Patient characteristics

Table 1. Patient characteristics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Sex	Female	Male	Male	Male	Male
Age (years)	58	66	45	60	65
Weight (kg)	57		73	77	92.5
Smoking	No	No	Yes	No	Yes
Comorbidities	Hypertension Diabetes mellitus	Prediabetes	Gout	Hypertension Hepatitis B Hepatitis C carrier	Obesity
Interval between symptoms and admission	9 days	7 days	10 days	8 days	6 days
Interval between admission and plasma	31 days	23 days	9 days	20 days	9 days
Complications prior to plasma transfusion	Bilateral upper extremity DVT SIADH	VAP Hypernatremia	None	VAP	None
Disease classification	Severe	Severe	Severe	Severe	Severe
Treatments	Plasma Diuretics	Plasma Diuretics	Plasma Diuretics Antibiotics	Plasma Antibiotics	Plasma CRRT Antibiotics
Proned	Yes	Yes	Yes	Yes	Yes
Extubated	No	No	Yes (day 29)	No	No
Deceased	Yes	Yes	No	Yes	Yes

Conclusion: In our patient cohort, the administration of CP did not improve laboratory markers or clinical outcomes. Some notable limitations of this study are the small sample size, and that the patients received CP late in their disease course. Further investigation is necessary to draw definitive conclusions about the utility of CP in the treatment of SARS-CoV2.

Disclosures: **All Authors**: No reported disclosures

560. Repurposing Eravacycline for the Treatment of SARS-CoV-2 Infections

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Session: P-21. COVID-19 Treatment

Background: The outbreak of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is seriously impacting health and economies all over the world. With more than 8 million diagnosed cases and close to 450.000 deaths worldwide by mid-June 2020, the need of safe and effective treatments is extremely urgent. Drug repurposing is a suitable approach to bring new treatments to the clinics in a very fast and cost-effective way.

Methods: We have applied an artificial intelligence screening technology based on molecular fields to find drugs that could inhibit the SARS-CoV-2 3-chymotrypsin-like cysteine protease (3CLpro) among a library of compounds with clinical experience, approved drugs and drugs in clinical development. The results were refined by covalent docking at the catalytic domain of the protein and thirty compounds were chosen for experimental validation on a protease assay with recombinant SARS-CoV-2 3CLpro. The compounds were also tested for their inhibition of SARS-CoV and MERS-CoV 3CLpro. Positive hits were further tested in a VeroE6 cell infection assay with pathogenic SARS-CoV-2 using nucleocapsid protein staining at 24h post infection as a readout.

Results: Eravacycline was identified at the top positions of the screening and its potent inhibitory activity was demonstrated in vitro against recombinant SARS-CoV-2, SARS-CoV and MERS-CoV 3CL proteases, with IC50 of 1.65, 10.04 and 16.36 μM respectively. In addition, eravacycline inhibited infection of VeroE6 cells by pathogenic strains of SARS-CoV-2, with an IC50 of 30.61 μM in the absence of drug induced cell toxicity.

Conclusion: Eravacycline is an FDA and EMA-approved antibiotic that was launched in the US in 2018. It is a safe drug that is known to accumulate in the lungs at concentrations that are compatible with its in vitro activity against SARS-CoV-2. This, together with its known antibacterial activity that could help prevent secondary infections in hospitalized COVID-19 patients, and the known anti-inflammatory actions of tetracyclines, warrant further research on the potential role of eravacycline for the treatment of patients with COVID-19 or infected with SARS-CoV-2 but with milder symptoms.

Disclosures: Núria Reig, PhD, SOM Biotech (Employee) Dong-Hae Shin, PhD full professor, SOM Biotech (Scientific Research Study Investigator)

561. Safety of Remdesivir vs Standard Care in Patients with Moderate Covid-19

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Session: P-21. COVID-19 Treatment

Background: Remdesivir (RDV) has been shown to shorten recovery time and was well tolerated in patients with severe COVID-19. Here we report safety of RDV in patients with moderate COVID-19.

Methods: We conducted an open-label, phase 3 trial (NCT04252664) in hospitalized patients with confirmed SARS-CoV-2 infection, evidence of pulmonary infiltrates, and oxygen saturation >94% on room air. Patients were randomly assigned to receive RDV (5 or 10 days) or standard of care (SOC). RDV was dosed intravenously at 200 mg on day 1, 100 mg daily thereafter. Adverse events (AEs) and laboratory abnormalities were evaluated through the day 11 data cut; safety data through day 28 will be presented at the meeting.

Results: 584 patients were randomized and treated (5d RDV: n=191; 10d RDV, n=193; SOC: n=200). Baseline characteristics were balanced among groups; median (range) age was 57y (12-95y), 39% were female and 19% Black, 39% had arterial hypertension, 15% hyperlipidemia, 11% asthma. Briefly, across both the 5d and 10d arms, RDV was well tolerated with a similar rate of Grade 3 or 4 AEs and fewer SAEs compared to SOC (Table). AEs more common with RDV vs SOC included nausea, headache, and hypokalemia. Overall, across the 3 arms, incidence of AEs leading to discontinuation and death were low and no clinically relevant changes in laboratory parameters were observed. In addition, median changes in renal and liver function tests from baseline were not statistically significant between the RDV 5d and RDV 10d groups compared to the SOC only group at d14 (Table 1).

Table 1.

Table 1. Safety of RDV vs SOC in patients with moderate COVID-ID through day 10

	RDV 5 Days (N = 191)	RDV 10 Days (N = 193)	SOC Only (N = 200)
Any AE	97 (51%)	106 (55%)	90 (45%)
AEs in ≥5% in any group			
Nausea	19 (10%)	18 (9%)	6 (3%)
Diarrhea	10 (5%)	10 (5%)	14 (7%)
Hypokalemia	9 (5%)	13 (7%)	4 (2%)
Headache	10 (5%)	10 (5%)	5 (3%)
Constipation	8 (4%)	5 (3%)	9 (5%)
Grade 3 or 4 AE	20 (10%)	21 (11%)	24 (12%)
RDV-related AE	36 (19%)	24 (12%)	NA
SAE	8 (4%)	7 (4%)	18 (9%)
AEs leading to discontinuation*	4 (2%)	7 (4%)	NA
Death¥	2 (1%)	2 (1%)	4 (2%)
Grade 3 or 4 lab abnormalities	23 (13%)	29 (16%)	33 (18%)
Renal and Liver Lab Parameters			
Change from Baseline in CrCl, mL/min median (Q1,Q3)**	2.4 (-7.2, 13.0)	5.1 (-7.8, 12.8)	0.4 (-9.7, 12.8)
Change from Baseline in AST U/L, median (Q1,Q3)**	-6 (-13, 3)	-2 (-13, 4)	-8 (-25, 14)
Change from Baseline in ALT U/L, median (Q1,Q3)**	6 (-4, 15)	4 (-6, 9)	1 (-11, 44)
Change from Baseline in Bilirubin mg/dL, median (Q1,Q3)**	0.10 (-0.10, 0.20)	0.10 (-0.07, 0.20)	0.00 (-0.20, 0.20)

* AEs leading to discontinuation included: 5d RDV, rash (n=2) and increased ALT and decreased heart rate (n=1 each); 10d RDV, transaminitis (n=2), increased AST and ALT (n=2), and increased ALT, increased blood alkaline phosphatase, and acute respiratory failure (n=1 each).

¥ Deaths included COVID-19 (n=3) and respiratory failure, acute respiratory distress syndrome, COVID-19 pneumonia with ascending thoracic aortic aneurysm, complete heart block, and cardiac arrest (n=1 each).

** p-value = non-significant.

CrCl, creatinine clearance by Cockcroft-Gault

Conclusion: RDV given for 5d or 10d was well tolerated in patients with moderate COVID-19. No clinically significant safety signals were observed with RDV vs SOC.

Disclosures: **Gerard J. Criner, MD**, **Gilead Sciences Inc.** (Scientific Research Study Investigator)**Regeneron** (Scientific Research Study Investigator) **Gerard J. Criner, MD**, NO DISCLOSURE DATA **Mi Young Ahn, MD**, **Gilead Sciences Inc.** (Scientific Research Study Investigator) **Gregory Huhn, MD**, **Gilead Sciences Inc.** (Grant/Research Support, Scientific Research Study Investigator)**Janssen** (Grant/Research Support)**Proteus** (Grant/Research Support)**US National Institutes of Health** (Grant/Research Support)**Viiv Healthcare** (Grant/Research Support) **Aruna Subramanian, MD**, **Gilead Sciences Inc.** (Scientific Research Study Investigator) **Carlos Lumbreras, MD**, **Gilead Sciences Inc.** (Scientific Research Study Investigator) **Stefan Schmiedel, MD**, **Gilead Sciences Inc.** (Scientific Research Study Investigator) **Robert H. Hyland, MD**, **Gilead Sciences Inc.** (Employee, Shareholder) **Vithika Suri, PhD**, **Gilead Sciences Inc.** (Employee, Shareholder) **Huyen Cao, MD**, **Gilead Sciences Inc.** (Employee, Shareholder) **Hongyuan Wang, PhD**, **Gilead Sciences Inc.** (Employee, Shareholder) **Devi SenGupta, MD**, **Gilead Sciences Inc.** (Employee, Shareholder) **Anand Chokkalingam, PhD**, **Gilead Sciences** (Employee) **Anu Osinusi, MD**, **Gilead Sciences** (Employee) **Diana M. Brainard, MD**, **Gilead Sciences** (Employee) **Yao-Shen Chen, MD**, **Gilead Sciences Inc.** (Scientific Research Study Investigator) **Yao-Shen Chen, MD**, NO DISCLOSURE DATA **Huldrych Günthard, MD**, **Gilead Sciences Inc.** (Scientific Research Study Investigator) **D Jose Sanz-Moreno, MD**, **Gilead Sciences**

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562. Tocilizumab for the Treatment of Severe COVID-19: A Retrospective, Multi-Center, Case-Matched Series

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Session: P-21. COVID-19 Treatment

Background: At the time of this writing, there is no FDA approved medication for the treatment of COVID-19. One medication currently under investigation for COVID-19 treatment is tocilizumab, an interleukin-6 (IL-6) inhibitor. It has been shown there are increased levels of cytokines including IL-6 in severe COVID-19 hospitalized patients attributed to cytokine release syndrome (CRS). Therefore, inhibition of IL-6 receptors may lead to a reduction in cytokines and prevent progression of CRS. The purpose of this retrospective study is to utilize a case-matched design to investigate clinical outcomes associated with the use of tocilizumab in severe COVID-19 hospitalized patients.

Methods: This was a retrospective, multi-center, case-matched series matched 1:1 on age, BMI, and days since symptom onset. Inclusion criteria included ≥ 18 years of age, laboratory confirmed positive SARS-CoV-2 result, admitted to a community hospital from March 1st – May 8th, 2020, and received tocilizumab while admitted. The primary outcome was in-hospital mortality. Secondary outcomes included hospital length of stay, total mechanical ventilation days, mechanical ventilation mortality, and incidence of secondary bacterial or fungal infections.

Results: The following results are presented as tocilizumab vs control respectively. The primary outcome of in-hospital mortality for tocilizumab (n=26) vs control (n=26) was 10 (38%) vs 11 (42%) patients, p=0.777. The median hospital length of stay for tocilizumab vs control was 14 vs 11 days, p=0.275. The median days of mechanical ventilation for tocilizumab (n=21) vs control (n=15) was 8 vs 7 days, p=0.139, and the mechanical ventilation mortality was 10 (48%) vs 9 (60%) patients, p=0.463. In the tocilizumab group, for those expired (n=10) vs alive (n=16), 10 (100%) vs 7 (50%) patients respectively had a peak ferritin > 600 ng/mL, and 6 (60%) vs 8 (50%) patients had a peak D-dimer > 2,000 ng/mL. The incidence of secondary bacterial or fungal infections within 7 days of tocilizumab administration occurred in 5 (19%) patients.

Conclusion: These findings suggest that tocilizumab may be a beneficial treatment modality for severe COVID-19 patients. Larger, prospective, placebo-controlled trials are needed to further validate results.

Disclosures: Christian Cheatham, PharmD, BCIDP, Antimicrobial Resistance Solutions (Shareholder)

563. Tocilizumab in the Treatment of Critical COVID-19 Pneumonia

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Session: P-21. COVID-19 Treatment

Background: The anti-interleukin-6 receptor monoclonal antibody tocilizumab has been proposed as a treatment for COVID-19 pneumonia although the efficacy remains unknown.

Methods: Patients with COVID-19 confirmed by nasal swab PCR for SARS-CoV-2 who were admitted to Stony Brook University Hospital in Suffolk County, New York between March 10th and April 2nd and received tocilizumab while undergoing mechanical ventilation in any intensive care unit were retrospectively analyzed from data available in the electronic medical record. Baseline characteristics and clinical outcomes were compared to mechanically ventilated patients admitted during the same time period who received standard hospital protocol.

Results: Forty-five patients received tocilizumab compared to seventy controls. Mean dose of tocilizumab given was 4.8mg/kg and mean time to receipt from initial intubation was 2.5 days. Baseline demographic characteristics, inflammatory markers, treatment with corticosteroids, and SOFA scores were similar between the two cohorts (Table 1). Patients who received tocilizumab had significantly lower Charlson co-morbidity index (2.0 versus 3.0, p = 0.01) and higher temperature (38.7 C versus 38.2 C, p = 0.004) than controls. There was no significant association between receipt of tocilizumab and the rate of extubation within fourteen days (44.4 percent versus 34.2 percent; OR = 1.53, 95% C.I. 0.71 – 3.30), discharge from hospital (51.1 percent versus 40.0 percent; OR = 1.568, 95% C.I. 0.737 – 3.337), or mortality (31.1 percent versus 41.4 percent; OR = 0.639, 95% C.I. 0.290 – 1.4407) (Table 2). Patients who were administered tocilizumab within two days of intubation had increased likelihood of extubation within fourteen days compared to those who were treated later (OR = 3.50, 95% C.I. 1.01 – 12.18). There was no observed increased risk of secondary infection in patients given tocilizumab (28.9 versus 25.7, OR = 1.1736, 95% C.I. = 0.507 – 2.714).

Table 1: Patient Demographics and Baseline Characteristics

	Tocilizumab (n=45)	Controls (n=70)	P-value
Mean age – yr (SD)	56.2 (14.7)	60.6 (13.4)	0.0935
Male – no (%)	29 (64.4)	51 (72.9)	0.3386
Race – no (%) White non-Hispanic	19 (42.2)	33 (47.1)	0.4416
Hispanic	20 (44.4)	27 (38.6)	
Black/AA	3 (6.7)	3 (4.3)	
Asian	3 (6.7)	11 (15.7)	
Mean BMI – kg/m^2 (SD)	30.7 (5.3)	31.3 (6.9)	0.5820
Tmax on ICU admission – degree C, mean (SD)	38.7 (0.82)	38.2 (0.89)	0.0042
C-reactive protein on ICU admission – mg/dL, median (IQR)	19.5 (15.7)	17.6 (18.0)	0.8120
Ferritin baseline – ng/mL, median (IQR)	1507 (1518)	1462[a] (1435)	0.8950
Interleukin-6 baseline – pg/mL, median (IQR)	81.6 (99.4)	92.3[b] (131.5)	0.6569
Corticosteroid treatment – no (%)	33 (73.3)	55 (78.6)	0.5178
Hydroxychloroquine treatment– no (%)	43 (95.6)	65 (92.9)	0.7030
SOFA score, median (IQR)	5.0 (3.0)	5.0 (5.0)	0.3539
Charlson Comorbidity Index, median (IQR)	2.0 (3.0)	3.0 (3.0)	0.0141

a) n = 68; b) n = 56

Table 2: Primary Outcomes

	Tocilizumab (n=45)	Controls (n=70)	OR (95% C.I.)	P-value
Extubation in 14 days – no (%)	20 (44.4)	24 (34.2)	1.533 (0.712-3.304)	0.2751
Discharged – no (%)	23 (51.1)	28 (40.0)	1.568 (0.737-3.337)	0.2429
Death – no (%)	14 (31.1)	29 (41.4)	0.639 (0.290-1.4407)	0.2658
Secondary infection – no (%)	13 (28.9)	18 (25.7)	1.1736 (0.507-2.714)	0.7081

Conclusion: Tocilizumab was not associated with a significant improvement in rate of extubation, hospital discharge, or reduction in mortality in this retrospective cohort study of mechanically ventilated patients with COVID-19 pneumonia. Further studies are needed to determine whether earlier treatment may result in improved outcomes.

Disclosures: **All Authors**: No reported disclosures

564. Tocilizumab Induces Rapid, Sustained Improvement of Inflammatory Markers in COVID-19.

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Session: P-21. COVID-19 Treatment

Background: Frequent observation of increasing fever and rising inflammatory markers late after onset of COVID-19 suggests Cytokine Release Syndrome (CRS, "Cytokine Storm") may contribute to pathophysiology. Tocilizumab (TCZ), a monoclonal antibody targeting the receptor for the pro-inflammatory cytokine, IL-6, is effective in suppressing pathological inflammation in several rheumatological diseases. After administering TCZ to COVID-19 patients with suspected CRS, we observed a sharp fall in inflammatory indices. We analyzed this effect using results from the first 19 COVID-19 patients receiving TCZ at our hospital.

Methods: Data for all patients with confirmed COVID-19 who received TCZ at our center, a 200 bed community hospital in New England, were extracted from the Electronic Medical Record, including demographics, body temperature, C-Reactive Protein (CRP), IL-6 levels, clinical severity on the Ordinal Scale for Clinical Improvement (OSCI), and clinical outcome (recovery/discharge home, partial recovery/discharge rehab, death). Results were tabulated and statistical significance of changes in indices pre- and post- TCZ assessed by Wilcoxon Signed-Rank Test.

Results: 19 patients received TCZ: 16 got 400mg x1, 2 got 400 mg x2, 1 got 660 mg x1. Median age was 64 years (range: 44–94), 68% male. Mean interval from symptom onset to receiving TCZ was 11.5 days. Mean IL-6 was 145 pg/mL. Demographics, OSCI