mSMART

Mayo Stratification for Myeloma And Risk-adapted Therapy

Management of Teclistamab Cytokine Release Syndrome (CRS) and Immune Cell Associated Neurotoxicity Syndrome (ICANS)

• Teclistamab was approved by FDA on October 25, 2022 for relapsed, refractory myeloma
  • After 4 prior lines of therapy AND
  • Exposure to proteasome inhibitor, IMiDs, and anti-CD38 antibody
• Package insert and REMS (Risk Evaluation and Mitigation System) provides guidelines for step up dosing adjustment for CRS and ICANS
• This consensus opinion specifically addresses acute management of CRS and ICANS
Options for Management of Teclistamab associated CRS

- Consider disease debulking whenever possible to reduce CRS risk during step-up dosing.
- For treatment centers with capability for outpatient monitoring and rapid escalation of inpatient care when needed, initial monitoring with Teclistamab doses can be done outpatient.
- Proactive intervention should be given early in the onset of CRS to reduce the likelihood of progression to higher grade.
- Prophylactic cytokine blockade with bispecific antibody is being studied and not standard of care at this time.

<table>
<thead>
<tr>
<th>Grading (ASTCT 2019 guideline)</th>
<th>Tocilizumab</th>
<th>Steroid</th>
<th>Other management considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (fever only, without hypotension or hypoxia)</td>
<td>Can be given. Can repeat dose q8hr if no improvement for up to 3 doses total.</td>
<td>Can be given. DEX 10 mg PO/IV. If given first, consider tocilizumab if no improvement in 4 hours.</td>
<td>Consider inpatient monitoring for institutions able to monitor outpatient depending on clinical escalation of symptoms and infrastructure support. Assess for infections.</td>
</tr>
<tr>
<td>Grade 2-4</td>
<td>Same as Grade 1. If no improvement after the first dose of toci, see other management section. Consider additional cytokine blockade such as siltuximab, anakinra.</td>
<td>DEX up to 10-20 mg PO/IV q6hrs. If no improvement within 24 hours, methylprednisolone 1000 - 2000 mg IV daily for up to 3 days, and taper q2-3 days as tolerated.</td>
<td>Inpatient monitoring. Cytokine panel monitoring if more than 1 dose of toci needed or scheduled steroid given. Consider alternative cytokine blockade. Monitor cardiac, renal and hepatic functions. If dysfunction not attributed to other causes, manage as refractory CRS.</td>
</tr>
</tbody>
</table>

## Options for Management of Teclistamab associated CRS

Additional medications have been used to manage CAR-T and T cell engagers associated severe CRS, HLH/MAS. Use may be off label usage and not covered by insurance.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting Dose</th>
<th>Comment(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anakinra</td>
<td>100 mg subQ BID</td>
<td>• IV doses can be given if concerns for subQ absorption. • Dose up to 48 mg/kg/day and 3500 mg/day IV for 3 days have been tolerated in infection and COVID-19. • Max dose: 100 mg bolus, 2mg/kg/hr IV.</td>
</tr>
<tr>
<td>Siltuximab</td>
<td>11mg/kg IV over 1-hour x 1</td>
<td>• If cytokine blockade in IL-6 strongly consider.</td>
</tr>
<tr>
<td>Basiliximab</td>
<td>20 mg IV x1</td>
<td>• If cytokine blockade in IL-2 strongly consider • Assess response after 6 to 8 hours; for robust responses additional doses can be given 4 days after the first.</td>
</tr>
<tr>
<td>Etoposide</td>
<td>150 mg/m^2 IV twice a week</td>
<td>• Not exceeding a cumulative dose of 2 grams.</td>
</tr>
<tr>
<td>Ruxolitinib</td>
<td>5mg po BID with a max of 20 mg po BID</td>
<td></td>
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<tr>
<td>Etanercept</td>
<td>25 mg subQ 2 times a week</td>
<td></td>
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<tr>
<td>Cyclosporine</td>
<td>trough of 200 to 250</td>
<td></td>
</tr>
<tr>
<td>Emapalumab</td>
<td>1 mg/kg IV 2 times a week</td>
<td>• Non-formulary treatment and may increase administration time. • If cytokine blockade in IFN-γ strongly consider. • Max Dose: 10 mg/kg IV 2 times a week.</td>
</tr>
</tbody>
</table>

v1 //last reviewed Jan 2023.
Management of Teclistamab associated CRS

CRS Grade

Grade 1
(fever only, without hypotension or hypoxia)

- **Tocilizumab** 1 dose

  - No improvement in 8 hours

  - **Tocilizumab** Repeat IV q8h (up to 3 doses total)

  - **Can start with Dexamethasone 10 mg PO/IV** 1 dose

- No improvement in 4 hours

  - **OR**

  - **Can start with Dexamethasone 10 mg PO/IV** 1 dose

Grade 2-4

- **Tocilizumab** Repeat IV q8h (up to 3 doses total)

  - **Can add Dexamethasone 10-20 mg PO/IV q6h**

    For progressive symptoms after the second dose of Tocilizumab consider alternative cytokine blockade

  - **Methylprednisolone** 1000-2000 mg IV daily x 3 days and taper over 2-3 days as tolerated.

Management considerations

Grade 1
- Consider inpatient monitoring for institutions able to monitor outpatient depending on clinical escalation of symptoms and infrastructure support
- Assess for infections

Grade 2-4
- Inpatient monitoring.
- Monitor cytokine panel and consider alternative cytokine blockade like siltuximab, anakinra.
- Monitor cardiac, renal and hepatic functions. If dysfunction not attributed to other causes, manage as refractory CRS.

v1 //last reviewed Jan 2023.
# Options for Management of Teclistamab associated ICANS

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<th>Grading (ASTCT 2019 guideline)</th>
<th>Steroid</th>
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<tbody>
<tr>
<td>Grade 1 (ICE score 7-9, awakens spontaneously, no seizure, motor deficits, increased ICP or cerebral edema)</td>
<td></td>
<td></td>
</tr>
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</table>
|  | • Consider DEX 10-20 mg PO/IV daily. | • If ICANS occurs during CRS and tocilizumab has not been given for CRS, tocilizumab can be given for CRS.  
• Consider initiating steroid for neurologic presentation that impacts patient safety.  
• Consider monitoring without steroid for dysphasia presentation alone.  
• Consider addition of Keppra for seizure prophylaxis. |
| Grade 2-4 | • DEX 10-20 mg PO/IV up to q6hr. De-escalate as quickly as tolerated when improved to Gr 1 or less.  
• Methylprednisolone, consider 2 mg/kg or up to 1000-2000 mg IV daily dose if symptoms continue to worsen despite DEX. |  |

Management of Teclistamab associated ICANS

ICANS Grade

Grade 1
ICE score 7-9, awakens spontaneously, no seizure, no motor deficits, increased ICP or cerebral edema

Grade 2-4

Dexamethasone
10-20 mg PO/IV daily

No
Symptom improvement

Yes
De-escalate & Taper off steroid as quickly as tolerated for symptoms <= Gr 1 not impacting ADL or patient safety

Methylprednisolone
2mg/kg OR 1000 - 2000 mg IV daily

No
Symptom improvement

Yes

Management considerations

Grade 1
- ICANS during CRS- Tocilizumab can be given for CRS
- Neurologic presentation impacts patient safety- Initiate steroids
- Dysphasia alone at presentation- Monitor without steroid
- Seizure prophylaxis- Add keppra

Grade 2-4
- Neurologic evaluation to rule out raised ICP, seizures, cerebral edema and infections