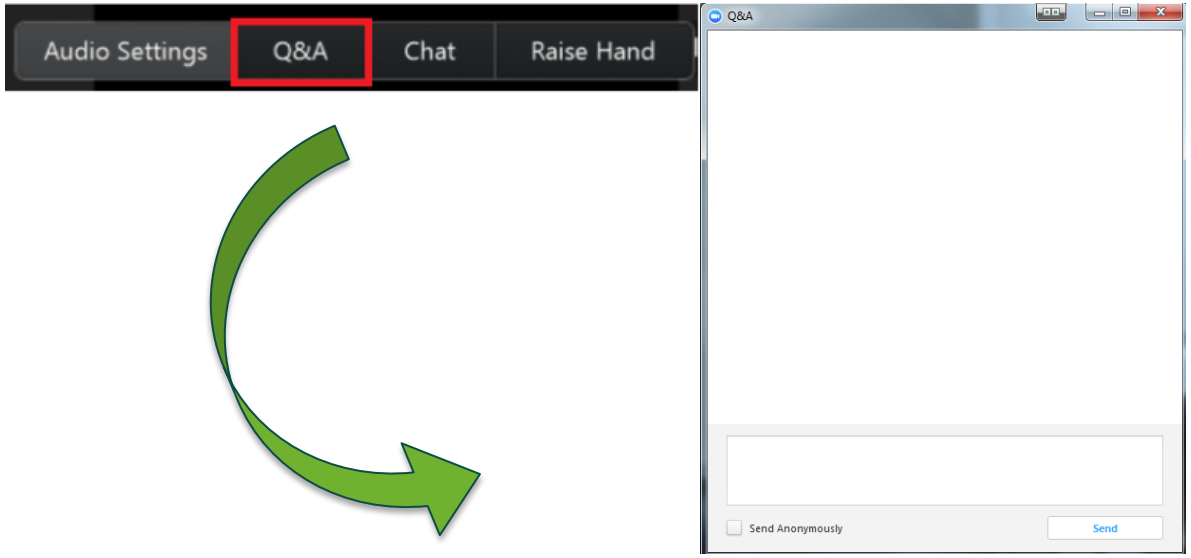
Clinical Insights: COVID-19 and the Liver

Case Studies and Updates

Webinar Series

Updates April 16, 2020

Submit your questions in the Q&A box at the top or bottom of your screen.



Questions will be answered at the end of the presentation.

Moderator

Elizabeth C. Verna, MD, MS

Columbia University Medical Center

Presenters

Oren K. Fix, MD, MSc, FAASLD

Swedish Medical Center

Ryan Kwok, MD, FACP

AASLD COVID-19 Working Group

Michael L. Schilsky, MD, FAASLD

Yale

New-Haven Hospital

Panelists

- **Kimberly Ann Brown, MD, FAASLD**
  Henry Ford Health System
- **Jaime Chu, MD**
  Icahn School of Medicine at Mount Sinai
- **Raymond T. Chung, MD, FAASLD**
  Massachusetts General Hospital
- **Oren K. Fix, MD, MSc, FAASLD**
  Swedish Medical Center
- **Patricia Harren, DNP**
  Columbia University Medical Center
- **Laura M. Kulik, MD**
  Northwestern University Feinberg School of Medicine
- **Brendan M. McGuire, MD**
  University of Alabama at Birmingham

AASLD COVID-19 Working Group

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Robert J. Fontana, MD, FAASLD	University of Michigan Hospitals and Health
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Elizabeth C. Verna, MD, MS	Columbia University Medical Center
Jorge A. Bezerra, MD, FAASLD	Cincinnati Children's Hospital Medical Center
Raymond T. Chung, MD, FAASLD	Massachusetts General Hospital

- Welcome and Introduction
  - Elizabeth Verna, MD
- Clinical Insights Updates
  - Oren K. Fix, MD, MSc, FAASLD
- Rapid Fire Journal Club
  - Ryan Kwok, MD
- Discussion of Audience Cases
  - Michael Schilsky, MD, FAASLD
- Q&A
- Closing

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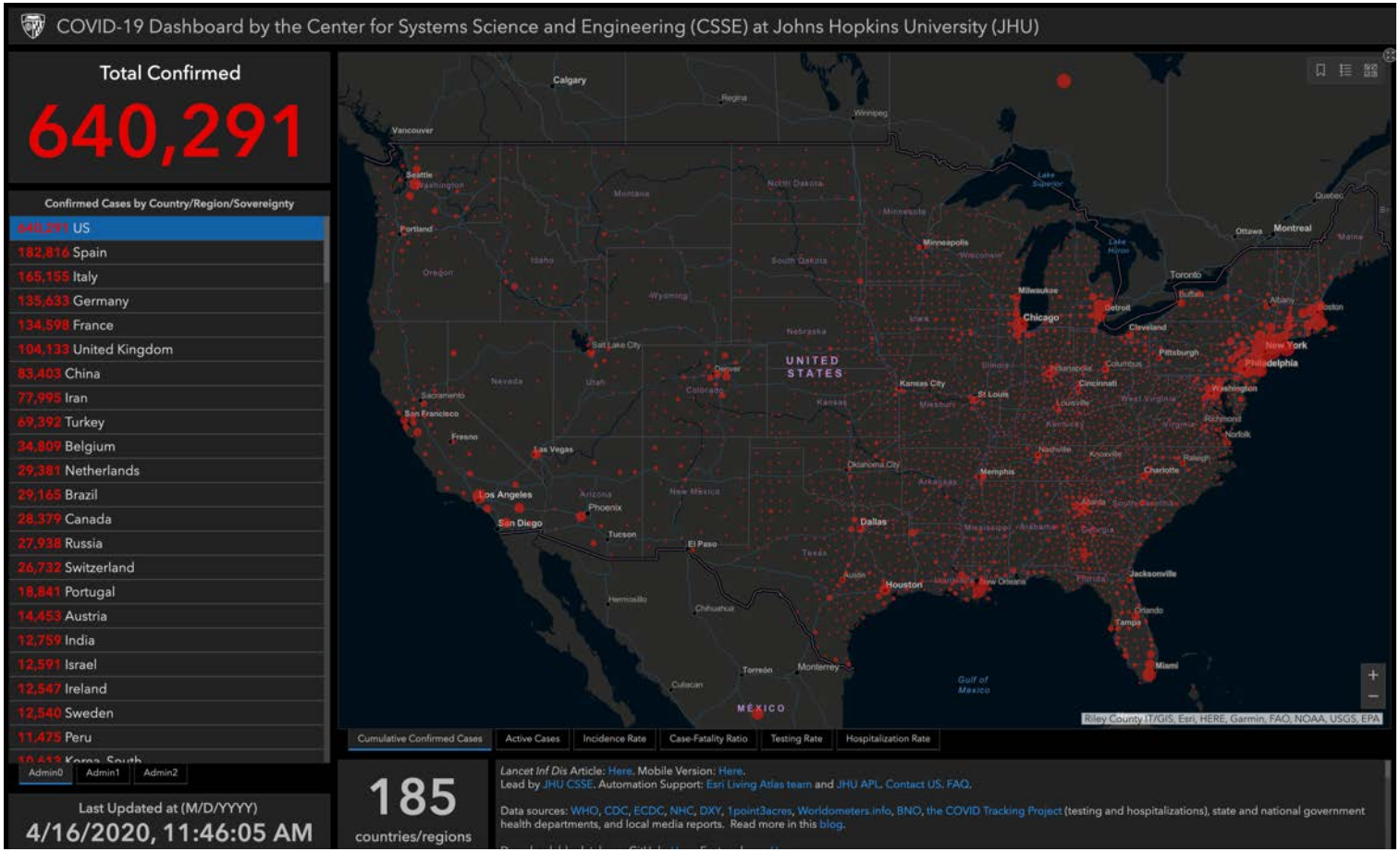
Introduction

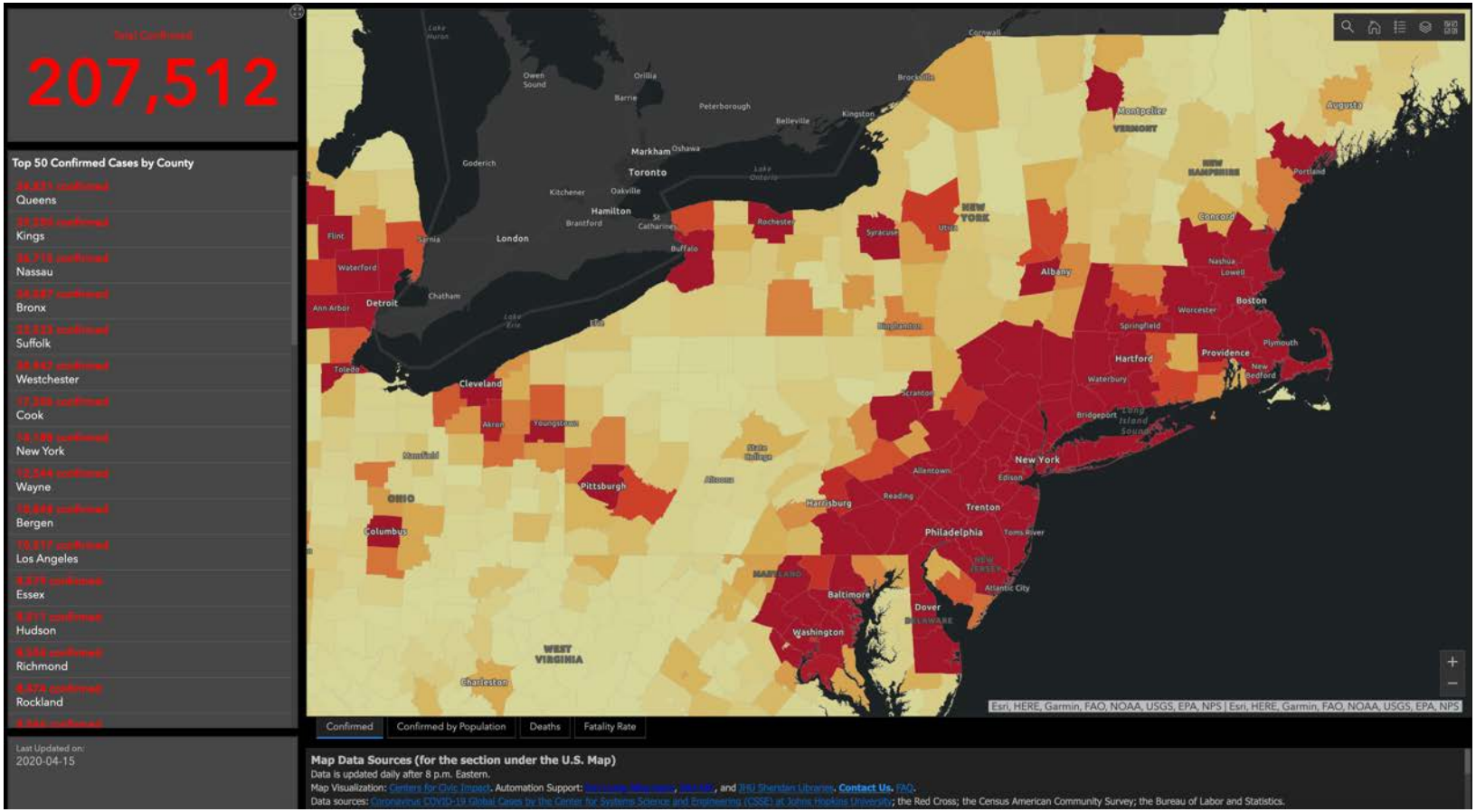
Elizabeth C. Verna, MD, MS
Associate Professor of Medicine
Columbia University Medical Center

Tracking the Spread of SARS-CoV-2 Across the US



https://coronavirus.jhu.edu/us-map
Accessed 4/16/2020

SARS-CoV-2 in New York State



https://coronavirus.jhu.edu/us-map
Accessed 4/16/2020

COVID-19 Among SOT at NYP

- As of 4/15/20, >150 SOT recipients with confirmed SARS-CoV2 at NYP
- 90 patients analyzed in detail
- Categorized by disease severity
  - Mild: outpatient
  - Moderate: general medical floor
  - Severe: mechanical ventilation, ICU admission, death

Pereira MP et al, Submitted

Patient Characteristics

	All (n=90)	Mild/Moderate Disease (n=68)	Severe Disease (n=22)	p-value
Age in years, median (IQR)	57 (46-68)	54.5 (39.5-64.5)	68 (56-74)	0.002
Male sex (%)	53 (59)	40 (59)	13 (59)	0.85
Organ Transplant (%)				0.68
Kidney	46 (51)	36 (53)	10 (48)	
Lung	17 (19)	12 (18)	5 (23)	
Liver	13 (14)	10 (15)	3 (14)	
Heart	9 (10)	6 (9)	3 (14)	
Dual-organ	5 (5)	4 (5)	1 (5)	
Years from transplant to diagnosis, median (IQR)	6.64 (2.87-10.61)	5.81 (2.85-11.01)	7.06 (2.87-10.02)	0.97
Within 1 month of txp (%)	3 (3)	2 (3)	1 (5)	0.72
Within 1 year of txp (%)	13 (14)	9 (13)	4 (18)	0.57
Comorbidities (%)				
HTN	58 (64)	39 (57)	19 (86)	0.02
DM	41 (46)	29 (43)	12 (55)	0.36
Chronic lung disease	17 (19)	11 (16)	6 (27)	0.28
Active cancer	3 (3)	0 (0)	3 (14)	0.002

Pereira MP et al, Submitted

Initial Hemodynamic and Laboratory Values among *Hospitalized Patients* with COVID-19

	All (n=65)	Moderate Disease (n=43)	Severe Disease (n=22)
Changes in IS (%)			
Decrease/hold antimetabolite	41/46 (89)	28/33 (85)	13/13 (100)
Decrease hold steroids	3/42 (7)	1/29 (3)	2/13 (15)
Decrease or hold CNI	9/54 (17)	4/37 (11)	5/17 (29)
Anti-viral treatment (%)			
Hydroxychloroquine	60 (92)	40 (93)	20 (91)
Azithromycin	44 (68)	28 (65)	16 (76)
Remdesivir	2 (3)	1 (2)	1 (5)
Immunomodulatory therapy (%)			
Bolus steroids	8 (12)	3 (7)	5 (24)
Tocilizumab	8 (12)	2 (5)	6 (27)
Mechanical Ventilation	19 (29)	0 (0)	19 (86)
ICU Admission (%)	19 (30)	0 (0)	19 (86)
Mortality (%)	10 (15)	0 (0)	10 (45)
Discharged (%)	18 (28)	16 (37)	2 (9)

Pereira MP et al, Submitted

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COVID-19 and the Liver: Case Studies and Updates

Oren K. Fix, MD, MSc, FAASLD
Medical Director, Liver Transplant Program
Swedish Medical Center, Seattle, WA

Clinical Associate Professor
Washington State University Elson S. Floyd College of Medicine

Clinical Insights Document

- First published online March 23rd
- Update posted online April 7th
- New update posted today
- Spanish and Portuguese translations available online
- *Hepatology* manuscript published online

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Click to check for updates

Released: April 16, 2020

CLINICAL INSIGHTS FOR HEPATOLOGY AND LIVER TRANSPLANT PROVIDERS DURING THE COVID-19 PANDEMIC

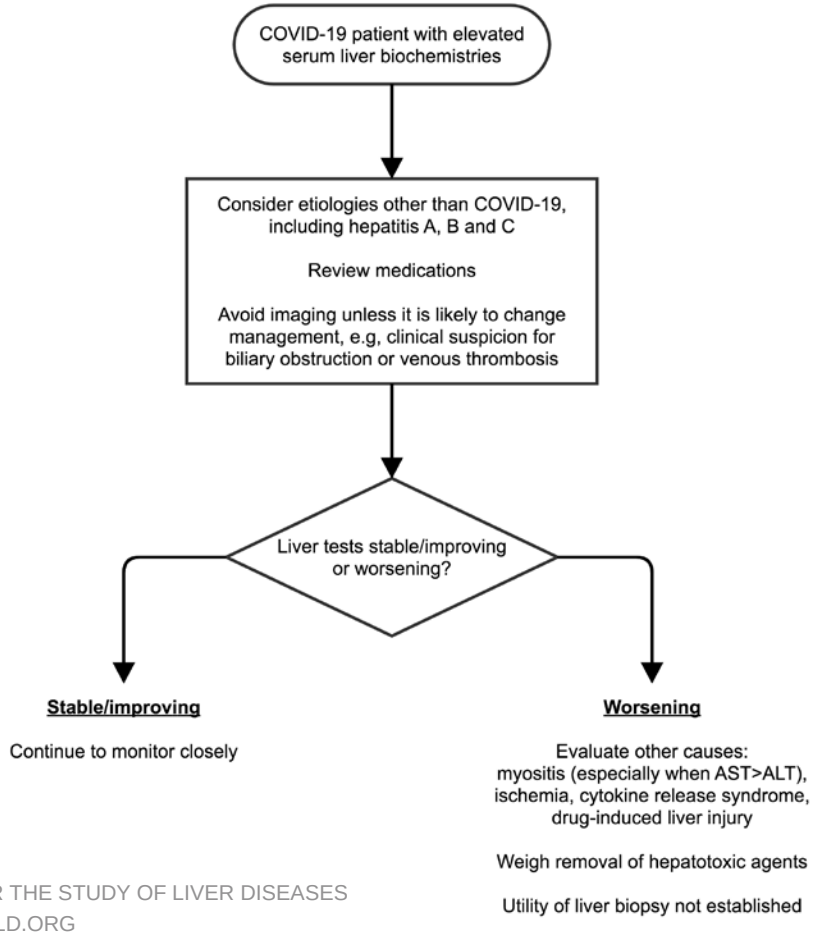
This is a "living" document that will continue to evolve and will be updated as new information becomes available.

Clinical Insights Document Major Changes: Chronic Liver Disease and COVID-19 Risk

- Emerging data suggest that patients with NAFLD may be at higher risk for COVID-19
- Patients with chronic liver disease and transplant recipients are potentially at increased risk for severe COVID-19 until further data become available

Clinical Insights Document Major Changes: Evaluation of Elevated Liver Biochemistries

- Consider etiologies unrelated to COVID-19, including other viruses such as hepatitis A, B, and C when assessing patients with COVID-19 and elevated liver biochemistries
- Updated Figure 1



Clinical Insights Document Major Changes: Treatment of Hepatitis B and C

- Proceed with treatment of hepatitis B and C in patients *without* COVID-19 as clinically warranted
- Initiating treatment of hepatitis B in a patient *with* COVID-19 is not routinely warranted but should be considered if there is clinical suspicion of a hepatitis B flare or when initiating immunosuppressive therapy
- Initiating treatment of hepatitis C in a patient *with* COVID-19 is not routinely warranted

Clinical Insights Document Major Changes: Liver Transplant Challenges

- Consider the following issues in hospitals with a high prevalence of COVID-19:
  - The risk of nosocomial transmission during the transplant admission
  - Difficulty obtaining procedures or other resources when complications arise
  - Limitations on family/caregiver visitation for a postoperative period that often relies on the engagement of caregivers

Clinical Insights Document Major Changes: Endoscopy

- Due to cancellations of elective/non-urgent endoscopy:
  - Consider, in the interim, primary prophylaxis with beta blocker therapy for patients with clinically significant portal hypertension or high risk of decompensation

Clinical Insights Document Major Changes: Masks

- Data suggest that a surgical mask worn by infected individuals may reduce the risk of transmission (source control)
- All healthcare workers should wear a surgical mask in patient care settings

Available Resources from AASLD

- Updated document available today at: https://www.aasld.org/about-aasld/covid-19-resources
- Future updates planned as new information becomes available
- Manuscript now available on *Hepatology* web site under Accepted Articles

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Rapid Fire Journal Club

Ryan M. Kwok, MD, FACP

Background / Definitions

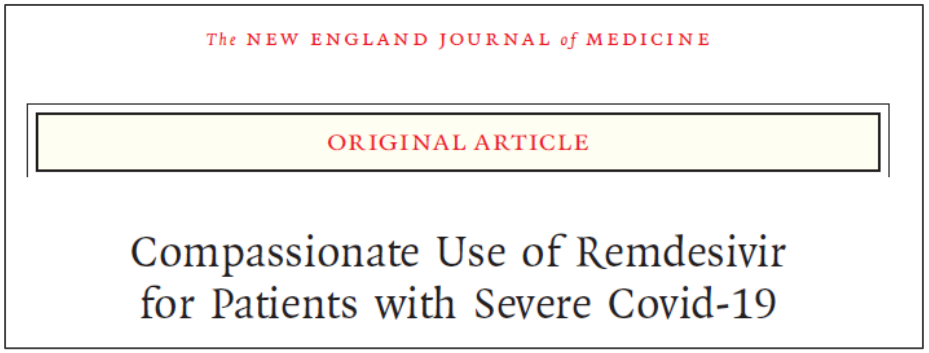
- No current proven effective therapy
  - Several off-label / compassionate use therapies
    - Remdesivir
    - Tocilizumab
    - Convalescent plasma
- Definitions
  - Severe
    - Resp ≥ 30 breaths / min
    - SpO2 ≤ 93% on RA or
    - PaO2/FiO2 ≤ 300 mmHg
  - Critical
    - Respiratory failure → ventilation
    - Shock
    - Organ failure requiring ICU admission

Diagnosis and treatment protocol for novel coronavirus pneumonia (6th interim edition). China NHCOTPSRO

Remdesivir

- Prodrug of a nucleotide analogue
  - Viral RNA polymerase inhibitor
- Activity against several virus families
  - Coronaviruses (e.g. SARS-CoV & MERS-CoV)
  - Filoviruses (e.g. Ebola)
- Safety demonstrated in Ebola virus

Mulangu S, et al. NEJM 2019; 381:2293-230



- Compassionate use protocol :
  - 10 day course (D1: 200mg IV, D2-9: 100mg IV)
- Hospitalized COVID-19 patients:
  - SaO2 ≤94% or requiring supplemental O2
  - CrCl >30mL / min
  - AST / ALT < 5x ULN
  - No other investigational agents

Grein J. et al. NEJM 2020

See Table 1

Compassionate Use of Remdesivir for Patients with Severe Covid-19

Grein J. et al. NEJM 2020

https://www.nejm.org/doi/full/10.1056/NEJMoa2007016

- 61 patients
  - 75% male, median age 64 years (IQR 48-71)
  - Median duration of symptoms before RDV = 12 days
  - Median Follow Up – 18 days

- 53 patients analyzed
  - 22 U.S., 22 Europe / Canada, 9 Japan
  - 8 unable to analyze
    - 7 without post-treatment data, 1 with dosing error
  - 13 (25%) patients did not receive full 10 day course

Results

- Mortality = 7/53 (13%)
  - 6/34 (18%) - invasive ventilation
  - 1/19 (5%) - noninvasive
- Risk of death increased with:
  - Baseline SCr – HR 1.91
  - Age >70 – HR 11.34

See Figure 1

Compassionate Use of Remdesivir for Patients with Severe Covid-19
Grein J. et al. NEJM 2020

https://www.nejm.org/doi/full/10.1056/NEJMoa2007016

See Figure 3

Compassionate Use of Remdesivir for Patients with Severe Covid-19
Grein J. et al. NEJM 2020

https://www.nejm.org/doi/full/10.1056/NEJMoa2007016

See Table 2

Compassionate Use of Remdesivir for Patients with Severe Covid-19

Grein J. et al. NEJM 2020

https://www.nejm.org/doi/full/10.1056/NEJMoa2007016

- 4 pts discontinued RDV prematurely
  - 2 due to elevated aminotransferases

Conclusions

See Figure 2

Compassionate Use of Remdesivir for Patients with Severe Covid-19
Grein J. et al. NEJM 2020

https://www.nejm.org/doi/full/10.1056/NEJMoa2007016

COVID-19 & Cytokine Storm

- Proposed pathogenesis of COVID-19 involves cytokine storm
  - IL-6, TNF-a, IL-12, etc.
  - IL-6 - alveolar-capillary blood / gas exchange dysfunction → impaired O2 diffusion

- Tocilizumab
  - Recombinant humanized anti-human IL-6 receptor monoclonal antibody
  - FDA indication :
    - Variety of rheumatologic conditions (RA, JRA, GCA)
    - Cytokine Release Syndrome - related to CAR T-cell therapy

Zhou Y, et al. BioRxiv 2020:2020.02.12.94576

Effective Treatment of Severe COVID-19 Patients with Tocilizumab

Xiaoling Xu[1,#*], Mingfeng Han[2,#], Tiantian Li[1], Wei Sun[2], Dongsheng Wang[1], Binqing Fu[3,4], Yonggang Zhou[3,4], Xiaohu Zheng[3,4], Yun Yang[5], Xiuyong Li[6], Xiaohua Zhang[2], Aijun Pan[5], Haiming Wei[3,4*]

- 21 patients
  - 86% male, median age 57 years (25-88 years)
  - All with severe or critical disease

Oxygen therapy	
High-flow oxygen	9/20 (45.0%)
Nasal cannula	7/20 (35.0%)
Invasive ventilation	2/20 (10.0%)
Noninvasive ventilation	1/20 (5.0%)
Mask oxygen	1/20 (5.0%)

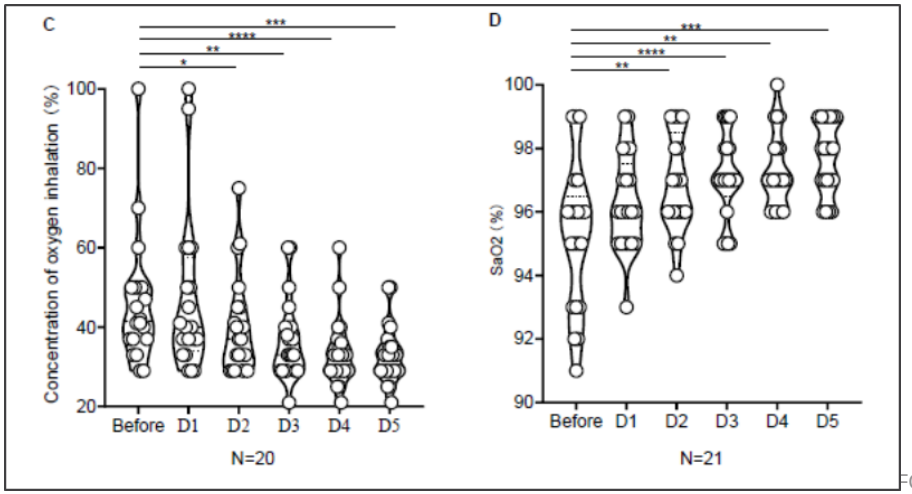
- Treated according to local protocol
  - Lopinavir, methylprednisolone
  - Tocilizumab (TCZ)
    - 400mg IV x1
      - No report on median time to dosing
    - 3 pts received a 2nd dose

Results

- No adverse events reported
- Improvement in all laboratory parameters and O2 requirements
- Hospitalized for 13.5 days after TCZ
  - 19/21 (91%) discharged
  - 2/21 (9%) remained hospitalized

Table 2 Laboratory Tests before and after Tocilizumab

	Range	Before the tocilizumab	After the tocilizumab		
			D1	D3	D5
White-cell count, ×10⁹/L	3.5-9.5	6.30 ± 2.77 (4/20, 20.0%)	8.05 ± 4.39 (8/18, 44.4%)	6.02 ± 3.05 (9/21, 42.9%)	5.25 ± 2.11 (2/19, 10.5%)
Lymphocyte percentage, %	20-50	15.52 ± 8.89 (17/20, 85.0%)	11.78 ± 11.36 (16/18, 88.9%)	16.93 ± 13.59 (14/21, 66.7%)	22.62 ± 13.48 (9/19, 47.4%)
C-reactive protein, mg/L	0-5	75.06 ± 66.80 (20/20, 100%)	38.13 ± 54.21 (17/18, 94.4%)	10.61 ± 13.79 (10/20, 50.0%)	2.72 ± 3.60 (3/19, 15.8%)
Procalcitonin, ng/ml	0-0.5	0.33 ± 0.78 (2/20, 10.0%)	0.21 ± 0.35 (2/16, 12.5%)	0.09 ± 0.13 (1/19, 5.3%)	0.12 ± 0.15 (1/18,5.6%)



Potential Risks

- Severe liver injury / liver failure

Transaminase Levels and Hepatic Events During Tocilizumab Treatment

Pooled Analysis of Long-Term Clinical Trial Safety Data in Rheumatoid Arthritis

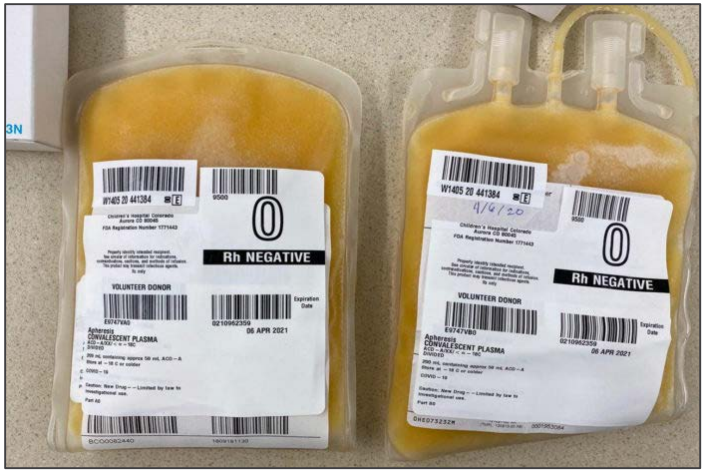
  - ALT elevations >ULN in 70.6%, >5x ULN in 2.9%
    - 2.5% stopped due to hepatic injury
  - Severe hepatic AE's to include ALF
- Theoretical risk for HBV reactivation
- Intestinal perforation
- Severe allergic reactions / anaphylaxis

Genovese MC, et al. Arthritis Rheumatol 2017; 69(9): 1751-61.
Jacobs B, et al. Arch Rheumatol 2018; 33(3): 372-5.

Convalescent Plasma Therapy

AASLD

- Adaptive immunotherapy in use for more than a century
- Successfully used in SARS, MERS, and 2009 H1N1 influenza with safety and efficacy
  - Meta-analysis of 32 studies in SARS and severe influenza
    - CP versus placebo / no therapy – reduction in mortality
      - OR 0.25 (95% CI, 0.14-0.45)
- 2009 H1N1 pandemic - significant reduction in viral load and cytokine burden



Mair-Jenkins J, et al. J. Infect. Dis. 2015; 211, 80–90.
Hung IF, et al. Clin Infect Dis. 2011;52(4):447-456.

Effectiveness of convalescent plasma therapy in severe COVID-19 patients

Kai Duan[a,b,1], Bende Liu[c,1], Cesheng Li[d,1], Huajun Zhang[e,1], Ting Yu[f,1], Jieming Qu[g,h,i,1], Min Zhou[g,h,i,1], Li Chen[j,1], Shengli Meng[b], Yong Hu[d], Cheng Peng[e], Mingchao Yuan[k], Jinyan Huang[l], Zejun Wang[b], Jianhong Yu[d], Xiaoxiao Gao[e], Dan Wang[k], Xiaoqi Yu[m], Li Li[b], Jiayou Zhang[b], Xiao Wu[d], Bei Li[e], Yanping Xu[g,h,i], Wei Chen[b], Yan Peng[d], Yeqin Hu[b], Lianzhen Lin[d], Xuefei Liu[g,h,i], Shihe Huang[b], Zhijun Zhou[d], Lianghao Zhang[b], Yue Wang[d], Zhi Zhang[b], Kun Deng[d], Zhiwu Xia[b], Qin Gong[d], Wei Zhang[d], Xiaobei Zheng[d], Ying Liu[d], Huichuan Yang[a], Dongbo Zhou[a], Ding Yu[a], Jifeng Hou[n], Zhengli Shi[e], Saijuan Chen[l], Zhu Chen[l,2], Xinxin Zhang[m,2], and Xiaoming Yang[a,b,2]

JAMA | Preliminary Communication

Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma

Chenguang Shen, PhD; Zhaoqin Wang, PhD; Fang Zhao, PhD; Yang Yang, MD; Jinxiu Li, MD; Jing Yuan, MD; Fuxiang Wang, MD; Delin Li, PhD; Minghui Yang, PhD; Li Xing, MM; Jinli Wei, MM; Haixia Xiao, PhD; Yan Yang, MM; Jiuxin Qu, MD; Ling Qing, MM; Li Chen, MD; Zhixiang Xu, MM; Ling Peng, MM; Yanjie Li, MM; Haixia Zheng, MM; Feng Chen, MM; Kun Huang, MM; Yujing Jiang, MM; Dongjing Liu, MD; Zheng Zhang, MD; Yingxia Liu, MD; Lei Liu, MD

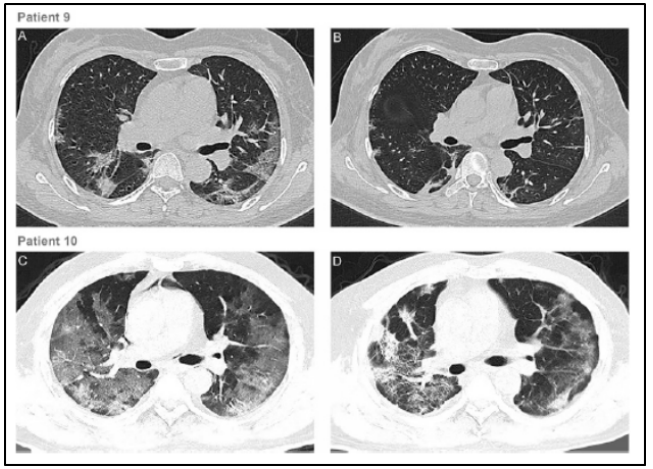
- 10 patients with severe COVID-19
  - 3/10 mechanically ventilated
  - 6/10 male, median age 52.5 years
  - CP administered 16.5 days after admission
    - 200mL x 1 transfusion
  - All treated with various additional therapies
    - Remdesivir, arbidol, ribavirin, peramivir, methylprednisolone

- 5 patients with critical COVID-19
  - 5/5 mechanically vented
  - 3/5 male, age range 36-73 years
  - CP administered 10-22d after admission
    - 200-250mL x 2 transfusions
  - All treated with various additional therapies
    - Lopinavir / ritonavir, IFN-α-1b, arbidol, favipravir, darunavir, methylprednisolone

Accessed from www.pnas.org/cgi/doi/10.1073/pnas.2004168117 on April 13, 2020
Shen C, et al. JAMA. Published online March 27, 2020. doi:10.1001/jama.2020.4783

Results

- All patients demonstrated improvement in clinical parameters after infusion
  - 4/8 (50%) mechanically vented patients extubated
  - Laboratory / radiographic parameters
    - IL-6, procalcitonin, CRP, AST/ALT, Lymphocyte counts
    - All patients with negative viral load after CP
    - Chest CT improvement
- No adverse / safety events reported

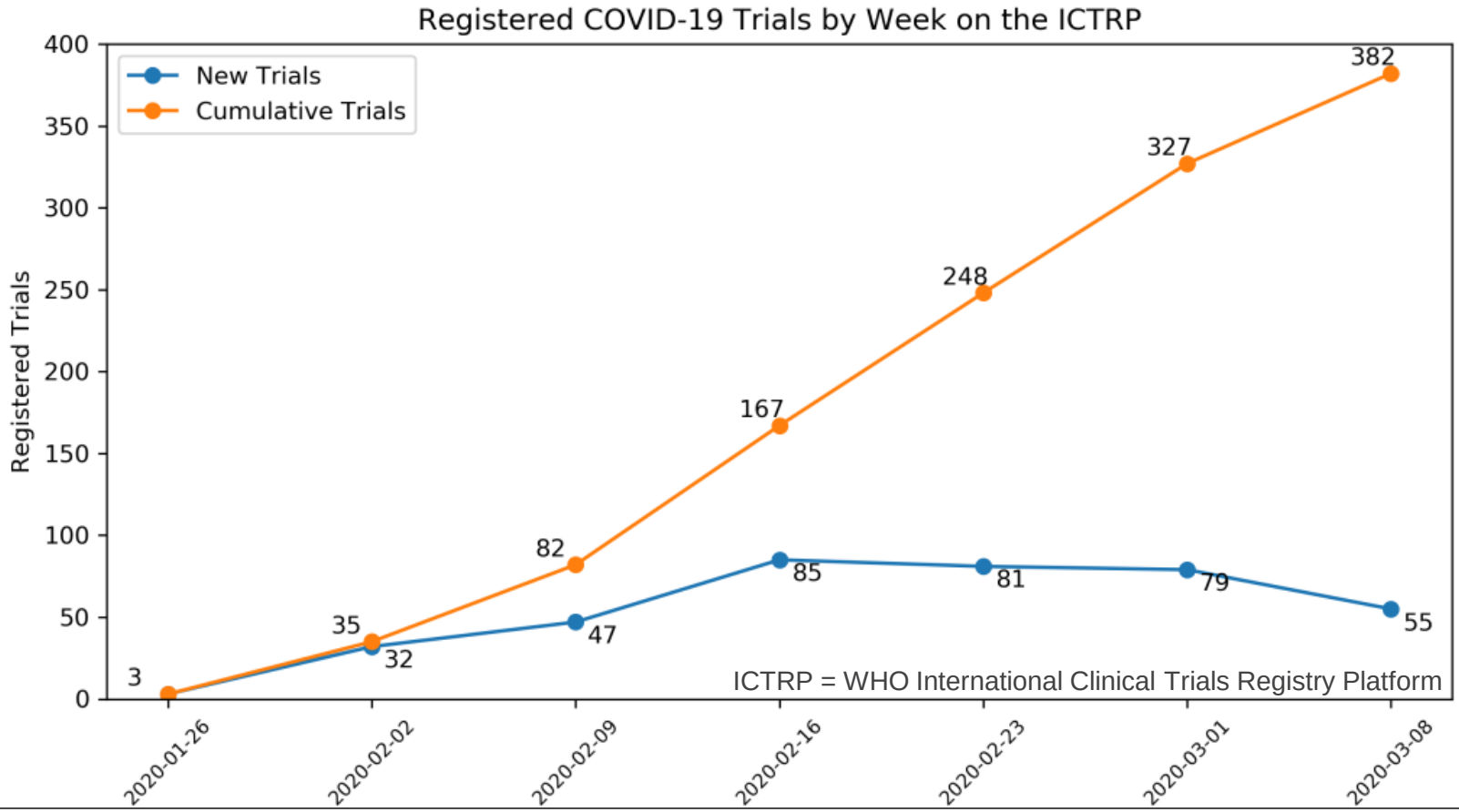


Summary

- Overall data encouraging

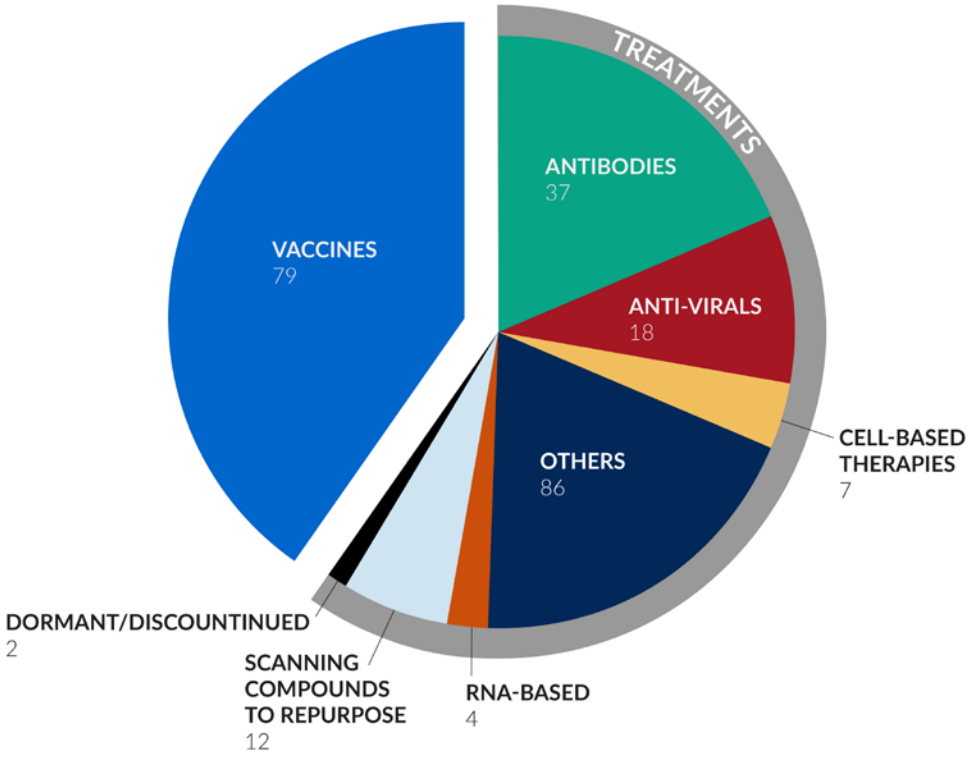
- Limitations
  - All trials are observational
    - Lack of randomization / controls limit conclusions
    - Confounded by additional therapies (CP, TCZ)
  - Relatively high percentage of patients on noninvasive O2 therapy
    - Spontaneous improvement?
  - Relatively delayed administration of treatments (median 16 days)
    - Bias toward healthier patients?

Tracking the Trials



Accessed from https://www.cebm.net/covid-19/registered-trials-and-analysis/ on April 13, 2020

Potential COVID-19 Treatments and Vaccines in Research Pipeline



Updated: April 9, 2020

Accessed from https://milkeninstitute.org/covid-19-tracker on April 13, 2020

IDSA Infectious Diseases Society of America

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Infectious Diseases Society of America Guide...

Abstract

Executive Summary and Background

Methods and Search Results

Recommendations 1 and 2: Hydroxychloroquine +/- azithromycin vs. no hydroxychloroquine +/- azithromycin for hospitalized patients

Recommendation 3: Lopinavir/ritonavir vs. placebo for confirmed COVID-19 pneumonia

Recommendations 4 and 5: Corticosteroids vs. no corticosteroids for hospitalized patients with/without ARDS

Recommendation 6: Tocilizumab vs. no treatment for severe COVID-19 pneumonia

Recommendation 7: Convalescent plasma vs. no convalescent plasma for hospitalized patients

Narrative summaries of treatments

Download

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

Published by IDSA, 4/11/2020

COVID-19 Guideline, Part 2: Diagnostics - *Coming Soon*

COVID-19 Guideline, Part 3: Infection Prevention - *Coming Soon*

Adarsh Bhimraj*, Rebecca L. Morgan**, Amy Hirsch Shumaker, Valery Lavergne**, Lindsey Baden, Vincent Chi-Chung Cheng, Kathryn M. Edwards, Rajesh Gandhi, William J. Muller, John C. O'Horo, Shmuel Shoham, M. Hassan Murad**, Reem A. Mustafa**, Shahnaz Sultan**, Yngve Falck-Ytter**

**Corresponding Author **Methodologist*

UPDATE (4/13/20): Language has been added to clarify that the guideline panel used the word "only" in recommendations about therapeutic agents with higher uncertainty and/or more potential for harm. See *Executive Summary* (second paragraph) and *Methods* section, Evidence to recommendations subsection (third paragraph).

Abstract

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AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

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CLINICAL INSIGHTS FOR HEPATOLOGY AND LIVER TRANSPLANT PROVIDERS DURING THE COVID-19 PANDEMIC

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Clinical Cases

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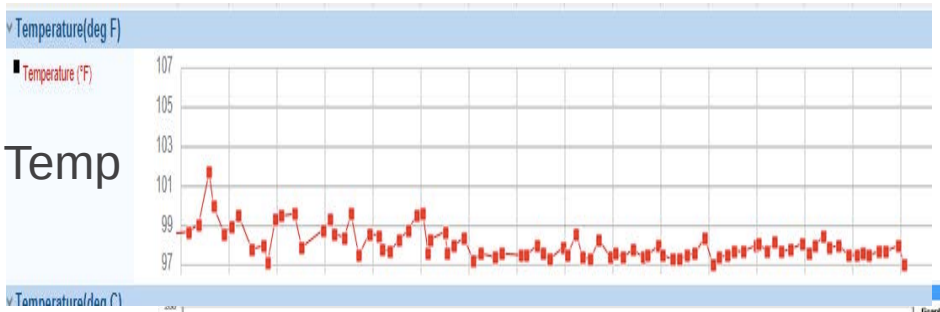
Case 1

- 60 yo transplanted for cryptogenic cirrhosis with HCC
- Early post transplant course complicated by c dificil colitis treated with oral vancomycin, delaying discharge until day 17.
- On the day of discharge patient was asymptomatic and nasopharyngeal swab for SARS-CoV2 was obtained due to potential in-hospital exposure (estimated to occur 4-5 days prior to discharge).
- Discharge immunosuppression - tacrolimus, prednisone, and prophylaxis with fluconazole, valganciclovir and trimethoprim sulfamethoxazole was given per protocol.
- The next day (POD 18) PCR test was positive for SARS-CoV2. The patient related no new symptoms, and her family was educated about precautions. She remained home.
- Lab testing was arranged at her home on POD 19 – no elevation ALT and AST, WBC 5, tacrolimus level 8.6, CRP 86 and Ferritin 694

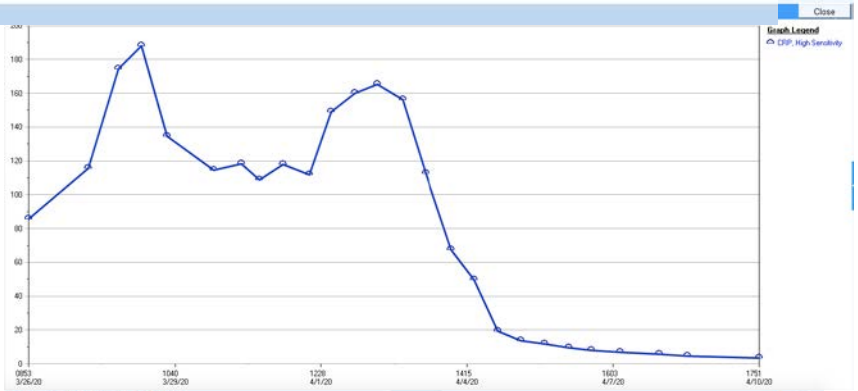
Case 1 cont'd

- Over the next 48 hours (POD 21) patient developed low grade fever and dyspnea and was re-admitted to the hospital. CXray was without infiltrate, O2 saturation was 97% on room air. CRP and ferritin were rising (see graph), D-dimer 4, troponin not elevated
- On POD 24 (12-13 days after exposure) oxygen saturation reduced from 95% to 87% on room air, and 2L NC was started. CXray was abnormal with new infiltrates (shown next slide)
- A single infusion of tocilizumab 580 mg was administered along with oral hydroxychloroquine, 800 mg the first day, 400 mg after for 5 days. ECG was monitored daily for QTc
- Trimethoprim sulfamethoxazole and fluconazole was stopped
- Throughout prednisone was maintained at 10 mg, and tacrolimus levels were monitored and kept at a level of 6-8
- Oxygen supplementation was continued for 5 more days with NC before it was no longer needed
- Liver tests showed mild changes (shown) but were mostly stable throughout

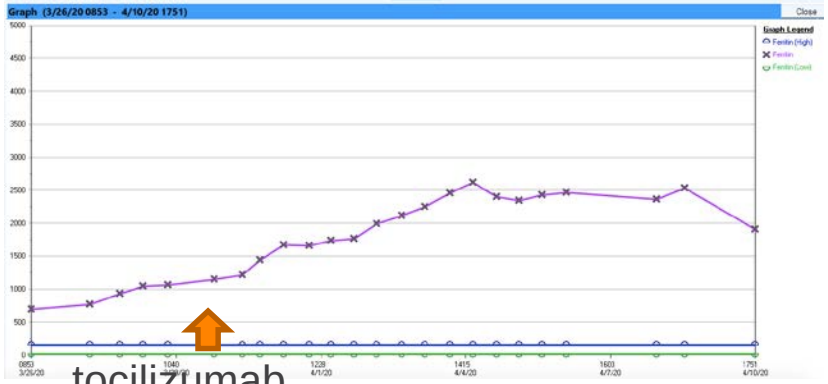
Temp



CRP

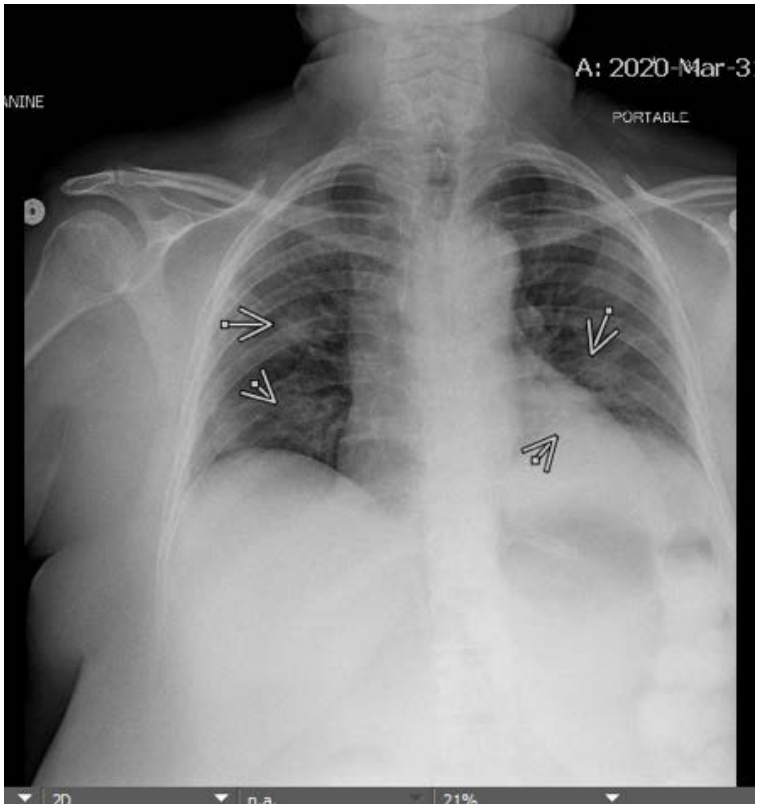


Ferritin



tocilizumab

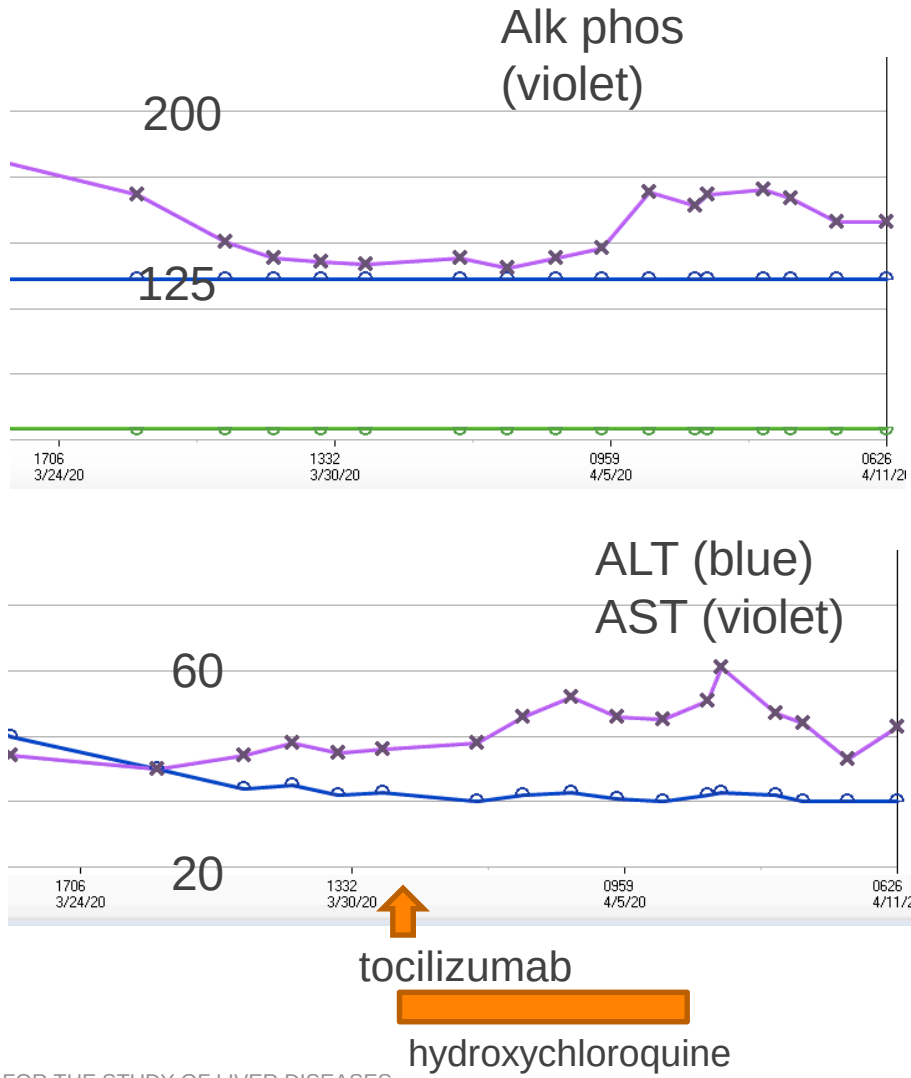
hydroxychloroquine



Arrows indicate infiltrate

Case 1 cont'd

- Patient asymptomatic and recovering in hospital, delayed discharge due to concerns at home
- Repeat nasal swab for SARS-CoV2 still positive by PCR 16 d after the first positive test (20-21 d after exposure)
- 5 days later (25-26 d after exposure) has equivocal PCR



Case 1 Discussion Points

- Even if testing for SARS-CoV2 is negative in donor and recipient, there is a risk for post transplant exposure
- Fever, dyspnea are common features of infection, paralleled by changes in inflammatory markers
- Immune suppression need not be lowered in patients post OLTx with mild and moderate COVID disease
- Therapy with anti-IL6 and hydroxychloroquine was initiated when there was a change from mild to moderate disease, likely better than waiting for severe disease
- Change in liver tests were minimal despite viremia and therapy
- Viral shedding is prolonged with immunosuppression

Case 2: (submitted by audience)

- 16 year old male with acute liver failure due to Hepatitis A
- Patient antibody to SARS CoV2 - IgM positive, Nasopharyngeal swab for SARS CoV2 - PCR positive
- To transplant or not to transplant ?

Case 2 Discussion Points

To transplant or withhold transplant is an ethical decision and you must consider the following principles:

- Principle of nonmaleficence
- Principle of beneficence
- Principle of justice – distributive justice

What we know:

- Outcomes for transplant with COVID19 unknown, however limited data from US and Europe suggests survival of most patients is possible, but deaths have occurred

Considerations in decision process:

- Must consider the condition of the recipient at the time of organ offer – assuming good oxygenation and no ARDS, his young age and lack of other co-morbid conditions and potential longevity after receiving the graft (years of benefit) – all favor proceeding with transplant.
- If any of these variables are different, the decision would need to be reconsidered as outcome might be less favorable.

Case 3 – Dr. Jaime Chu, The Mount Sinai Medical Center, NY

10 month old girl with history of biliary atresia s/p failed Kasai portoenterostomy, actively listed for LT

- Chief complaint: nasal congestion, increased work of breathing x 1 day
  - Telemedicine visit done the day prior to admission – significant for mild subcostal retractions, but otherwise afebrile (Tmax 99.2F), no cough, good disposition and hydration status
  - Repeat telemedicine visit the day of admission significant for increased subcostal retractions, nasal flaring, and grunting → sent to ED

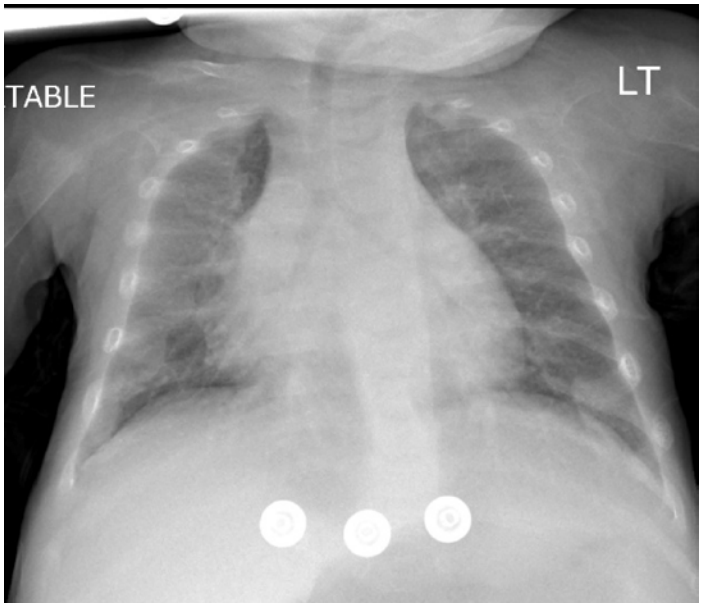
- Medical history: Kasai portoenterostomy done at DOL 46, failed biliary drainage, progressive ascites, on diuretics at home, no history of SBP or variceal bleed

- Social history: Mom reports no known sick contacts at home. Patient is Hispanic and lives in East Harlem, New York with Mom and 3 older sisters. Mom currently still working at an auto supply store and reports taking appropriate protective measures. Older sister had 1 episode of emesis yesterday, otherwise family members asymptomatic.

Initial presentation to ED:

- Vitals: Pulse 144 | Temp 37.6 °C (Rectal) | Resp 62 | SpO2 98% on RA
- Physical Exam:
  - Non-toxic appearing
  - HEENT: + scleral icterus, mild nasal flaring
  - Resp: tachypneic, clear to auscultation, subcostal retractions, intermittent grunting
  - Abdomen: soft and full with moderate ascites, +hepatosplenomegaly
  - Skin: + jaundice
- Labs:
  - WBC: 6.7, 30% PMNs, 37% lymphocytes, 15% atypical lymphocytes
  - Hgb 10.0, platelets 213,000
  - Creatinine < 0.2 mg/dL
  - INR 1.2, d-dimer 0.65 (lab range 0-0.5 ug/ml)
  - ALT/AST 161 / 308 (baseline ALT/AST 142/307)
  - T/d bili 23.3/16.9, GGT 257 (baseline bili 22.4/14.9, GGT 271)
  - CRP 2.9 mg/L, ferritin 99, procalcitonin 0.13 (normal < 0.49 ng/mL)

- CXR on admission: coarse pulmonary markings with peribronchial cuffing suggesting viral process
- Respiratory viral panel: negative
- Nasopharyngeal SARS-CoV-2 PCR: not detected
- Repeated nasopharyngeal SARS-CoV-2 PCR (24 hours later): not-detected
- Admitted to the Pediatric ICU on HFNC 8 LPM, 40% O2; Although negative for COVID-19 x 2, given patient's risk with ESLD, living in a highly endemic area, and clinical presentation + CXR, she is being treated as a presumed COVID case.
  - Ceftriaxone started for possible community-acquired pneumonia
  - Hydroxychloroquine 3.25mg/kg q12hrs x 4 days and Azithromycin x 5 day started
- Remains in-house: Initially weaned to 2 LPM, 21% O2 but on Day 7: recurrence of tachypnea requiring HFNC 8L at 21%, no change to admission CXR, liver tests remain stable.



Case 3 Discussion points

- By history alone it is not always clear who was the contagious contact
- GI symptoms in a sibling could have indicated others in the household were affected
- Current diagnostic testing by PCR has limitations
- Early admission led to timely recognition of disease worsening and institution of supportive care
- Continued monitoring and counseling about potential recurrent symptoms and concerns about secondary infections are warranted
- Treatments can be tried in patients with advanced liver disease, but monitoring for worsening of hepatic disease is needed

Panel Discussion

Please submit your questions to the Q&A Chat now.

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Upcoming COVID-19 Webinar

Thursday, April 30, 2020

5-6pm Eastern

Clinical Insights: COVID-19 and the Liver – Case Studies and Updates

Registration Now Open: http://www.aasld.org/COVID19

AASLD's COVID-19 Resources

Follow/Share: COVID-19 Resources Webpage: https://www.aasld.org/about-aasld/covid-19-resources

Join/Engage: COVID-19 Care Community on AASLD's online community, Engage. Open to all members. Log in to Engage with your AASLD user name and password.

Submit: *Hepatology, Liver Transplantation, Hep Commun* all accepting and fast tracking review of COVID-19 original articles, case reports