Management of CAR T-Cell Toxicities: Concordance Between Healthcare Providers and **Expert Consensus Recommendations in 2019 and 2020**

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Background

- CAR T-cell therapy has been a major innovative breakthrough for hematologic malignancies with 2 currently FDA-approved CAR T-cell products (tisagenlecleucel^[1] and axicabtagene ciloleucel^[2]) and several others in different stages of clinical investigation
- CAR T-cell therapies are associated with unique safety profiles and potentially serious toxicities, including cytokinerelease syndrome (CRS) and immune effector cell–associated neurotoxicity (ICANS)
- These adverse events (AEs) require vigilant monitoring and prompt recognition and management to ensure patient safety and optimal therapeutic benefit
- CCO developed an online Interactive Decision Support Tool to give healthcare providers (HCPs) case-specific, evidence-based consensus guidance from a panel of 5 interdisciplinary experts on the management of AEs due to CAR T-cell therapy
- Here, we report an updated comparison of planned CAR T-cell toxicity management among HCPs using the tool vs the expert consensus recommendations in the tool between the first 231 cases entered from 5/9/2019 through 9/18/2019 (Cohort 1) and the next 200 cases entered from 9/19/2019 through 7/31/2020 (Cohort 2)

	Recommendations Manage fever and constitutional symptoms as per grade 1 CRS: Acetaminophen and hypothermia blanket as needed for fever
Interactive Decision Support Tool	Administer IV fluids as needed
CAR-T Toxicity Mana Enter Patient Details Has the patient already received CA	Symptomatic management of constitutional symptom indicated 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4. 4.
Is the patient experiencing an adverse event? Yes [Change] Which adverse event is the patient experiencing? (i)	 If neutropenic, consider antibiotics If CRS is not resolving or symptoms are not consistent Maximize CRS management efforts with tocilizum Perform workup for HLH/MAS Evaluate for occult infections
 Cytokine release syndrome (CRS) Neurotoxicity (immune effector cell-associated neurotoxicity [ICANS]) with or wi concurrent CRS 	 Hypotension: Initiate tocilizumab at 8 mg/kg IV over 1 hour, not to exceed 800 If no improvement, repeat tocilizumab in 8 hours; do not exceed
What grade is the CRS? () Grade 1 () Grade 2 () Grade 3 () Grade 4 ()	 If hypotension persists after fluid boluses plus IL-6 antagonist, and initiate other hemodynamic monitoring methods Administer vasopressors as needed Transfer to ICU, obtain ECHO, and initiate other hemodynamic methods
	 Initiate dexamethasone* 10 mg IV every 6 hours If refractory, treat as CRS grade 4 Hypoxia: Administer supplemental oxygen, including high-flow oxygen delivered a ASBMT defines high-flow nasal cannula as oxygen delivered a Administer tocilizumab and corticosteroids* as above with supplemental based Administer tocilizumab and corticosteroids* as above with supplemental based Administer tocilizumab and corticosteroids* as above with supplemental based

The tool is online at: clinicaloptions.com/carttool

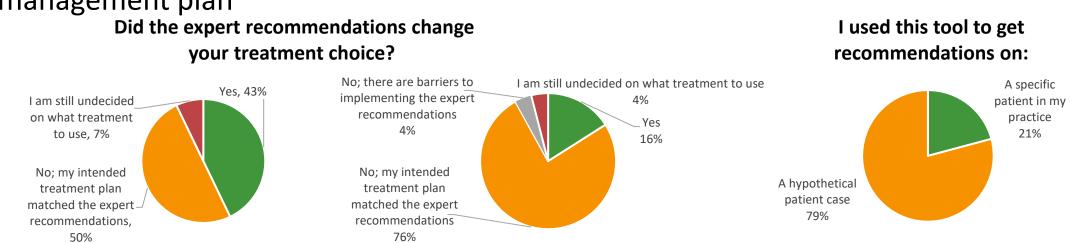
N = 431 cases entered by HCPs over 64 weeks (5/9/19 - 7/31/2020)

- Majority of cases had already received CAR T-cell therapy (n = 227)
- CRS was the most common AE case entered (n = 126; 67%)
 - In Cohort 1 71% of cases were CRS and 29% were ICANS vs 63% and 37%, respectively, in Cohort 2
- The proportion of the type of HCPs using the tool was comparable in both Cohorts, with 55% physicians, 22% nurses, and 23% pharmacists overall

Impact of the Tool on Clinical Practice

Of the 53 HCPs who answered the optional impact survey questions, 50% in Cohort 1 and 76% in Cohort 2 indicated that the tool recommendations confirmed their management plan

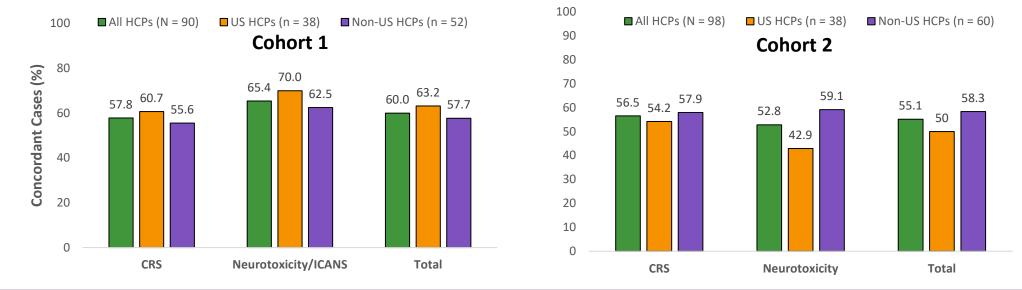
vour treatment choice?



Concordance of HCP Toxicity Management With Expert Recommendations

- In Cohort 1, 60% of cases managed concordant with expert recommendations (n = 54)
- In Cohort 2, 55% of cases managed concordant with expert recommendations (n = 54)

Cases Managed Concordant With Expert Recommendations, by Type of AE



These data suggest that many HCPs continue to suboptimally manage AEs associated with CAR T-cell therapy administration • Only 60% of HCPs' planned management of specific AEs was concordant with expert recommendations provided in the tool in cohort 1 vs 55% in Cohort 2 • In cohort 1, there was a significant difference in concordance with expert recommendations by grade, however, no significant difference was found in cohort 2 by grade, type of AE

- (CRS vs ICANS), or by region (US vs non-US HCPs)
 - Tocilizumab used more frequently by HCPs than expert recommendations for management of ICANS
 - Corticosteroids were used earlier in CRS (lower grades)
- improved confidence in CAR T cell therapy toxicity management over time

References:

1. Tisagenlecleucel package insert. 2. Axicabtagene ciloleucel package insert This presentation is the intellectual property of the author/presenter. Contact kmarcello@clinicaloptions.com for permission to reprint and/or distribute. The online tool is part of an educational program supported by educational grants from Celgene Corporation and Kite, A Gilead Company

Clinician receives casespecific management recommendations from

- expert panel
- Clinician is able to compare their intended management vs expert recommendations

mg/dose

eed 3 doses in 24 hours, with maximum of 4 doses total

d to maintain systolic blood pressure > 90 mmHg

initiate vasopressors, transfer patient to ICU, obtain ECHO,

onitoring methods, if not performed previously

livery and noninvasive positive pressure ventilation at > 6 L/min

portive care

d on duration of steroid use and/or if neutropenia present.



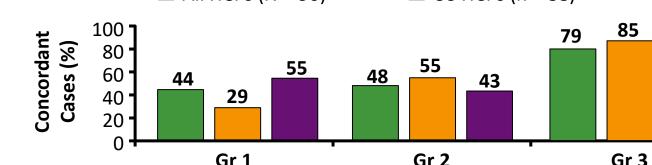


Results

Demographics and Cases Entered

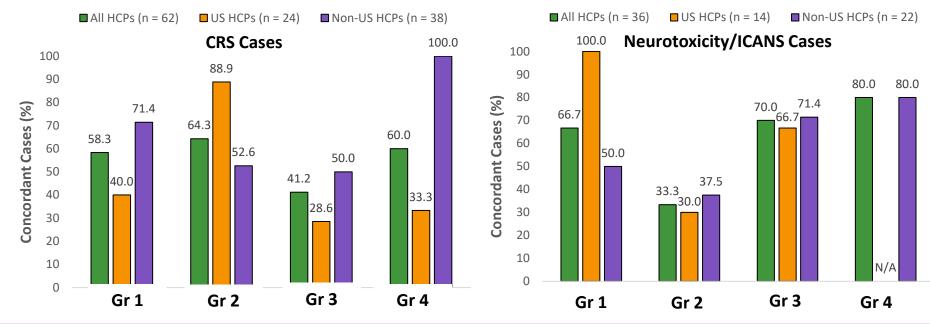


• **Cohort 1:** Significant difference in concordance by grade (*P* = .0417) Cases Managed Concordant With Expert Recommendations, by Grade All HCPs (N = 90) US HCPs (n = 38)



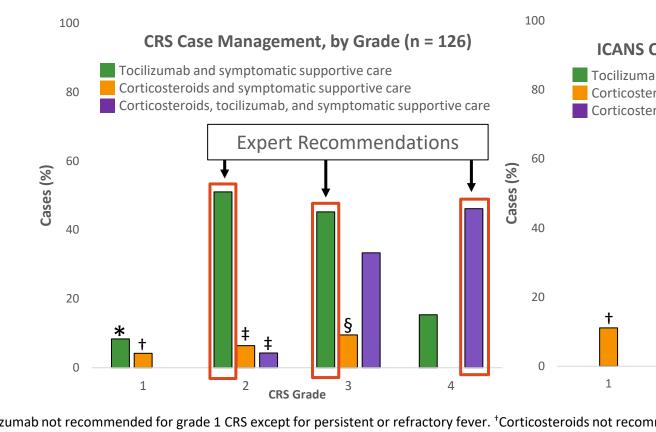
• **Cohort 2:** No significant difference in concordance by type of AE, grade of AE, or by region (US vs non-US HCPs)

Cases Managed Concordant With Expert Recommendations, by Grade for CRS and Neurotoxicity



Case Management by HCPs by AE and Grade

Pooled data from both cohorts: HCPs reported initiating corticosteroids more often than recommended by experts (eg, Grade 3 CRS and all grades of ICANS)

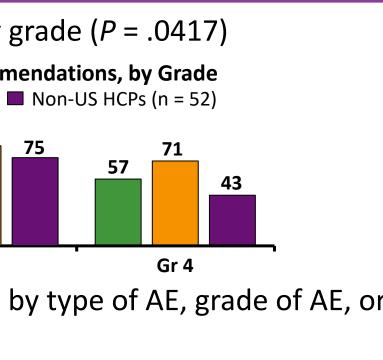


*Tocilizumab not recommended for grade 1 CRS except for persistent or refractory fever. *Corticosteroids not recommended for grade 1 CRS or grade 1 ICANS. *Corticosteroids recommended only for hypotension or hypoxia in patients at high risk for severe CRS and with continued hypotension/hypoxia after IL-6 antagonist, hypoperfusion signs, or rapid deterioration. [§] Corticosteroids recommended for hypotension or hypoxia. ^ITocilizumab only recommended if ICANS occurs concurrently with CRS necessitating intervention. The tool did not differentiate cases of ICANS that were concurrent with CRS

Conclusions

• Use of an online tool providing interactive, case-specific, evidence-based consensus recommendations can improve patient care and safety • A greater proportion of HCPs in Cohort 2 indicated that the expert recommendations confirmed/matched their intended management plan (76% vs 50% in Cohort 1) indicating potentially





ICANS Case Management, by Grade (n = 62) Tocilizumab and symptomatic supportive care corticosteroids and symptomatic supportive care osteroids, tocilizumab, and symptomatic supportive care Expert Recommendation