Philippine COVID-19 Living Clinical Practice Guidelines
Institute of Clinical Epidemiology, National Institutes of Health, UP Manila
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EVIDENCE SUMMARY

Should fatty acid supplements be used as adjunct treatment for patients with COVID-19?

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RECOMMENDATION

There is insufficient evidence to recommend the use of fatty acid supplements as adjunct treatment for patients with COVID-19. *(Low quality of evidence)*

Consensus Issues

There were no reported adverse events in the study that assessed the effect of addition of 1000mg omega-3-fatty acid supplementation to enteral feeding of hospitalized patients with COVID-19. There was no significant difference in reported adverse events between groups given fatty acid supplementation or placebo in critically-ill ICU patients (non-COVID).

In terms of cost, a capsule of 1000mg omega-3-fatty acid may cost less than Php 20.00 in the market. It was also remarked that patient preference may be affected because of the fishy taste.

Key Findings

There is low certainty of evidence based on one RCT (N=128) that compared omega-3-fatty acid supplementation of high-protein enteral feeding versus hi-protein enteral feeding alone in hospitalized patients with COVID-19, which showed significant reduction in mortality (available case analysis, RR 0.85, [0.73, 0.99]). The RCT did not report adverse events. Indirect evidence on adverse events from two meta-analyses of RCTs on critically-ill ICU patients (non-COVID), mostly with ARDS, given fatty acid supplementation versus control, showed that gastrointestinal adverse events were common but did not differ significantly between groups (RR 1.04, 95% CI 0.96, 1.13; moderate certainty of evidence).

Introduction

Essential fatty acids (EFA) are polyunsaturated fatty acids (PUFA) that are necessary for health, but must be provided by foods because they cannot be synthesized by the body. There are two families of EFA, omega-3 (ω-3) and omega-6 (ω-6). The main omega-3-fatty acids are alpha-linolenic acid (ALA), an essential fatty acid obtained from plant food (flaxseed, soybean, canola) and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), from shellfish and fish [1]. They can also be found in dietary supplements and prescription medications [2]. Linoleic acid is a polyunsaturated omega-6 fatty acid.

Omega-3-fatty acids and its bioactive lipid mediators may reduce inflammatory markers, reduce oxidative stress, mitigate hypercoagulation and thus, potentially lower the cardiovascular complications due to COVID-19 [3].

Omega-3-supplementation is recommended by the American Heart Association to prevent clinical CVD events in patients with prevalent CHD such as a recent MI [4] and as monotherapy or as an adjunct to other lipid-lowering agents in patients with hypertriglyceridemia [5].

In an app-based survey of 327,720 UK participants, the use of omega-3 fatty acids, was associated with a lower risk of SARS-CoV-2 infection by 13%(95%CI: [8%,16%]), after adjusting for potential confounders [6]. A cross-sectional study of 100 hospitalized patients with COVID-19 at a US medical center showed that there was no significant association between adequate levels (≥5.7%) versus inadequate levels (<5.7%) of omega-3 index (O3I, RBC EPA+DHA levels) and death (adjusted OR for age and sex 0.28 (0.03, 1.26 , P=0.11)] [7].

Three meta-analyses of RCTs (25 unique RCTs; N=1015 to 3574) that compared fatty acid supplements given to critically-ill adult patients with ARDS (non-COVID) in the ICU showed no significant difference in mortality between groups given and not given, although ventilation duration was significantly reduced (very low to low certainty of evidence) [8–10]. Adverse events in the 2 meta-analyses [8,9] did not differ significantly between groups.

Review Methods

We included studies with the following inclusion criteria:

P – Patients diagnosed with COVID-19
I – Oral fatty acid supplements plus Standard of care
C – Placebo or No treatment plus Standard of care
O – mortality, clinical deterioration/ development of ARDS, need for mechanical ventilation, hospital length of stay, time to clinical improvement/ recovery, improvement in Chest CT Scan/ X-ray, virologic clearance by PCR test, adverse effects
S – RCTs, CCTs, observational studies (cohorts, case-control studies, case reports)
Subgroup analysis - Severity of disease (mild, moderate, severe); Oxygen requirement (non-O2 requiring, O2 requiring, mechanically ventilated), age, comorbidity, dosage (if this is variable among studies)

We excluded virgin coconut oil since there is a separate Philippine Living COVID CPG review on this topic. We also excluded studies on prevention of COVID-19.

We searched the following until 3 April 2021:

a. COVID living evidence databases such as COVID-19 Open Living Evidence Synthesis: https://covid-nma.com/; Australian Guidelines for the Clinical Care of People with COVID-19 (https://covid19evidence.net.au/, WHO Therapeutics and COVID-19: living guideline: https://www.who.int/publications/i/item/therapeutics-and-covid-19-living-guideline and UpToDate.com
b. MEDLINE (through PubMed), CENTRAL, MedrXIV/BiorxIV, ChinaXIV, Clinicaltrials.gov, and WHO-ICTRP, using search strategies with the concepts of COVID and fatty acids

Results

Efficacy

We found one RCT (N=128) that investigated the addition of omega-3 1000 mg capsule into a high-protein formula (30 kcal/kg/d) through enteral feeding, compared to high-protein formula alone. Doaei et al. enrolled patients with COVID-19 who were critically ill and admitted to Razi Hospital in Iran from May to July 2020 (mean age 64-66 years, males 54-62%; BMI 27.4 to 27.7 kg/m2). The authors reported significantly higher survival rate at one month in the fatty acid group compared with the control group (21% vs 3%, P = 0.003) [11]. When we did available- case

analysis, where patients who died were included in the analysis, we found statistically significant reduction in mortality (29/35 vs 78/80; RR 0.85 [0.73, 0.99]). Sensitivity analysis was also done to consider the impact of missing data of 7/42 (17%) for FA group vs 6/86 (7%) for control group. Worst-case scenario sensitivity analysis, assuming that all missing participants in the fatty acid group died, changed the conclusion to no significant difference (36/42 vs 78/86; RR 0.95 [0.82, 1.09]), while conclusion for best case scenario remained unchanged but with a wider confidence interval (29/42 vs 84/86; RR 0.71 [0.58, 0.87]) [11]. Evidence for this study was downgraded to low certainty of evidence due to high risk of attrition bias that changed conclusion with worst-case sensitivity analysis, and imprecision (wide CI crossing line of appreciable benefit, RR<0.75).

Safety

The study by Doaei did not contain adverse event reporting on the use of fatty acids. Indirect evidence from two systematic reviews and meta-analyses on patients with non-COVID 19 ARDS showed that adverse effects were mostly gastrointestinal, such as diarrhea, nausea/vomiting and abdominal distension; they were common in both groups given and not given fatty acids (range, 14 to 52%) and not significantly different between the two (16%, 33/209 versus 14%, 30/218; RR 0.91, 95% CI [0.67 to 1.23]) [8]; 52%, 321/620 versus 50%, 310/616; RR 1.04, [0.96, 1.13], very low quality of evidence because of indirectness) [9].

Recommendations from Other Groups

The CDC, WHO and IDSA have no recommendations on the use of dietary supplements in the treatment nor prevention of COVID-19.

Research Gaps

There are 16 registered trials on fatty acid supplementation in patients with COVID-19 (Appendix 3).

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Appendix 1. Characteristics of Included Studies

Study ID	Sample Size	Participants (age, sex, clin severity, etc) (inclusion/exclusion)	Intervention (generic/brand name; dosage, duration)	Comparator (generic/brand name; dosage, duration)	Outcomes
Direct Evidence					
Doaei 2021	N=128	patients with COVID-19 who were hospitalized and critically ill (mean age 64-66 years, males 54-62%; BMI 27.4 to 27.7 kg/m2).	Omega-3 1000 mg capsule into a high-protein formula (30 kcal/kg/d) through enteral feeding,	High-protein formula through enteral feeding	Mortality Laboratory markers
Safety-Indirect Evidence					
Koekkoek 2019 meta-analysis Searched Jan 2018	24 RCTs (N=3574)	Critically ill adult patients (>95% of patients >18 y of age). 8 on ARDS 3 on sepsis 3 trauma 7 gen ICU	Enteral supplementation of FO (v-3 fatty acids) or FO-containing EN Excluded: Parenteral FO	control or placebo intervention.	mortality, ICU or hospital LOS, duration of mechanical ventilation, and infectious complications
Langlois 2018 meta-analysis Search date not stated	12 RCTs (N=1280)	intensive care unit (ICU) patients with ARDS	Omega-3-FA	Placebo	PaO2/FiO2 ratio evaluated early (3-4 days) and later (7-8 days), mortality, ICU/hospital length of stay (LOS), length of mechanical ventilation (MV) and infectious complications.

Appendix 2: GRADE Evidence Profile

FA compared to control for COVID (Doaei)

Certainty assessment							Summary of findings				
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With control	With FA		Risk with control	Risk difference with FA
Mortality (Available-case analysis) (follow up: 1 month)											
115 (1 RCT)	serious [a]	not serious	not serious	serious [c]	none	⨁⨁◯◯ LOW	78/80 (97.5 %)	29/35 (82.9 %)	**RR 0.85** (0.73 to 0.99)	975 per 1,000	**146 fewer per 1,000** (from 263 fewer to 10 fewer)
Mortality (Sensitivity analysis - Worst-case scenario) (follow up: 1 month)											

FA compared to control for COVID (Doaei)

Certainty assessment							Summary of findings				
128 (1 RCT)	serious [b]	not serious	not serious	not serious	none	⨁⨁⨁◯ MODERATE	78/86 (90.7 %)	36/42 (85.7 %)	**RR 0.95** (0.82 to 1.09)	907 per 1,000	**45 fewer per 1,000** (from 163 fewer to 82 more)

Mortality (Sensitivity analysis - Best-case scenario) (follow up: 1 month)

128 (1 RCT)	serious [b]	not serious	not serious	serious [c]	none	⨁⨁◯◯ LOW	84/86 (97.7 %)	29/42 (69.0 %)	**RR 0.71** (0.58 to 0.87)	977 per 1,000	**283 fewer per 1,000** (from 410 fewer to 127 fewer)

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. available-case analysis used due to lost to ffup due to discontinued enteral feeding
b. attrition bias for the lost to ff-up due to discontinued enteral feeding
c. wide CIs with lower limit crossing appreciable benefit of RR<0.75
Note: AE were not reported

Appendix 3: Characteristics of Ongoing Studies

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
1	Control of inflammatory parameters with omega-3 fatty acid supplementation in adult patients with parenteral nutrition and respiratory infection by SARS-CoV-2: randomized clinical trial COVID-19. EudrACT 2020-000705-86 Estimated primary completion date: 26-08-2020 Phase 4 RCT (N = 117) Spain; univ hospital	18-65 y.o. inclusion criteria: • Age ≥ 18 years. • Patients with at least 5 days of PN. • Baseline liver parameters before PN: GGT, alkaline phosphatase < 100 U/dL and direct bilirubin <1.2 mg/dL al inicio de NP. • Liver parameter alterations: GGT ≥ 300 U/dL, alkaline phosphatase ≥ 200 U/dL or direct bilirubin ≥1.8 mg/dL • Forseeing to receive at least 5 days of PN. • Admitted in the ICU of the Valle Hebron University Hospital Principal exclusion criteria: - Lipids administration contraindicated - Have a history of hypersensitivity of idiosincratic reactions to any component of intravenous lipid emulsions. - Home parenteral nutrition patients	TPN emulsion with 30% omega FA OMEGAVEN (Omega-3-Fatty Acids 90 10%)	NUTRIFLEX LIPID SPECIAL (Essential amino acids 56%; GLUCOSE ANHYDROUS PH EUR 158%; LONG-CHAIN TRIGLYCERIDES 5%) OMEGAFLEX SPECIAL (Essential amino acids 4%; GLUCOSE ANHYDROUS PH EUR 158%; Long chain TG 4%) OLIMEL N9 (Essential AA 57%; GLUCOSE ANHYDROUS PH EUR 11%; Long chain TG 4%) SMOFKABIVEN (Essential AA 5%; GLUCOSE ANHYDROUS PH EUR 125%; Long chain TG 36%) SMOFLIPID (Long chain TG 20%)	Primary end point(s): Primary end point is the change of liver function parameters: GGT ; from the value the day of inclusion to the end of PN. Secondary end point(s): Infection rate, hyperglycemia rate, hypertrygliceridemia rate, ICU and hospital length of stay.

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
		- Liver transplantation - Liver parameters alterations before PN: 20% above upper normal values			
2	A Randomised, Double-blind, Placebo Controlled Study of Eicosapentaenoic Acid (EPA-FFA) Gastro-resistant Capsules to Treat Hospitalised Subjects With Confirmed SARS-CoV-2 NCT04335032 Not yet recruiting November 9, 2020 - July 31, 2021 RCT (N=284)	Inclusion: 18 y.o. and up; moderate-severe COVID Exclusion: requiring oxygen support	EPA-FFA	placebo	Primary: time to treatment failure; Secondary: time to and amount of clinical improvement, change in recovery and survival rate
3	Use of a Medical Device, Viruxal Oral and Nasal Spray, for Treating the Symptoms of COVID-19 Via Application to the Naso- and Oropharyngeal Mucosa NCT04357990 Recruiting	Inclusion: 18 and up; symptomatic; mild-moderate disease. Exclusion: severe disease	Viruxal Oral and Nasal Spray	placebo spray	Primary: number of days until complete resolution of symptoms per group; number of hospital admissions per group. Secondary: number of days until reduction of symptoms; number of adverse events per group

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
	September 4, 2020 to March 2021 RCT (N=128) Iceland, National Hospital of Iceland				
4	Nebulised surfactant for the treatment of severe COVID-19 in adults (COV-Surf): A structured summary of a study protocal for a randomized controlled trial NCT04362059 EudraCT number: 2020-001886-35 Recruiting October 2020 - November 2021 RCT (N=12) England, 2 university hospitals	Inclusion: 18 and up; requiring endotracheal intubation. Exclusion: imminent expected death within 24 hours; stage 4 chronic kidney disease	lung surfactant	placebo	Primary: improvement in oxygenation; pulmonary ventilation. Secondary: adverse events, adverse device effects, change in pulmonary compliance, change in PEEP requirement of ventilatory support, clinical improvement, mechanical ventilation
5	An Investigation on the Effects of Icosapent Ethyl (VascepaTM) on Inflammatory Biomarkers in Individuals With COVID-19	Inclusion: 18 and up, symptomatic. Exclusion: hospitalized, life expectancy < 3 months, acute end-organ injury, active severe liver disease, pancreatitis,	icosapent ethyl	usual care	Primary: hs-CRP levels

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
	(VASCEPA-COVID-19) NCT04412018 Recruiting June - December 2020 RCT (N=100) Canada, Diagnostic and Cardiology clinic	pregnant, hemodynamic instability			
6	PREPARE-IT. Prevention of COVID19 With EPA in Healthcare Providers at Risk - Intervention Trial NCT04460651 Recruiting August 2020 - January 2021 RCT N=2000 Argentina, Clinic	Inclusion: 18 and up, medical workers, with exposure to aerosol-generating procedure w COVID patients, relatives of COVID-19 index cases, lab staff running COVID-19 tests	icosapent ethyl	placebo	Primary: COVID positive, highest mean WHO descriptive score of COVID-19. Secondary: hospital length of stay, mechanical ventilation, hospital admissions, rate of total events
7	Randomized, Open-label, Parallel Study to Investigate Safety and Efficacy of CARDIO Softgels Plus Best	Inclusion: 18-75 yo, former smoker, admitted, mild-moderate disease, not of child-bearing potential or	CARDIO softgel + standard of care	standard of care	Primary: oxygenation requirements. Secondary: clinical improvement, clinical status, CT or X-ray findings, time to clinical recovery, hospitalization period,

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
	Standard-of-care vs. Best Standard-of-care Alone on a Former Smoker and/or Steroid-resistant Asthma Population With COVID-19 Infection NCT04465513 Not yet recruiting August 2020 - August 2021 RCT (N=100) Canada	using birth control for duration of study. Exclusion: antiretroviral agents, oxygen support, uncontrolled hypotension, renal impairment, GI symptoms			amount of time on ventilator, ICU stay, QoL, all-cause mortality, temperature measurements, oxygen saturation measurements, COVID-19 QoL measurements
8	The Effect of Omega-3 Supplements on the Serum Levels of Selected Cytokines Involved in Cytokine Storm of Covid-19; A Randomized Clinical Trial in the Covid-19 Uninfected Jordanian People NCT04483271 Enrolling by invitation	Inclusion: 20-66 y.o. with no medical diagnosis of COVID-19 infection. Exclusion: chronic immune problems, pregnant, breastfeeding, using hormonal contraceptives	1000mg wild salmon and fish oil complex, which contains 300mg of omega3-FA	no intervention	Primary: IL-1 beta, IL-6, TNF alpha. Secondary: lipid profile, fasting blood glucose

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
	October - December 2020 RCT N=100 Jordan				
9	Omega-3 Supplementation for the Treatment of COVID-19 Infection-Related Olfactory Dysfunction NCT04495816 Recruiting August - November 2020 RCT N=176	Inclusion: 18 and up with olfactory dysfunction associated with COVID-19. Exclusion: pre-existing olfactory dysfunction, chronic rhinosinusitis, hsitory of sinus surgery, current use of nasal steroid sprays or omega-3 supplementation	omega-3 supplementation	placebo	Brief Smell Identification Test
10	A Pragmatic Randomized Trial of Icosapent Ethyl for High-Cardiovascular Risk Adults (MITIGATE) NCT04505098 Recruiting August 2020 - August 2021 RCT N=16500	Inclusion: 50 and up, no history of confirmed COVID-19, established ASCVD. Exclusion: receipt of IPE within 12 months before enrollment, omega-3 fatty acid usage, pregnant or planning to become pregnant, hospitalization for MI and/or elective PCI within past month, receiving triple anti-thrombotic therapy, stage D heart failure,	icosapent ethyl	usual care	Primary: moderate-severe confirmed viral URIs, worst clinical status due to URI. Secondary: all-case mortality, CV event, hospitalization, ED visits

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
	United States, California	severe liver disease, end-stage renal disease, metastatic cancer, institutionalized and/or palliative care			
11	A Randomized, Parallel-group Treatment, Quadruple Masked, Two-arm Study, to Assess the Effectiveness of Cod Liver Oil Compared to Placebo in the Prevention of Covid-19 and Airway Infections in Healthy Adults NCT04609423 Recruiting November 2020 - May 2021 RCT N=80000 Norway, university hospital	Inclusion: 18 years and older. Exclusion: renal failure, hypercalcemia, liver cirrhosis, sarcoidosis, granulomatous disease, pregnancy or planned pregnancy, vegan diet, age >75, previous COVID-19 disease	cod liver oil	corn oil	Primary: COVID positive; respiratory tract infection. Secondary: hospitalization due to COVID-19, ICU due to COVID-19, all-cause hospitalization, number of visits at GP for infections, number of GP visits
12	Resolving Inflammatory Storm in COVID-19 Patients by Omega-3 Polyunsaturated Fatty Acids - A Single-blind, Randomized, Placebo-	Inclusion: 18 and up, COVID-19 positive, requiring hospitalization. Exclusion: according to intervention contraindications, pregnancy and breastfeeding	docosahexaenoic acid(DHA) + eicosapentaenoic acid (EPA)	placebo	Primary: inflammatory biomarkers Secondary: length of hospital stay, ICU need, mortality

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
	controlled Feasibility Study NCT04647604 Recruiting June 2020 - April 2021 RCT N=40 Sweden				
14	Efficacy and Safety of Ozonised Oil (HOO) as Adjuvant Nutrition Supplement in COVID-19 Patients With Mild-to-Moderate Disease - HOO-COVID Project NCT04651387 Not yet recruiting January- June 2021 RCT N=74	Inclusion: 18-80 yo, COVID-19 severity score < 6, hospitalized < 48 hours. Exclusion: pregnancy and breastfeeding, severe COVID, ventilator, requiring oxygen support, liver failure, alcohol and drug abuse	ozonised oil capsule	standard of care	Primary: viral load. Secondary: virologic clearance, SaO2, hospitalization stay, ICU, COVID severity score, in-hospital mortality
15	Anti-inflammatory/Antioxidant Oral Nutrition Supplementation in COVID-19 (ONSCOVID19) NCT04323228	18-65 yrs old, SARS-COV-2 patients, stable, not requiring ICU admission	Enriched Oral Nutritional Supplement (ONS) (enriched in eicosapentaenoic acid, gamma-linolenic acid and antioxidants)	Control-ONS (iso-caloric - isonitrogenous product) will have the same macronutrient composition, calorie	Change from baseline score of Nutrition risk screening-2002; serum ferritin; IL-6;CRP; serum TNF-alpha;MCP-1 (Time frame: 3 months)

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
	Not yet recruiting May 1 - October 1, 2020 RCT (N=40) Saudi Arabia		14.8 g protein, 22.2 g fat, 25 g carbohydrate, 355 kcal, 1.1 g EPA, 450 mg DHA, 950 mg GLA, 2840 IU vitamin A as 1.2 mg β-carotene, 205 mg Vitamin C, 75 IU vitamin E, 18 ug Selenium, and 5.7 mg Zinc	density, and normal concentrations of vitamin A, C, E, Selenium and zinc	
16	Treatment with Omega-3 polyunsaturated fatty acids in COVID-19 patients. A single-blind, randomized, placebo-controlled feasibility study EUCTR2020-002293-28-SE RCT	18 years of age; COVID-19 positive or typical CT image of COVID-19 infection; Clinical status requiring hospitalization.	INTERVENTION: Trade Name: Omegaven IV Emulsion for infusion Other descriptive name: HIGHLY REFINED FISH OIL	Placebo	PRIMARY OUTCOME: Changes in a panel of inflammatory biomarkers measured in blood samples, urine samples and released from ex vivo stimulated leukocytes after 5 days of treatment. SECONDARY OUTCOME: 1. Changes in proresolving mediators after 5 days of treatment 2. Changes in omega-3 index in the erythrocyte fraction after 5 days of treatment 3. Changes in cardiac biomarkers (Troponin, NTproBNP) after 5 days of treatment

No.	Title/Study ID	**Participants (age, sex, clin severity, etc) (inclusion/exclusion)**	**Intervention (generic/brand name; dosage, duration)**	**Comparator (generic/brand name; dosage, duration)**	**Outcomes**
					4. Changes in biomarkers of organ damage (LD, creatinine) after 5 days of treatment 5. Changes in thrombosis and coagulation parameters (platelet count, coagulation) after 5 days of treatment 6. Changes in infectious load (PCT, SARS-CoV2-RNAemia, antibodies) after 5 days of treatment 7. Effects on clinical parameters (NEWS2, oxygen need, length of hospital stay, ICU need, complications, mortality)