Poster 57

Feasibility and Safety of Outpatient Administration of Chimeric Antigen Receptor T-cell Therapy: A Systematic Literature Review of Early U.S. Experience

Nausheen Ahmed,[1] Usuma Gergis,[2] Christopher Dieyi,[3] Babatunde Adedokun,[3] Clare Spooner,[3] Christine Fu,[3] Fang Sun,[3] and Javier Munoz[4]

[1]The University of Kansas Cancer Center, Kansas City, KS, USA; [2]Thomas Jefferson University Hospital, Philadelphia, PA, USA; [3]Kite, a Gilead Company, Santa Monica, CA, USA; and [4]Mayo Clinic, Phoenix, AZ, USA

BACKGROUND

- Chimeric antigen receptor (CAR) T-cell therapy has shifted the treatment paradigm for several hematological malignancies, including large B-cell lymphoma (LBCL)[1]
  - Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 CAR T-cell therapy approved for the treatment of relapsed or refractory LBCL[2,3]
- Historically, CAR T-cell therapy was largely administered inpatient due to the risk of serious adverse events (AEs), such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS)[4]
  - However, optimization of AE management strategies made since the approval of axi-cel have improved its safety profile and may enable adoption of outpatient administration of CAR T-cell therapy[5]
- Outpatient administration of CAR T-cell therapy may improve health system capacity, resource utilization, and treatment access, supporting the increasing need for delivery of the therapy in this setting[4]; thus, it is important to determine the feasibility and safety of CAR T-cell therapy administration in the real-world United States (US) setting

OBJECTIVE

- To conduct a systematic literature review (SLR) to understand the feasibility, safety, and healthcare resource utilization (HRU) related to outpatient CAR T-cell therapy in the US real-world setting with a focus on axi-cel

METHODS

Figure 1. SLR Study Design

SLR Data Source

- Embase and PubMed databases were searched to identify observational US studies published between January 2017 and June 2023 that reported on the use of axi-cel in an outpatient setting (alone or with other CAR T-cell therapies) and described outcomes of interest

Study Selection

- Study selection was conducted in 2 stages: (1) titles and abstracts (where available) then (2) full text articles from those identified in stage 1
- In both stages, 2 reviewers independently assessed content and discordant evaluations were resolved by consensus or in consultation with a third reviewer

Variables Extracted From Study Reports

- Patient population: baseline demographics and characteristics, CAR T-cell treatment received, and median follow-up time
- Characteristics of the outpatient program
- Healthcare resource utilization: inpatient admission rates (overall and in first 72 hours), time to admission, main reason for admission, and length of stay
- Safety: grade, time to onset and duration of CRS and ICANS; and tocilizumab and corticosteroid use
- Mortality rate and cause of death
- Rates of objective response and complete response

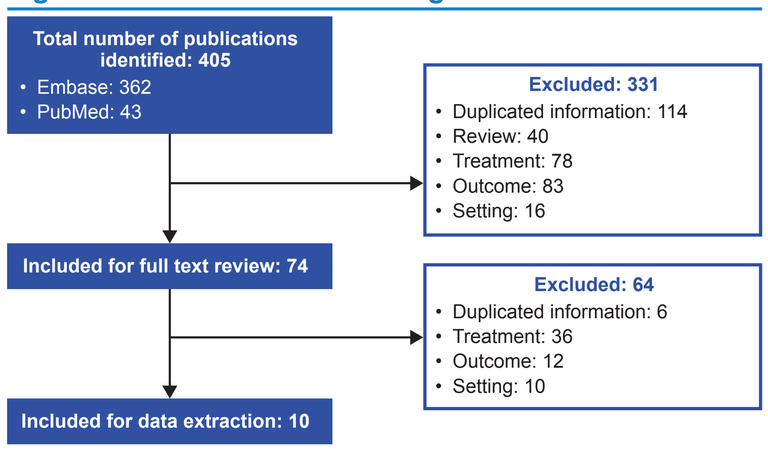
Statistical Analysis

- No quantitative summarization of the outcomes was done; however, the range of estimates across studies is reported

Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; SLR, systematic literature review; US, United States.

RESULTS

Figure 2. SLR Attrition Flow Diagram



- Our search identified 10 studies from 9 centers that reported their experience in administering axi-cel in the outpatient setting (**Figure 2**)

RESULTS

Table 1. Summary of HRU, Safety and Effectiveness Outcomes for CAR T-cell Therapy Outpatient Programs

Outpatient Program Information		Patient Characteristics				HRU Outcomes					Safety and Effectiveness Outcomes							
Center[a]	Practice Details	N (treatment)	Median Follow-up, days	Median Age, years	ECOG PS ≥1, %	Inpatient Admission, n (%)	Time to Admission (or Fever), days	Admission (or Fever) Within 72 Hours, n (%)	Main Reason for Admission (n)	Median Length of Stay, days	All Grade/ Grade ≥3 CRS, %/%	Any Grade CRS Median Onset/ Duration	All Grade/ Grade ≥3 ICANS, %/%	Any Grade ICANS Median Onset/ Duration	Tocilizumab/ Corticosteroid Use Among All Treated	Death, n (%)	Reason for Death	ORR/CR Rate, %/%
Mayo Rochester[6]	HBO practice: Lymphodepletion and CAR T-cell infusion in the HBO with daily monitoring until Day 7 and, thereafter as needed, until need for admission	64 (all axi-cel)	≥30	55-59	44	59 (92)	2	NR	Fever (51)	8	NR/NR	NR	NR/NR	NR	NR	0 (0), within 30 days post-infusion	NA	NR/NR
Mayo Rochester[7]	HBO practice: Lymphodepletion and CAR T-cell infusion in the HBO setting with daily monitoring until Day 7 and, thereafter as needed, until need for admission	39 (axi-cel: 7 brexu-cel: 7 ide-cel: 3 cilta-cel: 22)	≥30	65	ECOG ≥2: 0	32 (82)	1	NR	Fever (25)	7.5	79/3	NR	38/15	NR	Toci: 67% Corticosteroid: <1%	2 (5), within 30 days post-infusion	Toxicity	NR/NR
Vanderbilt[8]	Twice-daily outpatient monitoring for 14 days post-infusion; 1 overnight remote visit via telemedicine	13 (axi-cel: 9 brexu-cel: 4)	389	64	69	10 (77)	3.9	3 (23)	NR	7	92/0	Onset: 93.5 hours Duration: 3 days	54/15	NR	Toci: 69%	4 (31)	Relapse	NR/NR
University of Oklahoma HSC[9]	Daily outpatient monitoring for 14 days post-infusion; 3 visits per week from Days 15-28	21 (axi-cel: 13 tisa-cel: 6 brexu-cel: 1 liso-cel: 1)	NR	NR	NR	15 (71)	4	5 (24)	Fever (13), neurologic symptoms (2)	8	57/5	NR	29/5	NR	Toci: 33% Corticosteroid: 33%	6 (29)	Progression: 4 Infection: 2	At 6 months: 62/62
South Carolina[10]	Preemptive hospitalization on Day 0 after infusion, or daily follow-up	32 (axi-cel, brexu-cel, ide-cel total)	NR	NR	ECOG=2, 1 (3%)	28 (87.5)	2	27 (84.5)	NR	14	78/3	Onset: 2 days Duration: 3 days	38/16	Onset: 10 days Duration: 2 days	NR	3 (9)	NR	At 90 days: 72/63
Johns Hopkins[11,b]	Daily outpatient monitoring for 14 days post-infusion	47 (axi-cel: 29 tisa-cel: 10 brexu-cel: 8)	364	52-70	73	39 (83)	2-4	18 (38)	NR	7-10	74/2	Onset: NR Duration: 4-4.5 days	34/13	Duration: 5-10 days	Toci: 53%	0 (0)	NA	At 30 days: 47/19
Sarah Canon[12]	Remote patient monitoring (biometrics, clinical pathway questions)	>40 (axi-cel included)	≥30	NR	NR	26 (NR)	NR	NR	NR	NR	~65/0	NR	35/0	NR	NR	NR	NA	NR/NR
City of Hope[13]	Patient education, caregiver availability, 30 minutes distance from hospital for first 14 days, and 2 hours for the remaining 28 days	NR (axi-cel included)	NR	NR	NR	NR	NR	NR	NR	NR	NR/NR	NR	NR/NR	NR	NR	NR	NR	NR/NR
Intermountain Healthcare[14]	Daily triage visits and twice weekly visits with an advance practice provider	20 (axi-cel: 3 brexu-cel: 1 tisa-cel: 2 liso-cel: 14)	≥100	70	NR	10 (50)	NR	0 (0)	CRS (9)	NR	55/5	NR	45/20	NR	NR	2 (10)	Progression: 1 Infection: 1	NR/NR
Swedish Cancer Institute, Prisma Health, Jewish Hospital[15]	NR	51 (axi-cel: 23, brexu-cel: 4, liso-cel: 10, tisa-cel: 14)	≥30	65	NR	39 (75)	3	21 (40)	CRS (22)	5	39/0	NR	45/8	NR	Toci: 43%	NR	NR	NR

[a] Practice guidelines may vary by institution and change over time. [b] Presented results separately for ages <65 and ≥65 years. For medians, when the estimates could not be pooled, the data were reported as a range.
Axi-cel, axicabtagene ciloleucel; brexu-cel, brexucabtagene autoleucel; CAR, chimeric antigen receptor; cilta-cel, ciltacabtagene autoleucel; CR, complete response, CRS, cytokine release syndrome; ECOG PS, Eastern Cooperative Oncology Group performance score; HBO, hospital-based outpatient; HRU, healthcare resource utilization; HSC, Health Science Center; ICANS, immune effector cell-associated neurotoxicity syndrome; ide-cel, idecabtagene vicleucel; liso-cel, lisocabtagene maraleucel; ORR, objective response rate; NA, not applicable; NR, not reported; tisa-cel, tisagenlecleucel; toci, tocilizumab.

RESULTS

Outpatient Program Information and Patient Characteristics (Table 1)

- Most outpatient CAR T-cell therapy programs typically included a multidisciplinary team to coordinate patient care and monitored patients on-site or close to treatment centers for ≥14 days post-infusion; wearable devices or telemedicine were utilized by some
- Education of hospital staff, patients, and caregivers was a common practice, while some centers reported availability of nursing services 24 hours a day, 7 days a week for triage and admission, when needed
- Most studies reported outcomes pooled across multiple CAR T-cell therapies
- Median age of patients ranged from 52-70 years with ≥30 days of follow-up, where reported across studies

HRU Outcomes (Table 1)

- Reported post-infusion hospital admission rates ranged from 50%-92% with time to admission or fever ranging from 1-4 days and median length of stay ranging from 5-14 days
- Admission rates within 72 hours ranged from 23%-85%, where reported across studies

Safety and Effectiveness Outcomes (Table 1)

- Rates of any grade and Grade ≥3 CRS ranged from 39%-92% and 0%-5%, respectively
- Rates of any grade and Grade ≥3 ICANS ranged from 29%-54% and 5%-20%, respectively
- Reported tocilizumab and corticosteroid use ranged from 33%-69% and <1%-33%, respectively; though, limited studies reported these outcomes
- Mortality rates ranged from 0%-31% with the most common reason for death being progression or infection

CONCLUSIONS

- Early real-world US experience suggests that administering CAR T-cell therapy, including axi-cel, in the outpatient setting is feasible and has a comparable safety profile to inpatient infusion[16]
  - Rates of Grade ≥3 CRS and ICANS were similar to rates from inpatient CAR T-cell therapy
  - Mortality was predominantly due to progression and not due to CAR T-cell–related toxicity
- Limitations of this study include a small number of studies selected in the SLR, small sample sizes, and heterogenous data reported across all studies and CAR T-cell therapies
- Literature on the outpatient CAR T-cell therapy clinical experience is limited to mostly single institution reports; thus, more multicenter studies are needed to further understand and optimize the safety of outpatient CAR T-cell practice

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DISCLOSURES

CF: employment with Kite, a Gilead Company; stock or other ownership in Amgen and Gilead Sciences; and patents, royalties, and other intellectual property in Cellares.

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