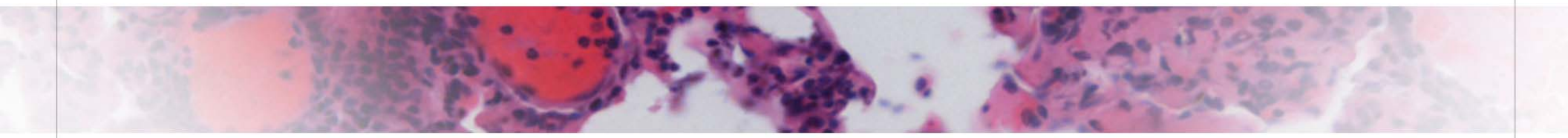

Real-World Effectiveness and Economic Impact Associated with Chimeric Antigen Receptor T-cell Therapy Among Older Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma in US

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Background

- Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma, with more than half of patients diagnosed over the age of 65 and approximately 30% of patients are over the age of 75.[1]
- Chimeric Antigen Receptor T-cell (CAR T) therapy has become a standard treatment for relapsed/refractory DLBCL.
- Though DLBCL is more prevalent in older patients, RWE data of CAR T use in older patients are scarce.
- The objective is to describe the RWE including effectiveness and economic impact associated with CAR T in older patients with relapsed/refractory DLBCL in the US.

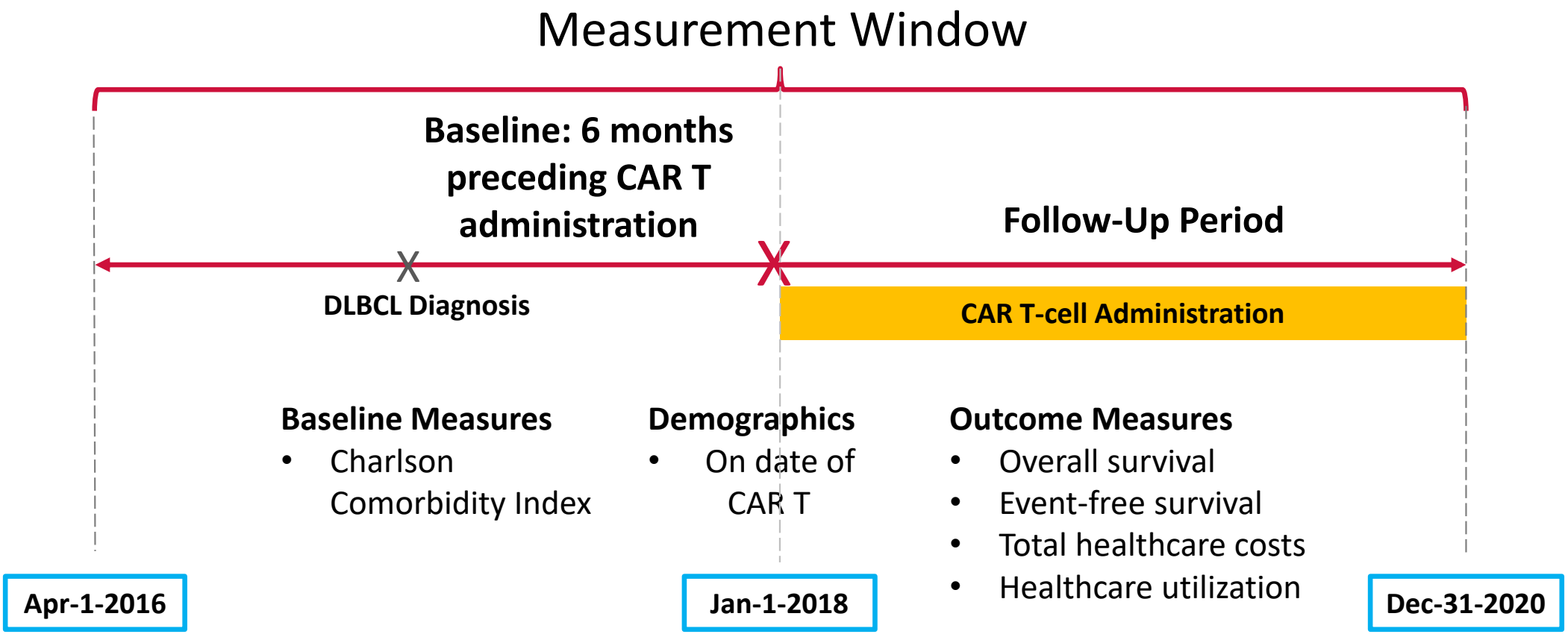
1. SEER 22 2015–2019

Data Source and Selection Criteria

100% Medicare Fee-for-Service Parts A/B/D from 4/1/2016 to 12/31/2020

- Inclusion
  - ≥ 1 inpatient or ≥ 2 outpatient claims
    - **diagnosis of DLBCL (ICD-10) between April 1, 2016 and December 1, 2020**
  - ≥ 1 claim for CAR T following diagnosis of DLBCL
    - **CAR T must have been administered on January 1, 2018 or later**
  - Aged 65+ on the date of CAR T administration
- Exclusion
  - Patients with evidence of clinical trial participation

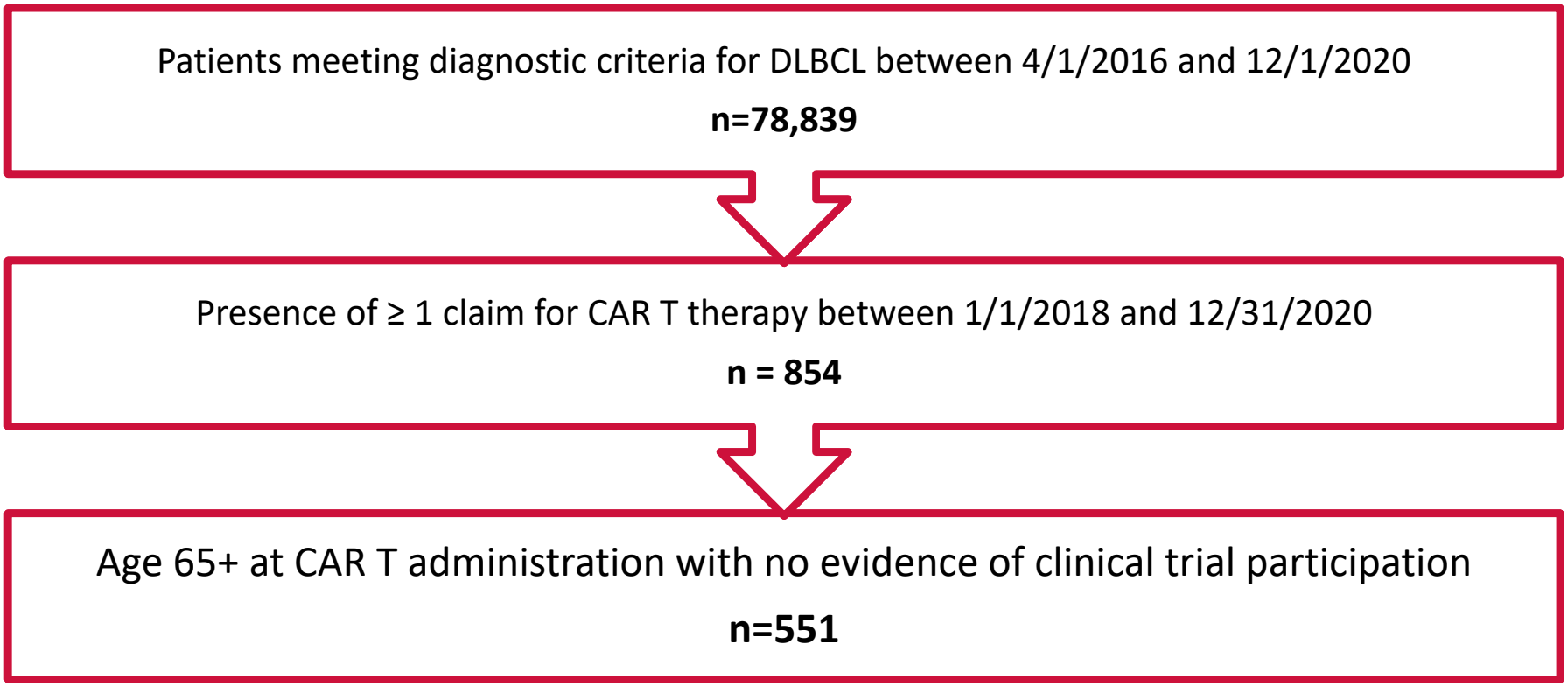
Study Design



Statistical analysis

- Analysis was stratified by three age groups
  - 65-69, 70-74, 75+
- Event: initiation of next treatment or death from any cause
- Bridging therapy: any DLBCL treatment within 28 days of CAR T administration
- Cox regression for EFS and OS
  - Variables of interest: Age, Sex, Comorbidity index, bridging treatment
- Healthcare utilization and costs were also stratified by CAR T administration setting
  - Inpatient vs outpatient

Patient population



CAR T-cell Therapy utilization in Older Patients

Among patients who received 3rd line treatment and beyond

Age group	% of CAR T use in 3L+
Age 65-69	19.2%
Age 70-74	22.1%
Age 75+	12.8%

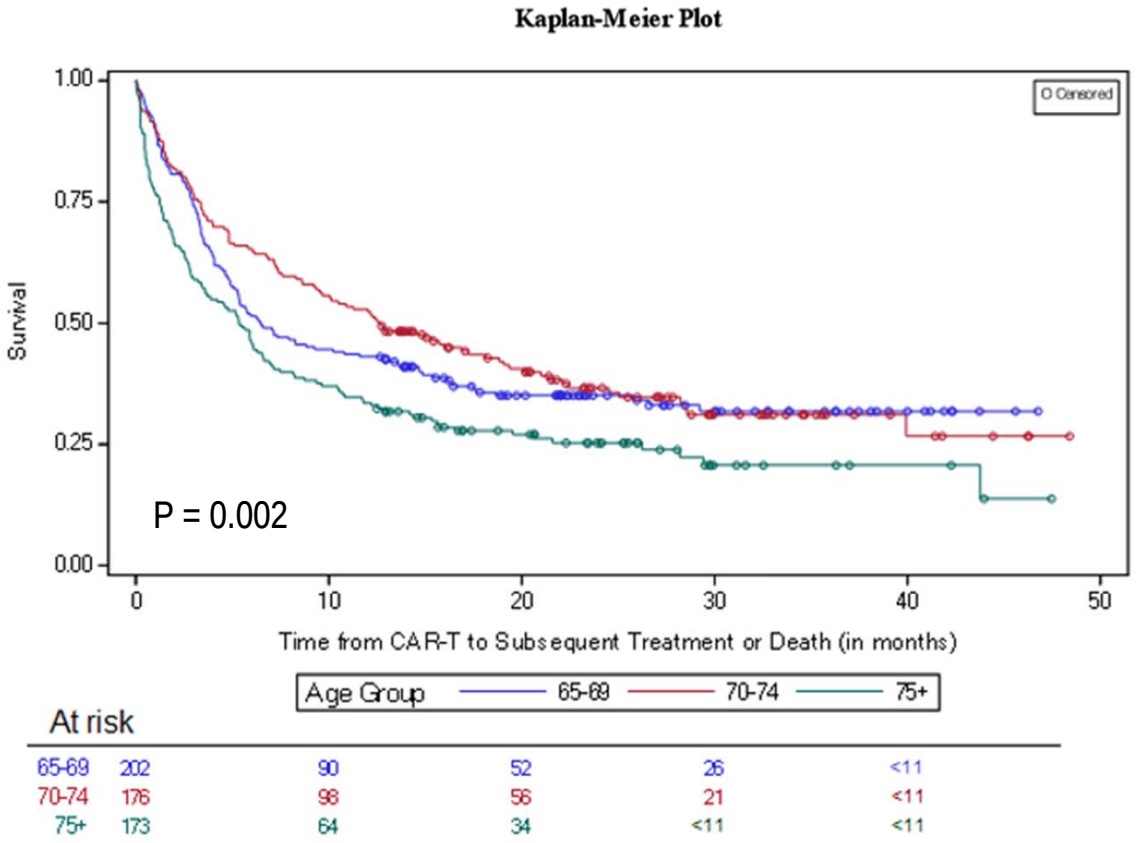
- **Only 1 in 5 received CAR T therapy in age 65-74**
- **Only 1 in 9 received CAR T therapy in age 75+**

Baseline Characteristics

	Age 65-69 n=202		Age 70-74 n=176		Age 75+ n=173		Full Sample n=551	
Median age (range)	67	(65-69)	72	(70-74)	78	(75-90)	**72**	(65-90)
Male (n,%)	108	53.50%	93	52.80%	98	56.60%	299	54.30%
Urban/Suburban Residence (n, %)	160	79.20%	142	80.70%	142	82.10%	444	80.60%
Median Charlson Comorbidity Index (range)	4	(0-15)	4	(0-15)	4	(0-15)	**4**	(0-15)
Bridging Therapies* (n,%)								
Any therapy	102	50.50%	69	39.20%	91	52.60%	262	**47.50%**
Chemotherapy or targeted therapy	64	31.70%	41	23.30%	55	31.80%	160	29.00%
Steroids*	<50	-	<50	-	23	13.30%	73	13.20%
Radiation*	<11	-	<11	-	13	7.50%	29	5.30%
CAR T Administration setting								
Inpatient (n,%)	171	84.70%	155	88.10%	130	75.10%	456	82.80%
Length of Stay (days, std)	19.7	12.4	24.2	21.2	20.5	13.1	**21.4**	16.2
Outpatient (n,%)	31	15.30%	21	11.90%	43	24.90%	95	17.20%

*Cell sizes < 11 patients have been suppressed to maintain patient confidentiality

Outcomes – Event-Free Survival

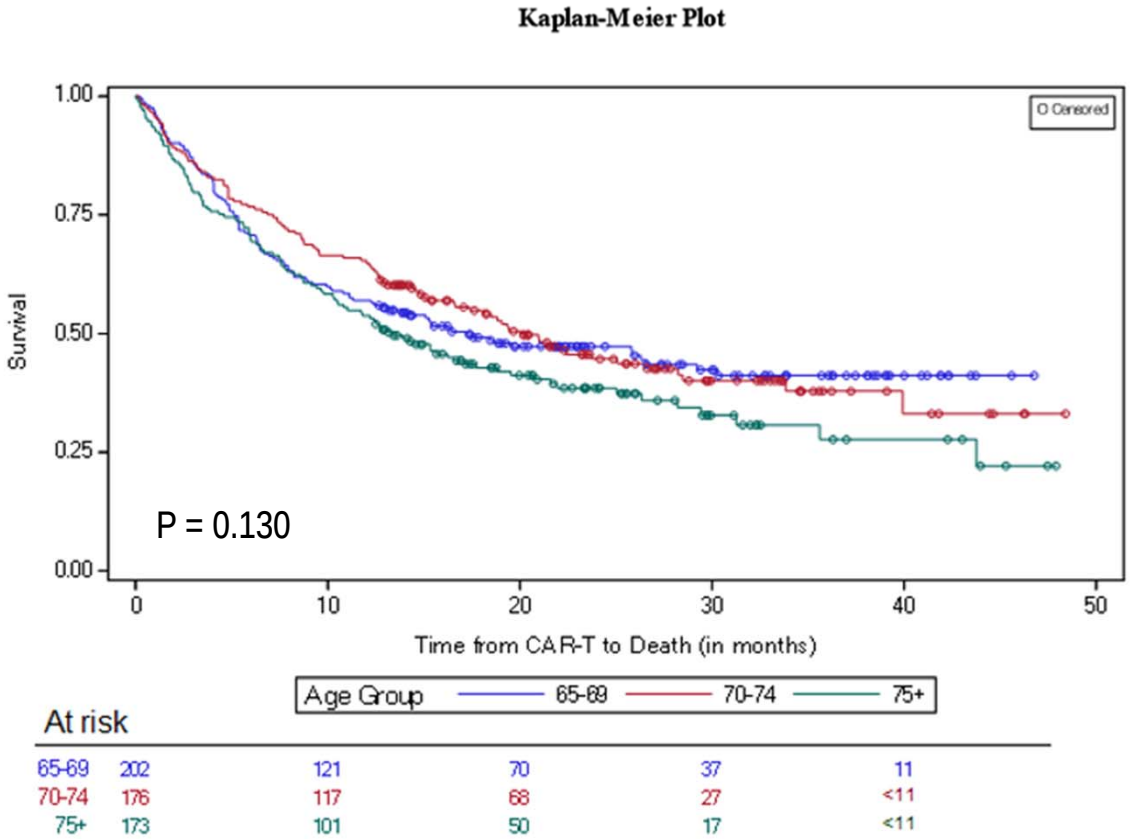


Median EFS in all patients

- 7.2 months (95%CI: 6.0 – 9.7)

Age group	Median EFS	1-year EFS
Age 65-69	6.5 months	43.1%
Age 70-74	12.6 months	51.7%
Age 75+	5.3 months	33.5%

Outcomes – Overall Survival



Median OS in all patients

- 17.1 months (95%CI: 14.2 – 21.0)

Age group	Median OS	1-year OS
Age 65-69	17.3 months	56.9%
Age 70-74	20.1 months	64.2%
Age 75+	13.4 months	53.8%

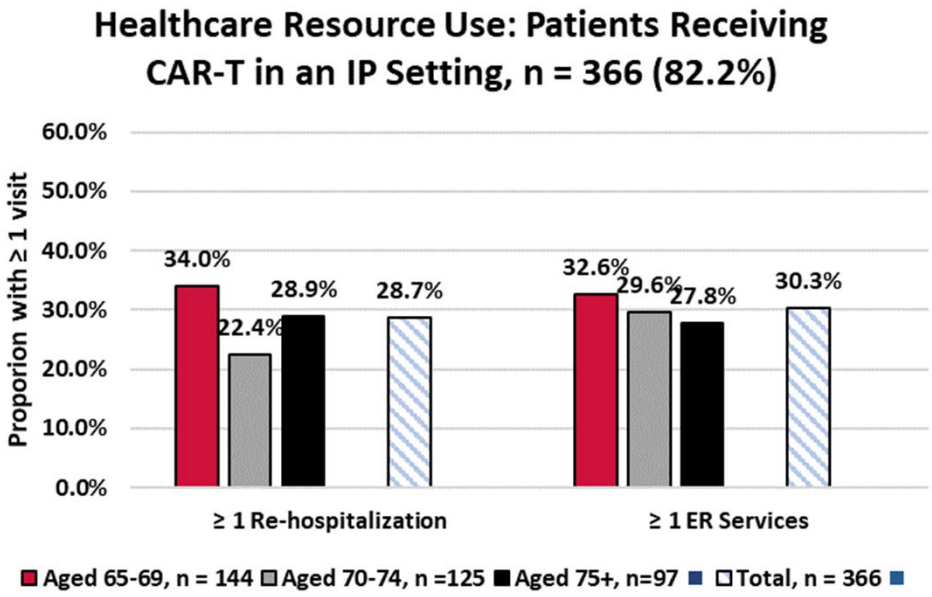
Risk factors for EFS

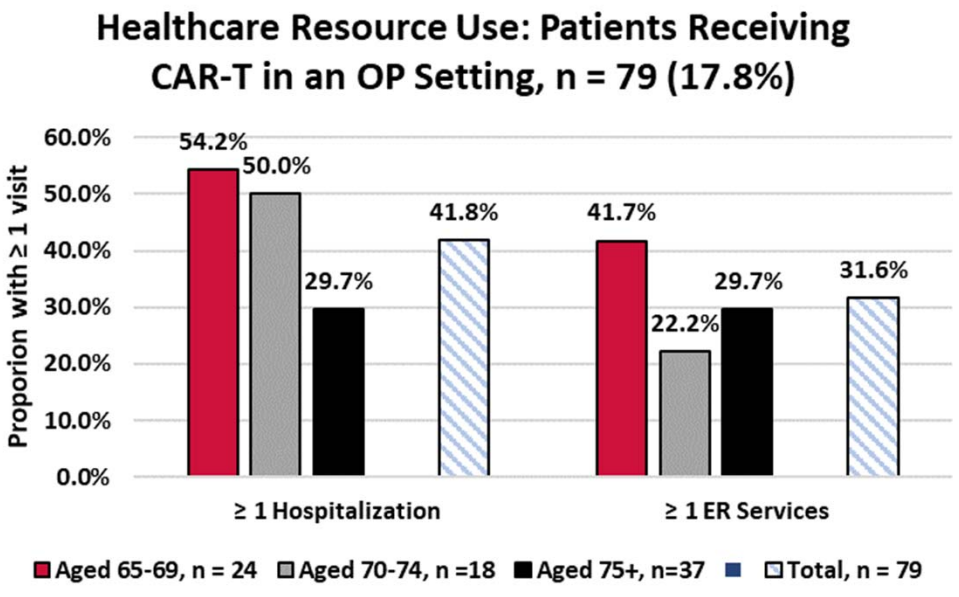
Characteristics		Univariate		Multivariate	
		HR	95%CI	HR	95%CI
Age groups	75+ vs. 65-69	**1.37**	1.07 - 1.74	**1.41**	1.10 - 1.82
	75+ vs. 70-74	**1.54**	1.19 - 1.98	**1.46**	1.13 – 1.89
Gender	Male vs. Female	1.01	0.81 – 1.22	0.92	0.75 – 1.14
Urban/Suburban Residence	Rural vs. Urban	1.14	0.88 – 1.47	Not included	-
Bridging therapy prior to administration	Present vs. Absent	**1.34**	1.09 – 1.64	**1.27**	1.03 – 1.56
Charlson Comorbidity Index	5+ vs. 0-4	**1.57**	1.28-1.94	**1.56**	1.26 – 1.92

Risk factors for OS

Characteristics		Univariate		Multivariate	
		HR	95%CI	HR	95%CI
Age groups	75+ vs. 65-69	1.25	0.96 – 1.62	1.20	0.91 – 1.58
	75+ vs. 70-74	1.29	0.98 – 1.70	1.20	0.90 – 1.58
Gender	Male vs. Female	1.05	0.85 – 1.33	1.00	0.80 – 1.26
Urban/Suburban Residence	Rural vs. Urban	1.22	0.93 – 1.60	Not included	-
Bridging therapy prior to administration	Present vs. Absent	**1.51**	1.19 – 1.86	**1.58**	1.26 – 1.99
Charlson Comorbidity Index	5+ vs. 0-4	**1.63**	1.30 – 2.05	**1.39**	1.11 – 1.75

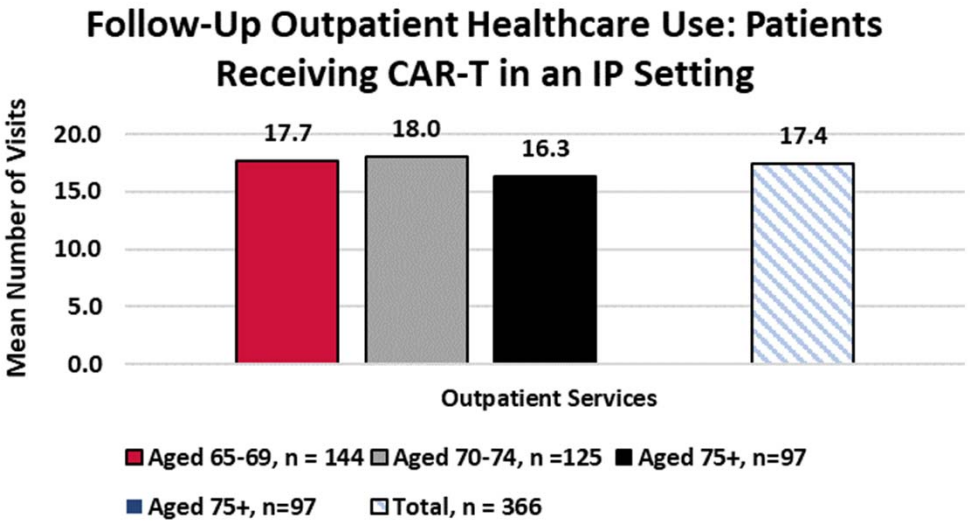
Outcomes – ER and inpatient utilization

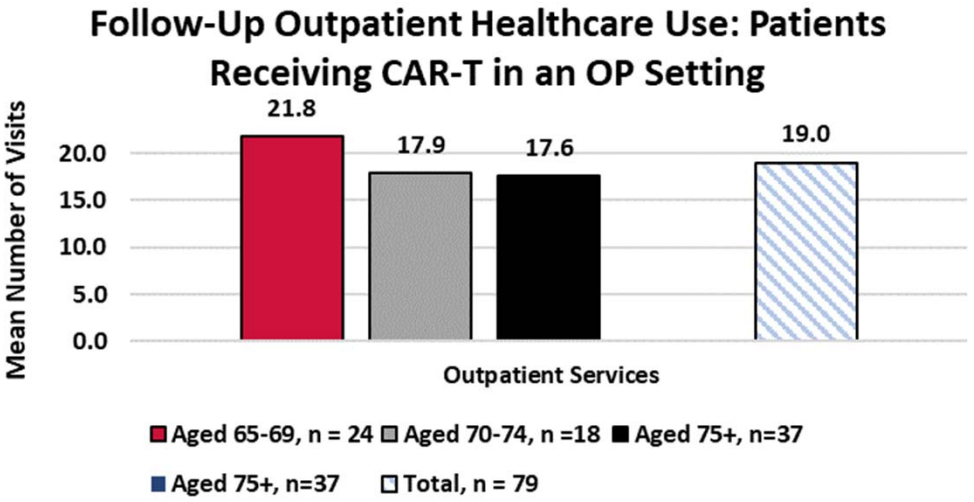




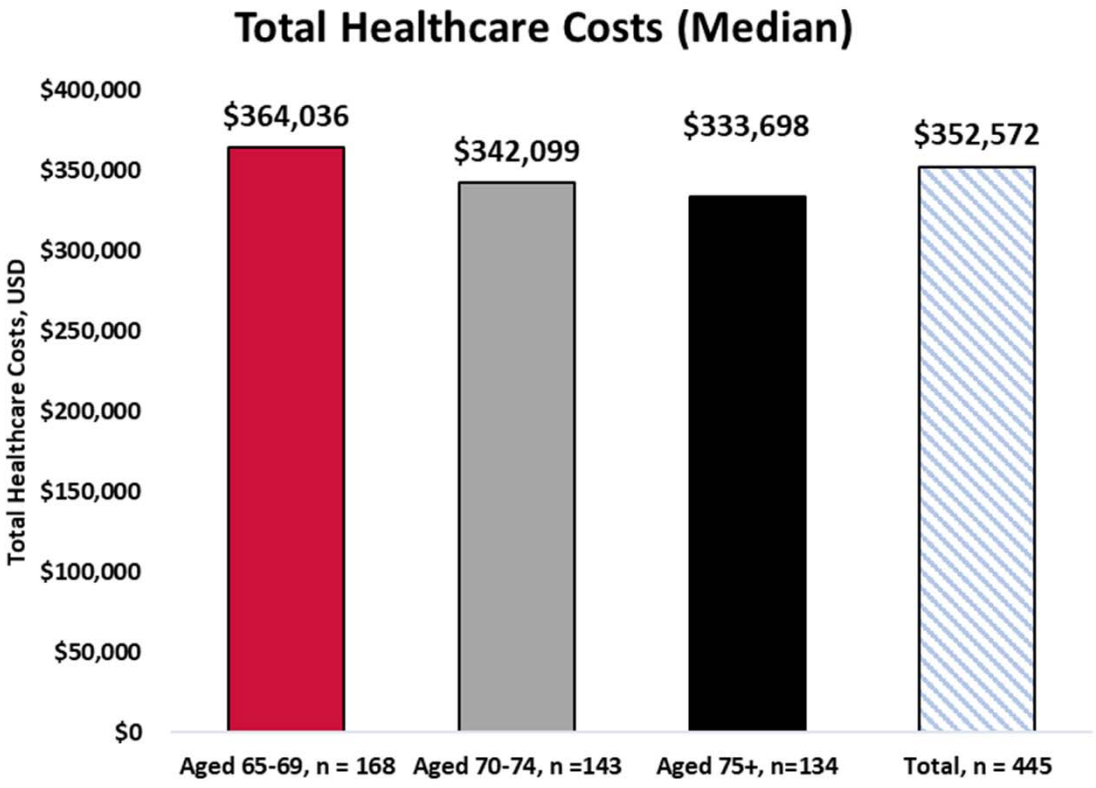
	Initial Hospitalization CAR T Administered	Follow-Up Hospitalizations	
		CAR T Administered in IP	CAR T Administered in OP
Hospitalization Length of Stay (Mean, SD)	21.4 (16.2)	7.6 (6.6)	7.5 (6.3)

Outcomes – Outpatient Utilization





Outcomes – Healthcare Costs



- Median total healthcare costs incurred during the 90-day period following CAR T administration were similar across age categories
- Mean costs presented a similar pattern:
  - Aged 65-69: $311,699
  - Aged 70-74: $296,192
  - Aged 75+: $271,767
  - Total sample: $294,692

Conclusions

- This is the largest and nationally representative RWE study in US in older patients with DLBCL who received CAR T therapy.
- CAR T therapy is associated with favorable EFS in older patients, comparable to outcomes observed among the pivotal phase 2 studies.
  - Less favorable EFS was observed in patients aged 75+
- CAR T therapy use in older patients was low, especially in patients aged 75+.
- Charlson Comorbidity Index was an independent risk factor for both EFS and OS.
- Healthcare costs associated with CAR T therapy were high.
- This study indicated that there is unmet need for more accessible, effective, and tolerable therapy in older patients, especially in patients aged 75+.