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Blood 142 (2023) 5150–5152

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

Real-World Incidence, Characteristics and Management of Cytokine Release Syndrome Induced By Chimeric Antigen Receptor T-Cell Therapy across Hematologic Malignancies

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Background: Cytokine release syndrome (CRS) is a potentially life-threatening, supraphysiologic response following immunotherapy resulting in the activation or engagement of endogenous or infused T cells and/or other immune effector cells. CRS occurs with varying frequency and severity, depending on the underlying disease and immunotherapy used, such as chimeric antigen receptor T-cell (CAR-T) therapy or off-the-shelf T-cell engaging bispecific antibodies. Limited research exists on the diagnosis and management of CRS in the real world. This study describes the real-world incidence, severity and clinical management of CRS induced by commercially available CAR-T therapies for diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), mantle cell lymphoma (MCL) and multiple myeloma (MM).
Methods: Real-world data (RWD) were obtained from the Flatiron Health, US, nationwide electronic health record (EHR)-derived, de-identified database of cancer patients within a network comprised primarily of community cancer practices. The Flatiron Health network also includes practices designated as academic sites by the National Cancer Institute; however, relative proportions of community/academic practices may vary depending on the study cohort. Data as of August 31, 2022, on CAR-T therapy, clinical characteristics and disease outcomes specific to CAR-T therapy, as well as CRS and its clinical management, were abstracted from unstructured documents in EHRs (in addition to routinely available structured data), in a cohort of patients receiving commercial CAR-T therapy. Specifically, data for CRS including treatments and resolution were abstracted based on explicit mention of and attribution to CRS in charts.
Results: Table 1 summarizes data by indication. Incidence of CRS ranged from 56% (104/185) in DLBCL to 72% (66/92) in MCL. Excluding categories with small numbers of cases (<15), CRS incidence also varied by individual CAR-T therapy and underlying indication and ranged from 35% for idecabtagene vicleucel in MM to 73% for brexucabtagene autoleucel in MCL. Highest incidence of Grade ≥2 CRS was observed among MCL patients, whereas Grade ≥3 CRS was most commonly observed among FL patients. Time to onset of CRS ranged from 0 to 16 days, with median onset between 3-4 days among lymphoma patients and earlier median onset of 1 day for MM patients. Median time to CRS resolution ranged from 2 to 6 days across indications. While 81-95% of patients received CAR-T therapy at an academic center, 5-14% received CAR-T therapy at a community center. Tocilizumab and corticosteroids were the most commonly used treatments for CRS, including 37-48% use of tocilizumab for Grade 1 CRS (Table 2).
Discussion: This study uniquely summarizes RWD on CRS following the use of commercially available CAR-T therapies across multiple hematologic malignancies, based on information from clinical notes abstracted retrospectively from EHRs. Consistent with the timing of approval of commercially available CAR-T therapies, the sample size for MM was limited compared with other malignancies. Safety events are typically under-reported in RWD sources, specifically for CRS when relying on information documented in patients' EHRs, compared with other published literature. In accordance with other RWD on CRS, grading criteria for CRS as well as vasopressor and oxygen use were not consistently reported in patients' EHRs. CAR-T treatments were predominantly administered in academic centers. Limited use in community practices was also observed; however, further information to accurately characterize the size and capabilities of community centers was not available in this database. Data also showed considerable use of tocilizumab to treat low-grade CRS, suggesting the need for additional evidence on its role to treat CRS beyond its current regulatory approval. Increased evidence generation, specifically from usual clinical practice, can contribute to increased awareness and knowledge about CRS diagnosis and management, and in turn realize the maximum potential of T-cell therapeutics.

Disclosures Chaudhary: *Genentech, Inc.:* Current Employment; *F. Hoffmann-La Roche Ltd:* Current equity holder in publicly-traded company. **Roy:** *Genentech, Inc.:* Current Employment, Current equity holder in publicly-traded company; *Amgen Inc:* Current equity holder in publicly-traded company, Ended employment in the past 24 months. **Lin:** *Genentech, Inc.:* Current Employment. **Tandon:** *F. Hoffmann La Roche Ltd:* Current Employment, Current holder of *stock options* in a privately-held company. **Kwan:** *F. Hoffmann-La Roche Ltd:* Current equity holder in publicly-traded company; *F. Hoffmann-La Roche Ltd / Genentch, Inc.:* Current Employment. **Kuebler:** *Genentech, Inc.:* Current Employment; *F. Hoffmann-La Roche Ltd:* Current equity holder in publicly-traded company. **Shewade:** *Genentech, Inc.:* Current Employment; *F. Hoffmann- La Roche Ltd employee stock options:* Current equity holder in publicly-traded company.

OffLabel Disclosure: Tocilizumab (ACTEMRA(R), RoActemra(R)) is indicated for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome in adults and pediatric patients 2 years of age and older

Table 1. CRS incidence and characteristics across indications

	DLBCL N=185	FL N=67	MCL N=92	MM N=42
CAR-T treatment setting,[1] n (%)				
Academic	150 (81.1)	60 (89.6)	76 (82.6)	40 (95.2)
Community	26 (14.1)	3 (4.5)	11 (12.0)	2 (4.8)
CAR-T therapy,[1] n (%)				
Axicabtagene ciloleucel	98 (53.0)	47 (70.1)	–	–
Tisagenlecleucel	59 (31.7)	13 (19.4)	–	–
Lisocabtagene maraleucel	23 (12.4)	6 (9.0)	–	–
Brexucabtagene autoleucel	–	–	91 (98.9)	–
Idecabtagene vicleucel	–	–	–	34 (81.0)
Ciltacabtagene autoleucel	–	–	–	7 (16.7)
Unknown/not documented	5 (2.7)	1 (1.5)	1 (1.1)	1 (2.4)
CRS incidence,[1–3] n (%)				
Any CRS	104 (56.2)	40 (59.7)	66 (71.7)	24 (57.1)
Grade 1	49 (26.5)	20 (29.9)	25 (27.2)	18 (42.9)
Grade 2	42 (22.7)	15 (22.4)	32 (34.8)	6 (14.3)
Grade ≥3	5 (2.7)	3 (4.5)	3 (3.3)	0 (0.0)
Median time to onset, days[4] [min, max]	3 [0, 15]	4 [0, 15]	4 [0, 12]	1 [0, 16]
Median duration, days[4,5] [min, max]	4 [1, 33]	5.5 [1, 20]	5 [1, 18]	2 [0, 8]

[1]Only reported data have been summarized and therefore percentages may not add to 100% due to missing data. [2]Data pertaining to CRS were abstracted from patients' EHRs with explicit mention of CRS. [3]RWD on CRS were available for the following commercial CAR-T therapies: axicabtagene ciloleucel, tisagenlecleucel, lisocabtagene maraleucel, brexucabtagene autoleucel, idecabtagene vicleucel, ciltacabtagene autoleucel. [4]Estimates have been calculated using data for those patients where CRS event dates were available with day-level granularity. [5]Estimates were based on cases with more than one instance of CRS assessment documented in patients' EHRs.

CAR-T, chimeric antigen receptor T-cell; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; EHR, electronic health record; FL, follicular lymphoma; MCL, mantle cell lymphoma; MM, multiple myeloma; RWD, real-world data

Table 2. Use of tocilizumab and corticosteroids to manage CRS

Grade 1 CRS treatment,[1–3] n (%)	**DLBCL N=49**	**FL N=20**	**MCL N=25**	**MM N=18**
Tocilizumab	18 (36.7)	8 (40.0)	12 (48.0)	7 (38.9)
Corticosteroids	8 (16.3)	5 (25.0)	7 (28.0)	1 (5.6)
Grade ≥2 CRS treatment,[1,3] n (%)	**DLBCL N=47**	**FL N=18**	**MCL[4] N=35**	**MM N=6**
Tocilizumab	35 (74.5)	12 (66.7)	30 (85.7)	6 (100.0)
Corticosteroids	21 (44.7)	8 (44.4)	22 (62.9)	3 (50.0)

[1]Only reported data have been summarized and therefore percentages may not add to 100% due to missing data.

[2]Data pertaining to treatments where available and distinctly attributable to CRS in patients' EHRs.

[3]Treatment data were unavailable in varying proportions across CRS grades, suggesting either lack of use of treatments or missing documentation.

[4]One patient with MCL received anakinra for CRS (Grade ≥2).

CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; EHR, electronic health record; FL, follicular lymphoma; MCL, mantle cell lymphoma; MM, multiple myeloma

Figure 1

https://doi.org/10.1182/blood-2023-174921