Practices in the care of the critically ill CAR patient

The goal of this research study is to learn more about the clinical practices at different intensive care units (ICUs) when complications occur after treating patients with Chimeric Antigen Receptor (CAR) therapy. The results of this study may help understand how research efforts can be allocated to better serve these patients. Further research in the care of CAR-related complications will help outcomes in this complex patient populations. If you agree to take part in this study, you will complete a questionnaire about your ICU's practices in the care, monitoring, and treatment of CAR patients with severe complications. The questionnaire should take about 10 minutes to complete. Your identity and your institution's identification will be kept strictly confidential and will be de-identified before analysis.

Consent Statement You have read the description of the study, and have decided to participate in the research project described here. You understand that you may refuse to answer any (or all) of the questions at this or any other time. You understand that there is a possibility that you might be contacted in the future about this, but that you are free to refuse any further participation if you wish.

You may withdraw your authorization at any time, in writing, for any reason as long as that information can be connected to you. You can learn more about how to withdraw your authorization by callin[redacted]or by contacting the study doctor.

ALL OF YOUR ANSWERS SHOULD REFLECT ONLY ADULT CAR PATIENTS

Hospital name	_____
Do you have an ICU solely for cancer patients?	◯ Yes ◯ No
Number of medical ICU beds	◯ 1-10 ◯ 11-20 ◯ 21-30 ◯ >30
What CAR products are being used in your institution? Choose all that apply	☐ Yescarta ☐ Kimryah ☐ Products from protocols ☐ Products created by our institution ☐ All
How many CAR patients are being treated a month in your institution?	◯ 1-5 ◯ 5-10 ◯ >10
Approximately how many CAR patients are admitted to your ICU a month?	_____
Approximately how many Kymriah patients have you treated in your ICU since FDA approval?	_____
Approximately how many Yescarta patients have you treated in your ICU since FDA approval?	_____

Are you already using the ASBMT guidelines for grading of CRS and ICANS (neurotoxicity)?	◯ Yes ◯ No ◯ Yes but some protocols require the older guidelines
What guidelines are being used at your institution for Managing CAR toxicities? Choose all that apply	☐ Own (unique to your institution) ☐ Penn Grading scale (Porter 2018) ☐ Lee (Blood, 2014) ☐ Neelapu (Nature 2018) ☐ Other
Specify which	_____
Is there a specialized group of physicians treating CAR patients in your ICU?	◯ Yes ◯ No (all ICU practitioners are trained)
Do you have a "committee" that helps monitor, review and create guidelines for the care of CAR patients in your institution?	◯ Yes ◯ No
Are you treating any patients with TCRs?	◯ Yes ◯ No
Do you have guidelines for antibiotic prophylaxis specific for this patient population?	◯ Yes ◯ No
Have you had any CAR patients in the ICU made DNR, no escalation of care or withdrawal of care?(due to patients preference, presence of multi organ failure, progression of disease)	◯ Yes ◯ No
Would you be interested in participating in future research projects involving critically Ill CAR patients?	◯ Yes ◯ No

Are you using the current ASBMT guidelines to grade CRS?	◯ Yes ◯ No
Do you ever admit patients with CRS grade 1 or 2 to the ICU?	◯ Yes ◯ No
Please comment on specifics that might be relevant to this decision of monitoring in ICU low grade toxicities	_____
Do you ever admit patients with CRS who are not on vasopressors, high flow nasal cannula or BiPAP, or require continuous renal replacement therapy?	◯ Yes ◯ No
First vasopressor of choice for shock in CRS?	◯ norepinephrine ◯ phenylephrine ◯ vasopressin ◯ angiotensin 2 agonist ◯ epinephrine ◯ dopamine
2nd vasopressor of choice?	◯ norepinephrine ◯ phenylephrine ◯ vasopressin ◯ angiotensin 2 agonist ◯ epinephrine ◯ dopamine
Third vasopressor of choice?	◯ norepinephrine ◯ phenylephrine ◯ vasopressin ◯ angiotensin 2 agonist ◯ epinephrine ◯ dopamine ◯ We don't use more than 2 vasopressors
What is your inotrope of choice in patients with CRS and cardiomyopathy?	◯ dobutamine ◯ milrinone ◯ epinephrine ◯ other ◯ Have not used any yet ◯ Choice depends on the clinical situation
How do you guide fluid resuscitation in these patients? Choose all that apply	☐ ml/kg of fluid bolus ☐ US guided ☐ Pulse pressure variation on arterial line ☐ Non-invasive modes of SVV, CO, SVR ☐ Other
What fluids do you usually use for their resuscitation? Choose all that apply	☐ NS ☐ Lactate ringers ☐ Albumin 5% ☐ 0.45% saline ☐ Other
Please specify "other"	_____

Do you always obtain an echocardiogram on your patients with hypotension/shock in view of CRS? (An echocardiogram obtained on the floors prior to ICU is considered a "yes")	◯ Yes ◯ No
Do you consider cardiomyopathy a frequent finding on your CART patients with CRS?	◯ Yes ◯ No
How do you treat respiratory failure in patients with CRS?	◯ We are aggressive with intubation and generally transition from HFNC to mechanical ventilation ◯ We give a trial of Bipap prior to intubation ◯ We avoid intubation as much as possible on these patients, therefore keep them as long as possible on HFNC or BiPAP ◯ N/A (have not experienced a patient with significant respiratory failure yet)
For how long do you do a BiPap trial on these patients?	◯ < 12 hours ◯ 12-24 hrs ◯ 24-48hrs ◯ >48hrs ◯ N/A (have not treated patients with Bipap)
Would you consider non-cardiogenic pulmonary edema (ALI/ARDS) a frequent finding in CAR patients with CRS?	◯ Yes ◯ No
Have your CAR patients required Renal replacement therapy?	◯ Yes ◯ No
Have you treated any patients with Hemophagocytic lymphohistiocytosis (HLH)?	◯ Yes ◯ No
Are there any other findings you have found to be significant or important to note on CART patients with CRS treated at your institution?	_____

Which are the ICU admission criteria for neurotoxicity in your ICU? Choose all that apply	☐ Easily controlled seizures (Ativan and one Anti-epileptic drug) ☐ Difficult to control seizures or status epilepticus ☐ Focal edema on brain MRI (independent of clinical status) ☐ Diffuse edema on MRI ☐ CARTOX/ICE score < 4 ☐ Motor deficits ☐ Depressed level of consciousness (Grade 3 or 4 on ASBMT consensus)
Do you ever admit to the ICU Grade 2 neurotoxicity for close monitoring?	◯ Yes ◯ No
Is this a frequent reason for ICU admission?	◯ Yes ◯ No
Is delirium a frequent reason for admission to the ICU?	◯ Yes ◯ No
Have you had any patients with ischemic stroke or intracranial hemorrhage?	◯ Yes ◯ No
State approximately how many	_____
Do you have any experience with external ventricular devices on this patient population?	◯ Yes ◯ No
How do you measure ICP in these patients? (choose all that apply)	☐ fundoscopy ☐ EVD ☐ ocular ultrasound ☐ We use mainly imaging to monitor for cerebral edema
Do you perform lumbar punctures on these patients?	◯ Yes -routinely ◯ No- never ◯ Yes but depends on the clinical situation
Specify the clinical situation	_____
What is your practice of EEGs on these patients?	☐ Always perform an EEG once symptoms begin ☐ We only perform EEGs if there is any clinical suspicion of seizures on the patient ☐ We only perform when neurotoxicity is >Grade2
How long is the EEG? choose all that apply	☐ Everyone gets a 24 hr EEG ☐ We start with a "spot"EEG and according to findings we perform longer EEGs ☐ We have no capability for 24 hr EEG
Do you perform routinely MRI brain?	☐ Yes ☐ No ☐ We try, however due to the patients clinical status it might not always be feasible

Have you treated patients with diffuse cerebral edema?	◯ Yes ◯ No
Have you treated any patients with only focal edema?	◯ Yes ◯ No
Does your aggressiveness in treatment vary between patients with focal vs diffuse edema (e.g: use of mannitol, hypertonic saline, EVD placement)?	◯ Yes ◯ No
What is you institutions preference for management of cerebral edema in this patient population?	☐ acetazolamide ☐ Hypertonic saline ☐ Mannitol ☐ Pharmacological coma ☐ Short course of hyperventilation ☐ EVDs to guide CPP ☐ Hypothermia
Does your institution use seizure prophylaxis?	◯ Yes ◯ No ◯ depends on the product
Which agent?	_____
Do you have specific protocols for the management of cerebral edema, seizures and status epilepticus on CART patients?	◯ Yes ◯ No- we use the institutional protocols used in our institution to treat ANY patient with cerebral edema or status epilepticus

Do you perform daily CRP and ferritin?	◯ Yes ◯ No
Do you perform serum cytokines on these patients? (choose all that apply)	☐ Yes daily or routinely ☐ No- we don't have the capabilities ☐ Only as needed
Which cytokines are you measuring?	_____
Do you feel any of these markers (cytokines, ferritin, CRP) play an important role in guiding treatment in the ICU?	◯ Yes ◯ No ◯ Sometimes
Have you ever performed flow cytometry to look for CARs (in serum or fluid) to help guide treatment?	◯ Yes ◯ No
What is the lowest grade of CRS and ICANS at which corticosteroids are administered in your institution? (Choose all that apply).	☐ Grade 1 CRS ☐ Grade 2 CRS ☐ Grade 3 CRS ☐ Grade 4 CRS ☐ Grade 1 ICANS ☐ Grade 2 ICANS ☐ Grade 3 ICANS ☐ Grade 4 ICANS
Find space below if you think of any specific examples or situations that require explanation:	_____
Which doses of corticosteroids have you used for the treatment of CRS or neurotoxicity/ICANS? Check all that apply	☐ Dexamethasone 10mg q/6hr, ☐ Dexamethasone 20mg q/6hr ☐ Solumedrol 250 mg q/12hr ☐ Solumedrol 500 mg q/12 hr (or 1gm single dose) ☐ Higher doses if needed
Once you have used >250 mg daily of solumedrol how do you taper?	◯ If patients responds rapidly we quickly taper the steroids and observe ◯ Independent of clinical response with such high doses of steroids we always taper slowly
Does your institution follow strict recommendations for tapering corticosteroids?	◯ Yes ◯ No-it all depend on the clinical response
Do you use >3 doses of tocilizumab to treat CRS?	◯ Yes ◯ No
How frequently do you dose tocilizumab? (e.g: q/8hrs)	_____
Do you use siltuximab for CRS and if so when?	◯ When the patient is refractory to tocilizumab ◯ Prior to using tocilizumab ◯ On any patient with grade 3-4 toxicity ◯ We don't use it

Do you use anti-IL-6 therapy (siltuximab, tocilizumab) for neurotoxicity?	◯ Never ◯ Only when associated to CRS symptoms
Have you used anakinra ?	◯ Yes ◯ No
When have you used anakinra? (choose all that apply)	☐ refractory grade 3-4 CRS ☐ refractory Grade 3-4 neurotoxicity ☐ Every time a patient is refractory to anti-IL6 treatment ☐ On every patient once they reach grade 3-4 toxicity
Have you used any of the following salvage treatments? Choose all that apply	☐ ATG ☐ etanercept ☐ suicide genes ☐ Ruxolitinib ☐ Other
Specify other	_____
Have you ever used continuous renal replacement therapy as a way to clear cytokines in patients with refractory CRS or neurotoxicity/ICANS?	◯ Yes ◯ No