

(97.24% CI, 44% to 96%;  $P = 0.002$ ) in 583 patients. In the final intention-to-treat analysis ( $N = 1057$ ), the adjusted relative risk reduction was 79% (95% CI, 50% to 91%;  $P < 0.001$ ) through Day 29 in recipients of sotrovimab ( $n=528$ ) vs. placebo ( $n=529$ ). Treatment with sotrovimab (ITT) resulted in a numerical reduction in the need for ER visits for illness management, hospitalization for acute illness management (any duration) or death (any cause) compared to placebo. No participants on sotrovimab required ICU admission, compared to 9 participants on placebo, of whom 4 participants required mechanical ventilation. No participants who received sotrovimab died, compared to 4 participants on placebo. The incidence of adverse events was similar between treatment arms and SAEs were numerically more common in the placebo arm.

**Conclusion.** Treatment with sotrovimab 500 mg IV resulted in a clinically and statistically significant reduction in progression of COVID-19 to hospitalization or death in patients with mild/moderate disease and was well-tolerated.

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### 503. In vitro Evaluation of Sitagliptin-HIV-1 Trans-activator Transcription Peptide Nano-formula for Antiviral Activity Against SARS-CoV-2: Drug Repurposing Approach

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**Session:** P-24. COVID-19 Treatment

**Background.** The outbreak of COVID-19 pandemic in China regarded as a major health/economic hazard. The importance of coming up with mechanisms for preventing or treating COVID-19 has been felt across the world. This work aimed at examining the efficiency of Sitagliptin (SIT) and human immunodeficiency virus type 1 (HIV-1) trans-activator transcription peptide (TAT) against SARS-CoV-2.

**Methods.** SIT-TAT nano-conjugates were prepared according to a full three-factor bi-level ( $2^3$ ) factorial design. SIT concentration (mM, X1), TAT concentration (mM, X2), and pH (X3) were selected as the factors. Particle size (nm, Y1) and zeta potential (mV, Y2) were assessed as responses. Characterization of the optimized formula for Fourier-transformed infrared (FTIR) and Transmission electron microscope was carried out. In addition, IC50 in Vero E6 cells, In vitro 3CL-protease inhibition and docking tests were investigated.

**Results.** The prepared complex's formula was as follows: 1: SIT: TAT molar ratio, whereas zeta potential and particle size values were at 34.17 mV and 97.19 nm, respectively. This combination did exhibit its antiviral potential against SARS-CoV-2 via IC50 values of 9.083 5.415, and 16.14  $\mu\text{M}$  for TAT, SIT-TAT, and SIT, respectively. In addition, the complex SIT-TAT showed a significant ( $P < 0.001$ ) viral-3CL-protease inhibitory effect (IC50 = 3.959  $\mu\text{M} \pm 0.011$ ) in comparison to isolated components (IC50 = 10.93  $\mu\text{M} \pm 0.25$ ) and TAT (IC50 = 8.128  $\mu\text{M} \pm 0.42$ ). This was further confirmed via in silico study. Molecular docking investigation has shown promising binding affinity of the formula components towards SARS-CoV-2 main protease (3-CL).

**Conclusion.** While offering significant binding interactions with protein's key pocket residues, an optimized formulation of SIT-TAT could guarantee both the enhanced delivery to the target cells and the improved cellular uptake. The presented

findings would guarantee further investigations regarding formula optimization against SARS-CoV-2.

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### 504. Case Series: Nasal Antimicrobial Photodisinfection (APDT) as Treatment Protocol for Asymptomatic and Early Stage COVID-19 Patients

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**Session:** P-24. COVID-19 Treatment

**Background.** Targeted reduction of SARS-CoV-2 viral load in the nose may mitigate the severity of lower tract respiratory disease as well as reduce hospitalization and mortality rates. Nasal Photodisinfection has been deployed for 10 years in Canadian hospitals reducing post-surgical infections. The objective of this work was to demonstrate effectiveness of APDT in early stage COVID-19 and asymptomatic carriers.

**Methods.** A cohort of 40 COVID-19 positive patients were treated with nasal photodisinfection (Steriwave) at a private clinic. All patients were previously identified by PCR as SARS-CoV-2 positive and admitted into the treatment cohort. BD rapid antigen nares testing was used before and after Photodisinfection treatment. Of the 40 patients, 13 were female and 27 were male. Age range was 9-56 years of age. Treatment involved 3-4 applications of photosensitizer and 16-24 minutes per patient of treatment time. Patients were followed up within 24 hours, 48 hours as well as day 5 and 6 and day 10/11. Patients filled out a COVID-19 score card.

**Results.** Results demonstrated APDT was capable of significant and rapid viral load reduction in COVID-19 carriers. 100% of patients were converted from positive rapid antigen test to negative. 60% of patients reported fever resolution within 24 hours. Fever resolution occurred in 100% of patients within 48 hours. Moreover, results demonstrated accelerated resolution of COVID-19 symptoms and significantly improved mental health benefits from reduction of COVID-19 related stress and anxiety. None of the patients experienced severe symptoms and no patients were hospitalized. Safety outcomes demonstrated no patient safety issues with only minor transient side effects (rhinorrhea, sneezing) observed. Moreover, the treatment procedure was pain-free and well tolerated by all patients.

**Conclusion.** Photodisinfection-based nasal decolonization anti-viral efficacy was demonstrated with improved outcomes for all patients treated in this case series. Significant rapid viral load reduction was confirmed by rapid antigen tests in all patients. More clinical studies are warranted in support of Photodisinfection based therapy for upper respiratory infections such as COVID-19.

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### 505. Impact of Remdesivir on SARS-CoV-2 Clearance in a Real-Life Setting: A Matched-Cohort Study

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COVID-BioB Study Group

**Session:** P-24. COVID-19 Treatment

**Background.** Evidence regarding the impact of remdesivir (RDV) on SARS-CoV-2 viral clearance (VC) is scarce. Aim of this study was to compare VC timing in COVID-19 patients who received RDV with those who did not.

**Methods.** Matched-cohort study conducted (25 February 2020-15 April 2021) at the IRCCS San Raffaele, Milan, Italy. The study enrolled hospitalized patients with pneumonia and a SARS-CoV-2 positive nasopharyngeal swab (NPS) at admission and at least one NPS during follow-up. Follow-up started at hospital admission and ended at the date of the first negative NPS (within 30 days after discharge). Patients who received RDV (cases) and patients who did not (controls) were matched based on age ( $\pm 5$  years), sex and PaO<sub>2</sub>/FiO<sub>2</sub> (P/F;  $\pm 10$  mmHg) values at admission. NPS were analyzed with RT-PCR. Results described as median (IQR) or frequency (%). Time to VC was estimated with Kaplan-Meier curve and compared with log-rank test.

**Results.** 648 patients were enrolled: 216 cases and 432 controls. Patients' characteristics at admission are reported in Table 1. VC was observed in 490 patients (75.6%) in a median time of 25 (16-34) days. Overall, time to VC was similar in patients receiving or not receiving remdesivir ( $p=0.519$ ). However, time to VC was different when considering both the use of RDV (yes vs no) and age ( $\leq$  or  $>$  63 years), as shown in Figure 1A. A significant finding was also observed considering the use of RDV and P/F values at admission ( $\leq$  or  $>$  200 mmHg), as reported in Figure 1B. Among the 490 patients who reached VC during follow-up, overall time to VC was similar in patients receiving or not receiving RDV ( $p=0.075$ ; Figure 2A); however, RDV use was associated with a higher probability of VC in the subgroup of patients with P/F admission values  $\leq 200$ mmHg ( $p=0.035$ ; Figure 2B), in the age group 55-65 years ( $p=0.025$ ; Figure 2C) and in patients with comorbidities ( $p=0.028$ ).

Table 1: Characteristics, respiratory function and laboratory values at admission of hospitalized patients according to the use of remdesivir

Variable	Category	Overall (n=648)	Remdesivir (n=216)	No remdesivir (n=432)	P-value
Age, years		64 (54 - 77)	63 (54 - 77)	64 (54 - 76)	0.817
Sex	Female	258 (39.8%)	86 (39.8%)	172 (39.8%)	1.000
Ethnicity	White	552 (85.2%)	174 (80.6%)	378 (87.5%)	0.025
Body Mass Index, Kg/m <sup>2</sup>		26.9 (24.4 - 30.5)	27.1 (24.2 - 31.0)	26.8 (24.5 - 30.1)	0.55
Duration of symptoms, days		8 (5 - 11)	7 (4 - 9)	8 (5 - 11)	0.009
Number of comorbidities					0.921
	0	228 (35.2%)	80 (37%)	148 (34.3%)	
	1	188 (29%)	61 (28.2%)	127 (29.4%)	
	2	124 (19.1%)	40 (18.5%)	84 (19.4%)	
	3	108 (16.7%)	35 (16.2%)	73 (16.9%)	
Neurological disorder/dementia		48 (7.4%)	19 (8.8%)	29 (6.7%)	0.343
Cardiovascular disease		177 (27.3%)	58 (26.9%)	119 (27.5%)	0.926
Cancer		91 (14%)	33 (15.3%)	58 (13.4%)	0.549
Diabetes		106 (16.4%)	30 (13.9%)	76 (17.6%)	0.260
Hypertension		305 (47.1%)	97 (44.9%)	208 (48.1%)	0.436
PaO <sub>2</sub> /FIO <sub>2</sub> , mmHg					0.802
	>200	302 (46.6%)	99 (45.8%)	203 (47%)	
	≤200	346 (53.4%)	117 (54.2%)	229 (53%)	
PaO <sub>2</sub> /FIO <sub>2</sub> , mmHg					0.416
	>100	473 (73%)	162 (75%)	311 (72%)	
	≤100	175 (27%)	54 (25%)	121 (28%)	
ALT, U/L		33.5 (22 - 53)	32 (21 - 51.5)	35 (23 - 56)	0.179
Creatinine, mg/dL		0.93 (0.78 - 1.15)	0.92 (0.76 - 1.09)	0.95 (0.78 - 1.19)	0.016
Lactic acid dehydrogenase, U/L		328.5 (265 - 422)	320.5 (261 - 408)	337.5 (265 - 425)	0.176
Lymphocytes, 10 <sup>9</sup> /L		1 (0.7 - 1.3)	0.9 (0.65 - 1.2)	1 (0.7 - 1.4)	0.002
C-reactive protein, mg/L		55.35 (26.3 - 110.2)	50.5 (25.5 - 96.05)	60.7 (26.9 - 116.8)	0.125
D-dimer, mcg/L		0.89 (0.51 - 1.69)	0.79 (0.42 - 1.42)	1.05 (0.61 - 1.99)	<0.0001
Interleukin-6, pg/mL		26.8 (9.3 - 53.9)	21.2 (6.5 - 39.9)	36.1 (13.7 - 69.6)	0.0001

FIGURE 1A. Time to viral clearance according to the use of remdesivir (yes vs no) and age ( $\leq 63$  years vs  $> 63$  years)

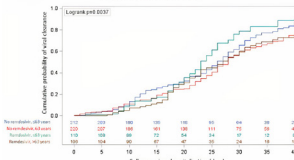


FIGURE 1B. Time to viral clearance according to the use of remdesivir (yes vs no) and PaO<sub>2</sub>/FIO<sub>2</sub> at admission ( $\leq 200$ mmHg vs  $> 200$  mmHg)

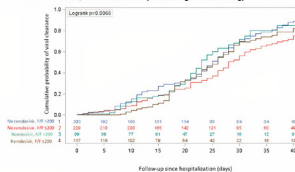
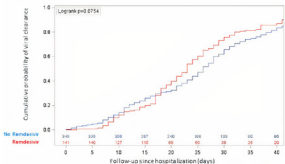
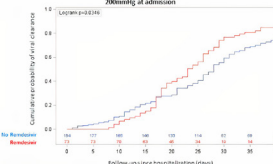


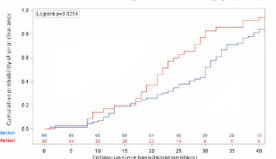
Figure 2. Panel A. Time to viral clearance according to remdesivir use



Panel B. Time to viral clearance according to remdesivir use in patients with a P/F ratio  $\leq 200$ mmHg at admission



Panel C. Time to viral clearance according to remdesivir use in the age group 55-65 years



Time to viral clearance among the 490 patients who reached VC during follow-up. Panel A: time to VC according to RDV use. Panel B: time to VC according to RDV and P/F ratio value at admission. Panel C: time to VC according to RDV in the age group 55-65 years.

**Conclusion.** Time to viral clearance was similar in patients receiving or not receiving remdesivir; however the use of RDV was associated with a benefit on time to viral clearance in younger patients and in those with a P/F ratio at admission  $\leq 200$  mmHg.

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**506. Outpatient Bamlanivimab, Casirivimab and Imdevimab for COVID-19: Single Center Feasibility Analysis**

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Session: P-24. COVID-19 Treatment

**Background.** Monoclonal Antibodies directed at the spike protein of SARS-COV-2 are approved by the FDA for Emergency Use for outpatients with COVID-19 who are at risk for severe complications. Here we present a single center experience using Bamlanivimab and Casirivimab/Imdevimab to prevent hospitalizations due to SARS-COV-2.

**Methods.** Adult patients who tested positive for SARS-COV-2 in our health system were offered outpatient monoclonal antibody infusion if: (1) testing was done within the previous 7 days, (2) the patient had fewer than 10 days of symptoms, (3) the patient was not currently hospitalized, and (4) met at least 1 of 8 criteria in the FDA EUA Fact Sheet for Bamlanivimab and Casirivimab/Imdevimab. Patients who met the criteria were offered the monoclonal antibody available at time of infusion. Those who declined antibody infusion were used as potential controls. The primary outcome was the discrepancy in hospitalization rates at 14-days past the infusion date for patients receiving the monoclonal antibody regimen versus 14-days past when those in control group would have been scheduled for infusion had they accepted. Secondary outcomes included emergency room visits, duration of hospitalization, and Intensive Care Unit stays. Coarsened exact matching (CEM) was used to obtain balance between treatment and control groups. A logistic regression model measured statistical differences between the groups.

**Results.** Between November 23, 2021 and February 8, 2021, 5567 patients were offered a monoclonal antibody infusion. A total of 894 patients completed infusion who were able to be matched with patients in the control group. Patients who received the infusion were statistically less likely to be hospitalized than those who did not receive the infusion (2.68% vs 6.70%,  $p<0.001$ ).

**Outcomes of Weighted Matched Data; Either Monoclonal Antibody**

Measure	Either Monoclonal Antibody				
	Received	Did Not Receive	Difference	p-value <sup>1</sup>	Significance
Effective Sample Size	894	3957			
Hospitalized	2.68%	6.70%	4.02%	<.001	***
ED Visit	2.68%	6.77%	4.09%	<.001	***
Hospitalized or ED Visit	5.15%	12.46%	7.32%	<.001	***

<sup>1</sup>Wald test of estimated coefficients using robust standard errors

**Conclusion.** This feasibility study shows reduction in hospitalization in patients who received monoclonal antibody versus standard care. It provides real-world information regarding using monoclonal antibodies as a tertiary prevention strategy to limit the progression of SARS-CoV2 infections, which will lead to improved clinical outcomes and decreased healthcare costs.

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**507. Impact of Baricitinib on Outcomes in Patients Treated with Remdesivir and Dexamethasone for SARS-CoV-2 Pneumonia: A Retrospective Cohort Study**

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Session: P-24. COVID-19 Treatment

**Background.** There is a lack of data specifically addressing the effects of triple therapy consisting of baricitinib plus remdesivir plus dexamethasone compared to dual therapy with remdesivir plus dexamethasone among patients with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pneumonia.

**Methods.** This retrospective study enrolled hospitalized adults with SARS-CoV-2 receiving supplemental oxygen without invasive mechanical ventilation (IMV) being treated baricitinib ( $\leq 10$  days) plus remdesivir ( $\leq 10$  days) plus dexamethasone ( $\leq 10$  days) or remdesivir ( $\leq 10$  days) plus dexamethasone ( $\leq 10$  days). The primary