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# Neuropsychological outcomes of patients with haematological malignancies undergoing chimeric antigen receptor T-cell therapy: protocol for a prospective study

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## ABSTRACT

**Introduction** Immune effector cell-associated neurotoxicity syndrome (ICANS) is a common side-effect of chimeric antigen receptor T-cell (CAR-T) therapy, with symptoms ranging from mild to occasionally life-threatening. The neurological, cognitive, psychiatric and psychosocial sequelae of ICANS are diverse and not well defined, posing a challenge for diagnosis and management. The recovery trajectory of the syndrome is uncertain. Patients are rarely examined in this population pretherapy, adding a layer of complexity to specifying symptoms pertinent solely to CAR-T treatment. We present a protocol of a prospective longitudinal research study of adult patients in a single Australian haematology service undergoing CAR-T therapy. The study will describe neurocognitive features specific to ICANS, characterise the underlying syndrome, capture recovery, identify predictors of differential postinfusion outcomes and determine a set of cognitive instruments necessary to monitor patients acutely.

**Methods and analysis** This is a prospective longitudinal study that comprises neuropsychological and neurological examinations occurring prior to CAR-T, during the acute post-treatment period, 28 days, 6 months and 12 months post infusion. Data will be sourced from objective psychometric measures, clinical examinations, self-report questionnaires of psychopathology and accounts of subjective cognitive complaint.

**Ethics and dissemination** This study aims to guide diagnosis, management and monitoring of neurocognitive features of CAR-T cell therapy. Results of this study will be disseminated through publication in peer-reviewed journals and presentations at scientific conferences. All procedures involving human subjects/patients were approved by the Peter MacCallum Cancer Centre Human Research Ethics Committee (21/145).

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Immune effector cell-associated neurotoxicity syndrome (ICANS) is a common side-effect of chimeric antigen receptor T-cell (CAR-T) therapy. Relatively little work has investigated the neurocognitive phenotype of ICANS, and even less is known about the long-term neuropsychological outcomes.

### WHAT THIS STUDY ADDS

⇒ The study will describe neurocognitive features specific to ICANS, characterise the underlying syndrome, capture recovery, identify predictors of differential postinfusion outcomes and determine a set of cognitive instruments necessary to monitor patients acutely.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The ultimate outcome of this study will be a set of evidence-based clinical guidelines relating to the preinfusion assessment and postinfusion monitoring of neurocognitive status in patients undergoing CAR-T therapy. This will improve clinical management and preinfusion counselling in this patient population.

## INTRODUCTION

Chimeric antigen receptor T-cell (CAR-T) therapy is an immunotherapy that modifies T-cells to target and eliminate cancer cells and is fast becoming a standard of care for some relapsed or refractory haematological malignancies.[1] Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) are common side-effects of CAR-T.[2] ICANS has been described in as high as over 60% of patients depending on a CAR-T product. The most commonly reported consequence is encephalopathy, which can range from mild cognitive and neurological deficits to obtundation,

stupor and even coma.[1] The onset tends to vary from days to weeks post infusion, with limited research available on neurocognitive recovery trajectory.[3] Although the literature has documented a diverse range of clinical features of ICANS, the syndrome has not been holistically characterised.[4]

This paper describes a protocol of an Australian prospective longitudinal study of adult patients in the haematology service undergoing CAR-T therapy. The aim is to investigate neurological, cognitive, psychiatric and psychosocial outcomes of the treatment, with an emphasis on characterisation of acute neurocognitive features of ICANS. The study will determine a set of cognitive and neurological instruments necessary to identify and monitor the syndrome acutely and investigate predictors of differential outcomes post infusion. Recovery is examined from an acute, subacute and long-term perspective. This paper outlines the rationale, design and methodology of the research project. The protocol includes clinical and paraclinical tools to help guide the overall management of CAR-T patients.

## Clinical features of ICANS

Accurate recognition of ICANS is essential for timely intervention and medical management. Description of clinical presentation varies across studies and can include focal weakness, apraxia, tremor, disturbance of speech and language, impaired attention, memory dysfunction, seizures, hallucinations, behaviour disturbance and emotional lability.[5] There has been, however, little consensus regarding a syndrome underpinning these symptoms, which complicates early detection, severity classification and our understanding of recovery. Neurotoxicity is typically treated with corticosteroids, which have the drawback of potentially reducing efficacy of CAR-T cells.[3] Understanding the syndrome evolution could help optimise dosage and duration of corticosteroid administration, subsequently improving therapy outcomes.

The commonly adopted measure of ICANS is the immune effector cell-associated encephalopathy (ICE) score.[6] The instrument comprises brief items on orientation, attention, handwriting, simple naming and ability to follow simple commands. Severity of ICANS is determined according to the ICE score out of 10 and patients' level of consciousness, motor function, evidence of seizures or elevated intracranial pressure.[1 3] Herr *et al*,[7] however, described a series of patients in whom neurocognitive symptoms predated decrease in the ICE score. Thus, this approach might adequately recognise early signs of mild impairment or capture recovery to complete resolution. Understanding syndromology of neurotoxicity is the first step in the development of new diagnostic instruments and evidence-based management strategies.

## Baseline significance

One of the key challenges in understanding CAR-T-related neurotoxicity is distinguishing new symptoms from pre-existing dysfunction. Both disease itself and cancer treatments are commonly associated with neurological and cognitive presentation. Patients become eligible for CAR-T if their cancer is refractory to or has progressed following prior lines of systemic therapy or stem cell transplantation, with many previously exposed to central nervous system (CNS) penetrating agents. Schroyen *et al*'s[8] systematic review demonstrated high prevalence of chemotherapy-induced leucoencephalopathy in patients with cancer, persisting for years following active treatment. Subjective cognitive complaints are prevalent in the oncology population, with physical and psychological factors (eg, poor sleep, fatigue, pain, anxiety and depression) commonly contributing to disruption in cognition. Thus, to adequately characterise ICANS, it is necessary to evaluate baseline cognitive, psychological and neurological status in patients pre-CAR-T.

## Recovery trajectory

Although ICANS is understood as an acute event typically resolving within several weeks, persisting symptoms have been reported. Research investigating neurocognitive recovery has been limited.[3] Maillet *et al*[9] examined 27 adult patients with relapsed B-cell lymphoma prior to CAR-T and 6–12 months post infusion. Forty-four per cent of their cohort experienced acute neurotoxicity. The authors found no difference in participants' neurocognitive status at review compared with baseline and a reduction in self-reported cognitive concerns, suggesting that ICANS had resolved. While these findings are consistent with the hypothesised acute nature of neurotoxicity, a large proportion of the cohort was excluded from follow-up due to disease progression. It is not clear if these patients followed the same trajectory. A wide follow-up interval also limits conclusions regarding ICANS duration.

Wang *et al*[10] conducted a cross-sectional study of patient-reported concerns in 60 individuals in the first year post-CAR-T (28 were included at <30 days, 13 at 30–90 days and 19 at >90 days post infusion). Commonly reported symptoms included pain, fatigue, sleep disturbance, drowsiness, lack of energy, malaise, weakness, headache and difficulty concentrating. Those who experienced grade 2–4 CRS and/or ICANS had greater reports of physical symptoms, sadness, irritability, difficulty speaking and interference with enjoyment of life >30 days post-CAR-T. The authors did not exclude patients with disease progression or have information on symptom profiles prior to infusion. Thus, distinguishing CAR-T-related contribution from possible effects of disease and other treatment is difficult. These findings provide valuable insight into subjective experience of CAR-T patients. Self-report questionnaires could be used to screen for patients who require clinical consultation and subsequent intervention.

## Risk of neurotoxicity

Identifying patients at risk of neurotoxicity is paramount for adequate medical management pre-CAR-T and post-CAR-T. Established risk factors for developing ICANS

**Table 1** Schedule of routine neurology and cognitive assessments

| Measures | Information collected | Baseline* | Post-CAR-T follow-up (days) | | | |
|---|---|---|---|---|---|---|
| | | | Acute/subacute† | | Long term | |
| | | | 14 (11–17) | 28 (25–31) | 180 (173–187) | 365 (358–372) |
| Neurological assessment | | | | | | |
| Clinical interview | Neurological symptoms and medical history | X | X | X | X | X |
| Neurological exam | Neurological status | X | X | X | X | X |
| Montreal cognitive assessment‡ | Cognitive screening instrument | X | X | X | X | X |
| Neuropsychological assessment | | | | | | |
| Semistructured clinical interview§ | Cognitive complaint, clinical presentation, demographic, medical, and psychiatric history | X | | X | X | X |
| Psychometric self-report questionnaires | | | | | | |
| EuroQol 5-dimension 5-level (EQ-5D-5L) | Quality of life | X | | X | X | X |
| Patient Reported Outcomes Measurement Information System Cancer Item Bank | Anxiety, depression, fatigue and pain interference | X | | X | X | X |
| Patient Reported Outcomes Measurement Information System Item Bank | Cognitive function, positive affect, sleep disturbance, general life satisfaction, and ability to participate in social roles and activities | X | | X | X | X |
| SPECTRA: Indices of Psychopathology | Psychopathology, subjective cognitive complaint and adaptive capacity | X | | X | X | X |
| Psychometric cognitive test battery | | | | | | |
| Digit span forward | Processing speed and attention | X | | X | X | X |
| Symbol Digit Modalities Test (oral)‡ | Processing speed and attention | X | | X | X | X |
| Trails Making Test A | Processing speed and attention | X | | X | X | X |
| Victoria Stroop Test Dots | Processing speed and attention | X | | X | X | X |
| Digit span back | Executive function | X | | X | X | X |
| Letter Fluency Test‡ | Executive function | X | | X | X | X |
| Trails Making Test B | Executive function | X | | X | X | X |
| Victoria Stroop Test Interference Score | Executive function | X | | X | X | X |
| Brief Visuospatial Memory Test-Revised‡ | Memory | X | | X | X | X |
| Rey Auditory Verbal Learning Test‡ | Memory | X | | X | X | X |
| Cookie Theft Picture§ | Language | X | | X | X | X |
| Category Fluency Test‡ | Language | X | | X | X | X |
| Sydney Language Battery Naming Test | Language | X | | X | X | X |
| Rey-Osterrieth Complex Figure Task (copy) | Visuospatial function | X | | X | X | X |
| Clock Drawing Test | Semantic function | X | | X | X | X |
| Test of premorbid function | Estimate of premorbid intellect | X | | | | |

*Baseline assessments occur at any point between completion of bridging therapy and commencement of conditioning lymphodepletion chemotherapy (ie, fludarabine and cyclophosphamide).
†In addition to the above schedule, ad hoc inpatient cognitive and neurological examinations occur acutely post-CAR-T as clinically appropriate.
‡Alternative test forms used at reviews in randomised order to minimise practice effects.
§Audio recording will be made.
CAR-T, chimeric antigen receptor T-cell.

Table 2 Description of cognitive instruments

| Test name | Description |
|---|---|
| Digit span (forward and backward) | On the forward subtest, participants listen to strings of numbers of progressively increasing length and repeat the digits in the order of presentation. On the backward subtest, participants repeat numbers in reverse order. |
| Symbol Digit Modalities Test (oral version) | The test comprises a coding key of nine abstract symbols, each paired with a one-digit number. The test sheet outlines the abstract symbols only, and participants verbally identify their corresponding numbers one-by-one by looking at the coding key. The goal is to identify as many numbers as possible in 90 s. |
| Trail Making Test | In the part A, participants use a pen to connect 25 numbers in an ascending order as quickly as possible. In the part B, participants alternate between connecting 13 accenting numbers and 12 letters in the alphabetical order. |
| Victoria Stroop Test | Participants are initially presented with 24 coloured dots and are asked to name colours of the dots as rapidly as possible. In the second part, they name ink colour of 24 neutral words. In the final part, participants name the colour of the ink for words with incongruent verbal content as quickly as possible. |
| Brief Visuospatial Memory Test-Revised | Participants view a display with six geometric figures arranged in a 2×3 array for 10 s. Once the display is removed, they are asked to draw the figures in their correct location using paper-and-pencil. The test comprises a total of three learning trials. After an approximate 25 min delay, participants draw the figures again from memory. On a subsequent recognition trial, participants are sequentially presented with 12 geometrical figures and identify which of the figures were on the original display. |
| Rey Auditory Verbal Learning Test | Participants hear a list of 15 nouns and are asked to recall as many as they can at the end of each of the five learning trials. They are then read a new list of 15 nouns and are asked to recall as many as they can. Following the distractor list, participants recall the nouns from the first list. After a 20-min delay, the first list is recalled again, followed by a recognition trial. |
| Verbal Fluency Test | On the Letter Fluency subtest, participants generate words that begin with a specific letter (F, A, and S in the standard form; B, H, and R in the alternate form) as quickly as possible within 1 min. Participants are instructed not to use names of people, places, or numbers, or to repeat the same word twice using a different ending. On the Category Fluency subtest, participants generate words that belong to a semantic category (animals and boys' names in the standard form; clothing and girls' names in the alternate form) as quickly as possible within 1 min. |
| Sydney Language Battery Naming Test | Participants are asked to name each of the 30 sequentially presented colour images depicting objects or animals ranging from high-frequency vocabulary words to more rare words. |
| Cookie Theft Picture | Participants are presented with a black-and-white picture and are instructed to describe everything that is happening in the scene. This process is recorded for later transcription. |
| Rey-Osterrieth Complex Figure Test (copy) | Participants copy the complex figure on a blank piece of paper. |
| Clock Drawing Task | On a blank piece of paper, participants are asked to draw the face of an analogue clock, including the numbers, and position hands of the clock indicating the time of 11:10. |
| Montreal Cognitive Assessment | Participants complete a 30-item screening instrument comprising measures a series of brief verbal and non-verbal tasks of memory, visuospatial function, attention and working memory, language, executive function and orientation to time and place. |
| Test of Premorbid Function | Participants read aloud 70 words of atypical grapheme to phoneme translations. |

include older age, active CNS disease, CAR-T cell dose and product (eg, higher incidence has been reported following axicabtagene ciloleucel), early onset of CRS and high disease burden.[11 12] The literature has suggested that serum markers, such as procalcitonin, ferritin, interleukin 6, C reactive protein and lactate dehydrogenase also might predict development of ICANS; however, the evidence is mixed.[12] There are no known cognitive markers predictive of development or severity of neurotoxicity. Identifying new risk factors and prodrome markers of ICANS would help establish uniform guidelines for medical care and implementing preventative strategies for those at high risk.[13]

## Project aims

The proposed research aims to investigate the neurocognitive, psychiatric and psychosocial outcomes of CAR-T therapy. By establishing a comprehensive neuropsychological and neurological baseline pretreatment, we will define acute neurocognitive features specific to ICANS

and severe CRS. Characterisation of the baseline cognitive status will extend beyond psychometric investigation to evaluating semiology of the cognitive complaint. The project will examine early signs associated with neurotoxicity, as well as define a set of instruments necessary to detect and monitor ICANS. Neuropsychological examinations will be completed by a clinical neuropsychologist, who will distinguish primary cognitive impairment underpinned by CAR-T-related processes from secondary cognitive dysfunction resulting from psychopathology, poor sleep, fatigue or pain. The study will also investigate predictive factors for developing neurotoxicity to facilitate close monitoring and preventative management of patients who are at high risk. Finally, both acute and long-term recovery will be examined post-CAR-T from a neurological, cognitive and psychosocial perspective. It is hoped that the research will contribute to optimising the overall management of CAR-T patients and improve recognition and referral pathways for neurocognitive dysfunction in this cohort.

## METHODS AND ANALYSIS

### Design

The study is a prospective longitudinal cohort study of adult patients undergoing CAR-T therapy at Peter MacCallum Cancer Centre (PMCC) haematology service. Patients will be initially examined at baseline, prior to CAR-T, and will be reviewed during the acute post-treatment period, 28 days, 6 months and 12 months post infusion. The project will also include cross-sectional recruitment of a matched healthy comparator group.

### Participants

#### Clinical cohort

The study will include patients undergoing CAR-T therapy who are at least 18 years of age and do not have an intellectual disability or history of significant neurological illness. All patients will complete a routine specialist cognitive assessment by a clinical neuropsychologist and a neurological examination by a treating neurologist pre-CAR-T and post-CAR-T. The findings from neuropsychological assessments will be included only for those proficient in English. Analyses will include data from baseline examinations of all patients who are planned for CAR-T; however, postinfusion follow-up sample will only comprise those who receive commercial products. All other participants will provide written informed consent.

#### Healthy controls

To collect optimal demographically adjusted psychometric normative data, healthy participants will be recruited to complete a single specialist cognitive assessment. Eligible participants will be over 18 years of age, be proficient in English, have adequate uncorrected or corrected eyesight to perceive examination material, not have cancer history, significant neurological or neurodevelopmental history and not have a current significant psychiatric condition. Healthy controls will be prospectively consented and will be matched to the clinical cohort on age, sex and education.

### Power and sample size

Based on clinical experience in the CAR-T programme, the following project aims to recruit 100 CAR-T patients. This sample size was determined based on the estimated patient throughput of the CAR-T programme within a reasonable timeframe and was confirmed by statistical power analysis as described below. The proportion of patients who develop ICANS following CAR-T therapy has been reported in 23%–67% of lymphoma cases and 40%–62% of patients with leukaemia.[1] Taking a conservative approach, we estimate that approximately 35% of our patients will develop ICANS of any grade. Thus, we expect to have 35 patients in the ICANS group and 65 patients in the non-ICANS group. This represents the expected number of patients to pass through the CAR-T programme as part of routine clinical care. Based on this samples size, the majority of analyses will be sensitive to small effect sizes. For example:

- For bivariate Pearson's correlations (eg, for examination of associations between continuous variables at baseline), this sample size would render the analyses sensitive to effect sizes of $r$=0.28 (power=80 %, alpha=5 %, sample size=100, two tailed).
- For dependent samples t-tests (eg, for examination of the mean change from baseline to post-CAR-T), this sample size would render the analyses sensitive to small effect sizes of $d$=0.28 (power=80 %, alpha=5 %, sample size=100, two tailed).
- For independent samples t-tests (eg, for comparisons of means between the anticipated 35 ICANS patients and the 65 non-ICANS patients), this sample size would render the analyses sensitive to medium effect sizes of $d$=0.59 (power=80 %, alpha=5 %, sample size=100, two tailed).
- For analysis of covariance for comparison across neuropsychological diagnostic groups with age included as a covariate, the sample size would render the analysis sensitive to a small effect size of $f$=0.09 (power=80 %, alpha=5 %, sample size=100, two tailed).

### Procedure

The neuropsychological assessment at each timepoint will include a clinical interview to elicit a cognitive complaint (if any), psychometric assessment of cognition and self-report online questionnaires on health, psychopathology, cognitive dysfunction and quality of life. The neurological assessment at each timepoint will include a clinical interview to collect medical history and elicit neurological complaint, a physical neurological examination and a screening measure of objective cognitive impairment. Table 1 details the schedule of routine assessments for the clinical cohort. Modified ad hoc inpatient examinations will be completed during acute postinfusion period,

as clinically indicated. Neurotoxicity will be monitored by inpatient ward staff via the ICE score,[6] and patients will undergo neuroimaging investigations as clinically indicated.

Medical history and demographic information will be obtained from patient charts and clinical interviews. Neuropsychology and neurology examinations will be primarily conducted at PMCC and the Royal Melbourne Hospital, with some follow-ups conducted via telehealth to minimise travel burden on participants.

## MEASURES

### Neurology assessment

The Montreal Cognitive Assessment[14] will be used as a screening measure of cognitive impairment during the neurological assessments. As part of standard of care, absolute values and patterns of laboratory markers (ie, C reactive protein, ferritin, lactic dehydrogenase and white blood cell count including lymphocyte count) will be collected pre-CAR-T and post-CAR-T. The current project will review the available laboratory data to analyse its value in predicting risk of ICANS.

### Semistructured clinical interview

A clinical interview will be conducted by a clinical neuropsychologist to elicit subjective cognitive complaint. Participants will be asked for permission to audio record baseline interviews to enable a focus on the descriptive quality of speech. Clinicodescriptive analysis of subjective cognitive complaint will contribute to describing baseline neuropsychological status specific to haematology patients compared with the healthy controls. Components of the psychometric examination and self-reported information will encompass quantitative analyses to clarify the mechanisms underlying typologies of cognitive complaint. This semistructured interview process was developed using clinical experience to mirror the standard care interview, and in alignment with previous interviews constructed to elicit detailed cognitive complaint. The interview is structured to probe circumstances in which cognitive dysfunction is likely to occur while obtaining features of frequency, contextualisation and recovery from cognitive failure. Recorded clinical interviews will be transcribed and analysed.

### Psychometric cognitive examination

A battery of psychometric cognitive instruments was selected to capture a range of cognitive dysfunction possible in this cohort. Five domains will be examined in accordance with the International Cognition and Cancer Task Force recommendations.[15] The processing speed and attention domain will be measured with the Trail Making Test Part A,[16] Victoria Stroop Test Dots,[17] Symbol Digit Modalities Test[18] and Digit Span forward from the Wechsler Adult Intelligence Scale 4th edition (WAIS-IV).[19] The executive function domain comprises the Trail Making Test Part B,[16] Letter Fluency Test from the Delis-Kaplan Executive Function System (D-KEFS),[20] Victoria Stroop Test interference score[17] and Digit Span backward from the WAIS-IV.[19] The memory domain will be measured with the Rey Auditory Verbal Learning Test[21] and the Brief Visuospatial Memory Test-Revised.[22] The language domain includes the Category Fluency Test from the D-KEFS[20] and the Sydney Language Battery Naming Test.[23] The visuospatial function domain will be measured using the Rey-Osterrieth Complex Figure Test Copy.[24] The Test of Premorbid Function[25] will be administered to estimate premorbid intellect. Table 2 details all cognitive instruments.

The raw scores will be converted into standardised z-scores based on the demographically adjusted normative data. A test score will be classified as impaired if the z-score ≤−1.5 SD.[15 26] A domain will be classified as impaired if at least two scores are impaired (or one score for the visuospatial function domain) or a z-score averages ≤−1.5 across tests in that domain. A patient will be classified as overall impaired if at least one domain is impaired.

### Questionnaires

Psychometric self-report online questionnaires measure domains of psychological, physical and psychosocial function relevant to our patients. Information collected via self-report measures will contribute to a holistic understanding of CAR-T patients experience and will aid in making a clinical distinction between primary and secondary cognitive dysfunction.

The SPECTRA Indices of Psychopathology measures psychopathology, subjective cognitive complaint and adaptive capacity. The instrument comprises 96 statements, to which participants respond on a 5-point Likert scale (1=not at all true; 5=completely true). The SPECTRA has good internal consistency in psychiatric patients ($\alpha$=0.74–0.95) and correlates with other measures of psychopathology.[27]

Instruments from the cancer bank of the Patient Reported Outcomes Measurement Information System (PROMIS)[28] will be included to examine symptoms specific to the oncology population (ie, anxiety, depression, fatigue and pain interference). We will also include measures from the broader PROMIS repository on subjective cognitive function, positive affect, sleep disturbance, general life satisfaction and ability to participate in social roles and activities. All questionnaires will be administered as computerised adaptive test, with the number of questions varying depending on response patterns.

Overall quality of life will be measured by the brief EQ-5D-5L questionnaire,[29] which examines health status across five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. For each item, participants will select out of five statements (1=no problems; 5=unable to/extreme problems). Overall health will be rated on the visual analogue scale 1–100.

## Discussion

When a patient is referred to a neurologist or a neuropsychologist in the context of a cognitive complaint or neurological dysfunction following CAR-T therapy, a clinician faces a challenge of establishing aetiology and predicting recovery. This research will characterise a neurocognitive syndrome of ICANS as distinguishable from symptoms accompanying other treatment. Our findings will facilitate early recognition of the syndrome and subsequently improve timely intervention. The research will develop evidence-based instruments for detecting and monitoring neurotoxicity. Through comprehensive baseline examinations and longitudinal follow-up, the study will capture patient journey for up to a year following CAR-T. Understanding the evolution of ICANS and its recovery will improve prognostication and counselling of patients and their families. Identifying new predictive markers for CAR-T-related complications will enhance implementation of appropriate preventative strategies.

This research will capture patients' experience, including their psychological status, quality of life and the impact of common physical symptoms, such as poor sleep, fatigue and pain. The findings will improve referral pathways to optimise daily function in this cohort. Collection of demographically matched healthy control group will allow for a robust definition of psychometric impairment distinguishable from cognitive fluctuation in the healthy population. The study aims to improve the overall clinical experience of haematology patients pre–CAR-T and post-CAR-T therapy.

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Anonymised data and the standardised proforma used to extract information on patient demographics and clinical characteristics can be shared on reasonable request from qualified investigators.



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