Dear Dr. Ebrahimi,

Thank you for your interest in clinical trial data being made available through the YODA Project. We are enthusiastic about your proposed research titled “Canagliflozin and Non-Alcoholic Fatty Liver Disease in Type 2 Diabetes (CaNAFLD) – A Post-Hoc Analysis of RCTs.” However, a clarification is required prior to completing the review of your data request. Please address the following question:

1. In this request, the authors outline a study focused on assessing the effect of canagliflozin vs. placebo on liver related outcomes in patients with T2DM and identifying subgroups that are most likely to benefit from treatment. Could the requestors clarify that the trials that are being requested contain the outcomes of interest for this study? In particular, do both trials have information for the primary and/or secondary outcomes outlined in the data request?

Author’s Reply:

Dear Reviewers,

We thank for the positive feedback and your request regarding the availability of the requested outcome parameters.

For the analysis of the primary outcome measure “change in ALT levels from baseline in the canagliflozin group compared to placebo”, ALT levels at different time points from baseline are needed. According to the final study protocols of the CANVAS (NCT01032629) and CANVAS R (NCT01989754) trials, ALT levels were routinely measured at study visits in both studies and should therefore be available for our analyses. The measurement of ALT levels has been stated in the Attachment 6 “Clinical Laboratory Tests” of the final CANVAS study protocol (document number: EDMS-ERI-13522077; version 12.0; page 126) as well as in the Attachment 1 of the final CANVAS-R protocol (document number: EDMS-ERI-65832346, version 8.0; page 85).

For the analysis of our secondary endpoints, the following additional laboratory parameters are needed: AST, GGT, HbA1c, white blood cell count, platelet count, albumin, triglycerides, and Bilirubin. All of those parameters were routinely measured at the study visits and should therefore be available. This can be seen in the Attachment 6 “Clinical Laboratory Tests” of the final CANVAS study protocol (document number: EDMS-ERI-13522077; version 12.0; page 126) as well as in the Attachment 1 of the final CANVAS-R protocol (document number: EDMS-ERI-65832346, version 8.0; page 85).

Furthermore, the clinical variables body mass index and body weight were regularly measured at study visits.

Yours sincerely,

Dr. Fahim Ebrahimi