Questions raised in the Webinar on COVID19 and Rare Respiratory Diseases

1. **Is chronic lung disease really is risk factor for severe/fatal COVID infection or is the comorbidity percentage of 12% in COVID patients just a reflection of the prevalence of chronic lung disease in the general population?**

   Thomas Wagner: We have to distinguish the risk of catching the virus from the risk of having a severe course of COVID-19: The risk of catching the virus may be increased in those patients with immunosuppression like in lung transplantation and in some patients with reduced mucosal defence; the risk of a severe course of the disease is more likely to be increased in those patients with significantly reduced pulmonary function, but we cannot reliably predict this due to lack of data. It is clear though, that there is no good reason to refuse ICU admission or treatment to patients with a rare disease of the respiratory system when SARS-CoV2 positive and showing more than a mild course of the infection.

2. **How will you adapt your clinic environment to safely see patients (to avoid cross infection) in the post COVID-19 era? hepa filters ?**

   Thomas Wagner/Michael Kreuter/Isabelle Fajac: A benefit-risk assessment is important when considering whether to see patients or not with rare diseases as consequences of a (overseen) deterioration of the underlying chronic lung disease may also be severe. All Health Care Providers (HCPs) had to change their practice and have adopted their logistics to avoid cross infection by segregation of patients who are known to be infected by SARS-CoV2 and other patients. Moreover, to avoid contamination, preventive measures are in place in all hospital areas for all present at the hospital, patients and staff, such as facial masks, regular hand hygiene and keeping at least 1 meter -distance between each other. We will certainly have to keep on doing this probably as long as population immunity with or without vaccination does not prevent most infections in our RD patients.

3. **How will the long term 'shielding' measures be sustainable? For patients in the high vulnerability group, do you think they will be likely to have to remain at home until a vaccine / treatment becomes available? Or given the relatively positive outcomes from the very limited data, is it likely that those in this category will re-integrate into society before a treatment becomes available?**

   Thomas Wagner: We all do not know how long which of the measures will have to be maintained and/or when and how they can be replaced by other means of reducing the different risks. We don't expect to return to what we had and did before until we have sufficient immunity with or without vaccination.

4. **As an idiopathic pulmonary arterial hypertension (PAH) patient, how safe is it for me to lead a regular life after the lock down is over and healthy people can leave their houses?**

   Marc Humbert: After the lock down it will take some time to be back to a normal life and everyone will have to be very cautious when they leave their houses. Until the pandemics has resolved PAH patients will still be recommended to
   - Stay at home as much as possible to reduce risk of being exposed.
   - Avoid crowds
   - Keep space between themselves and others.
   - Limit close contact to other people who are sick.

- Frequently wash their hands with soap for at least 20 seconds or use hand sanitizer with at least 60% alcohol content.
- Avoid touching their face, especially eyes, mouth and nose.
- Avoid all non-essential travel, even short trips.
- Cover mouth and nose with a cloth face cover when around others.

5. **Any exercise tips apart from corridor walks?**

   Marc Humbert/Michael Kreuter: The European ESC/ERS PH guidelines have suggested that PAH patients should be encouraged to be active within symptom limits. It was recommended that patients should avoid excessive physical activity that leads to distressing symptoms, but when physically deconditioned, patients may undertake supervised exercise rehabilitation. During the lock down period some sub maximal exercise can be performed within symptom limits after discussion with your PAH team. Also, patients with ILD are encouraged to be active on a daily basis; similar to PAH excessive physical activity leading to significant dyspnoea should be avoided and submaximal workout is recommended after discussion with your pulmonologist / ILD expert team. Potentially Yoga (where a 1stfeasibility trial showed some preliminary positive effects) could be a good substitute or if available (and after supervision of a physiotherapist) a Vibration Exercise Machine.

6. **For how long do you think it´s safe to put routine visits (lung function and infection monitoring) on hold?**

   Isabelle Fajac: As said during the webinar, it depends a lot on the severity of the disease. This is why regular videoconferences have to be put in place, so that the disease can be assessed and in case of need, further exploration can be planned.

7. **Any tips to boost the immune system for those on Tadalafil and Macitentan?**

   Answered during the Webinar by Geert Verleden (schort summary): Normally those patients who need immunosuppressive (IS) therapy should not think of stopping this; there seems to be an increased risk of catching the infection but, on the same time, from the little data we have there seems to be some protective effect of IS to prevent a severe course of COVID-19.

Questions which have been posted in EXABO after the webinar:

8. **It seems that children are less often infected by the new Coronavirus and especially that the course of the disease is on average less severe in children than in adults. Most children are said to be infected by adults, e.g. their parents. Now gradually the schools will open again and many fathers or mothers with PCD are afraid that their children might bring the infection home from school. However there are experts that say this is very unlikely as until now there are no or hardly any cases known where children did infect their parents.**
   Please let us know what you as expert think about the risk for parents to be infected by their children. *Male, Other country*

   Heymut Omran: The raised question is currently a research focus and not yet answered. Indeed, infected children show on average a more benign course of COVID-19. Children younger than 10 years of age are supposed to become less likely infected and in addition, once infected, might

less likely infect adults, because their cough is much weaker compared to the coughing of adults. However, other studies have demonstrated that young children probably can infect other individuals. Due to living within the same household, infected children might therefore infect their parents.

9. **Recently there was an article that looked at the role of ac2 cells playing a crucial role in who gets infected with COVID and who is less susceptible. Is there any correlation with ac2 cells and PCD? Also, are people with PCD more susceptible to bacterial infections vs. viral and does having more mucous present somehow "slow' down or inhibit viral penetration into host cells? Thank you!** *Female, 23, Other country*

   Heymut Omran/Thomas Wagner: : Assuming the questions raises the point that the new Corona virus uses the ACE2 receptor as entry site, we have to say, that so far we do not know of any correlation between cellular ACE2 receptor equipment and PCD. I do not know any data suggesting that PCD individuals are more likely to attract bacterial vs. viral infections. PCD individuals have an increased mucus viscosity but not as high as in cystic fibrosis individuals. I do not know any data that in PCD individuals increased mucus viscosity correlates with reduced viral penetration in host cells.

   Also, we do not have any data on the role of ACE2 inhibitors or ACE receptor blocking drugs. These drugs have been looked at extensively in COVID-19 because they are so widely used as blood pressure regulating drugs in arterial hypertension. The WHO and the CDC have unanimously stated that for now there is not sufficient evidence to warrant a generic recommendation to avoid or especially prescribe these drugs. The reason for some uncertainty lies in the physiological background of the behaviour of Corona viruses like SARS-CoV-2: They use the ACE receptors, which also can be found on airways mucosa cells as entry port to the cell and this is the start of the viral infection. ACE inhibitors and ACE receptor blocking agents are known to not only block these receptors (that would probably decrease the entry of virus into the cells) but also induce higher receptor concentrations on the surface of cells (that would make more “doors” for Corona virus to enter the cells). This theoretical approach has been tested and some hints might be interpreted in a way that these drugs increase the risk of a more severe course. But these were all patients with arterial hypertension and this is a risk factor by itself. If corrected for age and comorbidity, ACE inhibitors and receptor blocking drugs did not show an increased risk of a severe course. On the other hand, these drugs might show some beneficial effects if used in COVID-19 by interfering with the viral entry to teh cells, which is being tested in several clinical trials.

   For the time being, there is not sufficient evidence to stop treatment with these drugs in COVID-19 patients and, there is not sufficient data to start any of these drugs if COVID-19 infection occurs.

10. **Which prophylaxis scheme -if any- is proposed for CF patients?**

    So far, there is no prophylactic treatment for SARS-CoV2 infection identified for patients with CF or for the general population. Clinical trials studying this question are ongoing in healthcare professionals. Please go to https://www.ecfs.eu/covid-cf-project-europe for regular updates on prevalence and severity of COVID-19 in patients with CF in Europe.