Q&A: Coronavirus infection and immunomodulatory treatments in MS

Anders Svenningsson (ASV): Some initial comments on this topic that will be repeated in some answers but are the most important messages on this topic:

1. No MS medication makes it easier to ***become*** *infected by coronavirus. It is only* ***when*** *someone has become infected that some immunosuppressive treatment might be a risk for a more severe course of the infection. Therefore,* ***being alert about what areas travel should be avoided and being sensible about hand hygiene (see below) will take care of at least 99.9% of the risk of contracting a severe infection****. The overall risk to become infected as for now is extremely low in Sweden if behaving correctly.*

2. The immune defense for infections is a ***teamwork*** *of many players where each player is important but usually other players can make up for the loss of others. One (maybe the most important) player is unaffected by MS treatments and that is the mucosa immunity which is first-line defense to reduce the overall load of virus that gets into the body if exposed. If exposed and infected, other immediate systems kick in and as the third line of defense lymphocytes, which mainly are affected by MS medications, will start to work. If getting that far, however, these medications may make it more difficult for the body to clear the infection and the course may be longer and more severe than otherwise.*

2. The majority of infected individuals (about 80%) has a mild disease like a common upper airway infection. Mortality is now reported to be 0-3.6% with a much higher risk for people above 70 years of age and specifically individuals that have heart and/or lung disorders. For younger otherwise healthy individuals the mortality appears to be far lower than 0.5%. As otherwise healthy individuals with MS and immunosuppressive treatment (see below for how I "grade" them), overall risk is probably much lower for life-threatening infection than "ordinary" older people. The higher risk of more severe disease seen in men in China could be an influence of smoking, since over 50% of the men are smokers, but nearly none of the women.

The variation in death rates vary a lot between countries and at this point in time it is hard to calculate the number of people actually infected (for that we will need a validated serology test):

Globally: 93 000 infected, 3200 dead, estimated death rate 3.4%

China: 80 000 infected, 2900 dead, estimated death rate 3.6%

South Korea: 5500 infected, 28 dead, estimated death rate 0.5%

Italy: 3089 infected, 77 dead, estimated death rate 2.4%

Japan: 290 infected, 6 dead, estimated death rate 2.0%

Germany: 240 infected, 0 dead, estimated death rate 0%

Sweden: 52 infected, 0 dead, estimated death rate 0%

3. It is difficult to say anything for sure about how MS treatments might affect the disease course with coronavirus infections, since it is a new infection and we know that some agents are COMBATed (!) more by T cells and some more by B cells. Below is a ***very personal guess*** *of how I would grade the different MS medications; if no risk at all or if we don´t know.*

1. Autologous Hematologic Stem Cell Transplantation. In the immediate phase after cytotoxic therapy one needs to be isolated at hospital anyway but the first months at home after transplantation is also a high-risk period. Stay away from all possible sources of infection!

2. Lemtrada depletes both T- and B cells more or less completely initially. During that phase (a couple to several months), infection by a new agent should be considered very dangerous and should be avoided at any cost. When total lymphocytes start to return in blood and reaches levels above 0.5, I would assume that an infection with coronavirus will be handled quite well.

3. B-cell depleting therapies (rituximab and ocrelizumab) affects the capacity to build a strong immune response against a new infection or agent. This may result in infections taking longer to clear. It is entirely unclear if this also translates into a worse severity. However, it is important to say that we still lack information on how different factors may affect the course of coronavirus infections.

4. Agents that reduce T-cell numbers and function (fingolimod, cladribine, sometimes dimethyl fumarate, teriflunomide) may affect the capacity to create a strong immune response, but in general responses to vaccinations are pretty good. There seem to be slightly decreased T-cell activity, which increase the risk for herpesviruses, but not so clearly for different respiratory viruses. Also, here it is important to state that we don't yet know the effect on a coronavirus of these treatments.

5. Natalizumab is in my opinion unlikely to confer a strong risk for an aggravated course or an infection with coronavirus.

6. Interferons and glatiramer acetate (Copaxone) is most likely no risk at all in this context

1. How likely is it that those treated with rituximab will be infected by coronavirus?

*ASV: Most likely no increased risk at all to **GET** the infection. The primary defense lines for infections are the mucous membranes and they will remain completely intact also when on rituximab treatment. So taking the right precautions to avoid infections is the primary strategy as for everybody else. Most important is hand hygiene with hand washing, alcohol gels regularly of the hand, no touching of face, eyes and mouth with you hand unless you have washed them and/or used alcohol gels on them.*

2. What are the odds to survive corona if you have depleted all your B cells? Is it even a fair chance?

ASV: Mortality is now reported to be 0-3.6% out of which the vast majority are elderly people above 70 years old with concomitant heart and/or lung disease. Mortality for younger individuals are less than 0.5%. With almost 100 000 patients infected worldwide there are still no reports on how drugs such as B cell depleting drugs affect the disease course, even if they are quite frequently used. Of course, this is not proof that these drugs don´t affect the risk at all and it is good to be prudent and follow the directions from authorities of where not to go, try to keep away from "sneezers" and "coughers" and practice good hand hygiene. Then you will avoid infections at all.

As far as known there is NO risk to get infected from parcels of envelops coming in mail etc. Most cases infected have been from within the family.

3. Is there any special risk with natalizumab (Tysabri)?

ASV: Unlikely to affect risk.

4. I am changing from Dimetylfumarat (Tecfidera) to rituximab (Mabthera), does this increase my risk of having a more severe infection?

ASV: As you can see on my list above, I grade rituximab in this case giving an effect on the immune system that can make it more difficult than DMF to clear an infection if it passes the initial defense of the mucous membranes.

5. Is there any B-cell count value that could indicate if you have a higher risk or not (reference value)?

ASV: Hematologist use the value 20 cells per ul (0.02 x 10^9 per L) when they expect a vaccine to work so that value could be some kind of round figure in this context. But we still don´t know how important the B cell response is for this particular infection.

6. Is there any special treatment/precaution we should ask for by the health care in case we do get the infection? Any special treatments we need to have as soon as we arrive at the hospital just because we are on immunomodulatory treatments and have MS?

ASV: Cannot think of any.

7. Should one postpone planned rituximab treatment until we know how severe the pandemic becomes?

ASV: From all we know the excellent effect of rituximab will last long after somebody has started to get B cells back, we basically see no recurrence of disease also with a 1-year interval. For most individuals the disease is probably in remission for up to several years after having had a couple of rituximab infusions. So from that knowledge it is not a bad idea to postpone the next treatment another 6 months, maybe infusion interval can be increased for most patients. ***However****, I again want to reiterate that you all have the greatest power yourself to reduce the total risk by being sensible and that way avoid infection altogether.*

8. Can one replace the B cells in case it is needed by receiving blood or plasma?

ASV: This would be like a transplantation of bone marrow, which requires additional immunosuppression and thus probably not very helpful.

9. How is it with traveling by train through Sweden? Any higher risk?

ASV: Overall extremely low risk at this point.

10. I have a daughter with rituximab treatment who are going to school, but I am worried that there are going to be children there returning from abroad this week who might carry the virus without showing any symptoms. What do I do?

ASV: Just follow regular recommendations and the risk of getting infected in school should be minimal. I am sure that all schools give recommendations that pupils that has been travelling in countries with coronavirus should be alert to any sign of infection and in that case stay at home. That has to be trusted. As for now, reports claim no secondary case transmitted from children and also extremely low risk of transmitting the infection without symptoms.

11. Do I dare to go to Italy?

ASV: I wouldn't recommend that now. Regarding reimbursement of travels you already booked, you should discuss this with your neurologist.

12. Do I cancel any traveling, or can I go if I postpone the next infusion of rituximab? If my B-cell count is still on zero?

ASV: Depends on where you are going. If yet no case, there risk is minimal. On airports, just stay away from big crowds and sneezers and coughers. Use diligent hand hygiene. Don't pay attention to B-cell count in this case but rather if the journey may be a risk for infection by anyone.

13. How about treatment with Mavenclad?

ASV: Don't get infected immediately after the courses when lymphocytes are low. Somewhere 2 – 3 months after dose, the lymphocytes for most individuals are getting above 0.5 and risk of very serious infection drops.

"Final words" = most important!

MS treatments do not increase risk of becoming infected in the first place so with the following simple measures an infection can be avoided with more than 99.9 % certainty, so focus on that:

1. Stay as healthy as possible = eat healthy, sleep well and don't stress too much. This increase the resistance against all infections and is your best "insurance" for avoiding all kinds of infections, including coronavirus.

2. Do not travel to high-risk areas with lots of cases

3. Diligent hand hygiene including frequent washing, alcogels and NOT fiddle with your hands in eyes and mouth! You can skip shaking hands (use Japanese style greeting – its elegant I think…).

4. Spot coughers and sneezers and sneak away

5. Read official recommendations from authorities and follow them

- No symptoms = no (or extremely low) risk for transmitting disease

- Children appear to confer very low risk of transmitting coronavirus as it looks right now.

6. To keep updated with the latest information and high-risk areas for travel, refer to the WHO and your national CDC/health organization websites.

https://www.who.int/emergencies/diseases/novel-coronavirus-2019