Newsletter

Issue 26 · May 2026

RENAL LIFECYCLE TRIAL

Study progress

As of today, a total of **1,751 participants** have been randomized in our trial. We realize that during the last couple of weeks confusing messages have been sent to you about the end date for patient study inclusion. We apologize for this. Based on data that have become available only recently, we had to retract our initial stop date for inclusion. The cumulative incidence of endpoints in our trial appeared to have changed from an exponential increase to a linear increase. This means that the trial will last longer, unless more patients are included.

For **Spain, Singapore, the Netherlands and Belgium**, screening and inclusion timelines will be determined based on the new developments with respect to the number of primary endpoints collected. We will update you on this in due course.

Until screening is formally closed in each country, sites are kindly requested to **continue recruitment efforts** as planned and as fast as possible. We **thank all participating sites** for their ongoing commitment and significant contribution to the successful progress of the trial.

Open-label SLGT-2 inhibitor therapy

A recent data review showed that fortunately only a small number of participants have started open-label SGLT-2 inhibitors during the study. It is important to **avoid open-label SGLT-2 inhibitor use** during the study, because this will also decrease the chance of finding a treatment effect. whenever clinically feasible. We kindly ask investigators to remain mindful of this.

ALEA: OFF-Study notifications

For upcoming shipments of study medication, we aim to **align IMP supply** with the number of visits that are still expected at each site. Therefore, it is important that ALEA reflects when no further study medication dispensations are expected for a participant. This applies, for example, to participants who have died, continue follow-up without study medication, or have fully discontinued the study. **We kindly ask sites to fill in an OFF Study form should in ALEA for these participants**. **Important: when possible, always try to restart study medication**, even when there is a lag time of several weeks between stopping and restarting. **A temporary stop of study medication is for trial data quality always better than a definitive stop.** By the way, an OFF Study submission is technically difficult to reverse. Therefore, we ask that this form be completed only when it is certain that the participant will not restart study medication.

Discontinuation rates

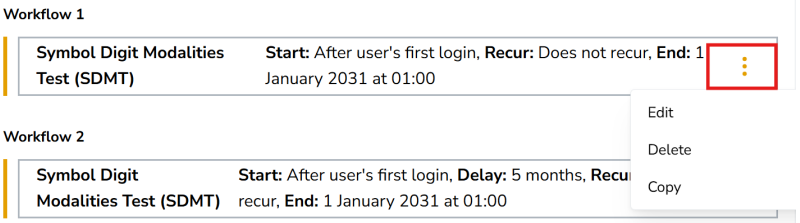
Recent study data shows that **overall discontinuation** of study medication over two years is around 20 percent. Discontinuations **occur gradually over the course** of the follow-up. Study drug discontinuation decreases the chance of finding a treatment effect. Continued **patient and research staff motivation** remains key to keep **study drug discontinuation as low as possible**. This will ensure complete and high-quality study data. We appreciate the commitment of all sites in supporting this.

Safety and Endpoint reporting

We would like to remind you to report only events that meet the study-defined reporting criteria. These include Serious Adverse Events (SAE), Adverse Events of Special Interest (AEoSI), Discontinuation Adverse Events (DAE) and study endpoints. Adverse Events that do not fall within these categories, **do not require reporting** in REDCap.
In addition, **timely reporting** of these events remain essential, especially for **study endpoints**. Prompt reporting of endpoints helps to keep the backlog as small as possible, which is crucial for this endpoint driven trial.

Orikami instructions after stop

When a participant withdraws from the study, it is important to also 'sign off' the participant in the Orikami dashboard (if participating in this sub-study). This ensures they do not receive notifications for follow-up assessments. You can 'sign off' a participant by deleting their schedules—using the three dots, as shown below.



Required documentation in case of Death

When a participant dies during the study, a specific set of forms is required to ensure complete study documentation. In the event of a participant's death, please complete the following forms in REDCap:

- Study Medication Termination form
- End of Study (EOS) form
- SAE report with the outcome marked as fatal

Timely completion of these forms supports complete and up-to-date safety data.

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