NDRS
NATIONAL DISEASE REGISTRATION SERVICE

NHS England

# Tisagenlecleucel for treating relapsed/refractory diffuse large B-cell lymphoma – data review

# About the NDRS

The National Disease Registration Service (NDRS) is part of NHS England. Its purpose is to collect, collate and analyse data on patients with cancer, congenital anomalies, and rare diseases. It provides robust surveillance to monitor and detect changes in health and disease in the population. NDRS is a vital resource that helps researchers, healthcare professionals and policy makers make decisions about NHS services and the treatments people receive.

The NDRS includes:

- the National Cancer Registration and Analysis Service (NCRAS) and
- the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS)

Healthcare professionals, researchers and policy makers use data to better understand population health and disease. The data is provided by patients and collected by the NHS as part of their care and support. The NDRS uses the data to help:

- understand cancer, rare diseases, and congenital anomalies
- improve diagnosis
- plan NHS services
- improve treatment
- evaluate policy
- improve genetic counselling

NDRS
NATIONAL DISEASE REGISTRATION SERVICE

National Disease Registration Service
The Leeds Government Hub
7&8 Wellington Place
Leeds
LS1 4AP

For queries relating to this document, please contact:
NDRSenquiries@nhs.net

NHS England

# Contents

# 1. Executive summary

## Introduction

The National Institute for Health and Care Excellence (NICE) appraised the clinical and cost effectiveness of tisagenlecleucel for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL) and transformed follicular lymphoma (TFL). The appraisal committee highlighted clinical uncertainty around estimates of overall survival (OS) in the evidence submission. As a result, they recommended the commissioning of tisagenlecleucel through the Cancer Drugs Fund (CDF) to allow a period of managed access, supported by additional data collection to answer the clinical uncertainty.

NHS England have evaluated the real-world treatment effectiveness of tisagenlecleucel in the CDF population, during the managed access period. This report presents the results of the use of tisagenlecleucel in clinical practice in England, using the routinely collected Systemic Anti-Cancer Therapy (SACT) dataset.

This report, and the data presented, demonstrate the potential within the English health system to collect real-world data to inform decision-making about patient access to cancer treatments via the CDF. The opportunity to collect real-world data enables patients to access promising new treatments much earlier than might otherwise be the case, whilst further evidence is collected to address clinical uncertainty.

The collection and follow up of real-world SACT data for patients treated through the CDF in England has resulted in analysis being carried out on 100% of patients and 99% of patient outcomes reported in the SACT dataset. NHS England are committed to providing world first, high-quality real-world data on CDF cancer treatments to be appraised alongside the outcome data from the relevant clinical trials.

## Methods

The NHS England Blueteq® system was used to provide a reference list of all patients with an application for tisagenlecleucel for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL) and transformed follicular lymphoma (TFL) in the CDF. Patient NHS numbers were used to link Blueteq applications to NDRS' routinely collected SACT data to provide SACT treatment history.

Between 1 February 2019 and 30 November 2022, 133 applications for tisagenlecleucel were identified in the Blueteq system. Following appropriate exclusions (see Figures 1 and 2), 124 unique patients who received treatment were included in these analyses. All patients were traced to obtain their vital status using the personal demographics service (PDS)[1].

# Results

124/124 (100%) unique patients with CDF applications were reported in the SACT dataset and were included in the final cohort.

At data cut off, outcomes were expected for all 124 patients, having all been identified as receiving the single infusion. Of the 124 patients, 123 had an outcome as completed as prescribed in the SACT dataset.

The median OS was 14.8 months [95% CI: 10.0, 21.8]. OS at 6 months was 72% [95% CI: 63%, 79%], 12 months OS was 52% [95% CI: 43%, 61%], OS at 18 months was 45% [95% CI: 36%, 54%], OS at 24 months was 37% [95% CI: 28%, 46%], OS at 36 months was 29% [95% CI: 20%, 39%].

An analysis on the use of intravenous immunoglobulin (IVIG) use was carried out, results showed that 15% of patients who received tisagenlecleucel also received IVIG treatment.

An OS sensitivity analysis was conducted for a cohort with at least 6 months' data follow-up in the SACT dataset. Results were consistent with the full analysis cohort.

# Conclusion

This report analysed SACT real-world data for patients treated with tisagenlecleucel for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL) and transformed follicular lymphoma (TFL) in the CDF. It evaluates OS and treatment outcomes for all patients treated with tisagenlecleucel for this indication.

# Introduction

Diffuse large B-cell lymphoma (DLBCL) and transformed follicular lymphoma (TFL) (ICD-10: C83.3 and C82.9) accounts for 2% of all cancer diagnoses in England. In 2020, 4,729 patients were diagnosed with either DLBCL or TFL (males 2,646, females 2,083)[2].

- tisagenlecleucel therapy is recommended for use within the Cancer Drugs Fund as an option for treating relapsed or refractory diffuse large B-cell lymphoma in adults after 2 or more systemic therapies, only if the conditions in the managed access agreement are followed[3].

# 2. Background to this report

## Using routinely collected data to support effective patient care

High quality and timely cancer data underpin NHS England's ambitions of monitoring cancer care and outcomes across the patient pathway. NHS England produces routine outcome reports on patients receiving treatments funded through the Cancer Drugs Fund (CDF) during a period of managed access using Systemic Anti-Cancer Therapy (SACT) data collected by the National Disease Registration Service (NDRS).

The CDF is a source of funding for cancer drugs in England[4]. From 29 July 2016 NHS England implemented a new approach to the appraisal of drugs funded by the CDF. The new CDF operates as a managed access scheme that provides patients with earlier access to new and promising treatments where there is uncertainty as to their clinical effectiveness. During this period of managed access, ongoing data collection is used to answer the clinical uncertainties raised by the NICE committee and inform drug reappraisal at the end of the CDF funding period[5].

NHS England analyse data derived from patient-level information collected in the NHS, as part of the care and support of cancer patients. The data is collated, maintained, quality-assured and analysed by the NDRS.

# NICE Appraisal Committee review of tisagenlecleuel for treating relapsed or refractory DLBC after 2 or more systemic therapies [TA567]

The NICE Appraisal Committee reviewed the clinical and cost effectiveness of the tisagenlecleucel infusion (Novartis Pharmaceuticals Ltd) in the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL) and transformed follicular lymphoma (TFL) [TA567] and published guidance for this indication in March 2019[6].

Due to the clinical uncertainties identified by the committee and outlined below, the committee recommended the commissioning of tisagenlecleucel for the treatment of relapsed/refractory DLBCL and TFL through the CDF for a period of 48 months, from February 2019 to February 2023. The drug will be funded through the CDF until NICE publish their final guidance.

During the CDF funding period, results from an ongoing clinical trial (JULIET[7]) evaluating tisagenlecleucel in the licensed indication is likely to answer the main clinical uncertainties raised by the NICE committee. Data collected from the JULIET clinical trial is the primary source of data collection.

Analysis of the SACT dataset provides information on real-world treatment patterns and outcomes for tisagenlecleucel for the treatment of DLBCL and TFL in England, during the CDF funding period. This acts as a secondary source of information alongside the results of the JULIET clinical trial[7].

The committee identified the key areas of uncertainty below for re-appraisal at the end of the CDF data collection;

- overall survival from the infusion of tisagenlecleucel
- the proportion of people who would need treatment for B-cell aplasia with intravenous immunoglobulin, and the duration of this treatment.

# Approach

Upon entry to the CDF, representatives from NHS England, NICE and the company (Novartis Pharmaceuticals Ltd) formed a working group to agree the Data Collection Agreement (DCA)[6]. The DCA sets out the real-world data to be collected and analysed to support the NICE re-appraisal of tisagenlecleucel. It also detailed the eligibility criteria for patient access to tisagenlecleucel through the CDF, and CDF entry and exit dates.

This report includes patients with approved CDF applications for tisagenlecleucel, approved through Blueteq® and followed up in the SACT dataset collected by NDRS in NHS England.

# 3. Methods

## CDF applications – identification of the cohort of interest

NHS England collects applications for CDF treatments through their online prior approval system (Blueteq®). The Blueteq application form captures essential baseline demographic and clinical characteristics of patients needed for CDF evaluation purposes. Where appropriate, Blueteq data are included in this report.

Consultants must complete a Blueteq application form for every patient receiving a CDF funded treatment. As part of the application form, consultants must confirm that a patient satisfies all clinical eligibility criteria to commence treatment. NDRS has access to the Blueteq database and key data items such as NHS number, primary diagnosis and drug information of all patients with an approved CDF application (which therefore met the treatment eligibility criteria).

The lawfulness of this processing is covered under Article 6(1)(e) of the United Kingdom (UK) General Data Protection Regulations (GDPR) (processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller). NHS England, through the National Disease Registration Service (NDRS), does have statutory authority to process confidential patient information (without prior patient consent) afforded through the National Disease Registries (NDRS) Directions 2021 issued to it by the Secretary of State for Health and Social Care, and has issued the NDRS Data Provision Notice under section 259 of the Health and Social Care Act 2012 regarding collection of the Blueteq data from NHS England.

NDRS in NHS England collates data on all SACT prescribed drugs by NHS organisations in England, irrespective of the funding mechanism. The Blueteq extract is therefore essential to identify the cohort of patients whose treatment was funded by the CDF.

# Tisagenlecleucel clinical treatment criteria

- the application is made by and that leucapheresis for and treatment with tisagenlecleucel-modified CAR-T cells will be initiated by a consultant haematologist or medical oncologist specifically trained and accredited in the use of systemic anti-cancer therapy and working in an accredited CAR-T cell treatment centre and who is a member of the National CAR-T Clinical Panel for DLBCL and TFL and a member of the treating Trust's DLBCL and TFL and CAR T cell multidisciplinary teams
- the patient has a confirmed histological diagnosis of DLBCL or TFL to DLBCL that as been either made by or reviewed and confirmed by a designated lymphoma stem cell transplant centre.
- the patient's disease has been re-biopsied unless a biopsy is unsafe in which case the patient must have progressive disease at previously known sites of active disease. In such situations the original diagnostic biopsy review is acceptable.
- the patient fulfils one of the following clinical scenarios relating to the definition of relapsed or refractory lymphoma.
    - has DLBCL and received 2 or more lines of systemic therapy and relapsed after the last line of systemic therapy OR
    - has DLBCL and received 2 or more lines of systemic therapy and was refractory to the last line of systemic therapy OR
    - has TFL to DLBCL and received 2 or more lines of systemic therapy since diagnosis of transformation and relapsed after the last line of systemic therapy OR
    - has TFL to DLBCL and received 2 or more lines of systemic therapy since diagnosis of transformation and was refractory to the last line of systemic therapy OR
    - has TFL to DLBCL, received an anthracycline-containing regimen before transformation, and after transformation then received 1 or more lines of systemic therapy and relapsed after the last line of systemic therapy OR
    - has TFL to DLBCL, received an anthracycline-containing regimen before transformation, and after transformation then received 1 or more lines of systemic therapy and was refractory to the last line of systemic therapy.
- the patient has been previously treated with a full dose anthracycline-containing regimen for his/her lymphoma.
- the patient has been previously treated with at least one anti-CD20 monoclonal antibody unless there is clear documentation of the determination of CD20 negative disease.
- the patient has not had stem cell transplantation (SCT) or has had an autologous or allogeneic SCT.
- the patient has not previously been treated with an anti-CD19 antibody-drug conjugate or if previously treated with an anti-CD19 antibody-drug conjugate that a biopsy of the relapsed/refractory disease has been done and has been shown to be CD19 positive.
- the patient does not have primary CNS lymphoma.
- the patient does not have known active CNS involvement by the lymphoma.
- the patient is aged 18 years or older on the date of approval for tisagenlecleucel by the National CAR-T Clinical Panel.
- the patient has an ECOG performance score of 0 or 1 or 2.

- the patient has sufficient end organ function to tolerate treatment with CAR-T cell therapy.
- the patient has either had no previous therapy with any genetically modified autologous or allogeneic T cell immunotherapy or the patient has been treated with doses of genetically modified autologous or allogeneic T cell immunotherapy within an abandoned dosing cohort in a first in human dose-escalation phase I clinical trial.
- 2 doses of tocilizumab are available for use in this patient in the event of the development of cytokine release syndrome.
- tisagenlecleucel-modified CAR-T cell therapy will otherwise be used as set out in its Summary of Product Characteristics (SPC).

## CDF applications - de-duplication criteria

Before conducting any analysis on CDF treatments, the Blueteq data is examined to identify duplicate applications. The following de-duplication rules are applied:

1. If two trusts apply for the tisagenlecleucel infusion used to treat relapsed/refractory DLBCL and TFL for the same patient (identified using the patient's NHS number), and both applications have the same approval date, then the record where the CDF trust (the trust applying for CDF treatment) matches the SACT treating trust is selected.

2. If two trusts apply for the tisagenlecleucel infusion used to treat relapsed/refractory DLBCL and TFL for the same patient, and the application dates are different, then the record where the approval date in the CDF is closest to the regimen start date in SACT is selected, even if the CDF trust did not match the SACT treating trust.

3. If two applications are submitted for the tisagenlecleucel infusion used to treat relapsed/refractory DLBCL and TFL and the patient has no regimen start date in SACT capturing when the specific drug was delivered, then the earliest application in the CDF is selected.

# Initial CDF cohorts

The analysis cohort is limited to the date the tisagenlecleucel infusion entered the CDF for this indication, onwards. Any treatments delivered before the CDF entry date are excluded as they are likely to be patients receiving treatment via an Early Access to Medicines Scheme (EAMS) or a compassionate access scheme run by the company. These schemes may have different eligibility criteria compared to the clinical treatment criteria detailed in the CDF managed access agreement for this indication.

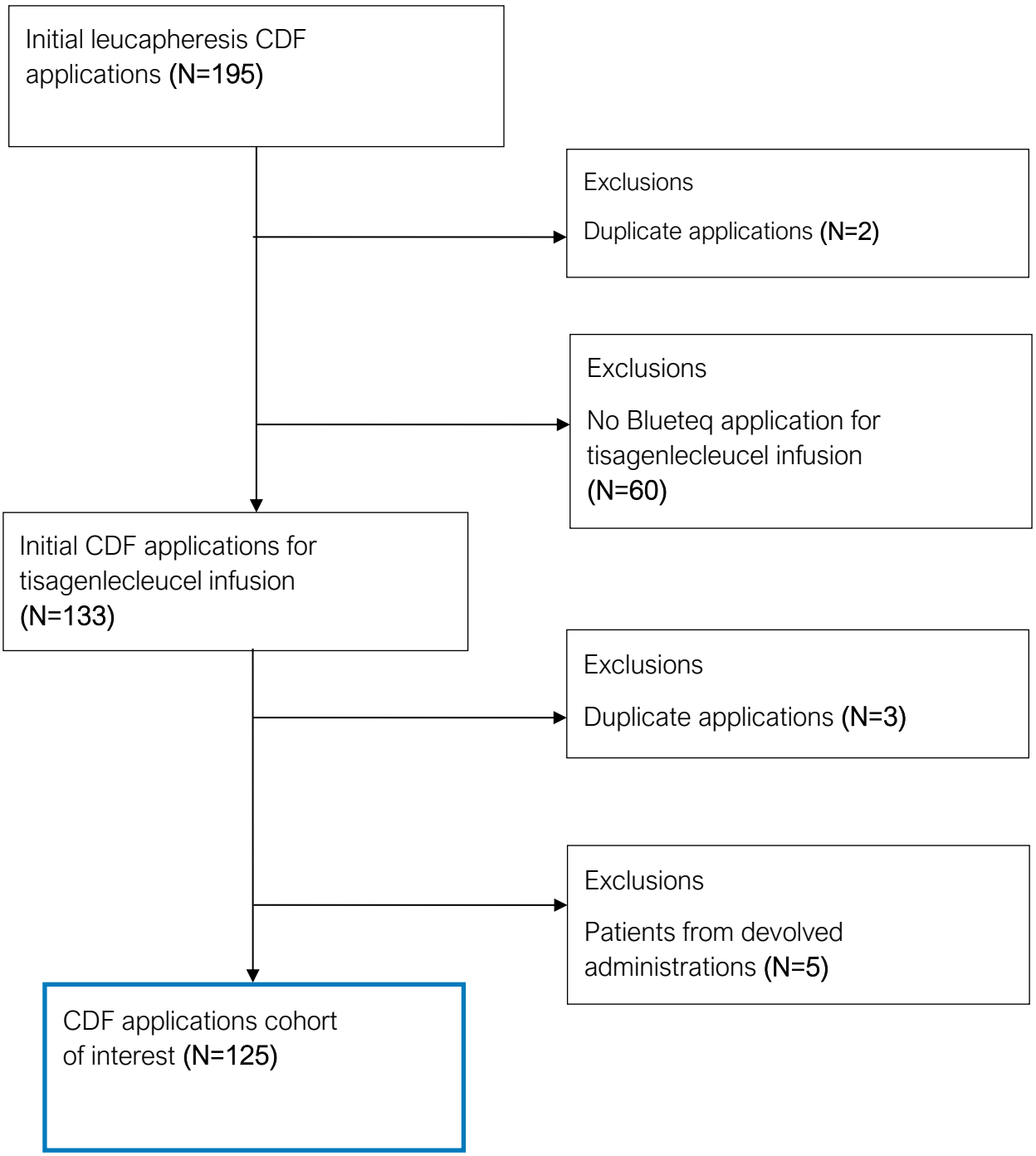
The CDF applications included in these analyses are from 1 February 2019 to 30 November 2022. A snapshot of SACT data was taken on 3 March 2023 and made available for analysis on 13 March 2023 and includes SACT activity up to 30 November 2022. Tracing the patients' vital status was carried out on 5 April 2023 using the Personal Demographics Service (PDS)[1].

Two CDF applications are required for tisagenlecleucel. The initial application is made at the point of leucapheresis and manufacture of the CAR-T cells, and a subsequent application is required at the point of infusion of the CAR-T cells. It was not possible to collect reasons why any subsequent infusion application was not made following a leucapheresis application.

There were 195 CDF funding applications for leucapheresis between 1 February 2019 and 30 November 2022, relating to 193 unique patients.

There were 133 applications for CDF funding for the tisagenlecleucel infusion, used to treat relapsed/refractory DLBCL and TFL between 1 February 2019 to 30 November 2022 in the NHS England Blueteq database. This relates to 125 unique patients after the exclusion of three duplicate application and five patients who were registered at GP practices in either Scotland, Wales, or Northern Ireland.

Figure 1: Derivation of the cohort of interest from all CDF (Blueteq) applications made for the tisagenlecleucel infusion for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL) and transformed follicular lymphoma (TFL) 1 February 2019 and 30 November 2022



# Linking CDF cohort to SACT

NHS numbers were used to link SACT records to CDF applications for tisagenlecleucel in the Blueteq system. Information on treatments in SACT were examined to ensure the correct SACT treatment records were matched to the CDF application; this includes information on treatment dates (regimen, cycle and administration dates) and primary diagnosis codes in SACT.

# Addressing clinical uncertainties

## Overall survival (OS)

OS is calculated from the CDF treatment start date, not the date of a patient's cancer diagnosis. Survival from the treatment start date is calculated using the patient's earliest treatment date[8] in the SACT dataset for the treatment of interest. Data items[9] used to determine a patient's earliest treatment date are:

- start date of regimen – SACT data item #22
- start date of cycle – SACT data item #27
- administration date – SACT data item #34

Additional explanation of these dates is provided below:

### Start date of regimen

A regimen defines the drugs used, their dosage and frequency of treatment. A regimen may contain many cycles. This date is generally only used if cycle or administration dates are missing.

### Start date of cycle

A cycle is a period of time over which treatment is delivered. A cycle may contain several administrations of treatment, after each treatment administration, separated by an appropriate time delay. For example; a patient may be on a 3-weekly cycle with treatment being administered on the 1st and 8th day, but nothing on days 2 to 7 and days 9 to 20. The 1st day would be recorded as the "start day of cycle". The patient's next cycle would start on the 21st day.

### Administration date

An administration is the date a patient is administered the treatment, which should coincide with when they receive treatment. Using the above example, the administrations for a single 3-week cycle would be on the 1st and 8th day. The next administration would be on the 21st day, which would be the start of their next cycle.

All patients in the cohort of interest are submitted to the PDS to check their vital status (dead or alive). Patients are traced before any analysis takes place. The date of tracing is used as the date of follow-up (censoring) for patients who have not died.

OS is calculated for each patient as the interval between the earliest treatment date where a specific drug was given to the date of death or date of follow-up (censoring).

OS (days) = Date of death (or follow up) - treatment start date

The patient is flagged as either:

Dead (event):

At the date of death recorded on the PDS.

Alive (censored):

At the date patients were traced for their vital status as patients are confirmed as alive on this date.

Lost to follow-up:

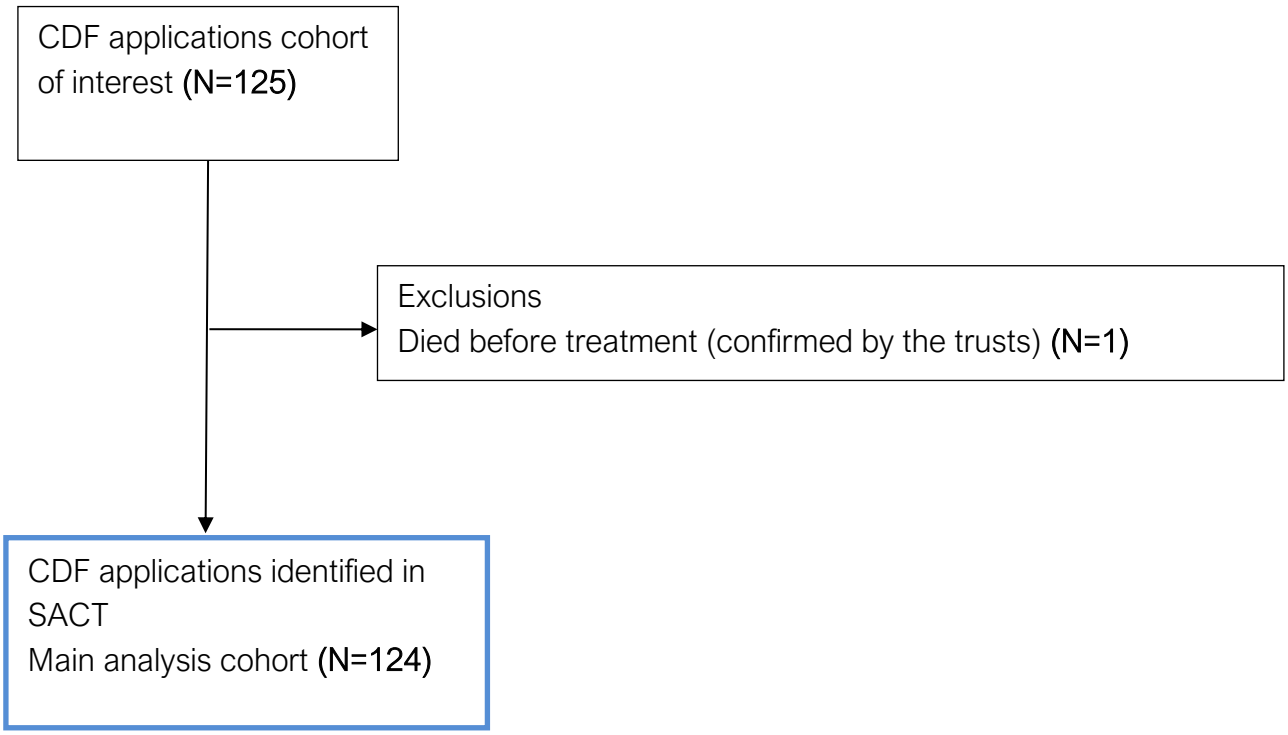
Where we cannot determine whether a patient is alive or not on the censor date; this happens when a patient cannot be successfully traced, for example, because they have emigrated or because important identifiers such as NHS number or date of birth contain errors, the patient's record will be censored at their last known treatment date in SACT. This is the date the patient was last known to be alive.

# 4. Results

## Cohort of interest

Of the 125 applications for CDF funding for the tisagenlecleucel infusion for the treatment of relapsed/refractory DLBCL and TFL, one patient died before treatment, all other patients were found in the SACT dataset[a] (see Figure 2).

**Figure 2: Matched cohort - SACT data to CDF (Blueteq®) applications for tisagenlecleucel infusion for the treatment of relapsed/refractory diffuse large B-cell lymphoma (DLBCL) and transformed follicular lymphoma (TFL) 1 February 2019 and 30 November 2022**




A maximum of 124 tisagenlecleucel infusion records are expected in SACT for patients who were alive, eligible and confirmed to have commenced treatment (Figure 2). 100% (124/124) of these applicants for CDF funding have a treatment record in SACT.

[a] The patient who died before treatment was confirmed by the relevant trust as a death before treatment by the SACT data liaison team.

# Completeness of SACT key variables

Table 1 presents the completeness of key data items required from SACT. Completeness is 100% for primary diagnosis, date of birth, gender, start date of regimen and start date of cycle. Administration is 99% complete and performance status at the start of regimen is 73% complete.

Table 1: Completeness of key SACT data items for the tisagenlecleucel infusion cohort (N=124)

| Variable | Completeness (%) |
|---|---|
| Primary diagnosis | 100% |
| Date of birth (used to calculate age) | 100% |
| Gender | 100% |
| Start date of regimen | 100% |
| Start date of cycle | 100% |
| Administration date | 99% |
| Performance status at start of regimen | 73% |

Table 2 presents the completeness of regimen outcome summary. A patient's outcome summary, detailing the reason why treatment was stopped, is only captured once a patient has completed their treatment for this indication. All 124 patients have received a single infusion of tisagenlecleucel and as such, a treatment completed as prescribed outcome is expected. Of the 124 patients that have received the single infusion, 123 have an outcome summary recorded in the SACT dataset 99% (123/124)[b].

Table 2: Completeness of outcome summary for patients that have ended treatment (N=124)

| Variable | Completeness (%) |
|---|---|
| Outcome summary of why treatment was stopped | 99% |

[b] All patients have received the tisagenlecleucel infusion, and as such should all have a treatment completed as prescribed outcome. 115 patients had an outcome of completed as prescribed, two patients had an outcome of patient choice for stopping treatment, five patients had an outcome of patient died and one patient had progressive disease.

# Completeness of Blueteq key variables

Table 3 presents the completeness of key data items required from Blueteq.

Table 3: Completeness of Blueteq key variables (N=124)

| Variable | Completeness (%) |
|---|---|
| Stem cell transplant | 100% |
| Confirmed histological diagnosis | 100% |
| Re-biopsied options | 100% |
| Relapsed or refractory and line of therapy | 96% |
| Bridging therapy | 100% |

# Patient characteristics

The median age of the 124 patients receiving the tisagenlecleucel infusion for treatment of relapsed/refractory DLBCL and TFL was 70 years. The median age in males and females was 69 and 70 years respectively.

Table 4: Patient characteristics (N=124)

| Patient characteristics[c] | | | |
|---|---|---|---|
| | | N | % |
| Gender | Male | 74 | 60% |
| | Female | 50 | 40% |
| Age | <40 | 2 | 2% |
| | 40 to 49 | 9 | 7% |
| | 50 to 59 | 13 | 10% |
| | 60 to 69 | 36 | 29% |
| | 70 to 79 | 59 | 48% |
| | 80+ | 5 | 4% |
| Performance status at the start of regimen | 0 | 24 | 19% |
| | 1 | 58 | 47% |
| | 2 | 8 | 6% |
| | 3 | 0 | 0% |
| | 4 | 0 | 0% |

[c] Figures may not sum to 100% due to rounding.

| Patient characteristics[c] | | | |
|---|---|---|---|
| | Missing | 34 | 27% |

# Blueteq data items

Table 5 shows the distribution of Blueteq data items.

Table 5: Distribution of key Blueteq data items (N=124)

| Blueteq data items[d] | | N | % |
|---|---|---|---|
| Stem cell transplant suitability | Has not had SCT | 112 | 80% |
| | Has had autologous SCT | 11 | 9% |
| | Has had allogeneic SCT | 1 | 9% |
| Confirmed histological diagnosis | Diffuse large B-cell lymphoma (DLBCL) | 92 | 74% |
| | Transformed follicular lymphoma (TFL) to DLBCL | 32 | 26% |
| Re-biopsied options | Re-biopsy has confirmed DLBCL | 72 | 58% |
| | Re-biopsy is unsafe, there is progressive disease at previously documented sites of active disease and previous histology was DLBCL | 32 | 26% |
| | Re-biopsy has confirmed transformed TFL to DLBCL | 20 | 16% |
| Relapsed or refractory and line of therapy | Has DLBCL and received 2 or more lines of systemic therapy and was refractory to the last line of systemic therapy | 57 | 46% |
| | Has DLBCL and received 2 or more lines of systemic therapy and relapsed after the last line of systemic therapy | 37 | 30% |
| | Has TFL to DLBCL and received 2 or more lines of systemic therapy since diagnosis of transformation and was refractory to the last line of systemic therapy | 16 | 13% |

[d] Figures may not add to 100% due to rounding.

| Blueteq data items | | N | % |
|---|---|---|---|
| | Has TFL to DLBCL and received 2 or more lines of systemic therapy since diagnosis of transformation and relapsed after the last line of systemic therapy | 6 | 5% |
| | has TFL to DLBCL, received an anthracycline-containing regimen before transformation, and after transformation then received 1 or more lines of systemic therapy and relapsed | 2 | 2% |
| | has TFL to DLBCL, received an anthracycline-containing regimen before transformation, and after transformation then received 1 or more lines of systemic therapy and was refractory | 1 | 1% |
| | Not captured | 5 | |
| Bridging therapy | Chemo(immuno)therapy only | 57 | 46% |
| | No bridging therapy at all | 15 | 12% |
| | Corticosteroids and chemo(immuno)therapy | 13 | 10% |
| | Chemo(immuno)therapy and radiotherapy ± corticosteroids | 11 | 9% |
| | Radiotherapy only | 11 | 9% |
| | Corticosteroids only | 10 | 8% |
| | Corticosteroids and radiotherapy | 7 | 6% |

# Treatment outcomes

Of the 124 patients with CDF applications, all have completed treatment after receiving a single infusion of tisagenlecleucel. 76 patients have since died (see Table 6).

**Table 6: Treatment outcomes for patients that received the tisagenlecleucel infusion for treating DLBCL and TFL (N=124)[e,f,g]**

| Treatment outcome | Frequency | Percentage |
|---|---|---|
| Completed treatment – received single infusion and are still alive | 48 | 39% |
| Completed treatment – died after single infusion | 76 | 61% |
| **Total** | **124** | **100%** |

[e] Figures may not sum to 100% due to rounding.
[f] Table 10 presents the outcome summary data for patients that have received the tisagenlecleucel infusion for the treatment of DLBCL and TFL.
[g]

# Overall survival (OS)

Of the 124 patients with a treatment record in SACT, the minimum follow-up was 4.1 months (124 days) from the last CDF application. Patients were traced for their vital status on 5 April 2023. This date was used as the follow-up date (censored date) if a patient is still alive. The median follow-up time in was 10.1 months (307 days). The median follow-up is the patients' median observed time from the start of their treatment to death or censored date.

Table 7: OS at 6, 12, 18, 24, 36-month intervals

| Time period | OS (%) |
|---|---|
| 6 months | 72% [95% CI: 63%, 79%] |
| 12 months | 52% [95% CI: 43%, 61%] |
| 18 months | 45% [95% CI: 36%, 54%] |
| 24 months | 37% [95% CI: 28%, 46%] |
| 36 months | 29% [95% CI: 20%, 39%] |

Figure 3 provides the Kaplan-Meier curve for OS, censored at 5 April 2023. The median OS was 14.8 months [95% CI: 10.0, 21.8] (450 days).

Figure 3: Kaplan-Meier survival plot (N=124)

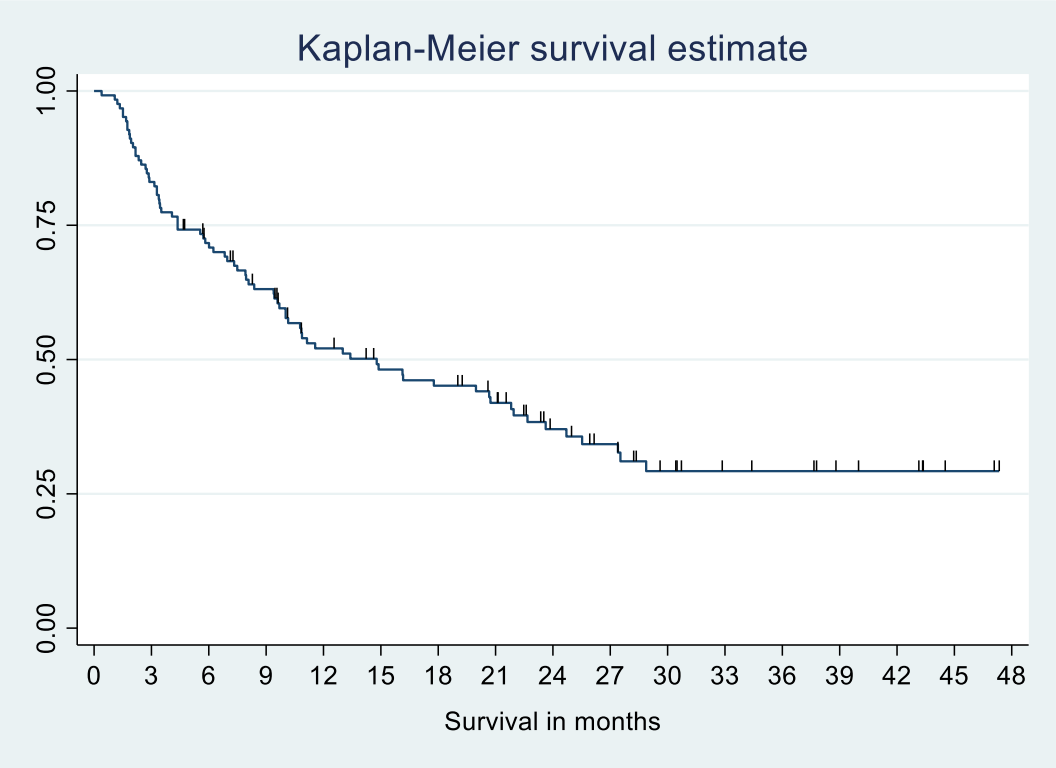


Table 8 and Table 9 show the number of patients at risk, the number of patients that were censored and the number of patients that died (events) from the time patients started treatment to the end of the follow-up period. The maximum follow-up period for survival was 50.1 months (1,524 days), all patients were traced on 5 April 2023.

Table 8: Includes the number of patients at risk, by quarterly breakpoints

| Time intervals (months) | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 | 45 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number at risk | 124 | 103 | 85 | 72 | 55 | 48 | 45 | 37 | 27 | 22 | 15 | 11 | 10 | 7 | 6 | 2 |

Table 9 shows that for all patients who received treatment, 48 were still alive (censored) at the date of follow-up and 76 had died (events).

Table 9: Number of patients at risk, those that have died (events) and those that are still alive (censored) by quarterly breakpoints

| Time intervals (months) | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 | 45 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Censored | 48 | 48 | 44 | 41 | 36 | 33 | 33 | 28 | 22 | 19 | 15 | 11 | 10 | 7 | 6 | 2 |
| Events | 76 | 55 | 41 | 31 | 19 | 15 | 12 | 9 | 5 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |

# Intravenous immunoglobulin (IVIG) use

All 124 patients who received the tisagenlecleucel infusion between 1 February 2019 and 30 November 2022 were followed up in the Medical Data Solutions and Services (MDSAS) immunoglobulin database on 18 April 2023.

Of the 124 patients, 18 (15%) patients received IVIG.

Table 10: Number and percentage of patients who received IVIG.

| Total number of patients | Patients who received IVIG | |
|---|---|---|
| | N | % |
| 124 | 18 | 15% |

# Sensitivity analysis

# 6-months follow up

## Overall survival (OS)

Sensitivity analyses were also carried out for OS on a cohort with at least six months follow-up. To identify the cohort, CDF applications were limited from 1 February 2019 to 5 October 2022.

Following the exclusions above, 119 patients (96%) were included in these analyses. The median follow-up time in SACT was 10.8 months (328 days). The median follow-up is the patients' median observed time from the start of their treatment to death or censored date.

Figure 4 provides the Kaplan-Meier curve for OS, censored at 5 April 2023. The median OS was 13.4 months [95% CI: 9.7, 21.8] (407 days).

Figure 4: Kaplan-Meier survival plot (N=119)

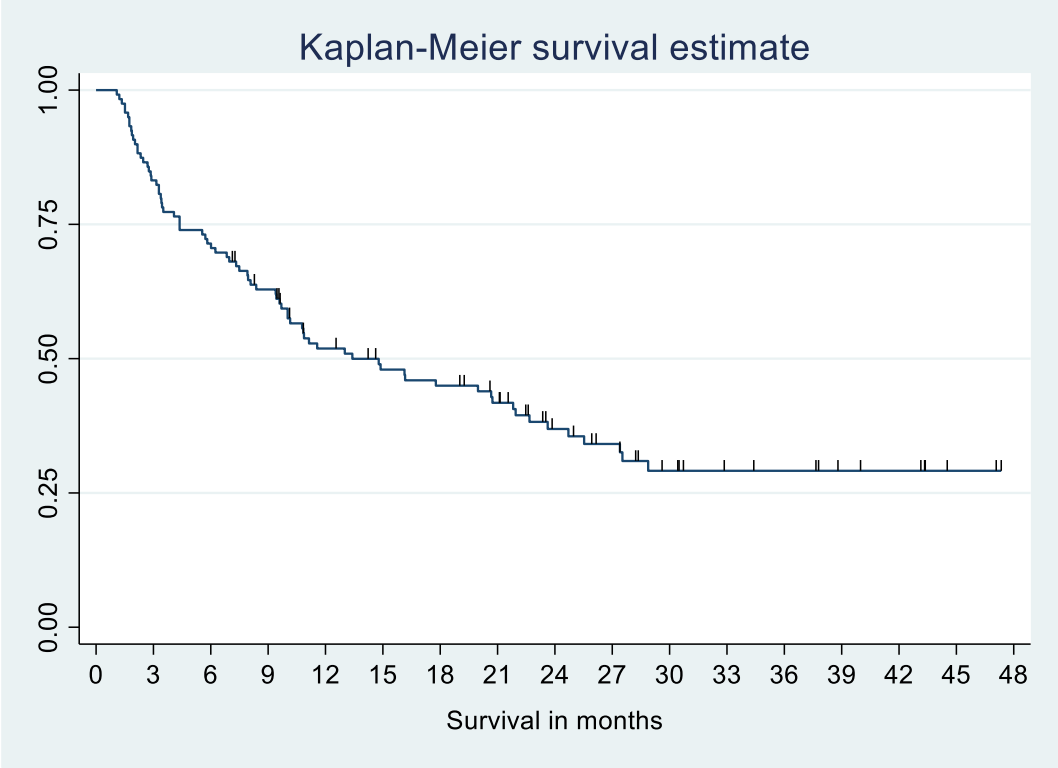


Table 11 and Table 12 show the number of patients at risk, the number of patients that were censored and the number of patients that died (events) from the time patients started treatment to the end of the follow-up period. The maximum follow-up period for survival was 50.1 months (1,524 days), all patients were traced on 5 April 2023.

Table 11: Includes the number of patients at risk, by quarterly breakpoints

| Time intervals (months) | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 | 45 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number at risk | 119 | 99 | 85 | 72 | 55 | 48 | 45 | 37 | 27 | 22 | 15 | 11 | 10 | 7 | 6 | 2 |

Table 12 shows that for all patients who received treatment, 44 were still alive (censored) at the date of follow-up and 75 had died (events).

Table 12: Number of patients at risk, those that have died (events) and those that are still alive (censored) by quarterly breakpoints

| Time intervals (months) | 0 | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 | 45 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Censored | 44 | 44 | 44 | 41 | 36 | 33 | 33 | 28 | 22 | 19 | 15 | 11 | 10 | 7 | 6 | 2 |
| Events | 75 | 55 | 41 | 31 | 19 | 15 | 12 | 9 | 5 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |

Table 13: Median OS, full cohort and sensitivity analysis

| Metric | Standard analysis:<br>Full cohort | Sensitivity analysis:<br>6 months follow-up cohort: |
|---|---|---|
| N | 124 | 119 |
| OS | 14.8 months [95% CI: 10.0, 21.8] (450 days). | 13.4 months [95% CI: 9.7, 21.8] (407 days). |

# 5. Conclusions

124 patients received the tisagenlecleucel infusion for the treatment of relapsed/refractory DLBCL and TFL [TA567] through the CDF in the reporting period (1 February 2019 and 30 November 2022). 124 patients were reported to the SACT dataset, giving a SACT dataset ascertainment of 100%. One patient with a CDF application died before treatment, this was confirmed by the trust responsible for the CDF application.

Patient characteristics from the SACT dataset show that 60% (N=74) of patients who received tisagenlecleucel infusion for the treatment of relapsed/refractory DLBCL and TFL were male, 40% (N=50) of patients were female. Most of the cohort were aged between 60 and 79, 77%, (N=95), and 73% (N=90) of patients had a performance status between 0 and 2 at the start of their regimen.

At data cut off, outcomes were expected for all 124 patients, having all been identified as receiving the single infusion. Of the 124 patients, 123 had an outcome as completed as prescribed in the SACT dataset.

The median OS was 14.8 months [95% CI: 9.7, 21.5]. OS at 6 months was 72% [95% CI: 63%, 79%], 12 months OS was 52% [95% CI: 43%, 61%], OS at 18 months was 45% [95% CI: 36%, 54%], OS at 24 months was 37% [95% CI: 28%, 46%], OS at 36 months was 29% [95% CI: 20%, 39%].

IVIG treatment use showed that 18 (15%) patients received IVIG after receiving the single infusion of tisagenlecleucel.

Sensitivity analysis was carried out on OS to evaluate a cohort for which all patients had a minimum follow-up of six months. Results showed a slight difference in the median OS but this was not statistically significant (full cohort = 14.8 months; sensitivity analysis cohort = 13.4 months).

# 6. References


1. The Personal Demographics Service (PDS). NHS Digital: 2023 [cited 2023 Apr]. Available from: hiips://digital.nhs.uk/Demographics

2. National Statistics. Cancer Registration Statistics, England: 2020. 2022 [cited 2023 Apr]. Available from: hiips://digital.nhs.uk/data -and-information/publications/statistical/cancer-registration-statistics/england-2020

3. National Institute for Health and Care Excellence: 2019 [cited 2023 Apr]. Available from: hiips://www.nice.org.uk/guidance/ta567/chapter/1 -Recommendations

4. Cancer Drugs Fund. [Internet]. NHS England: 2017 [cited 2023 Apr]. Available from: hiips://www.england.nhs.uk/cancer/cdf/

5. Appraisal and funding of Cancer Drugs. NHS England: 2016 [cited 2023 Apr]. Available from: hiips://www.england.nhs.uk/wp -content/uploads/2013/04/cdf-sop.pdf

6. National Institute for Health and Care Excellence: 2019 [cited 2023 Apr]. Available from: hiips://www.nice.org.uk/guidance/ta567/resources

7. Study of Efficacy and Safety of CTL019 in Adult DLBCL Patients (JULIET): 2015 [cited 2023 Apr] Available from: hiips://clinicaltrials.gov/ct2/show/NCT02445248

8. Systemic Anti-Cancer Therapy [Internet]: SACT: 2023 [cited 2023 Apr]. Available from: hiips://digital.nhs.uk/ndrs/data/data -sets/sact

9. CDF analytical methods. [Internet]. NHSD: 2019 [cited 2023 Apr]. Available from: hiip://www.chemodataset.nhs.uk/nhse_partnership/