

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

Matthew J. Frigault, MD¹; Megan Cartwright, PhD²; Krista Marcello²; Timothy Quill, PhD²; Daniel J. DeAngelo, MD, PhD³; Ilene A. Galinsky, NP³; Shilpa Paul, PharmD, BCOP⁴; Jae H. Park, MD⁵
 1. Massachusetts General Hospital; 2. Clinical Care Options, LLC; 3. Dana-Farber Cancer Institute; 4. MD Anderson Cancer Center; 5. Memorial Sloan Kettering Cancer Center.

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 cytokine-release 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)

Methods

The tool is online at: clinicaloptions.com/cartool



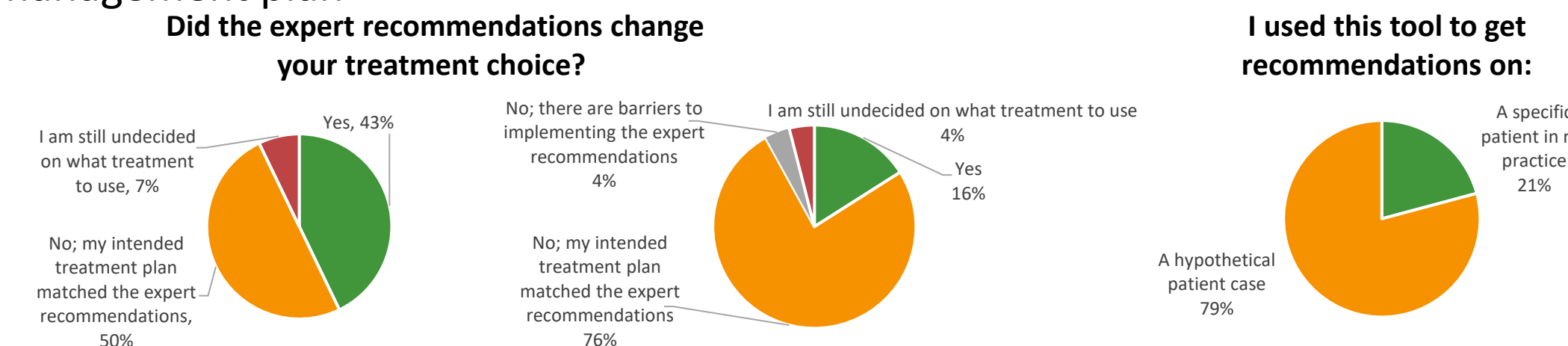
Results

Demographics and Cases Entered

- 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

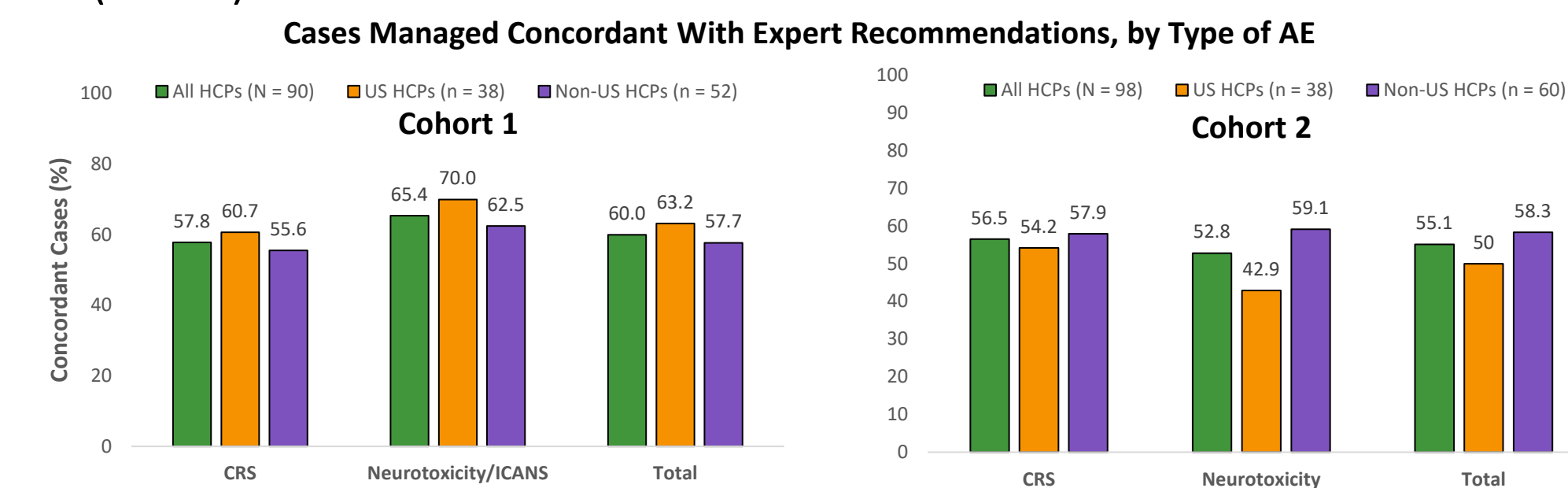
Impact of the Tool on Clinical Practice

- 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

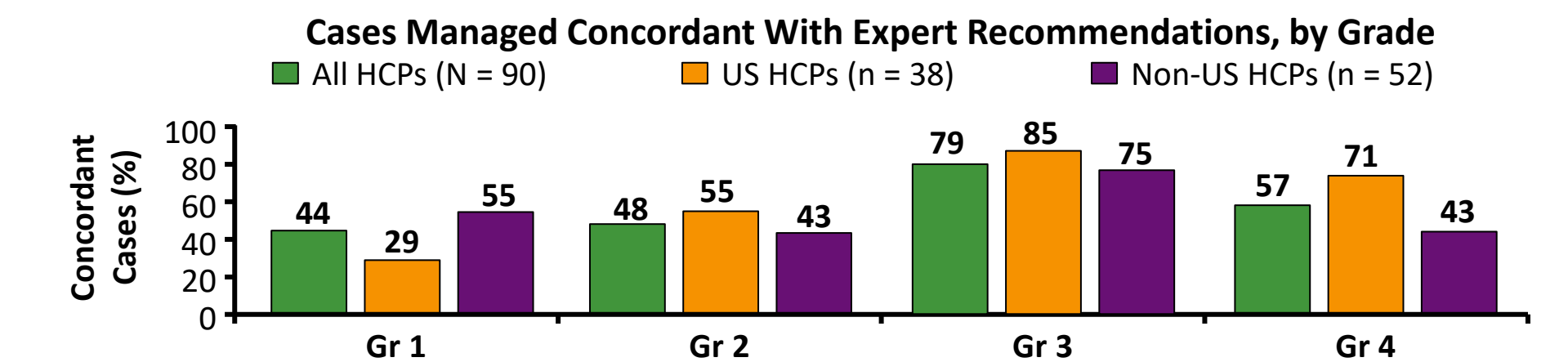


Concordance of HCP Toxicity Management With Expert Recommendations

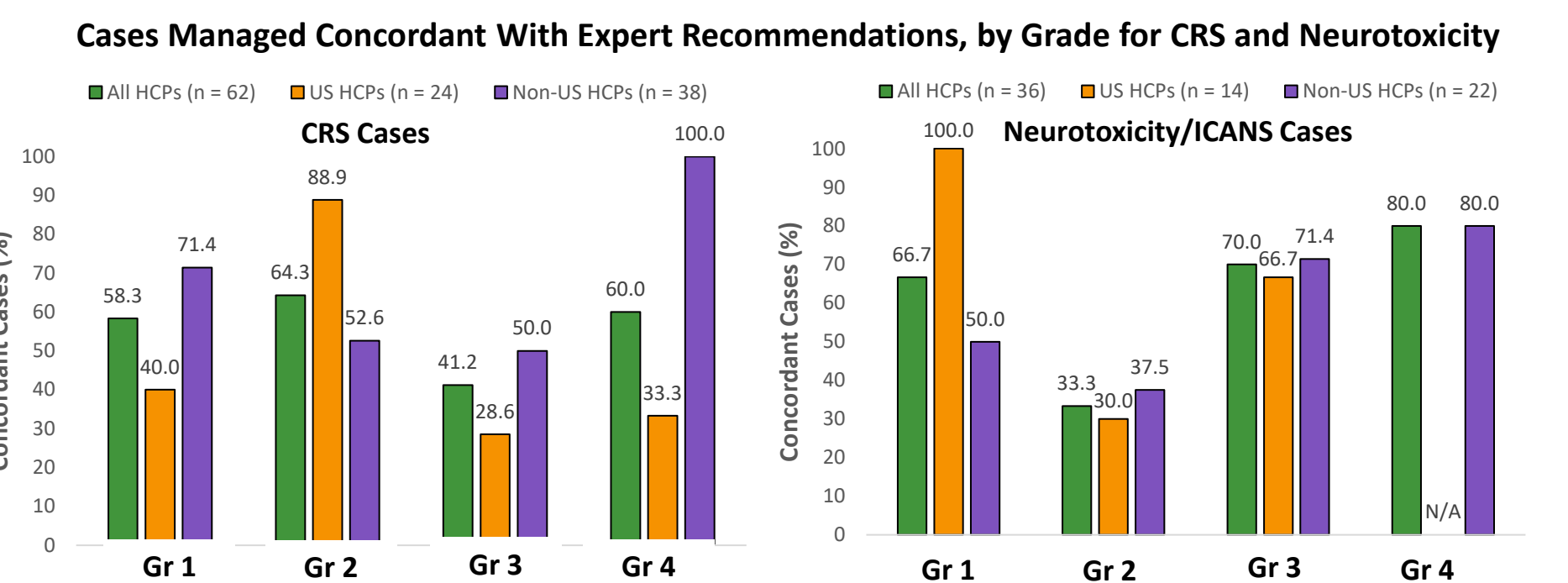
- In Cohort 1, 60% of cases managed concordant with expert recommendations (n = 54)
- In Cohort 2, 55% of cases managed concordant with expert recommendations (n = 54)



- Cohort 1:** Significant difference in concordance by grade (P = .0417)

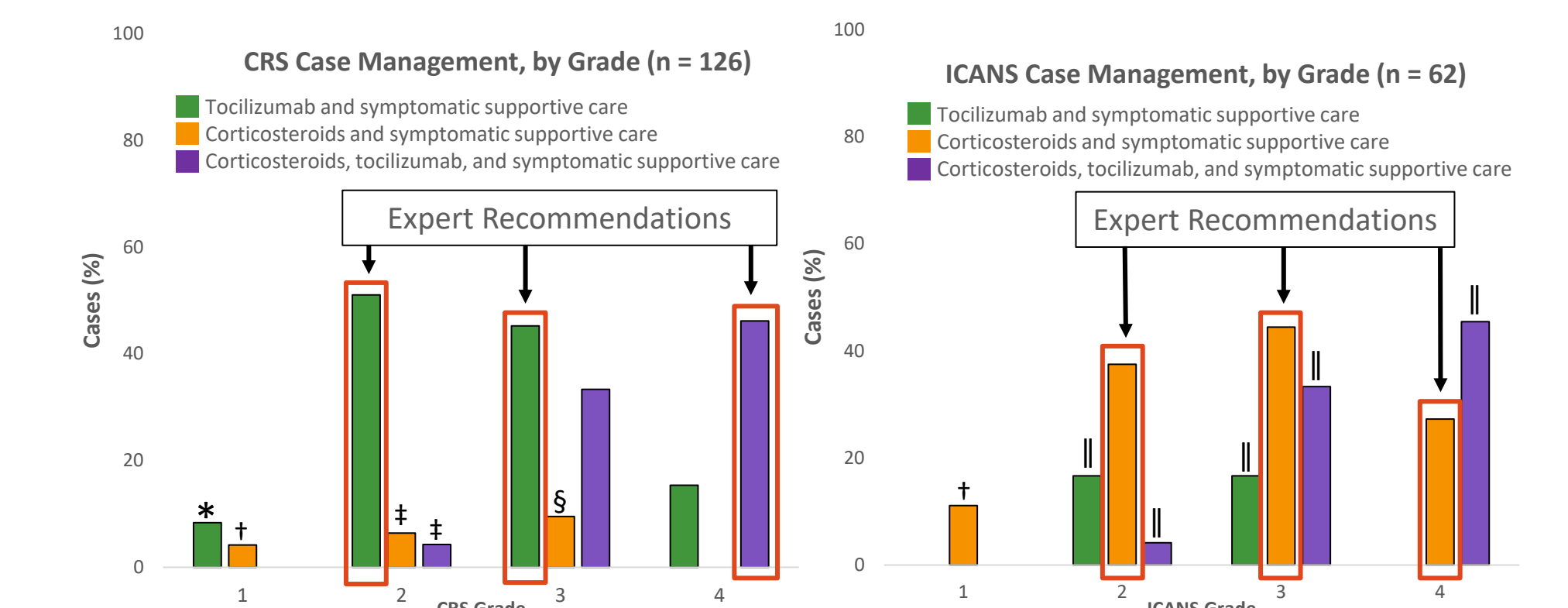


- Cohort 2:** No significant difference in concordance by type of AE, grade of AE, or by region (US vs non-US HCPs)



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. ††Tocilizumab only recommended if ICANS occurs concurrently with CRS necessitating intervention. The tool did not differentiate cases of ICANS that were concurrent with CRS

Conclusions

- 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)
- 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 improved confidence in CAR T cell therapy toxicity management over time

References:

- Tisagenlecleucel package insert.
- Axicabtagene ciloleucel package insert

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