HHS/ASPR COVID-19 Outpatient Therapeutics Mini-Series
Session #5— Managing Infusion Reactions
Wednesday, January 27, 2021 (12-1 PM ET)
Q/A Sheet

Date	Question	Answers		
27-Jan	What is the current guidance for using bamlanivimab in high risk patients who test positive for COVID after receiving 1st dose of COVID vaccine?	We have been administering it and delaying 2nd dose for 90 days.		
27-Jan	EUA lists 02 sat of 93 % required for infusion. Some organizations (State of Utah) use 90%. Thoughts?	Live answered.	90%	
27-Jan	Previous ASCP webinars had stated we were fine to compound BAM into a 250ml NACL using aseptic technique. However, last week it was stated that perhaps a sterile environment was needed. Thoughts?	Per the EUA Fact Sheet for bamlanivimab, aseptic technique is required.		
27-Jan	Do you have a protocol for pre-infusion of monoclonal? We have had patients sent to the ED because of poor 02Sat prior to infusion.	Zyrtec 10 mg, Pepcid 20 mg, Singulair 10 mg 30 min before infusion	Link to Dr Castells' presentation which includes the algorithm: https://iecho.unm.edu/sites/unm/download.hns?i=29251	A link to the resource library, a compilation of standing orders, training guides, SOPS, etc. can be found at https://hsc.unm.edu/echo/institute-programs/covid-19-response/us-covid19/hhs-aspr/miniseries.html
27-Jan	What is the acceptable 02Sat? Is it 93% ?	Lower than 90%		

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27-Jan	Is there guidance on dispensing bamlanivimab after receiving 2 doses of the COVID-19 vaccine? Does it have to be spaced out?	Use of Vaccines Prior to Bamlanivimab Treatment No analyses have been conducted to assess the impact of prior non-SARS-CoV-2 vaccines on the safety or effectiveness of bamlanivimab. No information is available regarding the safety or effectiveness of administering bamlanivimab after the first dose or completed series of a SARS-CoV-2 vaccine. For partially and fully vaccinated patients who subsequently test positive for COVID-19, prior receipt of a SARS-CoV-2 mRNA vaccine should not influence COVID-19 treatment decisions or the timing of such treatments.		
27-Jan	I would suppose that there are contraindications?	Patients with severe reactions to other monoclonals similar to the ones used for infusion.		
27-Jan	In SC, we have successfully treated over 5000 patients to date w/ mAb one dose infusion. We have had only 11 patients not able to complete treatment due to a mild to moderate allergic/hypersensitivity reaction w/ no anaphylactic episodes. Would like to hear more information on delayed	Stopping the infusions and using the algorithm in my slide which is shared can help continue infusion. Getting a tryptase level is extremely helpful in severe cases to understand the mechanism and be able to provide recommendations for re-infusion.		

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	hypersensitivity reactions w/ these mAbs. Thanks!			
27-Jan	Type I are both anaphylactic (IgE mediated) and anaphylactoid (non IgE mediated)? If yes, the latter then rate and dose dependent? Given no previous exposure, is the latter more likely with mAbs?	There is IgE and non IgE reaction, anaphylactoid is no longer a word in use . Both IgE and non IgE can induce the same symptoms and may need treatment with Epi and both elevated tryptase in blood.		
27-Jan	Will power points be available after the webinar?	Slide links were included with today's announcement and are also available on the mAb ECHO mini-series webpage. https://hsc.unm.edu/echo/institute-programs/covid-19-response/us-covid19/hhs-aspr/miniseries.html	Link to Dr Castells' presentation: https://iecho.unm.edu/sites/unm/download.hns?i=29251	
27-Jan	Thanks for sharing the Brighton scale. Very helpful in differentiating levels of hypersensitivity response.	We also use the Brwon scale which provide the indication for epi, grade 3 requires always Epi, grade 1 no needs and grade 2 depends on the evaluation of the reaction over time.		

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27-Jan	Have you seen SEVERE BLOOD PRESSURE ELEVATIONS rather than hypotension with immediate reactions (i.e. within 30 minutes following the administration of drug)? If seen, what is your opinion on giving epinephrine in those cases?	Yes, we have seen hypertension, we stop the infusion, use Benadryl depending on symptoms and avoid epi if SBP is >120.		
27-Jan	Will the slides be shared post meeting?	Slide links were included with ECHO's announcement and are also available on the mAb ECHO mini-series webpage at https://hsc.unm.edu/echo/institute-programs/covid-19-response/us-covid19/hhs-aspr/miniseries.html	Link to Dr Castells' presentation which includes the algorithm: https://iecho.unm.edu/sites/unm/download.hns?i=29251	
27-Jan	Have you seen severe cardiac events within 12 hours of the monoclonal infusion?	We have seen tachycardia and palpitations but no MI or severe cardiac events.		
27-Jan	Roughly how long does the tryptase level remain elevated following an anaphylactic reaction?	Live answered.		
27-Jan	It was my impression that the evidence for steroids in the acute management of anaphylaxis or infusion reaction was not definitive. Can you comment?	There is no room for steroids in the acute care of anaphylaxis, only Epi which can be used up to 3 times and H1 and H2 anti-histamines, fluids, oxygen and when the patient is stable, steroids to prevent delayed or protracted anaphylaxis.		

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27-Jan	I'm still confused if we can use the monoclonal antibodies while patients are getting the vaccine.	CDC has some guidance on this issue. See link at https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html Currently, there are no data on the safety and efficacy of mRNA COVID-19 vaccines in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Based on the estimated half-life of such therapies as well as evidence suggesting that reinfection is uncommon in the 90 days after initial infection, vaccination should be deferred for at least 90 days, as a precautionary measure until additional information becomes available, to avoid potential interference of the antibody therapy with vaccine-induced immune responses. This recommendation applies to persons who receive passive antibody therapy before receiving any vaccine doses as well as those who receive passive antibody therapy after the first dose but before the second dose, in which case the second dose should be deferred for at least 90 days following receipt of the antibody therapy.		

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27-Jan	What is the rationale for delaying mRNA COVID vaccination after mAb treatment? And what is the time delay prior to vaccination?	CDC has some guidance on this issue. See link at https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html Currently, there are no data on the safety and efficacy of mRNA COVID-19 vaccines in persons who received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment. Based on the estimated half-life of such therapies as well as evidence suggesting that reinfection is uncommon in the 90 days after initial infection, vaccination should be deferred for at least 90 days, as a precautionary measure until additional information becomes available, to avoid potential interference of the antibody therapy with vaccine-induced immune responses. This recommendation applies to persons who receive passive antibody therapy before receiving any vaccine doses as well as those who receive passive antibody therapy after the first dose but before the second dose, in which case the second dose should be deferred for at least 90 days following receipt of the antibody therapy.		

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27-Jan	I have a patient that got bamlanivimab for COVID who developed painful lymphadenopathy 2 weeks after receiving treatment (cervical, post-auricular, occipital). Any relationship? It worked well for her COVID symptoms/	Please be sure to report any suspected ADRs via MedWatch at https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program		
27-Jan	What is the level of supervision needed for managing MAb related infusions- can this be managed with a home infusion nurse with a MD available on phone?	Nurse with training is sufficient.		
27-Jan	What guidance would you give clinicians who are having trouble differentiating infusion reaction symptoms from COVID symptoms?	Live answered.		
27-Jan	A couple of questions: Are you providing monoclonal antibodies in an outpatient setting? Is it more difficult to manage patients who have had reactions in the outpatient setting versus in hospital? Besides epi/sq/im and Benadryl, do you administer solumedrol? How many patients in the outpatient setting, out of all of the patients who had a reaction to monoclonal antibody patients, how many required hospitalization > than 23 hours?	We have monoclonal infusions in our infusion center which is totally outpatient. Treatment of reactions requires training in anaphylaxis and hypersensitivity. We have had a frequency of less than 1/250000 cases that needed ER visit or hospitalization.		

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27-Jan	Please address the appropriate settings to administer these medications safely. Infusion centers, surgical centers, and hospitals are equipped with ACLS-certified staff, appropriate monitoring equipment, supplies (IV pumps for example), pharmacy services, RNs who are experienced starting IVs and administering multiple meds, and the like. Settings such as community health centers, prisons, long term care centers, etc. are not infusion centers.	Non-hospital settings (e.g., FQHCs, LTC, dialysis, corrections) are safely and successfully administering mAbs across the country. Many of these facilities are able to receive direct federal allocations of mAbs through the SPEED program. https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Pages/SPEED.aspx Per the EUA requirements, the administering facility needs to have access to meds and be able to activate EMS for potential severe infusion reactions.		
27-Jan	Could we address in a future session the potential challenges w/ the new variants esp. the one from South Africa on mAb efficacy? Thanks!	Live answered.		
27-Jan	Can you provide resources or more information for the 2-hour training you described for staff to learn more about managing infusion reactions/anaphylaxis? What kind of individuals do you train - hospital nurses or other?	A link to the "Resource Library", with a compilation of standing orders, training guides, SOPS, etc. can be found at https://hsc.unm.edu/echo/institute-programs/covid-19-response/us-covid19/hhs-aspr/miniseries.html		
27-Jan	How did you get nurses to staff the MAB clinic?	Live answered.		

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27-Jan	Do you hold infusion if o2 sat is less than 90%	The EUA excludes patients who require oxygen. The cutoff for an oxygen protocol is a facility/provider decision (it is not indicated in the EUA).		
27-Jan	What recommendations do you have for cleaning the room and portable HEPA filtration for COVID-19 positive? What are your recommendations on safeguarding others in the clinic setting?	For Safe-guarding others: Masks, social distancing and appropriate ventilation, e.g. HEPA filters.	For additional infection control guidance, go to Infection Control Guidance for Healthcare Professionals about Coronavirus (COVID-19) at https://www.cdc.gov/coronavirus/2019-nCoV/hcp/infection-control.html	
27-Jan	QUES - Are EDs able to & starting to provide mAb infusions ? Under what circumstances	Several weeks ago, a colleague in Michigan presented on the Michigan experience and in the first month almost 50% of the mAbs infusions were given in EDs.		
27-Jan	How do you envision the home infusion with infection control and protecting your staff?	CDC offers guidance for PPE and infection control practices that apply to a range of care settings, including guidance for donning/doffing PPE when entering/exiting the patient's home. All nurses are fit-tested for N-95 wear and equipped with the needed PPE.		

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27-Jan	Thank you. What would you do for the "next time" the therapy is given, knowing that allergic reaction could be worse and high BP would limit the use of epinephrine?	If there is a next, then risk stratification is done, skin testing evaluated depending on the initial reaction and if positive desensitization can be done with 3 bags 12 steps (5.8Hours) or if negative increase IV fluids, add calcium channel blocker or other BP medications. It is personalized to the patient initial reaction phenotype, severity and co-morbidities.		
27-Jan	I might have not got this question in. Is there a sterile environment required for constitution with the 250 cc NS?	Aseptic technique is required for drug preparation, which for home-based patients is performed at the bedside. A sterile environment is not required.		
27-Jan	WHAT IS THE REFUSAL RATE?	We have about 5% refuse after appointment made. We can't know who tells their provider in the office that they don't want it.		
27-Jan	We started using in hemodialysis unit. Would you try in patient with history of serious anaphylactic reaction from IV iron?	Anaphylaxis to IV iron is not a risk factor for reactions to monoclonals or chemotherapy. The patients are not at higher risk		
27-Jan	Joined late, apologies. What are your current staffing requirements?	Staffing is outlined by the EUA and local regulations regarding who may start IVs/ hang infusions.	You may find additional information in the mAb-Outpatient Administration Play book at https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Documents/COVID-Therapeutics-playbook_1Feb2021.pdf	

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27-Jan	This may seem tangential - but quite related: do our experts believe the isolation / ventilation (particularly for an outpatient clinic) have been sorted out? (what are the best isolation practices? - HEPA? just masks?)	Masks, distancing and appropriate ventilation, e.g. HEPA filters	For additional infection control guidance, go to "Infection Control Guidance for Healthcare Professionals about Coronavirus (COVID-19)" at https://www.cdc.gov/coronavirus/2019-nCoV/hcp/infection-control.html	
27-Jan	What recommendations would you make for facilities that do not regularly do infusions, but that have providers who want to use these. Also, for nursing homes across the country that are hesitant to do this even when they do other infusions.	We refer you to Dr. Jarrett's slides which outlines suggestions for "Staff Training" at https://hsc.unm.edu/echo/_docs/hhs-covid/1.27.21-jarrett.pdf		
27-Jan	With industry present: These dialyzable? Would think not significantly.	There is no hard data on the interaction between mAbs and dialysis membranes. In discussions with nephrologists and dialysis centers, the safest thing is to administer the mAbs post-dialysis.		
27-Jan	Will this chat be available on the website soon? Also, the link you gave I did not find the slides. Thx Kind regards	Links to today's slides were included in the announcement. The slides will also be posted to the mAb ECHO website in the next day or so. We will also post a Q&A transcript within 1-2 weeks.	A link to Dr Castells' presentation can be found at https://iecho.unm.edu/sites/unm/download.hns?i=29251	You should be able to download both presentations via the link in ECHO's announcement under the RESOURCES section.
27-Jan	The placebo must have been all ingredients except the med, not just NS?	In the BLAZE-1 study protocol, commercially available 0.9% sodium chloride was used as Placebo.	We are not providing placebo for Hospitalized & Ambulatory intravenous (IV) arms studies. Sites are using Normal Saline (0.9% sodium chloride) and 5% Dextrose for placebo.	

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27-Jan	Is there any consensus regarding the preferred corticosteroid (and dose) for managing infusion reactions?	Methyl prednisolone at 0.5 to 1 mg/kg or dexamethasone 20 mg.	There is not currently a recommendation for a specific corticosteroid.	
27-Jan	I have read that it seems to be talking about vaccine after MAB's not MAB's after vaccine. So, if my patient has already had the vaccine (95% of them at my facility have received the first dose), then they get COVID it is safe to give MABs? Then wait at least 90 days for the second dose?	We refer you to the CDC guidelines for the most updated information that addresses your question: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html		
27-Jan	We are trying to set this up in our outpatient clinic, we are not an infusion center, so struggling a little with what is required to mix this. Can the nurse just do it at point of care with sterile technique or is it required that a pharmacist mix this in special equipment?	Live Answered	Yes, it can be prepared bedside, using aseptic technique. You may also find additional information in the "mAb-Outpatient Administration Play Book" at https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Documents/COVID-Therapeutics-playbook_1Feb2021.pdf.	

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27-Jan	Thx unfortunately I missed that session	Sharing a link to the archive of recordings and PowerPoints. That presentation by William Fales was on January 6: https://hsc.unm.edu/echo/institute-programs/covid-19-response/us-covid19/hhs-aspr/miniseries.html		
27-Jan	If you desensitize a severe reaction and give the med, are they more likely to have a delayed reaction?	There are no severe delayed reactions after desensitization. In ours and other publications (Castells et all 2009, Sloane et al 2016, Isabwe et al 2018), 1-5 % of desensitizations have mild delayed symptoms, none anaphylactic and 99-95% have no symptoms		
27-Jan	Ques- one of the industry colleagues mentioned an NEJM article. Please provide a link :). Thx	**NEJM:** REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19 at https://www.nejm.org/doi/full/10.1056/NEJMoa2035002?query=recirc_curatedRelated_article		
27-Jan	Not sure if this was previously asked but when you decrease the infusion rate to 25-50%, do you keep the slower rate until the end of the infusion or when do you decide to bring the infusion rates up?	We resume the rate if the symptoms completely resolve and maintain at the slower rate if any mild symptoms persist.	Based on the severity of the reaction. When they feel well, go up on the infusion - if symptoms return slow infusion.	
27-Jan	While the size indicates these Ab are not likely dialyzable, do they adhere to the hemodialysis membrane?	There is no hard data on the interaction between mAbs and dialysis membranes. In discussions with nephrologists and dialysis centers, the safest thing is to administer the mAbs post-dialysis.		

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27-Jan	Rare severe reactions don't mean no severe reactions. It's essential to be properly trained and prepared for worst case scenarios. How can the best, safest practices be encouraged and supported for those with no experience in IV infusions who are looking to take this on? The actual requirements for doing this are very minimal.	We refer you to a NICA Resource entitled "COVID-19 Antibody Treatment FAQs: Infusion Providers" at https://infusioncenter.org/covid-19-antibody-treatment-faqs/#1478549326993-f03ab7c9-0037	You may find additional information in the mAb-Outpatient Administration Play book at https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Documents/COVID-Therapeutics-playbook_1Feb2021.pdf	A link to the resource library, a compilation of standing orders, training guides, SOPS, etc. can be found at https://hsc.unm.edu/echo/institute-programs/covid-19-response/us-covid19/hhs-aspr/miniseries.html
27-Jan	Is there a centralized process for monitoring and reporting outcomes data, outside of clinical trials?	No	We refer you to a Duke Margolis White Paper that provides insight on this at https://healthpolicy.duke.edu/publications/covid-19-monoclonal-antibody-treatments-using-evolving-evidence-improve-care-pandemic	
27-Jan	Any experience with infusing the mAb during the last hour of dialysis?	There is no hard data on the interaction between mAbs and dialysis membranes. In discussions with nephrologists and dialysis centers, the safest thing is to administer the mAbs post-dialysis.		

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27-Jan	Do you recommend the use of these on dialysis patients?	Dialysis centers are eligible to participate and receive direct allocations of mAbs. The EUA outlines the eligibility criteria, for more information go to: https://www.fda.gov/media/143894/download and https://www.fda.gov/media/143603/download		
27-Jan	If patient was hospitalized for COVID-19, but discharged within 10 days since symptoms onset, can they still get mAb therapy?	No. Hospitalization for COVID-19 is an exclusion criterion. A patient who is discharged within the 10 days still required hospitalization.		
27-Jan	With the dilution of Bam - there are two ways described in the documents one is directly mixing the Bam to 250 ml of NS and the other is withdrawing 70 ml of NS with final volume of 200 ml - which do you recommend and why ? Thanks	There have been updates to the EUA recommended dilution and administration instructions for Bamlanivimab, for the updated changes, go to https://www.fda.gov/media/143603/download.		

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27-Jan	Any thoughts or experience for giving mAb to inpatient who were admitted to the hospital, then develop COVID symptoms, such as hip fracture pts?	Bamlanivimab may be used in patients hospitalized for reasons other than COVID-19, so long as the terms and conditions of authorization are met. For example, a patient hospitalized for an elective orthopedic procedure who reports mild symptoms of COVID-19, confirmed with positive results of a direct SARS-CoV-2 viral test, may be appropriate for treatment with bamlanivimab if the patient is also at high risk for progressing to severe COVID-19 and/or hospitalization, as detailed in the Health Care Provider Fact Sheet (https://www.fda.gov/media/143603/download).		
27-Jan	To informed consent - the patient informational handout that has been provided is long and complex and not designed with health literacy in mind. Has anyone developed accessible informed consent processes/materials they can share?	A consent form is not required. The FDA and manufacturers provide the patient information sheets.		
27-Jan	Can mAb be given between vaccine dose 1 and 2?	We refer you to the CDC guidelines for the most updated information that addresses your question: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html		

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27-Jan	On the other side, if you have gotten mAbs, is the recommendation 30 days till you receive vaccine?	We refer you to the CDC guidelines for most updated information that addresses your question: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html		

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27-Jan	When is the optimal time to administer these MAbs?	The EUA authorizes casirivimab and imdevimab, administered together, as a single intravenous (IV) infusion as soon as possible after positive viral test for COVID-19 and within 10 days of symptom onset (https://www.fda.gov/media/143894/download). It is recommended that bamlanivimab be administered as soon as possible after positive viral test for SARS-CoV-2 and within 10 days of symptom onset. (https://www.fda.gov/media/143605/download)		
27-Jan	Whereas CDC is monitoring vaccine reactions in different ways including an app for vaccinated FDA is not monitoring any differently for mAb reactions?	As part of the EUA, FDA is requiring health care providers who prescribe the mAbs to report all medication errors and serious adverse events considered to be potentially related to the mAbs through FDA's MedWatch at https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program ADRs for vaccines can be reported at https://vaers.hhs.gov/		

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27-Jan	Thank you. Looking forward to more discussion on these issues I am experiencing in primary care	Thank you. We also refer you to a recording of past COVID-19 ECHO series, which covers a plethora of topics of interest at https://hsc.unm.edu/echo/institute-programs/covid-19-response/us-covid19/hhs-aspr/miniseries.html		
27-Jan	Thank you in advance for sharing the protocols soon.	A link to the resource library, a compilation of standing orders, training guides, SOPS, etc. can be found at https://hsc.unm.edu/echo/institute-programs/covid-19-response/us-covid19/hhs-aspr/miniseries.html		
27-Jan	Dr. Castells, the algorithm you showed had methylpred as first line. It was my understanding that steroids were not first line for infusion reactions or anaphylaxis. Can you comment?	Methyl prednisolone or any steroids do not treat anaphylaxis but treat infusion reactions and cytokine-release reactions.		
27-Jan	A post COVID patient with a serious rash that has resolved, would it be appropriate to obtain a Tryptase level?	No unless the patient had hypotension and other features of mast cell activation such as wheezing or gastrointestinal symptoms such as diarrhea.		