Increasing CAR T delivery capacity in certified healthcare facilities: An impact assessment of shifting resources from ASCT to CAR T in second-line treatment of diffuse large B-cell lymphoma

M SHAFEY[1], A DAVIES[2], I BALTADAKIS[3], A BARBER[4], E CHURCH[4], A LAWS[4], B DOBLE[5]

[1] Department of Medicine, University of Calgary, Calgary, AB, Canada. [2] Southampton NCRI/CR UK Experimental Cancer Medicines Centre, Southampton, UK. [3] Hematology-Lymphoma Department and BMT Unit, Evangelismos Hospital, Athens, Greece. [4] Lumanity, London, UK. [5] Kite, a Gilead Company, Santa Monica, CA, US.

Introduction

The use of chimeric antigen receptor T-cell therapy (CAR T) in second-line (2L) treatment of diffuse large B-cell lymphoma (DLBCL) is now considered standard of care, but CAR T certified healthcare facilities (CHCFs) often face capacity constraints due to competing priorities for resource allocation, making it challenging to invest in additional resources to increase centre capacity. The CAR T treatment pathway for DLBCL may require less inpatient and nursing time compared with the autologous stem cell transplant (ASCT) pathway.[1] Previous research has shown that CAR T treatment requires approximately 30% less staff time than ASCT, primarily due to fewer chemotherapy cycles, reduced outpatient visits and shorter hospital stays, with the treatment interaction time being roughly 37% shorter (30 versus 48 days).[1]

There may be additional resource offsets associated with increased 2L CAR T treatment due to reduced need and availability of subsequent therapies.[2] Patients treated with 2L CAR T are less likely to require subsequent therapies both because they are more likely to complete their 2L treatment pathway and, following 2L treatment, a higher proportion remain event-free. The largest and longest Phase III randomized control trial comparing CAR T with salvage chemotherapy +/- high dose therapy + ASCT in 2L DLBCL highlights this point, where 94% of patients in the CAR T arm completed treatment compared to only 36% in the comparator arm.[2] More than twice as many patients in the CAR T arm remained event-free at 2 years compared with the comparator arm (41% versus 16%).[3] Finally, for those patients that do require subsequent therapies, 57% of patients in the comparator arm received subsequent cellular therapy, showing that many patients who are referred for ASCT may later also require CAR T therapy in a third-line setting. [4,5]

Operations research can identify the potential impact of altering the case mix of ASCT and CAR T in 2L DLBCL on centre capacity, in terms of number of patients treatable in a year, and clinical benefits. It can also highlight the potential for investment in additional resources to expand capacity.

Objectives

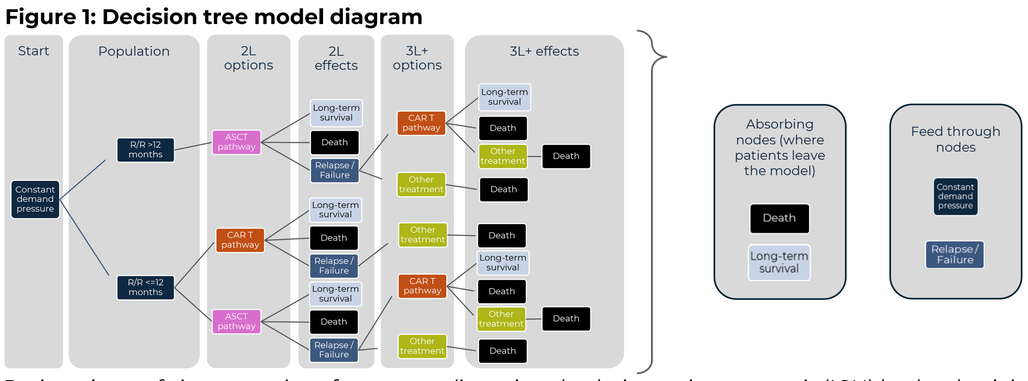
- Estimate the operational impact of shifting the case mix of patients with relapsed/refractory (R/R) DLBCL within 12 months after first-line therapy from a 2L ASCT pathway towards a 2L CAR T pathway.
- Assess the possible impact of investing in resources to increase CAR T treatment capacity.
- Evaluate the potential clinical benefits at the CHCF level of increasing capacity and shifting patients towards the CAR T pathway in 2L DLBCL.

Methods

Model Structure

A Microsoft Excel®-based decision tree model was developed to represent the patient trajectory in R/R DLBCL from the initiation of 2L therapy until either death or long-term survival following 2L or third-line (3L) treatment (Figure 1). The model assumes a constant demand pressure for the CHCF capacity.

Figure 1: Decision tree model diagram



Patients' use of six categories of resources (inpatient beds, intensive care unit (ICU) beds, physician time, nurse time, infusion chairs and functional services) are accumulated at each node. Functional services are defined as physical therapy, onco-psychological support, case management, dietary assistance, social work and technical assistance. Based on the 2L case mix of the centre and resources associated with each node, different amounts of each resource type are required to treat patients in the centre. Life years are accumulated in each node based on the average length of the pathway and an average general population life expectancy of 80 years.

Key Model Inputs

Resource use in the model is based on literature sources, with clinical inputs taken from relevant clinical trials or National Institute of Health and Care Excellence submissions (Table 1).

Table 1: Resource use per pathway

Resource type	ASCT pathway resources	CAR T pathway resources	Percentage change	Source
Inpatient bed days	10.8	7.1	**-34%**	Ring et al. (2022)[1]
ICU bed days	0.2	1.3	**733%**	Locke et al. (2021)[6]
Physician time (hours)	47.6	49.8	**5%**	Ring et al. (2022)[1]
Nurse time (hours)	299.9	191.9	**-36%**	Ring et al. (2022)[1]
Functional services (hours)	40.0	36.0	**-10%**	Ring et al. (2022)[1]
Infusion chair days	1.5	0.8	**-44%**	Lei et al. (2024)[7]

The model assumes the starting resources available for each of the resource categories is indicative of a hypothetical, medium-sized CHCF within a publicly funded healthcare system responsible for delivering the entirety of the CAR T and the ASCT pathways, from patient eligibility screening to hospital discharge. The centre is assumed to have the resources required to deliver 2L therapy to approximately 100 eligible patients.

Table 2: Centre resources available for the treatment of patients with 2L DLBCL, including 3L+ treatment

Resource type	Available centre resource
Inpatient bed days	3
ICU bed days	1
Physician time (hours)	3
Nurse time (hours)	13
Functional services (hours)	3
Infusion chair days	1

Analyses

All else equal, modifying the case mix alone changes the resource requirements in the CHCF, affecting the maximum possible patient throughput with the current resources available. Increasing investment in the constraining resource can further increase centre throughput. Three scenarios of varying 2L treatment case mix were explored:

- Scenario A: a new CHCF moving from 5% to 25% 2L CAR T.
- Scenario B: a maturing CHCF moving from 20% to 60% 2L CAR T.
- Scenario C: an established CHCF moving from 60% to 90% 2L CAR T.

At each starting case mix, the maximum patient throughput was calculated. Released resources were found by calculating the resource utilization in the new case mix while treating the same number of patients as the old case mix, and subsequently comparing this to the current centre setup. The maximum patient throughput with the new case mix was also calculated. After identifying the maximum treatable patients at the new case mix, one unit (bed, chair or full-time equivalent [FTE]) of the constraining resource was added to explore the impact on patient throughput of investing in additional resources. The maximum number of patients treated after changing the case mix, and investing in new resources, was subsequently combined with average expected life years for patients in each pathway to calculate the number of life years associated with the CHCF treatment mix.

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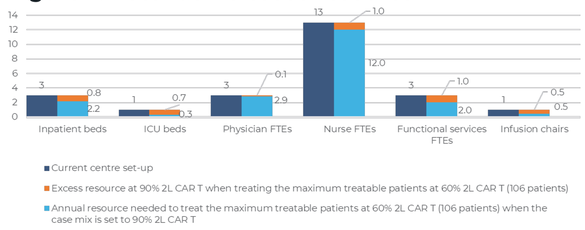
Results

Resources Released

When the 2L case mix is increased from 60% to 90% 2L CAR T in the eligible population, capacity is constrained by physician time, but all resource types have some degree of underutilization (Figure 2). With no change in centre capacity, the CHCF could reallocate 0.7 ICU beds, 0.5 infusion chairs, one nurse FTE and one functional services FTE.

Figure 2: Potential released resource



Centre Capacity With New Case Mix

Allowing these released resources to be utilized can increase centre capacity. Table 3 presents the maximum treatable patients in the centre at each modelled case mix. In all scenarios, the maximum 2L DLBCL patients treated in the CHCF increases with a shift to greater CAR T utilization. The greatest impact is in the maturing centre, which has the greatest shift in case mix moving from 20% to 60% CAR T.

Table 3: Maximum treatable patients changing only the centre case mix

Maximum treatable patients	Scenario A (5% -> 25%)	Scenario B (20% -> 60%)	Scenario C (60% -> 90%)
Before	93	96	106
After	97	106	110
Percentage change	4.6%	10.0%	4.3%

Investment in Resources

The impact of investing in one unit of the constraining resource, after changing the case mix, on the maximum number of treatable patients was evaluated for each scenario (Table 4).

In Scenario A, at 25% 2L CAR T, the addition of one full-time nurse increased capacity by 5.0% from 97 to 102. For Scenario B, at 60% 2L CAR T, adding one full-time nurse had minimal impact, with the number of treatable patients only increasing from 106 to 107, representing a 0.6% change.

In Scenario C, the addition of one full-time physician increased the number of treatable patients from 110 to 114, a 3.7% increase. These results highlight the varying impacts of resource investment on patient treatment capacity depending on the stage of CHCF development and the specific constraining resource which will be different for any specific centre.

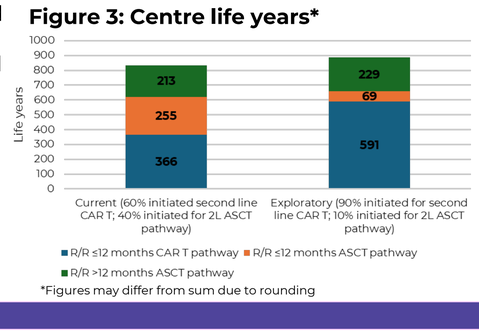
Table 4: Potential additional increased capacity from investment in centre resources

Maximum treatable patients	Scenario A (25%)	Scenario B (60%)	Scenario C (90%)
Resource category added	Nurse time (one full-time nurse)	Nurse time (one full-time nurse)	Physician time (one full-time physician)
Before	97	106	110
After	102	106	114
Percentage change	5.0%	0.6%	3.7%

Centre life years

Figure 3 shows the impact on life years expected in the centre, disaggregated by the patient's 2L treatment pathway in Scenario C with additional physician time available. By shifting the 2L case mix to 90% CAR T and making an investment in physician time, total centre life years increase from 835* to 889 years.

Figure 3: Centre life years*



*Figures may differ from sum due to rounding

Conclusions

Increasing the proportion of patients receiving 2L CAR T therapy within CHCFs leads to several important benefits. Increasing 2L CAR T uptake led to resources being released across all categories without changing centre capacity. These can be used to increase R/R DLBCL patient throughput without requiring additional investment in new resources.

In all scenarios explored, increasing the proportion of R/R DLBCL patients receiving 2L CAR T therapy increased the number of patients treatable in the CHCF. This increase in capacity was observed even when the centre was not optimally set up to deliver the new case mix. The greatest impact was seen in the maturing centre moving from 20% to 60% 2L CAR T, highlighting the potential for capacity expansion with strategic case mix adjustments and use of released resources.

Capacity can be substantially increased by investing in additional resources. The results show that an investment of one unit of the constraining resource category can lead to capacity increases. For example, adding one full-time nurse in Scenario A increased capacity by 5.0%, while adding one full-time physician in Scenario C increased capacity by 3.7%. These investments also led to an increase in expected life years for patients treated by the centre, with total life years increasing from 835 to 889 years when the 2L case mix is shifted to 90% CAR T and additional physician time is made available.

While these findings are based on specific scenarios and assumptions, they indicate that similar benefits could be realized in other centres. The potential for increased capacity, reduced patient burden and enhanced clinical outcomes underscores the value of considering both case mix adjustments and resource investments in CHCFs. These indicative results suggest that CHCFs could achieve important benefits by adopting similar strategies, ultimately improving the efficiency and effectiveness of 2L DLBCL treatment.

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Contact Information

Brett Doble, Director HEOR, Australia, Canada and Europe (ACE)
Kite, a Gilead Company
brett.doble@gilead.com