# Cost-Effectiveness of Axicabtagene Ciloleucel as Second-Line Therapy for Patients with Large B-Cell Lymphoma (LBCL) in the United States

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## INTRODUCTION

- ZUMA-7 (NCT03391466) is a global, randomized, phase 3 trial of axicabtagene ciloleucel (axi-cel), an autologous anti-CD19 CAR T therapy versus standard of care (SoC; salvage chemoimmunotherapy followed by high-dose therapy with auto-SCT for responders) in second-line large B-cell lymphoma (2L LBCL).[1]
- Axi-cel demonstrated a statistically significant and clinically meaningful improvement in event-free survival (HR 0.398 (95% CI, 0.308-0.514); P<0.0001), despite 56% of the SoC arm ultimately receiving subsequent CAR T therapy.[1]
- In order to inform healthcare decision making given the higher upfront cost, we conducted an economic evaluation of axi-cel versus SoC from a third-party United States (US) payer perspective in the 2L setting.

## METHODS

*Overview*

- A partitioned survival model divided patients into one of the three mutually exclusive health states: event-free (EF), post-event (PE) and death.
- Sub-states were used to model time on or off treatment to account for treatment related costs and adverse events:
  - In the EF state, patients were on-treatment with either 2L axi-cel or SoC.
  - Treatments in the PE state were based on the ZUMA-7 clinical trial.
- Outcomes include costs, life years (LYs) and quality-adjusted life years (QALYs) (discounted at 3.0% per year) and the incremental cost effectiveness ratio (ICER).

*Survival*

- Trial data were extrapolated based on statistical fit and clinical plausibility, using mixture cure modelling[2] where observed survival represents a blend of “statistically cured” and “non-cured” patients; this is assumed for both treatment arms given the precedent of long-term remission in the 2L LBCL setting.
- The model used a lifetime time horizon, with one month cycle lengths. Mean age of patients was based on all those enrolled in ZUMA-7 at 57.2 years.[1]

*Costs*

- Costs were inclusive of treatment-related, administration, disease management, and AE costs and are reported in 2021 US dollars. It was assumed that no LBCL-related resource use was incurred for those patients who remained event free after 5 years.

*Health outcomes*

- Utility inputs were sourced from literature and stratified by treatment and health state status. For patients surviving for at least five years, utility values were age- and gender-matched to the general population.
- No disutility values were applied to the model, as the potential influence of adverse events and other interventions were assumed to be captured by the on-treatment utility values.

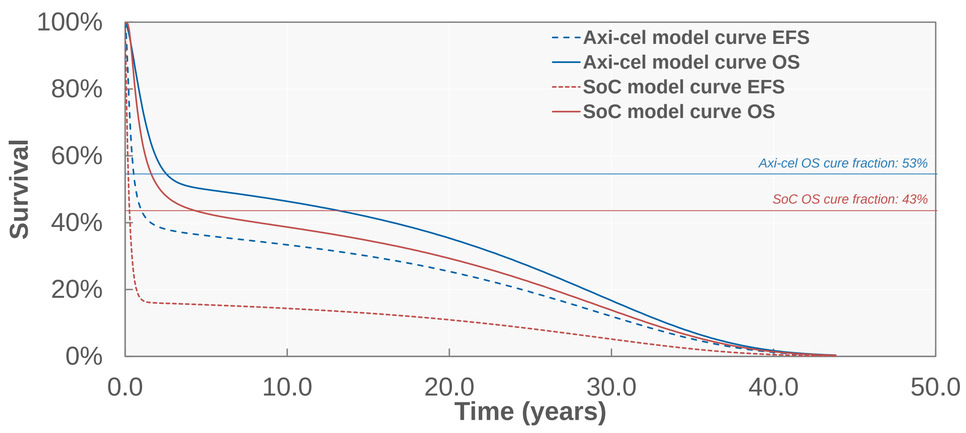
*Budget impact modelling*

- The budget impact was based on the difference of a future practice including CAR T therapy in the 2L versus the current practice without and included the cost of 2L treatments, AEs in the 2L as well as third-line (3L) treatments.
- It was estimated that 54/1,000,000 patients had LBCL[3], of these 15% had primary refractory and 25% had relapsed disease[4]; 70% relapsed within 12 months[5] and 50% were intended for auto-SCT[6].

## RESULTS

- Median OS was projected at 59 and 25 months for axi-cel and SoC, respectively (**Figure 1**).

**Figure 1. Modeled adjusted lifetime survival: OS and EFS**




## REFERENCES

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## RESULTS

- The average per patient incremental total costs were $111,303 higher with axi-cel; however, there were important cost offsets in subsequent therapy and disease management as compared to standard of care **(Table 1).**
  - Subsequent treatment costs represented ~60% of the total treatment-related costs for the SoC arm, of which a substantial amount was subsequent CAR T therapy costs.
  - The higher proportion of patients treated with axi-cel who remained event-free reduced disease management costs in the post-event health state, reducing the difference in cost between arms.

**Table 1. Mean incremental costs (discounted)**

| COSTS | AXI-CEL | SoC | △ |
|---|---|---|---|
| **TOTAL** | **$635,794** | **$524,491** | **$111,303** |
| **Total treatment** | **$546,786** | **$428,330** | **$118,374** |
| Second-line treatment-related | $449,786 | $95,319 | $354,467 |
| Subsequent treatment-related | $96,917 | $333,011 | -$236,093 |
| **Total disease management** | **$89,090** | **$96,161** | **-$7,071** |
| Event free | $49,769 | $23,195 | $26,575 |
| Post event | $21,751 | $40,010 | -$18,259 |
| Adverse Events | $3,432 | $18,047 | -$14,615 |
| Terminal care | $14,138 | $14,909 | -$771 |

- On average, each patient gained 1.37 QALYs with axi-cel vs. SoC; 74% of the QALYs gained for axi-cel were obtained in the event-free state.
- Over the lifetime time horizon, the incremental cost-effectiveness ratio (ICER) was estimated to be $81,369 per QALY gained for axi-cel vs. SoC, which is considered highly cost-effective in the US using a willingness to pay (WTP) threshold of $150,000/QALY **(Table 2**).

**Table 2. Cost-effectiveness results (discounted)**

| | AXI-CEL | SoC | △ |
|---|---|---|---|
| **LIFE YEARS** | **9.14** | **7.80** | **1.34** |
| **QALYs** | **7.08** | **5.71** | **1.37** |
| Event-free | 5.23 | 2.29 | 2.95 |
| Post-event | 1.84 | 3.42 | -1.58 |
| **TOTAL COSTS** | **$635,794** | **$524,491** | **$111,303** |
| **ICER, AXI-CEL vs. SoC** | | | **$81,369 / QALY** |

- One-way deterministic sensitivity analyses found that the ICER was most sensitive to subsequent treatment patterns in the SoC arm, the number of inpatient days for axi-cel administration and post-event utilities.
- Probabilistic sensitivity analysis found that, at a WTP threshold of $150,000 per QALY, axi-cel was cost-effective vs. SOC in 71% of the simulations.
- It was estimated that 9 patients in a million member plan would be eligible for axi-cel treatment as 2L LBCL patients. Lower and upper bound market share estimates led to a negligible cumulative budget impact per member per month (PMPM) **(Table 3).**

**Table 3. Budget impact results**

| | LOWER BOUND | | UPPER BOUND | |
|---|---|---|---|---|
| | Market share | PMPM | Market share | PMPM |
| **Year 1** | 2% | $0.001 | 6% | $0.004 |
| **Year 2** | 9% | $0.007 | 13% | $0.010 |
| **Year 3** | 12% | $0.009 | 16% | $0.013 |
| **Year 4** | 14% | $0.011 | 18% | $0.014 |
| **Year 5** | 16% | $0.013 | 20% | $0.016 |

## LIMITATIONS

- Cost of managing adverse events and related disutilities for subsequent treatments were not included in this economic analysis.
- As is common in economic analyses, mature OS data may result in different survival survival predictions. However, CAR T survival extrapolations have been validated in the 3L setting.

## CONCLUSION

- Findings from this study suggest a sizable improvement in quality and length of life for patients treated with axi-cel versus SoC.
- Cost offsets in subsequent CAR T use and reductions in disease progression led to a limited incremental cost difference resulting in a highly cost-effective ICER.
- This study suggests that axi-cel is a cost-effective treatment option that can address a critical unmet need while offering good value.