Buongiorno a tutti,

abbiamo il piacere di presentare quanto elaborato dal Dr. Domenico Mastrangelo

IL PRESIDENTE.

Autorizzazione all'uso in condizioni di emergenza (Emergency Use Authorization – EUA) pr il vaccinoBNT162b2 mRNA (Pfizer) per il COVD-19

Riguardo all'impiego del vaccinoPfizer-BioNTech COVID-19 e alle norme di legge per l'approvazione in condizioni di emergenza (Emergency Use Authorization – EUA), è opportuno sottolineare come tali norme siano, di fatto, disattese, ove si vada ad analizzare la documentazione fornita della Food & Drug Administration (FDA) e dagli enti regolatori preposti.

Nel documento ufficiale intitolato "Emergency Use Authorization for Vaccines to Prevent COVID-19: Guidance for Industry" (1)leggiamo: "La Food & Drug Administration pubblica questa guida, per fornire agli sponsor che lo richiedano, le raccomandazioni in base alle quali è possibile fare richiesta di approvazione per l'uso di vaccini, farmaci o altri prodotti, in condizioni di emergenza, relative alla sezione 564 della Legge Federale su cibi, farmaci e cosmetici (FD&C Act) 21 U.S.C. 360bbb-3, per un vaccino sperimentale per la prevenzione del COVID-19, per tutta la durata dell'emergenza legata alla pandemia di COVID-19".

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In base a quanto suggerito dalla stessa FDA, si assume che la "pandemia" di COVID-19 rappresenti un'emergenza sanitaria, che può giustificare l'uso di un prodotto (in questo caso non si tratta di un vaccino) sperimentale, idoneo a prevenirla.

Con Richard Horton (già editore capo di The Lancet) (2), tuttavia, possiamo osservare che il termine più appropriato per definire l'attuale "pandemia" di COVID-19, è quello di "sindemia", poiché, in questo caso, come sempre accade per l'influenza stagionale, sono due le categorie di patologia che interagiscono, all'interno della popolazione: l'infezione da SARS-CoV-2 e tutta una gamma di malattie non trasmissibili (NCDs = Non Communicable Diseases)

La "sindemia" non è soltanto una co-morbosità (ovvero l'associazione di due o più patologie, nello stesso individuo), ma si caratterizza per le interazioni biologiche e sociali tra condizioni diverse, che aumentano la suscettibilità dell'individuo stesso al danno o peggiorano l'andamento di una malattia. Nel caso del COVID-19, puntare alle malattie non trasmissibili (che si associano a quella infettiva), è un prerequisito per il successo terapeutico. Curare al COVID-19, significa curare anche l'ipertensione, l'obesità, il diabete, le malattie croniche (cardiovascolari, neurodegenerative, ecc.) e il cancro, che si possono associare alla malattia infettiva virale.

Riguardo, poi, alla condizione di "emergenza sanitaria pubblica", è degno di nota il fatto che, almeno in Italia, già dal mese di maggio del 2020, non si registravano più morti in eccesso (e dunque, la "pandemia" era terminata!) e le morti per COVID-19 risultavano sovrastimate (3),sebbene le autorità pubbliche nazionali non abbiano mai dichiarato la fine dell'"emergenza", che ancora continua alla data del presente comunicato, e promette di durare per tutto il 2022!

Pertanto, sebbene una vera emergenza sanitaria non esista, almeno in Italia, il vaccino sperimentale contro il COVID-19, viene attualmente usato, senza che vi sia alcuna prova dell'esistenza di un'emergenza di sanità pubblica.

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E' interessante, per altro, notare che le raccomandazioni della FDA sopra menzionate (1), stabiliscono che l'ente istituzionale americano conceda una EUA, dopo aver determinato che:

a."... l'agente chimico, biologico (in questo caso, il virus SARS-CoV-2), radiologico, ecc., può causare una malattia grave, che mette a rischio la vita delle persone", ma questo non è il caso del SARS-CoV-2, dato il basso tasso di mortalità (circa il 2% dei casi confermati da un tampone molecolare evidentemente inaffidabile e circa lo 0,02% dell'intera popolazione mondiale), e l'elevato tasso di "infezioni" (positività al test) asintomatiche (98%, appunto, dei positivi al test) (4, 5);

b."... sulla base della totalità dell'evidenza scientifica disponibile, inclusi i dati di sperimentazioni cliniche adeguate e ben controllate, se disponibili, è ragionevole credere che il prodotto possa essere efficacenel prevenire, diagnosticare o trattare tale malattia grave o pericolosa per la sopravvivenza, causata dal SARS-CoV-2 ...", ma anche questo non è il caso del vaccino Pfizer-BioNTech COVID-19. Di fatto, questo vaccino non previene l'infezione da SARS-CoV-2, ma riduce soltanto il numero dei casi sintomatici (6), per altro, in modo scarsamente significativo. Inoltre, riguardo alla dichiarata efficacia del 95%, nel prevenire lo sviluppo del COVID-19, dopo due iniezioni distanziate di 21 giorni, con Peter Doshi possiamo osservare che: "Nessuna delle sperimentazioni attualmente in corso è progettata per trovare una riduzione negli esiti più gravi della malattia, come il ricovero in ospedale, il ricovero in unità di terapia intensiva o la morte. Gli studi in corso, non sono neanche progettati per determinare se il vaccino sia in grado di interrompere la trasmissione del virus." (7)

c." ... I noti e potenziali effetti benefici del prodotto, quando usato nella diagnosi, nella prevenzione o nel trattamento della malattia grave o letale, sono di gran lunga superiori ai potenziali rischi impliciti nell'uso del prodotto stesso ...", e nemmeno questo è il caso del vaccine Pfizer contro il COVID-19, poiché, come abbiamo dimostrato nelle precedenti sezioni, le sperimentazioni cliniche

effettuate per studiare i profili di efficacia e sicurezza del vaccino, non consentono un'adeguata valutazione del rapporto tra rischi e benefici;

d." ... non esiste un'alternativa adeguata, approvata e disponibile al prodotto impiegato per la diagnosi, la prevenzione (il vaccino, appunto) o la terapia della malattia o condizione indicata ...", ed ancora, questo non è il caso della terapia del COVID-19, data la lista, completa ed esaustiva, fornita dal National Institutes of Health (NIH), con i risultati degli studi riguardanti un gran numero di possibili trattamenti della malattia, quali, tra gli altri:

a.Remdesivir(9-14);
b.Ivermectina(15-32);
c.Idrossichlorochina(33-39);
d.Chlorochina(40, 41);
e.Corticosteroidi(41-50);
f.Azitromicina (51-53);
g.Antivirali(54-56);
h.Plasma convalescente (57-64);
i.Immunoglobuline endovena(65);
j.Cellule staminali mesenchimali(66-69);
k.Interferoni(70-73);
l.Inibitori della Tirosin Chinasi(74-78);
m.Derivati dell'eparina (79-84);
n.Vitamina C (acido ascorbico)(85-89);
o.Vitamina D(90-94);
p.Zinco(95, 96) ... e altri ancora!

Da quanto sopra esposto, è possibile concludere che, riguardo all'impiego del vaccino BNT162b2 mRNA Covid-19 (Pfizer), nessuno dei requisiti legali per la richiesta di autorizzazione in situazioni di emergenza (EUA) è rispettatoe pertanto, l'impiego di

questo vaccino per vaccinazioni di massa, è da considerarsi illegale e, al tempo stesso, pericoloso.

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BIBLIOGRAFIA

1. https://www.fda.gov/media/142749/download
2. Horton R. Offline: COVID-19 is not a pandemic. Lancet. 2020 Sep 26;396(10255):874. doi: 10.1016/S0140-6736(20)32000-6. PMID: 32979964; PMCID: PMC7515561
3. Alicandro G, Remuzzi G, La Vecchia C. Italy's first wave of the COVID-19 pandemic has ended: no excess mortality in May, 2020. Lancet. 2020 Sep 12;396(10253): e27-e28. doi: 10.1016/S0140-6736(20)31865-1. Epub 2020 Sep 3. PMID: 32891216; PMCID: PMC7470816
4. http://www.salute.gov.it/portale/nuovocoronavirus/dettaglioContenutiNuovoCoronavirus.jsp?lingua=italiano&id=5338&area=nuovoCoronavirus&menu=vuoto
5. Roussel Y, Giraud-Gatineau A, Jimeno MT, Rolain JM, Zandotti C, Colson P, Raoult D. SARS-CoV-2: fear versus data. Int J Antimicrob Agents. 2020 May;55(5):105947. doi: 10.1016/j.ijantimicag.2020.105947. Epub 2020 Mar 19. PMID: 32201354; PMCID: PMC7102597
6. https://www.aifa.gov.it/documents/20142/1279946/FAQ-Vaccinazione_anti_COVID-19_con_vaccino_Pfizer_EN.pdf/81bf5487-f52e-5fcc-fb08-b96c980e017b
7. Doshi P. Will covid-19 vaccines save lives? Current trials aren't designed to tell us. BMJ. 2020 Oct 21;371:m4037. doi: 10.1136/bmj.m4037. PMID: 33087398
8. https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf
9. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of COVID-19 - final report. N Engl J Med. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32445440
10. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet. 2020;395(10236):1569-1578
11. Spinner CD, Gottlieb RL, Criner GJ, et al. Effect of Remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. JAMA. 2020;324(11):1048-1057
12. Goldman JD, Lye DCB, Hui DS, et al. Remdesivir for 5 or 10 days in patients with severe COVID-19. N Engl J Med. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32459919
13. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res. 2020;30(3):269-271

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14. Spinner CD, Gottlieb RL, Criner GJ, et al. Effect of Remdesivir vs standard care on clinical status at 11 days in patients with moderate COVID-19: a randomized clinical trial. JAMA. 2020;324(11):1048-1057
15. Yang SNY, Atkinson SC, Wang C, et al. The broad spectrum antiviral Ivermectin targets the host nuclear transport importin alpha/beta1 heterodimer. Antiviral Res. 2020; 177: 104760
16. Yang SNY, Atkinson SC, Wang C, et al. The broad spectrum antiviral Ivermectin targets the host nuclear transport importin alpha/beta1 heterodimer. Antiviral Res. 2020; 177: 104760
17. Arévalo AP, Pagotto R, Pórfido J, et al. Ivermectin reduces coronavirus infection in vivo: a mouse experimental model. bioRxiv. 2020; Preprint

18. Lehrer S, Rheinstein PH. Ivermectin docks to the SARS-CoV-2 spike receptor-binding domain attached to ACE2. In Vivo. 2020;34(5):3023-3026
19. Guzzo CA, Furtek CI, Porras AG, et al. Safety, tolerability, and pharmacokinetics of escalating high doses of Ivermectin in healthy adult subjects. J Clin Pharmacol. 2002;42(10):1122-1133
20. Chaccour C, Hammann F, Ramon-Garcia S, Rabinovich NR. Ivermectin and COVID-19: keeping rigor in times of urgency. Am J Trop Med Hyg. 2020;102(6):1156-1157
21. Chaccour C, Hammann F, Ramon-Garcia S, Rabinovich NR. Ivermectin and COVID-19: keeping rigor in times of urgency. Am J Trop Med Hyg. 2020;102(6):1156-1157
22. Bray M, Rayner C, Noel F, Jans D, Wagstaff K. Ivermectin and COVID-19: a report in Antiviral Research, widespread interest, an FDA warning, two letters to the editor and the authors' responses. Antiviral Res. 2020; 178: 104805
23. Zhang X, Song Y, Ci X, et al. Ivermectin inhibits LPS-induced production of inflammatory cytokines and improves LPS-induced survival in mice. Inflamm Res. 2008;57(11):524-529
24. Guzzo CA, Furtek CI, Porras AG, et al. Safety, tolerability, and pharmacokinetics of escalating high doses of Ivermectin in healthy adult subjects. J Clin Pharmacol. 2002;42(10):1122-1133
25. Yang SNY, Atkinson SC, Wang C, et al. The broad spectrum antiviral Ivermectin targets the host nuclear transport importin alpha/beta1 heterodimer. Antiviral Res. 2020; 177: 104760
26. Di Nicolantonio JJ, Barroso J, McCarty M. Ivermectin may be a clinically useful antiinflammatory agent for late-stage COVID-19. Open Heart. 2020;7(2)
27. Ahmed S, Karim MM, Ross AG, et al. A five-day course of Ivermectin for the treatment of COVID-19 may reduce the duration of illness. Int J Infect Dis. 2020; 103: 214-216
28. Wagstaff KM, Sivakumaran H, Heaton SM, Harrich D, Jans DA. Ivermectin is a specific inhibitor of importin alpha/beta-mediated nuclear import able to inhibit replication of HIV-1 and dengue virus. Biochem J. 2012;443(3):851-856
29. Chachar AZK, Khan KA, Asif M, Tanveer K, Khaqan A, Basri R. Effectiveness of Ivermectin in SARS-COV-2/COVID-19 Patients. Int J Sci. 2020; 9: 31-35
30. Elgazzar A, Hany B, Youssef SA, Hafez M, Moussa H, eltaweel A. Efficacy and safety of Ivermectin for treatment and prophylaxis of COVID-19 pandemic. Research Square. 2020
31. Niaee MS, Gheibi N, Namdar P, et al. Ivermectin as an adjunct treatment for hospitalized adult COVID-19 patients: a randomized multi-center clinical trial. Research Square. 2020
32. Khan MSI, Khan MSI, Debnath CR, et al. Ivermectin treatment may improve the prognosis

of patients with COVID-19. Arch Bronconeumol. 2020;56(12):828-830
33. Abella BS, Jolkovsky EL, Biney BT, et al. Efficacy and safety of hydroxychloroquine vs placebo for preexposure SARS-CoV-2 prophylaxis among health care workers: a randomized clinical trial. JAMA Intern Med.2020; Published online ahead of print
34. Rajasingham R, Bangdiwala AS, Nicol MR, et al. Hydroxychloroquine as pre-exposure prophylaxis for COVID-19 in healthcare workers: a randomized trial. Clin Infect Dis. 2020; Published online ahead of print
35. Yao X, Ye F, Zhang M, et al. In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clin Infect Dis. 2020;71(15):732-739
36. Boulware DR, Pullen MF, Bangdiwala AS, et al. A randomized trial of hydroxychloroquine as postexposure prophylaxis for COVID-19. N Engl J Med. 2020;383(6):517-525
37. Mitjà O, Corbacho-Monné M, Ubals M, et al. A cluster-randomized trial of hydroxychloroquine for prevention of COVID-19. N Engl J Med. 2020; Published online ahead of print
38. Liu J, Cao R, Xu M, et al. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. Cell Discov. 2020; 6:16
39. Maisonnasse P, Guedj J, Contreras V, et al. Hydroxychloroquine use against SARS-CoV-2 infection in non-human primates. Nature. 2020;585(7826):584-587
40. Vincent MJ, Bergeron E, Benjannet S, et al. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2005; 2: 69
41. Vincent MJ, Bergeron E, Benjannet S, et al. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J. 2005; 2: 69
42. Recovery Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with COVID-19 - preliminary report. N Engl J Med. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32678530
43. Rezk NA, Ibrahim AM. Effects of methyl prednisolone in early ARDS. Egypt J Chest Dis Tuberc. 2013;62(1):167-172
44. Tongyoo S, Permpikul C, Mongkolpun W, et al. Hydrocortisone treatment in early sepsisassociated acute respiratory distress syndrome: results of a randomized controlled trial. Crit Care. 2016;20(1):329
45. Jeronimo CMP, Farias MEL, Val FFA, et al. Methylprednisolone as adjunctive therapy for patients hospitalized with COVID-19 (Metcovid): a randomised, double-blind, Phase IIb, placebo-controlled trial. Clin Infect Dis. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32785710
46. Meduri GU, Golden E, Freire AX, et al. Methylprednisolone infusion in early severe ARDS: results of a randomized controlled trial. Chest. 2007;131(4):954-963
47. Meduri GU, Bridges L, Shih MC, Marik PE, Siemieniuk RAC, Kocak M. Prolonged glucocorticoid treatment is associated with improved ARDS outcomes: analysis of individual patients' data from four randomized trials and trial-level meta-analysis of the updated literature. Intensive Care Med. 2016;42(5):829-840
48. Tomazini BM, Maia IS, Cavalcanti AB, et al. Effect of dexamethasone on days alive and ventilator-free in patients with moderate or severe acute respiratory distress syndrome and

COVID-19: the CoDEX randomized clinical trial. JAMA. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32876695
49. Villar J, Ferrando C, Martinez D, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med. 2020;8(3):267-276
50. Writing Committee for the R-CAPI, Angus DC, Derde L, et al. Effect of hydrocortisone on mortality and organ support in patients with severe COVID-19: the REMAP-CAP COVID-19 corticosteroid domain randomized clinical trial. JAMA. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32876697
51. Rosenberg ES, Dufort EM, Udo T, et al. Association of treatment with hydroxychloroquine or azithromycin with in-hospital mortality in patients with COVID-19 in New York state. JAMA. 2020;323(24):2493-2502
52. Furtado RHM, Berwanger O, Fonseca HA, et al. Azithromycin in addition to standard of care versus standard of care alone in the treatment of patients admitted to the hospital with severe COVID-19 in Brazil (COALITION II): a randomised clinical trial. Lancet. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32896292
53. Arshad S, Kilgore P, Chaudhry ZS, et al. Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19. Int J Infect Dis. 2020; 97: 396-403
54. Chu CM, Cheng VC, Hung IF, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax. 2004;59(3):252-256
55. De Meyer S, Bojkova D, Cinatl J, et al. Lack of antiviral activity of darunavir against SARS-CoV-2. Int J Infect Dis. 2020; 97: 7-10
56. Hung IF, Lung KC, Tso EY, et al. Triple combination of interferon beta-1b, lopinavirritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, Phase 2 trial. Lancet. 2020;395(10238):1695-1704
57. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin (55-60) for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. J Infect Dis. 2015;211(1):80-90
58. Li L, Zhang W, Hu Y, et al. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19: a randomized clinical trial. JAMA. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32492084
59. Joyner MJ, Bruno KA, Klassen SA, et al. Safety update: COVID-19 convalescent plasma in 20,000 hospitalized patients. Mayo Clinical Proceedings. 2020. Available at: https://mayoclinicproceedings.org/pb/assets/raw/Health%20Advance/journals/jmcp/jmcp_ft95_6_8.pdf
60. Liu STH, Lin HM, Baine I, et al. Convalescent plasma treatment of severe COVID-19: a propensity scorematched control study. Nat Med. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32934372
61. Ahn JY, Sohn Y, Lee SH, et al. Use of convalescent plasma therapy in two COVID-19 patients with acute respiratory distress syndrome in Korea. J Korean Med Sci. 2020;35(14): e149

62. Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci US. 2020. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32253318
63. Cheng Y, Wong R, Soo YO, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. Eur J Clin Microbiol Infect Dis. 2005;24(1):44-46
64. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. J Infect Dis. 2015;211(1):80-90
65. Shao Z, Feng Y, Zhong L, et al. Clinical efficacy of intravenous immunoglobulin therapy in critical patients with COVID-19: A multicenter retrospective cohort study. medRxiv. 2020; Preprint. Available at: https://www.medrxiv.org/content/10.1101/2020.04.11.20061739v2
66. Shetty AK. Mesenchymal stem cell infusion shows promise for combating coronavirus (COVID-19)-induced pneumonia. Aging Dis. 2020;11(2):462-464
67. Leng Z, Zhu R, Hou W, et al. Transplantation of ACE2(-) mesenchymal stem cells improves the outcome of patients with COVID-19 pneumonia. Aging Dis. 2020;11(2):216-228
68. Shu L, Niu C, Li R, et al. Treatment of severe COVID-19 with human umbilical cord mesenchymal stem cells. Stem Cell Res Ther. 2020;11(1):361
69. Shetty AK. Mesenchymal stem cell infusion shows promise for combating coronavirus (COVID-19)-inducedbpneumonia. Aging Dis. 2020;11(2):462-464
70. Davoudi-Monfared E, Rahmani H, Khalili H, et al. A randomized clinical trial of the efficacy and safety of interferon beta-1a in treatment of severe COVID-19. Antimicrob Agents Chemother. 2020;64(9): e01061-20
71. Zhou Q, Chen V, Shannon CP, et al. Interferon-alpha2b treatment for COVID-19. Front Immunol. 2020; 11:1061), Interleukin Receptors Antagonists (Fisher CJ, Jr., Dhainaut JF, Opal SM, et al. Recombinant human interleukin 1 receptor antagonist in the treatment of patients with sepsis syndrome. Results from a randomized, double-blind, placebo-controlled trial. Phase III rhIL-1ra Sepsis Syndrome Study Group. JAMA. 1994;271(23):1836-1843
72. Fisher CJ, Jr., Slotman GJ, Opal SM, et al. Initial evaluation of human recombinant interleukin-1 receptor antagonist in the treatment of sepsis syndrome: a randomized, openlabel, placebo-controlled multicenter trial. Crit Care Med. 1994;22(1):12-21
73. Opal SM, Fisher CJ, Jr., Dhainaut JF, et al. Confirmatory interleukin-1 receptor antagonist trial in severe sepsis: a Phase III, randomized, double-blind, placebo-controlled, multicenter trial. The Interleukin-1 Receptor Antagonist Sepsis Investigator Group. Crit Care Med. 1997;25(7):1115-1124
74. Wieringa JW, van der Woude CJ. Effect of biologicals and JAK inhibitors during pregnancy on healthrelated outcomes in children of women with inflammatory bowel disease. Best Pract Res Clin Gastroenterol. 2020;44-45:101665
75. Owen C, Berinstein NL, Christofides A, Sehn LH. Review of Bruton tyrosine kinase inhibitors for the treatment of relapsed or refractory mantle cell lymphoma. Curr Oncol. 2019;26(2): e233-e240
76. Treon SP, Castillo JJ, Skarbnik AP, et al. The BTK inhibitor ibrutinib may protect against pulmonary injury in COVID-19-infected patients. Blood. 2020;135(21):1912-1915

77. Richardson P, Griffin I, Tucker C, et al. Baricitinib as potential treatment for 2019-nCoV acute respiratory disease. Lancet. 2020;395(10223):e30-e31
78. La Rosee F, Bremer HC, Gehrke I, et al. The Janus kinase 1/2 inhibitor ruxolitinib in COVID-19 with severe systemic hyperinflammation. Leukemia. 2020;34(7):1805-1815
79. Cohen AT, Davidson BL, Gallus AS, et al. Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial. BMJ. 2006;332(7537):325-329
80. Leizorovicz A, Cohen AT, Turpie AG, et al. Randomized, placebo-controlled trial of dalteparin for the prevention of venous thromboembolism in acutely ill medical patients. Circulation. 2004;110(7):874-879
81. Samama MM, Cohen AT, Darmon JY, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. Prophylaxis in Medical Patients with Enoxaparin Study Group. N Engl J Med. 1999;341(11):793-800
82. Lemos ACB, do Espirito Santo DA, Salvetti MC, et al. Therapeutic versus prophylactic anticoagulation for severe COVID-19: a randomized Phase II clinical trial (HESACOVID). Thromb Res. 2020; 196: 359-366
83. Barnes GD, Burnett A, Allen A, et al. Thromboembolism and anticoagulant therapy during the COVID-19pandemic: interim clinical guidance from the anticoagulation forum. J Thromb Thrombolysis. 2020;50(1):72-81
84. Cohen AT, Harrington RA, Goldhaber SZ, et al. Extended thromboprophylaxis with betrixaban in acutely ill medical patients. N Engl J Med. 2016;375(6):534-544
85. Fisher BJ, Seropian IM, Kraskauskas D, et al. Ascorbic acid attenuates lipopolysaccharideinduced acute lung injury. Crit Care Med. 2011;39(6):1454-1460
86. Fowler AA, 3rd, Syed AA, Knowlson S, et al. Phase I safety trial of intravenous ascorbic acid in patients with severe sepsis. J Transl Med. 2014; 12:32
87. Fowler AA, 3rd, Truwit JD, Hite RD, et al. Effect of vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: the CITRIS-ALI randomized clinical trial. JAMA. 2019;322(13):1261-1270
88. Fowler AA, 3rd, Fisher BJ, Kashiouris MG. Vitamin C for sepsis and acute respiratory failure–reply. JAMA. 2020; 323(8): 792-793
89. Moskowitz A, Huang DT, Hou PC, et al. Effect of ascorbic acid, corticosteroids, and thiamine on organ injury in septic shock: the ACTS randomized clinical trial. JAMA. 2020;324(7):642-650
90. Aranow C. Vitamin D and the immune system. J Investig Med. 2011;59(6):881-886
91. Lu D, Zhang J, Ma C, et al. Link between community-acquired pneumonia and vitamin D levels in older patients. Z Gerontol Geriatr. 2018;51(4):435-439
92. Martineau AR, Jolliffe DA, Hooper RL, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. BMJ. 2017; 356: i6583
93. Amrein K, Schnedl C, Holl A, et al. Effect of high-dose vitamin D3 on hospital length of stay in critically ill patients with vitamin D deficiency: the VITdAL-ICU randomized clinical trial. JAMA. 2014;312(15):1520-1530

94. National Heart Lung and Blood Institute PCTN, Ginde AA, et al. Early high-dose vitamin D3 for critically ill, vitamin D-deficient patients. N Engl J Med. 2019;381(26):2529-2540

95. te Velthuis AJ, van den Worm SH, Sims AC, Baric RS, Snijder EJ, van Hemert MJ. Zn(2+) inhibits coronavirus and arterivirus RNA polymerase activity in vitro and zinc ionophores block the replication of these viruses in cell culture. PLoS Pathog. 2010;6(11): e1001176
96. Xue J, Moyer A, Peng B, Wu J, Hannafon BN, Ding WQ. Chloroquine is a zinc ionophore. PLoS One. 2014;9(10): e109180)