Healthcare resource utilization and 2022 cost update of cytokine release syndrome and neurological toxicity in patients with relapsed and refractory multiple myeloma receiving idecabtagene vicleucel in KarMMa

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Introduction

- Relapsed and refractory multiple myeloma (RRMM) is associated with poor prognosis and decreased overall survival, especially among patients who are triple-class exposed (TCE)[1]
- Idecabtagene vicleucel (ide-cel, bb2121), a B-cell maturation antigen-directed chimeric antigen receptor (CAR) T cell therapy, demonstrated frequent, deep, and durable responses in TCE patients with RRMM in the phase 2, multicenter, single-arm KarMMa clinical trial (NCT03361748)[2]
- CAR T cell therapies are associated with 2 potentially serious adverse events (AEs): cytokine release syndrome (CRS) and neurotoxicity (NT)[2]
- These events have been observed across grades 1, 2, 3, and 4 and are associated with varying clinical and economic consequences
- Previous research assessed healthcare resource utilization (HCRU) and estimated 2020 costs of CRS and/or NT management in the KarMMa trial;[3] this study updates the estimated costs to 2022 values

Objective

- To report the 2022 HCRU and the cost of CRS and NT management for patients with RRMM who received ide-cel in the pivotal phase 2 KarMMa clinical trial, stratified by grade

Methods

Study population

- This analysis included 107 patients who received treatment with ide-cel as part of the phase 2 KarMMa clinical trial and experienced CRS and/or NT

Study methodology

- This retrospective study analyzed the individual patient-level case report forms detailing data among patients with RRMM treated with ide-cel in the KarMMa trial who experienced CRS and/or NT
- A 2-step methodology was utilized to quantify HCRU and associated costs:
  - Key CRS- and/or NT-related HCRU were identified per CRS/NT management guidelines post ide-cel administration from AE onset through resolution of AE, stratified by grade
    - HCRU, included hospital length of stay (LOS, standard inpatient [IP] and intensive care unit [ICU] days), diagnostics, procedures, and medications
  - Apply 2022 unit costs to each HCRU
- Key HCRU inputs are outlined in **Table 1**[4-9]
  - Facility costs were obtained from the HCUP NIS (2018),[4] OPPS (2022),[6] and peer-reviewed literature[5]
  - Medication cost data were obtained from Merative™ Micromedex® RED BOOK® (as of 2022) using WAC[9]
  - Diagnostic and procedure costs were obtained from the CMS 2022 first quarter CLFS,[7] PFS,[8] and the Durable Medical Equipment Fee Schedule,[10] OPPS (2022),[6] and peer-reviewed literature[5]
- Unit costs were measured from the healthcare system perspective, and adjusted to 2022 USD using the Consumer Price Index,[11] as needed

Outcomes

- The primary outcome was estimated 2022 post-infusion CRS and/or NT management-related costs, stratified by grade (**Figure 1**)
- Secondary CRS and/or NT management-related outcomes included:
  - Facility (IP stays and LOS, ICU stays and LOS)
  - Diagnostics (eg, laboratory tests and imaging)
  - Medications (excluding ide-cel; eg, tocilizumab, corticosteroids, antibiotics, or vasopressors)
  - Procedures (eg, dialysis and mechanical ventilation)

Statistical analyses

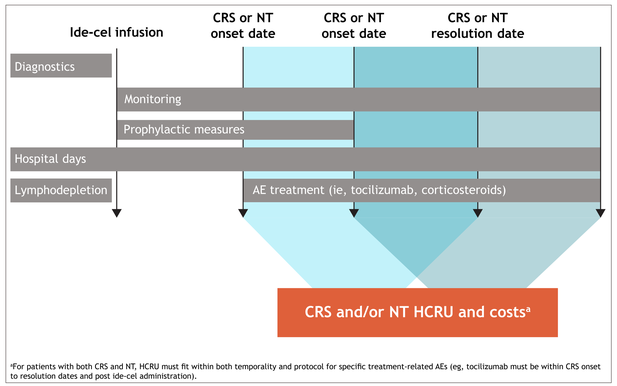
- Baseline patient characteristics, HCRU, and total costs were assessed descriptively by grade of CRS and/or NT

Table 1. Key HCRU inputs

Category	HCRU input[a]	2022 cost value or range (USD)	Data source
Facility	IP stay	2944/day	HCUP NIS 2018[b,4]
	ICU stay	9347/day	Dasta et al. 2005,[b] estimated cost without mechanical ventilation[5]
	Office visits	122/office visit	CMS Hospital OPPS 2022; national reimbursement rate[6]
Diagnostics	Diagnostic laboratory tests[c]	6–39/test	CMS CLFS 2022[7]
	Diagnostic tests[d]	10–1512	CMS PFS[8]/CMS Hospital OPPS 2022[6]
Medications[e]	Oncology Supportive Care (eg, granulocyte colony-stimulating factors, transfusions, anti-anemia drugs, antiemetics)	<1–15,600/dose	Merative™ Micromedex® RED BOOK® Online - WAC, 2022[9]
	Prophylactic treatments (eg, antibiotics, proton pump inhibitors, H2 blockers, seizure prophylaxis, intravenous immunoglobulin)		
	Other AE management (eg, antipyretics/ analgesics, tocilizumab and other anti-cytokine agents, corticosteroids, vasopressors)		
Procedures	Dialysis	672/day	CMS Hospital 2022; national reimbursement rate[6]
	Mechanical ventilation[f]	2875/day	Dasta et al. 2005[5]

[a]Only select HCRU inputs are presented in this table; does not represent the full facility, medication, diagnostic, and procedures included in cost calculations; [b]Inflated to 2022 USD; [c]Diagnostic laboratory tests included comprehensive metabolic panel, C-reactive protein, ferritin, complete blood count, coagulation panel, immunoglobulin, and cerebrospinal fluids; [d]Diagnostic tests included computerized tomography (CT) scan with contrast, magnetic resonance imaging (MRI) scan with contrast, positron emission tomography (PET) scan with contrast, electroencephalogram (EEG), electrocardiogram (ECG/EKG), and tumor biopsy; technical component and physician's component costs were included; [e]Cost of ide-cel was not included in this analysis; [f]Intubation was used as a proxy to indicate mechanical ventilation. CLFS, Clinical Laboratory Fee Schedule; CMS, Centers for Medicare & Medicaid Services; HCUP, Healthcare Cost and Utilization Project; NIS, National Inpatient Sample; OPPS, Outpatient Prospective Payment Systems; PFS, Physician Fee Schedule; USD, United States dollar; WAC, wholesale acquisition cost.

Figure 1. Method to identify HCRU and cost of CRS and/or NT management



[a]For patients with both CRS and NT, HCRU must fit within both temporality and protocol for specific treatment-related AEs (eg, tocilizumab must be within CRS onset to resolution dates and post ide-cel administration).

Results

Patient population

- 107 patients experienced CRS and/or NT (out of 128; 83.6%) and were included in the study:
  - 84 (78.5%) had CRS only and 23 (21.5%) had both CRS and NT; most patients (88.8%) were grade ≤ 2 and relatively few (11.2%) were grade ≥ 3 (**Table 2**)
  - Mean (SD) age was 60.2 (9.6) years
  - Patients were predominately male (59.8%), White (77.6%), and not Hispanic or Latino (81.3%)

CRS and NT management-related HCRU

- All patients were hospitalized during at least a portion of their AE event, and in some cases, this reflected an overlap with the trial protocol required stay of ≥ 14 days post ide-cel infusion (**Table 3**)
- 19 (17.8%) patients experienced an ICU stay during their AE event
- ICU admissions were more common (66.7%) and longer (median LOS, 8 days longer) in patients with more severe CRS/NT
- Most (64.5%) patients received tocilizumab + corticosteroids and some (15.9%) received vasopressors, with higher utilization with more severe CRS/NT (**Table 4**)
- Dialysis and intubation were rare, with higher rates among more severe CRS/NT (8.3% and 25.0%, respectively)

Table 2. Patient demographics and characteristics

Metric	Any CRS or NT	CRS only					Concurrent CRS and NT			All CRS and/ or NT	
AE grade	Any	Any	1	2	3	4	Any	CRS and NT ≤ 2	CRS or NT≥ 3	CRS and/or NT ≤ 2	CRS and/or NT ≥ 3
n (%)[a]	107 (100)	84 (78.5)	52 (48.6)	29 (27.1)	2 (1.9)	1 (0.9)	23 (21.5)	14 (13.1)	9 (8.4)	95 (88.8)	12 (11.2)
Age, years											
Mean (SD)	60.2 (9.6)	59.9 (9.5)	60.5 (8.9)	59.7 (10.6)	50.5 (2.1)	57.0 (-)	61.1 (10.3)	58.0 (10.5)	65.9 (8.5)	59.9 (9.6)	62.6 (9.5)
Median (range)	61(33–78)	60 (33–78)	61.5 (34–78)	60 (33–75)	50.5 (49–52)	57 (57–57)	64 (41–76)	60 (41–76)	67 (48–74)	60 (33–78)	66 (48–74)
Male, n (%)[b]	64 (59.8)	53 (63.1)	34 (65.4)	18 (62.1)	0	1 (100)	11 (47.8)	7 (50.0)	4 (44.4)	59 (62.1)	5 (41.7)
Race, n (%)[b]											
White	83 (77.6)	64 (76.2)	44 (84.6)	19 (65.5)	0	1 (100)	19 (82.6)	12 (85.7)	7 (77.8)	75 (78.9)	8 (66.7)
Ethnicity, n (%)[b]											
Not Hispanic or Latino	87 (81.3)	65 (77.4)	41 (78.8)	22 (75.9)	1 (50.0)	1 (100)	22 (95.7)	14 (100)	8 (88.9)	77 (81.1)	10 (83.3)
Hispanic or Latino	9 (8.4)	8 (9.5)	7 (13.5)	1 (3.4)	0	0	1 (4.3)	0	1 (11.1)	8 (8.4)	1 (8.3)

Lee criteria was used to determine CRS, while CTCAE version 4.03 was used to determine NT.
[a]Percentages are calculated using n/107; [b]Percentages are calculated within column as percentage of AE type and severity.
CTCAE, Common Terminology Criteria for Adverse Events; SD, standard deviation.

Table 3. Hospital stays and LOS (N = 107)

Metric	CRS only	Concurrent CRS and NT	All CRS and/or NT	
AE grade	Any	Any	CRS and/or NT ≤ 2	CRS and/or NT ≥ 3
n (%)[a]	84 (78.5)	23 (21.5)	95 (88.8)	12 (11.2)
AE-related hospital stay, n (%)[b]				
Standard IP	84 (100)	23 (100)	95 (100)	12 (100)
ICU	9 (10.7)	10 (43.5)	11 (11.6)	8 (66.7)
LOS, median (range), days				
Standard IP	5 (1–28)	9 (2–17)	6 (1–28)	10 (3–28)
ICU	3 (2–9)	5.5 (2–24)	3 (2–23)	5.5 (2–24)
Total	6 (1–28)	10 (2–41)	6 (1–28)	14 (4–41)

Lee criteria was used to determine CRS, while CTCAE version 4.03 was used to determine NT.
[a]Percentages are calculated using n/107; [b]Percentages are calculated within column as percentage of AE type and severity.

Table 4. Medications and procedures (N = 107)

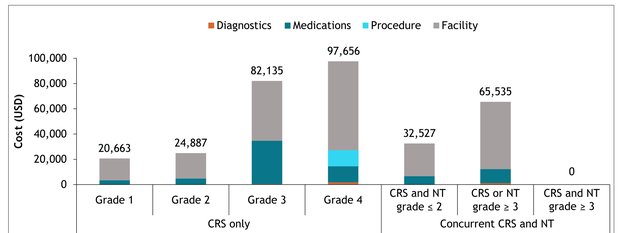
Metric	CRS only	Concurrent CRS and NT	All CRS and/or NT	
AE grade	Any	Any	CRS and/or NT ≤ 2	CRS and/or NT ≥ 3
n (%)[a]	84 (78.5)	23 (21.5)	95 (88.8)	12 (11.2)
Medications, n (%)[b]				
Tocilizumab only	0	0	0	0
Corticosteroids only	38 (45.2)	0	38 (40.0)	0
Tocilizumab + corticosteroids	46 (54.8)	23 (100)	57 (60.0)	12 (100)
Vasopressor	11 (13.1)	6 (26.1)	12 (12.6)	5 (41.7)
Procedures, n (%)[b]				
Dialysis	0	1 (4.3)	0	1 (8.3)
Intubation	1 (1.2)	4 (17.4)	2 (2.1)	3 (25.0)

Lee criteria was used to determine CRS, while CTCAE version 4.03 was used to determine NT.
[a]Percentages are calculated using n/107; [b]Percentages are calculated within column as percentage of AE type and severity.

CRS and NT management-related costs

- Median total costs were as follows: CRS only: grade 1= USD 20,663, grade 2 = USD 24,887, grade 3 = USD 82,135, grade 4 = USD 97,656; concurrent CRS/NT: grade ≤ 2, USD 32,527, and grade ≥ 3, USD 65,535 (**Figure 2**)
- Costs were primarily driven by hospital-related HCRU and fees
- Total CRS/NT costs ranged substantially (USD 5749-USD 315,629), and generally increased with severity
- Costs were highest among patients experiencing grade 4 CRS only and were consistently lower among patients with grade ≤ 2 CRS/NT than for patients with higher-grade CRS/NT

Figure 2. Median total 2022 cost of CRS and NT management



USD	n = 52	n = 29	n = 2	n = 1	n = 14	n = 9	n = 0
Facility	17,247	20,122	47,430	70,457	25,871	53,330	0
Procedure	0	0	0	12,713	0	0	0
Medications	3,415	4,765	34,352	12,790	6,550	11,073	0
Diagnostics	0	0	353	1,696	106	1,132	0
Total	20,663	24,887	82,135	97,656	32,527	65,535	0

Conclusions

- Findings suggest that a single infusion of ide-cel is associated with relatively low rates (11.2%) of severe (grade ≥ 3 and/or concurrent) CRS and/or NT
- Estimated HCRU and 2022 costs to manage severe CRS/NT were higher than those for patients with less severe, low-grade CRS/NT (grade ≤ 2 and/or nonconcurrent)
- CAR T cell therapies associated with lower-grade CRS/NT may limit HCRU and costs for CRS and NT management

References

1. Madduri D, et al. *Fut Oncol* 2021;17:503-515.
2. Munshi NC, et al. *N Engl J Med* 2021;384:705-716.
3. Hari P, et al. Poster presentation at the American Society of Hematology (ASH) Annual Meeting & Exposition; December 5-8, 2020; Virtual. Abstract 1958.
4. Introduction to the HCUP National Inpatient Sample (NIS) 2018. Healthcare Cost and Utilization Project - HCUP. Agency for Healthcare Research and Quality. https://www.hcup-us.ahrq.gov/db/nation/nis/NIS_Introduction_2018.jsp. Published November 2020. Updated April 5, 2021. Accessed March 25, 2023.
5. Dasta JF, et al. *Crit Care Med* 2005;33:1266-1271.
6. Hospital Outpatient Prospective Payment System (OPPS). U.S. Centers for Medicare and Medicaid Services. https://www.cms.gov/Research-Statistics-Data-and-Systems/Files-for-Order/LimitedDataSets/HospitalOPPS. Updated February 24, 2023. Accessed March 25, 2023.
7. Clinical Laboratory Fee Schedule U.S. Centers for Medicare & Medicaid Services. https://www.cms.gov/medicare/medicare-fee-for-service-payment/clinicallabfeesched. Updated April 6, 2023. Accessed March 25, 2023.
8. Physician Fee Schedule. U.S. Centers for Medicare & Medicaid Services. https://www.cms.gov/medicare/medicare-fee-for-service-payment/clinicallabfeesched. Updated April 6, 2023. Accessed March 25, 2023.
9. Merative. Merative™ Micromedex® RED BOOK® Online. http://www.micromedexsolutions.com. Accessed March 25, 2023.
10. Durable Medical Equipment, Prosthetics/Orthotics & Supplies Fee Schedule U.S. Centers for Medicare & Medicaid Services. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/DMEPOSFeeSched/DMEPOS-Fee-Schedule. Updated December 22, 2021. Accessed March 25, 2023.
11. Consumer Price Index. U.S. Bureau of Labor Statistics. https://www.bls.gov/cpi/tables/home.htm. Updated March 10, 2022. Accessed March 25, 2023.

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