**Markers of inflammation, oxidative stress, aging and CGM metrics in an adult Hybrid Closed Loop Trial**

**Aim:** Hyperglycaemia, hypoglycaemia and glucose fluctuations have been associated with inflammation, oxidative stress and cellular dysfunction. In Type 1 diabetes (T1D) insulin pump vs injection use is associated with major reductions in complications and CVD-related death. Suggested mechanisms include reduced inflammation, oxidative stress, insulin resistance and insulin dosage. We published (PMID:33055139) results of the first adult hybrid closed loop (HCL) pump trial, which improved all glucose metrics. We aimed to determine associations between HbA1c, CGM metrics and insulin delivery modality with measures of inflammation, oxidative stress, inflammation and biologic aging.

**Methods:** Trial data, including 3-weeks masked-CGM data pre-randomisation to 6-months Medtronic 670G HCL or usual care (no-CGM) and at trial-end. At baseline and trial-end biobanked samples were assayed: inflammation (sVCAM1, sICAM1, sE-Selectin, interleukin-6), oxidative stress (myeloperoxidase), adipokines/insulin resistance (adiponectin, resistin) by ELISA and biologic age markers (relative telomere length and mitochondrial DNA copy-number (mtDNA-cn)) by qPCR. All subject samples were in the same run with CVs (0.5-8%). Analyses include descriptives, correlations, ANCOVA with baseline-adjustments, t-test, or rank-sum equivalents, with significance at p<0.05.

**Results:** T1D adults (n=120), 47% male, 61% injection-users, mean(SD) age 44(12) yrs, T1D 24(12) yrs, HbA1c 7.4(0.9)%, Time-in-range (TIR) 55(13)% with no differences in demographics or research biomarkers by trial arm (HCL, n=61, usual care n=59).

At baseline, many biomarkers of inflammation, oxidative stress and biologic age correlated with age, diabetes duration, BMI and total-daily-insulin-dose.

Significant correlates (in delta biomarkers and delta glucose metrics (study-end–baseline) in all subjects (unless stated otherwise)): TIR with sVCAM1 (negatively) and resistin (positively); mtDNA-cn (negatively) with TIR and time-below-range, and (positively) with time-above-range and HbA1c. HCL-use was associated with increased resistin (median difference (95%CI) 0.68 (0.14, 1.23), p=0.0053).

**Conclusions:** In well-controlled T1D adults changes in HbA1c and CGM metrics correlated with measures of inflammation, insulin-resistance or mtDNA-cn, but few improved with HCL-use.