

Short-Term Costs Associated with Outpatient Use of Axicabtagene Ciloleucel in Second-Line Relapsed/Refractory Large B-Cell Lymphoma Based on Zuma-24 Clinical Trial

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INTRODUCTION

- Axicabtagene ciloleucel (axi-cel) is a CD19-directed genetically modified autologous chimeric antigen receptor T-cell (CAR T) therapy.[1]
- Axi-cel was the first CAR T therapy approved for treatment of adults with relapsed/refractory (R/R) large B-cell lymphoma (LBCL) by the US Food and Drug Administration (FDA) and by European Medicines Agency (EMA).[1,2]
- Additionally, axi-cel has proven cost-effective and has been recommended for reimbursement by leading health technology agencies, including the National Institute for Health and Care Excellence.[3,4]
- ZUMA-24 (NCT05459571) is a Phase 2, open-label, multicenter study to evaluate the safety and efficacy of outpatient administration of axi-cel with prophylactic corticosteroid use and early adverse event (AE) intervention in patients with R/R LBCL after ≥1 prior line of systemic therapy (2L+).[5]
- Through incorporation of these strategies, no patients in ZUMA-24 experienced grade 3+ cytokine release syndrome. Of the 23 patients who experience a neurologic event (54% grades 1 and 2) all but 3 had resolved as of data cutoff (median follow-up 7 months).[6]

OBJECTIVES

The objective of the analysis was to evaluate the short-term costs associated with outpatient use of axi-cel in 2L+ LBCL based on the results of the ZUMA-24 clinical trial.

METHODS

Study methodology

- This study utilized data collected in ZUMA-24 to determine the total health care resource utilization (HCRU) costs associated with outpatient axi-cel infusion.
 - A microcosting methodology was used to quantify HCRU and estimate the associated healthcare costs incurred pre- and post-infusion.
 - ZUMA-24 data provided the proportion of patients using various types of HCRU and the average number of services/units utilized per patient with HCRU.
 - Unit costs for each HCRU type were derived from public databases and literature and were applied to observed utilization.
 - Individual HCRU costs were aggregated to estimate average total costs per patient (excluding axi-cel infusion costs).
 - The cost calculator was developed in Microsoft Excel (version 2410).
- ### ZUMA-24 Study Population
- Key inclusion criteria were ≥1 prior line of systemic therapy for LBCL, Eastern Cooperative Oncology Group performance score (ECOG) 0-1 and adherence to prespecified institutional clinical monitoring requirements.
 - Key exclusion criteria include prior autologous or allogeneic stem cell transplant, and prior anti-CD19 or CAR T-cell therapy.

METHODS (CONTINUED)

HCRU and Cost Inputs (Table 1)

- HCRU data were sourced from the ZUMA-24 trial and included:
 - Pre-infusion treatments (lymphodepleting chemotherapy, bridging therapy, leukapheresis)
 - Laboratory tests (blood culture and microbiological procedures)
 - Diagnostic and imaging procedures (X-ray, CT, MRI, EEG, echocardiogram, EKG/ECG, electrocardiogram)
 - Hospitalizations (including both standard room and intensive care unit [ICU] for patients admitted to hospital after axi-cel infusion),
 - Supportive medications (tocilizumab, prophylactic steroids)
- Unit costs for HCRU were sourced from the 2024 Centers for Medicare and Medicaid Services fees schedules, RedBook, the Healthcare Cost and Utilization Project, and published literature.
- Costs are presented in 2024 USD and were inflated using consumer price index (CPI) for medical care in the US.
- It was assumed that costs of adverse event management (beyond steroid and tocilizumab use) are covered in the inpatient hospitalization costs.

Table 1. Inputs and costs used in the calculation

Model input category				
Pre-infusion	Patients with the procedure	Mean number of procedures (those with at least 1)	Cost per unit	Source
Leukapheresis	100%	1	\$1,172.79	[6], [8]
Bridging therapy	49%	1	\$2,282.46	[6], [9]
Lymphodepleting chemotherapy	86%	1	\$921.76	[6], [9]
Laboratory tests	Patients with the procedure	Mean number of procedures (those with at least 1)	Cost per unit	Source
Blood Culture	70%	2.52	\$10.32	[7], [10]
Microbiological procedures (Other)	27%	3.38	\$10.32	[7], [10]
Diagnostic and imaging procedures	Patients with the procedure	Mean number of procedures (those with at least 1)	Cost per unit	Source
Chest X-Ray	50%	2.00	\$33.62	[7], [11]
Other X-Ray	17%	1.60	\$51.93	[7], [11]
CT Brain	23%	1.29	\$1,480.51	[7], [11]
CT Other	33%	1.30	\$1,480.51	[7], [11]
EEG/EEG video monitoring	13%	1.25	\$350.19	[7], [11]
Echocardiogram	10%	1.00	\$196.06	[7], [11]
EKG/ECG	23%	1.43	\$14.31	[7], [11]
Electrocardiogram	10%	1.33	\$14.31	[7], [11]
MRI (Brain)	30%	1.33	\$326.88	[7], [11]
MRI (Other)	10%	1.00	\$484.33	[7], [11]
Hospitalizations Post-Infusion	Patients admitted	Mean length of stay per admission (days)	Cost per day	Source
Standard room	93%	8.1	\$3,275.97	[7], [12], 2020 dollars inflated to 2024 [13]
Intensive care unit (ICU)	13%	6.0	\$6,099.57	[7], [12], 2020 dollars inflated to 2024 [13]
Supportive medication	Patients hospitalized		Mean cost per event	Source
Cytokine release syndrome (CRS)	90%		\$17,424.40	[7], [11]

CT = computed tomography; EEG = electroencephalogram; EKG/ECG = Electrocardiogram; MRI = magnetic resonance imaging

RESULTS

- The estimated mean short-term cost of outpatient use of axi-cel in 2L+ LBCL (excluding drug acquisition) was \$72,477 per patient (**Figure 1**) including:
 - \$3,071 in leukapheresis, bridging therapy, and lymphodepleting chemotherapy costsand post-infusion costs:
 - \$28 in laboratory testing costs, \$1,397 in diagnostic and imaging procedure costs, \$52,299 in inpatient hospitalization costs, \$15,682 in supportive medication costs
- Costs for inpatient hospitalization were driven by all-cause hospital stays for the 93% of study patients who had inpatient care (mean length of stay per admission of 8.1 days) and 13% of patients requiring ICU (mean length of stay per ICU admission of 6.0 days).
 - Total mean inpatient hospitalization cost consists of \$46,200 attributable to hospitalization in standard room and remaining \$6,100 to ICU (**Figure 2**).
 - The biggest driver of 1st hospitalization was grade 1 adverse events

Figure 1. Estimated Mean Short-Term Cost of Outpatient Use of Axi-cel in 2L+ LBCL

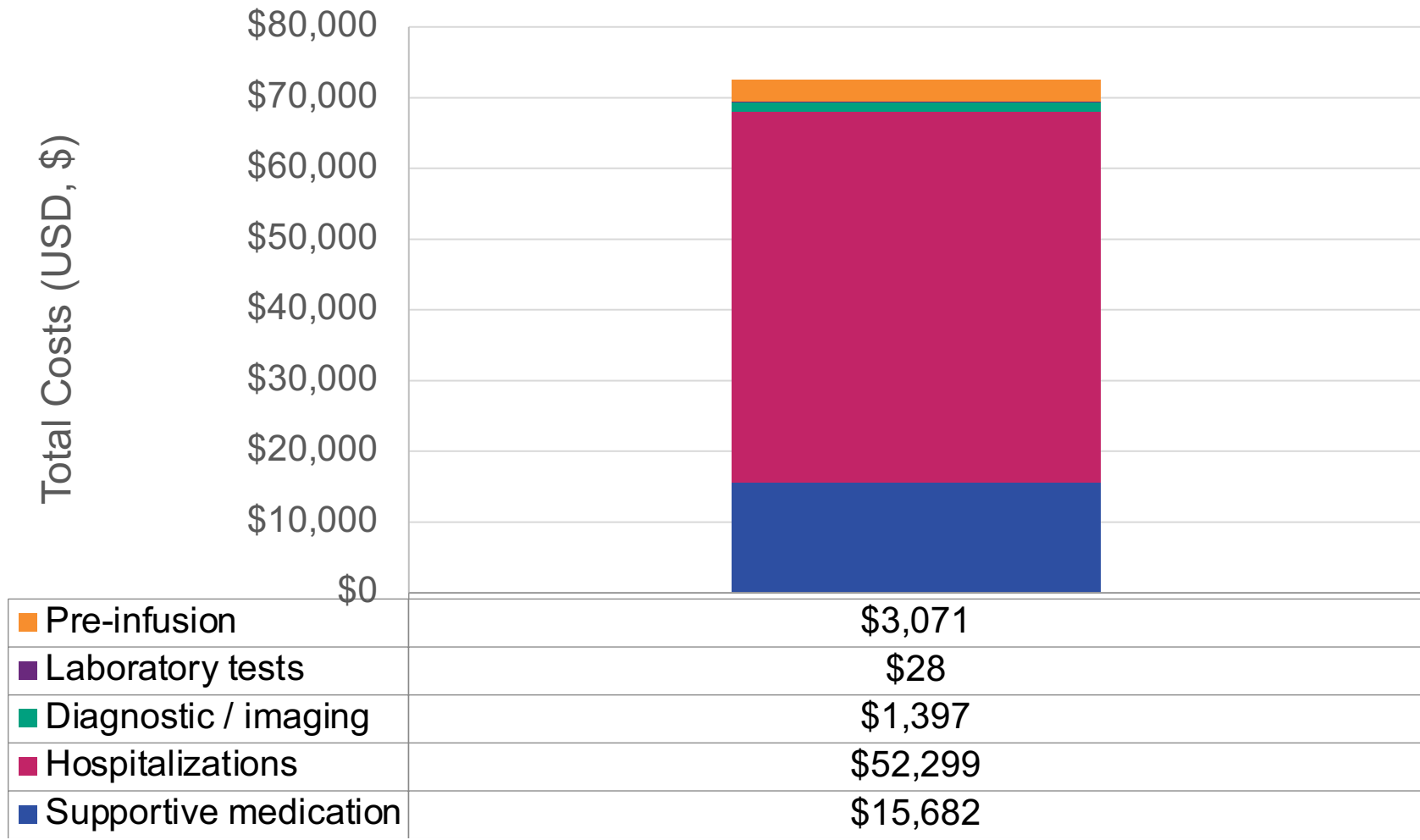
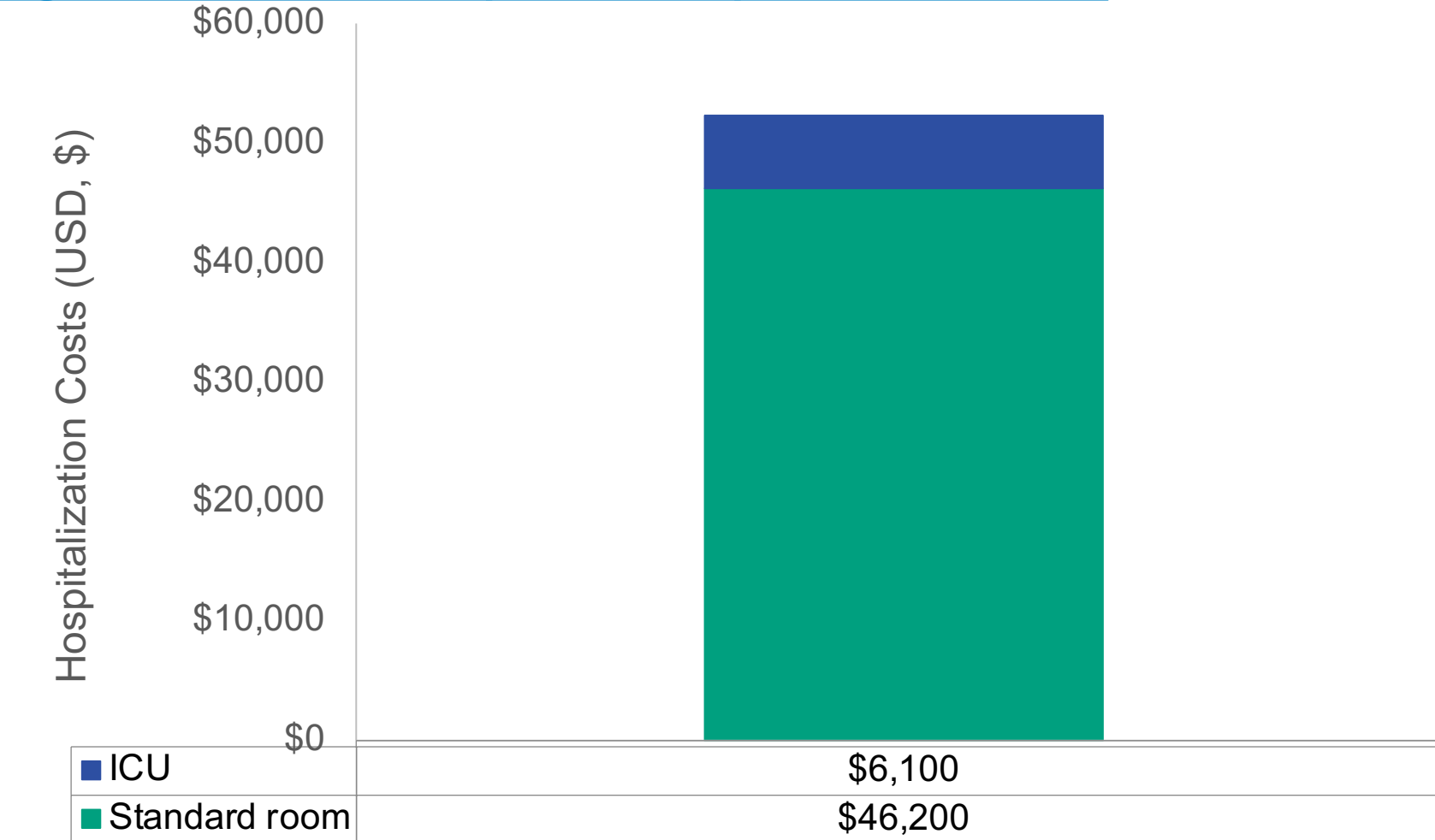


Figure 2. Total Mean Inpatient Hospitalization Costs



CONCLUSIONS

- A mean total cost of care of \$72,477 per patient was incurred for 2L+ LBCL patients treated with axi-cel in the outpatient setting, based on the ZUMA-24 study.
- The primary cost driver was hospitalizations (standard room and ICU days), which accounted for 72% of short-term costs (median follow-up: 7 months).
- For context, per-admission length of hospital stay admission was substantially shorter with outpatient axi-cel infusions than with inpatient infusions such as in the ZUMA-7 trial.[14]
- Out of 30 patients included in this study, grade 1 AEs were the reason 18 of 28 patients were hospitalized; Improved provider comfort with managing grade 1 AEs is likely to decrease hospitalization rates in the future.
- Using ZUMA-24 HCRU data this costing analysis reports manageable short-term costs with axi-cel administered in the outpatient setting for 2L+ LBCL patients.

LIMITATIONS

- Emergency room visits and remote monitoring costs were not considered in the analysis.
- This cost analysis utilized a short-term time horizon; longer-term costs can be considered upon availability of longer follow-up trial data.
- Presented analysis is US-based, further research is warranted ex-US.
- Most infusion-related AEs occur within the follow-up period examined here. However, research with longer follow-up may be warranted.

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