

Study progress

As of today, a total of **1,675 participants** have been randomized in our trial. We are also pleased to announce that Singapore has successfully enrolled its first 10 participants. In addition, the Netherlands has reached a significant milestone, surpassing 1,000 enrolled participants. We are well on track. Thank you all for your continued dedication and hard work !!!

Guidance from the Steering Committee

• Continue study medication after clinical events

Participants should remain on study medication (if possible) after events such as admission for heart failure or a kidney transplantation, or when starting dialysis.

• Management after primary endpoint of heart failure

When a participant reaches the primary endpoint related to heart failure, questions may arise regarding open-label SGLT-2 therapy. At this stage, there is no scientific evidence to support routine open-label treatment for dialysis patients, kidney transplant recipients or patients with advanced kidney disease. We kindly encourage sites to explain the rationale for continuing treatment to the patient because by doing so they will contribute to evidence to support informed decision-making for all future patients.

• Participants stopping medication at home

Some participants may stop taking study medication out of their own initiative. We encourage sites to discuss any interruptions proactively and to support participants in restarting medication whenever possible.

• Inclusion of ADPKD participants

We would like to emphasize that patients with ADPKD are eligible to be included in the study. By including such patients in our trial we may be able to deliver the first prospective evidence whether SGLT2i is beneficial in this patient group.

Practical reminder cognition sub-study

When entering data for the screening visit, please ensure that the “Yes” option is selected on the visit form if the participant is taking part in the cognition sub-study. Once this box is checked, the related question will automatically appear on the Informed Consent page. After both checkboxes have been completed, you will be able to enter the data for the Symbol Digit Modalities Test.

End of Study (EOS) form

When a participant fully ends participation in the study — e.g. due to withdrawal of consent, death, or any other reason — we kindly ask sites to complete the **End of Study (EOS) form** in REDCap. Please also ensure that the **Study Medication Termination form** is completed for these participants.

Follow-up without study medication

In our study, **participants must continue in follow-up** even after they have discontinued study medication, because of the **intention-to-treat design**. During this follow-up period, all applicable assessments will be performed even when not using medication, unless the participant withdraws consent completely. At the end of the overall study, the **final vital status** has to be recorded for all participants. Therefore, when a participant wants to stop study medication, it is important to ask whether they agree to collect this information at the overall end of the study. This permission should be recorded on the End of Study page in REDCap.

Cardiac Imaging Sub-studies Design Paper

A paper on the design of the cardiac imaging sub-studies of the Renal Lifecycle Trial has now been [published](#) in the Clinical Kidney Journal. The publication outlines the rationale and methodology of these sub-studies that are led by Lily Jakulj from Amsterdam and Sunil Badve and Clare Arnott from Sydney. It will provide important insights into the cardiac effects of dapagliflozin in patients with advanced CKD, dialysis, and kidney transplant recipients.

Request to submit ideas for substudies

Soon, the Steering Committee will start writing the definitive data analysis plan for the overall study. This plan, however, should also consider a brief description of other research questions that can be addressed using the data collected so far. We would like to invite you to share your ideas for substudies, including when possible a brief description (max half a page) outlining the title, objectives, hypotheses, and specific data required. These proposals will be reviewed for inclusion in the overall statistical analysis plan. The deadline for proposals is approximately 6 months from now. Please send them to: R.T.Gansevoort@umcg.nl