Appendix 1. World Health Organisation Trial Registration Dataset

Data Category	Information
Primary Registry and Trial Identifying Number	ClinicalTrials.gov (NCT03535935)
Date of Registration in Primary Registry	24 May 2018
Secondary Identifying Numbers	HMRF-14151731
Source(s) of Monetary or Material Support	Health and Medical Research Fund, Food and Health Bureau, Hong Kong
Primary Sponsor	The University of Hong Kong
Secondary Sponsor(s)	N/A
Contact for Public Queries	Prof TANG Chi-wai Sydney MD PhD Dr CHAN Kam-wa MSPH MD PhD Tel: +852 2255 3603 Email: scwtang@hku.hk / chriskwc@hku.hk
Public Title	Efficacy, Safety and Response Predictors of Adjuvant Astragalus Therapy for Diabetic Kidney Disease (READY)
Scientific Title	Efficacy, Safety and Response Predictors of Adjuvant Astragalus for Diabetic Kidney Disease (READY) – An Add-on, Assessor-blind, Parallel, Pragmatic Randomised Controlled Trial
Countries of Recruitment	Hong Kong SAR, China
Health Condition(s) or Problem(s) Studied	Diabetic kidney disease
Intervention (s)	Active comparator: Standard medical care with angiotensin converting enzyme inhibitor or angiotensin receptor blocker and oral hypoglycemic agents and/or insulin at stable dose Experimental arm: Semi-individualised dosage of astragalus on top of standard medical care
Key Inclusion and Exclusion Criteria	Ages eligible for study: between 35 and 80 years old Gender eligible for study: Both

	Healthy volunteers: Not accepted **Inclusion Criteria:** - diagnosed with type 2 diabetes for at least 5 years; - with an estimated glomerular filtration rate (GFR) ≥30 <90 mL/min/1.73m2 confirmed with repeat testing over three or more months calculated by the abbreviated MDRD study equation; - persistent macroalbuminuria with spot urine albumin-to-creatinine ratio (UACR) ≥ 300 mg/g confirmed by at least 2 out of 3 consecutive first morning void urine samples; - on stable dose of anti-diabetic drug including insulin for 12 weeks; - on stable dose of angiotensin-converting-enzyme inhibitor or angiotensin receptor blocker for 12 weeks; and - willing and able to give written informed consent **Exclusion Criteria:** - with known history of glomerulonephritis, polycystic kidney disease, systemic lupus erythematosus, any suggestive evidence of nondiabetic glomerulopathy; - with known history of kidney transplant; - with concurrent severe disorders of heart, brain, liver, and hematopoietic system, tumor and mental disorder; - with deranged liver function; - with poorly controlled blood pressure; - with known history of intolerance or malabsorption of oral medications; - with uncontrollable urinary infection; - experiencing pregnancy; or

	- participating in other clinical trial within 30 days
Study Type	Interventional Allocation: randomised Intervention model: parallel assignment (2 arms) Masking: Open label (Accessor of primary outcome measures blinded) Primary purpose: Treatment Phase: II/III Allocation concealment: Sealed opaque envelope prepared by an independent technical staff Sequence generation: computer generated random sequence
Date of First Enrollment	July 2018
Target Sample Size	118
Recruitment Status	Recruiting
Primary Outcome(s)	Changes in estimated glomerular filtration rate and spot urine to albumin ratio (time frame: 48 weeks)
Key Secondary Outcome(s)	Adverse events, changes in, glycated haemoglobin, lipids, blood pressure and other biomarkers

Appendix 2. Sample Consent form

Patient/Subject Information Sheet

1. STUDY TITLE

Efficacy, safety and response predictors of adjuvant astragalus for diabetic kidney disease (READY) – An open-label randomised controlled trial with responder regression analysis

2. INVITATION PARAGRAPH

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your family doctor if you wish to. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3. WHAT IS THE PURPOSE OF THE STUDY?

Modern pharmacologic therapy using blockers of angiotensin II is unable to fully suppress the progression of chronic kidney disease (CKD). As a result, many patients progress to end-stage kidney disease and require either dialysis or transplantation. Recently, research data shows that astragalus has anti-fibrotic effect, slower the progression to kidney disease and have been using in addition to routine medical care in Hong Kong. However, the actual pharmacological and therapeutic effect of astragalus are unclear. The present study lasting 48 weeks aims to investigate whether astragalus consumption stabilises renal function and reduces albuminuria.

4. WHY HAVE I BEEN CHOSEN?

You have CKD with unsatisfactory proteinuria control despite angiotensin blockade therapy, and are now being invited to participate in this study to investigate the potential beneficial effect of astragalus that is currently widely used in Hong Kong.

5. DO I HAVE TO TAKE PART?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. This will not affect the standard of care you receive.

6. WHAT WILL HAPPEN TO ME IF I TAKE PART?

You will be randomised by computer after thorough assessment to either receive guidance on astragalus consumption in addition to your standard medications or continue standard medications. The observation period of this study is 48 weeks, and you will be followed up at the clinic in the usual manner, but with additional blood and urine tests as appropriate. You will need to attend 6 extra clinic visits for Chinese medicine consultation in addition to your usual visits over the next 48 weeks.

7. WHAT DO I HAVE TO DO?

There are no lifestyle restrictions by participating in this study, except for the need of practicing contraception. As you have CKD, you will be given dietary advice on salt and protein restriction which are necessary even if you are not participating in this study. You will take the astragalus on top of your therapy for your present condition.

8. WHAT IS THE DRUG OR PROCEDURE THAT IS BEING TESTED?

Astragalus has been widely consumed for years in Hong Kong although with limited clinical evidence. According to existing best available evidence, astragalus has anti-fibrotic effect and could slower the progression to kidney disease. Currently, no adverse events have been confirmed to associate with the use of astragalus.

9. WHAT ARE THE ALTERNATIVES FOR DIAGNOSIS OR TREATMENT?

An alternative treatment option of chronic kidney disease is standard medical care with angiotensin receptor blocker or angiotensin converting enzyme inhibitor alone.

10. WHAT ARE THE SIDE EFFECTS OF TAKING PART?

Astragalus is generally well tolerated. There are no known side effects in addition to those of conventional treatment when astragalus is being used within the reference range of Pharmacopeia of China. Nevertheless, astragalus may have unknown side effects. Full evaluation will be performed and adequate monitoring will be exercised once you start taking it. You will need to attend 6 extra clinic visits in addition to your usual visits over the next 48 weeks. Any claims on loss or injury attributable to the study will be arranged by the University of Hong Kong.

11. WHAT ARE THE DISADVANTAGES AND RISKS OF TAKING PART?

The safety of the astragalus to the human fetus is unclear, therefore women with child-bearing potential must practice contraception.

12. WHAT ARE THE BENEFITS OF TAKING PART?

We hope that astragalus will help you. However, this cannot be guaranteed. The information we get from this study may help us treat future patients with CKD better.

13. WHAT IF NEW INFORMATION BECOMES AVAILABLE?

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

14. WHAT HAPPENS WHEN THE RESEARCH STUDY STOPS?

After the study stops, you will be advised whether or not to continue with astragalus according to clinical need. Astragalus will not be provided for free.

15. WHAT IF SOMETHING GOES WRONG?

Any claims on loss or injury attributable to the study will be arranged by the University of Hong Kong. If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal health service complaints mechanisms may be available to you.

16. WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?

You have the rights of access to personal data and publicly available study results, if and when needed.

Under the laws of Hong Kong (in particular the Personal Data (Privacy) Ordinance, Cap 486), you enjoy or may enjoy rights for the protection of the confidentiality of your personal data, such as those regarding the collection, custody, retention, management, control, use (including analysis or comparison), transfer in or out of Hong Kong, non-disclosure, erasure and/or in any way dealing with or disposing of any of your personal data in or for this study. For any query, you should consult the Privacy Commissioner for Privacy Data or his office (Tel No. 2827 2827) as to the proper monitoring or supervision of your personal data protection so that your full awareness and understanding of the significance of compliance with the law governing privacy data is assured.

By consenting to participate in this study, you expressly authorize:

- the principal investigator and his research team and the ethics committee responsible for overseeing this study to get access to, to use, and to retain your personal data for the purposes and in the manner described in this informed consent process; and
- the relevant government agencies (e.g. the Hong Kong Department of Health) to get access to your personal data for the purposes of checking and verifying the integrity of study data and assessing compliance with the study protocol and relevant requirements.

17. WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

The results of this study will be published in a medical journal. Your personal information will be kept confidential.

18. WHO IS ORGANISING AND FUNDING THE RESEARCH?

This study is supported by the Health and Medical Research Fund and you do not need to pay any extra cost. Your doctor will not be paid for including you in this study.

19. WHO HAS REVIEWED THE STUDY?

The Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster has reviewed and approved this study. After recruitment, Each patient will receive HK$150 for each blood/urine investigation visit related to this study as travel support.

20. CONTACT FOR FURTHER INFORMATION

In case of enquiry, you may contact Mr Chris Chan or Prof Sydney Tang at 2255 3207. You will be given a copy of this information sheet and a signed consent form to keep. Thank you for taking part in this study!

From the Division of Nephrology
Department of Medicine
University of Hong Kong
Queen Mary Hospital

PATIENT/SUBJECT CONSENT FORM

Title of Project: Efficacy, safety and response predictors of adjuvant astragalus for diabetic kidney disease (READY) – An open-label randomised controlled trial with responder regression analysis

Name of Researcher: Prof Sydney C.W. Tang

	Please initial box
1. I confirm that I have read and understood the information sheet dated __/__/__ for the above study and have had the opportunity to ask questions.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
3. I understand that sections of any of my medical notes may be looked at by responsible individuals from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.	☐
4. I agree to take part in the above study.	☐

_____	_____	_____
Name of patient	*Date*	*Signature*
_____	_____	_____
Name of Witness (if applicable)	*Date*	*Signature*
_____	_____	_____
Name of person taking consent (if different from researcher)	*Date*	*Signature*
_____	_____	_____
Researcher	*Date*	*Signature*

Copies to:

☐ Patient/Subject

☐ Researcher's File

☐ Hospital Record