

Ambulatory Glucose Profile (AGP)

REPORT

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Introduction

AGP is one of the most recent, innovative development being used to monitor glycemic variability in DM patients. We are able to get a glycemic variability curve, a median, a modal, various percentiles and statistical data generated through this device. (Saboo et al. 2018).

Articles review about Flash glucose monitoring(Libre)

Use of Ambulatory Glucose Profile for Improving Monitoring and Management of T2DM

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Abstract

Aim: To demonstrate glycemic variability in type 2 diabetic patients and consequent control of the same.

Methods: 108 patients with type 2 diabetes with an HbA1c level of 7.5-8.5% were selected for the study. A Freestyle Libre Pro AGP sensor was applied to the patients after explaining the patient about the same. Next, they were called for follow up at 3rd, 7th, 11th and 14th days. Based on the readings and graph obtained, diet and treatment changes were made on various follow-up days. The sensor was removed at the end of 14 days.

Results: Out of the 108 subjects, 106 completed the study. There were no adverse device effects. 98 patients had therapy changes while the rest had diet and lifestyle modifications. The mean HbA1c decreased from 7.96% to 7.03% by the end of 15 days. The glycemic variability curves helped in recognizing and treating masked or asymptomatic hypoglycemic events. It also graphically shows intervals of optimal and sub-optimal glycemia.

Conclusion: AGP is one of the most recent, innovative developments that are being used to monitor Glycaemic variability in DM patients. AGP is generated from the Flash Glucose Monitoring device which is like a CGM device attached to the patient for a maximum period of 14 days, which checks the ISF glucose at every 15 minutes. We are able to get a Glycaemic variability curve, a median, a modal, various percentiles and statistical data generated through this.

stress which plays a significant role in the pathogenesis of diabetic complications.⁴

Figure 1 shows the AGP sensor and the reader

The Ambulatory Glucose Profile consists of a small, round sensor – around the size of a 10 rupee coin that has to be applied on the back of the arm; it measures the interstitial blood glucose every 15 minute with the help of a small filament that is inserted subcutaneously. The glucose readings can be obtained by a reader. Each result shows ISF glucose value, showing the glycemic trend of the patient. It functions for a maximum of 14 days.

Figure 2 represents five curves of AGP represents five curves which demonstrate the median level of control and provide an index of variability in control at every hour of a typical day, both inter as well as intraday variability.⁵

FreeStyle Libre for glucose monitoring

Medtech innovation briefing

Published: 3 July 2017

[nice.org.uk/guidance/mib110](https://www.nice.org.uk/guidance/mib110)

- The main points from the evidence summarised in this briefing are from 5 studies (6 papers) involving 700 people. These include 2 randomised controlled trials, 1 including people with type 1 diabetes (n=241; the IMPACT study) and the other including people with type 2 diabetes (n=224; the REPLACE study). Three of the studies reported device accuracy compared with self-monitored blood glucose, with results ranging from 84% to 88% accuracy and from 99% to 100% clinical acceptability, using an error grid. One study reported device accuracy and acceptability of 97% to 99% compared with venous blood sampling. The evidence suggests that using FreeStyle Libre for up to 12 months reduces time spent in hypoglycaemia compared with self-monitoring of blood glucose using finger-prick tests, and reduces the average number of finger-prick blood glucose tests needed.

MEDICAL/ SURGICAL HX

Miss G,
64 years
old
female



Social History :

Single , works as Secretary
past 30 years.

Lives with brother

Past medical history:

Type 2 DM diagnosed 2012
Hba1c-6.8% (May 18), on
Metformin.

- Hypertension
- hyperlipidemia
- Recurrent UTI
- Gastritis and rectal polyp
on OGD/colonoscopy
(2016).

MEDICAL/ SURGICAL HX

On September 2018, admitted for obstructive jaundice and diagnosed with pancreatic mass. (histo non-diagnostic on EUS) .

Patient started Chemotherapy 7/12/18 – Folfirinox, 12 cycles for 6 month.

Whipple Operation/Total Pancreatectomy is done on 16/10/2018.

Patient has been doing SBGM at least 4 times daily.

Referred for Endocrinologist &DNE

Insulin dose:
Lantus 4 units bedtime,
Apidra 4/2/3 units



What is Folfirinox ?

FOLFIRINOX is the name of a combination of cancer drugs that includes:

- **FOL**
 - folinic acid (also called leucovorin, calcium folinate or FA)
- **F**
 - fluorouracil (also called 5FU)
- **Irin**
 - irinotecan
- **Ox**
 - oxaliplatin

Day 1

- Oxaliplatin as a drip into the vein over 2 hours
- Folinic acid as a drip into the vein over 2 hours at the same time with oxaliplatin.
- Irinotecan as a drip into the vein for 60 to 90 minutes.
- Fluorouracil as a injection into the vein for 5 minutes.
- Fluorouracil as an infusion over 46 hours given by a small portable pump.

Day 2

- Continue to have fluorouracil as an infusion given by a small portable pump.
- **Dexamethasone 4mg BD X 3 days.**

Day 3 to 14

- No treatment.

Diabetes and cancer are two diagnoses that individually overwhelm both patients and clinicians. Approximately 8–18% of people with cancer have diabetes. Together, these two diseases can pose formidable challenges to clinicians caring for this difficult patient population. Unfortunately, our knowledge of this topic is limited by insufficient evidence to determine how best to manage diabetes while simultaneously treating cancer. This article seeks to review some of the most common problems encountered by clinicians caring for these patients.

Diabetes Spectrum Volume 19, Number 3, 2006

Clinical Challenges in Caring for Patients With Diabetes and Cancer

Glucocorticoids

The use of glucocorticoids in patients with pre-existing diabetes typically wreaks havoc on postprandial glycemic control. Unfortunately, glucocorticoids are routinely used in many cancer treatment protocols. Glucocorticoid treatment for cancer patients usually consists of short-term therapy at a high dose. Lower-dose steroids are also used to prevent chemotherapy-induced nausea and vomiting. All patients should be screened for diabetes before initiating glucocorticoid therapy and routinely monitored thereafter. These medications raise blood glucose through increased insulin resistance, gluconeogenesis, glycogenolysis, and decreased insulin production and secretion.¹¹

insulin drips outside of the intensive care setting because of fear of hypoglycemia. Hourly glucose monitoring and insulin drip rate titrations place an added burden on the nursing staff. Regardless of the route or setting, insulin doses should be titrated daily as needed and should be tapered as glucocorticoid therapy is tapered to avoid hypoglycemia.^{11–17}

Tube Feeding and Total Parenteral Nutrition

Tube feeding and total parenteral nutrition (TPN) are frequently used in oncology to supplement or replace a regular diet for patients who cannot sustain their usual intake of nutritional requirements. Hyperglycemia is a frequent complication from both of

TPN is stopped abruptly. Gradually decreasing the infusion rate at least 1 hour before discontinuing TPN reduces the risk of hypoglycemia.²⁰

Nausea and Vomiting

Nausea and vomiting are common adverse drug reactions in some chemotherapy regimens. These reactions can occur in anticipation of therapy, acutely during or within 24 hours of the therapy, or may persist over an extended period of time after therapy. Breakthrough nausea and vomiting may occur, despite prophylactic treatment.

All patients should be screened for a history of nausea and vomiting before initiation of any chemotherapy. The history should include nausea and

Acute Hyperglycemia Associated with Anti-Cancer Medication

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Department of Internal Medicine, Center for Thyroid Cancer, National Cancer Center, Goyang, Korea

Hyperglycemia during chemotherapy occurs in approximately 10% to 30% of patients. Glucocorticoids and L-asparaginase are well known to cause acute hyperglycemia during chemotherapy. Long-term hyperglycemia is also frequently observed, especially in patients with hematologic malignancies treated with L-asparaginase-based regimens and total body irradiation. Glucocorticoid-induced hyperglycemia often develops because of increased insulin resistance, diminished insulin secretion, and exaggerated hepatic glucose output. Screening strategies for this condition include random glucose testing, hemoglobin A1c testing, oral glucose loading, and fasting plasma glucose screens. The management of hyperglycemia starts with insulin or sulfonylurea, depending on the type, dose, and delivery of the glucocorticoid formulation. Mammalian target of rapamycin (mTOR) inhibitors are associated with a high incidence of hyperglycemia, ranging from 13% to 50%. Immunotherapy, such as anti-programmed death 1 (PD-1) antibody treatment, induces hyperglycemia with a prevalence of 0.1%. The proposed mechanism of immunotherapy-induced hyperglycemia is an autoimmune process (insulinitis). Withdrawal of the PD-1 inhibitor is the primary treatment for severe hyperglycemia. The efficacy of glucocorticoid therapy is not fully established and the decision to resume PD-1 inhibitor therapy depends on the severity of the hyperglycemia. Diabetic patients should achieve optimized glycemic control before initiating treatment, and glucose levels should be monitored periodically in patients initiating mTOR inhibitor or PD-1 inhibitor therapy. With regard to hyperglycemia caused by anti-cancer therapy, frequent monitoring and proper management are important for promoting the efficacy of anti-cancer therapy and improving patients' quality of life.

Table 1 Summary of Results from Previous Studies Regarding Chemotherapy-Induced Hyperglycemia

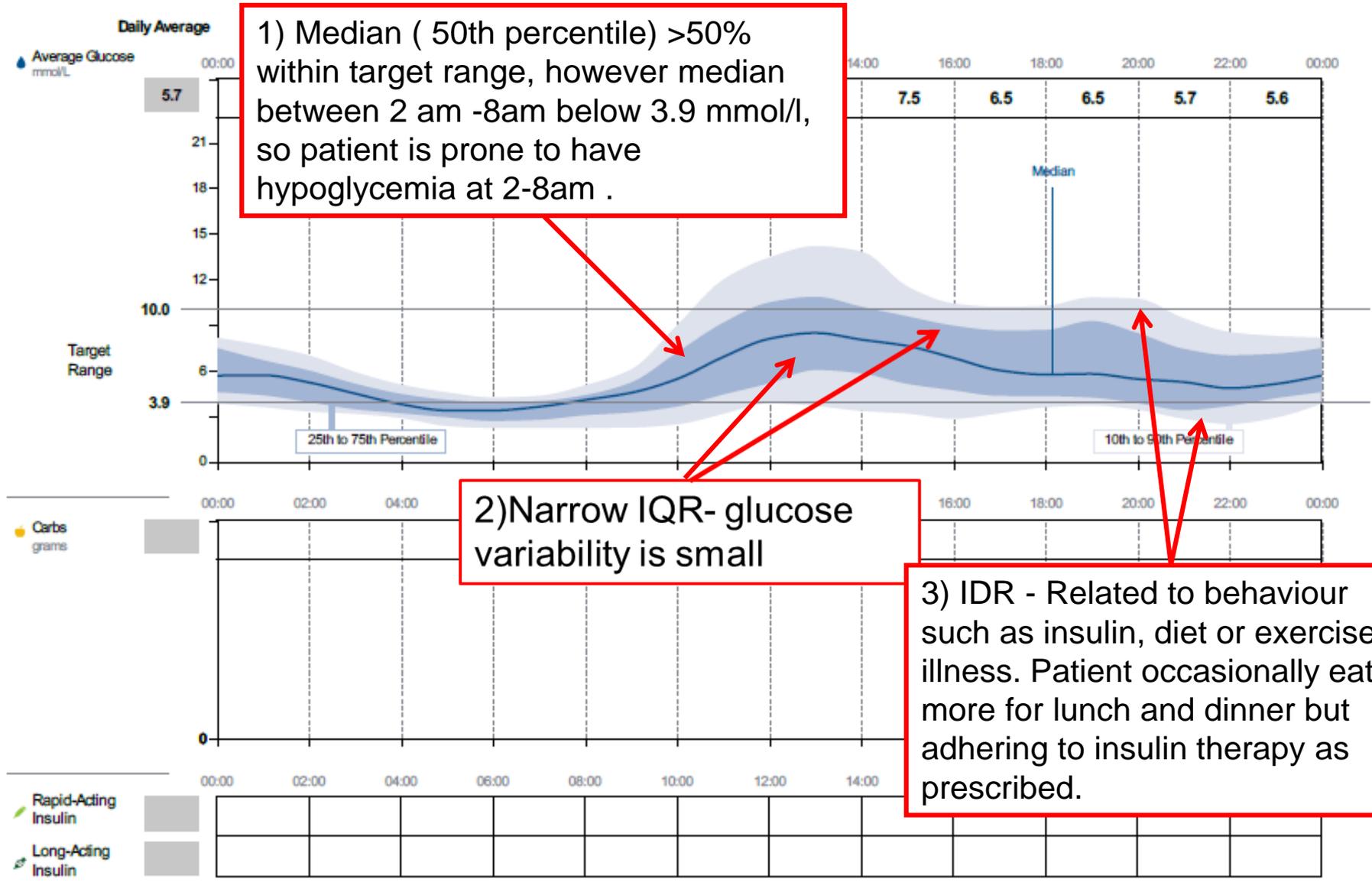
Study	Region	Study design	Setting (no. of patients, type of cancer, chemotherapy regimen)	Diagnostic tool for DM		Incidence	Risk factor(s)	Glucose-lowering therapy	Outcome
				Previous DM	New DM				
Feng et al. (2013) [11]	China	Retrospective	362, Colon cancer, 5FU (results incomplete for 44 patients)	FPG	FPG, OGTT	DM: 42 (11.6%) During treatment: 32 After treatment: 10 IFG: 41(11.3%) During treatment: 33 After treatment: 8	-	OAD: 22 (52.4%) LSM: 13 (30.9%) Observation: 7 (16.7)	Persistent: 31 (8.6%)
Lipscombe et al. (2013) [16]	Canada	Population-based, retrospective	Early-stage breast cancer vs. no breast cancer	History	2 Claims or 1 hospitalization	8.9% in patients who underwent adjuvant therapy, 10.0% in patients who did not undergo adjuvant therapy Age difference	-	-	-
Ji et al. (2013) [17]	China	Retrospective	119, Breast cancer, chemotherapy	OGTT	OGTT	DM: 21.8% Prediabetes: 43.7%	-	-	-
Lee et al. (2014) [18]	Japan	Retrospective	80, Lymphoma, CHOP	HbA1c	FPG/random glucose/bA1c	26 (32.5%)	Age ≥60 yr BMI >30 kg/m ² HbA1c >6.1%	Insulin: 3 LSM: 1	Persistent: 2 (2.5%)

AGP with inter-quartile and inter-deciles Range

Daily Patterns

19 January 2019 - 1 February 2019 (14 Days)

LibreView



1) Median (50th percentile) >50% within target range, however median between 2 am -8am below 3.9 mmol/l, so patient is prone to have hypoglycemia at 2-8am .

2) Narrow IQR- glucose variability is small

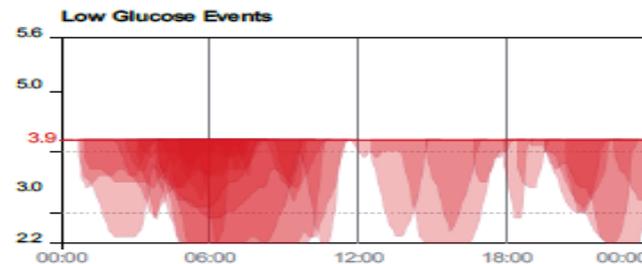
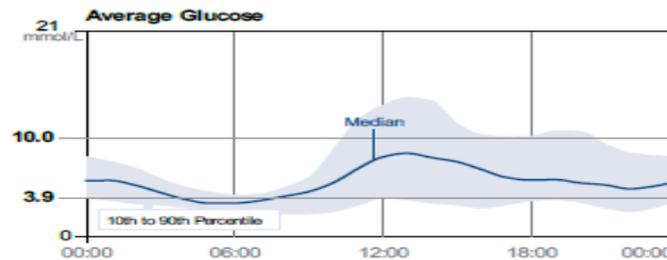
3) IDR - Related to behaviour such as insulin, diet or exercise, illness. Patient occasionally eats more for lunch and dinner but adhering to insulin therapy as prescribed.

Glucose

Estimated A1c **5.2 %** or **33 mmol/mol**

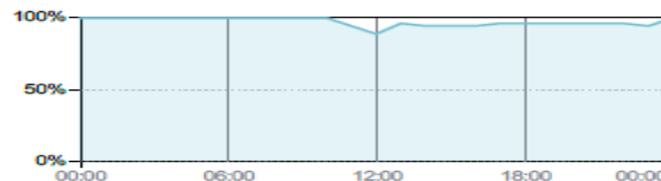
AVERAGE GLUCOSE	5.7 mmol/L
% above target	9 %
% in target	61 %
% below target	30 %

LOW GLUCOSE EVENTS	20
Average duration	341 Min



Sensor Usage

SENSOR DATA CAPTURED	98 %
Daily scans	7



DAILY CARBS _____ grams/day

INSULIN

RAPID-ACTING INSULIN _____ units/day

Meal _____

Correction _____

User Change _____

Manual _____

LONG-ACTING INSULIN _____ units/day

Total Daily Insulin _____ units/day

Comments

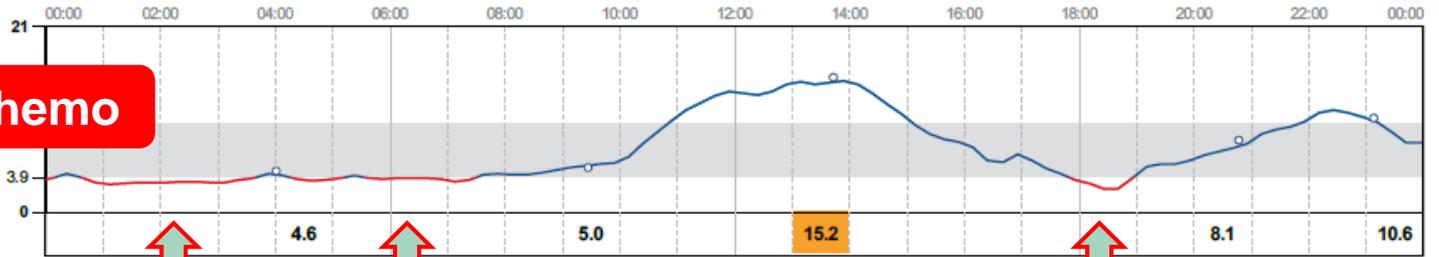
- Gaps found in the insulin data. 14 days in this reporting period have no recorded insulin events.
- Gaps found in food data. 14 days in this reporting period have no recorded food events.

On Jan 2019, patient started 3rd cycle of chemotherapy. Libre report shows: 20 low glucose events , average duration 341 mins. Hypoglycemia happen at 2-8 am. Patient wakes up with cold sweat and hunger .

SAT 19 Jan

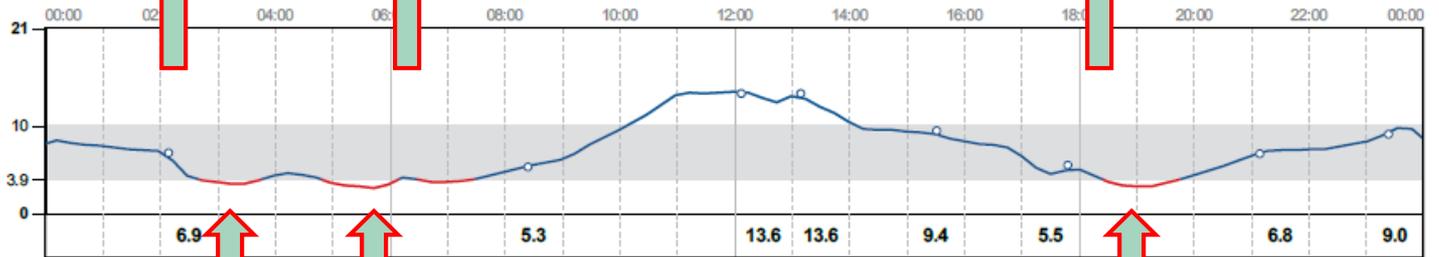
2nd day post-chemo

Glucose mmol/L



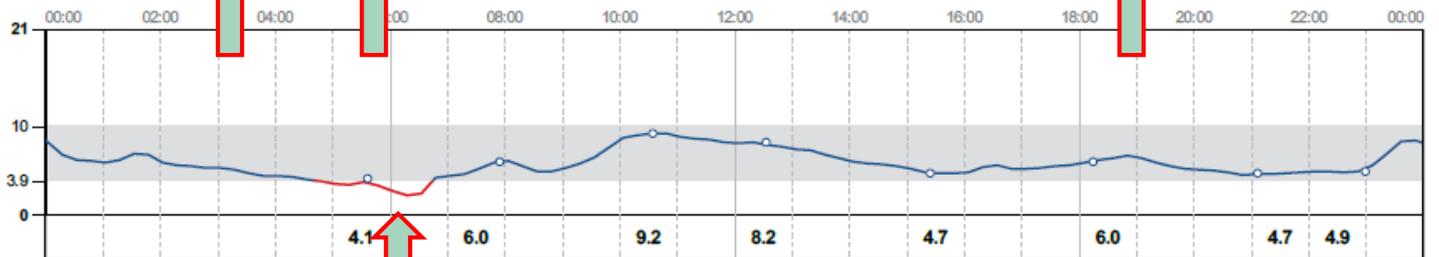
SUN 20 Jan

Glucose mmol/L



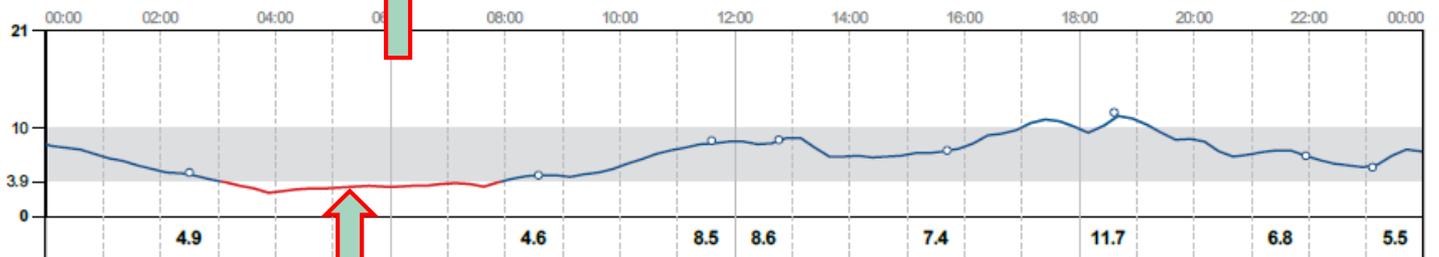
MON 21 Jan

Glucose mmol/L



TUE 22 Jan

Glucose mmol/L

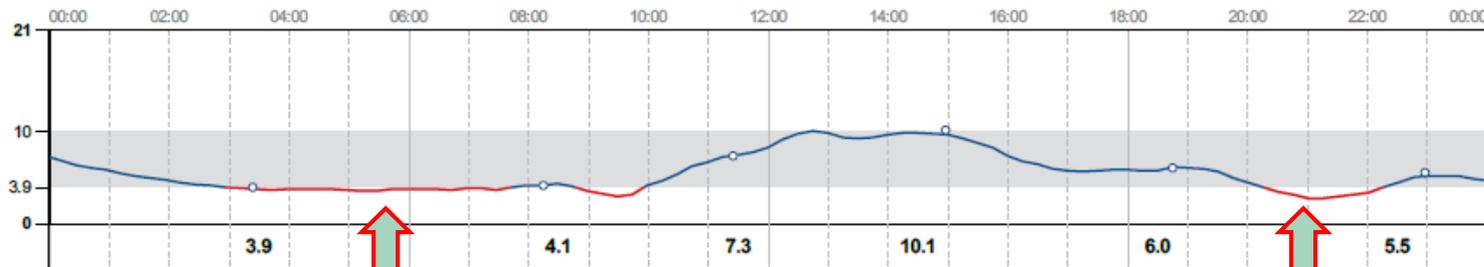


Hypoglycemia starts day 2 post chemotherapy.

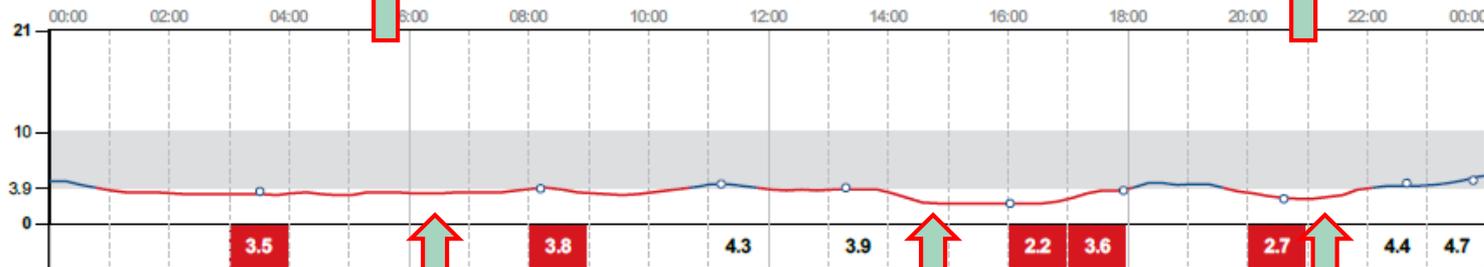
Daily Log

19 January 2019 - 1 February 2019 (14 Days)

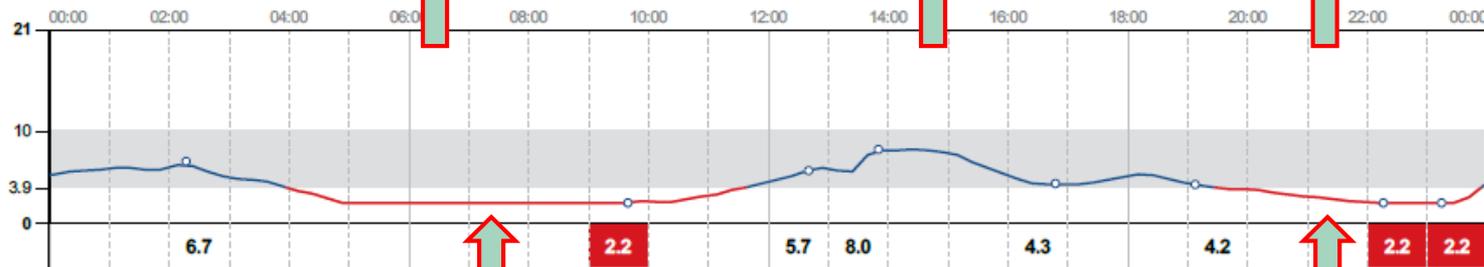
WED 23 Jan



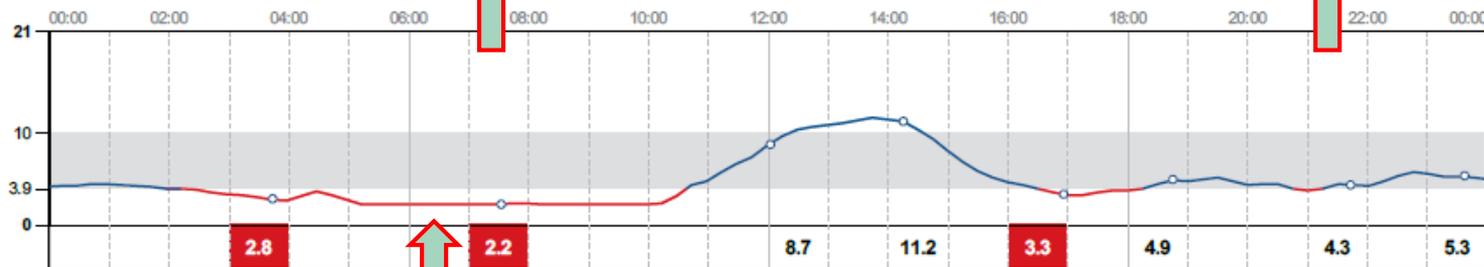
THU 24 Jan



FRI 25 Jan



SAT 26 Jan

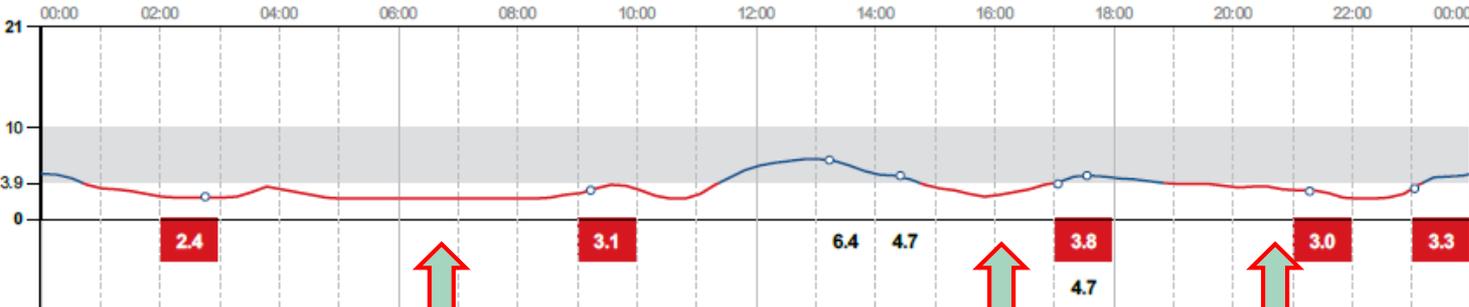


Hypoglycemia starts day 2 post chemotherapy.

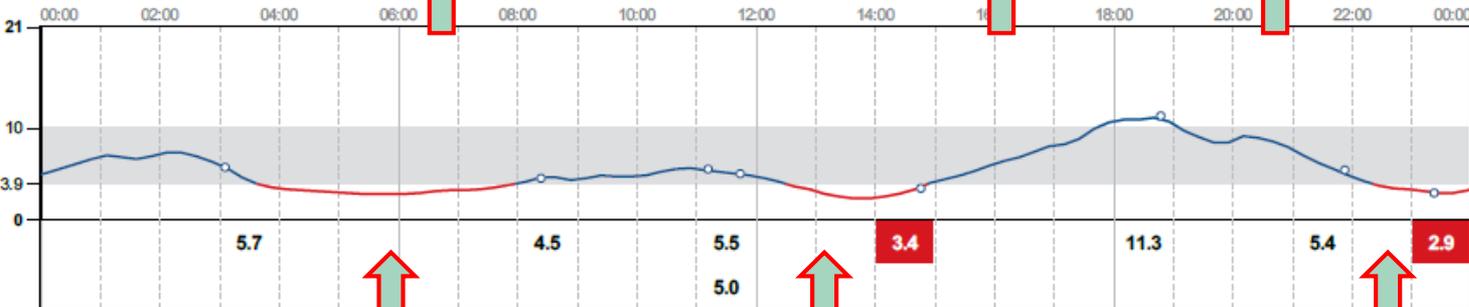
Daily Log

19 January 2019 - 1 February 2019 (14 Days)

SUN 27 Jan

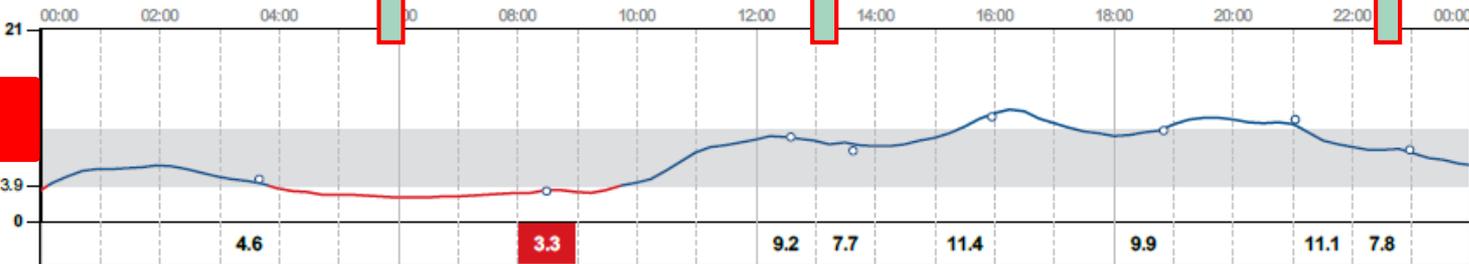


MON 28 Jan

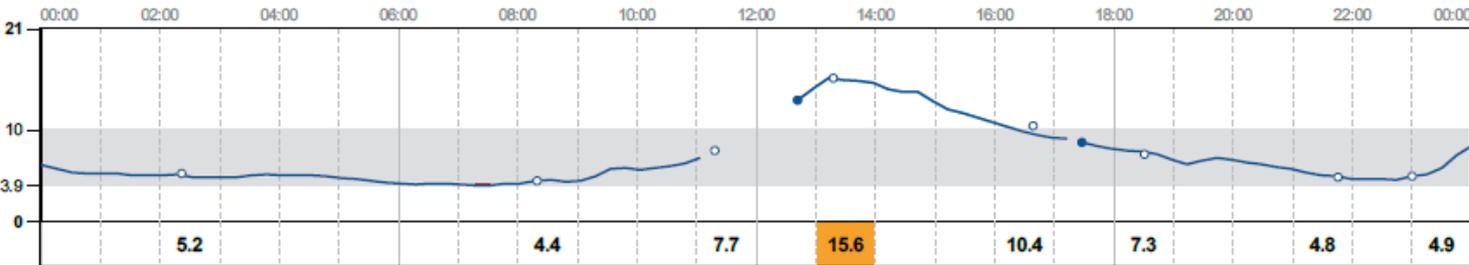


TUE 29 Jan

Chemo Day 1



WED 30 Jan



Hyperglycemia noted during chemotherapy.

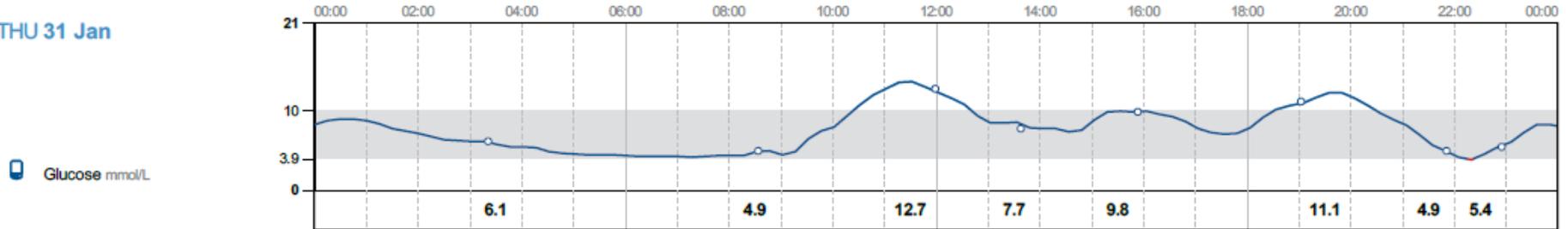
Ambulatory Glucose Profile

Daily Log

19 January 2019 - 1 February 2019 (14 Days)

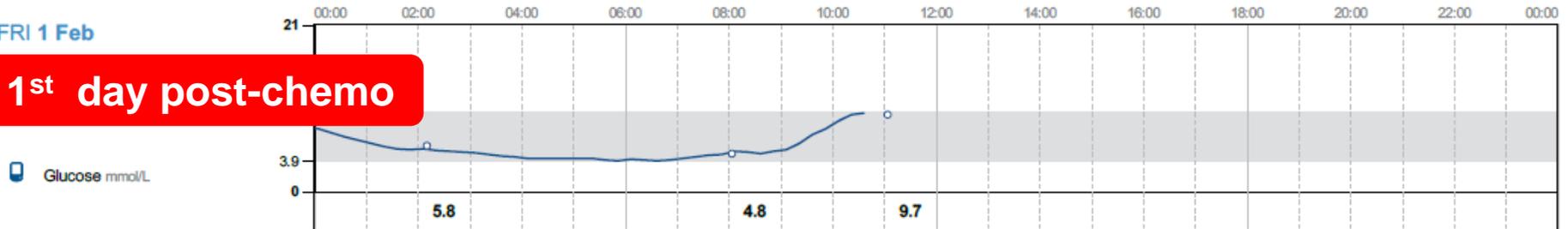
LibreView

THU 31 Jan



FRI 1 Feb

1st day post-chemo



Hyperglycemia noted during chemotherapy, hypoglycemia starts day 2 post chemotherapy.

Education and management

Chemotherapy - required higher doses of Lantus and Apidra

Post chemotherapy (irinotecan, oxaliplatin, folinic acid) – experienced hypo from D2, but PPG could still be high on D2-D3 and started decreasing thereafter

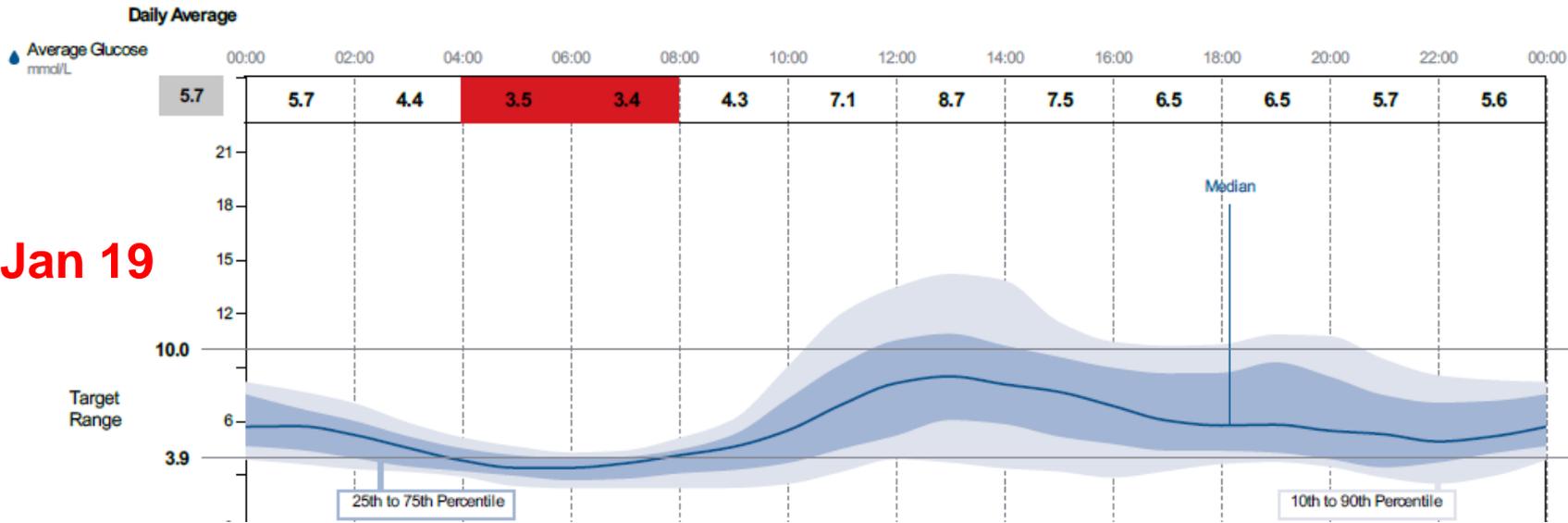
Lantus switched to morning due to hypoglycemia 2- 8 am.

Insulin Regime during chemotherapy **Lantus 5 OM, Apidra 6/5/8**

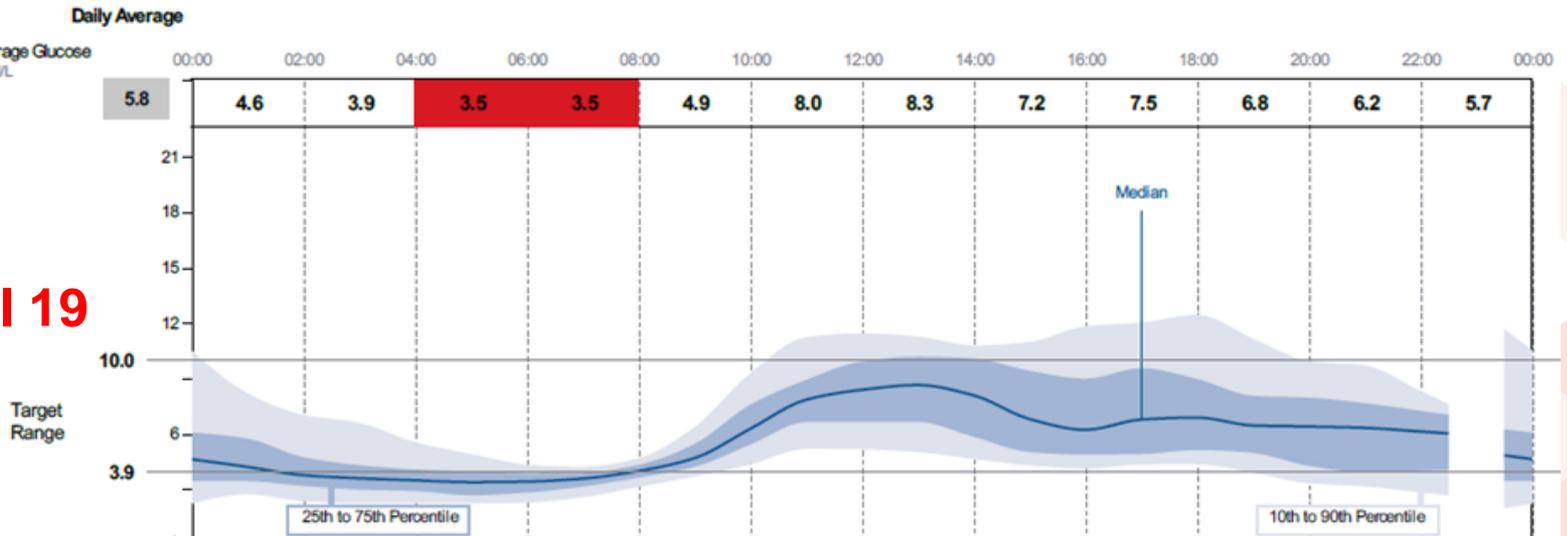
Insulin Regime Day 3 post chemotherapy **Lantus 3 OM, Apidra 4/4/5**

Due to the unstable blood sugar control, diabetes team follow up with Miss G closely either via phone or clinic visit.

Jan 19



April 19

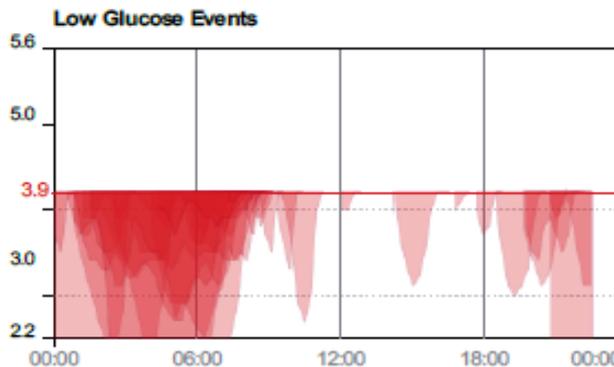
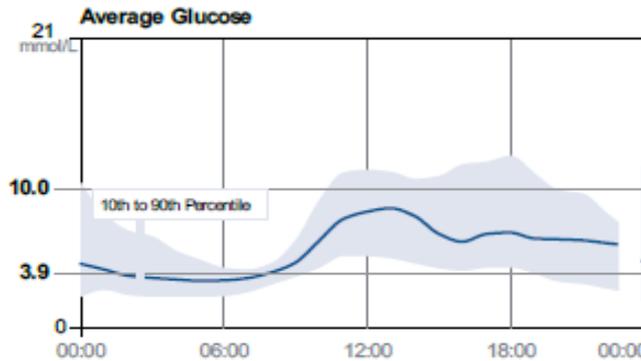


Compared April and January AGP, still has hypoglycemia but IQR and IDR shows lesser glucose variability .

Glucose

Estimated A1c 5.3 % or 34 mmol/mol

AVERAGE GLUCOSE	5.8 mmol/L
% above target	10 %
% in target	61 %
% below target	29 %



LOW GLUCOSE EVENTS	25
Average duration	238 Min

DAILY CARBS	grams/day
INSULIN	
RAPID-ACTING INSULIN	units/day
Meal	
Correction	
User Change	
Manual	
LONG-ACTING INSULIN	units/day
Total Daily Insulin	units/day

Comments

- Gaps found in the insulin data. 14 days in this reporting period have no recorded insulin events.
- Gaps found in food data. 14 days in this reporting period have no recorded food events.

Sensor Usage

SENSOR DATA CAPTURED	90 %
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Libre report showed that average duration of hypoglycemia has reduced to 238 min, although hypoglycemia event has slightly increase to 25 times with average 5.8 mmol/l, and 61% of blood glucose are in target on April 2019 (10th cycle of chemotherapy). Patient gains more insight in her overnight trends.

PRINTED: 22/04/2019

DOB: 21/08/1954

How patient and healthcare professionals feel about AGP?

For patient

- Convenience in monitoring of CBG without multiple finger pricks
- Minimize need for painful finger pricks
- Help patient in early recognition of hypo and hyperglycemia for early self management.
- Cost of sensor not economical

For healthcare professionals

- Finger pricks validation required as there is a variation of ± 2 mmol/L between finger pricks and interstitial fluid.
- Provides a better overall blood sugar profile of patient .
- For better management of diabetes medications, especially insulin, with AGP readings
- Help to detect hypoglycemia for patient who has hypoglycemia unawareness.

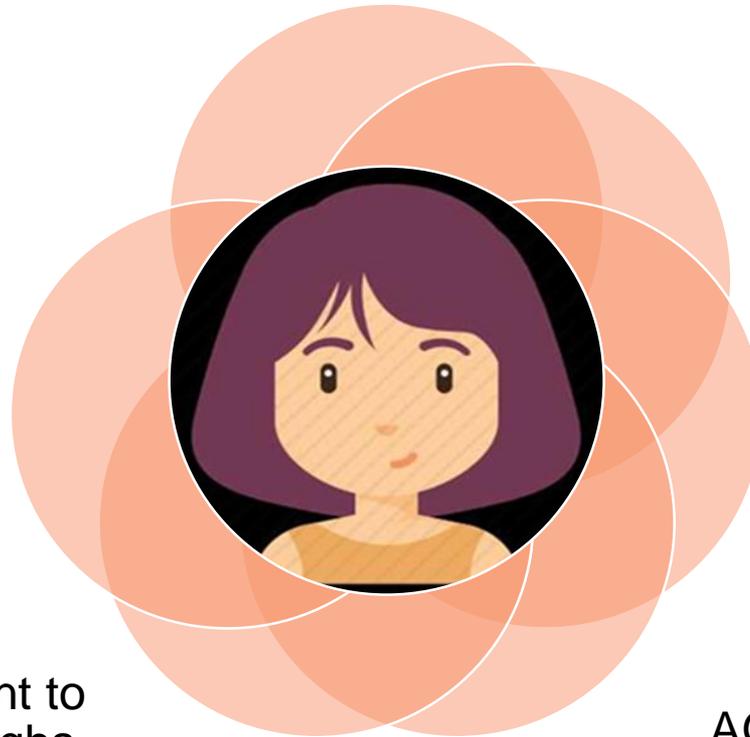
Conclusions

AGP helps to monitor patient's glucose closely so as to optimize glycemic control.

Trend arrows help to detect upcoming hyperglycemia or hypoglycemia.

Especially in our case study, patient is on chemotherapy with great fluctuations of blood sugar during and off treatment.

Helps patient and healthcare provide to gain confidence in intensifying treatment.



AGP helps us to fine tune insulin regime and controlling her blood sugar.

Definitely reduces the number of finger pricks per day with the use of AGP

AGP helps patient to recognize her highs and lows and administer treatment accordingly

AGP helps to reduce her hypoglycemic and hyperglycemic episodes.

Snapshot

19 January 2019 - 1 February 2019 (14 D)

Glucose

AVERAGE GLUCOSE	5.7 mmol/L
% above target	9 %
% in target	61 %
% below target	30 %

LOW GLUCOSE EVENTS	20
Average duration	341 Min

Sensor Usage

SENSOR DATA CAPTURED	98 %
Dailyscans	7

Snapshot

9 April 2019 - 22 April 2019 (14 Days)

Glucose

AVERAGE GLUCOSE	5.8 mmol/L
% above target	10 %
% in target	61 %
% below target	29 %

LOW GLUCOSE EVENTS	25
Average duration	238 Min

Sensor Usage

SENSOR DATA CAPTURED	90 %
Dailyscans	6

Snapshot

12 June 2019 - 25 June 2019 (14 Days)

Glucose

AVERAGE GLUCOSE	7.7 mmol/L
% above target	21 %
% in target	78 %
% below target	1 %

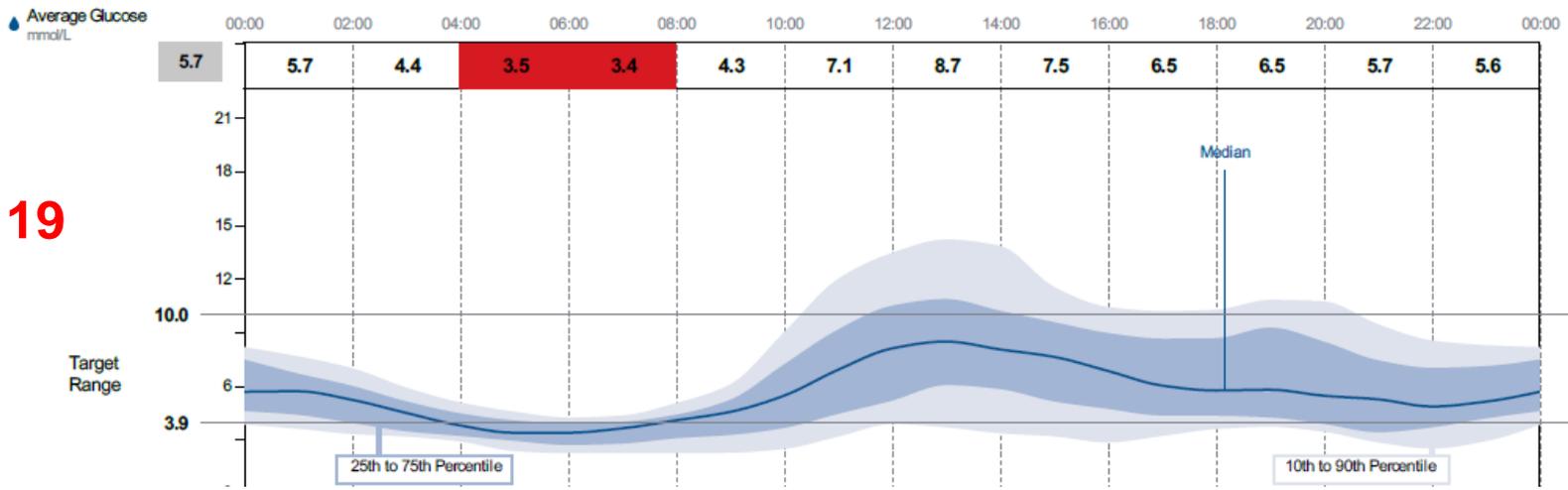
LOW GLUCOSE EVENTS	4
Average duration	75 Min

Sensor Usage

SENSOR DATA CAPTURED	87 %
Dailyscans	7

PRINTED: 01/02/2019

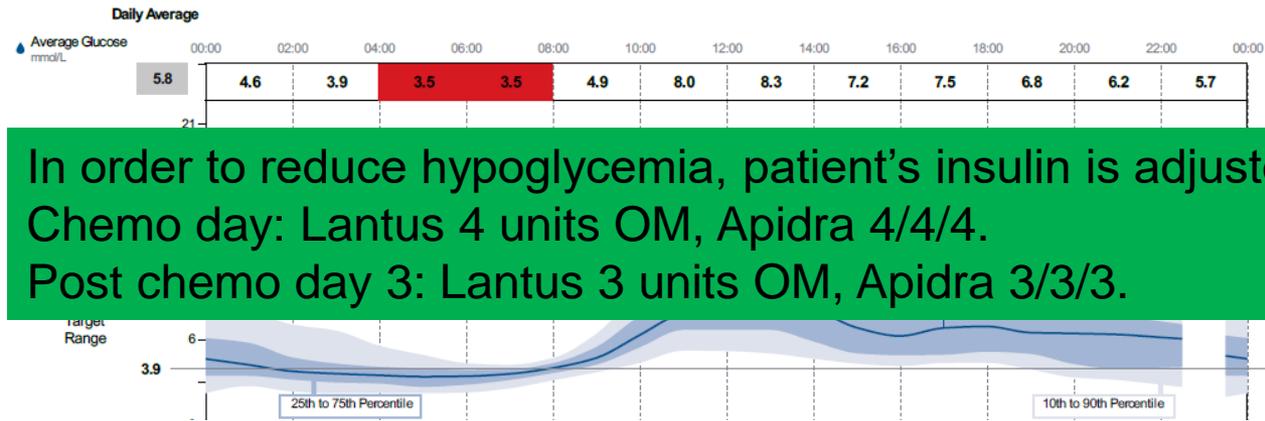
Jan 19



PRINTED: 22/04/2019

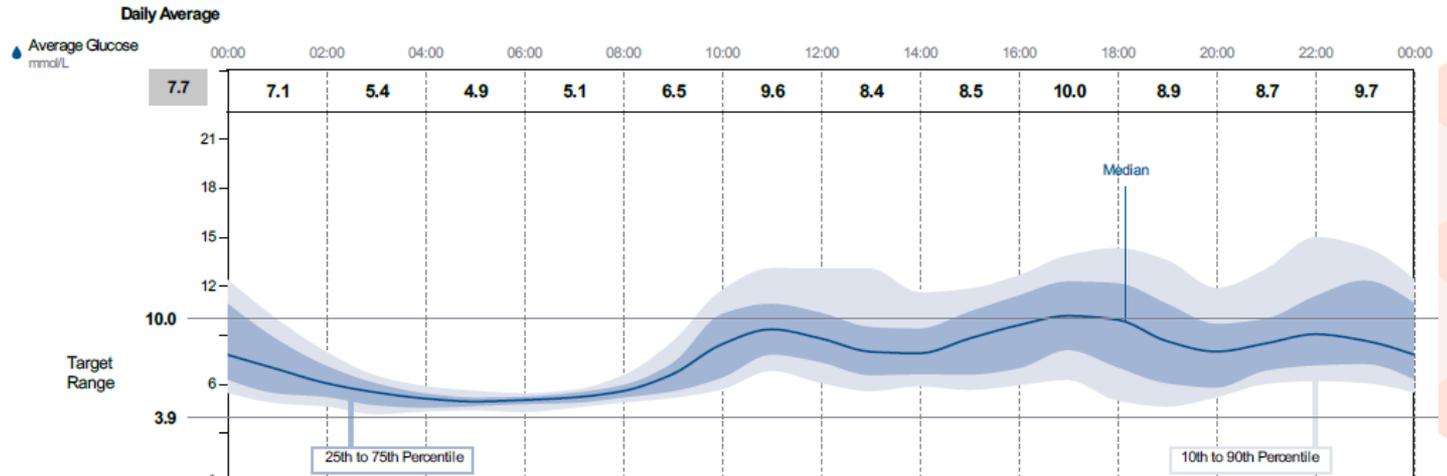
April 19

In order to reduce hypoglycemia, patient's insulin is adjusted:
 Chemo day: Lantus 4 units OM, Apidra 4/4/4.
 Post chemo day 3: Lantus 3 units OM, Apidra 3/3/3.



PRINTED: 25/06/2019

June 19



Special Thanks to :

All nurses at DOME Centre (CGH)

Dr. Eberta Tan (Consultant, CGH Endocrine)

Ms Nicole Lim (Abbott Diabetes Care)



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