Feasibility and preliminary effectiveness of virtual reality as a patient education tool for people with cancer undergoing immunotherapy: a protocol for a randomised controlled pilot study in a regional setting

Shannen R van der Kruk,1 Kate M Gunn,1 Hamish MacDougall,2 Donna Milne,3 Katherine Smith4, Rob Zielinski5,6

ABSTRACT

Introduction Patient education is a critical component of healthcare delivery. However, medical information and knowledge are complex and can be difficult for patients and families to comprehend when delivered verbally. The use of virtual reality (VR) to convey medical information to patients may bridge this communication gap and lead to more effective patient education. It may be of increased value to those with low health literacy and levels of patient activation, in rural and regional settings. The objective of this randomised, single-centre pilot study is to examine the feasibility and preliminary effectiveness of VR as an education tool for people with cancer. The results will provide data to inform the feasibility of a future randomised controlled trial, including sample size calculations.

Methods and analysis Patients with cancer undergoing immunotherapy will be recruited. A total of 36 patients will be recruited and randomised to one of three trial arms. Participants will be randomised 1:1:1 to receive VR, a two-dimensional video or standard care (ie, verbal communication and information leaflets). Feasibility will be assessed by recruitment rate, practicality, acceptability, usability and related adverse events. The potential impact of VR on patient-reported outcomes (ie, perceived information provision quality, knowledge about immunotherapy and patient activation) will be assessed and stratified by information coping style (ie, monitors vs blunters) whenever statistical analyses are significant.

The patient-reported outcomes will be measured at baseline, post-intervention and 2 weeks post-intervention. In addition, semistructured interviews will be conducted with health professionals and participants randomised to the VR trial arm, to further explore acceptability and feasibility.

Ethics and dissemination Ethics approval was obtained from the Greater Western Human Research Ethics Committee, New South Wales Local Health District (2022/ETH01760). Informed consent will be obtained from all participants. Findings will be disseminated via relevant conference presentations and publications in peer-reviewed journals.

Trial registration number ACTRN12622001473752.

STRENGTHS AND LIMITATIONS OF THIS STUDY

→ This pilot study will provide novel data regarding the feasibility and preliminary effectiveness of virtual reality as a patient educational tool for patients with cancer undergoing immunotherapy.

→ A novel immunotherapy knowledge quiz was created to assess patients’ understanding of immunotherapy.

→ Using a randomised, three-arm study design will reduce potential bias.

→ Due to the type of intervention, blinding of study participants and researchers delivering the intervention is not possible.

→ Results may not be fully generalisable to all rural patients and settings as this is a single-site study.

INTRODUCTION

People who are diagnosed with cancer are required to process and understand large volumes of information about their diagnosis, upcoming procedures, therapies and associated risks, to enable them to make informed decisions about their care.1 With the increasing emphasis on both patient-centred care (ie, ‘care that is respectful of and responsive to individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions’2) and shared decision-making, ensuring that this information is adequately comprehended is increasingly important.3,4 Currently, patient education relies heavily on the verbal communication between the patient and healthcare provider, and additional materials that are handed out, such as pamphlets or booklets. However, studies report that between 40% and 60% of patients cannot correctly report
the information provided by their healthcare provider 10–80 min after their consultation. Similar results are found among patients with cancer where they, on average, only recalled 60% of the information provided during the diagnostic and treatment planning phase. With the increased use of novel therapies, such as immunotherapy, and the introduction of a unique set of autoimmune adverse events (irAEs), new challenges have emerged for oncology nurses and oncologists in delivering patient education and managing irAEs. Immunotherapy side effects can be difficult to detect by patients and challenging to diagnose by primary care or emergency physicians. Not surprisingly, studies on immunotherapy found that patients with cancer had substantial knowledge deficits about immunotherapy, suggesting patients with cancer struggle to recall information provided by their oncologist. Thus, it is even more critical to bridge this communication gap when delivering immunotherapy to patients with cancer.

Virtual reality (VR) is an innovative and immersive technology that has the potential to improve the educational experience for patients with cancer receiving immunotherapy treatment. VR is a software/hardware application that allows users to be completely immersed into a virtual environment, or three-dimensional (3D) world, in very near real time, by using an interactive device and a head-mounted display. Compared with conventional text reading, VR has been shown to be associated with increased information retention and recall in memory, due to the user’s involvement and personal relevance. VR is increasingly being used as an education tool in the field of medicine, including the education of medical students and in surgical training. However, the use of VR as a patient education tool is much less well understood. A recent scoping review on the use of VR as a patient education tool highlights that VR has the potential to improve patient education and satisfaction, and reduce anxiety, but more research is required, particularly to investigate for whom education via VR might be most beneficial or potentially harmful. For example, evidence suggests that patients respond differently to medical information. Some patients may seek medical information related to their health (ie, monitors), whereas others deliberately avoid this information (ie, blunters). When given excessive information, patients who identify as blunters will experience more tension, which can result in depression and physical discomfort.

On the other hand, those who have a monitoring coping style desire more detailed information. Trialling these new approaches and bridging associated knowledge gaps are likely to be particularly beneficial for patients with cancer undergoing complex new treatments such as immunotherapy.

People affected by cancer who live outside of large metropolitan centres in Australia (ie, a setting described as regional or rural according to the Accessibility/Remoteness Index of Australia (ARIA) as defined by the Australian Bureau of Statistics), on average, experience worse cancer outcomes than their urban counterparts. While the reasons for this are complex, and not fully understood, contributing factors could be the lower levels of health literacy and patient activation (ie, a concept used to describe a patient’s knowledge, skills and confidence in managing their health conditions) in rural areas. Thus, finding new ways to improve patient education in these rural and regional settings may have particular value and positive implications for treatment initiation, adherence, continuation and survival, in rural and regional settings.

Objectives
The aims of this pilot study are to assess the: (1) feasibility of VR as an adjunctive patient educational tool for adult patients with cancer undergoing immunotherapy in a regional cancer centre, and (2) preliminary effectiveness of VR on perceived information provision, knowledge about immunotherapy and patient activation. The specific objectives, including hypotheses, of this pilot study are described in table 1.

METHODS AND ANALYSIS
The development of this protocol was guided by the Standard Protocol Items: Recommendations for Interventional Trials 2013 checklist and procedures.

Trial design
This multi-arm, randomised pilot study features a single-centre, three-arm design with a 1:1:1 allocation (figure 1). Patients undergoing immunotherapy will be recruited and randomised to one of two education intervention groups, or a control group that receives standard immunotherapy education. Those randomised to one of the intervention groups will either receive a VR-based or two-dimensional (2D)-based immunotherapy educational video intervention, in addition to standard care.

Study setting
The pilot study will be conducted at the Central West Cancer Care Centre (CWCCC), Orange Hospital, New South Wales (NSW), Australia. The interventions will be delivered by a credentialed clinical trial coordinator and overseen by the lead researcher (RZ), who is a senior oncologist and director of Clinical Trials Unit at Orange Hospital. The patients randomised to receive the VR intervention will undergo the intervention within the CWCCC under supervision by the trial coordinator. They will be appropriately monitored post-intervention for any adverse events. Online supplemental file 1 outlines the standard of care with the intervention timeline for immunotherapy education at this cancer centre.

Immunotherapy definition
In this study, immunotherapy refers to all cancer therapies that are based on specific immune checkpoint inhibitors (ICIs), including programmed cell death protein 1 and programmed death-ligand 1, and cytotoxic T
lymphocyte-associated protein 4. Patients who receive other forms of immunotherapy, such as adoptive cellular therapies (ie, cellular immunotherapy), which are based on the infusion of immune cells into the body to eliminate cancer, or cancer vaccines, which can be designed to have either therapeutic or prophylactic activity, will not be included.

Eligibility criteria
Inclusion criteria
Patients will be eligible to participate if they meet the following criteria: (a) are 18 years and over, (b) are diagnosed with a reportable cancer of any stage (eg, melanoma, kidney cancer, mesothelioma, lung cancer) that will be treated with ICIs, (c) are due to start only immunotherapy agents (ie, patients may not receive any other combined treatment, such as chemotherapy), (d) are able to understand English and (e) are able to give their own consent. All patients included in this pilot study will be receiving immunotherapy as standard treatment, and not as part of a clinical trial.

Exclusion criteria
Patients will be excluded if they: (a) have a condition that interferes with VR usage, including but not limited to seizures, facial injury precluding safe placement of headset and visual impairments, (b) have a prognosis of <3 months from the time of enrolment per treating oncologist, (c) receive other systemic cancer therapies in combination with immunotherapy, or (d) have a pre-existing severe mental health diagnosis or significant cognitive impairment, such as severe dementia that would impair their comprehension and/or ability to provide informed consent.

Exclusion in case of adverse events
The VR intervention will be performed under direct supervision by a trial coordinator with participants sitting on a chair or bed to ensure safety for trial participants. In the event participants experience unexpected symptoms that could be related to the VR, such as blurred vision, dizziness, light-headedness or nausea, the session will be stopped immediately. Any adverse events or unintended consequences will be managed and documented.

Table 1 Specific objectives and hypotheses of the pilot study

<table>
<thead>
<tr>
<th>Primary objectives</th>
<th>Hypotheses</th>
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<tr>
<td>Related to the feasibility</td>
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<tr>
<td>To assess the acceptability, usability and safety of VR as a patient educational tool in adult patients with cancer undergoing immunotherapy in a regional setting.</td>
<td>N/A</td>
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<tr>
<td>To assess accrual and practicality of conducting a definitive randomised controlled trial.</td>
<td>N/A</td>
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<tr>
<td>Related to the effect of the VR intervention on patient-reported outcomes</td>
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<tr>
<td>To examine the preliminary effectiveness of VR as a patient educational tool in adult patients with cancer undergoing immunotherapy, when compared with a 2D video and educational care as usual.</td>
<td>It is hypothesised that both the VR and 2D group will improve perceived information provision, knowledge of immunotherapy and activation of patients with cancer, compared with educational care as usual. However, it is hypothesised that the results will be more positive in the VR intervention group than in the 2D video group.</td>
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<table>
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<tr>
<th>Secondary objectives</th>
<th>Hypotheses</th>
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<tbody>
<tr>
<td>Related to the effect of the VR intervention on patient-reported outcomes over time</td>
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<tr>
<td>To explore the preliminary effectiveness of VR as a patient educational tool at 2 weeks post-intervention on perceived information provision, knowledge about immunotherapy and patient activation in adult patients with cancer undergoing immunotherapy, when compared with a 2D video and educational care as usual.</td>
<td>It is hypothesised that the use of VR as a patient education tool will result in improved perceived information provision, knowledge of immunotherapy and activation of patients with cancer, when compared with educational care as usual, overtime. It is also hypothesised that the results will improve more in the VR intervention group compared with a 2D video version of the VR experience.</td>
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<tr>
<td>Related to patient information coping styles</td>
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<td>To explore the preliminary effectiveness of VR as a patient educational tool on perceived information provision, knowledge about immunotherapy and patient activation in adult patients with cancer undergoing immunotherapy, stratified by patient information coping styles (ie, monitoring vs blunters).</td>
<td>It is hypothesised that results will have improved more in patients with cancer who identify as monitors (ie, those who seek for health information) compared with blunters (ie, those who prefer to avoid medical information).</td>
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2D, two-dimensional; N/A, not applicable; VR, virtual reality.
Recruitment and withdrawal

All patients, who are advised to undergo immunotherapy treatment during the recruitment period and who meet all eligibility criteria, will be invited to participate in this study. Verbal consent will be obtained 1–3 days after the consultation. The signed informed consent form will be collected by the oncologist or study coordinator on the day of the first education session (see online supplemental file 2). Patients will be free to withdraw from the study at any time point, without consequence.

Sample size

A rule of thumb for pilot studies is to include a minimum of 12 patients per trial arm, so this pilot study will aim to recruit a total of 36 patients with cancer. The results of this pilot study will then inform a power analysis for a future randomised controlled trial (RCT) study, if appropriate.

Randomisation

To ensure participants have an equal and independent chance of being selected in one of three trial arms, a research support unit will produce a computer-generated set of random allocations before the start of the study. The random set of allocations will be sealed in consecutively numbered opaque envelopes and given to participants by the oncologist, who will be concealed to group allocation. Randomisation will happen once the patient has returned a signed copy of the informed consent form.

Blinding

Due to the nature of the intervention, it is impossible to achieve blinding for the participants, those delivering the intervention and the outcome assessors. However, the statistician or researcher who will conduct the analyses will be blinded to treatment allocation.
Interventions

VR group (arm A)
Participants in the VR intervention group will receive immunotherapy education “as usual” plus an immersive, 3D 360° VR experience during or prior to commencing their first immunotherapy treatment. The VR intervention will be delivered by an experienced trial coordinator with the use of a gaming laptop (ie, Gigabyte AORUS 17G XC 17.3-inch Core i7 RTX 3070) and Oculus Quest 2 headset. The VR world shows patients how their immune system reacts to the immunotherapy treatment, what side effects may develop and what patients should do in case they experience any of these side effects (see online supplemental file 3). Participants will be seated throughout the session and will be able to interact within three ways: (1) they will be able to hold a white blood cell (T cell) and move it in space; (2) they will be able to ‘eye witness’ the process of being a foreign cell which is detected and destroyed by CD8 T Cells and (3) they will be able to ‘turn off’ the immune overstimulation by introducing steroid therapy into the scene. The VR experience lasts approximately 5–6 min.

2D video group (arm B)
Participants randomised to this group will receive education as usual and will be shown a 2D video on immunotherapy. The video will be a 2D replica of the immersive, 3D 360° VR experience patients receive when randomised to the VR group (arm A). Patients will watch the video (approximately 5–6 min in duration) on a laptop during or prior to commencing their first immunotherapy treatment.

Control group (arm C)
Participants allocated to the control group will receive education as per usual standard of care, which includes nurse-led verbal education on immunotherapy and provision of printed educational materials (eg, eviQ handouts).

All study groups
Regardless of group allocation, participants will all continue to receive standard medical care from their treating oncologist according to Australian oncology guidelines.

Outcome measures
Study outcomes were designed to determine the feasibility and preliminary effectiveness of VR as a patient education tool, which will determine whether a future RCT is feasible (table 2). Online supplemental file 4 demonstrates the baseline questionnaire for this pilot study.

Feasibility outcomes
The feasibility of VR as a patient education tool will be assessed by looking at the following:
1. Recruitment rate (ie, the number of patients approached, number consenting to participate and those eligible to be randomised).
2. Practicality of the intervention (ie, the degree to which it is possible to deliver the intervention in the event of limited resources, time or commitment).
3. Acceptability of the intervention by health professionals and patients with cancer, including satisfaction, via qualitative interviews.
4. Usability of VR as a patient education tool in the healthcare setting (eg, barriers and facilitators to VR use), via qualitative interviews.
5. Safety of the intervention (ie, VR-related adverse events).

Patient-reported outcomes

Patient information coping styles
Evidence suggests that patients respond differently to medical information. Some patients may seek medical information related to their health (ie, monitors), whereas others deliberately avoid this information (ie, blusters). This may affect how participants respond to the VR intervention; hence, monitoring and blunting coping styles will be assessed with the shortened version of the Threatening Medical Situations Inventory (TMSI). The shortened TMSI consists of two hypothetical situations, including experiencing headaches and dizziness, and considering heart surgery. Each description is followed by six items, three monitoring and three blunting coping styles (at random), for which participants are asked to score the items on a 5-point Likert scale (response options range from 1='not at all applicable to me' to 5='strongly applicable to me'). Blunting subscale scores will be subtracted from the monitoring subscale scores to calculate a sum score. Patients who have a sum score equal or below the median will be categorised as monitors. Subsequently, patients reporting a subscore above the median will be categorised as blusters. The internal consistency has shown to be good for both the monitor and blunting subscale (Cronbach's α>0.70), and test–retest reliability has been established as sufficient (Pearson correlation, 0.64–0.83).

Perceived information provision
The 25-item European Organization for Research and Treatment Quality-of-Life Group Information Questionnaire (EORTC QLQ-INFO25) will be used to evaluate the information received by patients with cancer about aspects of their disease and treatment. The EORTC QLQ-INFO25 questionnaire is composed of four multi-item subscales (ie, information about the disease, medical tests, treatment and other care services) and eight single-item scales. Patients rate the items on a 4-point Likert scale (ranging from 1='not at all' to 4='very much'), except for four items, which have a dichotomous (yes/no) response. Following the EORTC scoring manual, scores are transformed to a linear scale from 0 to 100, for which a higher score is seen as better-perceived information. The test–retest reliability has been established as good (intraclass correlation, 0.71–0.91).
Knowledge about immunotherapy

No standard method for the assessment of knowledge of immunotherapy of patients with cancer was identified in the literature. Therefore, a new immunotherapy study-specific, true/false questionnaire was drafted by a psycho-oncology researcher, with experience working as a clinical psychologist in a tertiary cancer centre (KMG), based on the true/false questionnaire format employed in a previously published study on the knowledge of patients with cancer and a list of key pieces of knowledge that need to be conveyed to immunotherapy patients (eg, eviQ). It was then reviewed and revised in an iterative process by an experienced oncologist (RZ) and clinical nurse researcher (DM). Twenty items were deemed adequate for assessing patient’s knowledge as a review showed that the majority of studies measuring patient’s knowledge in patient education use 20 items. The questionnaire broadly asks questions in the following categories: (a) the basic mechanism behind checkpoint immunotherapy, (b) mechanistic differences between chemotherapy and immunotherapy, (c) identification of likely and unlikely side effects attributable to immunotherapy, and (d) when to report problems to the cancer care team. The face validity of the questionnaire was tested by a group of experts and patients, then field tested with patients who were currently undergoing or had been treated with immunotherapy in the past. Comments and queries were collated, and the questionnaire was refined until a consensus was reached by DM and RZ.

Patient activation

The 13-item version of the Patient Activation Measure (PAM-13) will be used to measure patient activation. A critical component of immunotherapy education is to improve a patient’s ability to self-report side effects as early as possible in order to prevent or minimise the...
development of grade 3 or 4 toxicities, by implementing countermeasures such as steroids to limit the severity of the event. The PAM-13 is designed to measure the patient’s self-reported knowledge, skill and confidence in managing one’s health or chronic condition.\textsuperscript{38, 49} Participants are asked to score the items on a 5-point Likert scale (ranging from 1=‘strongly disagree to 5=‘strongly agree’) including an additional ‘not applicable’ option. A PAM score is calculated by dividing the raw score by the number of answered items (except non-applicable items) and multiplying by 13. The score will then be transformed to a linear interval scale of patient activation scores, ranging from 0 to 100, with higher scores indicating higher patient activation.\textsuperscript{50} Within the converted scale, patients will be categorised into one of four patient activation levels using cut-off points: score of ≤47 for level 1 (not having confidence to take an active role in their care); 47.1–55.1 for level 2 (not having knowledge and confidence to take action in self-management); 55.2–67.0 for level 3 (starting to take action but lacking necessary confidence and skills) and ≥67.1 for level 4 (adopting self-management behaviours with possible lack of maintenance of these behaviours).\textsuperscript{49, 50}

**Sociodemographic-related and disease-related outcomes**

Demographic characteristics will be obtained through a self-administered questionnaire at baseline, including age, gender, level of education, employment status and marital status. Area-level socioeconomic status will be obtained by postcode and will be derived from the Index of Relative Socioeconomic Disadvantage from the Socio-Economic Indexes for Areas.\textsuperscript{51} Remoteness will be classified according to ARIA, and will be categorised into major cities of Australia, inner regional Australia, outer regional Australia, remote Australia and very remote.\textsuperscript{52} Use of internet will be obtained by asking ‘How often do you use the internet?’, with answer options categorised into daily, weekly, monthly, never or unknown. Comorbidity will be assessed by presenting a list of comorbidities, for which answers will be categorised into no comorbidities, 1 comorbidity or >1 comorbidity. Type of cancer, stage of cancer and date of diagnosis will be obtained from hospital records with permission. Participants will also be asked whether anyone helps them with making medical decisions, if they have a smartphone and for how many hours (ie, 0–2, 3–4, 4–8, or more than 8 hours) they use electronic devices during the day.

**Data collection methods and timeline**

The time points for enrolment, interventions and assessments are summarised in **table 3.** Please note that days are estimates based on the average time frame of patients with cancer undergoing immunotherapy at the study’s cancer centre, and thus exact days may vary from patient to patient. It is anticipated that the study recruitment will

**Table 3** Participant data collection timeline

<table>
<thead>
<tr>
<th>Time points</th>
<th>Study period</th>
<th>Enrolment</th>
<th>Randomisation</th>
<th>Post-randomisation</th>
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<td>−t1</td>
<td>t0</td>
<td>t1</td>
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<tr>
<td>Enrolment</td>
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<td>Eligibility screening</td>
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<td>Verbal consent</td>
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<td>Baseline questionnaire</td>
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<td>Randomisation</td>
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<td>Interventions</td>
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<td>2D video</td>
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<td>Treatment as usual</td>
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<td>Knowledge</td>
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<td>Patient activation</td>
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<td>Qualitative interview</td>
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*Only participants in the VR intervention group will be interviewed.

†Qualitative interviews will be held 1–3 days after the patient’s first immunotherapy treatment session.

2D, two-dimensional; VR, virtual reality.
commence in July 2023 and will be completed 12 months later.

Enrolment (t1)
Patients will be referred to the oncologist for their first consultation (day 0). During this consultation, the oncologist will explain to the patient that immunotherapy is indicated for their cancer and will briefly outline the mechanism of action of immunotherapy, which includes verbal information and a printout (eg, NSW Cancer Institute eviQ immunotherapy https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/immunological/1993-management-of-immune-related-adverse-events). If a patient consents to receive immunotherapy, the oncologist will determine whether the patient is eligible to participate in the current study, and if so, explain the study to the patient. Those who are interested in participating will be provided with an envelope containing the participant information and consent form (PICF) and baseline questionnaire. The latter will include questions on the patient’s demographics, information coping style (ie, TMSI), perceived information provision (ie, EORTC QLQ-INFO25), knowledge quiz and activation assessment (ie, PAM-13). Over the next few days (days 1–3), the oncologist or study coordinator will call the patient to answer any questions and then verbally consent them into the study, and if consent is given, they will fill out the baseline questionnaire and bring the completed forms to their standard of care immunotherapy educational session. During the recruitment period, the oncologist will track the number of eligible patients approached and reasons for refusal on a case report form (see online supplemental file 5).

Randomisation (t0)
Upon the patient’s arrival to the standard of care education session (days 7–10), the oncologist or study coordinator will ask the patient for the completed forms. The study coordinator will check if the patient has consented to the study, which triggers randomisation to one of the three intervention arms: arm A—standard education+2D video; arm B—standard education+VR experience; arm C—standard education. The oncologist or study coordinator will countersign the PICF.

Post-randomisation (t1 and t2)
Following the standard of care education session, during which nurses take patients through the eviQ checklist, patients can start to receive their first immunotherapy treatment. This can occur on the same day of the education session or on a later day, depending on the distance to the treatment centre. While patients are receiving their first treatment, those randomised to the VR intervention group or 2D video group (arm A or arm B, respectively) will be given the additional education session, whereas participants in the control group will continue with standard of care. On the day of the first immunotherapy treatment, all patients will be given the first follow-up questionnaire (t1), which will include questions on the patient’s perceived information provision (ie, EORTC QLQ-INFO25), knowledge quiz and activation assessment (ie, PAM-13). A second follow-up questionnaire (t2), including the same questions, will be given to all patients approximately 2 weeks after their first immunotherapy treatment (day ±24). Patients will have been given a sealed envelope containing the questionnaire after their first treatment session and a trial nurse will phone the patient to complete it on a specific day. In addition, participants randomised to the VR intervention will be briefly interviewed about the feasibility of VR as a patient education tool, similar for health professionals. Interviews will be conducted by a member of the research team in person, over the telephone or via Zoom, depending on the patient’s preference (days 11–13). Box 1 details the topic guide for these interviews, which is based on literature and a methodological framework for the application of VR in healthcare.

Data management and monitoring
All patient-related data that are collected and analysed will be de-identified by assigning a randomly generated 4-digit, numerical code on receipt of the written PICF. Patient-reported outcome data will be transferred manually from the questionnaires to an electronic SPSS (version 25) database sheet. All collected data, including qualitative data, will be stored on a protected server of the NSW Health. As per the National Health Medical Research Council guidelines on the retention of clinical trial data, research data will be retained for 15 years following study completion, after which it will be permanently deleted from the server. Paper-based data will be stored in a locked office at the study site and will be destroyed after 15 years, by disposing of it in confidential bins that go to an office shredder.

The lead researcher (RZ) and research team will be responsible for monitoring data safety and integrity. Specific monitoring tasks will include:
- Monitoring patient accrual: data will be collected and analysed periodically during the recruitment period (ie, May 2023–May 2024), and reviewed by the lead researcher and project manager.
- Monitoring adverse events: all trial coordinators will be given an information education session on how to use the VR and the possible adverse events that may occur. If an adverse event is determined to be likely due to study participation or the immunotherapy,
Monitoring study progress: patient-reported outcome data will be collected by the research team and monitored by the lead researcher and, if necessary, by a biostatistician. The lead researcher and project manager will meet regularly to monitor recruitment and patient safety. Following publication of all study results, deidentified participant-level data may be made available on reasonable request to the lead researcher.

Data analysis plan

Feasibility outcomes

Recruitment data will be summarised using a rate and 95% CI using the Poisson distribution. Accceptability and appropriateness of study measures will be summarised using a proportion and 95% CI, which will be estimated using the Wilson method. The practicality of VR (ie, time spent by the study coordinator completing intervention-related activity) will be recorded in the study coordinator’s data collection instrument, including total time spent per patient as well as activity-specific time (eg, intervention preparation). Any adverse events related to the use of VR will also be recorded in the study coordinator’s data collection instrument. Means and SDs will be used to summarise time data. The feasibility outcomes will be judged against prespecified criteria, where appropriate (table 2).

Effectiveness outcomes

SPSS (version 25) will be used for descriptive and inferential statistical analysis to explore the feasibility and preliminary effectiveness of the VR on the dependent variables (ie, information provision, knowledge and patient activation). Data will be analysed according to the intention-to-treat analysis method. Linear, multilevel regression analysis, with random intercept on patient level to adjust for intradependency between repeated measures, will be used to assess the impact of VR on patient-reported outcomes (ie, information provision, knowledge and patient activation). An interaction term of information coping style and trial arm (control will be the reference group and will be compared with the intervention groups), with selected covariates (ie, demographic and clinical data obtained), will be added to assess the moderating effect of information coping style on the outcome measures. The analyses will be stratified by information coping style whenever the interaction term of coping style and trial arm is significant. To compensate for the multiple comparisons and control for type I error, Bonferroni will be employed. Statistical significance will be determined as p<0.05 (two tailed) and estimates will be presented with 95% CI.

Qualitative data

The acceptability and usability of the VR intervention will also be explored by using qualitative interviews with health professionals and participants who have experienced the VR intervention. Qualitative methods provide an additional layer of data that can inform intervention development and provide insights for a larger trial, when used concurrently with quantitative methods in a pilot study. For this reason, as well as not to burden patients, qualitative methods will be used to explore the acceptability and usability constructs, rather than adding quantitative methods. The interviews will be audio-recorded, transcribed and analysed using thematic framework analysis. Interview data that relate to the research questions will be arranged in an Excel spreadsheet. The researchers will first familiarise themselves with the data by reading and rereading the data and noting initial ideas. Thereafter, data will be coded, and codes will be collated into potential themes. Thematic maps will be constructed and discussed, after which the themes will be defined and presented alongside corresponding data.
Patient and public involvement
The research team tested the VR intervention as well as the knowledge questionnaire for face validity, comprehension and acceptability with patients in an iterative process that involved making revisions and then retesting content with other consumers. No further patient and public involvement for the pilot study is anticipated.

Ethics and dissemination
This study was approved by the Greater Western Human Research Ethics Committee, NSW Local Health District (ID: 2022/EHT01760) and registered in the Australian New Zealand Clinical Trials Registry (ID: ACTRN12622001473752). Informed consent will be obtained from all participants; on consent, each participant is assigned a randomly generated study identification code. All identifying information will be removed from the qualitative interview transcripts. The results will provide data to inform the feasibility of a future RCT, including sample size calculations. Findings will be published in peer-reviewed journals, and results will be shared broadly via conference presentations.

Author affiliations
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Contributors
All authors (SRvdK, KMG, HM, DM, KS and RZ) contributed to initial planning of the pilot study and to subsequent development of the protocol. The first author of this protocol paper (SRvdK) wrote the initial draft of the manuscript. All authors (SRvdK, KMG, HM, DM, KS and RZ) approved the final version of this manuscript.

Funding
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Competing interests
None declared.

Patient and public involvement
Patients and/or the public were involved in the design, conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication
Not required.

Provenance and peer review
Not commissioned; externally peer reviewed.

Supplemental material
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REFERENCES


Intervention Timeline

1. **Baseline: Referred to oncologist / first consultation with oncologist (day 0)**

When patients are referred to the oncologists, on the day of the first consultation, they often see the oncologist’s Basic Physician Trainee (BPT) or Registrar first where a detailed history and examination are performed which lasts around 40 minutes. Thereafter, they will have the consultation with the oncologist for around 15-20 minutes. During this period the oncologists explains to the patient that immunotherapy (IO) is indicated for their cancer and briefly outlines the mechanism of action of IO therapy. Lastly the oncologist will deliver the standard of care immunotherapy education.

Patients will be given verbal information, a printout (e.g., NSW Cancer Institute eviQ immunotherapy) and referred to literature on immunotherapy during the consultation with their oncologist.

After the consultation, an appointment will be made for the patient’s first treatment session and an appointment for a face-to-face standardised IO education session delivered by a nurse will be arranged. This usually takes place within 7-10 days of their oncologist appointment.

During the initial appointment the oncologist would explain the VR study to patients who have consented to undergo IO therapy. These patients will be provided with an envelope containing the “Participant Information and Consent Form” (PICF), “Informed Consent Form”, and “Baseline Questionnaire”. In the next few days, the oncologist/study coordinator would call the patient to verbally consent them onto the study. Patients would sign the PICF Patients and bring the completed forms to the first IO infusion appointment. The oncologist/study coordinator would counter sign the PICF

2. **Follow-up 1: First IO treatment appointment (day 7-10)**

Prior to their first treatment, patients are educated in what is involved in immunotherapy i.e., the mechanisms and side effects of IO. During this session, nurses take patients through a checklist (eviQ). This session can occur prior to their treatment or on the day of their treatment depending on the distance to the treatment centre.

Subjects participating in the VR study would have brought back the signed copy of the PICF and filled out the “Baseline Questionnaire”. The treatment nurse checks if the patient has consented to the study which triggers randomisation to one of the three intervention arms; Arm A – standard education + VR experience, Arm B – standard education + 2D Video, Arm C – standard education. Following the standardised education session, patients can start to receive their first IO treatment. Patients will be sitting in a chair in a room with other people (+/- 6) during treatment.

While patients are receiving their first IO treatment, they will be given the additional education intervention (Arm A or Arm B) and all patients will be given the follow-up questionnaire. They can fill this out during or after treatment.

Due to the nature of the intervention, patients and those delivering the intervention cannot be blinded to group allocation.
3. **Follow-up 2: Two weeks after first treatment (day +/- 24)**

Patients will be called for second follow-up. This is the usual standard of care for patients on IO therapy. Patients will be asked the same questions from the knowledge questionnaire, the EORTC QLQ-INFO25, and PAM-13.

Patients in Arm A (VR intervention) will also be asked some qualitative questions.

**Interventions**

**Virtual reality group – (Arm A)**

Participants in the immersive VR intervention group will receive care as usual plus an immersive, 360° VR experience. The VR intervention will be a 3D version of the 2D video that shows how the immune system responds to cancer cells, as well as what side effects may occur and what to do. This will be delivered whilst the patient is in the treatment chair.

The VR equipment will consist of:

- 4x Gigabyte AORUS 17G XC 17.3 inch Core i7 RTX 3070 gaming laptop. Model: AORUS 17G XC-8AU6430SH
- 4x Oculus Quest 2 128 GB

**2D video group (Arm B)**

The active control group will receive care as usual and will be shown an informative 2D video on immunotherapy. The video is made by the Cambridge University and can be found on their YouTube channel (www.youtube.com/watch?v=ntk8XsxVDd0). The video captures the behaviour of cytotoxic T cells – the body’s ‘serial killers’ – as they hunt down and eliminate cancer cells before moving on to their next target.

**Standard of Care group (Arm C)**

This will be the usual consultation with the consultant and the standardised nursing led education session before the first immunotherapy session.
Main Participant Information Sheet/Consent Form

Orange Hospital

Title: Assessing the Feasibility and Acceptability of a Virtual Reality educational module to improve cancer patients understanding of Immunotherapy

Protocol Number version 2.0

Local Sponsor: Western NSW LHD

Coordinating Principal Investigator/Principal Investigator: A/Prof Rob Zielinski
ph: (02) 6369 3380
rob.zielinski@health.nsw.gov.au

Associate Investigator(s)
(if required by institution)
Dr Kate Gunn, University of South Australia
Dr Hamish MacDougall, Sydney Local Health District
Dr Donna Milne, Peter MacCallum Cancer Centre
Shannen Van Der Kruk, University of South Australia
Katherine Smith, University of Sydney

Location Orange Health Service – 1530 Forest Road, Orange NSW 2800

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in a clinical research project. This is because you are diagnosed with cancer and have been prescribed immunotherapy medication. The research project is testing whether a virtual reality educational model will assist with your understanding of how immunotherapy will work.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research project.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend, or your local doctor.

Participation in this research is voluntary. If you don’t wish to take part, you don’t have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign and date the form in the consent section. By signing it you are telling us that you:

- Understand what you have read.
- Consent to take part in the research project.
- Consent to have the tests and treatments that are described.
- Consent to the use of your personal and health information as described.
You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The purpose of this research project is to determine if cancer patients find a virtual reality educational model helpful and useable. The main objective is to determine whether giving patients an extra virtual reality experience will improve their understanding of how immunotherapy drugs work and what type of side effects you might develop. By being better informed the researchers believe you will be able to identify side effects sooner which means they can be treated earlier.

Virtual reality is administered by wearing a headset with the aim of immersing a person into a simulated or computer generated world. It is not new technology and has been utilised in computer gaming as well as medical research. However, its role in how it might improve cancer education has not been greatly studied. The researchers hope to learn if virtual reality devices are easy to use and acceptable to cancer patients and also to determine if they help patients gain a better understanding of their immunotherapy treatment.

3 What does participation in this research involve?

This is a randomised pilot study where patients will be randomly allocated into one of three groups. All participants receive their cancer treatment. The only difference will be what type of immunotherapy education they receive.

In this project all participants will receive the standard of care education given to all patients about to embark on immunotherapy treatment. This education explains how the treatment works, how it is given and what side effects it may cause. The education is delivered by your treating doctor, the nurses administering the immunotherapy and information booklets.

Arm A participants will receive the standard of care education plus a 5-7 minute virtual reality experience. This will be delivered in the clinic room with your doctor/nurse present. You will wear an Oculus 2 Headset and be seated for the entire experience. The experience will transport you into the human body so you can experience and witness how the immune system detects and destroys cancer cells and how it interacts with your body. You will be able to interact with the cells in this experience.

Arm B participants will receive the standard of care education plus a 2D YouTube video of the virtual experience described above. You will not wear an Oculus Headset and the experience will not be interactive.

The group receiving the standard of care education described above will be the control arm, or Arm C.

- Arm A: Will receive Standard of Care (SoC) plus a virtual reality (VR) interactive experience;
- Arm B: Will receive SoC plus a 2 dimensional recording of the VR experience;
- Arm C: Will receive (SoC) immunotherapy education.

STUDY PROCEDURES

Various procedures will be performed each time you visit the site for immunotherapy treatment. Your study doctor might need to repeat any of these procedures at times other than those specified below if he/she feels it is necessary for your safety.

After your study doctor has determined that you meet all the criteria for participation, you will be given this Informed Consent Form by the study staff and you may review the document in detail. If you agree to take part in this research project, you must sign the consent form at the end of this document before any study procedures begin. However, signing this consent form does not mean that you are eligible for the research project.
This research project is made up of the following parts:

- Screening Period
- Immunotherapy Education

It is anticipated that you will be in this study for 6 weeks depending on how well you cope with the immunotherapy treatment. Refer to Table 1 for a summary of visits and study procedures.

**Screening Period**

There are no invasive screening tests to help the study doctor decide if you are eligible for this research project. The study doctor will ask you questions to determine if there is any medical condition that may increase your chances of not tolerating the VR experience, such as vertigo, dizziness, seizures.

The following Screening questions will be performed:

- Your demographic information (e.g., your age, postcode, marital status)
- A check of your current health status, medical history and previous/current treatments you were/are taking.

**Immunotherapy Education**

All participants will be randomly assigned to one of the three study arms. “Randomly assigned” means that you will be allocated to an education model by chance, like flipping a coin or drawing names out of a hat. You have a 33.3% (1 in 3) chance of being given the standard education experience, 33% chance of being given SoC + VR experience and a 33% chance of being given Standard of Care + YouTube video of the VR experience.

If you are found to be eligible to take part in this study, you will be assigned to one of three groups. On the day of your first immunotherapy treatment at Orange Hospital, you will receive the standard of care education from a nurse who will explain how immunotherapy works, what side effects you might experience and what to do if you experience any of the side effects. The nurse will also give you some pamphlets to read about immunotherapy.

If you are assigned to the group that undertakes the VR experience or watches a 2D video, you will have an additional session that will happen during your first immunotherapy treatment session.

You will be asked to complete some written questionnaires before and straight after your immunotherapy session, to help us understand if the type of education you received was effective (or not). You’ll be asked to complete the questionnaires again two weeks later.

If you are in the group who received the VR experience, we will also arrange a time with you a few days after your first immunotherapy session to ask you some questions to get your opinion about the VR experience and if it was helpful as an education tool (or not). This brief interview can take place on the phone, via video call (eg: Zoom) or in person if that is convenient.

**Administration of VR Experience**

If you are assigned to the group that receives the VR experience, the nurse will show you the VR headset you’ll wear and explain how it works. There may also be hand controllers that you can use to interact with the virtual reality world.

The nurse will help you put the headset on, and when you are comfortable, she will press a button on a laptop to start the VR experience. The VR experience will run for 5-7 minutes. In this time you will be taken through a 3D virtual experience where you will see and hear how the immunotherapy affects your cells, how it helps fight cancer and about some of the common side effects. There may also be hand controllers that you can use to interact with the virtual reality world. You will stay seated on a chair during the virtual reality experience.
If you feel unwell or uncomfortable at any time during the VR experience, let the nurse know and they will stop the VR experience straight away.

**Follow Up Period**

It is desirable that your local doctor be advised of your decision to participate in this research project. If you agree, your local doctor will be informed of your participation in this research project.

**Table 1 – Simplified study treatment schedule**

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Arm A – virtual reality</th>
<th>Arm B – 2D video</th>
<th>Arm C – SoC</th>
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<td>- Screening for eligibility</td>
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<td>- Verbal consent</td>
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<td></td>
<td>- Baseline assessment</td>
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<table>
<thead>
<tr>
<th>Week 2-4</th>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm C</th>
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<tr>
<td></td>
<td>- Informed consent</td>
<td>- Informed consent</td>
<td>- Informed consent</td>
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<td></td>
<td>- Randomization</td>
<td>- Randomization</td>
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<td></td>
<td>- First immunotherapy session</td>
<td>- First immunotherapy session</td>
<td>- First immunotherapy session</td>
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<tr>
<td></td>
<td>- Follow-up assessment 1</td>
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<table>
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<tr>
<th>Week 5</th>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm C</th>
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<tr>
<td></td>
<td>- Interview (20-30 minutes)</td>
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<tr>
<th>Week 5-6</th>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm C</th>
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<tbody>
<tr>
<td></td>
<td>- Follow-up assessment 2</td>
<td>Follow-up assessment 2</td>
<td>Follow-up assessment 2</td>
</tr>
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</table>

4 **What do I have to do?**

If you decide to be in this research project, there are certain requirements you must follow before, during, and after the research project. Some are listed below, but there could be others that your study doctor will discuss with you:

- You must be willing to attend all the scheduled visits (including screening, treatment and follow up visits) to the study site.
- If you decide to participate in this research study you will have to sign this consent and authorisation form.
- Keep your study appointments as listed above, including the follow-up visit. If you cannot keep an appointment, contact your study doctor or study staff to reschedule as soon as you know that you will miss the appointment.
- Tell your study doctor or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Ask questions as you think of them, and tell your study doctor or research staff if you change your mind about staying in the study.
- If you decide to take part in this research project, it is very important that you attend all visits as scheduled, including the follow-up visit.
- You must follow all instructions given to you while you are participating in this research project. If you do not, you may be removed from the research project. If you are unsure about what you are supposed to do, ask the study doctor.

5 **Other relevant information about the research project**

Participation in the study will not require any additional travel time as the intervention and questionnaires will be arranged when you are already at the hospital for treatment.
If you agree to take part in this research project, you will be one of about 36 participants. This research project is open to male and female participants, who meet all of the requirements. You’ll be eligible to participate if you meet the following criteria:

- are 18 years and over,
- are diagnosed with a reportable cancer of any stage (e.g., melanoma, kidney cancer, mesothelioma, lung cancer) that will be treated with immunotherapy,
- are due to start only immunotherapy agents (i.e., patients may not receive any other treatment, such as chemotherapy or radiotherapy),
- are able to understand English, and
- are able to give their own consent

All patients who will be included in this pilot study will be receiving immunotherapy as standard treatment, and not as part of a clinical trial.

**Costs**

There are no additional costs associated with participating in this research project, nor will you be paid. All medical care required as part of the research project will be provided to you free of charge.

**6 Do I have to take part in this research project?**

Participation in any research project is voluntary. You should not feel obligated to agree to participate. If you decide not to participate, tell your study doctor. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Orange Hospital.

If you decide to participate, you will be told of any important new information that is learned during the course of this research project, which might affect your willingness to continue participation in this research project.

**7 What are the alternatives to participation?**

You do not have to take part in this research project in order to receive immunotherapy treatment at this hospital.

**8 What are the possible benefits of taking part?**

You may or may not directly benefit from participating in this research project. Your participation in the study may benefit other participants in the future by giving important information about the use of virtual reality experiences in cancer immunotherapy education.

**9 What are the possible risks and disadvantages of taking part?**

It is possible that you may feel motion sickness using the virtual reality goggles. You may also experience other virtual reality side effects associated with wearing a virtual reality headset, which could include any of those listed below.

- General discomfort
- Fatigue
- Headache
- Eyestrain
- Difficulty focusing
- Increased salivation
- Sweating
- Nausea
- Difficulty concentrating
- Fullness of head
- Blurred vision
- Dizzy (eyes open)
- Dizzy (eyes closed)
- Vertigo
- Stomach awareness
- Burping

One or more of these side-effects might be experienced by any one study participant.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get, even if you do not think these problems are caused by the study. Please understand that you are free to withdraw at any time during the study. If you are worried about anything while in this study, please speak to the researchers or please call the Principal Investigator on the telephone number on page 1.

Although unlikely, it is possible that you could feel upset when answering questions about your experiences with the virtual reality. If you do find any of the questions upsetting or don't want to answer a question, you don't have to, and a researcher will be available to talk with you about this.

10 What if I withdraw from this research project?

You are free to stop participating in this study at any time. If you stop, you will not lose any medical benefits except for any benefits that you might have been receiving in connection with this research project.

If you decide to withdraw from the research project, please tell your study doctor and you will be asked to sign a “Withdrawal of Consent” form. They can tell you about stopping all or part of the research project activities, discuss any health risks or special requirements linked to withdrawing and what other care is available for you.

If you do withdraw your consent during the research project, the study doctor and relevant project team members will not collect additional personal information from you. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must inform the study doctor.

11 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons, such as:

- Unacceptable side effects
- The research project is stopped by the sponsor for reasons not related to you

The study doctor or the sponsor may stop your participation in the research project for a variety of reasons. The study doctor will tell you if this happens. These may include the following reasons:
You are not able to complete the study procedures as required
You do not consent to continue in the research project after being told of changes in the research that may affect you, or for any other reason.

Part 2  How is the research project being conducted?

12  What will happen to information about me?

The study will gather certain personal information about you. This information will be held by Orange Hospital and will be re-identifiable.

Your data will be stored by Orange Hospital, the Sponsor, for a minimum of 15 years after the completion of the research project and will be accessed by the Sponsor. It will be disclosed only with your permission, or as required by law.

Your treating doctor/s will be notified of your participation in this study and the exchange of clinically relevant information noted by the trial doctor in the conduct of the trial will occur.

Unless required by law, only your doctor, the study team, the Sponsor and Far West Human Research Ethics Committee will have access to data which identifies you by name or from which your identity is otherwise apparent or can be reasonably ascertained.

Your medical files may be reviewed at the hospital (or study doctor’s office) or remotely (outside of the study centre) in order to check the information and verify the clinical study procedures, without breaking your confidentiality. If your medical files are reviewed remotely, the records will include your participant code but will not include your name or other directly identifiable information, unless these records will be reviewed directly through the study centre’s secure electronic medical records portal.

All personal information will be used only for the purpose of administering your participation in this study and in accordance with the laws governing the protection and privacy of personal information under Australian privacy legislation.

In most cases, you have the right to access personal information collected from you in connection with the study and request corrections of any such personal information that is incorrect.

13  Complaints and compensation

If you are injured as a result of your participation in this trial, you may be entitled to compensation. There are two avenues that may be available to you to seek compensation.

1) Sponsors of clinical trials in Australia have agreed that the guidelines developed by their industry body, Medicines Australia, will govern the way in which compensation claims from injured participants are managed by sponsors.

However, as guidelines, they do NOT in any way dictate the pathway you should follow to seek compensation. The sponsor is obliged to follow these guidelines.

These guidelines are available for your inspection on the Medicines Australia Website (www.medicinesaustralia.com.au) under Policy – Clinical Trials – Indemnity and Compensation Guidelines. Alternatively, your study doctor can provide you with a hard-copy of the guidelines.

2) You may be able to seek compensation through the courts.

It is the recommendation of the independent ethics committee responsible for the review of this trial that you seek independent legal advice before taking any steps towards compensation for injury.
14 **Who is organising and funding the research?**

This research project is being conducted and sponsored by the Central West Cancer Care Centre located within the Orange Hospital. Orange Hospital is a part of Western NSW Local Health District which is a part of the NSW Government.

Project costs are being covered by funding received from Cancer Care West NSW Inc, AstraZeneca Australia, Bristol Myers Squibb and Roche Australia.

The Sponsor may benefit financially from this research project if, for example, the project assists the Sponsor to obtain approval for the virtual reality experience.

You will not benefit financially from your involvement in this research project.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to the Sponsor, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

15 **Who has reviewed the research project?**

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC).

Greater Western Human Research Ethics Committee has reviewed and approved this study in accordance with the National Statement on Ethical Conduct in Human Research (2018) incorporating all updates.

This Statement has been developed to protect the interests of people who agree to participate in human research studies. Should you wish to discuss the study or view a copy of the Complaint procedure with someone not directly involved, particularly in relation to matters concerning policies, information or complaints about the conduct of the study or your rights as a participant, you may contact the Greater Western HREC on 02 6330 5948.

16 **Further information and who to contact**

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor Associate Professor Robert Zielinski on 02 6369 3380.

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

<table>
<thead>
<tr>
<th>Reviewing HREC name</th>
<th>Greater Western Human Research Ethics Committee.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HREC Executive Officer</td>
<td>Phil Sanders</td>
</tr>
<tr>
<td>Telephone</td>
<td>02 6330 5948</td>
</tr>
<tr>
<td>Email – Delete if not required</td>
<td><a href="mailto:phil.sanders@health.nsw.gov.au">phil.sanders@health.nsw.gov.au</a></td>
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</tbody>
</table>
Main Consent Form

Title
Assessing the Feasibility and Acceptability of a Virtual Reality educational module to improve cancer patients understanding of Immunotherapy

Protocol Number
V2.0

Local Sponsor
Orange Hospital

Coordinating Principal Investigator/Principal Investigator
A/Professor Robert Zielinski

Associate Investigator(s)
Dr Kate Gunn, University of South Australia
Dr Hamish MacDougall, Sydney Local Health District
Dr Donna Milne, Peter MacCallum Cancer Centre
Shannen Van Der Kruk, University of South Australia
Katherine Smith, University of Sydney

Location
Orange Health Service – 1530 Forest Road, Orange NSW 2800

Declaration by Participant

Participant Signature of Consent:

In signing this section, I confirm that:

- I am aged between 18 - 90 years old.
- I have read the Participant Information Sheet, or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the project.
- I understand, I will be informed in a timely manner, of any information that may impact my willingness to continue participation in the study.
- I give permission for my local doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Orange Health Service concerning my personal information (including full date of birth, race and ethnicity), disease and treatment for the purposes of this project. I understand that such information will remain confidential.
- I understand that my medical files may be reviewed remotely, and will include my study participant number, unless these records will be reviewed directly through the study centre’s secure electronic medical records portal.
• I agree that if I decide to withdraw and leave the research project, the information and
data collected about me up to the point when I withdraw may continue to be used.
• I have had an opportunity to ask questions and I am satisfied with the answers I have
received.
• I freely agree to participate in this research project as described and understand that
I am free to withdraw at any time during the research project without affecting my
future health care.
• I allow the study doctor and his/her study staff to complete the study procedures
outlined in this information sheet.
• I understand that I will be given a signed copy of this document to keep.
• I do not give up any of my legal rights by signing this Consent Form

Name of Participant (please print) ________________________________________________
Signature ____________________________ Date ____________________________

[The below witness section will be required for any Participant who is unable to read]
Under certain circumstances (see Note for Guidance on Good Clinical Practice CPMP/ICH/135/95
at 4.8.9) a witness* to the informed consent process may be required. If a participant is unable to
read, an impartial witness should be present during the entire informed consent discussion.

By signing the consent form, the witness attests that the information in the consent form and any
other written information was accurately explained to, and apparently understood by the
participant, and that informed consent was freely given by the participant.

☐ Not Applicable

Name of Witness* to the
Informed Consent process
(please print) ________________________________
Signature ____________________________ Date ____________________________

*Witness is not to be the investigator, a member of the project team or their delegate.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe
that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) ________________________________
Signature ____________________________ Date ____________________________

†A senior member of the research team must provide the explanation of, and information concerning, the research
project.

Note: All parties signing the consent section must date their own signature.
1. Demographic Questions

1. What gender do you identify with?
☐ Male ☐ Female ☐ Other _______________________

2. What is your date of birth (e.g., 11 November 1967)? ____________________

3. What is your postcode? ______________

4. What is your marital status?
☐ Married or living with a partner
☐ Separated/ divorced
☐ Widowed
☐ Never married

5. Do you rely heavily on other people to help make your medical decisions?
☐ Yes ☐ No

6. If the answer is yes, what is your relationship to this person?
_______________________________________

7. What is the highest educational qualification you have completed?
☐ Did not finish primary school
☐ Finished primary school
☐ Finished high school
☐ Trade certificate, apprenticeship, diploma or certificate from a college or TAFE
☐ Degree or diploma from a university
☐ Postgraduate degree

8. What is your employment situation?
☐ Full-time employment
☐ Part-time employment
☐ Not employed and not looking for a job
☐ Not employed and looking for a job
☐ Retired

9. How often do you use the Internet?
10. Do you have a smartphone?
☐ Yes ☐ No

11. How many hours do you use computers, smartphones, tablets during the day?
☐ 0-2 hours
☐ 3-4 hours
☐ 4-8 hours
☐ More than 8 hours

12. Do you currently suffer from any conditions that affect your judgement or decision making (e.g., dementia, psychosis, schizophrenia)?
☐ Yes ☐ No

13. If the answer is yes, what is the name of the condition?
______________________________
(If the answer is yes, potential participant will be screened for suitability for participation in study)

14. Do you have any of the following comorbidities? (Multiple answer options possible)
☐ None
☐ Hypertension (use non-medical terms)
☐ Cardiovascular/ Heart disease
☐ Hypercholesterolemia
☐ Diabetes, type 2
☐ COPD
☐ Chronic kidney disease
☐ Chronic liver disease
☐ Other b: ________________________

* Cardiovascular disease includes cardiomyopathy and heart failure.

b Other includes anaemia, asthma, inflammatory bowel disease, epilepsy, chronic respiratory insufficiency, endocrine disorders, connective tissue diseases, neurologic disorders, chronic pancreatitis, immunocompromise, and organ transplant.
15. When were you diagnosed with cancer (e.g., 25 March 2021)?
________________________________________

16. What type of cancer were you diagnosed with (e.g., melanoma, kidney cancer, lung cancer)?
________________________________________

17. What stage were you diagnosed with (e.g., stage III or IV)?
________________________________________

18. What type of cancer treatment(s) have you had in the past?
☐ Chemotherapy
☐ Hormone therapy
☐ Immunotherapy
☐ Radiotherapy
☐ Surgery
☐ Targeted therapy
☐ I have not had any treatment in the past
☐ Combination of the above, namely: __________________________

19. What type of cancer treatment(s) are you currently receiving?
☐ Chemotherapy
☐ Hormone therapy
☐ Immunotherapy
☐ Radiotherapy
☐ Surgery
☐ Targeted therapy
☐ Combination of the above, namely: __________________________

20. What is the goal of your treatment (e.g., cure, prolong)?
________________________________________
2. Patient information processing style (Threatening Medical Situation Inventory)

1. Imagine you suffer from headaches and dizziness for some period of time already. You visit your doctor. He or she tells you things don’t look too well and refers you to a specialist for a rather trying medical examination. Please indicate for each statement below to what degree it is applicable to you, by encircling your answer:

   - 1 = not at all applicable to me
   - 2 = not very much applicable to me
   - 3 = a tiny bit applicable to me
   - 4 = rather applicable to me
   - 5 = strongly applicable to me

<table>
<thead>
<tr>
<th>Monitoring</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. I plan to ask the specialist as many questions as possible</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>b. I plan to start reading about headaches and dizziness</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>c. I determine to inform myself at other instances and doctors first</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Blunting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. I think things will turn out to be alright</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>e. For the time being I try not to think of unpleasant outcomes</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>f. I am not going to worry: such an examination is less worse than suffering from headaches all the time</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

2. Imagine you have heart complaints. Your specialist advices an operation. He tells you you will have to wait four months for it and that it is not certain whether the operation will be effective. Please indicate for each statement below to what degree it is applicable to you, by encircling your answer:

   - 1 = not at all applicable to me
   - 2 = not very much applicable to me
   - 3 = a tiny bit applicable to me
   - 4 = rather applicable to me
   - 5 = strongly applicable to me

<table>
<thead>
<tr>
<th>Monitoring</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. I decide to deepen myself into heart surgery as much as possible</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>b. I decide to contact patients who have the same problem, to get information</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
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<td>---</td>
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</tr>
<tr>
<td><strong>c. I decide to do research on the failing percentage of the surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blunting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>d. I assume the operation will benefit me</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>e. I am thinking: it will all turn out alright</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>f. The next few months, I plan to do as many enjoyable and useful things as possible</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
3. Perceived information provision (EORTC QLQ-INFO25)

We are interested in the information you have received about aspects of your disease and its treatment, in order to improve your health care. Please answer ALL questions.

<table>
<thead>
<tr>
<th>During your current disease or treatment, how much information have you received on:</th>
<th>Not at all</th>
<th>A little</th>
<th>Quite a bit</th>
<th>Very much</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 The diagnosis of your disease?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2 The extent (spread) of your disease?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>3 The possible causes of your disease?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>4 Whether the disease is under control?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>5 The purpose of any medical tests you have had or may undergo?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>6 The procedures of the medical tests?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>7 The results of the medical tests you have already received?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>8 The medical treatment (chemotherapy, radiotherapy, surgery or other treatment modality)?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>9 The expected benefit of the treatment?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>10 The possible side-effects of your treatment?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>11 The expected effects of the treatment on disease symptoms?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>12 The effects of the treatment on social and family life?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>13 The effects of the treatment on sexual activity?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>14 Additional help outside the hospital (e.g., help with daily activities, self-help groups, district nurses)?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>15 Rehabilitation services (e.g., physiotherapy, occupational therapy)?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>16 Aspects of managing your illness at home?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>17 Possible professional psychological support?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>18 Different places of care (hospitals/outpatient services/home)?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>19 Things that you can do to help yourself get well (rest, contact with others...)?</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>20 Have you received written information?</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21 Have you received information on CD or tape/video?</td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>22</td>
<td>Were you satisfied with the amount of information you have received?</td>
<td>Not at all</td>
<td>A little</td>
</tr>
<tr>
<td>---</td>
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<td>------------------------------------------------------------------</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>23</td>
<td>a) Do you wish to receive more information?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) If yes, please specify on which topics?</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>a) Do you wish that you had received less information?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) If yes, please specify on which topics?</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>Overall has the information you have received been helpful?</td>
<td>Not at all</td>
<td>A little</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4. Knowledge questions

Please answer True or False to each of these immunotherapy statements.

<table>
<thead>
<tr>
<th>Statement</th>
<th>True</th>
<th>False</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Your own immune system can be used to attack cancer cells and shrink tumours.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2. Your immune system is found only in lymph nodes.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>3. Cancer cells have worked out a way of hiding from your immune system.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>4. Immunotherapy treatment works by helping your own immune system to destroy cancer cells.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>5. Immunotherapy can make your immune system overactive. This is the main reason why you can develop side effects.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>6. Immunotherapy uses similar techniques to chemotherapy to attack cancer cells and tumours.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>7. Just like chemotherapy, immunotherapy can weaken your immune system and make you more likely to develop infections.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>8. Immunotherapy and chemotherapy cause almost the same types of side effects.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>9. Delayed treatment of an out-of-control immune system can be life threatening.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>10. Loose, frequent bowel motions can be a problem/symptom caused by an overactive immune system.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>11. An itch can be a problem/symptom caused by an overactive immune system.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>12. A dry cough can be a problem/symptom caused by an overactive immune system.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>13. Unusual or unexplained fatigue or tiredness can be a problem/symptom caused by an overactive immune.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>14. A headache can be an unusual and rare problem/symptom caused by an overactive immune system.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>15. You need to develop some side effects to be sure that immunotherapy is shrinking your cancer.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>16. If you need steroids to treat an immunotherapy side effect, this will reduce the effectiveness of immunotherapy working to fight your cancer.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>17. The longer you leave it before reporting side effects to your doctor or nurse, the more likely it is that you will need to come to the hospital to fix it.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>18. Your treating team is really busy, so you should only contact them when you think you are that unwell that you will likely need to be admitted to hospital.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>19. It is safe for you to wait to see if side effects, such as diarrhoea, improve before letting your treating team know.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>20. You need to let your treating team know if you are worried about how you are feeling.</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
5. Patient Activation (PAM-13)

If the statement does not apply to you, circle N/A.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Agree</th>
<th>Strongly Agree</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>When all is said and done, I am the person who is responsible for taking care for my health</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>2.</td>
<td>Taking an active role in my own health care is the most important thing that affects my health</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>3.</td>
<td>I am confident I can help prevent or reduce problems associated with my health</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>4.</td>
<td>I know what each of my prescribed medications do</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>5.</td>
<td>I am confident that I can tell whether I need to go to the doctor or whether I can take care of a health problem myself</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>6.</td>
<td>I am confident that I can tell a doctor concerns I have even when he or she does not ask</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>7.</td>
<td>I am confident that I can follow through on medical treatments I may need to do at home</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>8.</td>
<td>I understand my health problems and what causes them</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>9.</td>
<td>I know what treatments are available for my health problems</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>10.</td>
<td>I have been able to maintain (keep up with) lifestyle changes, like eating right or exercising</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>11.</td>
<td>I know how to prevent problems with my health</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>12.</td>
<td>I am confident I can figure out solutions when new problems arise with my health</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>13.</td>
<td>I am confident that I can maintain lifestyle changes, like eating right and exercising, even during times of stress</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>
Virtual reality as a patient education tool for people with cancer undergoing immunotherapy

Case Report Form

Participant ID: ______________________
Name of investigator: ______________________

Date of recruitment: ___ (Day) ___ (Month) ___ ___ ___ (Year)
Date of trial completion: ___ (Day) ___ (Month) ___ ___ ___ (Year)
Participant ID: ___________________

### Research stages: Assessment table

<table>
<thead>
<tr>
<th></th>
<th>t-1</th>
<th>t0</th>
<th>t1</th>
<th>t2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for declining to participate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eligibility screening</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Verbal consent</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Signed Consent Form</td>
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<td></td>
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<tr>
<td>Baseline questionnaire</td>
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<tr>
<td>AEs</td>
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<td></td>
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</tr>
<tr>
<td>Follow-up questionnaire 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up questionnaire 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drop-outs with reasons</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: Items with “☒” are required to be checked. Please tick the correspondent boxes (“☒”) once assessment is completed. AEs: adverse events.
Participant ID: ___________________

### Selection criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is 18 years and over</td>
</tr>
<tr>
<td>2. Is diagnosed with a reportable cancer of any stage (e.g., melanoma, kidney cancer, mesothelioma, lung cancer) that will be treated with immunotherapy</td>
</tr>
<tr>
<td>3. Is due to start only immunotherapy agents (i.e., patients may not receive any other treatment, such as chemotherapy or radiotherapy)</td>
</tr>
<tr>
<td>4. Is able to understand English</td>
</tr>
<tr>
<td>5. Is able to give their own consent</td>
</tr>
<tr>
<td>6. Will be receiving immunotherapy as standard treatment; not as part of a clinical trial</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion criteria*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Has a condition that interferes with VR usage, including but not limited to seizures, facial injury precluding safe placement of headset, and visual impairments</td>
</tr>
<tr>
<td>2. Has a prognosis of &lt;3 months from the time of enrolment per treating oncologist</td>
</tr>
<tr>
<td>3. Receives other systemic cancer therapies in combination with immunotherapy</td>
</tr>
<tr>
<td>4. Has a pre-existing severe mental health diagnosis or significant cognitive impairment, such as severe dementia that would impair their comprehension and/or ability to provide informed consent</td>
</tr>
</tbody>
</table>

*In the event participants experience unexpected symptoms that could be related to the VR, such as blurred vision, dizziness, light-headedness, or nausea, the session will be stopped immediately. Any adverse events or unintended consequences will be documented and assessed.

### Informed consent

Date of signing informed consent: __ __ (Day) __ __ (Month) __ __ __ __ (Year)
Participant ID: ________________

**Reasons for declining study participations**

The following is a guide for the wording to be used when asking patients for their reason/s for declining participation in the study.

For our research purposes we are interested in why patients may not want to participate in the virtual reality study. However, you don’t have to give us a reason and we will fully understand. We don’t want you to feel pressured to change your mind about participating in the study, and whatever you decide, it will in no way affect the healthcare you receive from your doctor.

For patients who indicate that they would be comfortable to share their reason, provide a printed copy of the form below or provide the options verbally and record on the form.

<table>
<thead>
<tr>
<th>Potential reasons</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concern about the effects of VR (e.g.: motion sickness, feeling scared etc)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncomfortable with immersion in a virtual world</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unsure about the use of the technology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concerned that it may not be effective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Don’t want to commit to the extra time required (e.g.: for questionnaires, interviews)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preference for the standard education only</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other (please describe): _______________________________________________________
___________________________________________________________________________
___________________________________________________________________________
___________________________________________________________________________
___________________________________________________________________________

<table>
<thead>
<tr>
<th>Drop-out</th>
<th>Yes*</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did the participant drop out</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*See page 7
Adverse events

<table>
<thead>
<tr>
<th>Potential adverse events</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>General discomfort</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Fatigue</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Headache</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Eye strain</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Difficulty focusing</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Fullness of the Head</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Dizziness with eyes closed</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Vertigo</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

Other (please describe):

___________________________________________________________________________
___________________________________________________________________________
___________________________________________________________________________
___________________________________________________________________________

Date of adverse event: __ __ (Day) __ __ (Month) __ __ __ __ (Year)

Severity of adverse event: ☐ none; ☐ mild; ☐ moderate; ☐ severe

Please describe how the adverse event was resolved:
___________________________________________________________________________
___________________________________________________________________________
___________________________________________________________________________
___________________________________________________________________________

Participant ID: ___________________
Participant ID: ________________

(Attach Allocation Card Here)
Form for Withdrawal of Participation

Title
Assessing the Feasibility and Acceptability of a Virtual Reality educational module to improve cancer patients understanding of Immunotherapy

Protocol Number
2.0

Project Sponsor
Western NSW LHD

Coordinating Principal Investigator/Principal Investigator
A/Prof Rob Zielinski ph:
(02) 6369 3380
rob.zielinski@health.nsw.gov.au

Associate Investigator(s)
Dr Kate Gunn, University of South Australia
Dr Hamish MacDougall, Sydney Local Health District
Donna Milne, Peter MacCallum Cancer Centre Shannen
Van Der Kruk, University of South Australia
Katherine Smith, University of Sydney

Location
Orange Health Service – 1530 Forest Road, Orange NSW 2800

Declaration by Participant
I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Orange Health Service

Name of Participant (please print) ______________________________
Signature __________________________ Date __________________________

Declaration by Study Doctor/Senior Researcher*
I have given a verbal explanation of the implications of withdrawal from the research project, and I believe that the participant has understood that explanation.

Name of Study Doctor/Senior Researcher* (please print) ________________________________
Signature __________________________ Date __________________________

* A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.

Version 1.0, 7 November 2022