Participant Information Sheet

THIS IS FOR YOU TO KEEP

Temporary Withholding of Immunosuppressant in Rheumatic Diseases and Lupus (TWIRL) Study

Short title: TWIRL Study
Coordinating Principal Investigator: Associate Professor Alberta Hoi
Principal Investigator: A/Prof Alberta Hoi, MBBS, FRACP, PhD
Associate investigators: A/Prof Ian Woolley, A/Prof Claire Dendle, Prof Eric Morand, A/Prof Vera Golder, Dr Kathryn Connelly, Dr Laura Eades, Dr Kristy Yap, Dr Raychel Barallon, Miss Celine Shi
Location: Monash Health, 246 Clayton Road Clayton

Part 1 - What does my participation involve?

1. Introduction:

You are invited to take part in the TWIRL study, which stands for Temporary Withholding of Immunosuppressant in Rheumatic diseases and Lupus. This is a randomised controlled study to examine a safer and evidence-based way of using immunosuppressant, balancing the risk of infection in the immunocompromised group of patients. We want to know if temporarily withholding (stopping) mycophenolate in stable lupus patients can improve their vaccine response to Influenza vaccination.

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

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 participate, you may want to discuss 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 regardless of whether you participate.
If you decide you want to take part in the research project, you will be asked to sign 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 a randomized controlled study?

A randomised control study is when participants are randomly assigned to one of two groups: one (the experimental group) receiving the intervention that is being tested, and the other (the comparison group or control) receiving an alternative (conventional) treatment or procedure. The two groups are followed up to see if there are any differences between them in the outcome.

3. What is the purpose of this research?

Mycophenolate is an immunosuppressant that is widely used as a treatment for systemic lupus erythematosus (SLE). Its biological effects involve a reduction in immune cell functions, which in turn reduce systemic or organ related inflammation and damage. The benefits of using mycophenolate in SLE need to be carefully balanced against unintended side effects such as increased risk of infection or blunting of vaccine responses. One strategy to counteract these effects is the temporary withdrawal of the immunosuppressant, which allows for the immune system to recover and effectively respond to a vaccine or infection. Our study will examine the effects of withdrawing mycophenolate for a short period in SLE patients to improve their immune responses to the seasonal influenza vaccination while safely maintaining disease control.

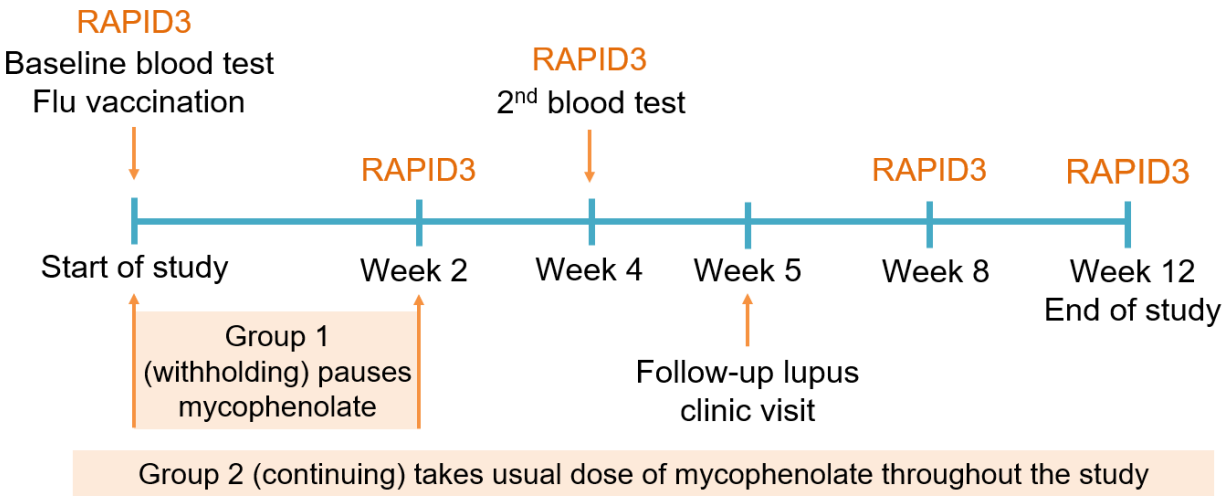
4. What does participation in this research involve?

If you agree to take part in this research project, we will organise for you to receive your seasonal influenza vaccination through Monash Health. You will be contacted by our study coordinator to schedule two (2) in-person blood tests at Monash Medical Centre Clayton. Where possible, we will aim to schedule these blood tests to coincide with your routine lupus clinic blood test collection. In this way, blood samples for this study can be obtained at the same time as your routine blood collection. We will put aside no more than 50ml (approximately 3.5 tablespoons) of blood towards this study at each visit, in addition to the blood taken as part of your routine lupus clinic tests. We will also seek permission to access your immunisation history through your Medicare record. The schedule for the two (2) in-person blood tests will be as follows:

1. First blood test (baseline)
    - A blood sample for the study (approximately 50mL or 3.5 tablespoons) will be collected alongside your routine lupus clinic blood tests
    - You will receive the seasonal influenza vaccine from Monash Immunisation Service
    - At this visit you will be randomised to either the experimental group (Group 1) and stop use of mycophenolate for two (2) weeks following the vaccination; or the comparison/control group (Group 2) and continue to use mycophenolate as per usual.
2. Second blood test
    - To take place four weeks after administration of the seasonal influenza vaccine
    - If you were randomised to Group 1, this appointment will take place two (2) weeks after you have resumed use of mycophenolate
    - An additional blood sample for the study (approximately 50mL or 3.5 tablespoons) will be collected alongside your routine lupus clinic blood tests

From the time of receiving the influenza vaccination, your involvement in the study will last twelve (12) weeks. In addition to the blood tests outlined above, you will be asked to complete a health questionnaire called "RAPID3" at certain points in the study. You will be asked to complete the RAPID3 either in-person on paper, or invitations to complete the RAPID3 questionnaire will be sent to you electronically via email. Participants will be asked to complete the RAPID3 questionnaire five (5) times over the course of the study: once prior to receiving the influenza vaccine and then at 2, 4, 8 and 12 weeks after receiving the influenza vaccine. Please refer to timeline below. You will also be asked to fill out some "influenza checker" questions at 4 and 8 weeks after receiving the influenza vaccine. Your answers to these questions will help us track whether you have contracted influenza and how severe the infection is. Participants who are randomised to Group 1 will receive messages via email to remind them to recommence use of mycophenolate at the end of the 2-week withholding period.

We will provide you with a pathology request slip for a nasopharyngeal swab which we ask that you have collected if you develop symptoms suggestive of influenza, ideally within 5 days of symptom onset. It is standard of care to clarify the nature of the pathogen, where possible. Please advise Dr Hoi or the study coordinator if you have a swab collected. We also ask that you please also complete the symptom diary (provided) every day until symptoms resolve. You should seek your usual care with your doctor if you develop symptoms suggestive of influenza. By taking part in this research project, you will be offered the seasonal influenza vaccine. You will not receive any other personal benefits by taking part in this study. There is no new medication involved. We hope to understand if there is a safer way of handling immunosuppressant during the vaccination process.



5. Other relevant information about the research project.

All study investigators are rheumatologists, infectious disease physicians, immunologists and scientists based at Monash Health or Monash University. The project will aim to recruit about 80 patients.

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

Your participation is voluntary. Whether you take part or not will have no effect on the medical care you currently receive.

7. What are the possible benefits of taking part?

The advice regarding temporary withholding of immunosuppression has been inconsistent due to a lack of available data. We are conducting this randomised control study with the hope of further advancing our understanding on the effects of temporary interruption of mycophenolate and provide scientific evidence for the safety of this practice in patients with systemic lupus erythematosus. Findings in SLE studies can also guide management of mycophenolate use in other autoimmune diseases. Any reversibility of immunosuppressive effect of mycophenolate may also be relevant in the context of concurrent infection. By taking part you will not receive any specific benefit other than being offered the seasonal influenza vaccine, as recommended by the National Immunisation Program.

8. What are the possible risks and disadvantages of taking part?

You will need to attend Monash Medical Centre Clayton for the study blood tests and to receive the seasonal influenza vaccine, which may be an inconvenience. Ideally, we will try to schedule the blood tests for TWIRL to coincide with your routine blood collection for your usual lupus clinic appointment. In the event this is not possible, extra visits for blood collection for the TWIRL study may be required and this may be an inconvenience. You may experience some discomfort associated with the two blood collections as part of the study, in the form of pain and bruising. For participants randomised to Group 1 (experimental group halting mycophenolate use for 2 weeks following administration of vaccine), there is a theoretical risk of disease flares. The study design is such that you will be observed closely and under the care of a Monash Lupus Clinic doctor. We believe the risk of disease flare is low, but its occurrence is recorded as an outcome of interest. Your health is our priority above all else and any participant who agrees initially to take part in this study has the right to withdraw from the study at any point. The questionnaires we ask you to complete are short (<5 minutes).

9. What will happen to my test samples?

The blood samples for this study will be processed by Monash Pathology, the Burnet Institute and Biobanking Victoria. Blood samples will be initially collected by a study investigator, study coordinator or Monash Pathology, and then will be temporarily stored at Biobanking Victoria before being sent to the Burnet Institute for processing and analysis. Any excess sample will be returned to the Australian Lupus Registry & Biobank for storage under HREC 14262A, and future use may be subjected to written approval of specific HREC approval.

10. Will I be given the results of the research project?

Upon completion of the study, a summary of results can be provided to you at your request. Other findings will be made publicly available through conference abstracts at national or international scientific conferences presented by investigators, or publication in peer-reviewed journals.

Part 2 – How is this research being conducted?

11. Human Research Ethics Committee (HREC) Review

This project has been approved by the Monash Health Human Research Ethics Committee. All research will be carried out according to the National Statement on Ethical Conduct in Human Research 2018.

12. Use of clinical and biological data for research purposes

By signing the consent form, you consent to the study doctors and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. All blood samples will be de-identified and coded. It will be possible to re-identify the sample as yours using the code. This information will only be available to the active investigators of this study. Blood samples supplied for this study may be stored for future research.

Your health records and any information collected and stored by the study doctor during the research project may be reviewed for the purpose of verifying the procedures and the data. This review may be done by the ethics committee which approved this research project, regulatory authorities and authorised representatives of Monash Health /Monash University, or as required by law. By signing the consent form, you authorise release of, or access to, this confidential information as noted above.

Your health information will be held for at least 7 years following completion of the study. The data will be stored in a password protected file on a Monash Health secure server and only accessed by the investigator team.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your express permission.

13. Research funding

This study is supported by Arthritis Australia Project Grant (2023).

14. Complaints and further information:

For matters relating to research at the site at which you are participating, the details of the local clinical contact person are:

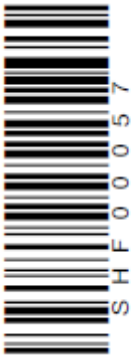
Clinical contact person

Name	A/Prof Alberta Hoi
Position	Principal study doctor & Head, Monash Lupus Clinic
Telephone	(03) 9594 4899
Email	Alberta.Hoi@monash.edu

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:

Reviewing Human Research Ethics Committee (HREC) approving this research and HREC Executive Officer details

Reviewing HREC name	Monash Health Human Research Ethics Committee
HREC Executive Officer	HREC Executive Officer
Telephone	(03) 9594 4611
Email	Research@monashhealth.org



Participant Consent Form (Adult)

Temporary Withholding of Immunosuppressant in Rheumatic Diseases and Lupus (TWIRL) Study

Short title: TWIRL Study
Coordinating Principal Investigator: Associate Professor Alberta Hoi
Principal Investigator: A/Prof Alberta Hoi, MBBS, FRACP, PhD
Associate investigators: A/Prof Ian Woolley, A/Prof Claire Dendle, Prof Eric Morand, A/Prof Vera Golder, Dr Kathryn Connelly, Dr Laura Eades, Dr Kristy Yap, Dr Raychel Barallon, Miss Celine Shi
Location: Monash Health, 246 Clayton Road Clayton

Declaration by Participant

- 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 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 project without affecting my future health care.
- I understand that I will be given a signed copy of this document to keep.
- I understand that I can withdraw my consent to participate in this research project by completing a "Withdrawal of Consent" form.
- I understand that, if I decide to discontinue the study, I may be asked to attend follow-up visits to allow collection of information regarding my health status. Alternatively, a member of the research team may request my permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.

Use of samples for future research

☐ By checking this box, I consent for samples obtained in this study to be stored and used for future research.

Participant's Name (printed): …….

Signature: …… Date: ……

Interpreter's Name (as needed) (printed): …….

Signature: …… Date: ……

Declaration by 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.

Researcher's Name (printed): …….

Signature: …… Date: ……

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

Note: All parties signing the consent section must date their own signature. If the consent process takes place over the phone (due to COVID), a verbal consent is accepted together with a "confirmation of consent" written by the consenting doctor and the date.

Form for Withdrawal of Participation (Adults)

NOTE: COMPLETION OF THIS FORM IS OPTIONAL. A PARTICIPANT MAY WITHDRAW FROM THE STUDY WITHOUT COMPLETION OF THIS FORM.

Temporary Withholding of Immunosuppressant in Rheumatic Diseases and Lupus (TWIRL) Study

Short title: TWIRL Study
Coordinating Principal Investigator: Associate Professor Alberta Hoi
Principal Investigator: A/Prof Alberta Hoi, MBBS, FRACP, PhD
Associate investigators: A/Prof Ian Woolley, A/Prof Claire Dendle, Prof Eric Morand, A/Prof Vera Golder, Dr Kathryn Connelly, Dr Laura Eades
Location: Monash Health, 246 Clayton Road Clayton

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 Monash Health.

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, the research project. Note: All parties signing the consent section must date their own signature. If the withdrawal process takes place over the phone (due to COVID), a verbal withdrawal is accepted together with a "confirmation of withdrawal" written by the doctor and the date.