Observed Glycemic and Psychosocial Benefits in the Prospective Bigfoot Unity Real World Study (BURST): A 12-Month Analysis

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Background

- The Bigfoot Unity System integrates Abbott FreeStyle Libre 2 CGM data into a smart insulin pen cap and mobile app enabling clinician-directed insulin dose recommendations and real time alerts.
- The objective was to analyze prospective, real world, 12-month glycemic control for System users on multiple daily injections (MDI).

Methods

- BURST is a prospective, single arm real world study (NCT05088265). We conducted a final 6 and 12-month, 100+ person per-protocol analysis. The protocol, consent forms and data collections forms were approved by the JAEB Center for Health Research (JCHR) institutional review board (IRB).
- Participants reported baseline demographics, adverse events and other surveys electronically. Either at-home kit or electronic medical record HbA1c data were collected. De-identified CGM and other System data, collected after System initiation, were transferred from the sponsor to JCHR for analysis.
- The per-protocol cohort included all participants with baseline and 6-month HbA1c and ≥50% CGM data availability at 6 months, reflecting N=125 of 232 in the study; 100 had 12-month data.
- An expanded cohort (N=176) with any HbA1c or GMI after ≥3 months was also analyzed to assess drop-out bias.
- Patient reported outcomes (PRO) included the 28-item Type 1 Diabetes Distress Scale (T1-DDS) and the Hypoglycemia Confidence Scale (HCS) at baseline, and 6 and 12 months; scores calculated as described.[1,2]
- Serious adverse events were categorized as follows: Severe hypoglycemia (loss of consciousness or impairment where assistance was required by a third party); Diabetic ketoacidosis (DKA; reported DKA diagnosis from a healthcare facility); Serious hyperglycemia (treated in a healthcare facility other than DKA).
- A longitudinal linear regression model was used to test HbA1c and PRO change from baseline. Recently, similar interim 6-month results with more detailed methods, results and discussion have been published.[3]

Results

- Median age was 58 years, 58% were White non-Hispanic, 86% had type 2 diabetes (T2D) and 14% type 1 diabetes (T1D; Table 1).
- There was substantial HbA1c improvement from baseline (prior to System use) to 3, 6, 9 and 12 months (Figure 1) with a low percentage of time below range (TBR; Table 2).
- Improvement was evident quickly after initiation of the System; mean glucose management indicator (GMI) was calculated to be 7.7 ± 1.0% in the first 2 weeks and remained stable through 6 (7.6 ± 1.0%) and 12 months (7.5 ± 1.0%).
- There was significant decrease from baseline in total diabetes distress with a corresponding rise in hypoglycemia confidence (Table 2).
- Several subgroups (Table 3) showed similar HbA1c outcomes; those in a rural setting, those with shorter diabetes duration and higher baseline HbA1c had more improvement, likely due to higher baseline HbA1c. A smaller group of T1D individuals had similar HbA1c improvement (Table 3) but slightly higher percent TBR and time above range (TAR) and slightly less HCS improvement (Table 4). An expanded cohort of participants with less strict use requirements had similar HbA1c and PRO outcomes and CGM metrics (Table 4).
- Six severe hypoglycemia events in 4 participants (incidence 4.5 events per 100 person years) occurred in the per protocol cohort; no DKA/severe hyperglycemia occurred (8 severe hypoglycemia events in 6 participants and 1 DKA event occurred in the expanded cohort); no events were related to the System.

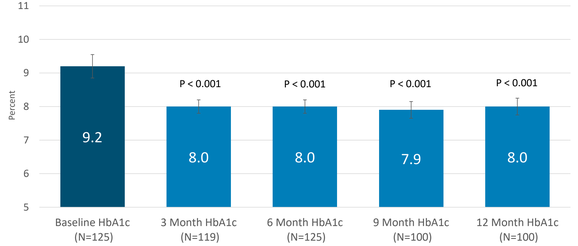

Figure 1: Comparison of Baseline to 3- through 12-Month HbA1c The median timing of baseline HbA1cs prior to System start was 15 days. Data represent mean and 95% confidence interval.

Table 1: Patient Characteristics

Per-Protocol Cohort (N=125)	
Age in years, median (range)	58 (22-82)
Female, n (%)[a]	76 (63)
Type 2 Diabetes, n (%)	108 (86)
BMI, mean (SD)[a]	34.9 (8.1)
Basal Dose at Baseline (Units), median (quartiles)	30 (20, 50)
Race/Ethnicity, n (%)[a]	
White non-Hispanic	70 (58)
Black/African-American	38 (31)
Hispanic or Latino	9 (7)
Other[b]	4 (3)
Prefer not to answer	0 (0)
Duration of Prior CGM Use, n (%)[a]	
No prior CGM use	65 (54)
Less than 6 months	12 (10)
6 months - <1 year	7 (6)
≥ 1 year	37 (31)

[a]Four (4) were missing data on baseline surveys; [b]Other race: 1 participant selected Native Hawaiian/Other Pacific Islander and 3 selected multiple races.

Table 2: Glycemic, Use and PRO Outcomes

Per-Protocol Cohort	Baseline (N=125)	Month 6 (N=125)	Month 12 (N=100)[f]
HbA1c (%), mean (SD)	9.2 (1.8)	8.0 (1.3)[b]	8.0 (1.2)[b]
Mean Glucose (mg/dL), mean (SD)	221 (51)[c]	179 (41)	177 (43)
Percent Time 70-180 mg/dL, mean (SD)	30 (27)[c]	58 (23)	59 (24)
Percent Time >180 mg/dL, mean (SD)	69 (31)[c]	41 (24)	40 (25)
Glucose Management Indicator (%), mean (SD)	-	7.6 (1.0)	7.5 (1.0)
Percent Time >250 mg/dL, mean (SD)	-	15 (17)	15 (18)
Percent Time <70 mg/dL, mean (SD)[d]	-	1.0 (1.4)	1.1 (1.6)
Percent Time <54 mg/dL, mean (SD)[d]	-	0.03 (0.14)	0.05 (0.19)
Glucose Coefficient of Variation (%), mean (SD)	-	31 (7)	31 (7)
Daily Rate of Sensor Scans, median (quartiles)	-	5.3 (3.8, 8.0)	4.4 (2.9, 6.6)
Daily Rate of Rapid-Acting Insulin Doses, median (quartiles)	-	2.4 (1.7, 3.0)	2.0 (1.4, 2.9)
Weekly Rate of Long-Acting Insulin Doses, median (quartiles)	-	7.0 (6.3, 7.3)	6.5 (5.3, 7.0)
# Participants with ≥1 Rapid-Acting Insulin Dose Adjustments, n (%)	-	21 (17)	10 (10)
# Participants with ≥1 Long-Acting Insulin Dose Adjustments, n (%)	-	16 (13)	10 (10)
Diabetes Distress Scale, Total Score, mean (SD)[e]	2.4 (1.0)	1.7 (0.6)[b]	1.5 (0.5)[b]
Hypoglycemic Confidence Scale, mean (SD)[e]	2.8 (0.7)	3.2 (0.7)[b]	3.3 (0.6)[b]

[a]One was missing data for CGM and dosing parameters at 12 months (N=99); [b]For 3 measures assessed at baseline, 6 and 12 months (HbA1c, T1-DDS, HCS), there was significant change from baseline to 6 and 12 months (p<0.001); estimates, confidence intervals, and p-values calculated using a longitudinal linear model with p-values adjusted for multiplicity using the two-stage adaptive Benjamini-Hochberg procedure; [c]Baseline values were estimated from the baseline HbA1c value using formulas from Beck et al.[4] [d]Robust means and SD are reported. [e]Some participants in the cohort had missing surveys; N=114 at baseline, N=117 at 6 months and N=103 at 12 months.

Table 3: HbA1c Subgroup Analysis

Per-Protocol Cohort		N[a]	Baseline HbA1c	12 Month HbA1c	Interaction P-value[b]
Age	25-<50 years	32/25	9.8 ± 2.2	7.9 ± 1.3	0.02
	50-<65 years	51/41	9.5 ± 1.8	8.2 ± 1.4	
	≥65 years	42/34	8.6 ± 1.4	7.9 ± 1.1	
Diabetes Duration	≤ 10 years	42/33	9.8 ± 2.2	7.7 ± 1.2	0.003
	> 10 years	79/64	9.0 ± 1.5	8.1 ± 1.2	
Baseline HbA1c	<8.0%	28/22	7.2 ± 0.5	7.1 ± 1.0	<0.001
	≥8.0%	97/78	9.9 ± 1.6	8.2 ± 1.2	
Race/Ethnicity	Non-White or Hispanic	51/40	9.7 ± 1.9	8.3 ± 1.4	0.34
	White non-Hispanic	70/57	8.9 ± 1.7	7.8 ± 1.1	
Urban/Rural	Rural	25/18	9.7 ± 2.0	7.5 ± 1.3	0.004
	Urban	100/82	9.1 ± 1.8	8.1 ± 1.2	
Income	<$100,000	94/79	9.3 ± 1.9	8.0 ± 1.2	0.14
	≥$100,000	18/13	8.7 ± 1.4	8.2 ± 1.1	
Education	<Bachelor's	85/71	9.4 ± 1.9	8.0 ± 1.2	0.47
	≥Bachelor's	35/25	9.0 ± 1.6	7.9 ± 1.3	
Pre-Study Sensor	Non-CGM user	65/49	9.2 ± 1.9	7.9 ± 0.9	0.71
	CGM user	56/48	9.3 ± 1.8	8.1 ± 1.5	
Type of Diabetes	T1D	17/13	9.3 ± 1.4	8.4 ± 1.5	ND
	T2D	108/87	9.2 ± 1.9	7.9 ± 1.2	

[a]Numbers reflect baseline/12 month N as some had missing data; [b]Interaction was tested using longitudinal linear model with a study period by subgroup interaction term. CI and p-values were adjusted for multiplicity using the two-step adaptive Benjamini-Hochberg procedure. Type of diabetes subgroup was added post-hoc and no interaction testing was performed.

Table 4: Cohort Comparisons

Per-Protocol Cohort vs Expanded Cohort		Per-Protocol[a] (N=125)	Expanded Cohort[b] (N=176)
6-Month Change from baseline	HbA1c, mean (95%CI) [p-value]	-1.2 (-1.5, -0.9) [<0.001]	-1.3 (-1.5, -1.0) [<0.001]
	T1-DDS, mean (95%CI) [p-value]	-0.7 (-0.9, -0.5) [<0.001]	-0.8 (-0.9, -0.6) [<0.001]
	HCS, mean (95%CI) [p-value]	0.4 (0.3, 0.5) [<0.001]	0.4 (0.3, 0.5) [<0.001]
6-Month CGM parameters	Percent CGM use, median (IQR)	85 (74, 91)	81 (66, 90)
	Percent Time 70-180 mg/dL, mean (SD)	58 (23)	56 (25)
	Percent Time <70 mg/dL, mean (SD)	1.0 (1.4)	1.0 (1.5)
	Percent Time >180 mg/dL, mean (SD)	41 (24)	43 (25)
Per-Protocol T1D vs T2D		**Per-Protocol T1D[a] (N=17)**	**Per-Protocol T2D[a] (N=108)**
6-Month Change from baseline	HbA1c, mean (95%CI) [p-value]	-1.1 (-1.7, -0.4)	-1.3 (-1.6, -0.9)
	T1-DDS, mean (95%CI)	-0.7 (-1.1, -0.3)	-0.7 (-0.9, -0.5)
	HCS, mean (95%CI)	0.2 (-0.2, 0.6)	0.4 (0.3, 0.6)
6-Month CGM parameters	Percent CGM use, median (IQR)	84 (72, 95)	85 (74, 90)
	Percent Time 70-180 mg/dL, mean (SD)	45 (22)	60 (23)
	Percent Time <70 mg/dL, mean (SD)	2.0 (1.8)	0.8 (1.2)
	Percent Time >180 mg/dL, mean (SD)	53 (23)	39 (23)

[a]Some participants in the per protocol cohort had missing PRO surveys; N=114 (N=17 T1D, N=97 T2D) had baseline data and N=117 (N=15 T1D, N=102 T2D) had data at 6 months. [b]At baseline all N=176 had a baseline HbA1c; at 6 months, data was available for N=168 participants with GMI being used as a proxy for HbA1c for 15 (9%) of participants; For T1-DDS, N=156 and 154 contributed data at baseline and 6 months; For HCS, N=154 contributed data at baseline and 6 months; for 6-month CGM parameters N=157 contributed data; estimates, confidence intervals, and p-values were calculated using a longitudinal linear model utilizing multiple imputation for missing data. P-values have been adjusted for multiplicity using the two-stage adaptive Benjamini-Hochberg procedure.

Conclusions

- Within this study consisting of primarily older adults with T2D using MDI, durable glycemic improvement with reduced diabetes distress and increased hypoglycemic confidence occurred using the System for 6 months and was sustained through 12 months. The ~1.2% HbA1c improvement occurred with little hypoglycemia; the average percent time <70 and <54 mg/dL suggests most met established targets of <4% and <1%, respectively.[5-7]
- Based on the 2-week GMI estimate compared with baseline and 3- to 12-month HbA1c, there was rapid glycemic improvement observed within the first 2 weeks of System use that remained stable through 12 months.
- It is notable that the group was on average above the critical T1-DDS threshold at baseline (>2.0), indicating clinically relevant diabetes distress, but then fell below that threshold at 6 and 12 months.[8] Similarly, the average baseline hypoglycemia confidence was below the clinically meaningful threshold (<3.0) indicating low confidence but increased above that threshold at 6 and 12 months.[2] Additionally, the estimated minimally clinically important difference (MCID) for the T1-DDS total score is 0.19 in a T1D population;[8] comparing the observed average improvement (~-0.7) with the MCID suggest most participants had clinically meaningful improvement.
- A median of 7.0 long-acting doses a week in month 6 is encouraging. Given that the vast majority reported taking 2 (38%) or 3 (45%) meals per day at baseline, our findings of a median of 2.4 rapid-acting doses per day in month 6 also suggest minimal missed meal injections. However, dosing events appear reduced at 12 months.
- Severe hypoglycemia and DKA (at 4.5 and 0.5 events per 100 person years) are in line with other literature with estimates ranging between 7-130 and 4-8 events per 100 person years in insulin requiring diabetes.[9-11]
- To mitigate potential dropout bias in the per-protocol analysis and maximize analyzable data without requiring stringent System use, we conducted our expanded cohort analysis which demonstrated similar glycemic and PRO improvement, System use, and safety outcomes. Thus, we do not believe that the incompleteness of data for some participants was an appreciable source of bias.
- The T1D subgroup was small which limits interpretation (Table 3 & 4), but there may be slightly higher percent TBR (2% vs 0.8%) and TAR (53% vs 39%) and slightly less HCS improvement (0.2 vs 0.4-point) compared to the T2D subgroup, respectively. These findings are consistent with similar MDI populations.[12,13]
- Limitations of this study include the single-arm study design with no concurrent control group and relatively small sample size in the per protocol cohort. The study design also did not include baseline CGM metrics.

References/Acknowledgements

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