Concept for early treatment of COVID-19 for people with increased risk of severe disease

(For all elderly and for all people with relevant comorbidities of any age)

Available from:

http://freepdfhosting.com/c1e7323cd0.pdf

Important note:

This is only a theoretical concept and not a real treatment recommendation!

This concept should be evaluated by controlled and randomized trials, and then be modified or optimized!

I. Removal of all legal restrictions against the accessibility and the use of agents needed for PREP, PEP or therapy (unachievable)

II. Preexposure prophylaxis (PREP)

Vitamin D supplementation

(if possible, daily doses dependent on the results of a vitamin D blood test; also available as self (home) test)

Possible advantageous role of: curcumin, magnesium, vitamin C, polyunsaturated fatty acids (PUFA), vitamin B12, zinc, probiotics like beta-glucans, herbal TCM and others

for

(a) theoretical (mechanistic) reasons, (b) because of *in vitro* data or (c) based on experiences with other respiratory infections,

but no direct evidence of prophylactic effect from clinical trials in the case of COVID-19 available so far.

Tinospora cordifolia extract (Guduchi) (BID)

III. Postexposure prophylaxis (PEP) / periexposure prophylaxis / ring prophylaxis

Continuation of established PREP methods

Local preexposure prophylaxis with iota-carrageenan (e.g. Algovir effect nose spray)

Local prophylaxis with povidone-iodine (PVP-I) – nasal tract and oropharyngeal application *(see http://freepdfhosting.com/35f285c9f2.pdf)*

(e.g., preexposure prophylaxis with carrageenan because of its longlasting effect due to its good retention on the mucosal surface, **postexposure prophylaxis with PVP-I** to kill all of the virus that survived carrageenan exposure, since PVP-I in concentrations about 0.5 – 1.25 % will kill of the virus which comes in contact with PVP-I without damaging the nasal mucosa and the respiratory epithelium, e.g. the ciliary beat frequency).

Carrageenan has the advantage of a long-lasting effect, whereas PVP-I is stronger with regard to virus inactivation. Whereas iota-Carrageenan inhibits the virus only by 80 – 90 %, what cannot be increased by higher doses (saturation effect), PVP-I is able to inhibit the virus completely, while its protective effect cannot be expected to last as long as carrageenan. This favors a concept of carrageenan as PREP, whereas PVP-I should be used directly following a risky exposure.

Umifenovir – at best in therapeutic dose (600 mg per day; 200 mg TID); doses of 200 mg/day are also effective to reduce the risk of symptomatic COVID and the severity of the disease, but the effect is much smaller than with 600 mg/day and one cannot expect to avoid symptomatic disease with the same certainty than 600 mg/day. However, one may also consider 100 mg TID as a compromise. For pharmacokinetic reasons, 100 mg TID are expected to be much more effective than 200 mg once a day or 100 mg BID.

(*see http://freepdfhosting.com/863ed84c7f.pdf).*

Tinospora cordifolia extract (Guduchi) (BID)

Liposomal lactoferrin (drinkable) (lower dose than treatment dose) + **zinc** (lower dose)

IV. Early treatment of symptomatic disease

OPTIMUM: individualized therapy based on regular blood examinations

(may be based on the "minimum concept" of phase IV + individualized adjuvants to that)

Only if an individualized therapy based on regular blood examinations is not possible:

Basal concept:

Continuation of methods described in III (PREP, local PVP-I prophylaxis nasal and oral/throat)

Umifenovir 600 mg/day (200 mg TID)

Favipiravir (if available for outpatients)

Lysosomal lactoferrin (drinkable) in combination with zinc

Fluvoxamine (dose escalation as usually recommended)

Clarithromycin (500 mg TID)

Pentoxifylline (400 mg TID)

Dipyramidole (50 mg TID) or regular thromboprophylaxis if possible

Indomethacin (25 mg BID or 75 mg slow release once daily); but avoid proton pump inhibitors for gastrointestinal protection (better: famotidine)

Doxycycline 200 mg/day

Magnesium (at least 150 mg/day), vitamin B 12 (0,5 mg/day), vitamin D (at least 1000 IU/day), **zinc, vitamin C (high dose; better: lysosomal encapsulated for better resorption)** *(see http://freepdfhosting.com/35f285c9f2.pdf)*

Beta-Glucan (supplement)

Tinospora cordifolia extract (Guduchi) (BID)

Lianhua Qingwen Kapseln (3 x 3 or 3 x 4 capsules as recommended by the producer)

Possibly: Spirulina, N-Acetylcysteine, Glucosamine, Sulforaphane, Ambroxol inhalation

Advanced concept:

Baricitinib for the prevention of cytokine storm syndrome (or to dampen them in case they already occurred) *(see http://freepdfhosting.com/35f285c9f2.pdf)* (as far as there is no contraindication) (in combination with an antiviral)

In hospital:

Combination of Baricitinib + Remdesivir

Recombinant human GCSF

Thromboprophylaxis

V. In case of deterioration in spite of the advanced concept of phase IV:

In addition to IV:

Convalescent plasma (early enough before own antibodies rise to titres with are comparable to CP)

It is important that CP has high antibody titres. The reduction of mortality is directly correlated with the antibody titre. The higher the titre, the higher the chance that the patient will survive!

The same applies to the time of administration: the earlier CP is given in the course of the disease, the higher the chance of survival!

and/or

nafamostat + second antiviral (favipiravir or remdesivir)

dexamethasone

Because of its anticoagulant activity, anticoagulation by dipyramidole or enoxaparin has to be adapted to nafamostat treatment to avoid overdoses of anticoagulating agents.

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VI. In case of deterioration in spite of the concept for phase V:

At the latest (!), this is now the point of time when "early" treatment was definitely unsuccessful and hospitalization and individualized treatment become inevitable.

However, RCTs have to show whether patients who follow this concept until now (including the advanced concept of phase IV and phase V) can progress so far that they need phase VI at all?

Whereas the treatment until phase V is at least theoretically possible in an outpatient and ambulatory setting (with infusions on an ambulatory base), hospitalization is now inevitable.

Beside possible need for oxygen, treatment **must** now be directed by individual blood parameters, e.g.

High IL-6: **Tocilizumab**

High inflammatory markers in general: **methylprednisolone or dexamethasone**

If tocilizumab fails: **methylprednisolone** as rescue therapy.

These are only examples of possibilities which are still available in this situation. It is beyond the scope of this concept for early treatment to discuss advanced and late treatment stages which should be individualized in any case.

Very important:

In any patient with increased risk for severe disease, the treatment should be under close monitoring of blood parameters from the beginning of symptomatic disease.

Blood should be monitored for parameters of (hyper)inflammation, lymphocytopenia, neutrophils, lymphocytes-to-neutrophils ratio, platelet ratiios, CD4+ T cells, CD8+ T cells, cytokines, parameters of iron metabolism (Fe, ferritin and others) and also for parameters associated with coagulation.

Vitamin D level should be examined in the first blood test in order to supplement an oral bolus of vitamin D if it is found too low (beyond the daily recommended supplementary dose).

At best, therapy is based on blood monitoring and individualized from the beginning of the disease in every person with increased risk of severe disease!

Because of the risk of infection of medical staff and other patients, it is difficult for infected outpatients to get blood examinations and a blood-parameter based individualized therapy. Infected people under quarantine are not allowed to visit doctors, and it is obviously not possible to establish a regional "home visit system" by nurses who take blood and administer e.g. enoxaparin on a regular base since the home of an infected person with symptomatic COVID disease has to be regarded as a highly infective setting, or because of the lack of manpower, equipment, PPE, PREP and because of costs and regulations or the lack of adequate structures adapted to these demands.

For that reason, phases III, IV and V of this concept are empirical if the therapy cannot be based individually on blood examinations. In a favorable situation when regular blood tests are established, the results of blood tests will lead the treatment in an individualized way, and this may results in deviations from this concept. This is of course much better than empirical treatment without blood tests.

So in first line, one should try to develop an individualized treatment concept for all infected people with increased risk based on regular blood examinations; only if this is not possible, the recommendations of phase IV and V should be considered.

So phases IV and V of this concept have to be regarded not as a supposed "best option", but instead as a the response to a desperate situation when regular blood tests and individualized therapy based on blood tests are not available!

Based on:

Registrierte Studien zur Chemoprophylaxe von COVID-19 (Präexpositionsprophylaxe, Postexpositionsprophylaxe)

http://freepdfhosting.com/bedd8b1c79.pdf

Chemoprophylaxis against COVID-19 is needed more urgently than ever before

http://freepdfhosting.com/9686575098.pdf

Frühe unspezifische systemische und lokale Therapieoptionen gegen COVID-19 ?

http://freepdfhosting.com/1c7f0ba1e1.pdf

Early unspecific systemic and local therapeutic options in COVID-19 disease ?

http://freepdfhosting.com/35f285c9f2.pdf

Early results from chemoprophylaxis trials against COVID-19

http://freepdfhosting.com/863ed84c7f.pdf

Sammlung von Studien von unmittelbarer therapeutischer Relevanz für SARS-CoV-2

http://freepdfhosting.com/2d4f1a9d90.pdf

(note: the version in the link is from the middle of June. The link cannot be updated any more because newer versions of this data collection include some direct quotations from original papers longer than one sentence so that they cannot be published any longer in the internet for copy right reasons. Thus in spite of continued actualization of that data base, it is no longer possible to make the newer versions available to the public.)

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