Issue Brief:

CAR T-cell Therapy Provider and Patient Characteristics

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THE MORAN COMPANY

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YESCARTA™ (axicabtagene ciloleucel) – a CAR T-cell therapy (or chimeric antigen receptor T-cell therapy) for adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy, was approved in 2017 by the US Food and Drug Administration (FDA).[1] While YESCARTA is considered a transformative therapy, there has been significant concern regarding access to YESCARTA and other CAR T-cell therapies. The Moran Company (TMC) was asked to use Medicare claims data to identify characteristics of the hospitals that provide, and patients who receive CAR T-cell therapy. This report presents the findings from our analysis using 2018 and 2019 Medicare claims data.

Highlights of Our Findings:

- Our sample consisted of 897 Medicare patients receiving CAR T-cell therapy at 69 hospitals between 2018 to 2019.
- Approximately 57% of CAR T cases were paid under the Inpatient Prospective Payment System (IPPS), and most CAR T-cell therapy cases were performed in the inpatient setting by urban teaching hospitals.
- Roughly 54% of all CAR T cases identified in Medicare claims were part of a clinical trial.
- Most CAR T-cell therapy patients were between the ages of 65 and 74 years (62.9%), male (60.3%), and white (84.1%).
- Approximately 13% of CAR T-cell therapy patients were dually eligible for both Medicare and Medicaid and 17% were disabled.

Background on CAR T-cell Therapy

According to the National Cancer Institute, CAR T-cell therapy is a type of treatment in which a patient's T cells are used to attack cancer cells. T cells are taken from a patient's blood and the gene for a receptor that binds to a protein on the patient's cancer cells (called a chimeric antigen receptor (CAR)) is added to the T cells in a laboratory where they are grown. The treatment is then delivered to the patient via infusion.[2] Prior to the summer of 2020, the FDA had approved two CAR T-cell therapies – KYMRIAH™ and YESCARTA. KYMRIAH was approved for treatment of adults with r/r large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.[3,4] YESCARTA was approved for the

[1] Food and Drug Administration. Package Insert – YESCARTA. https://www.fda.gov/media/108377/download.
[2] National Cancer Institute. NCI Dictionary of Cancer Terms: CAR T-cell therapy. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy.
[3] Food and Drug Administration. Package Insert – KYMRIAH. https://www.fda.gov/media/107296/download.
[4] KYMRIAH is also indicated for patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

treatment of adult patients with r/r large B-cell lymphoma after two or more lines of systemic therapy, including DLBCL not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.[5] KYMRIAH and YESCARTA are the focus of this issue brief. In July 2020, the FDA approved TECARTUS™ for r/r mantle cell lymphoma.[6] Clinical trials of CAR T-cell therapies for other cancers are ongoing.

Clinical trials have found CAR T-cell therapy highly effective. Clinical trials of YESCARTA show 82% of eligible patients with large B-cell lymphoma responded to CAR T-cell therapy, and 54% achieved complete remission.[7] However, access to CAR T-cell therapy is limited. This is partly due to the highly specialized nature of CAR T-cell therapy. Only providers with specialized expertise and certification can provide CAR T-cell therapy. Additionally, when CAR T-cell therapies first came to market, many stakeholders assumed hospital billing practices would result in very large losses (perhaps as much as $200,000 or more) when treating Medicare patients. This precluded some providers from participating. However, The Moran Company's analysis of claims data for the years since these therapies first became available suggests that while there have been reimbursement challenges under Medicare for some providers, reimbursement has been better than expected.

The table below presents trends in Medicare reimbursement for CAR T-cell therapies between quarter 4 of 2018 and quarter 4 of 2019 based on TMC's analysis of Medicare Inpatient Standard Analytic Files (SAFs). Quarterly average Medicare payments ranged from $340,364 to $404,095 during the 5 quarters. During this same period, TMC's analysis using the MedPAR data revealed that the average cost to treat patients using CAR T-cell therapy was roughly $426,000.[8] While the average Medicare payment was generally lower than the average treatment cost, the difference was smaller than many stakeholders had anticipated prior to the availability of data. In fact, 30% of the claims were paid more than $426,000 (the average cost of treatment) suggesting some providers are better able to recoup their expenses than the others. New Technology Add-on Payments (NTAPs) and outlier payments have been instrumental in improving Medicare reimbursement. The table below also presents the NTAPs and outlier payments during the period.

[5] YESCARTA Package Insert.
[6] Food and Drug Administration. Package Insert – TECARTUS. https://www.fda.gov/media/140409/download
[7] Dana Farber. CAR T-Cell Therapy for Lymphoma. https://www.dana-farber.org/cellular-therapies-program/car-t-cell-therapy/car-t-cell-therapy-for-lymphoma/#:~:text=The%20clinical%20trials%20of%20Yescarta,%2C%20no%20sign%20of%20cancer).
[8] The cost to treat patients was calculated using the charges available in the MedPAR data and adjusting for provider specific cost to charge ratio.

Table 1. Medicare Reimbursement Trends for CAR T-cell Therapies

	2018, Q4	2019, Q1	2019, Q2	2019, Q3	2019, Q4
Total Discharges	24	32	46	31	49
Average Medicare Payment	$ 387,337	$ 387,459	$ 340,364	$ 358,727	$ 404,095
Median Medicare Payment	$ 391,904	$ 396,062	$ 368,921	$ 383,382	$ 382,946
Average NTAP	$ 145,084	$ 156,711	$ 129,012	$ 141,517	$ 196,025
Median NTAP	$ 186,500	$ 186,500	$ 162,205	$ 167,910	$ 224,514
Average Outlier Payment	$ 153,325	$ 143,409	$ 110,848	$ 112,022	$ 115,573
Median Outlier Payment	$ 135,853	$ 137,500	$ 110,074	$ 113,838	$ 72,807

*Note: Only non-clinical trial discharges (discharges that do not have a clinical trial indicator and have drug charges>373,000) from IPPS hospitals are included in this table because accurate payment information is available only for these discharges.

In response to concerns regarding reimbursement for CAR T-cell therapy, in the FY 2021 IPPS Final Rule, CMS established a separate CAR T-cell therapy DRG that will help mitigate hospitals' financial losses.[9] This could alleviate hospitals' hesitation to provide CAR T-cell therapy thereby improving access. However, based on TMC's projections, 63% of cases—not hospitals—are still projected to be paid less than the full treatment cost for CAR T-cell therapy patients.

The primary aim of this analysis is to understand the characteristics of hospitals that provide CAR T-cell therapy and to provide descriptive information about patients who undergo CAR T-cell therapy.

Methods

We used Medicare claims data for 2018 and 2019 available in the 100% Inpatient and Outpatient Standard Analytic Files (SAFs). In the inpatient SAFs, claims with International Classification of Diseases, Tenth Revision, Procedure Coding System (ICD-10-PCS) codes 'XW033C3', and 'XW043C3' were identified as CAR T-cell therapy claims. In the outpatient SAFs, claims with Healthcare Common Procedure Coding System (HCPCS) codes 'Q2040', 'Q2041', 'Q2042' were identified as CAR T-cell therapy claims. Claims with no payments in both the inpatient and outpatients SAFs were excluded from our analysis.

[9] CMS. FY 2021 IPPS Final Rule, 85 FR 58432.

Indicators of whether the provider was paid based on the Inpatient Prospective Payment System (IPPS), provider teaching status, and urban status were created by matching the Medicare provider number available in the claims data to provider characteristics available in Inpatient Impact File. We considered all inpatient and outpatient CAR T-cell therapy claims with an ICD-10, clinical modification (ICD-10-CM) code of 'Z006' clinical trial cases. In addition, consistent with Medicare's definition of CAR T-cell therapy clinical trial cases in the FY 2021 IPPS Final Rule, we also consider cases with drug charges below $373,000 as clinical trials.

Patient characteristics such as age, gender, race, dual-eligibility, and disability status were obtained from the Medicare denominator file.

Results

Table 2. Description of Study Sample

Provider Characteristics	Number of Hospitals	Number of Patients	Inpatient Stays N, (Percentage)	Length of Inpatient Stay Mean, (Standard dev.)
TOTAL CASES	69	897	855 (95.3%)	17.52 (10.35)

In total, our sample consisted of 897 CAR T-cell therapy patients receiving treatment at 69 hospitals. Most patients (95.3%) received CAR T-cell therapy in the inpatient setting, and the average length of stay (LOS) among those patients was approximately 18 days.

Provider Characteristics

I. Payment System

Table 3. Sample Distribution by Payment System

Payment System	Number of Hospitals	Number of Patients (%)	Length of Inpatient Stay (Mean, Std dev.)
Inpatient IPPS	60	510 (56.8%)	16.40 (10.20)
Inpatient PPS-Exempt	8	345 (38.5%)	19.16 (10.36)
Outpatient	12	42 (5.7%)	-

In general, acute care hospitals are paid by Medicare Part A based on prospectively set rates. This payment system is referred to as the Inpatient Prospective Payment System (IPPS). However, certain cancer hospitals, children's hospitals, psychiatric facilities, and certain rural hospitals are excluded from payment under the IPPS and are referred to as PPS-exempt hospitals. Of most importance for CAR T-cell therapy, there are 11 cancer hospitals that are designated by Medicare as PPS-exempt and are instead paid under a different payment methodology. All outpatient cases are paid by Medicare Part B.

The majority of CAR T-cell therapy cases (510 patients, 56.8%) in our sample were paid under the IPPS. Of the remaining 387 patients, 345 patients (38.5%) received inpatient care in a PPS-exempt hospital, and 42 patients (5.7%) received care in the outpatient setting. Almost all hospitals that provided outpatient CAR T-cell therapy also provided treatment in the inpatient settings (11 out of 12 hospitals). CAR T-cell therapy patients who were treated inpatient by PPS-exempt providers had longer LOS (~19 days) than cases treated by providers paid under IPPS (~16 days).

II. Teaching Status

Table 3. Sample Distribution by Provider Teaching Status

Teaching Status	Number of Hospitals	Number of Patients (%)	Length of Inpatient Stay* (Mean, Std dev.)
Major Teaching	56	842 (93.9%)	17.73 (10.44)
Other	13	55 (6.1%)	14.35 (8.49)

*Note: Length of stay variable is based on inpatient stays only

Most hospitals providing CAR T-cell therapy were major teaching hospitals (56 hospitals or 81% of all hospitals),[10] and approximately 94% of all CAR T-cell therapy patients were treated at these hospitals. Of the remaining 13 hospitals, most were minor teaching hospitals. Only a very few cases (< 2%) were treated in non-teaching hospitals. LOS at major teaching hospitals was, on average, three days longer than LOS at other hospitals.

III. Clinical Trials

Table 4. Sample Distribution by Clinical Trial Status

Hospitals by Clinical Trial Status	Number of Hospitals	Number of Patients (%)	Length of Inpatient Stay* (Mean, Std dev.)
Clinical Trials Only	16	57 (1.4%)	15.33 (13.33)
Clinical Trials and Non-Clinical Trials	37	Clinical – 424 (37.6%)	16.83 (9.76)
		Non-Clinical - 372 (53.5%)	18.40 (10.50)

[10] We consider hospitals with resident-to-bed ratio >/= 0.25 as major teaching hospitals, and hospitals with resident-to-bed ratio > 0 and resident-to-bed ratio < 0.25 as minor teaching hospitals. Hospitals with no residents are considered non-teaching hospitals.

Non-Clinical Trials Only	16	44 (7.5%)	20.41 (9.53)
All Clinical Trials	53	481 (53.6%)	16.66 (9.40)
All Non-Clinical Trials	53	416 (46.4%)	18.63 (10.40)

*Note: Length of stay variable is based on inpatient stays only

Clinical trials were conducted in nearly 77% of hospitals providing CAR T-cell therapy (53 of the 69 hospitals). However, less than 25% of hospitals performed clinical trials only. Approximately 54% of all CAR T-cell therapy cases were clinical trial cases. In general, clinical trial cases had shorter LOS (~17 days) compared to non-clinical trial cases (~19 days).

IV. Location

Table 5. Sample Distribution by Provider Location

Provider Location	Number of Hospitals	Number of Patients (%)	Length of Inpatient Stay* (Mean, Std dev.)
Urban	69	897 (100.0%)	17.52 (10.35)
Rural	-	-	-

*Note: Length of stay variable is based on inpatient stays only

Between 2018 and 2019, CAR T-cell therapies were provided exclusively in urban hospitals. Thus, if patients in rural areas were to receive CAR T-cell therapy, they had to travel to urban provider locations.

Patient Characteristics

I. Age, Gender, and Race

Table 6. Sample Distribution by Patient Age, Gender and Race

Patient Characteristics		Number of Patients (%)	Length of Inpatient Stay* (Mean, Std dev.)
Age Group	64 and Younger	170 (19.0%)	16.35 (8.54)
	65 to 74	564 (62.9%)	18.15 (11.43)
	75 and Older	163 (18.2%)	16.56 (7.97)
Gender	Male	541 (60.3%)	17.23 (9.95)

	Female	356 (39.7%)	17.94 (10.93)
Race	White	754 (84.1%)	17.52 (10.67)
	Other	143 (15.9%)	17.51 (8.58)

*Note: Length of stay variable is based on inpatient stays only

The majority (62.9%) of patients in our sample who received CAR T-cell therapy were between the ages of 65 and 74. On average, patients in the 65 to 74 years age group had longer LOS (~18 days) compared to patients who were younger than 65 (~16 days) and patients who were 75 and older (~16 days). Approximately 60% of the CAR T-cell therapy cases in our analysis were male, and the majority were white (84.1%). LOS did not differ significantly by gender or race.

II. Dual-eligibility Status

Table 7. Sample Distribution by Patient Dual-eligibility Status

Dual-eligibility Status	Number of Patients (%)	Length of Inpatient Stay (Mean, Std dev.)
Dual-eligible	114 (12.7%)	18.53 (10.70)
Not Dual-eligible	783 (87.3%)	17.37 (10.30)

*Note: Length of stay variable is based on inpatient stays only

Dual-eligible patients are those beneficiaries who are enrolled in both Medicare and Medicaid. Approximately 13% of CAR T-cell therapy patients were dual-eligible. Dual-eligible patients had slightly longer LOS (~18 days) compared to non-dual-eligible patients (~17 days).

III. Disability Status

Table 8. Sample Distribution by Patient Disability Status

Disability Status	Number of Patients (%)	Length of Inpatient Stay (Mean, Std dev.)
Disabled	148 (16.5%)	16.46 (8.69)
Not Disabled	749 (83.5%)	17.73 (10.64)

*Note: Length of stay variable is based on inpatient stays only

In addition to those aged 65 and older, Medicare also covers certain people with disabilities who are under age 65. Patients who qualify for Medicare based on disability are generally younger than and more likely to be dually eligible compared to other Medicare patients. Approximately 17% of CAR T-cell therapy cases in our sample were Medicare beneficiaries with a disability.

LOS for disabled beneficiaries was about a day shorter (~16 days) for those that were disabled compared to those that were not disabled (~17 days).