Poster 401

‘Don’t keep me waiting’: estimating the impact on lifetime survival and QALYs of reduced vein-to-vein time for LBCL patients treated with CAR T in the 3L+ setting

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INTRODUCTION

- Chimeric antigen receptor T-cell (CAR T) therapy production requires a multistep process which includes leukapheresis, manufacturing, transport and storage, and lastly infusion.[1]
- The time from leukapheresis to infusion is known as ‘vein-to-vein time’ (V2VT)[2], during which a patient’s condition may deteriorate, highlighting the potential importance of V2VT for patient outcomes.[3]
- This modelling study aims to isolate the impact of V2VT on potential lifetime outcomes for patients with relapsed/refractory large B-cell lymphoma (r/r LBCL) treated with CAR T therapy in the 3L+ setting, using the best available evidence.

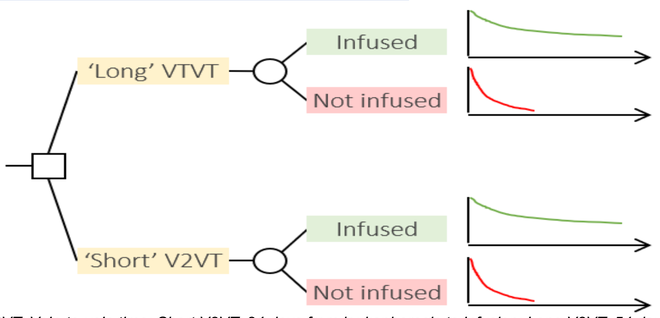
OBJECTIVES

- To compare the lifetime outcomes of a hypothetical cohort of patients receiving CAR T therapy for the treatment of r/r LBCL in the 3L+ setting, but with differing V2VTs.

METHODS

- A decision tree model with outcomes associated with a ‘long’ or ‘short’ V2VT was developed in MS Excel (**Figure 1**).
- Model outputs included Life Years (LYs) and Quality Adjusted Life Years (QALYs)

Figure 1. Simplified model schematic



V2VT: Vein-to-vein time; Short V2VT: 24 days from leukapheresis to infusion; Long V2VT: 54 days from leukapheresis to infusion. Square nodes represent decision gates. Circular nodes represent probability nodes. The graphs to the right of the diagram represented modelled lifetime outcomes based on published data.

- In the absence of a single source of data, the model was informed by a variety of published literature including clinical studies of CAR T therapies that reported data on time from leukaphereses to infusion and % of leukapheresed patients who were successfully infused, as well as studies that investigated the relationship between survival and V2VT, and differences in survival for infused vs non-infused patients (**Table 1**).[4-10]

Table 1. Data inputs used in model

Input	Source
Definition of ‘long’ or ‘short’ V2VT	Median V2VT reported from pivotal CAR T trials in 3L+ LBCL setting: ZUMA-1 (24 days)[4], JULIET (54 days)[5] , and TRANSCEND-NHL (37 days).[6]
Probability of infusion	Linear regression model based on proportion infused and median V2VT from published trials.[4-6]
Lifetime outcomes – non-infused patients	Mixture cure modelling using survival data from real-world evidence for base-case analysis and sensitivity analysis.[7-8]
Lifetime outcomes – infused patients	Mixture cure modelling using survival data from real-world evidence for base-case analysis[7] and sensitivity analysis.[8-9]
Efficacy of ‘long’ vs ‘short’ V2VT for infused patients	Hazard ratio (1.25) applied to the infused patient outcomes.[7]
Quality-adjusted life years (QALYs)	An average of utility weights (0.6845) for progression-free and progressed patients from NICE TA559[10]

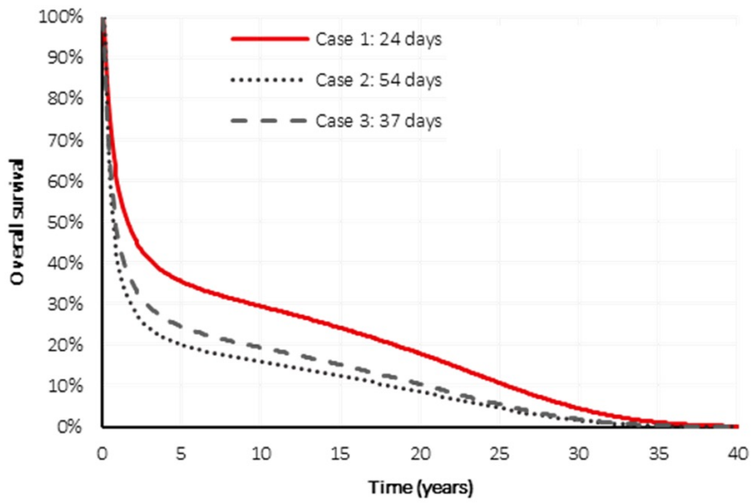
V2VT: Vein-to-vein time; HR: Hazard ratio. QALYs: Quality-adjusted life years

- In order to isolate the effect of V2VT on survival, efficacy outcomes were assumed to be equivalent across the different CAR T therapies and efficacy data for axi-cel were applied in the model due to the limited availability of relevant published data to inform model inputs.
- A range of sensitivity analyses were conducted in order to test the robustness of the results.
- Finally, the per-patient results were scaled using an epidemiology model to estimate the population outcomes if all LBCL 3L+ CAR T eligible patients in the US had a reduced V2VT. Epidemiology estimates were taken from NICE resource impact report[11] but modified for the US population.[12]

RESULTS

- Survival projections were modelled for the three hypothetical patient cohorts with different V2VTs (**Figure 2**).
- An estimated 2,700 3L+ LBCL patients were assumed to be eligible for CAR T in the US.[12]

Figure 2. Modelled survival outputs with differing V2VT times



- Median overall survival for the three hypothetical patient cohorts were 19.5 months, 8.5 months and 10.5 months for case 1, 2, and 3 respectively.
- Reducing V2VT from 54 to 24 days led to a 3-year gain in life expectancy (4.2 vs 7.7 additional LYs), and an additional 2 QALYs (2.9 vs 5.3) per patient (**Table 2**).
- A smaller reduction in V2VT (37 to 24 days) produced 2.6 additional LYs, or 1.8 additional QALYs (not shown).

Table 2. Base case per patient and population level results

	Total per-patient outcomes		Incremental per patient outcomes		Incremental US population outcomes	
	LYs	QALYs	LYs	QALYs	LYs	QALYs
‘Short’ V2VT: 24 days	7.68	5.26	-	-	-	-
‘Long’ V2VT: 54 days	4.24	2.90	**3.44**	**2.36**	9,328	6,385

V2VT: Vein-to-vein time; Short V2VT: 24 days from leukapheresis to infusion; Long V2VT: 54 days from leukapheresis to infusion. LYs: Life years; QALYs: Quality-adjusted life years; US: United States.

- Extensive sensitivity analyses were performed and all analyses showed that a shorter V2VT time led to an improvement in outcomes (**Table 3**).
- The sensitivity analyses demonstrates that outcomes are largely driven by the post-infusion outcomes as a function of V2VT, and the probability of infusion as a function of V2VT parameters.

Table 3. Sensitivity analyses incremental results on LYs

Scenario number and description		LYs: Per-patient	LYs: US population
Base case results		**3.44**	**9,328**
1	Probability of infusion not affected by V2VT	1.98	5,375
2	Post-infusion survival not affected by V2VT[9]	0.94	2,537
3	Switch non-infused survival source[8]	3.43	9,305
4	Switch HR cut-offs (to <28 vs ≥28 to <40 vs ≥40)	3.71	10,050
5	Change ‘long’ V2VT to ‘short’ V2VT[4-5]	2.60	7,040
6	Change ‘short’ V2VT to 30 days	3.02	8,174

V2VT: Vein-to-vein time; HR: Hazard ratio; Short V2VT: 24 days from leukapheresis to infusion; Long V2VT: 54 days from leukapheresis to infusion. LYs: Life years; US: United States.

DISCLOSURES

SV, MR, HS, and ZH: Employment or leadership position - Kite, A Gilead company; Stock ownership - Kite, A Gilead company. **AB, MEJ, WS**: Employment or Leadership position: Delta Hat Limited; Research funding: Delta Hat Limited has received funds from for-profit healthcare companies for research. **RM, MP, GC**: Consultant, research funding, or advisory role for Kite/Gilead.

DISCUSSION

- In the real-world setting, there are multiple factors that can impact V2VT for patients receiving CAR T, and delays during this multi-step process may impact patient outcomes.
- Our study synthesizes publicly available real-world data to demonstrate a potential difference in survival outcomes based on V2VT.
- Our modelling demonstrated that outcomes were primarily determined by a higher probability of reaching infusion and, subsequently, improved outcomes were demonstrated for infused patients compared with those not infused. Outcomes were improved across a range of tested sensitivity analyses.

Strengths:

- The first study to estimate a formal relationship between V2VT and infusion success using regression model.
- Incorporation of current real-world evidence for infused and non-infused outcomes.
- A modular, relatively simple and transparent model design which serves as a foundation from which further work can be conducted when additional data may become available.

Limitations:

- Due the lack of available evidence, the model is reliant on range of sources with limited granularity. Thus, we are unable to fully interrogate the relationship between V2VT and survival, while removing potential confounders. Availability of rich real-world patient data with long-term follow-up data is needed to robustly estimate the relationship between V2VT and long-term survival.
- As a result, and as is common in modelling studies, a number of key assumptions were made, including: generalisation of the HR[7]; impact of bridging; and assuming no difference in efficacy across therapies. However, we performed a range of sensitivity analyses to test the potential impact of these assumptions.
- Data from older studies reflect the reality of outcomes for patients treated when these studies were conducted[4-6]. Since our analysis is reliant on available published evidence it may not be entirely reflective of contemporary outcomes, for example we did not formally interrogate the impact of bridging on outcomes. This provides opportunity for additional research.
- In the absence of direct, comparative evidence, our analysis is limited to outcomes based on patients treated with axi-cel.[7] Further differences due to varying levels of efficacy across different CAR T-cell therapies might be expected, however due to data limitations we were not able to make this comparison.

CONCLUSIONS

- Our modelling study suggests that V2VT may be an important predictor of outcomes in R/R LBCL.
- Further, our findings suggest better outcomes associated with a shorter V2VT highlights that timely and effective CAR T manufacturing may be important for optimizing patient outcomes.
- Efforts to shorten all steps in the process from leukapheresis to infusion may be key to further improve outcomes for patients treated with CAR T therapies.
- While data in this area is sparse, we hope our study may prompt further data collection and reporting for V2VT in general, including proxy measures for patients who are not infused. This would allow for specific investigations to be undertaken, including the reasons why V2VT can vary across individuals, regions, and the impact of bridging strategies on patient outcomes.

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