

Recommendations regarding Covid-19 vaccination in patients undergoing instillation therapy for NMIBC

Theoretically, there should be no reason not to administer **intravesical mitomycin** with the BioNTech/Pfizer mRNA vaccine at the same time, since MMC has low immunosuppressive potential when retained in the urinary bladder. And SARS-CoV-2 mRNA vaccines (eg. from BioNTech/Pfizer or Moderna) are considered as a dead/inactivated vaccine, not a live vaccine.

This is in contrast to **intravesical BCG** which may show overlap in known side effects related to administration of mRNA-based COVID-19 vaccines. However, there appears to be no consensus re. a recommended delay of vaccination after intravesical BCG instillation. We have previously recommended a delay of at least 1 week, the British BAUS has recommended a delay of 6 weeks in 2010. Of note, these recommendations relate to influenza, not COVID-19 vaccination.

The “Recommendations from the EAU NMIBC Guidelines Panel applicable during the COVID-19 pandemic” did not include the topic of COVID-19 vaccines yet.

Following short literature review and consultation with relevant, the following can be summarized:

There is no high level evidence in the literature supporting either not giving inactivated vaccine (as the Covid-19 vaccines are) during BCG or just giving it irrespectively. However, there are some scarce recommendations involving flu-vaccines etc.

Generally, the recommendation is that there should not be given two live vaccines at the same time. But this is not a relevant problem relevant here as known upcoming vaccines for Covid19 are not live vaccines. Regarding simultaneous vaccine administration, it is slightly more complicated but there are very few issues. When giving up to 6 to 7 different vaccines to a person before sending them to exotic work places, vaccines are most often given with 3-5 days interval if there are two vaccines depending on the same pathways. So from that perspective, patients should not be given the vaccine during BCG induction therapy because of identical immune response pathways are utilized. However, vaccine can safely be given up to 1 week before or minimum 1 week after BCG if the patient is otherwise asymptomatic. Whether it affects the efficacy of either the BCG or the Covid19-vaccine is not clear but from a theoretical perspective, it might actually be improved for both! Naturally not sufficiently investigated to recommend it to be given simultaneously.

The biggest issue is if patients experience side effects after either the vaccine or BCG – risk of side effects are not necessarily higher per se even if given simultaneously. But if a patient develops fever the first day after BCG AND Covid-vaccine, you cannot know which caused it. Therefore, this should be avoided. However, as most symptoms develop within hours to days, one week abstinence between treatments should be quite sufficient.

So recommendations for now would be to give the BCG as planned if already initiated and then postpone vaccine to 1 week after the last instillation. If the patient is scheduled for vaccine within short time, vaccine should be given and BCG started a minimum of 1 week thereafter.

MMC in the bladder is not believed to cause significant interference on the vaccine or systemic immune system per se. However, based on the argument with side effects where you would like to be able to discriminate, the same recommendations regarding 1 week before or after can be recommended.

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December 2020