PARTICIPANT INFORMATION SHEET AND CONSENT FORM
(Phase 1b – Multiple Ascending Dose)

Short Title:	A Study to Evaluate the Safety and Tolerability of YCT-529 in Healthy Male Participants
Protocol Number:	YCT-529-02
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Ethics Number:	2024 FULL 20396

This is the Second time that YCT-529 will be studied in humans.
You will not get any health benefit from the drug used in this study; but there are risks of you having a drug reaction, injury, or illness.

You are invited to take part in a clinical research study. This study will test an experimental drug, named YCT-529, that may potentially be used as a means of male contraception. YCT-529 is an investigational product because it has not been approved by the New Zealand MedSafe or other drug regulatory authorities.

This study has multiple parts, and you are being asked to participate in the Phase 1b part. This Participant Information Sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. We expect this will take about 30-60 minutes. You do not have to decide today whether or not you will participate in this study. Before you decide, you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

Please make sure you have read and understood all the pages of this document including the consent form.

1 WHY ARE WE DOING THE STUDY?

1.1 Purpose

YCT-529 is being developed as a potential non-hormonal, oral contraceptive for males. The purpose of this study is to evaluate the safety and tolerability of multiple doses of YCT 529 in healthy male participants. You have been invited to participate in this study as you have decided to have a vasectomy (a procedure which is considered permanent and not reversible) and you are waiting for the procedure **OR** you have, in the opinion of the investigator, have made a firm decision not to father children in the future.

YCT-529 is designed to target and block a receptor required for sperm production. It is hoped that YCT-529 may be able to reduce sperm count and sperm motility (movement) in a reversible manner to provide an option for a non-hormonal male contraceptive. This study is the first-time multiple doses of YCT-529 will be given to humans and thus, the potential effects and risks of the investigational medicine are not yet known and may include a potential risk of impairing fertility irreversibly (becoming sterile).

YCT-529 has been studied in healthy male participants in a Phase 1a single ascending dose study conducted internationally. The current study is made up of two parts. The Phase 1b part is investigating multiple ascending doses and the Phase 2a part will be an expansion study. You are being invited to take part in the Phase 1b part of this study.

The purpose of the Phase 1b part of the study is to:

- Evaluate how safe and well tolerated YCT-529 is, in healthy male participants.
- Measure levels of YCT-529 in the blood over time, following multiple doses.
- Measure the effect of YCT-529 on sperm count and motility.

1.2 Study Design

Up to 50 healthy male participants will take part in this study. The Phase 1b part will consist of up to 20 healthy male participants. This part of the study requires a 7-night stay and a 4-night stay at the New Zealand Clinical Research (NZCR) unit. The study will also include up to 14 scheduled clinic visits and 17 follow-up video calls. This study may also enrol participants internationally (in Australia).

Every person in the study will receive 28 doses of YCT-529. Each dose will be given by mouth as a tablet(s), with a glass of water. You will receive the investigational medicine in a fasted state (without food for at least 10 hours).

Up to 5 cohorts are planned for this part of the study. Each group will be made up of 4 participants. Your assigned group will depend on when you join the study. Doses of up to 180mg YCT-529 are planned for this study. Details for the dosing groups, including the planned doses, are as follows:

Cohort	Dose of YCT-529	Frequency
1	15 mg	28 doses given orally once daily for 28 days
2	30 mg	
3	90 mg	
4	TBD	
5*	TBD	

* Cohort 5 is an optional cohort. Dose is to be determined (TBD).

Dose groups will be enrolled in order. You will be told which dose group you will be in. You will also be told, in writing, if any changes are made to the planned dose for your group.

Blood samples and other tests to measure investigational medicine levels and effects on the body will be collected at specific time points during the study. Your safety will be monitored, and any changes in your health will be recorded.

1.3 Nature and Sources of Funding of the Study

This research project is being conducted and funded by YourChoice Therapeutics and locally sponsored in New Zealand by Research Associates Ltd, which helps conduct and monitor the study in New Zealand. Southern Star Research will be the Contract Research Organisation (CRO) that will also help with the conduct of the study in New Zealand.

By taking part in this research study, you agree that data generated from your assessments throughout the study, will be provided to YourChoice Therapeutics, Research Associates Ltd, and Southern Star Research. The knowledge gained from this data may lead to new discoveries, which would assist them in obtaining approval for a new drug and benefit the sponsor financially. There would be no financial benefit to you from these discoveries.

New Zealand Clinical Research (NZCR) will receive a payment from YourChoice Therapeutics for undertaking this research project.

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

1.4 Approval by Ethics Committee.

This study has been reviewed by an independent group of people called a Health and Disability Ethics Committee (HDEC). The ethical aspects of this research project have been approved by the **Northern A** Ethics Committee.

A description of this clinical study will be available on http://www.ClinicalTrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

2 WHAT WOULD YOUR PARTICIPATION INVOLVE?

Participation in this study will last approximately 24 weeks, including a screening, dosing, and follow-up period. If you are required to attend the 6 additional follow-up visits your participation in the study will last up to approximately 44 weeks. If you wish to participate in this study, you will be asked to sign this consent form before any study assessments can be performed.

The details of the study and tests performed are discussed and shown below. During the screening period, assessments will be done to check whether the study is suitable for you. The day you have your first dose of YCT-529 is called Day 1 and all other days are counted back or forward from this.

The results of the screening assessments will determine whether or not you can take part in the study. However, even if all your results are normal, you may not be guaranteed a place. We may screen more participants than we need and so you may be asked to be a reserve. This will mean you will be asked to come to the clinic and undergo the tests and procedures until the point that we have enrolled enough eligible participants for the cohort. You will then be discharged and where possible we will try to include you in a later cohort.

2.1 Tests and Procedures

Collection of Demographic Information
At your Screening visit, the study staff will record your demographic information, such as your name, age, sex, race/ethnicity, address and phone number.

Physical Examination:
During the study, the doctor will perform a physical examination to check your health. Your height and weight will also be measured to calculate that your Body Mass Index (BMI) is within range for the study.

Electrocardiogram (ECG) and Holter Monitoring:

- An ECG measures the electrical activity of your heart, using 12 wires attached to your chest and limbs with sticky pads.
- You will wear a Holter monitor (a machine that periodically records the heart rhythms) for a period of 24 hours prior to first dose, and for a period of 48 hours after first dose (for 72 hours total). Starting on Day 28 you will wear the monitor for a period of 48 hours. You will carry the Holter monitor in a pocket or pouch worn around your neck or waist.

Vital Signs:
Vital signs include recordings of your pulse, blood pressure, breathing rate, and temperature.

Tele-health (video call) Visit:
On dosing days, where other tests and procedures do not need to take place, a video call visit will occur. During this visit study staff will ensure your dose is taken and ask you questions about your health. If needed, you may be asked to attend a clinic visit instead of a video call visit. If you do not have a device that can be used for a video call, one will be provided at no cost to you.

Biological Samples:
Blood and Urine samples:
At clinic visits, blood samples are taken by direct vein puncture. On Day 1 and Day 28, a cannula (thin plastic tube) will be inserted into a vein in your arm to take blood samples. If your cannula stops working, direct vein punctures will be used. Blood and urine samples will be collected:

- To monitor your safety (blood cells, clotting, chemistry, fats, liver function, kidney function, heart function, physical health)
- To screen for recreational drugs such as cannabis, methamphetamine, and opiates. You will also have a breath test performed to screen for the presence of alcohol
- To screen for specific infections (HIV, Hepatitis B, Hepatitis C)
- To measure the amount of YCT-529 in the blood (pharmacokinetics)
- To measure the effect of YCT-529 on immune markers and hormones in the blood (pharmacodynamics)

Semen Samples

- During this study, you will be required to provide semen samples for the researchers to see if the investigational medicine is having an effect on sperm count and sperm motility.
- There are certain sperm parameters that are required for eligibility in this study. A doctor will discuss these results with you if your sperm sample is not within study criteria.

Note that you will attend appointments at an independent fertility clinic at a different location to the study clinic to provide these semen samples.

Alcohol Breath Testing
You will be screened for the presence of alcohol via a breathalyser. You will blow into the mouthpiece for a few seconds to measure the presence of alcohol on your breath.

Psychosexual Self-reporting Diary:
You will be asked to complete a self-reporting diary through an application at the screening visit, daily from Day -1 to Day 31 and then at each of the follow up visits. You will be asked to answer sexually related questions that are used to determine your overall sexual drive. Completion of the questionnaire through an application will be discussed further in the document. If you experience any issues using the application, you will receive a paper copy of the diary to complete. If you would prefer to complete the psychosexual self-reporting diary on paper, please inform the study staff.

Mandatory Sperm Sample storage (Sperm Banking)
In order to participate in this study, you must consent to provide a semen sample that will be collected at a fertility clinic prior to dosing. This sample will be cryopreserved (frozen) and stored at the fertility clinic until the end of the study, and for 10 years thereafter, at no cost to you. If you request a change of location for your sperm sample storage, this will be at your own expense. If your sperm parameters return to normal ranges of fertility (as per WHO - World Health Organisation, guidelines and published data), your stored sperm sample will be destroyed. If you request a change of location for your sperm sample storage, this will be at your own expense. It is possible your sperm counts will not return to normal levels. The banked sperm is intended as a precaution to this event. Any questions you may have about sperm banking can be addressed by the fertility clinic. **If you do not wish to have your sperm stored at a fertility clinic for the abovementioned timeframe, then you should not participate in this study.** You may also request to have your cryopreserved samples destroyed.

Study Schedule

Period	Screening	In-clinic period						Dosing					
Study Day	**-28 to -2**	**-1**	**1**	**2**	**3**	**4**	**5, 6**	**7**	**8, 9**	**10**	**11, 12, 13**	**14**	**15, 16**	**17**
Questions about my health	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Admission to the unit		X												
Discharge from the unit								X						
Clinic Visit	X	*In patient (7-nights)*								X		X		X
Tele-health (Video Call)									X		X		X	
Physical Exam [a]	X	X	X	X	X	X	X	X		X		X		X
Vital Signs	X	X	X	X	X	X	X	X		X		X		X
ECG	X	X	X	X	X	X	X	X		X		X		
Holter Monitoring [b]		X	X	X	X									
BMI (Height & Weight)	X													
Dose Administration			X	X	X	X	X	X	X	X	X	X	X	X
Blood Sampling	X	X	X	X	X	X		X		X		X		X
Urine Sampling	X	X		X		X		X				X		
Urine drug test	X	X										X		
Alcohol breath test		X												
Semen Sample	X													
Psychosexual Diary Completion	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Period	Dosing					In-clinic period				Follow-Up			
Study Day	**18, 19, 20**	**21**	**22, 23**	**24**	**25, 26**	**27**	**28**	**29, 30**	**31**	**35, 42, 49**	**56**	**84**	**112 EOS [b]**
Questions about my health	X	X	X	X	X	X	X	X	X	X	X	X	X
Admission to the unit						X							
Discharge from the unit									X				
Clinic Visit		X		X		*In patient (4-nights)*					X	X	X [c]
Tele-health (Video Call)	X		X		X					X			
Physical Exam [a]		X		X		X	X	X	X		X	X	X
Vital Signs		X		X		X	X	X	X		X	X	X
ECG		X					X		X		X	X	X
Holter Monitoring [c]							X	X					
BMI (Height & Weight)													
Dose Administration	X	X	X	X	X	X	X						
Blood Sampling		X		X			X	X	X		X	X	X
Urine Sampling		X					X		X		X	X	X
Urine drug test		X					X				X	X	X
Semen Sample		X					X			X [d]	X	X	X
Psychosexual Diary Completion	X	X	X	X	X	X	X	X	X	X	X	X	X

[a] Full physical exam will be performed at screening. At other visits these examinations will be symptom driven

[b] EOS = End of Study, if your Day 28, 42 and 56 semen samples show your sperm parameters have returned to baseline normal values taken at the beginning of the study, Day 112 will be your last study visit. If your sperm parameters are not within the baseline normal values taken at the beginning of the study, you will need to return to the clinic for additional safety follow-up visits on Day 140, 168, 196, 224, 252 and 280. Once your sperm parameters return to baseline you may no longer need to attend these visits. These study procedures will be done on each of the additional safety follow-up visits.

[c] Holter monitoring prior to last dose (Day 28), and for 48 hours after.

[d] A semen sample will be collected on Day 42, but not Day 35 or Day 49.

Additional Visits (Safety Follow-up Visits):

If your Day 28, 42 and 56 semen samples show that your sperm parameters are not within normal ranges, you will return to the fertility clinic and NZCR clinic for additional safety follow-ups on Day 140, 168, 196, 224, 252, and again on Day 280. If your sperm parameters return to baseline levels, you may not be required to attend all the follow ups. Study staff will let you know if this applies to you. If you are required to attend these additional visits you will be appropriately reimbursed for your time and inconvenience ($100 less tax per visit) and any reasonable travel costs that are associated with this visit.

By signing this document, you understand that you may be asked to attend additional visits at a fertility clinic and at the NZCR clinic following study completion and agree to attend this additional follow-up visit if required.

2.2 Who Can Take Part in this Study?

You have been invited to participate in this study as you have decided to have a vasectomy and are waiting for the procedure **OR** you have, in the opinion of the investigator, made a firm decision not to father children in the future.

To take part in this study you must:	
✓	Be able to give informed consent and follow the study procedures.
✓	Be aged 28 – 70 years, inclusive.
✓	Have a BMI (Body Mass Index) between 18.0 kg/m^2 – 35.0 kg/m^2 and you must weigh at least 55 kgs.
✓	Meet one of the following criteria: Have decided to have a vasectomy and are waiting for the procedure **or** have, in the opinion of the investigator, made a firm decision not to father children in the future.
✓	Must meet sperm health criteria, your study doctor will explain this to you in detail.

You cannot take part in this study if you:	
✗	Have a partner that is pregnant or lactating
✗	Have a history of a significant medical problem, mental health problem or severe allergy.
✗	Have taken any prescription medication (excluding paracetamol) or over-the-counter vitamins, herbal remedies or supplements within 14 days prior to screening.
✗	Have used cannabis or any recreational drugs within 30 days prior to screening.
✗	Have participated in another clinical trial involving an investigational medicine within 30 days prior to dosing.
✗	Have a history of androgen (sex hormone) deficiency due to testicular disease or hormonal imbalances.
✗	Have taken hormone therapy within 90 days prior to screening.

✕	Have a history of alcohol or drug abuse within 2 years prior to screening
✕	Have consumed 5 or more cigarettes (or the equivalent in nicotine products) per week within 3 months prior to screening.

If you think that any of the above applies to you, or you have one of the conditions described, please discuss these with your study doctor for more thorough assessment to see if you can take part in this study or not. Additionally, there are other criteria that you will need to meet in order to be eligible for the study, but the study doctor will discuss this with you at your screening visit.

2.3 Study Instructions

It is important that you follow the instructions you are given and attend all scheduled clinic visits. It is also possible that the study doctor may schedule extra visits or tests for you, if considered necessary. In the event that an assessment is not performed on the day outlined within the Schedule of Activities within this document, the assessment may be performed at your next study visit.

You will be given a Participant Identification Card if you participate in this study, stating the name of the study and the study doctor's contact information. This card should be carried with you at all times so that you can contact the study doctor at any time and so you can show it to any other doctor, dentist, or pharmacist that you might visit while in this study.

At each visit, the study staff will ask you questions about your health and the medications you are currently taking. You should always report any changes in your health, unusual feelings, or symptoms to the study staff. It is also important that you do not start, stop, or make changes to any of the medications you are currently taking without first discussing this with your study doctor.

Please inform the study doctor or staff if you decide to stop taking YCT-529 for any reason. If you stop taking the investigational medicine for any reason (either your choice or on the advice of your study doctor) your study doctor will ask you to continue to attend the unit for follow-up assessments.

When you are an inpatient with us, we will provide you with all of your meals. Meals play an important role in clinical trials due to their relationship with metabolism of the investigational medicine (the way that the investigational medicine is processed and broken down by the body). By signing this document, you are agreeing that you will be compliant with all meal requirements on this study. In certain cases, we are able to cater for dietary requirements, please discuss this with the study team before joining the study.

Restrictions:

- You must not consume grapefruit, pomegranates, star fruit, or Seville oranges from 7 days prior to admission until Day 56.
- You must not consume vitamins or herbal supplements within 14 days prior to dosing until Day 56.
- You must not smoke more than 4 cigarettes a week (or equivalent amount of nicotine) during the study.
- You must refrain from consuming food containing poppy seeds for 72 hours prior to screening, within 72 hours prior to admission, and until Day 56.
- You must not consume any caffeine or xanthine containing products (i.e., coffee, tea, chocolate, soda) within 24 hours prior to admission.
- You must not consume any alcohol in the 24 hours prior to your screening visit, and for at least 48 hours prior to admission. You should not drink more than 7 drinks per week until Day 56 (and

spread them out if possible). Alcohol could impact your liver and kidney function and impact your safety test results.

- You must be fasted (no food, only water) for at least 10 hours prior to your screening visit and all in-clinic follow up visits. You also must have fasted for 10 hours prior to each dose of the investigational medicine and for 2 hours afterwards. Study staff will remind you prior to each visit that you need to be fasted.
- You must refrain from strenuous exercise for at least 72 hours prior to screening, 72 hours prior to admission, through until Day 31. Strenuous exercise will impact your muscle and liver function which could make it harder for the study team to monitor your body's response to the investigational medicine.
- You must not donate blood during the study period.
- You must not use cannabis or recreational drugs during the study period.
- You must minimise exposure to sunlight and must not use sunbeds. You are advised to wear sunglasses and clothing that minimizes exposure to sunlight and use sun cream on exposed areas when going outdoors from the time you take your last dose until 10 days after that.
- You should refrain from ejaculating for 2 days but not more than 5 days prior to your sperm sample collection appointments. Study staff will remind you of this prior to each visit.

At admission, your bag will be checked for prohibited items (e.g., drinks or foods, etc.). Any prohibited items will be removed and returned to you on discharge from the unit.

3 WHAT ARE THE POSSIBLE BENEFITS, COSTS AND RISKS TO YOU PARTICIPATING?

3.1 Benefits

This study is not designed to provide you with any therapeutic benefits. The information from this study might help to develop better long-term contraceptive options for males.

3.2 Reimbursement and Costs

All tests required to be done for this study will be paid for by YourChoice Therapeutics and there will be no cost for you to participate in this study.

You will be reimbursed the sum of $10,700 (before tax), following the final study visit**.** However, the timing of reimbursement is flexible and can be adjusted to suit your needs – please discuss this with study staff if you have any concerns regarding your reimbursement. **We are required to deduct withholding tax at the applicable rate you have declared in the IR330C form**. You will be responsible for any other tax obligations (e.g., ACC). If you are GST registered, it may be possible for you to submit a GST invoice. Contact paymentforms@nzcr.co.nz if you would like to discuss this further.

The payment will be made after you complete the study, to cover your time and inconvenience. If you are receiving a benefit or allowance, your usual payments may be affected. Your tax statement will state that you were paid from your dosing day through to your final study visit.

To be able to participate in the clinical study you must be eligible to work in NZ for the entire duration of the study. If you are no longer eligible to work in NZ during the study, you will be withdrawn from the study and your reimbursement will be a pro-rata of the total amount.

You will be reimbursed for travel and parking (if you use personal transport) or you can use uber or taxi for your study visits, which can be arranged and paid for by NZCR if you live in the metropolitan area.

Please discuss arranging study transport with the site study staff. If you live outside this area, we will discuss your travel costs individually. Full reimbursement requires completion of all visits according to study requirements. If you are withdrawn from the study for medical reasons, having received trial medication, you will receive reimbursement in full.

If you leave the study of your own choice or are released from the study for non-medical reasons, you will receive a partial reimbursement (a pro-rata reimbursement) according to how far you contributed to the study.

In order to meet dosing requirements, additional (reserve) participants may be admitted to the unit. If you are invited to attend the study as a reserve, you will be asked to either; admit to the unit on Day -1 just for the day (**day reserve**) or admit to the unit on Day -1 and stay overnight (**night reserve**). If you are a reserve, and you are not required to be dosed, you will be reimbursed for your time and inconvenience (day reserve = $150 or night reserve = $350).

If you complete the screening visit assessments and are found not eligible for the study, you will not receive any reimbursement.

3.3 Possible Risks and Disadvantages?

Medications often cause side effects. You may have none, some or all the effects listed below, and they may be mild, moderate, or severe. There may also be unknown side effects from taking YCT-529 alone or with other drugs you may be taking. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

What are the Risks or Side Effects of YCT-529?

This is the first time YCT-529 will be administered to humans repeatedly. Single doses of up to 180 mg of YCT-529 were found safe and tolerable in humans. Animal studies have been done with YCT-529 to predict what type of side effects might occur in people as well as the effect of YCT-529 on sperm. However, animal studies do not always predict human responses to investigational medicines. Single and repeat doses of the investigational medicine of up to 108 days have been given to animals but have not given rise to any major safety concerns.

Single doses given to animals were well tolerated with minor side effects including vomiting and changes of protein levels (e.g. enzymes) in the body. When animals were given the investigational medicine at high doses for 4-5 days, side effects included changes in the animals' liver and kidney function, which in some cases resulted in death. These effects occurred at doses equivalent to a human dose of 330 mg or higher, which is more than 20 times higher than the initial dose that will be given in this study as a daily dose. High doses administered to animals did not appear to cause effects to the heart, lungs or central nervous system. Lower doses given to animals for up to 28 days were well tolerated.

The recovery of spermatogenesis (sperm production and sperm function) after repeated dose administration and subsequent interruption of the investigational medicine has been confirmed in 3 out of 4 animal species tested (mouse, dog, and monkey). The one species that did not have recovery (rat) has fundamental differences in how sperm production is controlled and initiated. Thus, it is not felt to represent a good model for how human sperm production could resume after stopping YCT-529.

Before you receive investigational medicine YCT-529, sample(s) of your sperm will be collected and stored. The sample will be cryopreserved (frozen) and maintained in storage at no cost for you until the end of the study and for a period of 10 years thereafter in case your sperm parameters have not returned to normal fertility levels.

Fertility and Virility:
There is a potential risk that YCT-529 could affect your fertility and these effects may not be reversible. YCT-529 is designed to decrease your fertility (e.g. sperm count and sperm motility). This impairment of fertility was reversible in 3 out of 4 animal species tested, but there is a risk that your fertility will not return, and you may become sterile. Animal research also suggests that YCT-529 does not alter testosterone and that it does not affect virility (libido/sex drive).

Kidney and Liver toxicity:
At very high doses the investigational medicine was found to affect liver and kidney function in animals. The planned starting dose in this study is 15 mg. This dose has been selected based on the evidence from the studies in animals and humans and is projected to be safe. Your liver and kidney function will be monitored closely by blood test, throughout the study.

Phototoxicity:
YCT-529 has the potential to cause phototoxicity (sensitivity to sunlight) from UV light and further testing for potential phototoxicity is needed. Therefore, you are strongly advised to refrain from prolonged UV exposure and to wear protective clothing and sunscreen when venturing outdoors for 10 days after your last dose of investigational medicine.

The doses planned for this study in people are lower than the doses that were safe in animals. The study will begin with low doses of YCT-529 that will be gradually increased if the investigational medicine is well tolerated. However, as noted above, animal studies do not always predict human response to investigational medicines. Among side effects that could occur, some could be life-threatening.

As with other investigational medicines, YCT-529 may cause an immune reaction or allergic reaction. Symptoms may include rash, flushing, itching, sneezing or runny nose, abdominal pain, diarrhoea, swelling of face, tongue or throat, dizziness, lightheaded or fainting, trouble breathing, irregular or racing heart rate, and seizures. These reactions can be life-threatening / fatal.

What are the Risks or Side Effects of Study Procedures?

Blood Sample Collection & Cannulas:
Risks include bruises, swelling with itching, and slight bleeding. The area may become inflamed. In rare cases, it may result in a blood clot, an infection or nerve damage. As needles can cause pain, you may feel light-headed or faint.

ECG Tests and Holter monitoring:
Sometimes the sticky pads used to attach the ECG leads can cause skin irritation (redness / itchiness).

Physical Examination:
During this examination you may be asked to remove some items of clothing so a full examination can be done. You can request a chaperone to be with you at the time of the physical examination, please ask one of our research nurses.

Psychosexual self-reporting diary:
During the treatment period you will be required to complete a diary questionnaire that outlines different questions and scale rating of your sexual desires and impulses. Some of these questions may make you feel slightly uncomfortable.

3.4 Contraception

Reproductive Risks for Sperm in Sexually Active Participants

The effects of YCT-529 if passed on through semen are unknown, but there is a risk it may cause birth defects or foetal deaths. **You are responsible for informing your sexual partner of these possible risks.**

If you are sexually active and have any partner who is of child-bearing potential (meaning a partner who may become pregnant) it is very important that you use contraception during this study. You and your partner must use one of the methods of contraception listed below, from at least your first dose of investigational medicine through until at least 28 days after your last dose:

A highly effective method (less than 1 pregnancy per 100 people using the method for one year) e.g.

- Implant contraceptive (e.g., Jadelle®)
- Intra-uterine device (IUD) containing either copper or levonorgestrel (e.g., Mirena®)
- Sterilization (e.g., bilateral tubal ligation ('clipping or tying tubes') or hysterectomy)

OR an effective method (5 - 10 pregnancies per 100 people using the method for one year) e.g.

- Injectable contraceptive (e.g., Depo Provera)
- Oral Contraceptive Pill (combined hormonal contraceptive pill or progestogen-only 'mini-pill' that are associated with inhibition of ovulation)

You and your partner must also use a barrier method of contraception, from your first dose of investigational medicine through until Day 56 (or 28 days after your last dose of investigational medicine). Barrier methods of contraception include:

- Condoms (external or internal) – not to be used together due to increased risk of breakage
- Diaphragm ('cap')

Please note that barrier methods alone are not highly effective methods of contraception.

Total abstinence from heterosexual intercourse during the entire period of risk associated with the investigational medicine (from dosing until at least Day 56 or 28 Days after your last dose) is considered an acceptable form of contraception, if this is in line with your preferred and usual lifestyle.

If a pregnancy occurs, you must report this to the study doctor as soon as possible. Your partner will be asked to give consent for their information and their infant's information to be collected for monitoring purposes.

You must also agree not to donate sperm, from dosing until at least 120 days after your last dose of the investigational medicine.

4 WHAT WOULD HAPPEN IF YOU WERE INJURED IN THE STUDY?

As this research study is for the principal benefit of its commercial sponsor YourChoice Therapeutics, if you are injured as a result of taking part in this study you **won't** be eligible for compensation from Accident Compensation Corporation (ACC).

However, YourChoice Therapeutics has satisfied the **Northern A** Health and Disability Ethics Committee that approved this study that it has up-to-date insurance for providing participants with compensation if they are injured as a result of taking part in this study.

New Zealand ethical guidelines for intervention studies require compensation for injury to be at least ACC equivalent. Compensation should be appropriate to the nature, severity and persistence of your injury and should be no less than would be awarded for similar injuries by New Zealand's ACC scheme.

Some sponsors voluntarily commit to providing compensation in accordance with guidelines that they have agreed between themselves, called the Medicines New Zealand Guidelines (Industry Guidelines). These are often referred to for information on compensation for commercial clinical trials. There are some important points to know about the Industry Guidelines:

- On their own they are not legally enforceable and may not provide ACC equivalent compensation.
- There are limitations on when compensation is available, for example compensation may be available for more serious, enduring injuries, and not for temporary pain or discomfort or less serious or curable complaints.
- Unlike ACC, the guidelines do not provide compensation on a no-fault basis:
- The Sponsor may not accept the compensation claim if:
    - Your injury was caused by the investigators, or;
    - There was a deviation from the proposed research plan, or;
    - Your injury was caused solely by you.

An initial decision whether to compensate you would be made the by the sponsor and/or its insurers.

If they decide not to compensate you, you may be able to take action through the Courts for compensation, but it could be expensive and lengthy, and you might require legal representation. You would need to be able to show that your injury was caused by participation in the trial.

You are strongly advised to read the Industry Guidelines and ask questions if you are unsure about what they mean for you.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

5 WHAT WILL HAPPEN TO MY TEST SAMPLES?

Blood and urine samples will be collected throughout the study. These samples will be used for various tests. Some of the samples will be used for regular routine blood counts and blood chemistry, to monitor your general health. All these routine samples will be sent to LabPlus for testing and destroyed after 3 months by internationally accepted means.

You will have a semen sample collected and cryopreserved (frozen) at the beginning of the study. This semen sample will be collected and stored at Fertility Associates in Remuera, Auckland for the duration of the study, and for 10 years thereafter (unless sperm parameters return to normal levels). It will then be destroyed by internationally accepted means.

Other semen samples will be collected during the study. These samples will be initially stored at Fertility Associates in Remuera, Auckland for sperm analysis. They will then be sent to the central laboratory (Agilex) in Thebarton Australia for testing and destroyed after 2 years by internationally accepted means.

All other study samples (pharmacokinetics and pharmacodynamics) will be sent to a central laboratory (Agilex) in Thebarton, Australia for testing and destroyed after 2 years by internationally accepted means.

The maximum amount of blood collected from each participant during the study will be up to approximately 460 mL. For comparison, a standard blood donation at a blood collection centre, is about 470 mL. Samples collected by NZCR will be identified by your study number, year of birth, initials, and sex, to allow study doctors to quickly respond to any abnormal results. Before the results of these tests are sent to the Sponsor, your identifiable information will be removed and replaced with a code.

The proposed blood tests include a screening test for HIV and for viral Hepatitis B and C. Signing the consent form means that you agree to have this testing performed. It is important to understand that a positive screening test does not necessarily mean you have the disease. Should you receive a positive screening result for HIV or either Hepatitis B or C, then the study doctors will provide initial counselling and medical advice and will assist in arranging any follow up tests that you require. HIV, Acute (newly diagnosed) and Hepatitis B/C are all 'notifiable diseases', which means that it is required by law to notify government health authorities of any new cases.

5.1 Are There Any Cultural Considerations?

You may hold beliefs about sacred and shared values about your tissue samples and/or data originating from this tissue. The cultural issues associated with sending your tissue samples and data overseas and/or storing your tissue and data should be discussed with your family/whānau as appropriate. If you wish to know more about the study, we can arrange for an Investigator to come and talk to you and your whānau. NZCR are committed to preserving and upholding mauri through karakia and the handling of samples. You are invited to perform a karakia at the time of sample collection, please inform staff if you would like any assistance. However, due to your samples being sent to countries outside of New Zealand, a karakia will not be able to be performed at the time of your sample disposal.

Personal and health information is a tāonga and will be treated accordingly. The following data sovereignty principles are in place to ensure that the data generated from this research is protected and may benefit Māori now and into the future. The principles included are whakapapa, whanaungatanga, rangatiratanga, kotahitanga, manaakitanga and kaitiakitanga. Clinical trials are often driven by Sponsor companies overseas and involve very few Māori as participants.

Consideration of Tikanga and Tiriti obligations are highly valued at NZCR, whereby staff attend Tiriti and Tikanga workshops to acknowledge and understand Māori cultural values and principles. NZCR also maintain contact with the Office of the Chief Advisor Tikanga across Te Whatu Ora Waitemata and Te Toka Tumai Auckland.

Before deciding whether to participate in this study or not, it may be appropriate to discuss your participation with your whanau/family/Kaumatua/hapu/Iwi and consider both the potential risks and benefits that may be involved. If you need cultural support, please let us know and we will arrange this for you. For additional cultural support or tikanga advice, please contact your local Māori support contact listed at the end of this document.

6 WHAT ARE THE RIGHTS OF PARTICIPANTS IN THE STUDY?

6.1 Participation is Voluntary

Participation in any research project is voluntary. 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. This will not affect your relationship with NZCR.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

6.2 New Information

Sometimes during the course of a research project, new information becomes available about the medication that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project, you may be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, they will explain the reasons and arrange for your regular health care to continue.

6.3 Privacy and Confidentiality and Right to Access Information Collected During the Study

What will Happen to my Information?

During this study, the study doctors, researchers, nurses and other NZCR staff will record information about you and your study participation. This includes the results of any study assessments. Information such as your name, sex, age, race/ethnicity, address and phone number will be on the demographics page for the study so we can identify you correctly at visits and contact you. This information may be used to obtain health records (detailed below) but is not supplied to anyone overseas.

If needed, **information from your hospital records and your usual doctor (GP) may also be collected**, and your GP will be notified about your participation in the study. You cannot take part in this study if you do not consent to the collection of this information.

Type of information	Where is it stored?	Who can access it?
Identifiable Information – *this information can be traced back to you*		
• Information collected from you • Laboratory results • Health Diary (back up paper diary if required or requested) • Fertility Clinic for the collection and storage of your semen sample	• **Paper**: stored securely under restricted access at NZCR. Following study completion paper forms are transferred to a secure site and stored for 15 years, then destroyed • **Electronic**: stored on secure NZCR servers (in New Zealand and Australia)	• NZCR staff • Your GP / usual doctor • Local laboratory staff to process and report your screening and safety tests • Sponsor/CRO monitors to ensure the study is run properly and data is collected accurately • Representatives from the Sponsor if you make a compensation claim as a result of study-related injury. Identifiable information is required to assess your claim • Ethics committee, regulatory authorities, and sponsor/CRO representatives if the study or site is audited • Medical Officer of Health for positive test results for a notifiable disease (i.e., Hepatitis B/C) • The study doctor may share your information with other people, in the rare event of a serious threat to public health or safety, or to the life or health of you or another person OR if the information is required in certain legal situations

My Clinical Diary Account Registration requires Identifiable Information – *this information can be traced back to you*		
• Contact Details (email address)	• **Electronic**: will be stored-on a secure platform, Zelta (in Australia, USA and France), and will be retained for up to 15 years. Storage will comply with local and/or international data security guidelines.	• Merative (Zelta)
De-identified (coded) Information – *this information is only labelled with your unique study ID*		
• Study assessment results are uploaded into the study database to be analysed • Health diary recorded in the My Clinical Diary application.	• **Electronic**: will be stored-on a secure platform, Zelta (in Australia, USA and France) and will be retained for up to 15 years. Storage will comply with local and/or international data security guidelines.	• The Sponsor, for the purposes of this study. • People and companies working with or for the Sponsor, for the purposes of this study. • Regulatory or other governmental agencies worldwide.
Anonymised Information – *this information cannot be traced back to you (code removed)*		
• All de-identified information for which the code has been removed	• **Electronic**: stored on a secure sponsor-managed database	• Access not restricted

Future Research Using Your Information

Your coded information may be used for future research related to YCT-529 or male contraception.

This future research may be conducted overseas. You will not be told when future research is undertaken using your information. Your information may be shared widely with other researchers or companies. Your information may also be added to information from other studies, to form much larger sets of data.

You will not get reports or other information about any / some research that is done using your information.

Your information may be used indefinitely for future research unless you withdraw your consent. However, it may be extremely difficult or impossible to access your information or withdraw consent for its use once your information has been shared for future research.

Security and Storage of Your Information

During the study, your information will be stored on paper forms at NZCR and electronically on secure servers. When the study has finished, paper forms will be transferred to a secure site and stored for at least 15 years, then destroyed. De-identified information in electronic form will remain on a secure platform and will be retained indefinitely. Storage will comply with local and/or international data security guidelines.

Risks

Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. While the risk is currently very small, the chance that someone might access and misuse your

information (for example, by making it harder for you to get or keep a job or health insurance) might increase in the future as people find new ways of tracing information.

Your coded information is being sent overseas. Other countries may have lower levels of data protection than New Zealand. There may be no New Zealand representation on overseas organisations which make decisions about the use of your information. There is a risk that overseas researchers may work with information in a way that is not culturally appropriate for New Zealanders.

Rights to Access Your Information and Results

You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

Please ask if you would like to access your screening and safety tests during the study.

If you have any questions about the collection and use of information about you, you should ask a study doctor.

7 WHAT WILL HAPPEN AFTER THE STUDY ENDS, OR IF I WANT TO PULL OUT?

7.1 If You Decide to Withdraw

You may withdraw your consent for the collection and use of your information at any time, by informing your Study Doctor. Please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing, such as follow up visits.

If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you. Information collected up until your withdrawal from the study will continue to be used and included in the study. This is to protect the quality of the study.

You will be asked to attend NZCR for a final visit, known as an early termination visit. You will have the same safety procedures performed as those listed in the Day 14 visit.

7.2 Why the Study Might be Unexpectedly Stopped

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects and safety issues
- Poor recruitment
- Poor study conduct

7.3 Results

When the research project ends the study data must be analysed, so the results of the study may not be available until about a year after the research finishes. The study doctors and/or Sponsor may decide to discuss or publish the results of the study. This may include publication in journals, presentation at conferences or other professional forums. In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you. If you do not wish to receive a summary of the study results when they become available, then please inform NZCR staff.

8 Use of Technology (" My Clinical Diary ") Application

During the study, you will be asked to use technology to complete the psychosexual health diary.

Whilst you are on the study you will be asked to answer sexually related questions that are used to determine your overall sexual impulse. In order to complete this questionnaire, you will need to log into a patient portal ("My Clinical Diary"). The My Clinical Diary Zelta ePRO application is an application which you will be asked to download on your smart phone or similar devices (any Apple IOS or Android supported devices). There are no costs associated to you with the use of the application.

During screening, the study staff will help you set up the application and show you how to use it. During your scheduled clinic visits, study staff will review the diary information with you and collect additional information as necessary.

How is your Data Protected when using the "My Clinical Diary" Application?
The "My Clinical Diary" Application is provided by Zelta. In order to take part in this study and use this application, you will need to accept the application's Terms and Conditions, which are standard conditions regarding privacy of data and are discussed further below. You will need to download this application for the purpose of the study, and the application can be deleted from your device at the end of the study

The information that you enter into the application will be stored on Zelta platform, on a secure data server in Australia, USA and France. The platform that will be used is secure and complies with the regulations to protect the privacy of your health information.

Your email address (identifiable information) will be used to set up your "My Clinical Diary" account. This information will be sent overseas to Zelta, but it will not be sent to the Sponsor. All of your information that is obtained within the "My Clinical Diary" application will be encrypted (unreadable form) while being transferred from the application on your personal device to the study server. This will help to prevent unauthorised access and keep your identity safe, although the risk of unauthorised access cannot be eliminated completely.

Additionally, the application will be password protected and only you can access your own login. For the protection of your privacy, you must not give your login information to anyone. If you are aware, or think that your login information has been compromised, change your password immediately and notify the study staff.

The Sponsor will see the data that is collected from the "My Clinical Diary" Application (i.e., your responses to questions). However, the Sponsor will not see any of your personal identifiable information. Your de-identified information will be added to the data of other study participants and made available to groups of certified Investigators working on the study for analysis.

What are the risks?
The system has been designed to protect your privacy and personal health information. However, because personal information is being transmitted over the internet, there is still some risk of accidental disclosure of your personal identifiable medical information.

For more details on the privacy policies for the "My Clinical Diary" application please use the link below: https://www.merative.com/zelta-privacy

9 WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns, or complaints about the study at any stage, you can contact:

Dr. Rohit Katial, Principal Investigator
Phone: 0800STUDIES
Email: latitude.auckland@nzcr.co.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@advocacy.org.nz
Website: https://www.advocacy.org.nz/

Māori cultural support is available through:

Auckland:

The Office of the Chief Advisor Tikanga, He Kamaka Waiora, Te Whatu Ora (Health New Zealand) – Waitemata and Auckland

Mobile: 021 0203 1167
Phone: 09 486 8320 ext 43204
Email: hkwresearch@waitematadhb.govt.nz

Christchurch:

Dr. Matea Gillies
Mobile: 027 4105 025
Email: gillies-lamb@xtra.co.nz

Waikato:

Te Puna Oranga Māori Health Service, Te Whatu Ora (Health New Zealand) - Waikato

Phone: (07) 8343644
Email: research@waikatodhb.health.nz

Wellington:

Glen Alexander
Mobile: 022 4993 099
Email: glen.alexander1968@gmail.com

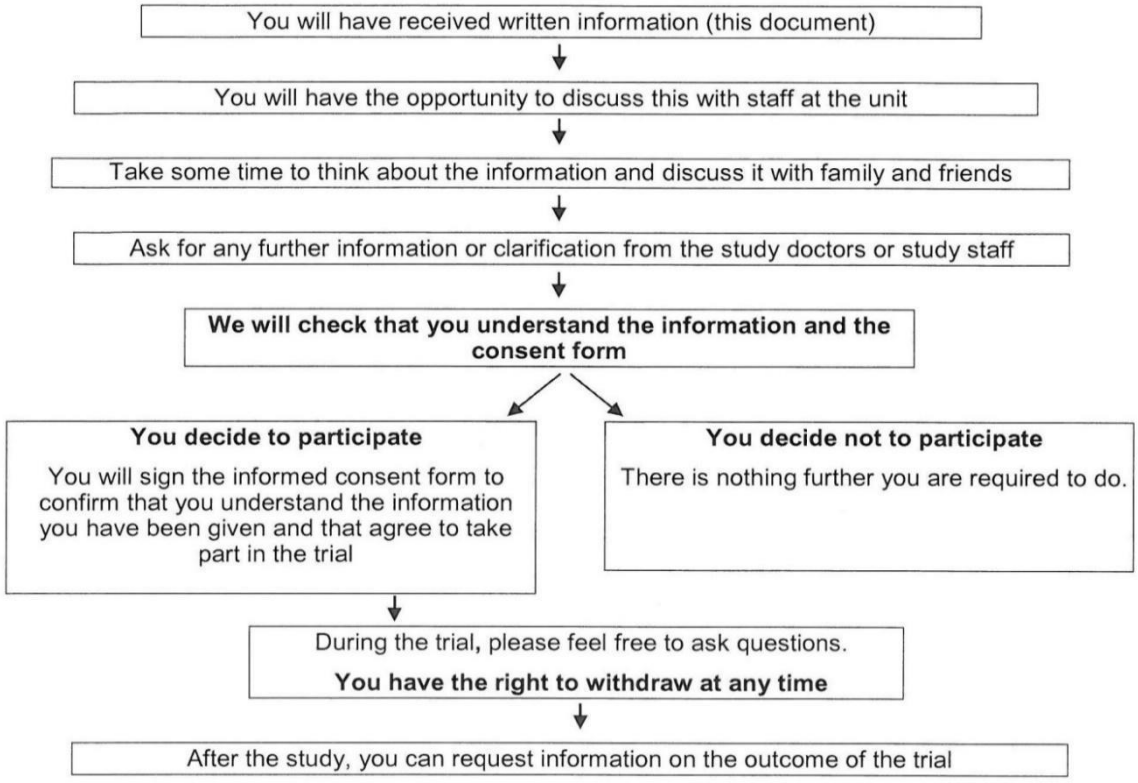
You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Email: hdecs@health.govt.nz

10 WHAT ABOUT ANY OTHER QUESTIONS I MAY HAVE?

11 DO I HAVE TO DECIDE STRAIGHT AWAY?

No, you do not have to decide straight away. You should take some time to consider whether or not to participate, we will be in touch in a week or so to discuss your decision**.** The following steps are useful in helping you reach a decision.



CONSENT FORM
(Phase 1b – Multiple Ascending Dose)

Short Title:	A Study to Evaluate the Safety and Tolerability of YCT-529 in Healthy Male Participants
Protocol Number:	YCT-529-02
Principal Investigator:	Dr. Rohit Katial

***Please let study staff know if you require an interpreter*.**

Declaration by participant:

- I have read the Participant Information Sheet, or have had it read to me in a language I understand, and I fully comprehend what it says.
- I have been given sufficient time to consider whether or not to participate in this study.
- I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.
- I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.
- I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.
- I consent to the research staff collecting and processing my information, including information about my health (including information collected from my GP and other Health Providers).
- If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.
- I understand that there may be risks associated with the medication in the event of my partner becoming pregnant. I undertake to inform my partner of the risks and to take responsibility for the prevention of pregnancy.
- I agree to my tissue samples being sent overseas, and I am aware that these samples will be disposed of using established guidelines for discarding biohazard waste.
- I agree to an approved parties including Sponsor or CRO representatives for monitoring and auditing, auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.
- I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.
- I understand the compensation provisions in case of injury during the study.
- I know who to contact if I have any questions about the study in general.
- I understand my responsibilities as a study participant.
- I understand that I will receive a summary of the study results and if I do not wish to receive this, I will inform site staff.
- I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.

Statement by Participant I hereby consent to take part in this study. I understand that I will receive a signed copy of this consent form for my records.

_____ (full name)

_____ (signature)

__ __ / __ __ __ / __ __ __ __ (Date DD/MMM/YYYY)

Statement by Consenter (Investigator/designee) I have discussed this study with the above-named participant. The participant appeared to fully understand the information provided about the study.

_____ (full name)

_____ (signature)

_____ (project role)

__ __ / __ __ __ / __ __ __ __ (Date DD/MMM/YYYY)