Combined therapy of Covid-19 infection

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SARS-CoV-2 virus effects body in two ways. It directly interacts and effects the host cell causing disturbence in it´s functioning or even it´s destruction. Indirectly the virus effects the host by effecting functioning of it´s immune system.
Successful Covid-19 therapy must target all these effects at once. I will try to present that we can achieve this goal now and without the need to wait for new medication to be developed. The more over clinical trial testing only one medication cannot detect benefits of combined therapy.

I will advocated bellow mentioned therapy as meeting criterias for successfull Covid-19 therapy:

severe cases:
- infusion of hrACE2 receptor
- low dose antimalarics like Plaquenil 400mg 1-0-1 for 2 days, than 400mg 1-0-0 for next 3 days
- macrolides: azithromycin 500 1-0-0 up to 10 days (if needed)
  or clarithromycin 500 1-0-1 as long as needed
- high dose vitamin C therapy: 200mg/kg/day - ARDS; 100mg/kg - in respiratory distress
- per oral vitamin D: 1-0-0
  10 000 I.U./D. in case vit. D bellow 100 nmol/ml
  6 000 I.U if vitamin D above 100 nmol/ml
  /100 nmol/l follows Vitamin D society recommandation for optimal vitamin D level/
- Zn
- fibrate 150 0-0-1
- milgamma 1 amp. 1x/week

moderate cases:
- isoprinosine 1g 1-1-1-1 for 7-10 days
- low dose antimalarics
- macrolides
- high dose vitamin C therapy
- per oral vitamin D
- per oral vit. B for 5 days
- Zn
- fibrate 150 0-0-1 in patients with sufficient level of vitamin D.

mild cases:
- isoprinosine 1g 1-1-1-1 for 7-10 days
- macrolides
- per oral vitamin C in high doses
  D
  B
- fibrate 150 0-0-1 in patients with sufficient level of vitamin D.
- Zn

preventive medication in general population:
- isoprinosine 1 g 1-1-1 or Imunor 1x/week for 4 weeks
- Broncho Vaxom 10 days/month for 3 months
- vitamin D longterm dose 6 000 I.U/d

- vitamin C 500 mg/den longterm/d
- Zn 20mg/5-7 days in a month
- vit. B 5-7 days in a month

preventive medication in population highly exposed to Covid-19:
- isoprinosine 1g 1-0-1 for 10 days than 20 days off; repeat 2x
- Broncho Vaxom 10 days/month for 3 months
- vitamin D, C, B
- Zn
- combination with Imunor ?

More detailed reasoning for the therapy:

Infusion of hrACE2 :

main objectives:
- virus load reduction
- managing severity of the course of disease by regulating virus load in body

reasonig:
SARS-Co-V2 and flu viruses infect human cells by utilizing ACE2 receptor. There is no way for the virus to get inside the cell without binding to the ACE2 receptor. Bioengineered ACE2 receptor was manufactured and tested as safe in humans. There has been presented that hrACE2 receptor infused in human body serves as a false beacon for Covid-19 virus. This way hrACE2 was showen to eliminate SARS-Co-V2 virus form 30 000 copies/ml bellow detection limits of quantitative PCR in severe Covid-19 patient in 72 hours. Clinical trial in critically ill ARDS patients was performed in 2017 in an attempt to proof effect of hrACE2 on immunity processes involved in ARDS. hrACE2 was found not to be effective in this respet but was found to be safe. Of course there was no idea that anything like SARS-Co-V2 would come at that time. hrACE2 was not tested in severe flu for unknown reasons. (I guess manufacturer had no idea of flu virus utilising ACE2 receptor which is my impression from discussing hrACE2 with manufacturer). As mentioned above hrACE2 receptor successfully underwent I. and II. stage of clinical trials and was proofed safe. The more over there should be no ethical issues in using this drug since no human fatal cells are involved in it´s production.

literature:

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30418-5/fulltext
https://pubmed.ncbi.nlm.nih.gov/28877748/
https://www.cell.com/cell/fulltext/S0092-8674(20)30399-8
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2042670/

artificial ACE2 - company web page:
https://www.apeiron-biologics.com/
name of the drug: APN01

note:
Any lab with the capability to work with SARS-Co-V2 can easily establish pharmacodynamics interference among hrACE2 and almost any drug or combinations of drugs in few days. So there is easy way to make tabulations of supposed effectivness of hrACE2 for viral dose and patient medication. This way more accurate control of the course of disease could be achived.

High dose vitamin C:

main objectives:
- post Covid-19 fibrosis prevention
- cytokine storm prevention
- effects on hematopoiesis

reasoning:
To my knowledge high dose vitamin C is the only drug capable of preventing postinfectious fibrosis in ARDS. This was presented in enterovirus/rhinovirus ARDS case study presented by Fowler. The more over there was presented case study showing rapid improvement in ARDS Covid-19 patient treated with azithromycin and HCQ. At the same time high dose vitamin C was used in Covid-19 patients to prevent cytokine storm. Animal studies demonstrated immunomodulative and lung protective effects.

literature:
https://www.amjcaserep.com/download/index/idArt/925521
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5295174/
https://academic.oup.com/jn/article/136/10/2611/4746705
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3329599/
in Chinese: https://mp.weixin.qq.com/s/bF2YhJKiOfe1yimBc4XwOA
https://transmedcomms.biomedcentral.com/articles/10.1186/s41231-017-0012-x
https://riordanclinic.org/journal-article-archive/continuous-intravenous-vitamin-c-in-the-cancer-treatment-reevaluation-of-a-phase-i-clinical-study/

Fibrate:

Fenofibrate was demonstrated to cause 2-log virus load reduction in lung epithelium culture. Fenofibrates are safe and widely used in contemporary medicine. Therefore possible benefits outweighs costs if cost benefit evaluation would be made in Covid-19 patients. Longest possible time gap in vitamin D and fenofibrates administration is recommanded.

literature:
http://huji.org.ar/wp-content/uploads/2020/07/Final-Manuscript_merged-The-SARS-CoV-2-Transcriptional-Metabolic-Signature-in-Lung-Epithelium.pdf

Antimalarics:

main objectives:
- cell susceptibility reduction to Covid-19 (by glycosilation of ACE2)
- viral load reduction (interference with Covid-19 intracellular replication and exocytosis)
- immunomodulation (HCQ is commonly used to reduce severity of revmat. arthritis etc.)

HCQ hrACE2 interaction:
I was not able to find out if active cell metabolic processes are needed for glycosilation of ACE2 caused by HCQ. but this issue can be easily resolve in any lab working with SARS-Co-V2 virus.

literature:
https://pubmed.ncbi.nlm.nih.gov/16115318/

https://www.sciencedirect.com/science/article/abs/pii/S0953620520303356
https://www.medrxiv.org/content/10.1101/2020.08.20.20178772v1?s=09
https://www.sciencedirect.com/science/article/pii/S1201971220305348
https://calexicochronicle.com/wp-content/uploads/2020/08/AAAA-ebook-Medical-Studies-Support-MDs-Prescribing-Hydroxychloroquine-for-Early-Stage-COVID-3rd-Edition.pdf

Macrolydes:
- interference with Covid-19
- immunomodulation (I was suprised to be told that marolydes and doxycylin were developed as immunosuppressive agensts leter were repurposed to antibiotics)
- prevention of bacterial superinfection

literature:
https://www.jstage.jst.go.jp/article/bst/advpub/0/advpub_2020.03058/_article/-char/ja/
https://www.sciencedirect.com/science/article/pii/S1201971220305348

Isoprinosine:
in Czech: https://www.orthodont-cz.cz/data/files/Isoprinosine-informace%20pro%20zdravotn%C3%ADky.pdf