Investigating overall quality of life in patients with diffuse large B-cell lymphoma undergoing CAR T-cell therapy

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Abstract

Background Some adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) are eligible for chimeric antigen receptor T-cell (CAR T-cell) therapy. Although this novel immunotherapy can be life-extending, it can also lead to significant morbidity and mortality from associated toxicities. Patients with DLBCL are known to experience a poor quality of life, which may deteriorate or improve depending on their response to CAR T-cell therapy.

Aim To investigate the quality of life of patients receiving CAR T-cell therapy.

Method The design was a pilot prospective observational cohort study. Data were collected using two self-reported measures of health-related quality of life. The eight participants were asked to complete the questionnaires before commencing treatment and at 30 days, three months, six months, nine months, 12 months and 18 months post treatment.

Results One key result was that five participants out of eight had a reduced quality-of-life score at 30 days post treatment compared with baseline. However, the three patients who responded well to treatment experienced, on the whole, an improved quality of life. Five of the eight participants died during the data collection period and only three participants were able to complete the questionnaires at all time points.

Conclusion CAR T-cell therapy can offer some patients with DLBCL an improved quality of life, but there appears to be a reduction in quality of life at around 30 days post treatment, which may in part be due to treatment-related toxicities. Patients should be allocated a key worker and given the contact details of a member of the clinical team at the tertiary referral centre to ensure they have consistent support before, during and after treatment.

Citation

Peer review
This article has been subject to external double-blind peer review and checked for plagiarism using automated software

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Conflict of interest
None declared

Acknowledgements
The author would like to thank the South Wales Bone Marrow Transplant team and its director Dr Keith Wilson (consultant haematologist) and the CAR T-cell therapy clinical team led by Dr Ceri Jones (consultant haematologist). The author would also like to thank their MSc supervisor, Jane Hopkinson, professor of nursing and interdisciplinary cancer care at Cardiff University.

Accepted
28 February 2024

Published online
May 2024

Keywords
blood cancers, cancer, cancer care, cancer treatments, immunotherapy, non-Hodgkin lymphoma, patients, patient outcomes, professional, quality of life

Background
Diffuse large B-cell lymphoma (DLBCL) is a high-grade (fast growing) type of non-Hodgkin lymphoma, which affects the lymphocytes. The most common symptom is a painless swelling in the neck, groin or armpit which may be accompanied by profuse night sweats, fluctuating high temperatures with no obvious cause, loss of weight and fatigue (Friedberg and Fisher 2008, Cancer Research UK 2024). DLBCL is the most common type of non-Hodgkin lymphoma and has a 60-70% five-year overall survival rate (Li et al 2018). In the UK around 5,500 people per
Early clinical trials have demonstrated remarkable remission rates for patients with relapsed or refractory haematological malignancies who have been treated with CAR T-cell therapy (Gill and Porter 2014, Zahid et al 2020, Kankeu Fonkoua et al 2022, National Cancer Institute 2022). However, this treatment can also lead to significant morbidity and mortality from associated toxicities (Zahid et al 2020), which include cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome (ICANS), cytopenia, infection, tumour lysis syndrome and acute anaphylaxis (Shaikh and Shaikh 2024).

Due to the complexity of CAR T-cell therapy, and the often precarious health status of the patients, NHS England has established two UK-wide clinical panels which are responsible for reviewing eligible patients to ensure they meet the clinical criteria specified by NICE (2023) and by the marketing authorisation for the medicine used in the infusion and for prioritising patients. The panels are clinically led, with patient and public voice representation, and decisions are made based on unanimous consent between the clinical and provider members (Welsh Health Specialised Services Committee 2019a, 2019b).

Patients approved for treatment by the clinical panels receive CAR T-cell therapy at a tertiary referral centre as inpatients and remain in hospital for around two weeks after receiving the infusion due to the high risk of toxicities. Following discharge, patients are advised to stay at a location within half an hour of the treatment centre for around a month – in Wales, where the author works, patients who live further away from the treatment centre are provided with hotel accommodation.

Quality of life

Evidence suggests that some patients, particularly those aged ≥65 years, have an impaired quality of life at initial DLBCL diagnosis (Kelly 2012, Jensen et al 2013, Maziarz et al 2019). In addition, given that CAR T-cell therapy is a novel treatment with potentially life-threatening side effects and that patients are offered it when other treatments have failed, it is important to monitor patients’ quality of life before, during and after treatment.

At the time of writing, the author was unable to identify any published UK studies exploring the quality of life of patients with DLBCL receiving CAR T-cell therapy and identified only a small number of studies on this topic from other countries. Connor Johnson et al (2023) in the US and Maziarz et al (2019) in the US and Germany both emphasised the importance of including early time points when investigating quality of life in this patient population.

The author undertook a pilot prospective observational cohort study in Wales to explore quality of life in this patient population, including at 30 days post treatment. As far as the author is aware, this is the first nurse-led study on this topic in the UK. For space reasons this article discusses one key result from the study.

**Aim**

To investigate the quality of life of patients receiving CAR T-cell therapy.

**Method**

**Setting and design**

This was a pilot prospective observational cohort study, which involves following a study cohort over a period of time, collecting data on their experiences and tracking their outcomes. The setting was a tertiary referral centre in Wales.

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**Implications for practice**

- **Chimeric antigen receptor T-cell (CAR T-cell) therapy can extend the life of patients with diffuse large B-cell lymphoma (DLBCL), but it also has potentially life-threatening side effects.**

- **Patients with DLBCL who receive CAR T-cell therapy need support, advice and reassurance before, during and after treatment.**

- **Patients need to be given a key worker and the contact details of a member of the clinical team at the tertiary referral centre.**

- **Pre-CAR T-cell therapy counselling can help patients prepare for the likely deterioration in their health status before they experience any improvement.**

- **Patients can benefit from having a clinical nurse specialist present at pre-treatment counselling to help them understand information and to coordinate referral to psychology services as appropriate.**
Participants
NHS Wales refers all eligible patients to the dedicated clinical panel in line with the access criteria in the Welsh Health Specialised Services Committee (2019a, 2019b) service specification regarding CAR T-cell therapy. All patients who had been approved for CAR T-cell therapy by the clinical panel and had been referred for treatment to the tertiary referral centre in Wales were contacted by the author and asked whether they would like to participate in the study. Participants were recruited at different times, depending on when they had been referred, between December 2020 and December 2021. Over that period, ten patients were referred to the centre, but two relapsed and died while waiting for treatment. Eight patients took part in the study. Inclusion and exclusion criteria are shown in Box 1.

Data collection tools


Data analysis
The author collected participants’ responses to the EQ-5D-5L and FACT-Lym questionnaires at each time point and entered the data into a database developed for the study and stored in a secure and password-protected IT system. The results were displayed as graphs and bar charts and were presented to, and discussed with, the CAR T-cell therapy clinical team at the participating hospital.

Ethical considerations
Ethical approval was given by the Wales Research Ethics Committee and by the participating hospital’s research and development department. A consent form was attached to the questionnaires and included permission for anonymised data to be used to support future research and to be shared anonymously with other researchers.

A licence was issued for the author to use the EQ-5D-5L and FACT-Lym questionnaires for the study at the participating site.

Since many participants had a precarious health status, the author and the clinical team discussed each person’s results at each time point to decide whether it was in their best interest to continue with the study or whether they should withdraw.

Results
Eight patients participated in the study, four men and four women, with a median age of...
Participants had previously received two or more lines of chemotherapy and were eligible for CAR T-cell therapy. Participants’ overall quality-of-life scores, as measured on the EQ VAS, are shown in Figure 1. Five of the eight participants had a lower quality-of-life score at the 30-day time point compared with baseline. Three participants responded well to treatment over the study period (participants 1, 3 and 6); for participants 1 and 3, the quality-of-life score was higher at the 30-day time point and at the end of the study period compared with baseline; for participant 6, the quality-of-life score was lower at the 30-day, 12-month and 18-month time points compared with baseline, but was at or above baseline at the three-month, six-month and nine-month time points (Figure 1). This suggests that patients who respond well to CAR T-cell therapy experience, on the whole, an improved quality of life.

Participant 1’s overall quality-of-life score decreased at nine- and 12-months post treatment and participant 6’s overall quality-of-life score decreased at 12- and 18-months post treatment (Figure 1). Further investigation revealed that one of these two participants had contracted coronavirus disease 2019 (COVID-19) and had been admitted to hospital, while the other had developed recurrent chest infections which led to a prolonged admission to the intensive treatment unit.

A poor response to treatment combined with the development of serious toxicities meant data collection was not fully completed for all eight participants (Figure 1). Although the intention was to capture participants’ quality-of-life scores post relapse, some were too unwell to continue to take part in the study, which highlights one of the challenges of research in this patient group. One participant had died before, and two had died around, the 30-day time point (participants 2, 4 and 8); one participant was unable to continue to take part after the 30-day time point and died five months after treatment (participant 7); and one participant was unable to continue to take part after the nine-month time point and died 14 months after treatment (participant 5) (Figure 1).

**Discussion**

This article reports one key result from the pilot study, namely that most participants had a reduced overall quality-of-life score at 30 days post treatment. This emphasises the need for patients who are scheduled to receive CAR T-cell therapy to have additional support before receiving treatment to discuss and plan for a potential deterioration in quality of life in the first few weeks following treatment. Patients with DLBCL who are scheduled to receive CAR T-cell therapy have already undergone many challenging treatment regimens and are about to receive a treatment that could extend their life or induce toxicities that could have severe adverse and irreversible effects. In addition, patients receive CAR T-cell therapy in a designated tertiary referral centre that may not be their local hospital, so they may not have access to their previous care worker and clinical support team.

Quality of life at 30 days post treatment

Maziarz et al (2019) and Jim et al (2018) recognised that the early assessment of quality of life in patients receiving CAR T-cell therapy is crucial, particularly since patients may experience short-term toxicities. Most participants who took part in the present study had developed cytokine release syndrome, neutropenia and/or thrombocytopenia by the 30-day time point, which may partly explain the reduction in their quality-of-life scores at that point. In addition, participants had been recently discharged from the inpatient setting where they had received CAR T-cell therapy, and some were staying in temporary accommodation because they lived more than half an hour away from the treating centre. These patients were therefore unable to return to their normal daily life.
The deterioration in overall quality-of-life scores at 30 days post treatment, and the fact that most participants had developed toxicities by that point, emphasise the importance of providing patients with a key worker, such as a clinical nurse specialist (CNP), at the treating centre to coordinate their treatment and care. In addition, patients should be provided with the contact details of a designated person from the CAR T-cell therapy clinical team who they can contact at any time during and after treatment to discuss concerns about symptoms and/or a deterioration in their condition.

This result also emphasises the importance of providing patients with robust pre-CAR T-cell therapy counselling so that they understand, and are prepared for, the likelihood that they will experience a deterioration in their health status before they experience any improvement. Patients with cancer who are informed about potential side effects of treatments, and have a better understanding of their condition, have been shown to have more positive outcomes (Chelf et al 2001).

Pre-CAR T-cell therapy counselling involves an in-depth explanation of the treatment, the potential side effects and toxicities and the potential adverse and positive outcomes, which may be challenging for patients to hear and/or understand. However, providing this information is essential to enable them to make an informed decision about whether to accept the treatment. Having a CNP present at the pre-CAR T-cell therapy counselling session is important, as they can help patients make sense of the information they are being given. In addition, patients may be signposted to psychology services, which the CNP can help to coordinate and ensure they are referred to relevant services.

**Value of quality-of-life assessments**

Data collected from patient-reported quality-of-life assessments may provide nurses and other healthcare professionals with meaningful information that could be used to inform interventions to improve patients' health status (Fayers and Bottomley 2002). Fallowfield (2002) suggested that quality-of-life research can provide vital information about the effects of a disease and its treatment on patients' physical, social, emotional and functional well-being and can have a prognostic function in terms of helping to predict which patients may benefit most from certain treatments. Quality-of-life data can also be a useful ‘layer of information’ that can be used to guide patients and healthcare professionals’ decision-making (Elsaway et al 2022).

Patrick et al (2019) suggested that patient-reported outcome measures and quality-of-life tools are gaining more importance since they enable patients to provide information that cannot always be identified by technology or observation, and that such tools have an essential role in the treatment of patients with cancer. Jones et al (2020) discussed the potential of patient-reported outcomes (PROs) to improve clinical care but suggested that one of the barriers to doing this effectively was the challenge of individualising PROs. The researchers suggested there is a need to develop a new method that measures individual patients’ PROs – which they call ‘precision PROs’ – which involves selecting, using and interpreting PROs tailored to the individual to support patient-centred care (Jones et al 2020).

### Involving patients with cancer in research

The recruitment rate for the present study was high since all eligible patients who were offered the opportunity to take part in the study consented to do so. In addition, although the study was undertaken at the height of the COVID-19 pandemic, and despite having gone through systemic anticancer therapy treatments, the participants were keen to be involved in a research project that they regarded as important for their care.

Previous research has suggested that patients who participate in research can feel a sense of empowerment, which may lead to positive attitudes about taking part and which may in turn enhance their adherence to research instructions and result in positive outcomes (Castillo et al 2012). A literature review of attitudes to, and participation in, clinical trials in oncology found that there may be many benefits for patients who are treated in a hospital that is engaged with research (Ellis 2000). In addition, Lakeman et al (2013) suggested that participating in research can involve beneficial therapeutic processes for patients, such as exploring their experiences and feeling heard.

In the present study, five of the eight participants experienced a relapse and died during the data collection period. This emphasises the importance of acknowledging that patients undergoing this potentially life-extending therapy remain immunocompromised after treatment and are at risk of treatment-related toxicities, which can have a negative effect on their overall quality of life and health status.

Further research on quality of life in patients with DLBCL who undergo CAR T-cell therapy is required to inform practice. This study was undertaken with a small number of patients in a single centre in Wales, therefore a multicentre study involving a larger patient sample would provide a more robust and generalisable result.
support a more robust statistical analysis and a deeper exploration of themes. In addition, using standardised data collection tools would enable a comparison of results.

Limitations
The main limitation was the small sample size. In addition, the nature of participants’ health condition meant that many relapsed during the study period and were too unwell to continue to participate; five of the eight participants died before the end of the data collection period. The study was undertaken during the COVID-19 pandemic, which could have adversely affected participants’ overall quality-of-life scores; many patients with DLBCL that the author has worked with have expressed extreme concern about contracting COVID-19 as this would prevent them from receiving CAR T-cell therapy.

Conclusion
Information extracted from patient-reported quality-of-life questionnaires may provide nurses and other healthcare professionals with meaningful data that could be used to inform interventions to improve patients’ health status. A key result of this pilot study, which used two quality-of-life questionnaires, suggests that the overall quality of life of patients with DLBCL who receive CAR T-cell therapy is lower around 30 days post treatment compared with baseline. Patients should therefore be provided with robust pre-treatment counselling and be supported by a key worker at the tertiary referral centre before treatment commences to help prepare them for the potential challenges ahead. In patients who respond well to treatment, quality of life appears to improve compared with baseline. However, although CAR T-cell therapy can extend the life of patients with DLBCL, it has a high risk of toxicities which can lead to significant mortality in this population. Further research on quality of life in patients with DLBCL who undergo CAR T-cell therapy is required to inform practice.

References