Job Certificate

Job Info Fields

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Document Number:	HQ21TSM00031

Classification Fields

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Job Type:	Promotional
Country Compliance Classification:	
Target Audience:	Healthcare Practitioners
Subtype:	Sales Material
Job Description:	The new iSelling for Tresiba
Geographical Use (Global Only):	Global

Date Fields

Date of Certification:	04/04/2022
Planned Date of First Use:	04/04/2022

Signature text:

I hereby confirm that I have examined the final form of the material, and relevant related documentation, and in my belief it is in compliance with relevant local legislation and instructions (e.g. SOPs, code, etc.).

Role	Signature
Compliance Certification Medical Approved	BAMK (Balamurali K) bamk@novonordisk.com 29-Mar-2022 10:08:06 GMT+0000
Business Certification BU Insulins Approved	HDUI (Hans Duijf) hdui@novonordisk.com 04-Apr-2022 13:56:59 GMT+0000

Let TRESIBA® help patients with type 2 diabetes

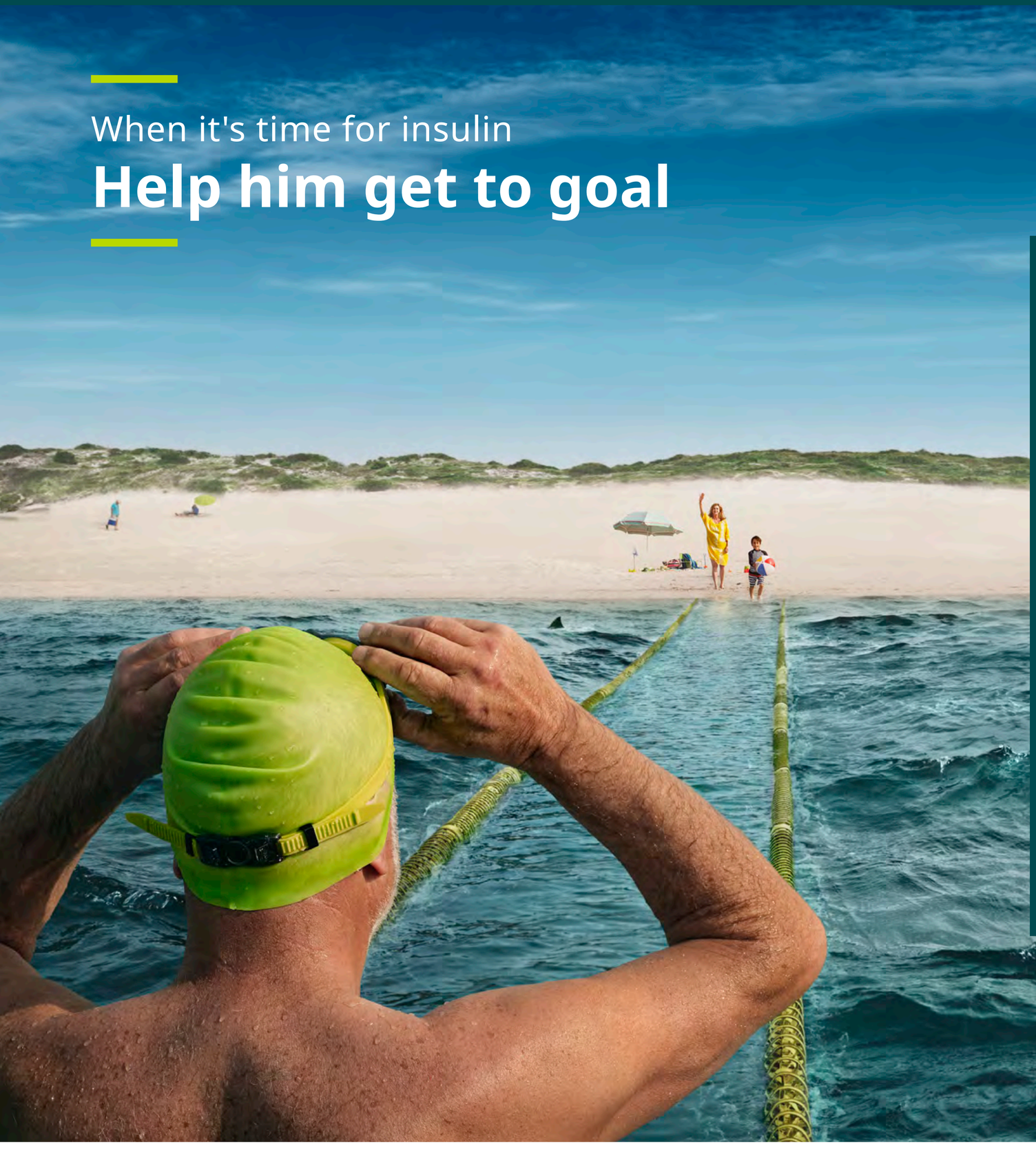
get to goal with a lower risk of hypos vs glargine U100 & glargine U300[1-3]

R | SmPC | aPI

TRESIBA®
insulin degludec [rDNA origin] injection

When it's time for insulin

Help him get to goal



7/10

patients

living with type 2 diabetes on insulin do not reach **HbA_{1c} ≤7%**[4]

This may be due to:

- fear of hypos[5,6]
- poor adherence[5]
- lack of dose adjustment.[7]

POSSIBLE CONSEQUENCES

Type 2 diabetes – possible consequences

Hospital admission[8]

Renal failure and blindness[9]

Falls due to hypoglycaemia[10]

Lower limb amputation[8]

Coronary heart disease[11]

Stroke[11]

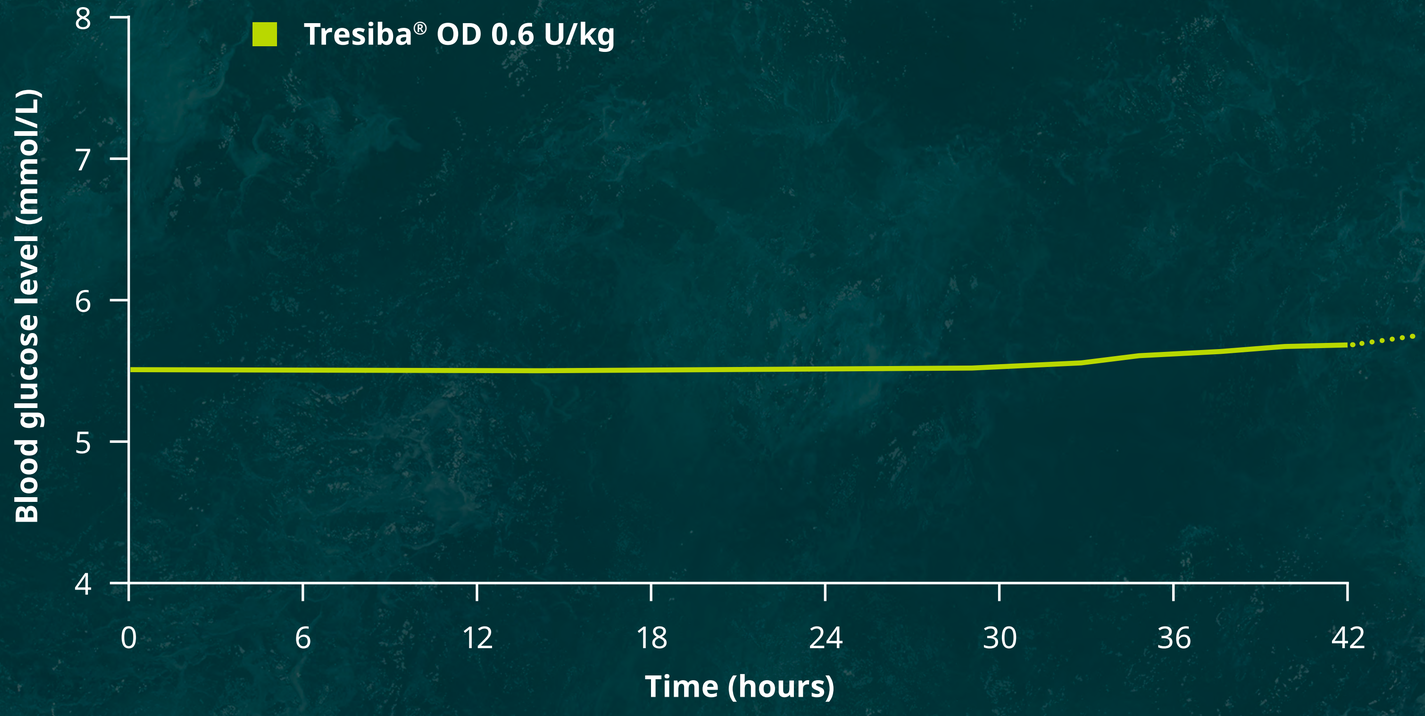
Once-daily TRESIBA®:

Day-to-day stability

VARIABILITY

Duration of action – beyond 42 hours[12,13]

Mean glucose profile in a 42-hour clamp study in adults with type 1 diabetes (n=66)[13]



UNIQUE MOLECULE

Once-daily TRESIBA®:

Day-to-day stability

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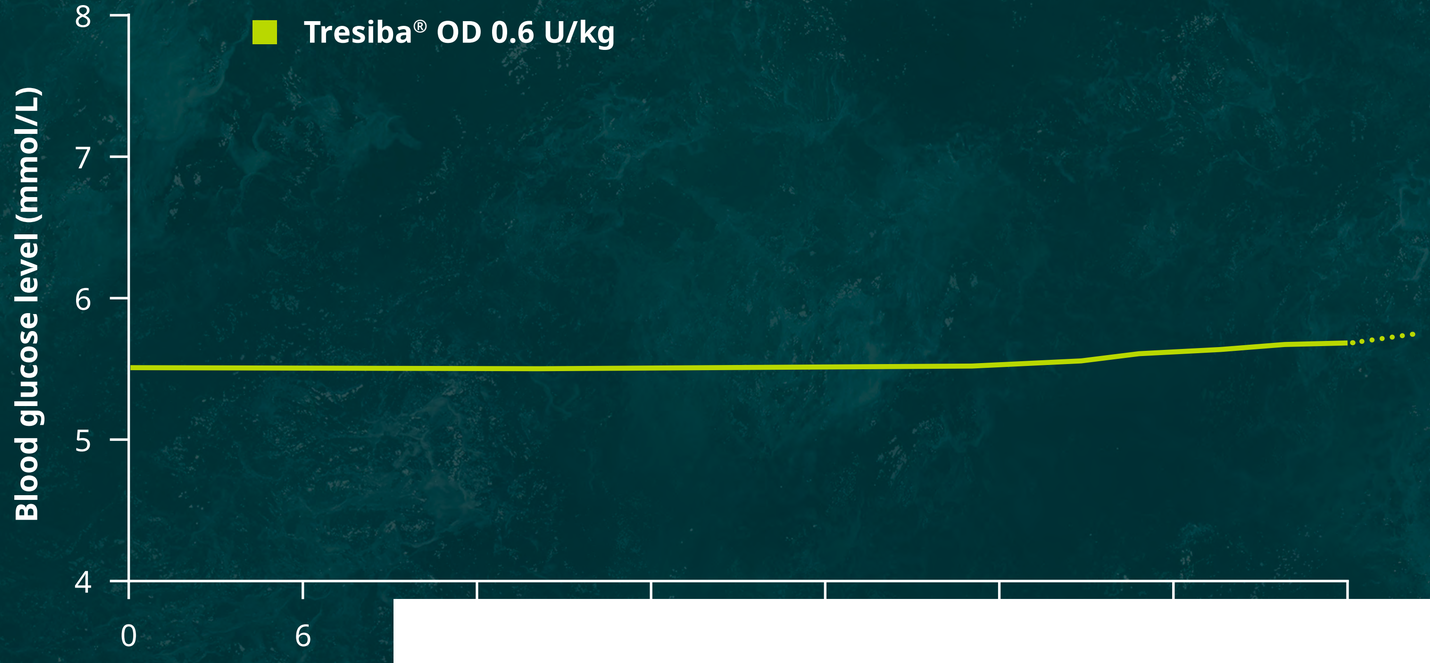


42-hour euglycaemic clamp on day 8 under steady-state conditions with once-daily dosing.[13]
OD (once-daily).

Patients deserve adaptability

TRESIBA® allows flexibility around daily injection routines[12,14]

REGULAR TIME

✓

8 am

Example patient injection routine.

He can adapt injection time to fit in with his life

EARLY-MORNING SWIM	ROAD TRIP	MORNING WITH GRANDSON
INJECTION TIME	**INJECTION TIME**	**INJECTION TIME**
10 am	**6 am**	**12 pm**
		
POSTPONE DOSE	PREPONE DOSE	POSTPONE DOSE

Having to inject basal insulins at a fixed time each day may complicate adherence and compromise glycaemic control[15]

With Tresiba®, an ultra-long (>42 hour) duration of action allows for flexibility in day-to-day dosing time when needed[12,14]*

* Establishing a routine is important; Tresiba® should be dosed once daily, with a minimum of 8 hours between doses.[12]

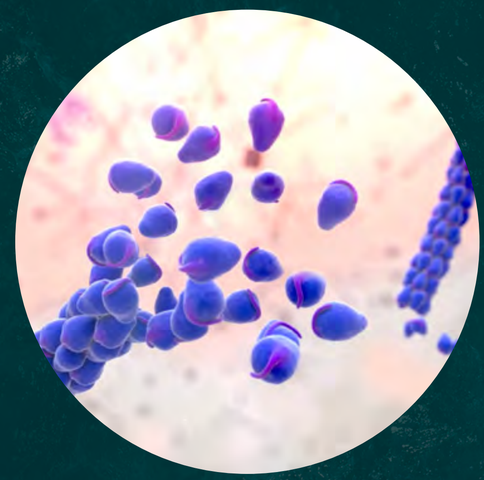
There is no clinical experience with flexibility in dosing time of Tresiba® in children and adolescents.[12]
The image shown is a model and not a real patient.

UNIQUE MOLECULE

Benefit from the unique TRESIBA® molecule[12,16]

Slow, consistent release:

After injection, Tresiba® molecules bind to form chains[12,13,16]



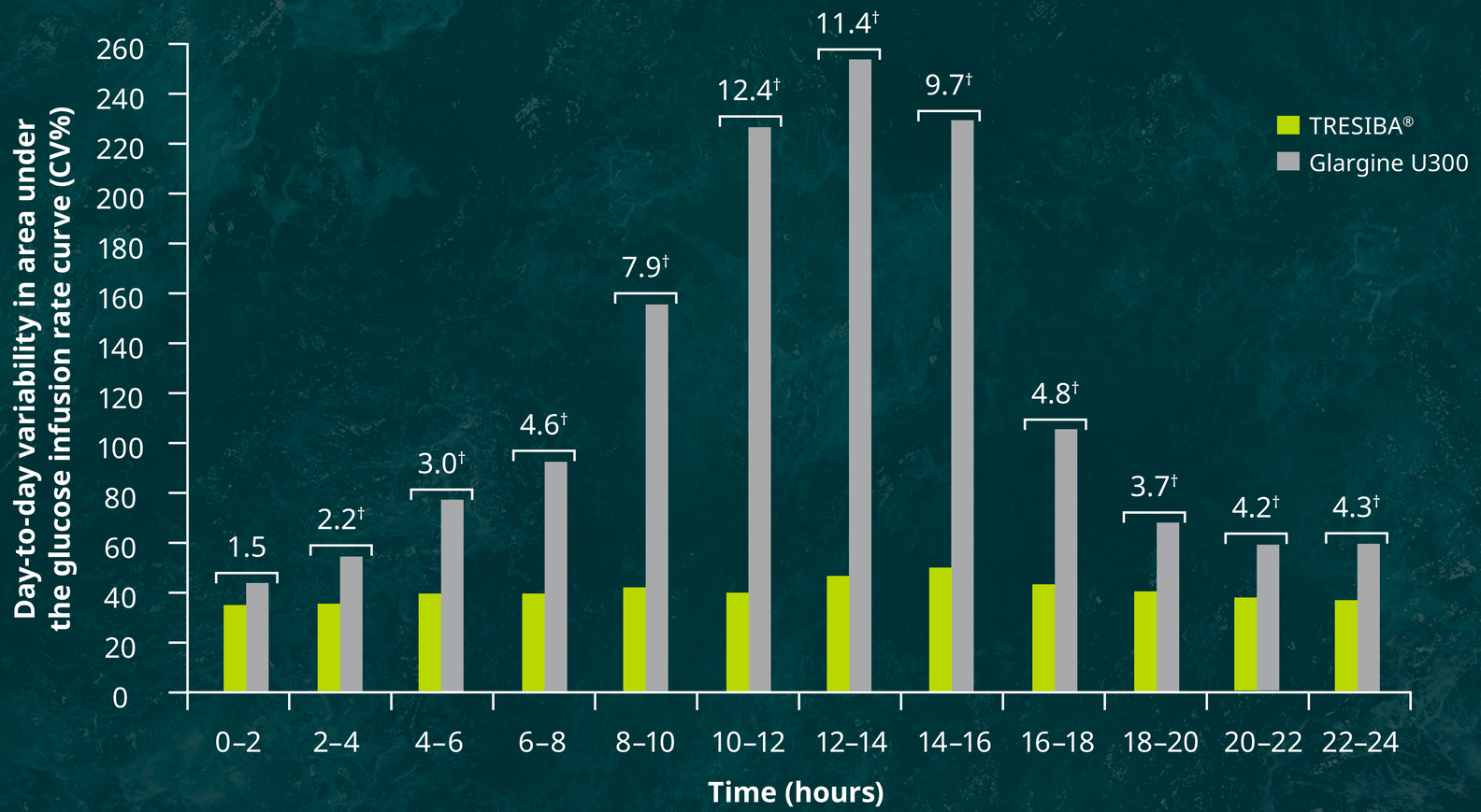
Individual molecules are then slowly and consistently released into the circulation[12,13,16]

Play molecule animation

UNIQUE MOLECULE

TRESIBA® offers lower day-to-day variability in glucose-lowering effect vs glargine U300[17,18]*

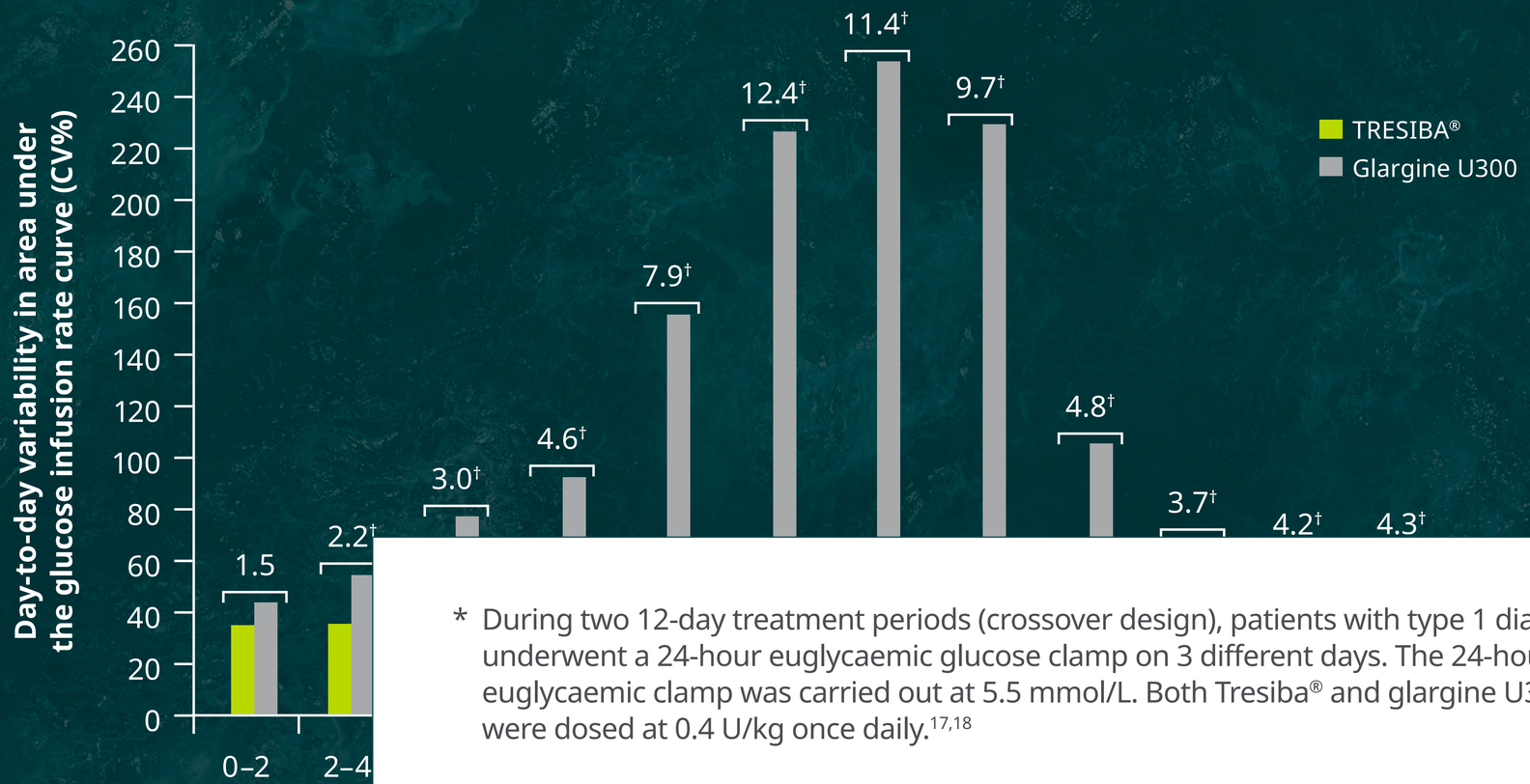
Slow, consistent release:



* In patients with type 1 diabetes in a PK/PD study.[17,18]
† $p<0.05$.

TRESIBA® offers lower day-to-day variability in glucose-lowering effect
vs glargine U300[17,18]*

Slow, consistent release:



* In patients with type 1 diabetes in a PK/PD study.[17,18]
† $p<0.05$.

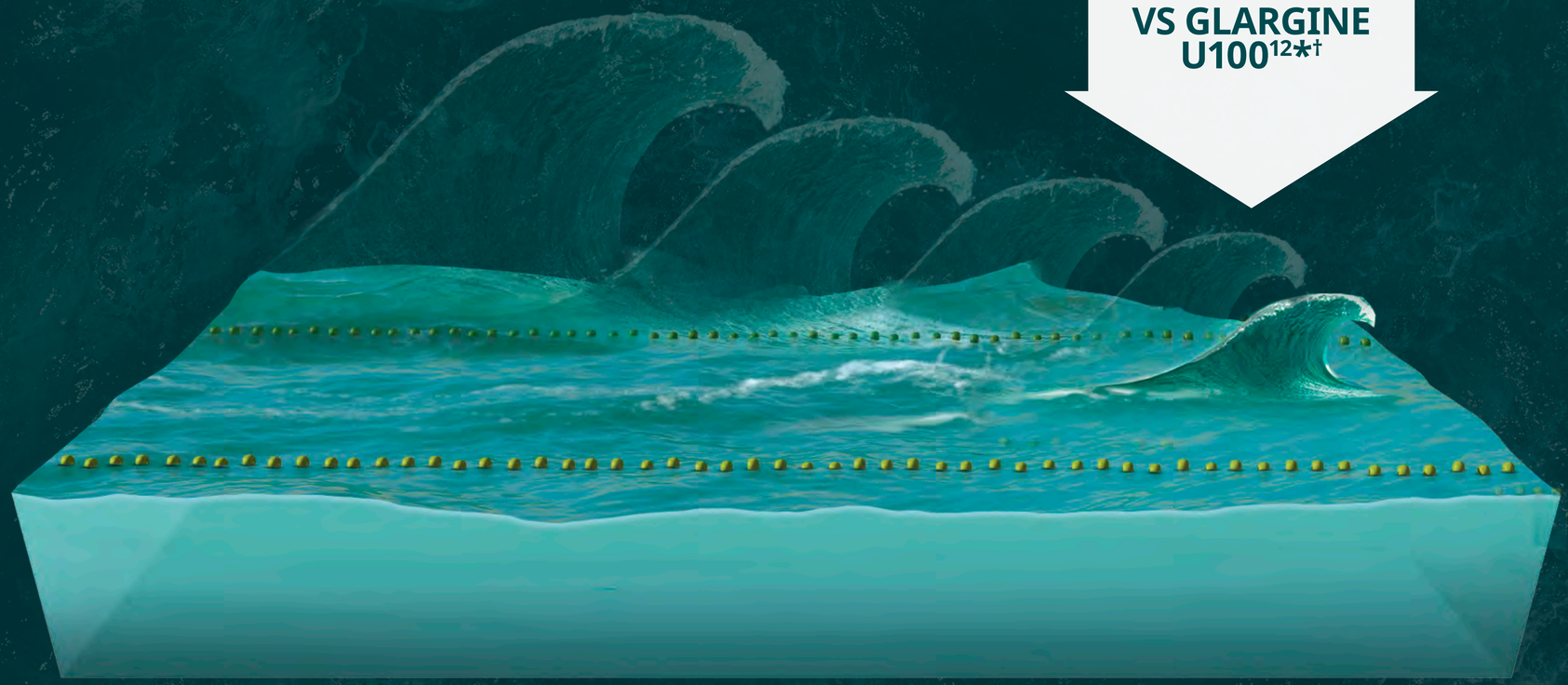
* During two 12-day treatment periods (crossover design), patients with type 1 diabetes underwent a 24-hour euglycaemic glucose clamp on 3 different days. The 24-hour euglycaemic clamp was carried out at 5.5 mmol/L. Both Tresiba® and glargine U300 were dosed at 0.4 U/kg once daily.[17,18]

CV (coefficient of variation). PD (pharmacodynamic). PK (pharmacokinetic).

UNIQUE MOLECULE

With TRESIBA® you can help give them daily predictability[12,17,18]

SIGNIFICANTLY LOWER DAY-TO-DAY VARIABILITY WITH TRESIBA® VS GLARGINE U100[12]*†

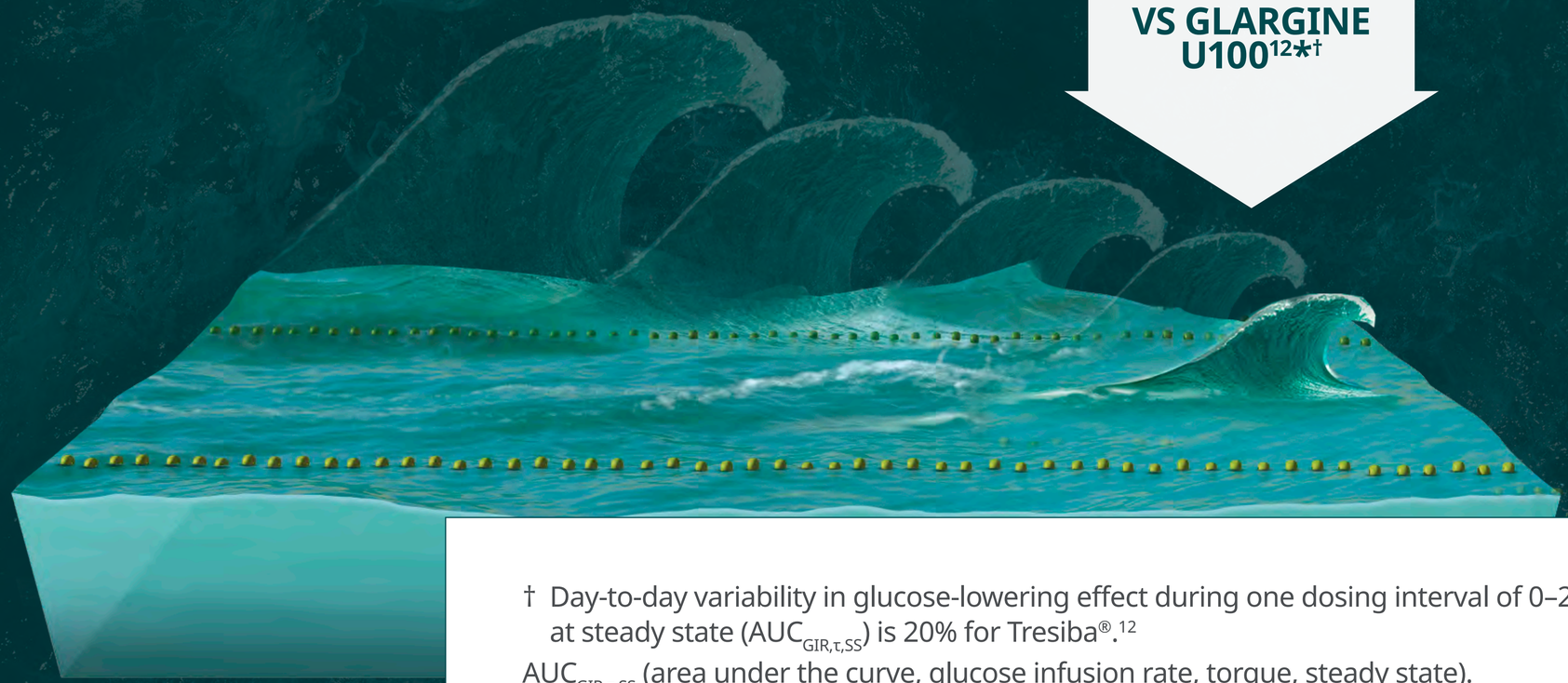


* In glucose-lowering effect in patients with type 1 diabetes in a PK/PD study.

UNIQUE MOLECULE

With TRESIBA® you can help give them daily predictability[12,17,18]

SIGNIFICANTLY LOWER DAY-TO-DAY VARIABILITY WITH TRESIBA® VS GLARGINE U100[12]*†



† Day-to-day variability in glucose-lowering effect during one dosing interval of 0–24 hours at steady state ($AUC_{GIR,\tau,SS}$) is 20% for Tresiba®.[12]

$AUC_{GIR,\tau,SS}$ (area under the curve, glucose infusion rate, torque, steady state).
PD (pharmacodynamic). PK (pharmacokinetic).

* In glucose-lowering effect in patients with type 1 diabetes in

UNIQUE MOLECULE

Getting to goal in the real world[3]

In the **CONFIRM** study, patients with type 2 diabetes **treated with Tresiba®** achieved:

↓ **.27%**

Significantly greater reduction in HbA_{1c} vs glargine U300[3]*

↓ **27%**

Reduced likelihood of treatment discontinuation vs glargine U300[3†]

CONFIRM

Getting to goal in the real world[3]

In the **CONFIRM** study, patients with type 2 diabetes **treated with Tresiba®** achieved:

↓ **.27%**

Significantly greater reduction in HbA_{1c} vs glargine U300[3]*

↓ **27%**

Reduced likelihood of treatment

* Estimated treatment difference in HbA_{1c} –0.27%; (*p*=0.03).[3]

† Treatment with Tresiba® was 27% less likely to result in treatment discontinuation than treatment with glargine U300 (HR 0.73; *p*<0.001).[3]

CONFIRM was a retrospective, real-world study in insulin-naïve patients.[3]

HR (hazard ratio).

You can significantly increase patients' Time in Range (TiR)[19]

More than HbA_{1c}

Patients with type 2 diabetes using Tresiba® significantly increased their Time in Range vs glargine U100 in the SWITCH PRO trial[19]*

~21 minutes more **TiR** per day[19†]

= **125 hours** more **TiR** per year with Tresiba®[19†]

Tresiba® significantly reduced nocturnal hypoglycaemic episodes (level 2) vs glargine U100[19‡]

TRESIBA® insulin degludec [rDNA origin] injection

You can significantly increase patients' Time in Range (TiR)[19]

More than HbA_{1c}

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~21 minutes more **TiR** per day[19†] = **125 hours** more **TiR** per year with Tresiba®[19†]

* Insulin-treated patients with type 2 diabetes at increased risk of hypoglycaemia, *p*=0.03.[19]

† Mean TiR was 72.11% Tresiba® vs 70.68% glargine U100, *p*=0.03.[19]

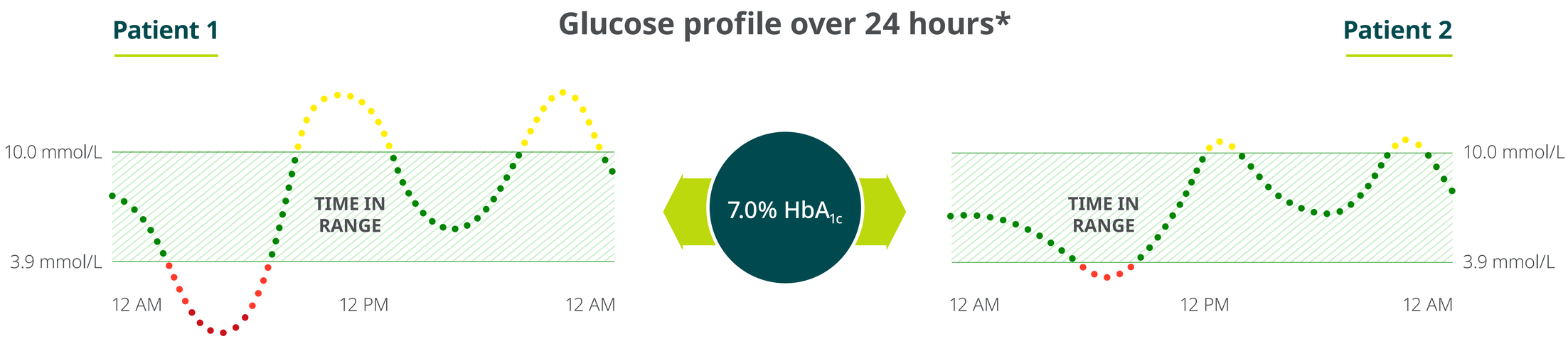
‡ Clinically significant nocturnal (00:01–05:59 am) episodes, defined as ≥2 consecutive FGM readings at level 2 <3.0 mmol/L, separated by 15 minutes: 31.1 patient-years of exposure vs 40.9, respectively (treatment rate ratio 0.76), 24% reduction.[19]

FGM (flash glucose monitoring). TiR (Time in Range).

Time in Range

Glycaemic control is more than HbA_{1c}

Patients with the same HbA_{1c} can have very different daily glucose patterns, glycaemic variability and Time in Range[20]

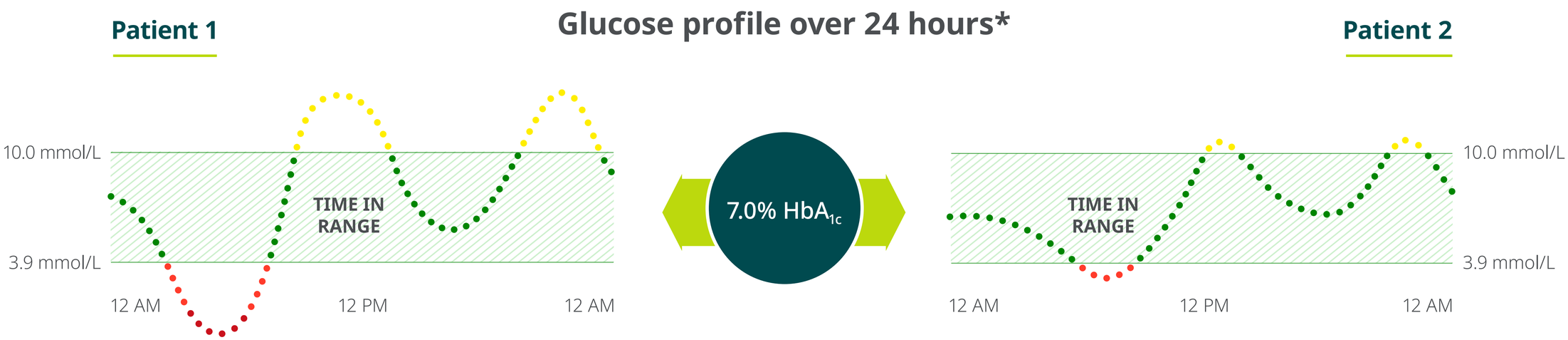


- 36% of patients with type 2 diabetes say having their blood glucose on target all day is the most important factor for a positive frame of mind.[21†]
- More Time in Range means fewer hypos and hypers.[22]

* Diagram is for illustrative purposes only and does not represent an actual patient profile.

Time in Range

Glycaemic control is more than HbA_{1c}
Patients with the same HbA_{1c} can have very different daily glucose patterns, glycaemic variability and Time in Range[20]



- 36% of patients with type 2 diabetes say ha
  for a positive frame of mind.[21†]
- More Time in Range means fewer hypos ar

* Diagram is for illustrative purposes only and does not repr

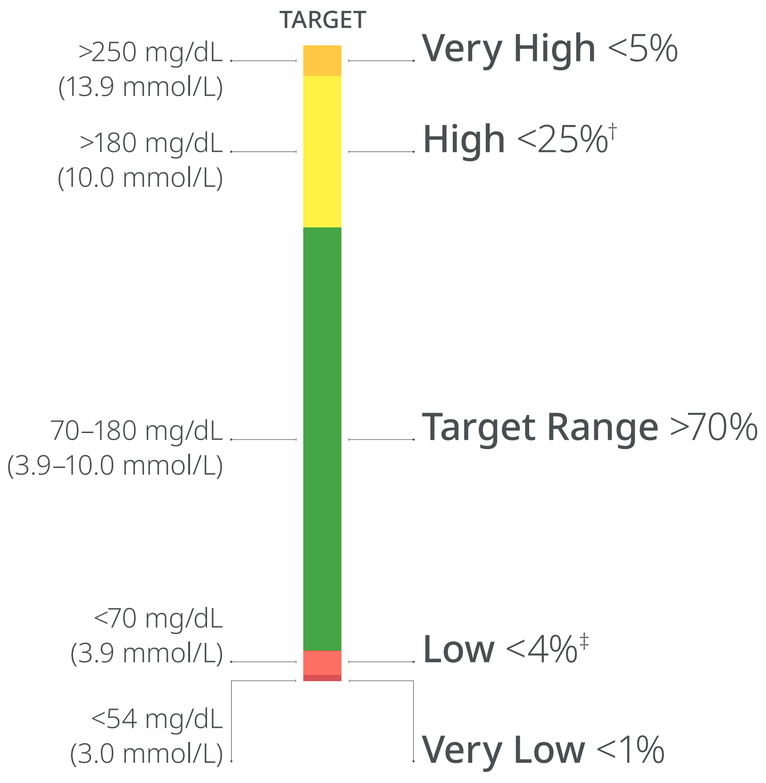
† Patients with type 2 diabetes on insulin (N=1,154).[21]

ADA (American Diabetes Association). TiR (Time in Range).

Affiliates are responsible for reviewing the promotional material against local label, more stringent relevant local legislation, and if relevant local code of conduct (cf. S.O.P 100965 "Approval of Promotional Material in Novo Nordisk") before distribution.

Patients should spend >70% of the day in target glucose range[22]*

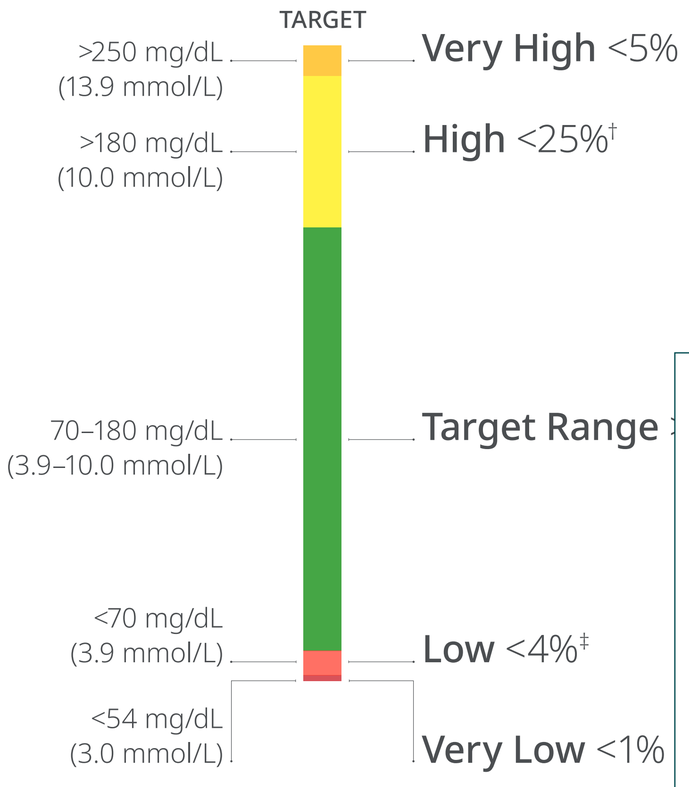
ADA daily time targets for patients with type 2 diabetes[22]*



In real life, patients with type 2 diabetes may spend only 55% of their day in recommended **Time in Range**[23§]

Patients should spend >70% of the day in target glucose range[22]*

ADA daily time targets for patients with type 2 diabetes[22]*



* For older or high-risk patients, the TiR target is lowered to >50% and time below range reduced to <1% at <70 mg/dL (<3.9 mmol/L).[22]

† Includes % of values >250 mg/dL (13.9 mmol/L).[22]

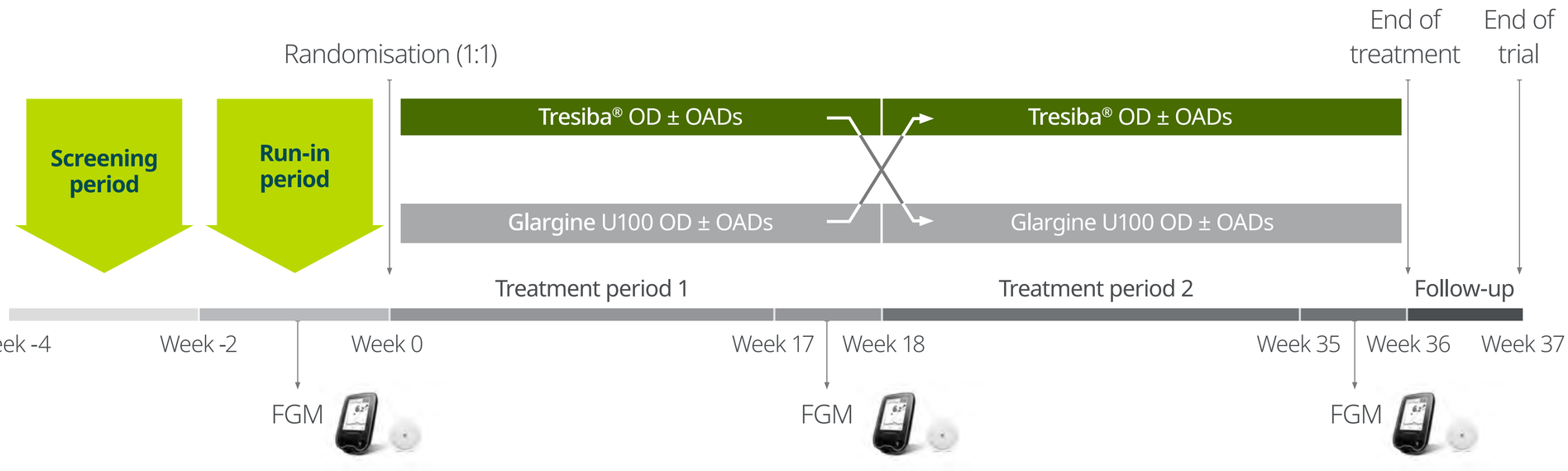
‡ Includes % of values <54 mg/dL (3.0 mmol/L).[22]

§ From a multicentre, randomised study in patients with type 2 diabetes (N=158) to assess the effectiveness of CGM. Patients were assigned CGM (n=79) or usual care (n=79). Time spent in range is reported at baseline.[23]

ADA (American Diabetes Association). CGM (continuous glucose monitoring). TiR (Time in Range).

SWITCH PRO trial design[19]

498
insulin-treated patients with type 2 diabetes at increased risk of hypoglycaemia



Trial characteristics

- Randomised 1:1
- Open-label
- Crossover
- Multicentre

Primary endpoint

- % of TiR (3.9–10.0 mmol/L) during the 2-week maintenance periods (weeks 17–18 and 35–36)

Secondary endpoints

- Overall and nocturnal time in tight glycaemic target range (3.9–7.8 mmol/L)
- Mean HbA_{1c} and glucose levels (based on FGM) during the 2-week maintenance periods

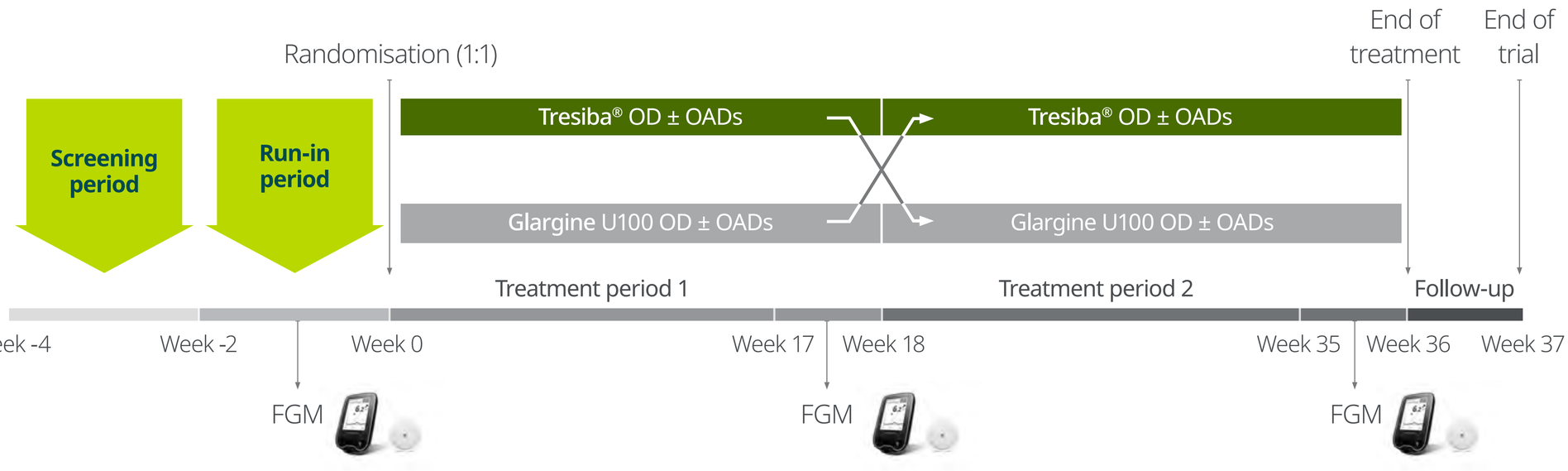
Exploratory endpoints

- Time in hypoglycaemia alert range (level 1: 3.0–3.8 mmol/L)
- Time in clinically significant hypoglycaemia (level 2: <3.0 mmol/L)
- Overall and nocturnal clinically significant hypoglycaemic episodes*
- Glycaemic variability
- Mean insulin dose

All measured by FGM during the 2-week maintenance periods

SWITCH PRO trial design[19]

498
insulin-treated patients with type 2 diabetes at increased risk of hypoglycaemia



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- Time in hypoglycaemia alert range (level 1: 3.0–3.8 mmol/L)

* 00:01–05:59 inclusive, defined as ≥2 consecutive FGM readings <3.0 mmol/L, separated by 15 minutes.[19]

FGM (flash glucose monitoring). OADs (oral anti-diabetic drugs). OD (once daily). TiR (Time in Range).

Helping to avoid the downside

Fear of hypos is a barrier to insulin adherence in

87%

of patients with type 2 diabetes[5]

46%

of patients with type 2 diabetes experience at least one hypo every month[24]*

Hypos impact patient behaviour[25]

- Reducing insulin dose[25]
- Skipping injections[25]
- Avoiding physical exercise[25]

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Hypos impact patient behaviour[25]

- Reducing insulin dose[25]
- Skipping injections[25]
- Avoiding physical exercise[25]

* Hypoglycaemia was patient-reported and defined as non-severe (managed by the patient alone), severe (ADA definition: blood glucose ≤3.9 and requiring third-party assistance) and nocturnal (occurring between midnight and 06:00).[24]

ADA (American Diabetes Association).

TRESIBA® – the reassurance patients with type 2 diabetes need to get to goal

CONCLUDE

R | SmPC | aPI

TRESIBA® insulin degludec [rDNA origin] injection

Reassurance from consistently few hypos

BEGIN

Vs
glargine U100

42%

reduction in nocturnal hypos[26†]

SWITCH 2

Vs
glargine U100

30%

reduction in overall hypos[1‡]

DEVOTE

Vs
glargine U100

40%

reduction in severe hypos[2§]

CONFIRM*

Vs
glargine U300

30%

reduction in hypos[3¶]

ReFLeCT*

After switching from other basal insulins

54%

reduction in overall hypos[27‖]

✔ **Without compromising glycaemic control[1-3,26,27]**

i

Reassurance from consistently few hypos

* Real-world evidence studies.

† (p=0.002).[26]
Data from the extension trial set.[26]
In the BEGIN ONCE LONG trial, in insulin-naïve patients with type 2 diabetes, confirmed hypoglycaemic episodes included either episodes confirmed by self-monitored blood glucose corresponding to plasma glucose value <3.1 mmol/L (<56 mg/dL) or severe episodes requiring assistance. Episodes occurring between 00:01 and 05:59 (both inclusive) were classified as nocturnal.[26]

‡ (p<0.001). Maintenance period.[1]
In the SWITCH 2 trial, in patients with type 2 diabetes, overall hypoglycaemia was defined as severe or BG-confirmed (<3.1 mmol/L [<56 mg/dL]) with symptoms, and severe hypoglycaemia was defined as an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions, neurological recovery following the return of plasma glucose to normal, or both (ADA definition).[1]

§ (p<0.001).[2]
In the DEVOTE trial, in patients with type 2 diabetes at high risk of CV events, severe hypoglycaemic episodes were independently adjudicated using the ADA definition.[2]

¶ (p<0.05).[3]
CONFIRM was a retrospective, real-world study.[3]
In the CONFIRM study, in insulin-naïve patients with type 2 diabetes, hypoglycaemia was recorded by the treating clinician and defined according to International Classification of Diseases codes 9 and 10.[3]

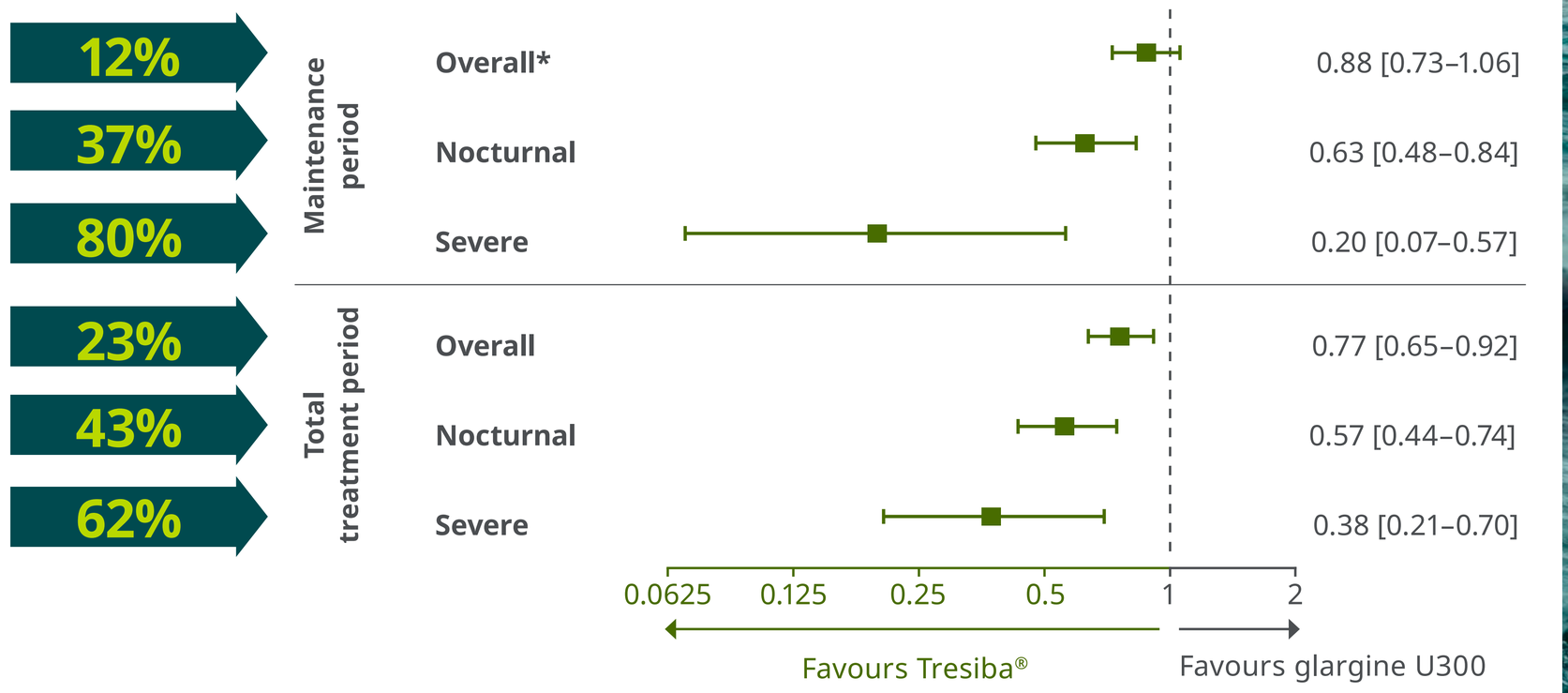
‖ (p<0.001).[27]
ReFLeCT was a prospective, real-world study.[27]
In the ReFLeCT study, in patients with type 2 diabetes, overall hypoglycaemia was defined as any event recorded as hypoglycaemia in patients' diaries irrespective of symptoms, blood glucose or time of day.[27]

ADA (American Diabetes Association). BG (blood glucose). CV (cardiovascular).

Based on CONCLUDE, which would you choose?[28]

Reduction in hypo
rates with TRESIBA® vs glargine U300

The primary endpoint* (superiority on rate of overall symptomatic hypoglycaemia in the maintenance period) for Tresiba® vs glargine U300 was not met (not statistically significant, although numerically lower; rate ratio: 0.88; 95% CI: 0.73 to 1.06).[28]



✔ **Without compromising glycaemic control[28†]**

Based on CONCLUDE, which would you choose?[28]

Reduction in hypo
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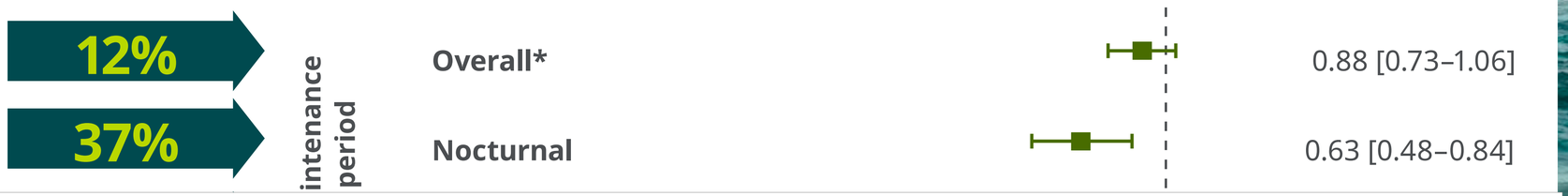
The primary endpoint* (superiority on rate of overall symptomatic hypoglycaemia in the maintenance period) for Tresiba® vs glargine U300 was not met (not statistically significant, although numerically lower; rate ratio: 0.88; 95% CI: 0.73 to 1.06).[28]



* Primary endpoint of the study was not met.[28]

† *Post hoc* analysis that assessed change from baseline to end of treatment showed lower HbA_{1c} in patients treated with Tresiba® vs glargine U300 (estimated treatment difference –0.10%; 95% CI: –0.18 to –0.02).[28]

The pre-specified confirmatory secondary hypoglycaemia endpoint, nocturnal symptomatic hypoglycaemia during the maintenance period, is considered exploratory as it could not be controlled for the family-wise type I error.[28]

Secondary endpoints should not be interpreted independently of the primary endpoint.[28]

Overall symptomatic hypoglycaemia was defined as severe or BG-confirmed.[28]

Nocturnal symptomatic hypoglycaemia was defined as severe or BG-confirmed, occurring between the times of 00:01 and 05:59.[28]

Severe hypoglycaemia was defined as an event requiring third-party assistance as per the ADA definition.[28,29]

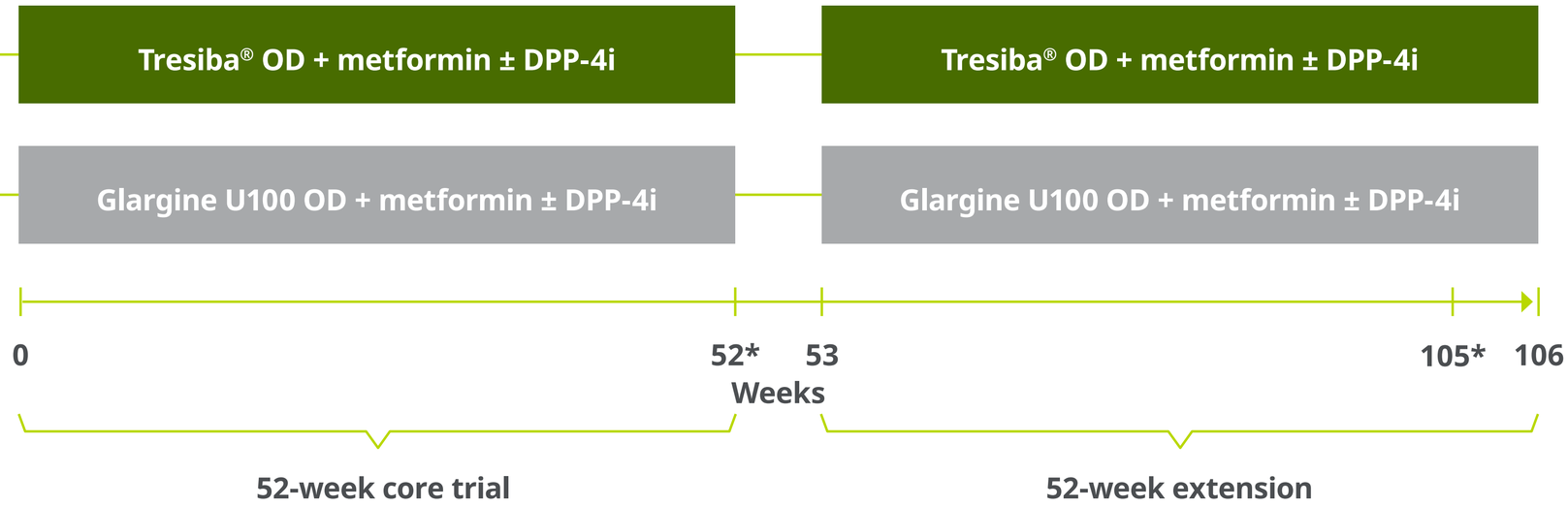
BG-confirmed events were defined as BG <3.1 mmol/L (<56 mg/dL), with symptoms.[28]

ADA (American Diabetes Association). BG (blood glucose). CI (confidence interval).

BEGIN ONCE LONG trial design[26]

1,030

insulin-naïve patients with type 2 diabetes, inadequately controlled with OADs



Trial characteristics

- Randomised 3:1 (Tresiba® OD:glargine U100 OD)
- Open-label
- Treat-to-target
- Non-inferiority

Primary endpoint

Non-inferiority in HbA_{1c} reduction

Aim of extension

Assessed long-term safety and tolerability

Patients who completed the core phase and entered the extension maintained their prior randomisation treatment. Basal insulin was titrated to a target FPG of 3.9–4.9 mmol/L.[26]

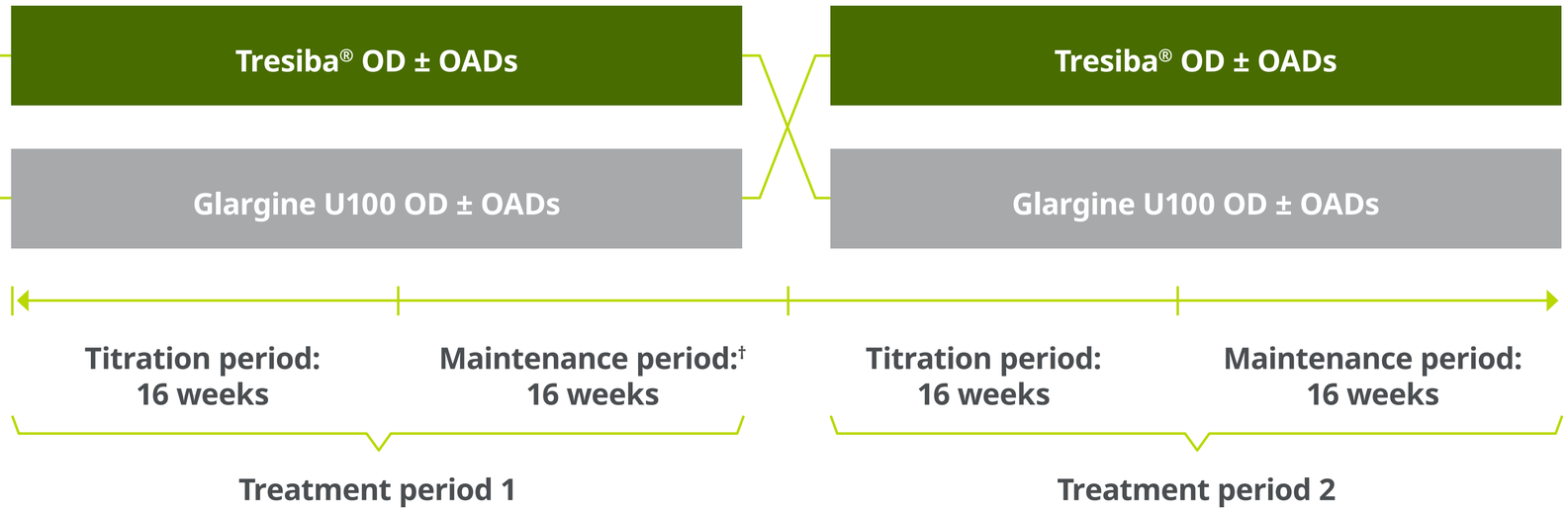
In the BEGIN ONCE LONG trial, confirmed hypoglycaemic episodes included either episodes confirmed by self-monitored blood glucose corresponding to plasma glucose value <3.1 mmol/L (<56 mg/dL) or severe episodes requiring assistance. Episodes occurring between 00:01 and 05:59 (both inclusive) were classified as nocturnal.[26]

* 1-week washout period at week 52 and week 105. 105 weeks = 104 weeks' exposure.[26]

DPP-4i (dipeptidyl peptidase-4 inhibitor). FPG (fasting plasma glucose). OADs (oral anti-diabetic drugs). OD (once daily).

SWITCH 2 trial design[1]

721
adult patients with type 2 diabetes on basal insulin ± OADs*



Trial characteristics
- Randomised 1:1
- Double-blind
- Crossover
- Treat-to-target

Primary endpoint
Change in rates of overall hypoglycaemic episodes during the maintenance period

Secondary endpoints
Change in rates of nocturnal hypoglycaemic episodes and the proportion of patients experiencing one or more severe hypoglycaemic episodes, both in the maintenance period

Overall and nocturnal hypoglycaemia reductions were significant in the maintenance period and based on rate ratios (pre-specified analysis). Reduction in rates of overall (23%) and nocturnal (25%) hypoglycaemia were also significant for the full trial period. Severe hypoglycaemia reductions were not significant in the maintenance period, although the reduction in rate for the full trial period (51%) was statistically significant.[1]

In the SWITCH 2 trial, overall hypoglycaemia was defined as severe or BG-confirmed (<3.1 mmol/L [<56 mg/dL]) with symptoms, nocturnal hypoglycaemia was defined as episodes occurring between 00:01 and 05:59 (both inclusive), and severe hypoglycaemia was defined as an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions, neurological recovery following the return of plasma glucose to normal, or both (ADA definition).[1]

* For patients previously treated with BID basal insulin, a 20% dose reduction was applied at randomisation.[1]

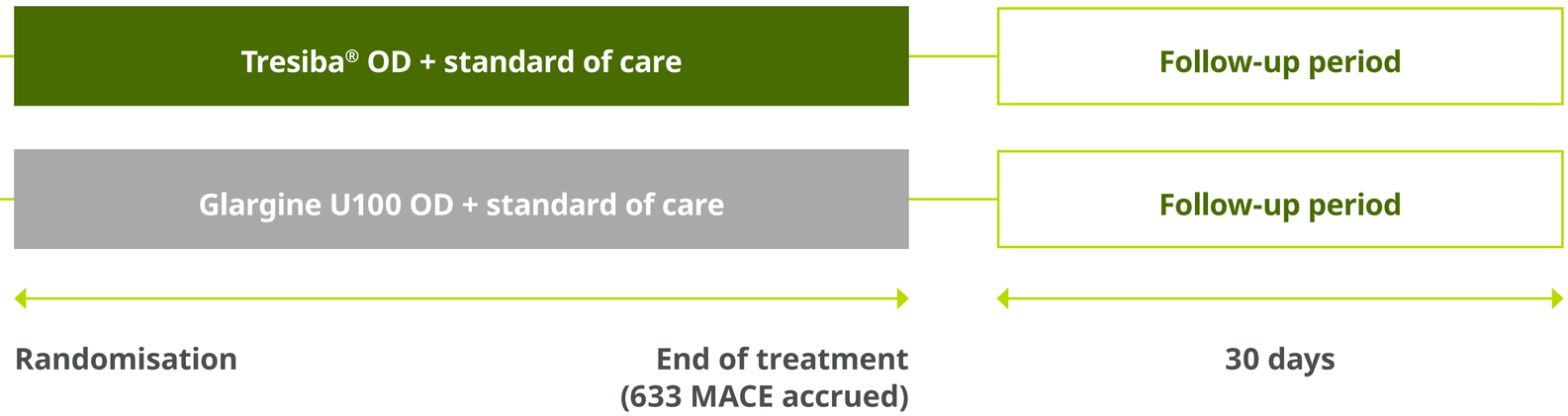
† Only patients who were exposed in the first maintenance period contributed to the maintenance period analysis.[1]

ADA (American Diabetes Association). BG (blood glucose). BID (twice daily). OADs (oral anti-diabetic drugs excluding sulfonylurea and meglitinides). OD (once daily).

DEVOTE trial design[2]

7,637
patients with type 2 diabetes at high risk of CV events

Trial characteristics
- Randomised
- Double-blind
- Multicentre and international
- Event-driven
- Independently adjudicated



Primary outcome
The first occurrence of MACE

Secondary outcome
Change in the number and incidence of adjudicated events of severe hypoglycaemia

In the DEVOTE trial, nocturnal hypoglycaemia was defined as episodes occurring between 12:01 and 05:59. Severe hypoglycaemic episodes were independently adjudicated using the ADA definition. MACE was defined as CV death, non-fatal MI and non-fatal stroke.[2]

ADA (American Diabetes Association). CV (cardiovascular). MACE (major adverse cardiovascular event). MI (myocardial infarction). OD (once daily).

CONFIRM real-world study design[3]

4,056
insulin-naïve patients with type 2 diabetes

RETROSPECTIVE DATA EXTRACTION

- **Insulin-naïve** (minimum 12 months) → **Tresiba®** (minimum 3 months)
- **Insulin-naïve** (minimum 12 months) → **Glargine U300** (minimum 3 months)

6 months pre-initiation — **3 months** — **Initiation of basal insulin** — **3 months** — **6 months post-initiation**

Primary endpoint

Change in mean HbA_{1c} from initiation to 6 months of follow-up

Secondary endpoints*

Change in rates of hypoglycaemic episodes from initiation to 6 months of follow-up

Change in proportion of patients with ≥1 episode of hypoglycaemia from initiation to 6 months of follow-up

As with all real-world studies, CONFIRM was not randomised. Therefore, this study carries the limitations of real-world evidence.[3]

POTENTIAL STUDY LIMITATIONS:[3]

- **Potential under-reporting of hypoglycaemia (however, this is the case in both CONFIRM treatment arms, meaning the rate ratio and the odds ratio are expected to be preserved)**
- **Short follow-up period of 3–6 months (however, this corresponds to the time in which the largest changes in HbA_{1c} tend to occur and is commonly used in many clinical trials)**
- **The study only provides evidence of prescribed basal insulin, not actual use (whether or not the medication was picked up at the pharmacy)**

In the CONFIRM study, HbA_{1c} values were estimated using repeated-measure analysis of covariance, treatment as factor and subject as random effect.[3]

Reduction in mean HbA_{1c} was also significant (p=0.03; baseline HbA_{1c} values – Tresiba®: 9.6 ± 2.2; glargine U300: 9.5 ± 2.1).[3]

Hypoglycaemia was recorded by the treating clinician and defined according to International Classification of Diseases codes 9 and 10.[3†]

* Rate of hypoglycaemic episodes and proportion of patients with hypoglycaemia were estimated over a period of 180 days (pre- or post-initiation of basal insulin) using negative binomial and logistic regression, respectively and a generalised estimating equation approach.[3]

† This definition differs from key Novo Nordisk RCTs with Tresiba® e.g., SWITCH 2 and DEVOTE.

CI (confidence interval). RCT (randomised controlled trial).

ReFLeCT real-world study design[27]

611

patients with type 2 diabetes on other basal insulins switched to Tresiba®

Study characteristics

- Multinational
- Real-world
- Prospective
- Observational
- Hypo data collected using patient diaries

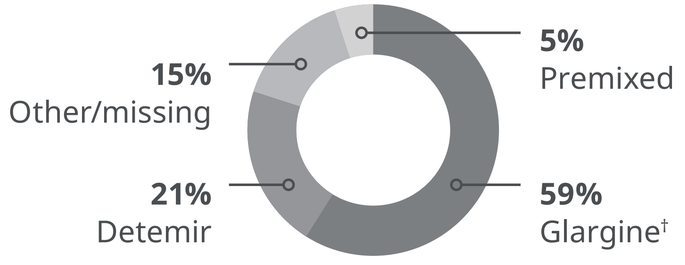
Primary endpoint

Change in number of overall hypoglycaemic episodes in patients before and after switching to Tresiba®

Secondary endpoints

Change in the number of severe, non-severe and nocturnal hypoglycaemic events, HbA_{1c}, FPG, daily insulin dose, body weight, DTSQ-s and SF-36® v2 health status survey scores

Previous basal insulin therapy



POTENTIAL STUDY LIMITATIONS:[27]

- **Real-world data are generated outside a controlled clinical trial setting, the main methodological difference from RCTs being that patients are not randomised to treatment groups.**
- **The absence of a comparator group means that a treatment effect cannot be isolated from a study effect.**
- **Hypoglycaemia rates captured in ReFLeCT may be due to selection bias of the patients enrolled – so it is possible that patients with frequent hypoglycaemia were overrepresented.**

In the ReFLeCT study, overall hypoglycaemia was defined as any event recorded as hypoglycaemia in patients' diaries irrespective of symptoms, blood glucose or time of day. Nocturnal hypoglycaemia was defined as an event (either severe or non-severe) occurring between 00:01 and 05:59 (both inclusive), regardless of whether the patient was awake or woken up. Severe hypoglycaemia was defined as an episode requiring assistance of another person to actively administer carbohydrate, glucagon, or take other corrective actions (ADA definition). Non-severe hypoglycaemia was defined as either an event with or without symptoms accompanied by a BG measurement ≤3.9 mmol/L (70 mg/dL) or an event with symptoms not accompanied by a BG measurement but assumed to be caused by a BG ≤3.9 mmol/L (70 mg/dL).[27]

* Patients were only expected to attend visits that were part of routine clinical practice.[27]

† Data to differentiate glargine U100 or U300 were not collected.[27]

ADA (American Diabetes Association). BG (blood glucose). DTSQ-s (Diabetes Treatment Satisfaction Questionnaire status version). FPG (fasting plasma glucose). RCT (randomised controlled study). SF-36® v2 (Short Form-36 version).

CONCLUDE – designed to demonstrate TRESIBA® safety profile[28,29]

1,609
insulin-treated patients with type 2 diabetes

Screening and randomisation: 2 weeks

Tresiba® ± OADs — **n=703**

Titration: 16 weeks | Variable maintenance period: up to 36 weeks* | Maintenance period: 36 weeks† | Follow-up: 30 days

Total treatment period: up to 88 weeks

Glargine U300 ± OADs — **n=706**

Trial completers

Trial characteristics
- Randomised 1:1
- Open-label
- Multinational
- Treat-to-target

Aim
To investigate the effect of Tresiba® and glargine U300 on hypoglycaemia in insulin-treated patients with type 2 diabetes

Primary endpoint
Superiority on rate of overall symptomatic hypoglycaemia with Tresiba® vs glargine U300 during the maintenance period

Secondary endpoints
- Basal insulin dose at end of treatment
- Rate (during the maintenance period) vs glargine U300 of nocturnal symptomatic hypoglycaemia and severe hypoglycaemia
- Rates (during the total treatment period) vs glargine U300 of overall symptomatic, nocturnal symptomatic and severe hypoglycaemic events

During the trial conduct, a protocol amendment was implemented due to an unusual and potentially unsafe reporting pattern of glycaemic values and hypoglycaemic episodes related to the glycaemic data collection system. The protocol amendment and ensuing actions ensured that patient safety and the scientific integrity of the trial were not compromised.[28,29]
Overall symptomatic hypoglycaemia was defined as severe or BG-confirmed.[28]
Nocturnal symptomatic hypoglycaemia was defined as severe or BG-confirmed, occurring between the times of 00:01 and 05:59.[28]
Severe hypoglycaemia was defined as an event requiring third-party assistance as per the ADA definition.[28,30]
BG-confirmed events were defined as BG <3.1 mmol/L (<56 mg/dL), with symptoms.[28]
* The duration of the variable maintenance period was dependent on each patient's individual randomisation date and/or approval of the amended protocol by health authorities and local ethics committees, if applicable.[28]
† Primary and secondary endpoints related to hypoglycaemia were assessed during the maintenance period.[28]
ADA (American Diabetes Association). BG (blood glucose). OADs (oral anti-diabetic drugs).

TRESIBA® once-daily

Everyday use for every day

TRESIBA®
insulin degludec [rDNA origin] injection

Start TRESIBA®

FlexTouch®

TRESIBA® FlexTouch®

Smart pens

NovoPen®6 Dialoq®

In patients with type 2 diabetes

Starting is simple

with once-daily TRESIBA®[12]

NEW
to insulin

10
units per day[12]*

SWITCHING
from
once-daily
insulin

1:1
dose conversion[12]*

SWITCHING
from twice-daily
insulin or
glargine U300

Consider
20%
dose reduction[12]*

After reaching steady state, titrate based on the average of two preceding FPG measurements[14†]

Above target
+2
UNITS

On target
maintain dose

Below target
-2
UNITS

Patient models and examples for illustration only.

* Followed by individual dose adjustments.[12]
As Tresiba® takes between 2–3 days to reach steady state, blood glucose levels may be slightly higher on the first few days.[13,31]

SMART WAY TO USE TRESIBA®

In patients with type 2 diabetes

Starting is simple

with once-daily TRESIBA®[12]

NEW
to insulin

10
units per day[12]*

SWITCHING
from
once-daily
insulin

1:1
dose conversion[12]*

SWITCHING
from twice-daily
insulin or
glargine U3

Consider
20%

After reaching steady state, titrate based on the average of two preceding FPG measurements[14†]

Above target
+2
UNITS

On target
maintain dose

Below target
-2
UNITS

† ADA-recommended FPG goal is 4.4–7.2 mmol/L (80–130 mg/dL) for many adults with diabetes.[32]

ADA (American Diabetes Association). FPG (fasting plasma glucose).

Patient models and examples for illustration only.

* Followed by individual dose adjustments.[12]
As Tresiba® takes between 2–3 days to reach steady state, blood gluc
may be slightly higher on the first few days.[13,31]

TRESIBA® is available in FlexTouch®

Easy to use[33–37]

- **≥85%** of patients rated FlexTouch® easier to use than SoloSTAR®* or KwikPen®[37†]

Confidence in insulin delivery[33–35,38,39]

- **96%** felt confident in managing daily injections with FlexTouch®[39‡]

Preferred by patients[33–35,39]

- **100%** of patients would recommend FlexTouch®[39‡]

Tresiba® FlexTouch® U100

- **Pen contains 300 total units[12]**
- **Up to 80 units in one injection[12]**
- **1-unit dose adjustments[12]**

Tresiba® FlexTouch® U200

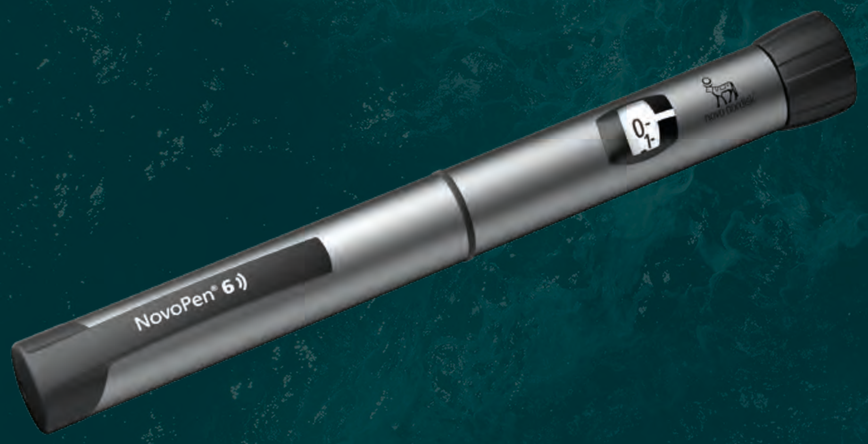
- **Pen delivers the same dose in half the volume of U100[12]**
- **Patients who need higher doses can inject up to 160 units in one injection[12]**
- **2-unit dose adjustments[12]**

* Glargine U100 units/mL. † In two usability studies (n=59) and n=79.[37]
‡ Randomised study, N=222.[39]

Smart ways to use TRESIBA®

NovoPen® 6 | NovoPen Echo® Plus | Dialoq®

NovoPen® 6 can help improve patients' Time in Range (TiR)[40]



~2 hours
more **TiR** every day
after using NovoPen® 6[40]*

Study subjects not limited to patients using Tresiba.®

Reliable insulin dose recording†

- Smart insulin pens automatically record insulin dosing data which can be transfered to compatible apps‡

Potential for informed, personalised consultations based upon patients' individual injection data†

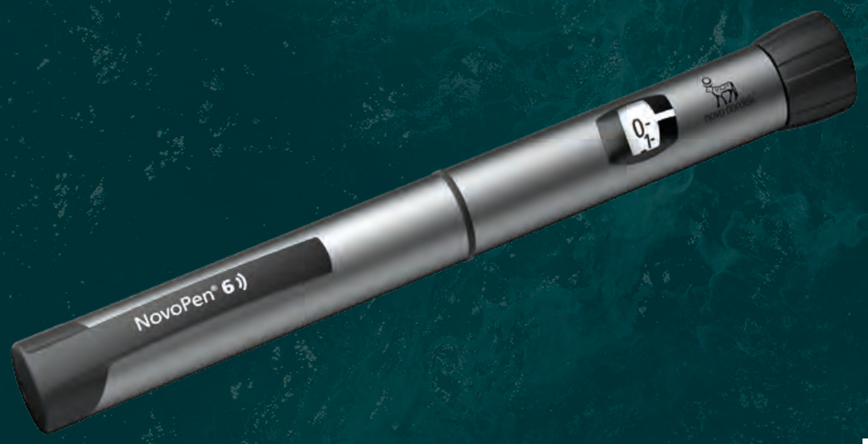
- Provides insights for personalised consultations

NP6 NPE+ Dialoq

Smart ways to use TRESIBA®

NovoPen® 6 | NovoPen Echo® Plus | Dialoq®

NovoPen® 6 can help improve patients' Time in Range (TiR)[40]



~2 hours
more **TiR** every day
after using NovoPen® 6[40]*

Study subjects not limited to patients using Tresiba.®

Reliable insulin dose recording†

- Smart insulin pens automatically record insulin dosing data which can be transfered to compatible apps‡

* In an observational study of patients with type 2 diabetes (N=94), TiR significantly increased by a mean of 1.9 hours/day (p<0.001) from baseline to follow-up period (on average >180 days). There was an 8.5% absolute difference in time spent in range (3.9–10.0 mmol/L, p<0.001); this is expected to correspond to ~0.4–0.7% improvement in HbA_{1c}. Significantly less time was spent experiencing hyperglycaemia (p=0.003) or level 2 hypos (p=0.005).[40]

† Self-reported diabetes information can often be unreliable.[41] Automatic logging may be more reliable than manual logging.

‡ Compatible with the following apps: mySugr®, Freestyle LibreLink, glooko® and Decom®.

TiR (Time in Range).

Affiliates are responsible for reviewing the promotional material against local label, more stringent relevant local legislation, and if relevant local code of conduct (cf. S.O.P 100965 "Approval of Promotional Material in Novo Nordisk") before distribution.

TRESIBA®
insulin degludec [rDNA origin] injection

Smart ways to use TRESIBA®

NovoPen® 6

NovoPen Echo® Plus

- Automatically records the last 800 injections
- Dose memory display of the amount and time since last injection
- Wireless transfer of patient data via Near Field Communication (NFC) technology
- In-use battery life of at least 4 years*

- 60-unit maximum dose
- 1-unit dose increments

- 30-unit maximum dose
- 0.5-unit dose increments

Dialoq®

- Automatically records and stores at least 3 months of doses (maximum 1,200 doses)
- Automatically records the insulin type†, number of units dosed, and the time and date of all injected and flow check doses

- Wireless transfer of patient data via Bluetooth®-enabled technology
- 2-year battery life

Note: Dialoq® can only be promoted once awarded the CE mark.

* No need to recharge. † The device memory will send a log including the insulin type. The Dialoq® device will show a medicine type as unsupported if it is not known.

Study subjects not limited to patients using Tresiba®

Insulin pens just got smarter

Broad range of partners

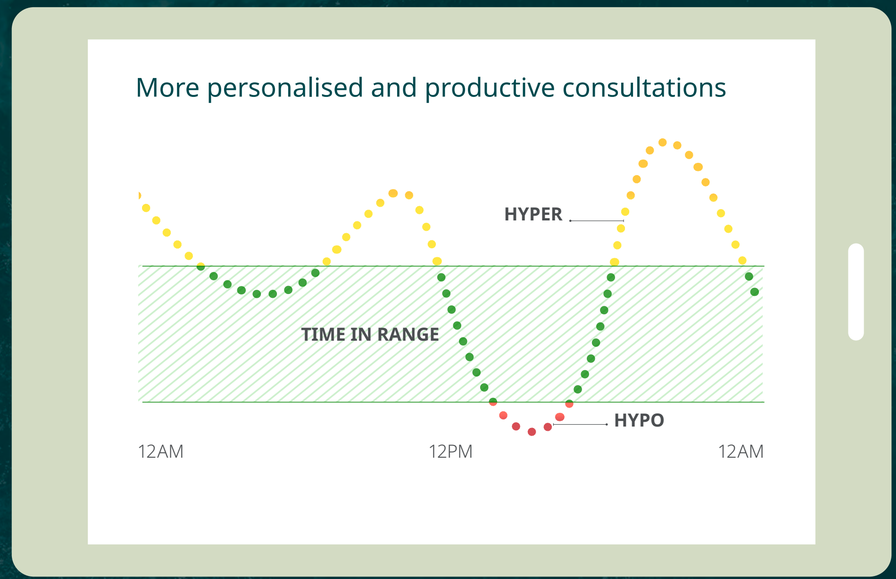
Glucose data ••••• Insulin dose data

mySugr

FreeStyle LibreLink

glooko

Dexcom



Insulin dose recording

NovoPen® 6 | Dialoq®

Support for treatment with TRESIBA®

Consent

Potential for informed, personalised consultations based upon patients' individual injection data[42]*

* When used in combination with a compatible app. NovoPen® 6 & NovoPen Echo® are compatible with the following apps: mySugr®, Freestyle LibreLink / LibreView, Glooko® and Dexcom®.

Currently, NovoNordisk® smart pen integrations are in process and not fully in place for all partners' solutions. Availability and timing will differ from partner to partner and country to country.

TRESIBA® – summary of benefits

for patients with type 2 diabetes

Reduction in HbA_{1c} vs glargine U100[1,2]

Can significantly increase **Time in Range** vs glargine U100[19]

42 HR

Flat and stable, with duration of action beyond 42 hours[12,13]

To help reassure patients of **few hypos**[1-3,26*]

* Compared with glargine U100 or glargine U300.[1-3,26]

HQ21TSM00031 Approval date: March 2022.

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