Increased Time in Range with Ultra Rapid Lispro Treatment in Participants with Type 2 Diabetes: PRONTO-Time in Range

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Supplementary Material

Supplementary Table 1. List of ethics review boards

Ethics Review Board's Name and Address
Central Ethics Review Boards
IntegReview Ethical Review Board 3815 S. Capital of Texas Highway, Suite 320, Austin, TX, 78704 United States (2020-2021)
Advarra Inc. 6100 Merriweather Drive, Suite 600, Columbia, MD, 21044 United States (2021- present)
Advarra Inc. 6940 Columbia Gateway Drive, IRB Suite 110, Columbia, MD, 21046 United States (2020-2021)
Local Ethics Review Boards
SUNY Upstate Medical University 750 East Adams Street, Room 1109 at Weiskotten Hall, Syracuse, NY, 13210 United States
St. Agnes Hospital 900 Caton, Baltimore, MD, 21229 United States

Supplementary Table 2. Target glucose values for adjustment of insulin dosing

Time of target glucose measurement	**CGM glucose**	
Fasting and premeal	Target	100 mg/dL (5.6 mmol/L)
	Range	80 to <110 mg/dL (4.4 to <6.1 mmol/L)
Prebedtime	Range	80 to <110 (4.4 to <6.1 mmol/L)
1-2 hour or peak postprandial	Target	< 140 (7.8 mmol/L)

CGM, continuous glucose monitoring.

Supplementary Table 3. Basal insulin dosing strategy

A. Basal insulin hypoglycemia assessment

Hypoglycemic events in the previous week	Basal insulin change
Two or more nocturnal hypoglycemia events occur or one severe hypoglycemia event occurs at any time of the day	Decrease the basal insulin dose to the previous lower dose (or by 10% if this is first dose).
One nocturnal hypoglycemia event occurs	Do not increase basal insulin dose. Consider decrease in basal insulin dose if clinically indicated.
No nocturnal events occur	Titrate the basal insulin dose as described below.

B. Basal insulin dosing adjustment algorithm

If fasting glucose CGM pattern is:	Adjust the basal insulin dose by:
<80 mg/dL (<4.4 mmol/L)	Decreasing dose to previous lower dose[a]
80-109 mg/dL (4.4-6.1 mmol/L)	No adjustment
110-129 mg/dL (>6.1-7.2 mmol/L)	Increasing by 1-2 units
130-149 mg/dL (>7.2-8.3 mmol/L)	Increasing by 2-4 units
150-179 mg/dL (>8.3-9.9 mmol/L)	Increasing by 4-6 units
≥180 mg/dL (≥10.0 mmol/L)	Increasing by 6-8 units

[a]If there is no previous dose because this was the first assigned dose, then the basal dose should be decreased by 10% in consultation with the investigator. Adapted from Bartley et al. 2008[1] and Bolli et al. 2009.[2] Basal and prandial insulin doses could be decreased at any time if clinically indicated such as for hypoglycemia. CGM, continuous glucose monitoring

Supplementary Table 4. Prandial insulin dosing strategy

A. Prandial insulin dose assessment

Prandial insulin dose assessed	**Corresponding CGM glucose value for review**
Fasting or morning premeal	Previous day premidday meal glucose value
Midday premeal	Previous day preevening meal glucose value
Evening premeal	Previous day bedtime glucose value

B. Prandial insulin adjustment algorithm

CGM glucose <80 mg/dL (<4.4 mmol/L)	**CGM glucose 80–109- mg/dL (4.4–6.1 -mmol/L)**	**CGM glucose >109 mg/dL (>6.1 mmol/L)**
Decrease by one unit	No change	Increase by one unit

Adapted from Bergenstal et al. 2008[3] and Edelman et al. 2014.[4] Basal and prandial insulin doses could be decreased at any time if clinically indicated such as for hypoglycemia. CGM, continuous glucose monitoring.

Supplementary Table 5. Proportion of participants achieving key CGM targets

Target CGM glucose range	Baseline % n = 153	Week 12 % n = 133	Odds ratio [95% CI] of Week 12 / baseline	p-value
>70% TIR 70 to 180 mg/dL	28.10	48.12	4.36 [2.22, 8.58]	<0.001
<1% TBR <54 mg/dL	66.67	71.43	1.34 [0.67, 2.67]	0.407
<5% TAR >250 mg/dL	38.56	53.38	2.61 [1.43, 4.75]	0.002

CGM, continuous glucose monitoring; TAR, time above range; TBR, time below range; TIR, time in range.

Supplementary Table 6. Glucose variability

Coefficient of variation for glucose (24-hour)	Baseline n = 153	Week 12 n = 133	Week 12 Change from baseline n = 133	p-value
Within-day (%)	29.5 (0.53)	29.4 (0.33)	0.0 (0.33)	0.938
Between-day (%)	30.8 (0.57)	29.6 (0.42)	-0.9 (0.42)	0.028
Overall (%)	34.2 (0.59)	32.9 (0.38)	-1.2 (0.38)	0.003

Data are LSM (SE).

Supplementary Table 7. Insulin treatment satisfaction questionnaire results

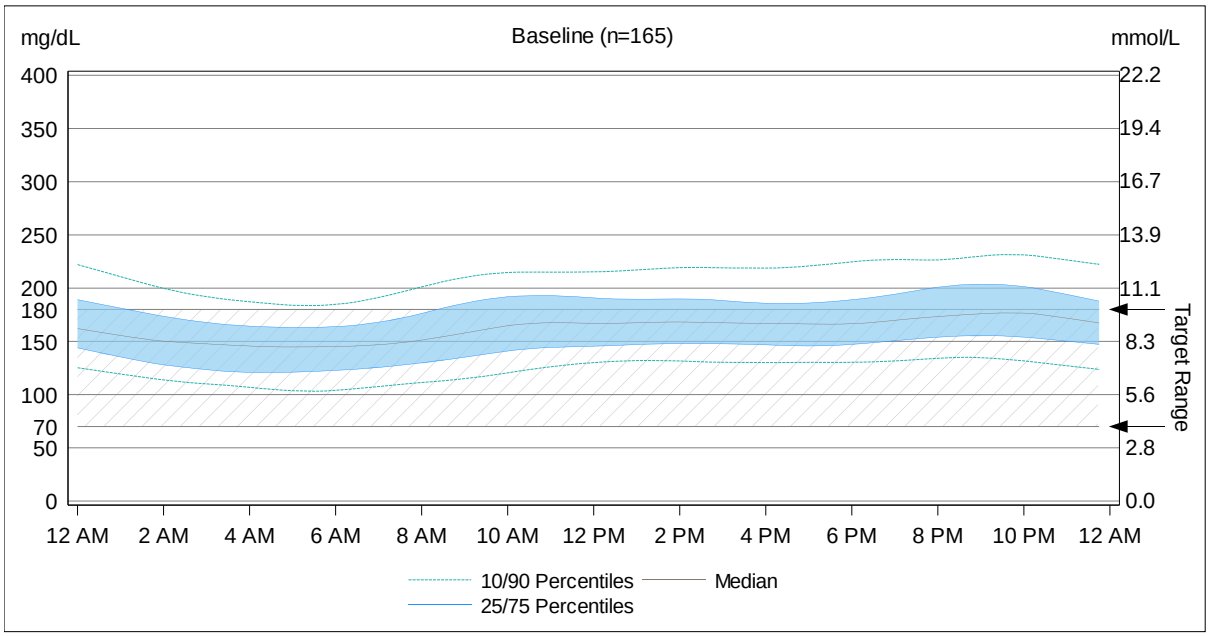
Transformed score	Baseline LSM (SE) n = 160	Week 12 LSM (SE) n = 154	Week 12 change from baseline LSM (SE) n = 154	p-value
Glycemic control	60.5 (2.04)	77.1 (1.55)	16.9 (1.55)	<0.001
Hypoglycemic control	70.8 (1.76)	73.4 (1.59)	2.5 (1.59)	0.113
Insulin delivery device satisfaction	74.6 (1.66)	81.9 (1.20)	7.9 (1.20)	<0.001
Inconvenience of regimen	76.4 (1.66)	82.5 (1.31)	6.2 (1.31)	<0.001
Lifestyle flexibility	63.3 (2.05)	67.0 (1.74)	3.6 (1.74)	0.038
Total	69.1 (1.50)	76.4 (1.12)	7.4 (1.12)	<0.001

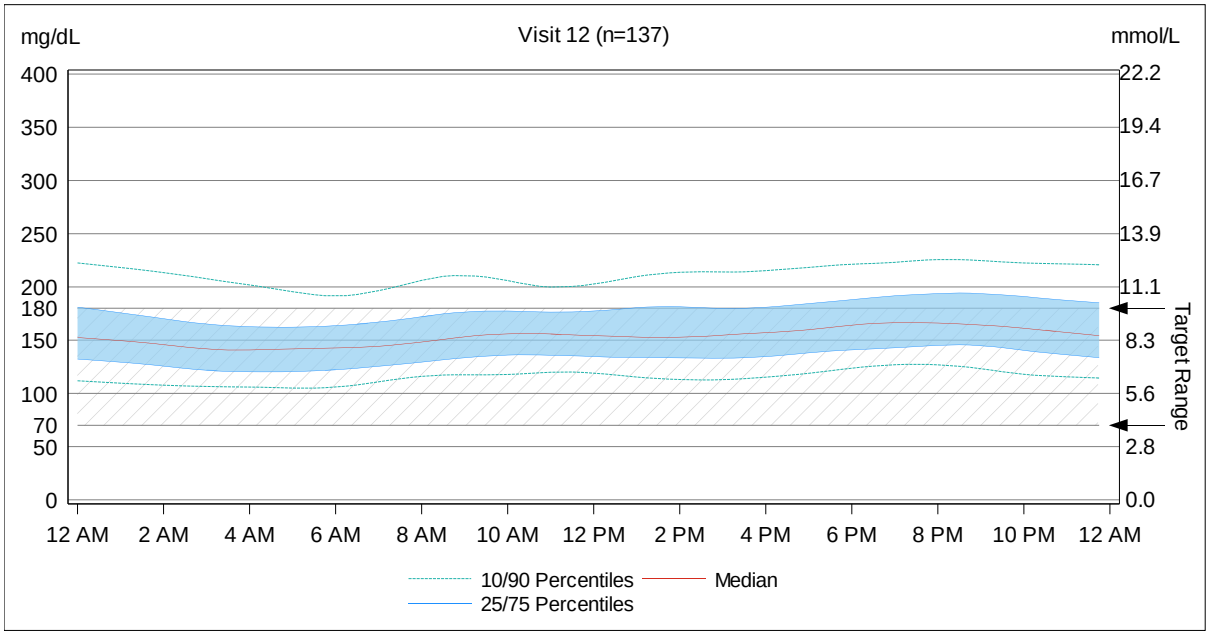
Data are LSM (SE).

Supplementary Table 8. Participants' mealtime insulin experience questionnaire results

Likely include mealtime insulin routine	**Week 12** **n (%)** **n = 153**
Very unlikely	9 (5.9)
Unlikely	1 (0.7)
Not sure	11 (7.2)
Likely	34 (22.2)
Very likely	98 (64.1)

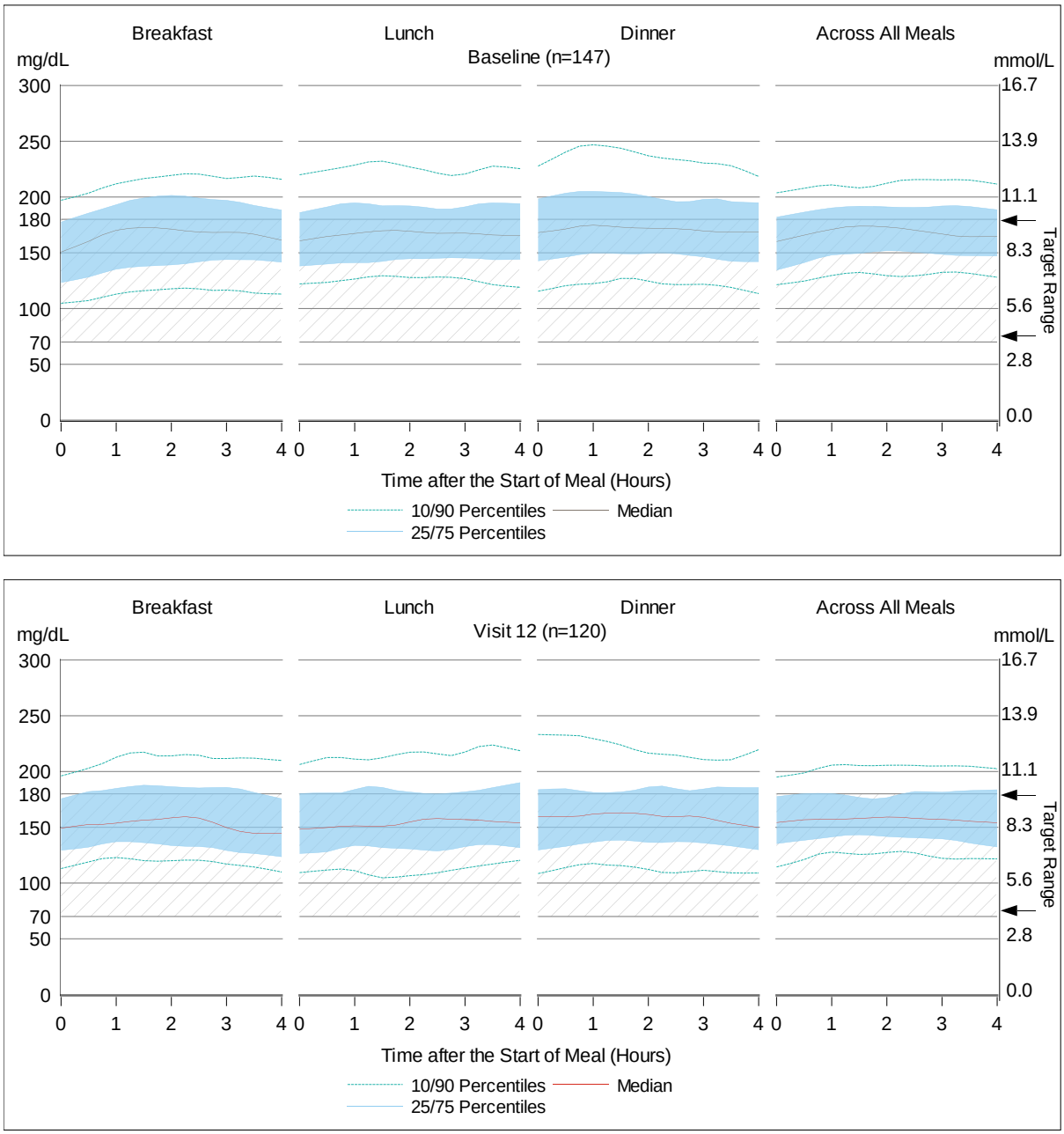
Supplementary Figure 1. Median and percentile hourly ambulatory glucose profiles over 24 hours at baseline and Week 12





Glucose percentile curves are calculated from the locally weighted polynomial regression (0.30 smoothing)

Supplementary Figure 2. Median and percentile hourly ambulatory glucose profiles 0–4 hours postmeal at baseline and Week 12



Glucose percentile curves are calculated from the locally weighted polynomial regression (0.30 smoothing)

References

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