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Chimeric Antigen Receptor (CAR) Cell Therapy Toxicity Assessment and Management

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CTCAE = Common Terminology Criteria for Adverse Events; CRS = Cytokine Release Syndrome
Chimeric Antigen Receptor (CAR) Cell Therapy Toxicity Assessment and Management

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INITIAL EVALUATION

Patient receiving CAR cell therapy → Monitoring\(^1\) of patient per protocol to include:
- Vital signs
- Neurological status
- History
- Physical exam
- Lab results\(^2\)
- Cardiac monitor, EKG, and/or ECHO
- Consider seizure prophylaxis\(^3\)
- Refer to Tumor Lysis in Adult Patients Algorithm for prophylaxis in patients with high tumor burden

Does patient have either?

Yes →
- Determine if patient has Cytokine Release Syndrome (CRS)\(^4\) and/or Neurotoxicity\(^5\)
- Determine the grade of CRS\(^6\) and/or Neurotoxicity\(^7\)
- See pages 6-7 for Management of CRS
- See page 9 for Management of Neurotoxicity

No →

\(^1\)Neurology Team and Critical Care Team to follow patient starting from day of cell infusion.
\(^2\)C-reactive protein and ferritin daily starting on cell infusion day (in addition to normal lab monitoring)
\(^3\)If permitted by protocol, recommended seizure prophylaxis is levetiracetam 500 mg – 750 mg twice daily for 30 days starting from day of cell infusion.
\(^4\)The patient may have CRS if the following are present within the first 3 weeks of CAR cell therapy infusion:
  - Fever (temperature greater than or equal to 38\(^\circ\)C)
  - Hypotension (SBP less than 90 mmHg)
  - Hypoxia (Needing oxygen to maintain oxygen saturation greater than 90%)
  - Organ toxicity (See Appendix C for Grading)
\(^5\)The patient may have neurotoxicity if the following are present:
  - Somnolence
  - Confusion
  - Encephalopathy
  - Dysphasia
  - Seizure
  - Incontinence or motor weakness
  - Tremor
  - Agitation
\(^6\)See Appendix A for Grading of CRS
\(^7\)See Appendix E for Grading of Neurotoxicity

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Appendix A: Grading of CRS
Note: CRS grade should be determined at least twice daily and any time there is a change in patient’s status

<table>
<thead>
<tr>
<th>Category</th>
<th>Sign/Symptom</th>
<th>CRS Grade 1</th>
<th>CRS Grade 2</th>
<th>CRS Grade 3</th>
<th>CRS Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vital signs</td>
<td>Temperature greater than or equal to 38°C</td>
<td>Yes</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td>SBP less than 90 mmHg</td>
<td>No</td>
<td>Responds to IV fluids or low-dose vasopressor</td>
<td>Requires high-dose or multiple vasopressors</td>
<td>Life-threatening</td>
</tr>
<tr>
<td></td>
<td>Needing Oxygen to maintain O₂ saturation greater than 90%</td>
<td>No</td>
<td>FiO₂ less than 40%</td>
<td>FiO₂ greater than or equal to 40% and/or requiring BiPAP</td>
<td>Requires ventilator support</td>
</tr>
<tr>
<td>Organ Toxicity</td>
<td>See Appendix C</td>
<td>Grade 1</td>
<td>Grade 2</td>
<td>Grade 3 or grade 4 transaminitis</td>
<td>Grade 4 except grade 4 transaminitis</td>
</tr>
</tbody>
</table>

1Grade 1 CRS may manifest as fever and/or grade 1 organ toxicity.
2For grades 2, 3, or 4 CRS: any one of the criteria other than temperature is sufficient.
3See Appendix C and CTCAE, version 4 for grading of organ toxicity.
4See Appendix B for definition of high-dose vasopressors.

Appendix B: Definition of High-dose Vasopressors

<table>
<thead>
<tr>
<th>Vasopressor</th>
<th>Definition of High-dose Vasopressor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine monotherapy</td>
<td>Greater than or equal to 20 mcg/minute</td>
</tr>
<tr>
<td>Dopamine monotherapy</td>
<td>Greater than or equal to 10 mcg/kg/minute</td>
</tr>
<tr>
<td>Phenylephrine monotherapy</td>
<td>Greater than or equal to 200 mcg/minute</td>
</tr>
<tr>
<td>Epinephrine monotherapy</td>
<td>Greater than or equal to 10 mcg/minute</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>Vasopressin + norepinephrine equivalent of greater than or equal to 10 mcg/minute</td>
</tr>
<tr>
<td>Combination vasopressors (not including vasopressin)</td>
<td>Norepinephrine equivalent of greater than or equal to 20 mcg/minute</td>
</tr>
</tbody>
</table>

FiO₂ = Fraction of inspired oxygen; SBP = Systolic blood pressure; BiPAP = Bilevel Positive Airway Pressure

Vasopressin equivalent equation: norepinephrine equivalent dose = [norepinephrine (mcg/minute)] + [dopamine (mcg/kg/minute) / 2] + [epinephrine (mcg/minute)] + [phenylephrine (mcg/minute) / 10].

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**Appendix C: CTCAE grading of common organ toxicities**

<table>
<thead>
<tr>
<th>Category</th>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac</strong></td>
<td>Sinus tachycardia</td>
<td>Asymptomatic, No intervention needed</td>
<td>Symptomatic, non-urgent intervention indicated</td>
<td>Urgent intervention indicated</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Arrhythmia or heart block</td>
<td>Asymptomatic, No intervention needed</td>
<td>Symptomatic, non-urgent intervention indicated</td>
<td>Urgent intervention indicated</td>
<td>Life-threatening</td>
</tr>
<tr>
<td></td>
<td>Ejection fraction decreased</td>
<td>-</td>
<td>EF 40-50% or 10-19% drop from baseline</td>
<td>EF 20-39% or greater than or equal to 20% drop from baseline</td>
<td>EF less than 20%</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td>Pleural effusion</td>
<td>Asymptomatic, No intervention needed</td>
<td>Symptomatic, intervention indicated</td>
<td>Symptomatic with respiratory distress; needs surgical intervention (chest tube or pleurodesis)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Pulmonary edema</td>
<td>Minimal dyspnea on exertion</td>
<td>Moderate dyspnea on exertion; medical intervention indicated; limits instrumental ADL</td>
<td>Dyspnea at rest; oxygen indicated; limits self-care ADL</td>
<td>Life-threatening; urgent intervention or ventilatory support indicated</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td>Nausea</td>
<td>Loss of appetite without alteration in eating habits</td>
<td>Oral intake decreased without dehydration or weight loss</td>
<td>Inadequate oral caloric or fluid intake; receiving tube feeding or TPN</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>1-2 episodes / 24 hours</td>
<td>3-5 episodes / 24 hours</td>
<td>Greater than 6 episodes / 24 hours; receiving tube feeding or TPN</td>
<td>Life-threatening</td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
<td>Increase of 1-3 stools/day over baseline</td>
<td>Increase of 4-6 stools/day over baseline</td>
<td>Increase of greater than 6 stools/day over baseline; limits self-care ADL</td>
<td>Life-threatening</td>
</tr>
</tbody>
</table>

CTCAE= Common Terminology Criteria for Adverse Events; EF = Ejection fraction; ADL = Activities of daily living

1Ejection fraction may be increased with Cytokine Release Syndrome, but is not graded.
# Chimeric Antigen Receptor (CAR) Cell Therapy Toxicity Assessment and Management

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## Appendix C: CTCAE grading of common organ toxicities - continued

<table>
<thead>
<tr>
<th>Category</th>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatic</strong></td>
<td>AST or ALT increased</td>
<td>Greater than ULN to 3 x ULN</td>
<td>Greater than 3 x ULN to 5 x ULN</td>
<td>Greater than 5 x ULN to 20 x ULN</td>
<td>Greater than 20 x ULN</td>
</tr>
<tr>
<td></td>
<td>Total bilirubin increased</td>
<td>Greater than ULN to 1.5 x ULN</td>
<td>Greater than 1.5 x ULN to 3 x ULN</td>
<td>Greater than 3 x ULN to 10 x ULN</td>
<td>Greater than 10 x ULN</td>
</tr>
<tr>
<td><strong>Renal</strong></td>
<td>Urine output decreased</td>
<td>-</td>
<td>-</td>
<td>Oliguria (less than 80 mL / 8 hours)</td>
<td>Anuria (less than 240 mL / 24 hours)</td>
</tr>
<tr>
<td></td>
<td>Acute kidney injury</td>
<td>Creatinine 1.5-2 x above baseline</td>
<td>Creatinine 2-3 x above baseline</td>
<td>Creatinine greater than 3 x baseline or greater than 4 mg/dL</td>
<td>Life-threatening; dialysis indicated</td>
</tr>
<tr>
<td><strong>Coagulopathy</strong></td>
<td>Disseminated Intravascular Coagulation (DIC)</td>
<td>Laboratory findings with no bleeding</td>
<td>Laboratory findings with bleeding</td>
<td>Papules and/or pustules covering greater than 30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL</td>
<td>Papules and/or pustules covering any percent BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection with IV antibiotics indicated; life threatening consequences</td>
</tr>
<tr>
<td><strong>Skin</strong></td>
<td>Rash aciform</td>
<td>Papules and/or pustules covering less than 10% BSA, which may or may not be associated with symptoms of pruritus or tenderness</td>
<td>Papules and/or pustules covering 10 - 30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; associated with psychosocial impact; limiting instrumental ADL</td>
<td>Papules and/or pustules covering greater than 30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; limiting self care ADL; associated with local superinfection with oral antibiotics indicated</td>
<td>Papules and/or pustules covering greater than 30% BSA with or without associated symptoms; limiting self care ADL</td>
</tr>
<tr>
<td></td>
<td>Rash maculo-papular</td>
<td>Macules/papules covering less than 10% BSA with or without symptoms (e.g., pruritus, burning, tightness)</td>
<td>Macules/papules covering 10-30% BSA with or without symptoms (e.g., pruritus, burning, tightness); limiting instrumental ADL</td>
<td>Macules/papules covering greater than 30% BSA with or without associated symptoms; limiting self care ADL</td>
<td>-</td>
</tr>
</tbody>
</table>

Note: For toxicities not listed here, please refer to CTCAE, version 4 for grading.

AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; ULN = Upper limit of normal; BSA = Body surface area

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### Appendix D: Management of CRS and Organ Toxicity

<table>
<thead>
<tr>
<th>CRS Grade</th>
<th>Sign/Symptom</th>
<th>Management</th>
</tr>
</thead>
</table>
| Grade 1   | Fever or grade 1 organ toxicity | • Acetaminophen and hypothermia blanket as needed for fever  
• Ibuprofen if fever is not controlled with above; use with caution or avoid if thrombocytopenic  
• Assess for infection with blood and urine cultures, and chest x-ray  
• Consider antibiotics and filgrastim (if neutropenic)  
• IV fluids as needed  
• Symptomatic management of constitutional symptoms and organ toxicities |
| Grade 1   | Hypotension   | • IV fluid bolus of 500 – 1000 mL normal saline; repeat as necessary to maintain SBP greater than 90 mmHg.  
• Tocilizumab 8 mg/kg (maximum 800 mg/dose) IV every 6 hours as needed for up to 3 doses / 24 hours  
• If hypotension persists after two fluid boluses, start vasopressors, transfer patient to ICU, and obtain ECHO  
• In patients at high-risk for CRS or if hypotension persists after 1-2 doses of tocilizumab, may use dexamethasone 10 mg IV every 6 hours  
• Manage fever and constitutional symptoms as in Grade 1 CRS |
| Grade 2   | Hypoxia       | • Use supplemental oxygen as needed  
• Use tocilizumab with or without corticosteroids as in hypotension  
• Manage fever and constitutional symptoms as in Grade 1 CRS |
| Grade 2 organ toxicity | Manage organ toxicity as per standard guidelines  
Use tocilizumab with or without corticosteroids as in hypotension  
Manage fever and constitutional symptoms as in Grade 1 CRS |

1High risk for severe CRS:  
• High tumor burden  
• Co-morbidities (a score of 3 or greater using the Hematopoietic Cell Transplantation Comorbidity Index; for solid tumor patients – prior solid tumor excluding non-melanoma skin cancer will not be counted)  
• Age greater than or equal to 60 years  
• Early onset CRS (less than 3 days from cell infusion).  

SBP = Systolic blood pressure
## Appendix D: Management of CRS and Organ Toxicity

<table>
<thead>
<tr>
<th>CRS Grade</th>
<th>Sign/Symptom</th>
<th>Management</th>
</tr>
</thead>
</table>
| **Grade 3** | **Hypotension** | • IV fluid boluses as needed as in Grade 2 CRS  
• Tocilizumab 8 mg/kg (maximum 800 mg/dose) IV every 6 hours as needed for up to 3 doses / 24 hours if not administered previously  
• Use vasopressors as needed  
• Transfer patient to ICU and obtain ECHO if not done already  
• Start dexamethasone 10 mg IV every 6 hours\(^1\)  
• Manage fever and constitutional symptoms as in Grade 1 CRS |
| | **Hypoxia** | • Use supplemental oxygen as needed  
• Use tocilizumab and corticosteroids as above  
• Manage fever and constitutional symptoms as in Grade 1 CRS |
| | **Grade 3 organ toxicity or grade 4 transaminitis** | • Manage organ toxicity as per standard guidelines  
• Use tocilizumab and corticosteroids as above  
• Manage fever and constitutional symptoms as in Grade 1 CRS |
| **Grade 4** | **Hypotension** | • Manage as in Grade 3 CRS |
| | **Hypoxia** | • Mechanical ventilation |
| | **Grade 4 organ toxicity excluding transaminitis** | • Manage as in Grade 3 CRS |

\(^1\)Alternatively, methylprednisolone has also been used at doses ranging from 1 mg/kg IV every 12 hours to 500 mg IV every 12 hours for 3 days, followed by rapid taper (250 mg every 12 hours x 2 days, 125 mg every 12 hours x 2 days, and 60 mg every 12 hours x 2 days). Corticosteroid taper may be individualized depending on toxicity.
Chimeric Antigen Receptor (CAR) Cell Therapy
Toxicity Assessment and Management

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Appendix E: Grading of Neurotoxicity

<table>
<thead>
<tr>
<th>Sign/Symptom</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somnolence1</td>
<td>Mild drowsiness / sleepiness</td>
<td>Moderate somnolence, limiting instrumental ADL</td>
<td>Obtundation or stupor</td>
<td>Life-threatening needing urgent intervention or mechanical ventilation</td>
</tr>
<tr>
<td>Confusion1</td>
<td>Mild disorientation / confusion</td>
<td>Moderate disorientation, limiting instrumental ADL</td>
<td>Severe disorientation, limiting self-care ADL</td>
<td></td>
</tr>
<tr>
<td>Encephalopathy1</td>
<td>Mild limiting of ADL</td>
<td>Limiting instrumental ADL</td>
<td>Limiting self-care ADL</td>
<td></td>
</tr>
<tr>
<td>Dysphasia1</td>
<td>Dysphasia not impairing ability to communicate</td>
<td>Dysphasia with moderate impairment in ability to communicate spontaneously</td>
<td>Severe receptive or expressive dysphasia, impairing ability to read, write or communicate intelligibly</td>
<td></td>
</tr>
<tr>
<td>Seizure1</td>
<td>Brief partial seizure; no loss of consciousness</td>
<td>Brief generalized seizure</td>
<td>Multiple seizures despite medical intervention</td>
<td>Life-threatening; prolonged repetitive seizures</td>
</tr>
<tr>
<td>Incontinence or motor weakness2</td>
<td>-</td>
<td>-</td>
<td>Bowel / bladder incontinence; Weakness limiting self-care ADL, disabling</td>
<td>-</td>
</tr>
<tr>
<td>Tremor1</td>
<td>Mild symptoms</td>
<td>Moderate symptoms; limiting instrumental ADL</td>
<td>Severe symptoms; limiting self care ADL</td>
<td></td>
</tr>
<tr>
<td>MD Anderson 10-point Neurotoxicity grade2</td>
<td>Mild (7-9)</td>
<td>Moderate (3-6),</td>
<td>Severe (1-2), grade 1 and 2 papilledema with CSF OP less than 20 mmHg; Critical (obtunded; convulsive status epileptics; motor weakness; grade 3, 4 and 5 papilledema; CSF OP greater than or equal to 20 mmHg; cerebral edema)</td>
<td></td>
</tr>
</tbody>
</table>

1 Grading per CTCAE, version 4  
2 See Appendix G for Simplified 10-point Neurologic Examination

ADL = Activities of daily living; OP = Opening pressure

Note: For toxicities not listed here, please refer to CTCAE, version 4 for grading.
# Chimeric Antigen Receptor (CAR) Cell Therapy Toxicity Assessment and Management

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## Appendix F: Management of Neurotoxicity

<table>
<thead>
<tr>
<th>Grade</th>
<th>Management</th>
</tr>
</thead>
</table>
| Grade 1 | Vigilant supportive care; aspiration precautions  
Daily simplified neurologic examination as in Appendix G  
Fundus exam to assess for papilledema  
MRI brain and diagnostic lumbar puncture with OP; MRI spine if focal signs exist  
Daily 30 minute EEG; if no seizures detected on EEG, continue levetiracetam  
If EEG shows non-convulsive status epilepticus, treat as per algorithm in Appendix H  
Consider Tocilizumab 8 mg/kg (maximum 800 mg/dose) IV if associated with Grade 2 or greater CRS  
Manage as per Grade 1  
Consider ICU transfer if associated with Grade 2 or greater CRS  
Tocilizumab 8 mg/kg (maximum 800 mg/dose) IV if associated with Grade 2 or greater CRS |
| Grade 2 | Manage as per Grade 1  
Tocilizumab 8 mg/kg (maximum 800 mg/dose) IV every 6 hours for up to 3 doses / 24 hours if not administered previously  
Consider corticosteroids (e.g. dexamethasone 10 mg IV every 6 hours or methylprednisolone 1 mg/kg IV every 12 hours) for worsening symptoms despite tocilizumab. Continue corticosteroids until reversal of toxicity is seen and taper over 1-2 weeks.  
Low grade (1 & 2) papilledema with CSF OP less than 20 mmHg, see Appendix I  
Consider ICU transfer if associated with Grade 2 or greater CRS  
Consider repeat neuro-imaging (CT or MRI) every 2-3 days if persistent neurotoxicity greater than or equal to grade 3 |
| Grade 3 | Manage as per Grade 3  
ICU monitoring  
High-dose corticosteroids [e.g. methylprednisolone IV 1,000 mg/day x 3 days followed by rapid taper (250 mg every 12 hours x 2 days, 125 mg every 12 hours x 2 days, and 60 mg every 12 hours x 2 days)]. Continue until reversal of toxicity is seen and taper over 2 weeks.  
For convulsive status epilepticus, treat as per Appendix J  
High grade (3, 4, & 5) papilledema, CSF OP greater than or equal to 20 mmHg, or cerebral edema, see Appendix I |
| Grade 4 | “Orientation to year, month, city, hospital, President: 5 points  
Ability to write a standard sentence (e.g. National bird is the bald eagle): 1 point  
Name 3 objects (point to clock, pen, button): 3 points  
Count backwards from 100 by tens: 1 point  
Normal – score 10  
Mild neurotoxicity – score 7-9  
Moderate neurotoxicity – score 3-6  
Severe neurotoxicity – score 1-2, mild papilledema (grade 1 or 2) with CSF OP less than 20 mmHg  
Critical neurotoxicity – Obtunded / stuporous and/or any new motor weakness and/or convulsive status epilepticus, and/or higher grade papilledema (grade 3, 4, or 5), CSF OP greater than or equal to 20 mmHg, cerebral edema seen on neuro-imaging |

---

Appendix G: Simplified 10-Point Neurologic Examination

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Normal</td>
</tr>
<tr>
<td>7-9</td>
<td>Mild neurotoxicity</td>
</tr>
<tr>
<td>3-6</td>
<td>Moderate neurotoxicity</td>
</tr>
<tr>
<td>1-2</td>
<td>Severe neurotoxicity</td>
</tr>
<tr>
<td>1</td>
<td>Critical neurotoxicity</td>
</tr>
</tbody>
</table>

OP = Opening pressure

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Chimeric Antigen Receptor (CAR) Cell Therapy
Toxicity Assessment and Management

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Appendix H: Management of Non-convulsive Status Epilepticus

- Assess ABC / airway protection / high flow O2, check blood glucose
- Lorazepam 0.5 mg IV × 1 with additional 0.5 mg IV every 5 minutes (to a maximum cumulative dose of 2 mg) to control electrographical seizures
- Levetiracetam 500 mg IV bolus
- If seizures persist, transfer to ICU and add a second agent phenobarbital at a loading dose of 60 mg IV
- Maintenance doses after resolution of status epilepticus
  - Lorazepam 0.5 mg IV every 8 hours × 3 doses
  - Increase levetiracetam to 1,000 mg IV every 12 hours
  - Phenobarbital 30 mg IV every 12 hours
- Acetazolamide 1,000 mg IV followed by 250 mg-1000 mg IV every 12 hours (adjust dose based on renal function and acid/base balance)

Appendix I: Management of Cerebral Edema

<table>
<thead>
<tr>
<th>Grade 1 and 2 papilledema with CSF OP less than 20 mmHg without cerebral edema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetazolamide 1,000 mg IV followed by 250 mg-1000 mg IV every 12 hours (adjust dose based on renal function and acid/base balance)</td>
</tr>
</tbody>
</table>

- Use high-dose steroids as per Grade 4 neurotoxicity along with the following measures for management of cerebral edema
- Elevate head of bed to 30 degrees
- Hyperventilation to achieve target PaCO2 of 28-30 mmHg for 24 hours
- Hyperosmolar therapy with either mannitol 20% or hypertonic saline (3% or 23.4%)
  - Mannitol: initial dose 0.5-1 g/kg; maintenance dose 0.25-1 g/kg every 6 hours (metabolic profile and serum osmolality every 6 hours; hold mannitol if serum osmolality greater than or equal to 320 mOsm/kg or osmolol gap greater than or equal to 40)
  - Hypertonic saline: initial dose 250 mL of 3% hypertonic saline, maintenance dose 50-100 mL/hour (electrolytes every 4 hours; hold infusion if serum sodium greater than or equal to 155 mEq/L)
- Hypertonic saline: initial dose 250 mL of 3% hypertonic saline, maintenance dose 50-100 mL/hour (electrolytes every 4 hours; hold infusion if serum sodium greater than or equal to 155 mEq/L)
  - Hypertonic saline: initial dose 250 mL of 3% hypertonic saline, maintenance dose 50-100 mL/hour (electrolytes every 4 hours; hold infusion if serum sodium greater than or equal to 155 mEq/L)
- Imminent herniation: initial dose 30 mL of 23.4% hypertonic saline (may repeat in 15 minutes)
- If patient has ommaya reservoir, drain CSF to target OP less than 20 mmHg
- Consider neurosurgery consultation, IV anesthetics for burst-suppression EEG
- Metabolic profile every 6 hours; daily Head CT; and adjust above medications to prevent rebound cerebral edema, renal failure, electrolyte abnormalities, hypovolemia and hypotension.

Appendix J: Management of Convulsive Status Epilepticus

- Assess ABC / airway protection / high flow O2, check blood glucose
- MERIT team to evaluate for transfer to ICU
- Lorazepam 2 mg IV × 1 with additional 2 mg IV to a total of 4 mg to control electrographic seizures
- Levetiracetam 500 mg IV bolus
- If seizures persist, transfer to ICU and add a second agent phenobarbital at a loading dose 15 mg/kg IV
- Maintenance doses after resolution of status epilepticus
  - Lorazepam 0.5 mg IV every 8 hours × 3 doses
  - Increase levetiracetam to 1,000 mg IV every 12 hours
  - Phenobarbital 1-3 mg/kg IV every 12 hours
  - Continuous EEG if seizures are refractory

ABC = Airway, breathing, circulation; OP = Opening pressure

Approved by the Executive Committee of the Medical Staff on 09/27/2016
Chimeric Antigen Receptor (CAR) Cell Therapy Toxicity Assessment and Management

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

SUGGESTED READINGS


Chimeric Antigen Receptor (CAR) Cell Therapy Toxicity Assessment and Management

This practice consensus algorithm is based on majority expert opinion of the CAR Cell Therapy Toxicity Assessment and Management work group at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following providers:

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