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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

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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.

Grading (ASTCT 2019 guideline)[1]	**Tocilizumab**	**Steroid**	**Other management considerations**
Grade 1 (fever only, without hypotension or hypoxia)	• Can be given. • Can repeat dose q8hr if no improvement for up to 3 doses total.	• Can be given. DEX 10 mg PO/IV. • If given first, consider tocilizumab if no improvement in 4 hours.	• Consider inpatient monitoring for institutions able to monitor outpatient depending on clinical escalation of symptoms and infrastructure support • Assess for infections
Grade 2-4	• 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.	• 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.	• 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.

1. Lee DW et al. BBMT 2019; 25: 625-638. PMID:30592986.

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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

Medication	Starting Dose	Comment(s)
Anakinra	100 mg subQ BID	• 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.
Siltuximab	11mg/kg IV over 1-hour x 1	• If cytokine blockade in IL-6 strongly consider.
Basiliximab	20 mg IV x1	• 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.
Etoposide	150 mg/m^2 IV twice a week	• Not exceeding a cumulative dose of 2 grams.
Ruxolitinib	5mg po BID with a max of 20 mg po BID	
Etanercept	25 mg subQ 2 times a week	
Cyclosporine	trough of 200 to 250	
Emapalumab	1 mg/kg IV 2 times a week	• 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.

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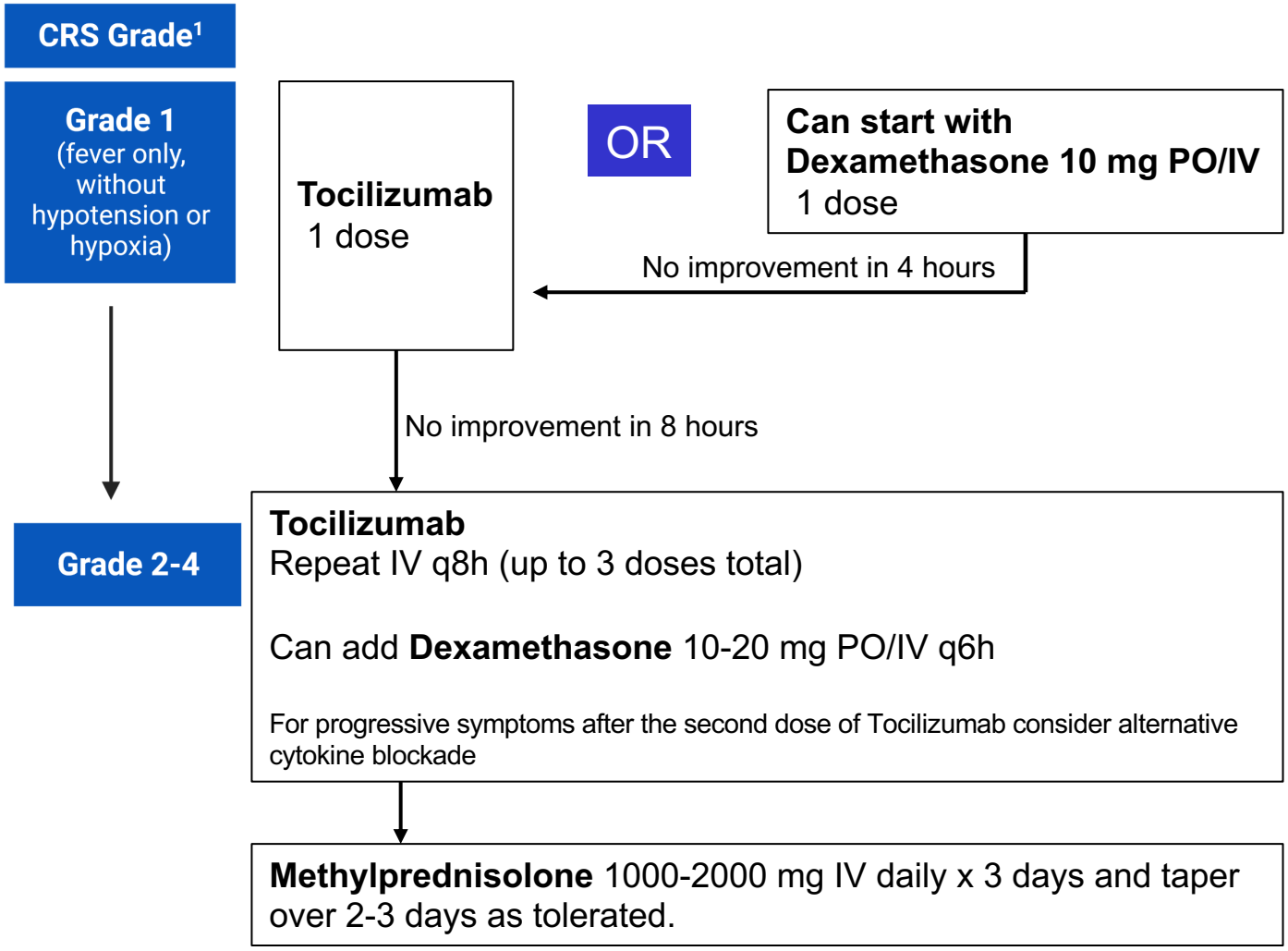
Management of Teclistamab associated CRS



Management considerations

Grade1

- 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.

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Options for Management of Teclistamab associated ICANS

Grading (ASTCT 2019 guideline)[1]	Steroid	Other management considerations
Grade 1 (ICE score 7-9, awakens spontaneously, no seizure, motor deficits, increased ICP or cerebral edema)	• 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.	• Neurologic evaluation as appropriate to rule out increased intracranial pressure (ICP), cerebral edema, seizure, and infections.

1. Lee DW et al. BBMT 2019; 25: 625-638. PMID:30592986.

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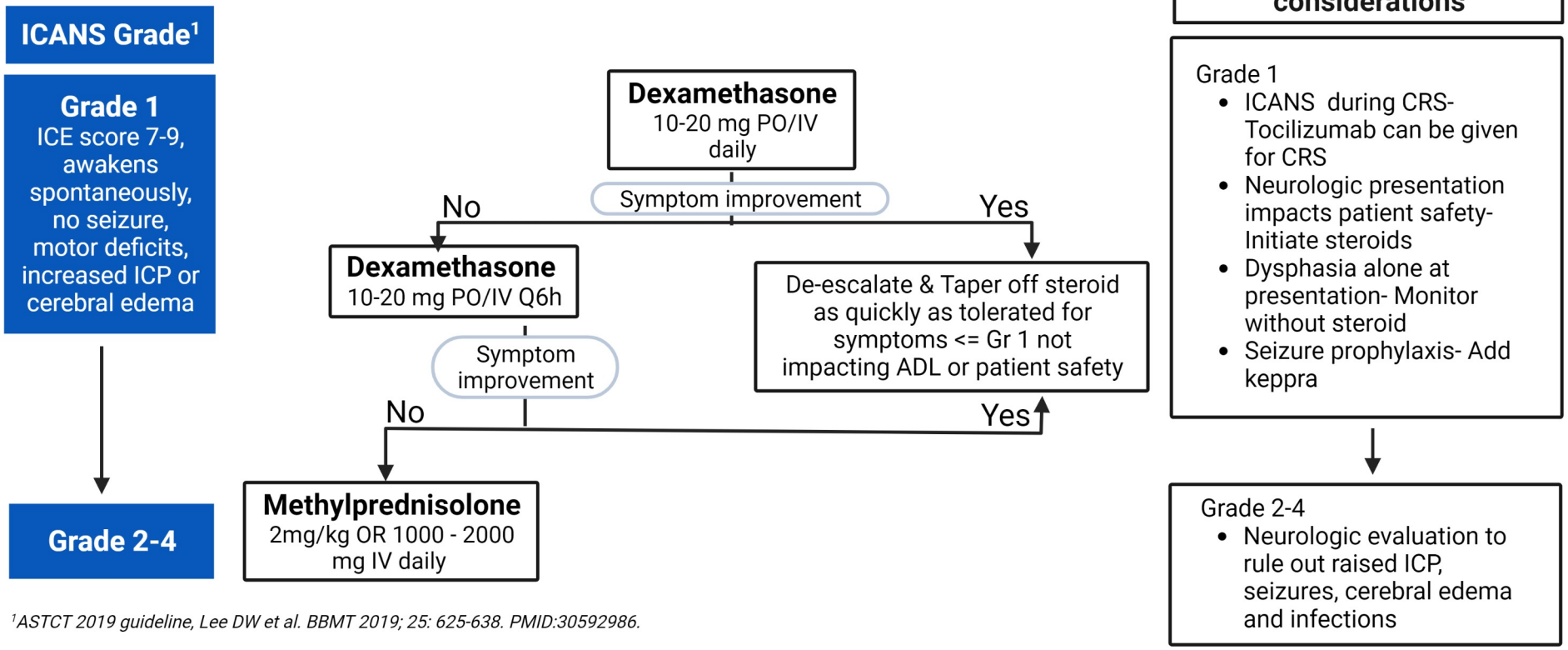
Management of Teclistamab associated ICANS



[1]*ASTCT 2019 guideline, Lee DW et al. BBMT 2019; 25: 625-638. PMID:30592986.*