

SUPPLEMENTARY DATA

Supplementary Table 1. Subject demographics and baseline characteristics (with units stated in parenthesis).

Characteristic	Value
Cohort	19 (11F,8M)
Age (yrs)	23.0 (10.0)
Weight (kg)	86.1±22.8
BMI (kg/m²)	28.2±6.0
Duration of diabetes (yrs)	11.0 (11.8)
Total daily insulin (TDD) (U)	56.3±18.4
Total daily insulin per kg (U/kg)	0.67±0.19
HbA1c (%)	8.0±1.7
HbA1c (mmol/mol)	63.8±18.4

Supplementary Table 2. Non-responder subjects during the study. The differences (Δ) are calculated as Zone-MPC AP outcomes minus SAP outcomes. Subjects #2 to #6 had increased mean glucose during closed-loop (CL) while Subjects #1, #2, #4, #5 and #6 had decreased time in 70-180 mg/dL during CL. Non-responders had a baseline HbA1c that was slightly higher than that of responders (8.3±2.9 vs. 7.9±0.8%; $p=0.43$) but mean SAP glucose that was slightly lower (147±20 vs. 160±11 mg/dL; $p=0.18$), though neither difference was statistically significant.

#	Subject	Site	HbA1c	SAP Mean BG (mg/dL)	SAP % time in 70- 180	SAP % time < 70	SAP % time > 180	Δ Mean BG (mg/dL)	Δ % time in 70- 180	Δ % time < 70	Δ % time > 180	Percent time in CL
1	23007	SU	8.2	165	65.3	0.73	33.95	-2.33	-0.35	-0.44	0.79	93.9
2	23009	SU	8.0	143	76.75	2.60	20.63	6.08	-2.3	-1.75	4.05	90.9
3	23002	SU	6.7	144	69.44	7.12	23.43	4.78	0.89	-3.91	3	87.5
4	23004	SU	6.3	131	80.33	5.59	14	23.68	-8.83	-4.37	13.21	94.6
5	23005	SU	14.0	175	54.46	1.7	43.83	9.76	-3.9	-0.75	4.66	80.5
6	48806	BDC	6.4	122	88	3.79	8.21	17.39	-7.9	-2.72	10.63	89.5

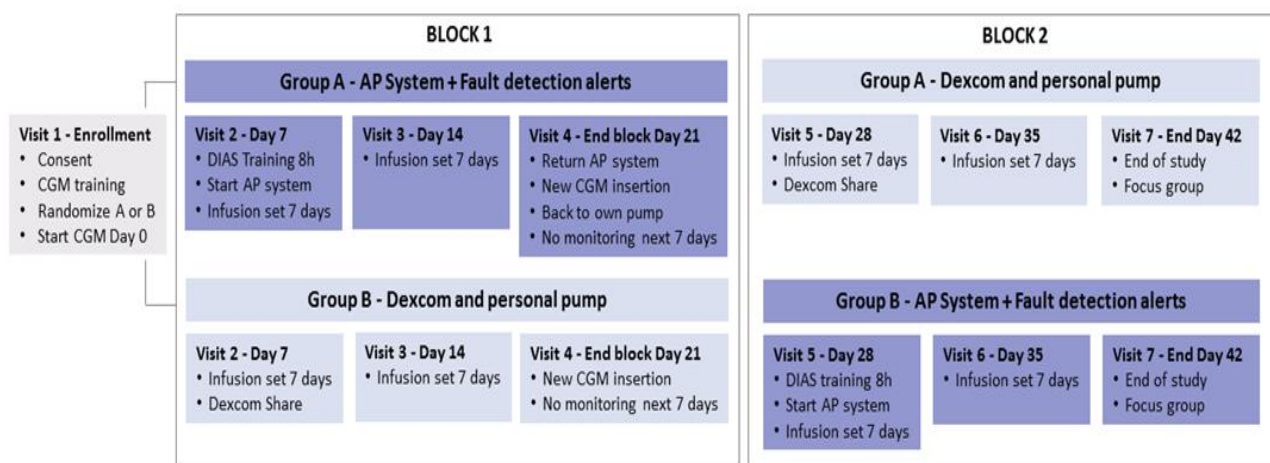
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Supplementary Table 3. Change (Δ) in glycemic metrics (Zone-MPC AP outcomes minus SAP outcomes) in the two sequences of the study: AP followed by SAP and SAP followed by AP. No period-specific differences were found for primary and secondary outcomes as assessed by rank-sum test. The data are shown as median (IQR).

Metric	AP followed by SAP (N=10)	SAP followed by AP (N=9)	p-value
Δ %Time < 50 mg/dL	-0.1 (0.3)	-0.0 (0.2)	0.368
Δ %Time < 60 mg/dL	-0.7 (0.5)	-0.3 (0.7)	0.356
Δ %Time < 70 mg/dL	-1.5 (1.0)	-0.8 (2.1)	0.549
Δ %Time in 70 - 140 mg/dL	6.0 (8.4)	8.1 (12.7)	0.905
Δ %Time in 70 - 180 mg/dL	5.9 (12.6)	11.1 (15.4)	0.604
Δ %Time > 180 mg/dL	-4.1 (11.4)	-10.5 (17.7)	0.720
Δ %Time > 250 mg/dL	-2.7 (2.0)	-1.7 (4.3)	0.549
Δ %Time > 300 mg/dL	-1.0 (1.6)	-0.2 (1.6)	0.278
Δ Mean glucose (mg/dL)	-7.6 (10.7)	-10.7 (19.5)	0.720
Δ Median glucose (mg/dL)	-6.1 (14.3)	-12.8 (24.2)	0.842
Δ SD glucose (mg/dL)	-4.8 (16.7)	-4.9 (10.0)	0.968
Δ CV glucose	-0.0 (0.1)	-0.0 (0.1)	1.000
Δ Mean glucose at 06:00 (mg/dL)	-24.2 (38.2)	-17.0 (28.8)	0.400

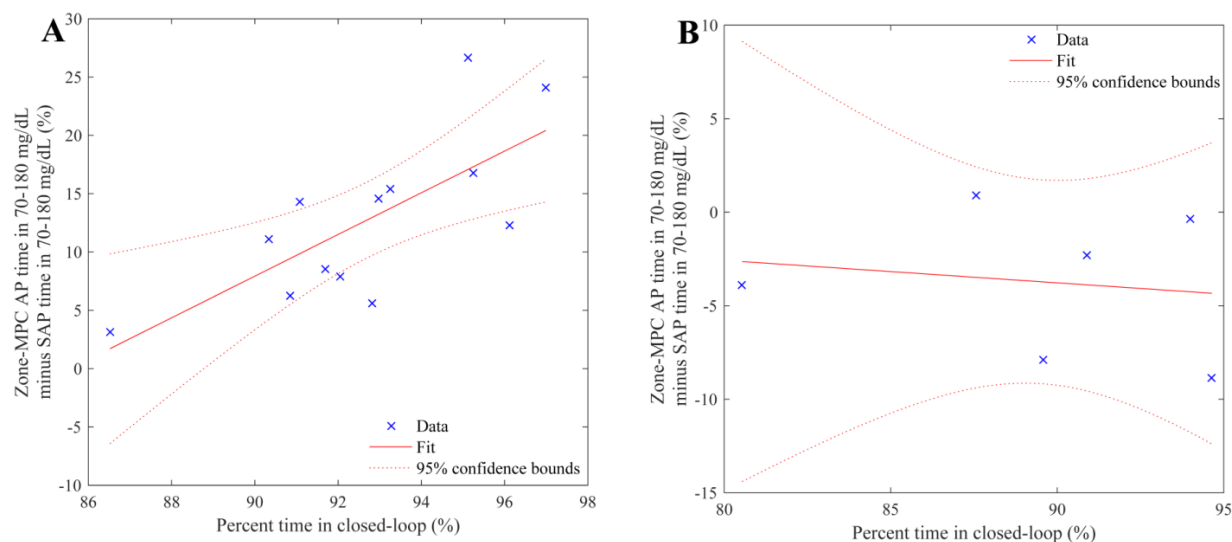
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Supplementary Figure 1. Flowchart of clinical trial plan.



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Supplementary Figure 2. Analysis on relationship between changes in time in 70-180 mg/dL, from Zone-MPC AP to SAP, and percent time closed-loop was active for responders (A) vs non-responders (B). For responders, the percent time in closed-loop is strongly correlated (sub-figure A, $R^2 = 0.49$, $\beta_1 = 1.78$ ($p = 0.007$), 95% CI = [0.57 2.99]) with the outcome whereas completely unrelated (sub-figure B, $R^2 = 0.02$, $\beta_1 = -0.12$ ($p = 0.78$), 95% CI = [-1.28 1.03]) for non-responders



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Supplementary Figure 3. Analysis on relationship between time < 70 mg/dL and time > 180 mg/dL changes, from Zone-MPC AP to SAP, and percent time closed-loop was active. For change in percent time < 70 mg/dL (sub-figure A, $R^2 = 0.000975$, $\beta_1 = 0.01$ ($p = 0.9$), 95% CI = $[-0.17 \ 0.19]$), there was no correlation with percent time in closed-loop as subjects spent very small amount of time in hypoglycemia. For change in percent time > 180 mg/dL (sub-figure B, $R^2 = 0.31$, $\beta_1 = -1.53$ ($p = 0.014$), 95% CI = $[-2.72 \ -0.34]$), the time spent in closed-loop correlates with decrease in hyperglycemia.

