Cellular Therapies in Community Oncology : Operational Protocols

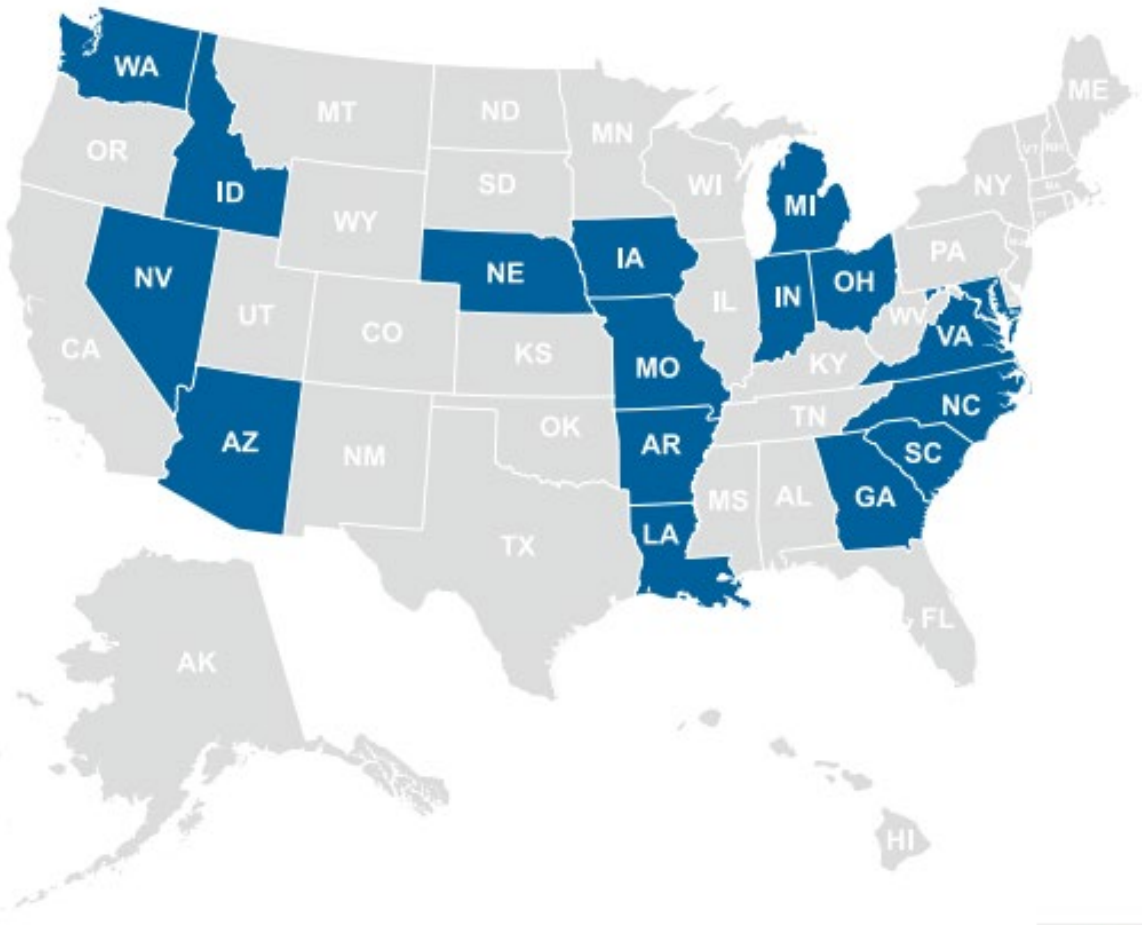
Brooke Peters, PharmD, BCOP

Brooke.Peters@aoncology.com

Outline

- Discuss multidisciplinary challenges and considerations for initiation of cellular therapies in the community oncology setting
- Review an example of a standard operating procedure for initiation of cellular therapies in a community oncology practice
- Review an example of a standard operating procedure for treatment of CRS/ICANS for community oncology practices and their local hospitals

American Oncology Network (AON)



103 Physicians

86 Advanced Practitioners

1328 Staff members

18 States

Cellular Therapy Initiation Challenges

- Hospital admission requirements
  - Relationships with local hospitals may or may not already be established
- New toxicity recognition and management
  - Both clinic staff and local hospital staff are likely unfamiliar with recognition and management of CRS/ICANS
  - Clinic and hospital may not have tocilizumab on-hand
- REMS requirements
  - REMS training for providers, nurses, pharmacy staff for both the clinic and the local hospital

CRS: cytokine release syndrome

ICANS: Immune effector cell-associated neurotoxicity syndrome

Initiation of Cellular Therapies SOP

- Purpose
  - To establish guidance for providers and clinic staff seeking to initiate cellular therapies (**bispecific T-cell-engaging therapies**).
- Process description
  - Outline cellular therapy initiation processes for providers, nursing leadership, financial staff, and pharmacy staff.

SOP: standard operating procedure

Initiation of Cellular Therapies SOP

- Outline roles/responsibilities
  - The **provider** is responsible for:
    - Identifying patient requiring cellular therapy
    - Notifying Clinic Nurse Manager of intent to initiate cellular therapy
    - Completing REMS training (if applicable)
    - Entering appropriate treatment orders for intended patient
  - The **Nurse Manager** is responsible for:
    - Notifying Regional Clinical Pharmacist, Clinic Financial Manager, and Regional Director of Nursing of intent to initiate cellular therapy
    - Notifying local hospital of intent to initiate cellular therapy
    - Notifying manufacturer of intent to initiate cellular therapy (if applicable)
    - Coordinating internal staff training

Initiation of Cellular Therapies SOP

- Outline roles/responsibilities (continued)
  - The **pharmacy staff** is responsible for:
    - REMS pharmacy registration (if applicable)
    - Ensuring that Oncology Supply recognizes REMS-complete status (if applicable)
    - Ordering appropriate drug/equipment for drug preparation/administration
  - The **Financial Counselors** and Clinic Financial Manger are responsible for:
    - Confirming that insurance authorization and financial assistance is obtained, if applicable

Initiation of Cellular Therapies SOP

- Introduce cellular therapy requirements

	Blincyto	Kimmtrak	Tecvayli	Lunsumio
Bispecific T-cell-engager	☑	☑	☑	☑
Risk of CRS/ICANS	☑	☑	☑	☑
REMS requirement	X	X	☑	X
Requires hospital admission admission	☑	☑	☑	X
Financial assistance available	☑	☑	☑	☑
Requires tocilizumab on-hand in clinic	X	X	Clinic Discretion	

Initiation of Cellular Therapies SOP

- Provide preparation/administration instructions
  - Blincyto (blinatumomab)
    - First FDA-approved 12/4/2014. Indications include CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% and relapsed or refractory CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL). See package insert
  - Kimmtrak (tebentafusp)
    - FDA-approved 1/25/22 for HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma. See package insert
  - Tecvayli (teclistamab)
    - FDA-approved 10/25/2022 for relapsed/refractory multiple myeloma after at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. See package insert
  - Lunsumio (mosunetuzumab)
    - FDA-approved 12/22/2022 for relapsed/refractory follicular lymphoma after two or more lines of systemic therapy. See package insert

Mosunetuzumab (Lunsumio)

Approvals & Indications	• **Follicular lymphoma, relapsed or refractory (after two or more lines of systemic therapy)** ○ (21-day treatment cycles) 1 mg IV over at least 4 hours on C1D1, 2 mg IV over at least 4 hours on C1D8, 60 mg IV over at least 4 hours on C1D15, 60 mg IV over 2 hours on C2D1 if cycle 1 infusions were tolerated, and 30 mg IV over 2 hours on day 1 of all subsequent cycles if previous infusions were tolerated.	
Mechanism of Action	T-cell engaging bispecific humanized monoclonal antibody that binds to the CD3 receptor expressed on the surface of T-cells and CD20 expressed on the surface of lymphoma cells and some healthy B-lineage cells	
Hazardous	Non-hazardous (though not classified by NIOSH)	
Route	IVPB	
Premedication	• Premedicate prior to each cycle 1 and cycle 2 dose; administer in cycle 3 and beyond if patient experienced cytokine release syndrome (any grade) with the previous dose. • Premedications to include dexamethasone 20 mg IV at least 1 hour prior to mosunetuzumab infusion, diphenhydramine 50 PO or IV and acetaminophen 500 to 1,000 mg PO at least 30 minutes prior to mosunetuzumab infusion.	

Preparation	• Withdraw volume equal to the volume of mosunetuzumab dose from NS or 1/2NS
	  ○ Infusion bag volume to be used based on dose of mosunetuzumab:
	  ▪ 1-2 mg: 50 or 100 mL
	  ▪ 30 mg: 50, 100, or 250 mL
	  ▪ 60 mg: 100 or 250 mL
	• Use infusion bags made only of polyvinyl chloride (PVC) or polyolefin, such as polyethylene or polypropylene
	• Visually inspect vial for particulate matter and/or discoloration; do not use if solution is discolored, cloudy, or contains visible foreign particles
	• Withdraw the mosunetuzumab dose from vial and add to infusion bag.
	• Mix gently by slowly inverting the bag; do not shake	

Administration Instructions	Infuse IV over at least 4 hours in cycle 1; if cycle 1 infusions are tolerated, infuse over 2 hours in cycle 2 and beyond. Do not infuse through an inline filter.	
Storage/Stability	**Unused Vials/Syringes**	**Completed Admixture**
	Fridge	Fridge: 24 hours Room temp: 16 hour
Monitoring	• CBC with differential (monitor throughout treatment). • Verify pregnancy status prior to treatment initiation (in patients who could become pregnant). • Monitor for signs/symptoms of cytokine release syndrome (CRS) and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS). Please see RN-JBI-041-ATT1. • Monitor for signs/symptoms of infection (including opportunistic infections) prior to and during treatment and for signs/symptoms of tumor flare	

Initiation of Cellular Therapies SOP

- Hospital coordination
  - Clinic Nurse Manager to engage with local hospital at which patient will receive inpatient doses and/or may be treated for cytokine release syndrome (CRS)

	Blincyto	Kimmtrak	Tecvayli	Lunsumio
Requires hospital admission admission	☑	☑	☑	X
Risk of CRS/ICANS	☑	☑	☑	☑

    - If hospital contact previously established, reach out to available contact as early as possible to inform hospital staff of intent to initiate cellular therapy. *If no contact is established, alternative instructions provided*.
    - Inform hospital staff of REMS requirement, if applicable
    - Provide treatment plan orders from EMR (if treatment requires hospital admission) and **cytokine release syndrome treatment protocol** (even if administration of the bispecific T-cell engager will be entirely outpatient)
    - Ensure that **tocilizumab** can be kept on-hand in the hospital
  - Provide an outline of inpatient vs outpatient treatment schedule for drugs that require admission

Initiation of Cellular Therapies SOP

- Clinic Nurse Manager (or Regional Clinical Pharmacist, or Regional Director of Nursing) to notify **manufacturer representative** of intention to initiate cellular therapy
  - Coordinate nursing staff training with manufacturer
  - Manufacturer to reach out to local hospital staff to coordinate training and financial conversations as needed. Inform manufacturer of which local hospital will be administering drug, if applicable
  - Please use local contacts or the contacts below. If no contact listed, please reach out to Regional Clinical Pharmacist to determine appropriate contact if needed.
    - Kimmtrak (Immunocore): medical.information@immunocore.com
    - Tecvayli (Janssen): *name*@its.jnj.com and *name* @its.jnj.com (please include "ACTIVATION REQUIRED" in subject)
    - Lunsumio (Genentech): *name*@gene.com
  - For the first administration of a particular therapy at your site, please provide the following information to the manufacturer representative:
    - Clinic Nurse Manager contact information
    - Regional Clinical Pharmacist contact information
    - Regional Director of Nursing contact information
    - Provider contact information
    - Which Hospital for step-up dosing (if applicable)
    - Key Hospital Contact (i.e. Pharmacists, hospital admin.) if known

Initiation of Cellular Therapies SOP

- Initiate REMS training, if applicable

	Blincyto	Kimmtrak	Tecvayli	Lunsumio
REMS requirement	X	X	☑	X

  - Tecvayli (teclistamab) REMS:
    - Providers: https://tecvaylirems.com/#Main/Prescribers
      - Review training materials
      - Complete knowledge assessment
      - Complete and submit Prescriber Enrollment Form
      - Ultimately responsible for patient education
    - Pharmacy staff: https://tecvaylirems.com/#Main/Pharmacies
      - Designate an authorized representative for the clinic (can be a pharmacist, pharmacy technician, registered nurse, or any responsible individual assigned by the clinic
      - Review Pharmacy and Healthcare Setting Training Program Documents and share with clinic staff
      - Complete and submit Pharmacy and Healthcare Setting Enrollment Form
      - Please reach out to procurement to confirm that REMS-complete status documented by OS for Tecvayli ordering
    - Nurses:
      - Ensure that patient has been educated and has received Janssen-provided wallet card. If no wallet cards available, download “patient wallet card” handout here

Initiation of Cellular Therapies SOP

- Determine CRS Risk and establish tocilizumab stock in clinic and/or local hospital, as

	Blincyto	Kimmtrak	Tecvayli	Lunsumio
Bispecific T-cell-engager	☑	☑	☑	☑
Risk of CRS/ICANS	☑	☑	☑	☑
Requires tocilizumab on-hand in clinic clinic	X	X	Clinic Discretion	
Any grade CRS	14.2%	89%	72.1%	44%
Grade 3-4 CRS	4.9%	0.8%	0.6%	2%
Typical timing of CRS (most common) common)	2 days after infusion start start	1st 3 doses (inpatient)	1st 3 doses (inpatient)	C1D1 or C1D15
Tocilizumab use	Not reported	0.4%	36.4%	7.8%

  - Tocilizumab is not required on-hand in clinic, but **must be kept on-hand at local hospital** whether doses of drug are given in the hospital or not. If provider prefers for tocilizumab to be kept on-hand in clinic, it may be procured.
  - Tocilizumab orders that are specific to CRS should be maintained in an emergency pocket within the nucleus. Please store these separately from Actemra stock maintained for SIS (Specialty Infusion Services) patients. See RN-JBI-041-ATT1 Cytokine Release Syndrome for instructions for ordering and storing tocilizumab for CRS.

Initiation of Cellular Therapies SOP

- Billing/coding tools and financial assistance links provided for financial counselors

CRS Treatment Protocol: Components

- Background/mechanism of CRS/ICANS
- Typical signs/symptoms of CRS/ICANS
- Grading tools
  - ASTCT provided in our protocol because it is most commonly used to grade CRS/ICANS in trials with bispecific T cell engagers
- Treatment recommendations for CRS/ICANS
- Logistics
  - How to place order for treatment for CRS/ICANS in the EMR
  - How to procure and store tocilizumab for the treatment of CRS
- Patient education

Treatment Recommendations for CRS/ICANS

Table 2: CRS Management

Grade	Work-Up	Supportive Care	Treatment	Drug-Specific Considerations
			Outpatient	
1	• Infection work-up (blood and urine cultures, chest radiography) • Cardiac telemetry and pulse oximetry oximetry	Fever: • 1st line: acetaminophen 2nd line: ibuprofen • Maintenance IV fluids for hydration hydration • If not on seizure prophylaxis, initiate levetiracetam 500 mg PO twice daily if at higher risk of seizure, such as those with seizure seizure history, CNS disease, concerning EEG findings, or neoplastic brain lesions If neutropenic: • Treatment setting as per standard of care for febrile neutropenia • Initiate broad-spectrum antibiotics • Consider filgrastim	• Consider tocilizumab 8 mg/kg (max 800 mg) x1 dose for persistent fever lasting greater than 3 days, if fever presented within 72 hours of infusion, or in patients with significant symptoms, symptoms, comorbidities, and/or are elderly	• For Tecvayli: withhold until CRS resolves, add premedication prior to next dose if not already ordered ordered (dexamethasone 16 mg, acetaminophen 500-1000 mg, diphenhydramine 50 mg)[4]. • For Lunsumio: withhold until CRS resolves, add premedication prior to next dose if not already ordered ordered (dexamethasone (20 mg, acetaminophen 500-1000 mg, diphenhydramine 50 mg). If Lunsumio infusion paused for CRS CRS and symptoms resolve, may resume at previous rate. Otherwise ensure CRS symptoms symptoms resolved at least 72 hours prior to next Lunsumio dose.[4]

Table 2: CRS Management (continued)

Grade	Work-Up	Supportive Care	Treatment	Drug-Specific Considerations
			Inpatient	
2	Same as grade 1 1	Fever management as per grade 1 <u>Hypotension:</u> • IV fluid bolus 500-1000 mL; repeat once as needed needed to maintain normal BP • If hypotension persists after IV fluids, tocilizumab, and steroids, start vasopressors, transfer to ICU, obtain ECHO, and refer to further management as as in Grade 3 or 4 CRS <u>Hypoxia:</u> • Supplemental oxygen as needed • If hypoxia persists but is stable with low-flow nasal nasal cannula, continue close monitoring • If hypoxia increases, refer to further management as in Grade 3 or 4 CRS	• Administer tocilizumab 8 mg/kg (max 800 mg) x1 IV over 1 hour o Tocilizumab may be repeated every 8 hours for up to 3 doses in a 24-hour period (up to a maximum of 4 doses per CRS episode) • Consider dexamethasone 10 mg* IV for 1 dose for persistent hypotension after 2 fluid boluses and 1-2 doses of anti-IL6 therapy, reassess in 6 hours or earlier if clinically indicated.	• For Tecvayli: see grade 1 plus hospitalize for 48 hours hours after next dose of Tecvayli • For Lunsumio: see grade 1 plus consider hospitalization for the next dose. If infusion paused for CRS and symptoms resolve, may resume at 50% 50% previous rate and consider starting next dose at at 50% rate. For recurrent grade 2, see grade 3 Lunsumio instructions. • For Kimmtrak: Use 2 mg/kg methylprednisolone equivalent instead of dexamethasone 10 mg. If persistent (lasting 2-3 hours) or recurrent, administer administer corticosteroid premedication (dexamethasone 4 mg) at least 30 minutes prior to next dose.
3	Same as grade 1, plus: Obtain ECHO (if hypotension)	Fever management as per grade 1 <u>Hypotension:</u> • Transfer to ICU • IV fluids boluses as per grade 2 • Use vasopressors as needed <u>Hypoxia:</u> • High-flow supplemental oxygen	• Administer tocilizumab as in grade grade 2 (if not administered previously) • If on one vasopressor and/or grade 3 hypoxia: dexamethasone[1] dexamethasone[1] 10 mg IV every 6 6 hours and rapidly taper once symptoms improve to grade 1 or less • If on two vasopressors: dexamethasone[1] 10-20 mg IV every 6 hours	• For Tecvayli: see grade 2 for first occurrence of grade grade 3 with duration less than 48 hrs. For recurrent grade 3 or first occurrence >48 hrs, permanently discontinue Tecvayli. • For Lunsumio: see grade 2 except hospitalization and and 50% infusion rate <u>required</u> for next dose. For recurrent grade 3, permanently discontinue. • For Kimmtrak: see grade 2 plus withhold Kimmtrak and resume at the same dose level when CRS has resolved. • For Blincyto: Withhold until resolution. Administer dexamethasone 8 mg (instead of 10 mg) Q8H for up to 3 days then taper over 4 days. Resume at 9 mcg daily and increase to 28 mcg daily[5] after 7 days if without adverse reaction.

Table 2: CRS Management (continued)				
Grade	Work-Up	Supportive Care	Treatment	Drug-Specific Considerations
		Inpatient		
4	Same as grade 3	Fever management as per grade 1 Hypotension: • IV fluid boluses and vasopressor use as in grades 2 and 3 Hypoxia: • Positive pressure ventilation	• Administer tocilizumab as in grade 2 (if not administered previously) • Methylprednisolone 1000 mg/day in divided doses IV for 3 days[2] followed by rapid taper[3]	• For Tecvayli: permanently discontinue • For Lunsumio: permanently discontinue • For Kimmtrak: Use 2 mg/kg methylprednisolone equivalent instead of dexamethasone 10 mg. Permanently discontinue • For Blincyto: See grade 3 treatment, discontinue permanently

1. Or methylprednisolone equivalent
2. Increase to methylprednisolone 1000 mg 2 times per day if not improving (per NCCN and ASCO)
3. 250 mg IV every 12 hours for 2 days, 125 mg IV every 12 hours for 2 days, and 60 mg IV every 12 hours until CRS improvement to G1 (per ASCO)
4. See table 2 in Tecvayli package insert or Lunsumio package insert for instructions for restarting Tecvayli after a dose delay
5. If <45 kg, resume at 5 mcg/m2/day and increase to 15 mcg/m2/day after 7 days if without adverse reaction

Table 5: ICANS Management

ICANS Grade	No Concurrent CRS	Additional therapy if concurrent CRS	Drug-Specific Considerations
1	Supportive care If not on seizure prophylaxis, consider initiating levetiracetam 500 mg PO twice daily	Administer tocilizumab 8 mg/kg (max 800 mg) x1 IV over 1 hour Dexamethasone[1]	For Tecvayli: withhold Tecvayli until ICANS resolves[4]
2	Supportive care Consider dexamethasone[2] 10 mg IV x two doses and reassess. Repeat every 6-12 hours if no improvement. Continue until grade 1 or less then taper.	Tocilizumab as per grade 1 If refractory to 1st dose of tocilizumab, Consider dexamethasone[2] 10 mg IV x two doses and reassess. Repeat every 6-12 hours if no improvement. Continue until grade 1 or less then taper.	For Tecvayli: see grade 1 plus hospitalize for 48 hours after next dose of Tecvayli For Lunsumio: withhold until ICANS resolves to grade 1 or less for at least 72 hours[4]
3	ICU care recommended Consider repeat neuroimaging every 2-3 days if symptoms persist Dexamethasone[2] 10 mg IV every 6-12 hours. Continue until grade 1 or less then taper.	Tocilizumab as per grade 1 If refractory to 1st dose of tocilizumab, give dexamethasone[2] 10 mg IV x 1 dose, may repeat every 6-12 hours if no improvement. Continue until grade 1 or less then taper.	For Tecvayli: see grade 2 for first occurrence of grade 3. For recurrent grade 3 permanently discontinue Tecvayli. For Lunsumio: for first occurrence, see grade 2. For recurrent grade 3, permanently discontinue For Blincyto: Withhold for at least 3 days and until grade 1 or less. Resume at 9 mcg daily and increase to 28 mcg daily[5] after 7 days if without adverse reaction. If reaction occurred at 9 mcg dose, takes >7 days to resolve, or patient experiences >1 seizure, permanently discontinue
4	ICU care, consider mechanical ventilation Treatment of status epilepticus per institutional guidelines High-dose corticosteroids (e.g. methylprednisolone 1000 mg 1-2 times per day x 3 days, followed by rapid taper)[3]	Tocilizumab as per grade 1 High-dose corticosteroids (e.g. methylprednisolone 1000 mg 1-2 times per day x 3 days, followed by rapid taper)[3]	For Tecvayli: permanently discontinue For Lunsumio: permanently discontinue For Blincyto: permanently discontinue

1. Consider dexamethasone if refractory to 1st dose of tocilizumab.
2. Or methylprednisolone equivalent
3. Increase to methylprednisolone 1000 mg 2-3 times per day if not improving
4. See table 2 in Tecvayli package insert or Lunsumio package insert for instructions for restarting Tecvayli after a dose delay
5. If <45 kg, resume at 5 mcg/m2/day and increase to 15 mcg/m2/day after 7 days if without adverse reaction

CRS Treatment Protocol: Components

- Background/mechanism of CRS/ICANS
- Typical signs/symptoms of CRS/ICANS
- Grading tools
  - ASTCT provided in our protocol because it is most commonly used to grade CRS/ICANS in trials with bispecific T cell engagers
- Treatment recommendations for CRS/ICANS
- Logistics
  - How to place order for treatment for CRS/ICANS in the EMR
  - How to procure and store tocilizumab for the treatment of CRS
- Patient education

CRS Treatment Logistics: EMR Orderset

Cytokine Release Syndrome Orderset v8.0 (Practice)

Include ordersets defined for: ☑ My practice ☐ Me

Components:

☑	Name	Value	Instructions
☑	Tylenol (Acetaminophen Oral)	650mg	Administer PO.
☑	Decadron IV (Dexamethasone inj)	10mg	**PRN** Administer only PRN as directed by provider for hypotension refractory to tocilizuma Administer in 50ml NS over 20 min. Usual dose is dexamethasone 4 to 10 mg IV. Per NCCN recommended for patients with grade 2 CRS and hypotension refractory to tocilizumab. How idecabtagene vicleucel (Abecma) and lisocabtagene maraleucel (Breyanzi), may consider de early-onset CRS (<72 hours after infusion) in the absence of hypotension.
☑	0.9%NS 500ml	500ml	Administer as directed for hypotension
☑	Actemra (Tocilizumab)	8mg/kg	Administer over one hour. Do not mix with other medications. Dose should not exceed 800m total volume Withdraw a volume of 0.9% Sodium Chloride injection, equal to the volume of th patient's dose from the infusion bag or bottle
☑	CBC		With Differential.
☑	CMP		
☑	CL1	*	
☑	RN- Cellular Therapy Initiation & CRS Management	*	See attached JBI and SOP
☑	Medication Guide	Required	Patient to be Given the Medication Guide Handout https://dailymed.nlm.nih.gov/dailymed/medguide.cfm?setid=2e5365ff-cb2a-4b16-b2c7-e35c6
☑	Managed Care	Required	Please approve Drug
☑	Alert!!!	*	**Dose should not exceed 800mg.**
☑	Consent for Therapy	Required	A consent must be signed by the patient prior to the start of treatment. Consent forms are found in Operational Excellence

CRS Treatment Logistics: Tocilizumab Ordering

Ordering tocilizumab (Actemra®) for CRS Emergencies - AON

Providers and Clinical Nurse Managers should assess the need to maintain tocilizumab (Actemra) on hand **at least 3-4 days prior to initiating any therapy** that may require the use of tocilizumab for CRS purposes.

Clinical Nurse Manager should work with their clinic pharmacy staff to:

- Place the MyService Ticket titled “Nucleus – Add/Delete Pocket”
  - Indicate Drug Name as Actemra and the Drug Unit Size as 200mg
  - Once the ticket has been submitted, procurement will add in the following Emergency Kit – Actemra item to the clinic’s nucleus. Confirmation will be sent by procurement once this has been completed
- Pharmacy staff member or clinical nurse manager must place an order of up to order of **8 x 200mg (800mg dose)** vials of Actemra under this newly created bin and submit it to procurement for processing.
  - Actemra is dosed at 8mg/kg, so individual patients doses needed may differ per patient. An order of 4 vials of 200mg will ensure that any ordered dose (up to 800mg) can be obtained from the emergency stock ordered.
- Upon delivery of the Actemra vials, Pharmacy staff must follow all current procedures for restocking into emergency kit bins within the nucleus.

The steps above are necessary to ensure that clinics maintain their Actemra Emergency stock completely separate from other Actemra stock, especially in clinics that may also be using Actemra for non-CRS purposes.

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Cytokine Release Syndrome and Related Side Effects

American Oncology Network

- Cytokine release syndrome, or CRS, is a systemic inflammatory response that occurs when the immune system is over-activated.
- CRS may occur in response to infection or receipt of certain medications, such as chimeric antigen receptor (CAR) T-cell therapy or bispecific T-cell engaging antibodies.
- Symptoms of CRS may include flu-like symptoms (fever, chills, body aches), low blood pressure, or difficulty breathing.
- Immune effector cell-associated neurotoxicity syndrome, or ICANS, is a neurological condition that may occur with or without CRS. Symptoms of ICANS include confusion, dizziness, headaches, or hallucinations.

- You will be closely monitored for these symptoms after receiving therapy with a risk for CRS or ICANS.
- Occasionally, these symptoms can become severe enough to require inpatient admission for management.
- Early recognition of these symptoms may result in less severe complications.

Contact your health care provider immediately if you experience any of these symptoms or note any changes in behavior:

Chills	Headaches
Fever	Dizziness
Low blood pressure	Hallucinations
Difficulty breathing	Seizures
Confusion	Anxiety

Drug Name and Clinic contact information:

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AON PHARMACY OPERATIONS

CRS Treatment Protocol: Patient Education

AON AMERICAN ONCOLOGY NETWORK, LLC

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Brooke Peters, PharmD, BCOP

Brooke.Peters@aoncology.com