RESOLUTION

of Teleconference «Omicron: new challenges, new treatment opportunities»

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Kyiv, Ukraine

Almost 7 000 health care specialists have registered to participate in the Teleconference «Omicron: new challenges, new treatment opportunities».

Within the framework of the event the leading specialists and experts in the sphere of infectious diseases, pulmonology and therapy have shared their expert opinions and experience related to management of patients with COVID-19. The event acquired international format due to involvement of the leading infectious disease specialist from Romania Dr. Oana Săndulescu, MD, PhD, Associate Professor at the Department of Infectious Diseases, Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, Bucharest.

Seven main reports were offered to the participants for review and discussion and they were dealing with the following issues:

- Clinical laboratory peculiarities of Omicron variant of SARS-CoV-2: treatment methods.
- Surveillance of patients with COVID-19 in the hospital and outpatient phases.
- Target therapy of COVID-19 in modern clinical practice.
- Monoclonal antibodies against SARS-Cov-2: what's new?
- Steroid therapy in COVID-19.
- Place and time for antibacterial therapy in COVID-19.

Conclusions and decisions based on discussion of reports:

1. Within 2021 rapid increase in the number of cases of SARS-CoV-2 breakthrough infection in countries with a high rate of completed primary vaccination demonstrated that it is impossible to overcome COVID-19 in such a way. Consequently, it has become clear that a comprehensive approach is required, particularly the earliest possible initiation of specific pharmacotherapy to reduce viral load and prevent hospitalization of patients at risk.

2. The main factor of pathogenesis of COVID-19 is three-dimensional S-glycoprotein, containing three RBD S1-subunits, being a key antigen determinant and immunologic target. Accordingly, one of the most promising areas of therapy has been the use of monoclonal antibodies (mAbs), which disable binding of SARS-Cov-2 with ACE2 receptor, prevent virus penetration into the target cell and stop its replication. Use of mAbs for antiviral target therapy helps to neutralize SARS-CoV-2 in patients at risk of progression and severe form of COVID-19.

3. Regdanvimab is a highly-effective medicine for target treatment of coronaviral disease (COVID-19), being a recombinant human monoclonal antibody IgG1, that binds with receptor-binding domain (RBD) of SARS-CoV-2 adhesive protein, and in such a way it disables its penetration into cells and further extension of SARS-CoV-2. The efficiency interval is 7 days, which is longer than that of peroral

SARS-CoV-2 direct-acting antiviral preparations, and it makes it possible to conduct antiviral therapy with Regdanvimab both at the hospital and outpatient stage when diagnosed on time. Regdanvimab reduces by 72% the risk of emergency hospitalization or death of patients with a high risk of progression, as well as by more than 50% the need for emergency hospitalization or oxygen-therapy of patients with diagnosed pneumonia. Regdanvimab reduces viral load by 39% less than placebo on day 7; in treatment reduces time until clinical recovery by at least 4.73 bed-days; has tolerance at placebo level.

4. The molecular mechanism of development of COVID-19, defined as cytokine storm (cytokine release syndrome, CRS), provided an opportunity to isolate therapeutic interventions that could be influenced by the pharmaceuticals already available. Edaravone is an ischemic cascade inhibitor, acceptor of ROS and APLA both in water and lipid environment. In addition to the anti-stroke effect, edaravone has numerous pleiotropic effects, including anti-inflammatory, anti-cytokine, immunomodulatory, anti-apoptotic, anti-necrotic, antifibrotic actions, protects the pulmonary surfactant and numerous organs from damage due to ischemia/reperfusion. Thus, it acts as an ischemic cascade blocker and the most auxiliary drug in the prevention and treatment of cytokine storm caused by COVID-19, acute lung injury /ARDS. Edavaron therapy, initiated in early and/or second transition phase, can prevent progression to cytokine storms in high-risk patients.

5. Clinical and pre-clinical data support the claim that endothelium is a key target organ for COVID-19. Thus, COVID-19 can be considered a systemic vascular disease affecting several organs due to endothelium damage. Amino acid metabolism has been shown to be a decisive factor in the pathophysiology of COVID-19; in particular, in patients with coronavirus infection, a decrease of L-arginine levels in plasma has been reported along with an increase of arginase activity, especially in severe forms. According to the data of randomized, double, blind, placebo-controlled research conducted by G. Fiorentino and co-authors adding of peroral L-arginine to the standard therapy for patients with severe COVID-19 significantly reduces the length of hospitalization and reduces the need for respiratory support. Adding of combination of L-arginine and L-carnitine to the standard hospital therapy contributes to the alleviation of the disease.

6. Hyperosmolar crystalloid solution is appropriate for the control of intoxication syndrome. According to the results of open research with blind assessment of RHD RheoSTAT-CP0698, administration of hyperosmolar crystalloid solution to patients with pneumonia by intravenous infusion at a dose of 200-400 ml/day for 3 days significantly improves clinical condition and reduces manifestations of (poly-) organ insufficiency and endogenous intoxication. Low volume infusion therapy contributes to rapid normalization of volume of blood circulation, stabilization of hemodynamic parameters, acid-alkali, electrolyte and gas composition of blood, significantly improves saturation and reduces tachypnoea. The therapy definitely has positive impact on kidney function parameters and inflammation symptoms. The administration of the drug in this mode has a favorable safety profile: it does not result in fluid overload, pulmonary edema, pleural fluid or other serious undesirable effects, nor does it result in a clinically significant increase in endogenous blood lactate. RheoSTAT-CP0698 research justifies reasonability of use of hyperosmolar crystalloid solution within complex treatment of pneumonia.

7. A complication of coronaviral disease is bacterial infection, which is an indication of empirical antibacterial therapy in patients with COVID-19. It is recommended to use the 3rd generation cephalosporins (for example, cefoperazone + sulbactam) in combination with macrolide for initial treatment of bacterial complications. It they are not efficient enough the 4th generation fluoroquinolones are prescribed, for example, moxifloxacin coming as a concentrate for preparing of infusion solution 20 mg/ml in 20 ml bottle. It allows to conduct highly effective antibacterial therapy in accordance with approved international and national standards with maximum availability for Ukrainian patients and possibility of optimization of infusion therapy (qualitatively and quantitatively).

8. WHO strongly recommends systemic treatment with corticosteroids (low doses of intravenous or oral dexamethasone or hydrocortisone) for 7-10 days for adults with severe or critical disease. They say that systemic corticosteroids reduce mortality within 28 days in patients with severe or critical disease, as well as reduce the need for invasive lung ventilation. At the same time, WHO does not recommend the use of systemic corticosteroids in patients with mild COVID-19. In patients with mild COVID-19 and a high risk of severe progression, it is advisable to consider inhaled corticosteroids. The protective action of inhaled glucocorticosteroids in case of COVID-19 decreasing the viral load is considered. The study of use of dry powder budesonide 1600 mcg in case of mild COVID-19 demonstrated reduction of hospital admissions, shorter period of symptoms, reduction of residual effects of COVID-19 on the 14th and 28th day.

9. COVID-19 has a wave-like progression: the first wave is characterized by mild symptoms, after a temporary improvement it transforms into the second wave (the so-called lung phase), which is significantly heavier and often has lethal ending. Therefore, it is important to prescribe treatment preventing the first wave from passing to the second wave at an early stage of COVID-19. This can be achieved by controlling the replication of the SARS-CoV-2 virus, suppressing inflammation, protecting pneumonocytes, alleviating the effects of oxidant stress and minimizing possible disruptions of the coagulation system. Today we have proof for reasonable use of the following medicines for patients with mild progression of COVID-19:
   1. Dry powder budesonide, which is able to inhibit SARS-CoV-2 virus replication through impact on ACE2 receptors, to reduce viral load, to decrease levels of IL-6 and TNF directly in pulmonary tissue.
   2. Parenteral acetylcysteine, which is used for inhalation or injection, creates high concentration of active principle in lungs and in such a way provides powerful lung-protective effect.
   3. L-arginine in the form of oral solution is used to correct endothelial dysfunction, inhibit excessive adhesion of platelets and immune-thrombosis at COVID-19.

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