Chimeric Antigen Receptor T-cell (CAR-T) Therapy Real-World Assessment of Total Cost of Care and Clinical Events for the Treatment of Relapsed or Refractory Lymphoma among 15 Million Commercially Insured Members

B. Sahli[1], D. Eckwright[1], E. Darling[1], P.P. Gleason[1,2], J. Leach [1,3]. [1]Prime Therapeutics LLC, Eagan, MN, United States; [2]University of Minnesota College of Pharmacy, Minneapolis, MN, United States; [3]Minnesota Oncology, St. Paul, MN, United States.

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BACKGROUND

- Axicabtagene ciloleucel is FDA approved, October 2017, to treat relapsed or refractory B-cell lymphoma after two or more lines of systemic therapy.[1] Tisagenlecleucel (originally approved for acute lymphoblastic leukemia [ALL]) is also approved, May 2018, to treat relapsed or refractory B-cell lymphoma after two or more lines of systemic therapy.[2]
- CAR-T therapy involves a complex process of T-cell extraction through lymphophoresis, ex-vivo transfection with a genetically modified viral vector, re-administration of the patient's modified T-cells, and hospital inpatient stay and management of adverse reactions such as cytokine release syndrome or neurotoxicity.
- The 2018 ICER report on CAR-T therapies for B-cell cancers suggests axicabtagene ciloleucel at a price of $340,797 would achieve the $100,000/QALY threshold, and at $524,015 would achieve $150,000/QALY. These proposed prices were based on the total discounted lifetime cost of approximately $617,000 for care of a patient's B-cell cancer.[3]
- The published wholesale acquisition cost (WAC) for both products is $373,000. Little has been established using real-world evidence identifying CAR-T episode total cost of care (TCC) and post-administration clinical events among the commercially insured population.

OBJECTIVE

- Evaluate real-world integrated medical and pharmacy claims data to characterize: utilization, total episode costs and post-administration events in members receiving CAR-T treatment for relapsed or refractory B-cell lymphoma in the commercially insured population.

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PATRICK GLEASON, 800.858.0723, ext. 5190
pgleason@primetherapeutics.com

METHODS

- Analysis was conducted using integrated pharmacy and medical claims data among an average of 15 million commercially insured members.
  - Members were identified from January 2018 to June 2020 with a CAR-T drug claim line allowed cost of >$250,000
  - Age 18 years and older
  - Lymphoma diagnosis and no leukemia or ALL diagnosis
  - Members were required to have continuous enrollment through an 86-day CAR-T episode of 30 days prior to and 56 days post the CAR-T administration date **(see Figure)**
- CAR-T drug utilization was identified through claims analysis for an HCPCS code, NDC, GPI specific to each drug product, or by CAR-T revenue codes or ICD-10 procedure codes indicated for CAR-T services.
- There were no specific inclusion criteria for use of previous lines of chemotherapy or bone marrow transplant prior to CAR-T for members to be included in the analytic population.
- The 86-day CAR-T episode total cost of care included all-cause pharmacy and medical costs. Costs are defined as the plan-paid allowed amounts plus member cost share. The CAR-T (drug claim line) specific costs and non-CAR-T drug costs were further separated and reported as components of the total episode cost.

Outcome Events

- For all non-financial outcome events, members were followed from the CAR-T episode end date, as long as enrollment allowed, up to the time of the end of the analytic period (Oct. 31, 2020 **[see Figure]**). Member disposition status and time to event (TTE) were reported at the end of the analytic period. Each member was assigned to one of the following mutually exclusive groups:
  - Experienced any claims-identified clinical event
  - Disenrolled without experiencing a claims-identified clinical event
  - Enrolled and did not experience a clinical event as of the analytic end date Oct. 31, 2020
- If a member experienced a clinical event (CE) post CAR-T administration plus 56 days, the CEs were identified as listed below and all events were counted independently such that a member could have more than one event.
  - Any subsequent chemotherapy drug not including supportive medications (e.g., antiemetics, colony stimulating factor or megestrol acetate)
  - Bone marrow transplant (BMT), including any allogeneic or autologous hematopoietic stem cell transplant
  - Death or hospice

RESULTS

- Among 15 million commercially insured members over the two and half year analysis period, we identified 74 members meeting all inclusion and exclusion criteria **(Table 1)**. Members were 59% male with an average age of 55 years ranging from 18 to 76 years old. Outcome events (disposition status and clinical event) assessment follow-up period averaged 288 days, with a range of 26 to 990 days, after the initial 56 day CAR-T episode.
- The mean 86-day CAR-T episode TCC was $711,884 (median $610,999) with the mean CAR-T drug cost at $527,547 (median $411,278) **(Table 2)**. The mean episode non-CAR-T drug cost was $184,337 (median $144,711).
- The disposition status of 74 members **(Table 3)** was: 29 (39%) members experienced a clinical event (CE), 21 (28%) members had no CE and disenrolled during follow-up or ceased all claim activity, and 24 (32%) remained enrolled with no CE, as of October 2020.
- Specific non-mutually exclusive CEs include: 22 (30%) of the 74 members received subsequent chemotherapy, four (5%) had a BMT, and 13 (18%) had an identified death or hospice; nine members experienced more than one specific type of CE.

LIMITATIONS

- There is potential for uncertainty on the exact cost of the CAR-T drug in this analysis. Though the claims are settled and we have confidence in the total paid amounts for members in aggregate, there exists the potential that a line item cost for a drug incurred within a hospitalization episode may not represent exactly what was intended by the facility and payer as a result of documentation, billing and payment procedures.
- Discontinuation without a clinical event may inadequately represent actual clinical events due to lack of visibility of events once a member leaves a plan or due to insufficient representation of mortality information in claims data. Death is identified through hospital discharge status. If a member died outside of a hospitalization or the discharge status was not coded to represent a death, then our report did not record this clinical event.
- These results represent commercially insured lives from many different clients of a national pharmacy benefit manager. The findings cannot be extrapolated to populations such as Medicare/Medicaid and may differ from other commercially insured populations with different attributes.

FIGURE

CAR-T Episode and Follow-up Analysis Timeline

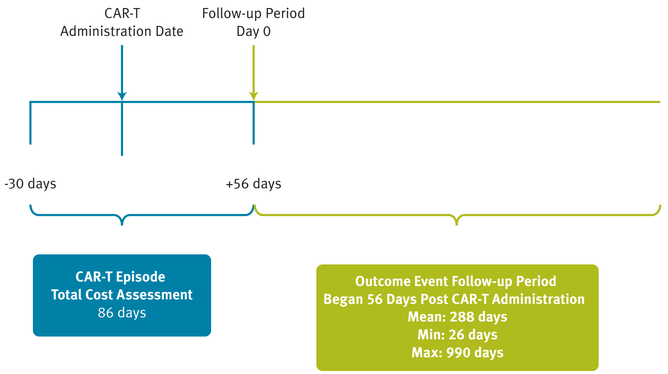

TABLE 3

Disposition Status of 74 Members Receiving CAR-T Therapy for B-cell Lymphoma

Outcome	Members n = 74	Mean TTE [SD] Days	Median TTE [min, max] Days
Experienced a Clinical Event*	29 (39%)	228 [217]	139 [59, 887]
Disenroll**, no Clinical Event	21 (28%)	253 [167]	209 [26, 599]
Enrolled***, no Clinical Event	24 (32%)	390 [264]	290 [112, 990]
All members	74 (100%)	288 [230]	203 [26, 990]

Chimeric Antigen Receptor T-cell (CAR-T) drugs include axicabtagene ciloleucel and tisagenlecleucel.
CAR-T claims were identified for members between Jan. 1, 2018 and June 30, 2020.
TTE = Time to Event post CAR-T episode completion (i.e., after the 56 days post CAR-T administration date), SD = Standard Deviation
*Clinical events are defined as: subsequent chemotherapy, death/hospice or bone marrow transplant. See Table 4 for further detail.
**Disenrolled prior to October 2020.
***Enrolled as of October 2020.

TABLE 1

CAR-T B-cell Lymphoma Utilizing Members Study Population Identification among 15 Million Commercial Lives

Study Criteria	N (%)
Members with CAR-T Claim*	105
Members 18 years or Older	89 (85%)
Continuously Enrolled for CAR-T Episode**	82 (78%)
Had Lymphoma Dx, No ALL Dx. – Final Analytic Population	74 (70%)

*Chimeric Antigen Receptor T-cell (CAR-T) drugs include axicabtagene ciloleucel and tisagenlecleucel with members having a claim between Jan 1, 2018 and June 30 2020.
**CAR-T episode was defined as 30 days prior to and 56 days post the CAR-T administration date.
Dx = Diagnosis, ALL = Acute Lymphoblastic Leukemia.

TABLE 2

CAR-T B-cell Lymphoma Episode Costs among 74 Members

Cost Category	Mean [SD]	Median [min, max]
CAR-T Drug Claim	$527,547 [$302,836]	$411,278 [$275,244, $2,101,934]
Episode Non-CAR-T Drug Claim	$184,337 [$129,422]	$144,711 [$15,363, $748,597]
Total Episode	$711,884 [$304,894]	$610,999 [$358,980, $2,235,658]

A CAR-T episode was defined as 86 days (30 days prior to until 56 days after the CAR-T administration date).
Episode costs include any medical or pharmacy cost incurred during the CAR-T episode time period.
CAR-T drug claim was reported as the cost on the claim line associated with the CAR-T drug.
SD = Standard Deviation.

TABLE 4

Clinical Events among 74 Members Receiving CAR-T Therapy for B-cell Lymphoma

Clinical Events	Members, non-mutually exclusive (n = 74)	Mean TTE [SD] Days	Median TTE [min, max] Days
Subsequent chemotherapy	22 (30%)	263 [238]	148 [59, 887]
Death/hospice	13 (18%)	297 [143]	290 [87, 512]
BMT	4 (5%)	245 [108]	340 [121, 342]

Chimeric Antigen Receptor T-cell (CAR-T) drugs include axicabtagene ciloleucel and tisagenlecleucel.
CAR-T claims were identified for members between Jan. 1, 2018 and June 30, 2020.
Bone marrow transplant (BMT) includes any allogeneic or autologous hematopoietic stem cell transplant.
TTE = Time to Event post CAR-T episode completion (i.e., after the 56 days post CAR-T administration date), SD = Standard Deviation.

CONCLUSIONS

- Among 15 million commercially insured lives with integrated medical and pharmacy claims data, we found 74 members with a CAR-T episode having substantial variation in total cost of care and clinical experience.
- Total 86-day episode cost was 74% CAR-T drug and 26% all other treatment cost with a wide range from $358,980 to $2,235,658; 12% of episodes were over $1 million in total cost.
- With the 74 analyzable members having an average 288 days post-episode (i.e., 56 days after CAR-T administration) follow-up, we found 39% of members did not have a durable CAR-T response for B-cell lymphoma. Among the members analyzed, providers initiated subsequent chemotherapy in 30%, in the absence of clear guidelines.
- These data inform managed care activities such as developing performance metrics and value-based contracting with providers and pharmaceutical manufacturers. Additionally, these data are important in actuarial forecasting for CAR-Ts utilization and costs given the pipeline potential for increased volume of treated patients and spend.

REFERENCES

1. Food and Drug Administration, Yescarta (axicabtagene ciloleucel). Accessed at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/yescarta-axicabtagene-ciloleucel.
2. Food and Drug Administration, Kymriah (tisagenlecleucel), Accessed at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/kymriah-tisagenlecleucel.
3. Chimeric Antigen Receptor T-Cell Therapy for B-Cell Cancers: Effectiveness and Value. *Institute for Clinical and Economic Review.* March 2018. Accessed at: https://icer.org/wp-content/uploads/2020/10/ICER_CAR_T_Final_Evidence_Report_032318.pdf.