

On the website of the American Society of Transplantation (ATS), prof. Umberto Maggiore, transplant-nephrologist working in Azienda Ospedaliera-Universitaria Parma, Italy, has answered some important questions in a web-forum. Working in the focus of the European epidemic, he has unique experience of which we may learn. His contribution can be found at the ATS Outstanding Questions in Transplantation Research Forum. Unfortunately, this site has no open access. For your convenience prof. Luuk Hilbrands (*Chair of the ERA-EDTA WG Descartes, Radboud UMC Nijmegen, The Netherlands*) has therefore made a summary of some of the most crucial questions and answers that prof. Maggiore addressed.

Has any institution modified its protocol on the frequency of lab check?

Most institutions in Italy have rescheduled the regular visits for later dates. The general approach for transplant recipients with only mild flu-like symptoms (fever ≤ 37.5 , °C unless it is an obvious UTI) or asymptomatic patients with known COVID-19 exposure outside the hospital, is close outpatient monitoring. However, according to local rules, subjects with fever > 37.5 °C should ask the GP for a home visit, or call 112. Sometimes, transplant recipients may call us right away, upon experiencing symptoms and we may decide to follow-up closely, entirely over the phone.

What is the incidence of AKI in transplant patients

We cannot say whether or not AKI incidence in renal transplant recipients with COVID-19 and pneumonia is different from the rest of the population. As for them, AKI is definitely a risk indicator of the severity of the disease.

Is there a need to place a hold on immunomodulation protocols for high cPRA ESRD listed patients? It appears that the risk posed by COVID 19 outweighs the reasonable benefits in this set of patients.

An approach adopted by most centers, even in areas where the spread of the disease is limited, is to interrupt all transplant requiring lympho-depleting agents because lymphopenia is most important indicators of poor outcome in patients with COVID-19 with pneumonia. Transplants for hyperimmune patients is currently limited in these centers to the ones on urgent waiting list for exhausted vascular access.

Testing the donors

Donor testing is mandatory. Since the risk of donor-derived transmission is possible (RAemia was reported in at least 15% in one case series; Huang C, et al. Lancet 2020), donors at risk of infection should not be accepted.

Incidence in the general population.

In general, experience so far indicates a similar trend of infections in transplant recipients compared to general population. For severe forms of COVID-19 mortality rate may be increased.

The incidence of COVID-19 does not seem to be increased. Someone has speculated that may be caused by the alleged antiviral properties of CNI. But it is more likely related to the fact that such patients are already used to follow common rules to prevent infection risk

Tacrolimus withdrawal versus reduction

It is possible that in some patients CNI reduction (which may prevent the risk of acute rejection) may be preferred over complete withdrawal on CNI, because of direct CNI favorable effect of viral replication or because of CNI anti-inflammatory action. Pending the results of clinical studies CNI withdrawal vs reduction may be established on a case by case basis depending on the severity of pneumonia:

1) patients who are suffering from extensive pneumonia and who may require intubation may benefit from improved viral clearance by unleashed cytotoxic T cells (i.e. complete CNI withdrawal) along with administration of anti-inflammatory agents such as tocilizumab (or pulse steroids)

2) moreover, as to anti-viral drugs, every patient undergoing treatment with ritonavir-boosted drugs must reduce tacrolimus by 1/20-1/50 to maintain the same blood levels. Therefore, the dose should be reduced even further (i.e. less than 1/50) if you are willing to "reduce" CNI rather than stop CNI altogether. The problem of reduced Tac metabolism in those patients may be further aggravated by the reduced hepatic clearance in the course of MOF.

Therefore, I still believe that in patients with extensive pneumonia, especially those undergoing treatment with ritonavir-boosted antiviral regimes, may be safer to completely withdraw Tac in the first place