Job Certificate

Job Info Fields

Document Name: Tresiba® self led e-detail aid 2022_Updated EXPECT claims
Document Number: HQ22TSM00023

Classification Fields

Product Name: Tresiba
Job Type: Promotional
Country Compliance Classification:
Target Audience: Healthcare Practitioners
Subtype: Sales Material
Job Description: The new iSelling for Tresiba in self led e-detail aid format
Geographical Use (Global Only): Global

Date Fields

Date of Certification: 9/16/2022
Planned Date of First Use: 9/19/2022

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.).

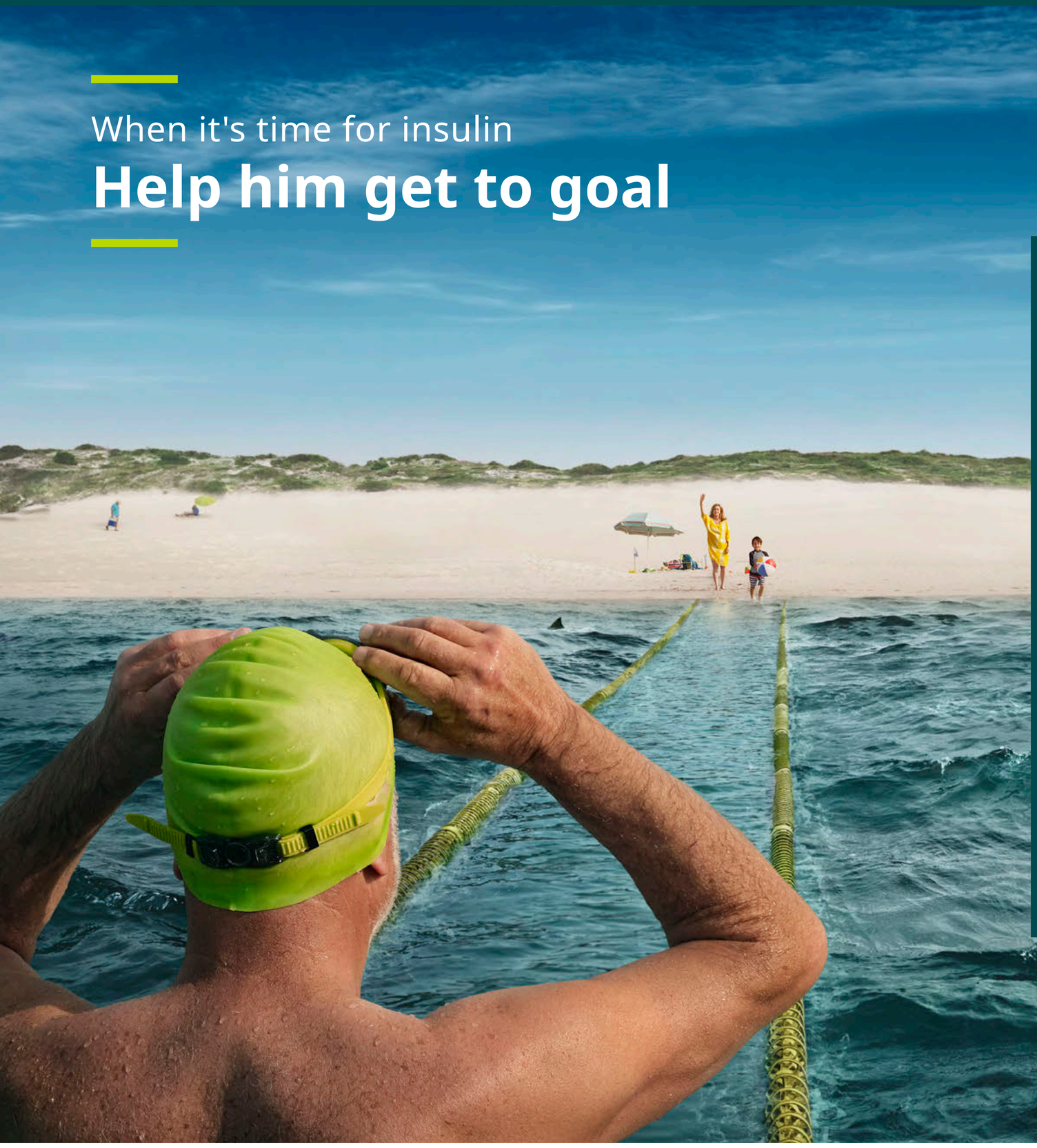
Role	Signature
Business Certification BU Insulins Approved	HDUI (Hans Duijf) hdui@novonordisk.com 14-Sep-2022 14:24:30 GMT+0000
Compliance Certification Medical Approved	BAMK (Balamurali K) bamk@novonordisk.com 16-Sep-2022 05:03:37 GMT+0000

Let TRESIBA® help patients with type 2 diabetes

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

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

novo nordisk®

R | SmPC | aPI

TRESIBA®
insulin degludec [rDNA origin] injection

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]

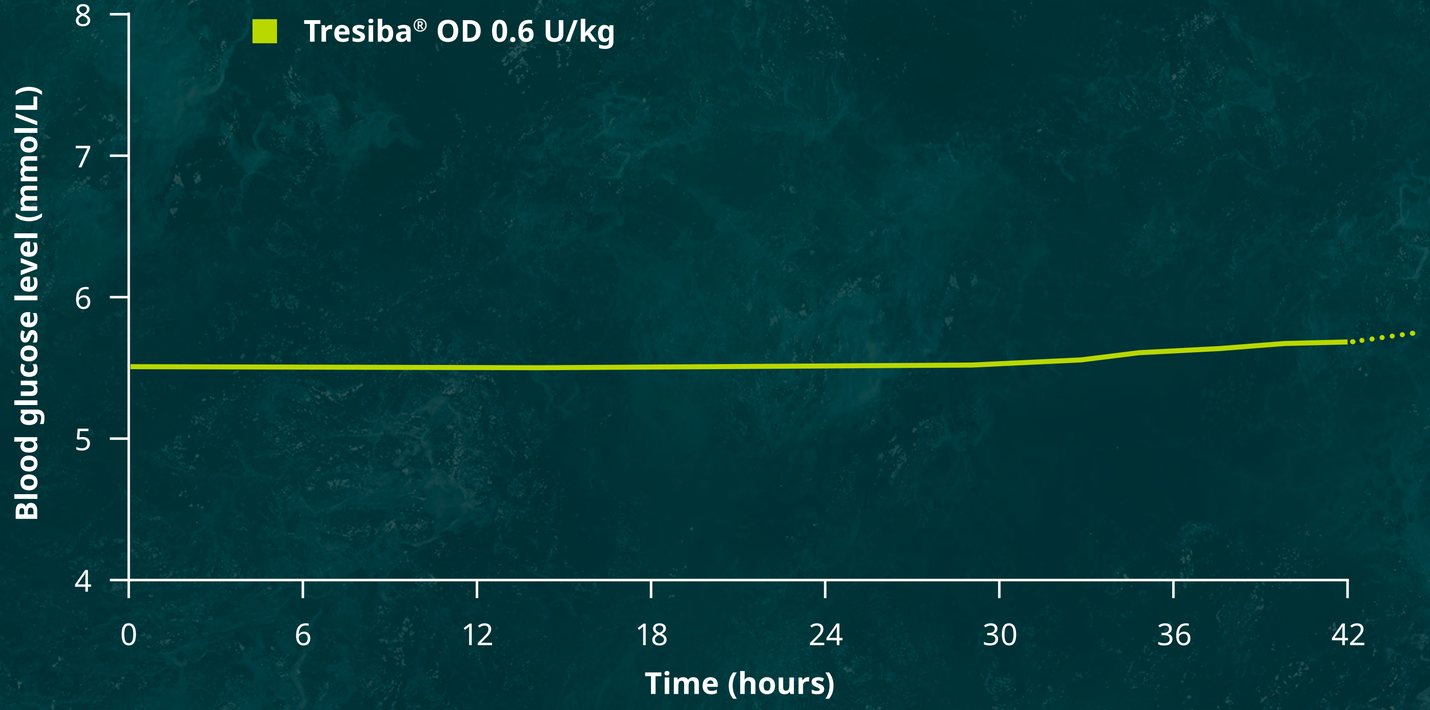
Stroke[11]

Once-daily TRESIBA®:

Day-to-day stability

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]



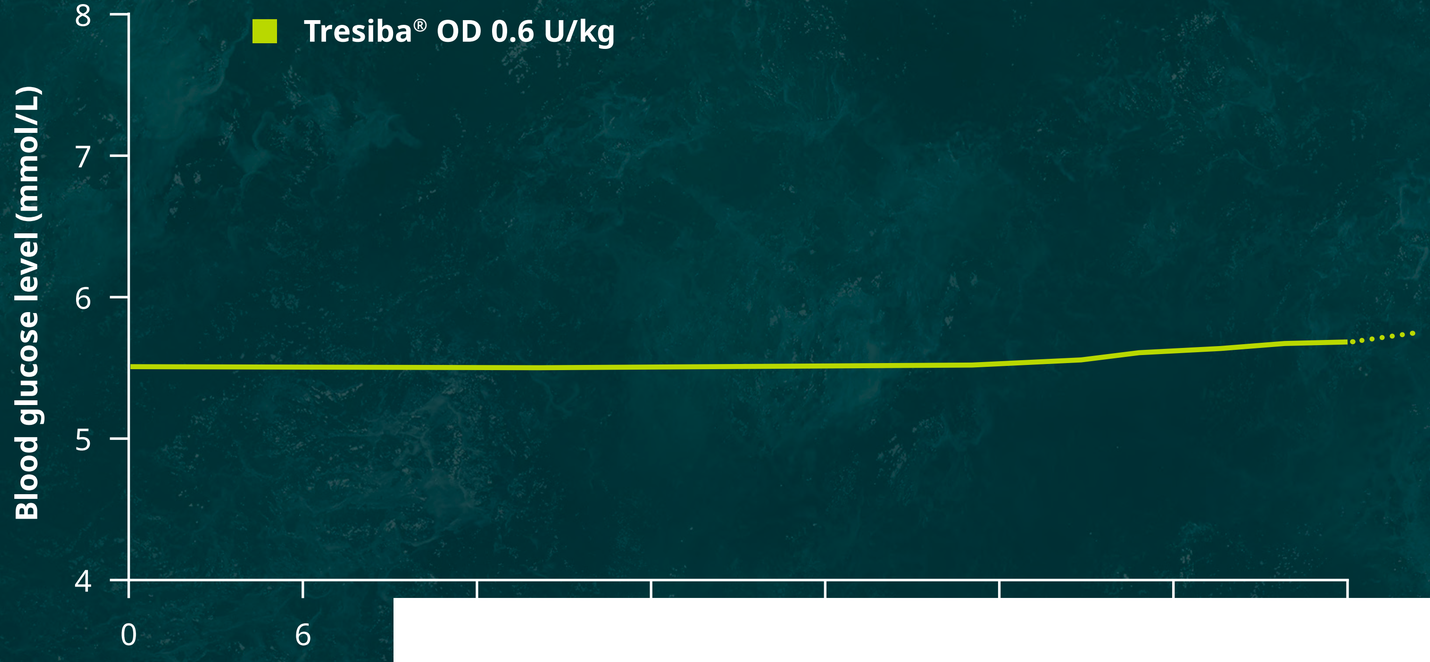
UNIQUE MOLECULE

Once-daily TRESIBA®:

Day-to-day stability

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]



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

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

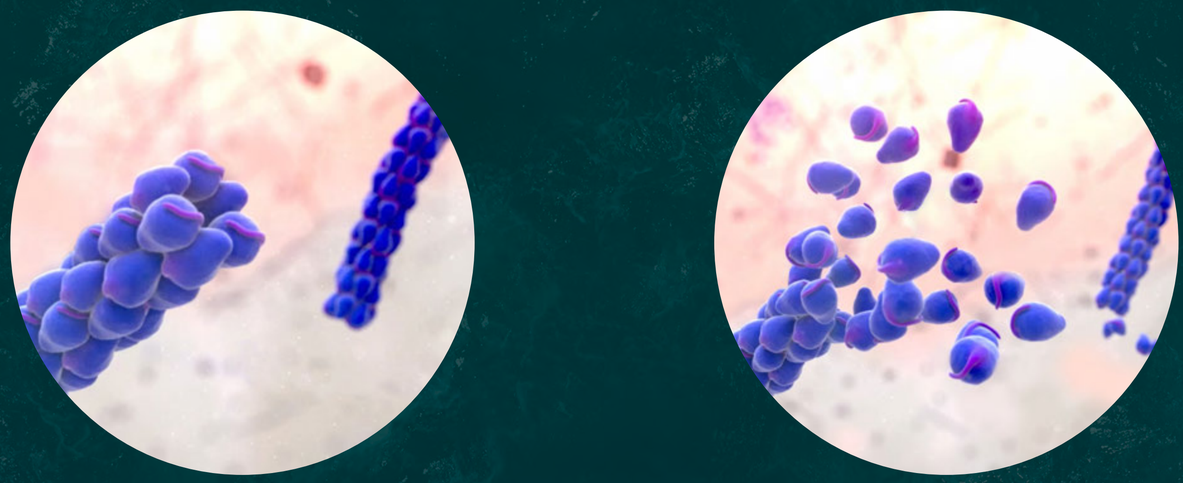
Example patient injection routine.

* 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]

UNIQUE MOLECULE

Benefit from the unique TRESIBA® molecule[12,15]

Slow, consistent release:



Play molecule animation

After injection, Tresiba® molecules bind to form chains[12,13,15]

Individual molecules are then slowly and consistently released into the circulation[12,13,15]

UNIQUE MOLECULE

Getting to goal in the real world[3]

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

↓ **.27%**

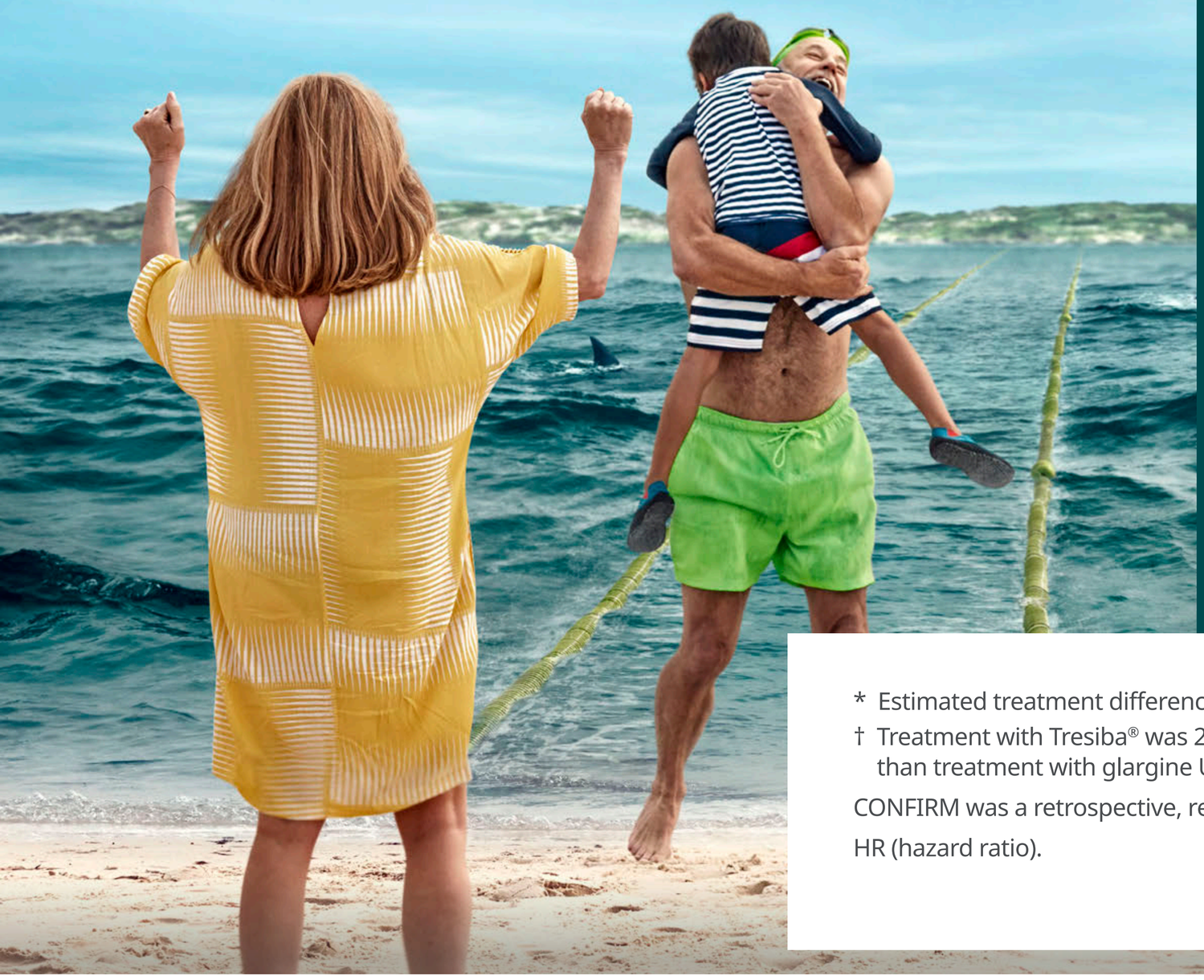
Significantly greater reduction in HbA_{1c} vs glargine U300[3]*

↓ **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)[16]

More than HbA_{1c}

Target TiR

Patients with type 2 diabetes using Tresiba® significantly increased their Time in Range vs glargine U100 in the SWITCH PRO trial[16]*

~21 minutes more **TiR** per day[16†]

= **125 hours** more **TiR** per year with Tresiba®[16†]

Tresiba® significantly reduced nocturnal hypoglycaemic episodes (level 2) vs glargine U100[16‡]

You can significantly increase patients' Time in Range (TiR)[16]

More than HbA_{1c}

Target TiR

Patients with type 2 diabetes using Tresiba® significantly increased their Time in Range vs glargine U100 in the SWITCH PRO trial[16]*

~21 minutes more **TiR** per day[16†] = **125 hours** more **TiR** per year with Tresiba®[16†]

* Insulin-treated patients with type 2 diabetes at increased risk of hypoglycaemia, *p*=0.03.[16]

† Mean TiR was 72.11% Tresiba® vs 70.68% glargine U100, *p*=0.03.[16]

‡ 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.[16]

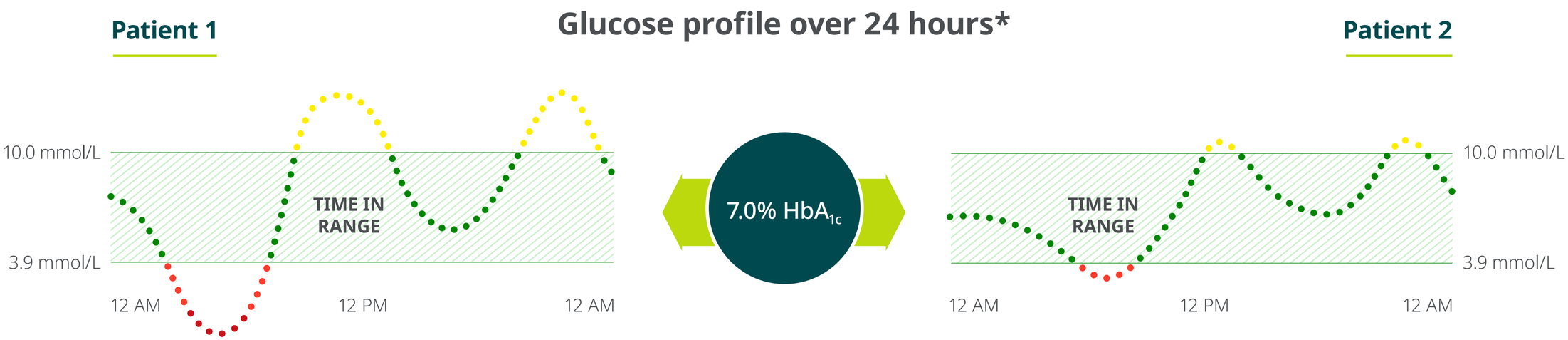
FGM (flash glucose monitoring). TiR (Time in Range).

TRESIBA®
insulin degludec [rDNA origin] injection

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[17]

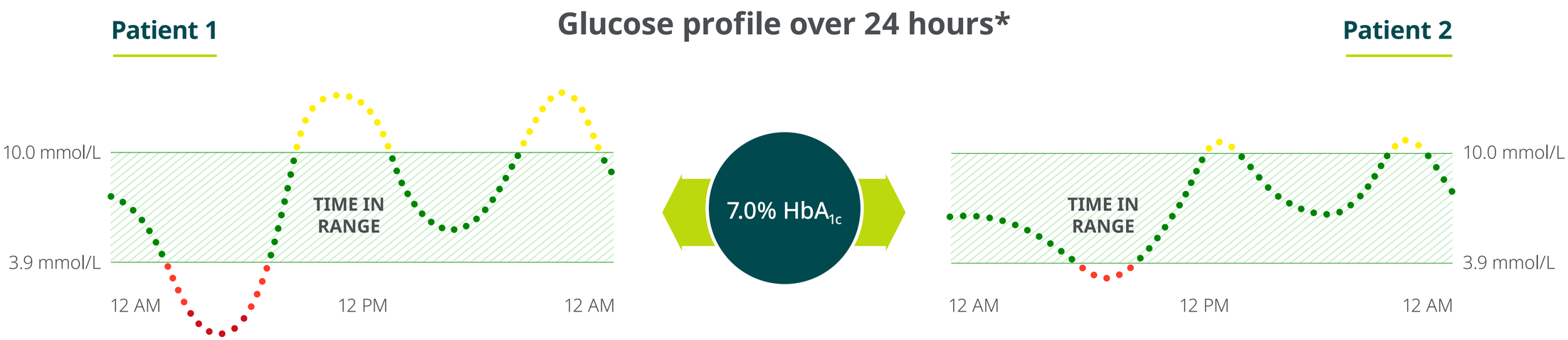


- 36% of patients with type 2 diabetes say having their blood glucose on target all day is the most important factor for a positive frame of mind.[18†]
- More Time in Range means fewer hypos and hypers.[19]

* 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[17]



- 36% of patients with type 2 diabetes say ha
  for a positive frame of mind.[18†]
- More Time in Range means fewer hypos ar

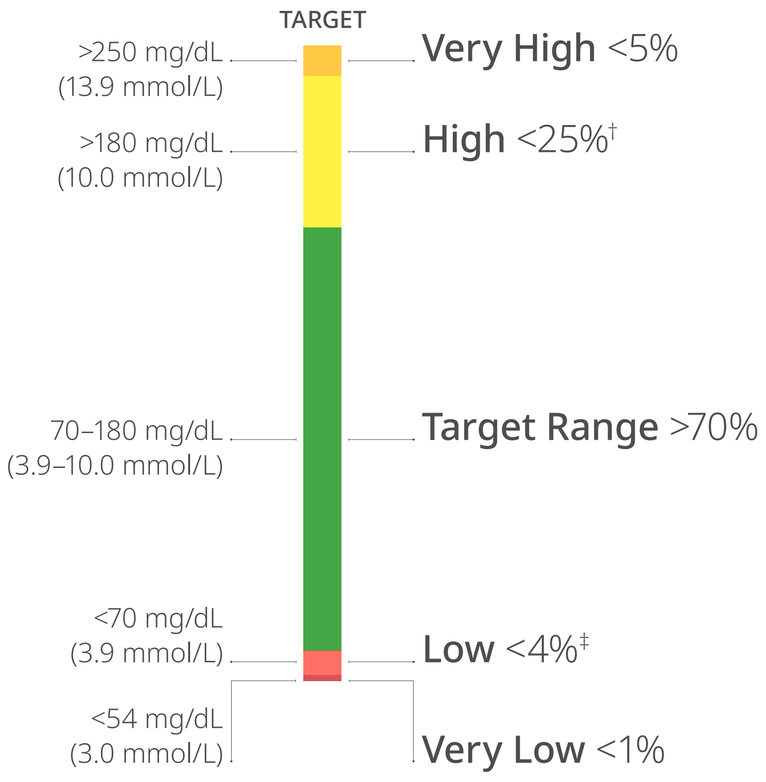
* Diagram is for illustrative purposes only and does not repr

† Patients with type 2 diabetes on insulin (N=1,154).[18]

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

Patients should spend >70% of the day in target glucose range[19]*

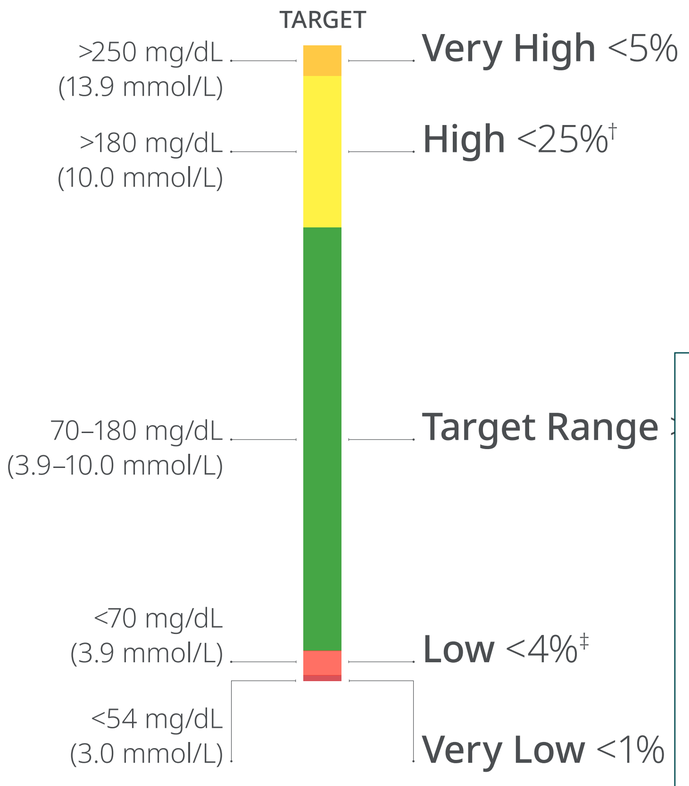
ADA daily time targets for patients with type 2 diabetes[19]*



In real life, patients with type 2 diabetes may spend only 55% of their day in recommended **Time in Range**[20§]

Patients should spend >70% of the day in target glucose range[19]*

ADA daily time targets for patients with type 2 diabetes[19]*



* 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).[19]

† Includes % of values >250 mg/dL (13.9 mmol/L).[19]

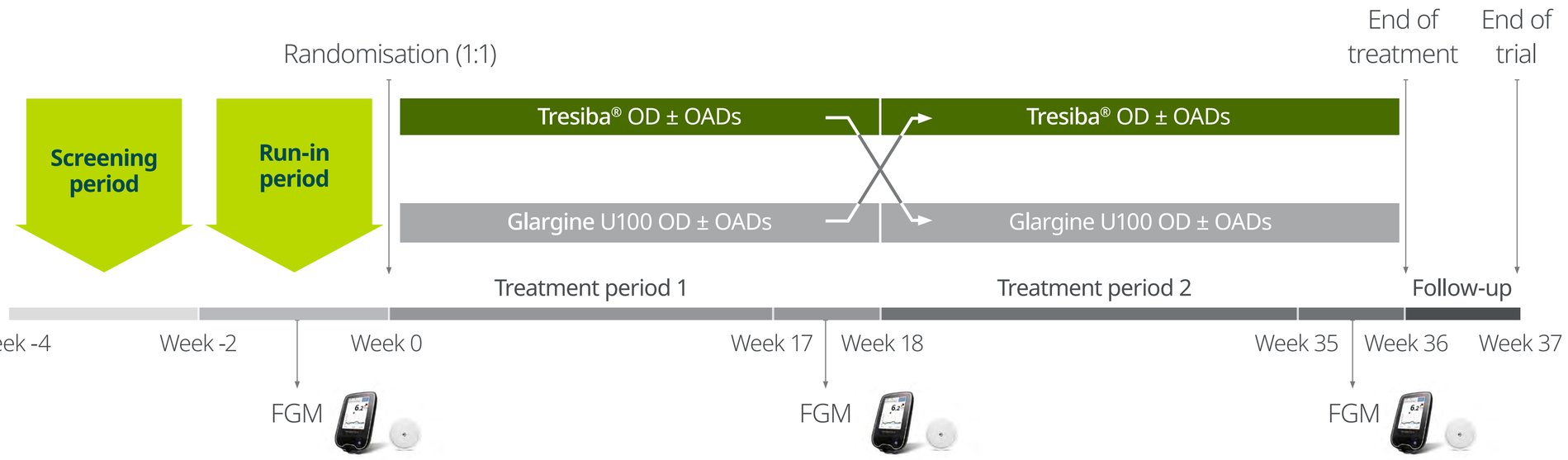
‡ Includes % of values <54 mg/dL (3.0 mmol/L).[19]

§ 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.[20]

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

SWITCH PRO trial design[16]

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

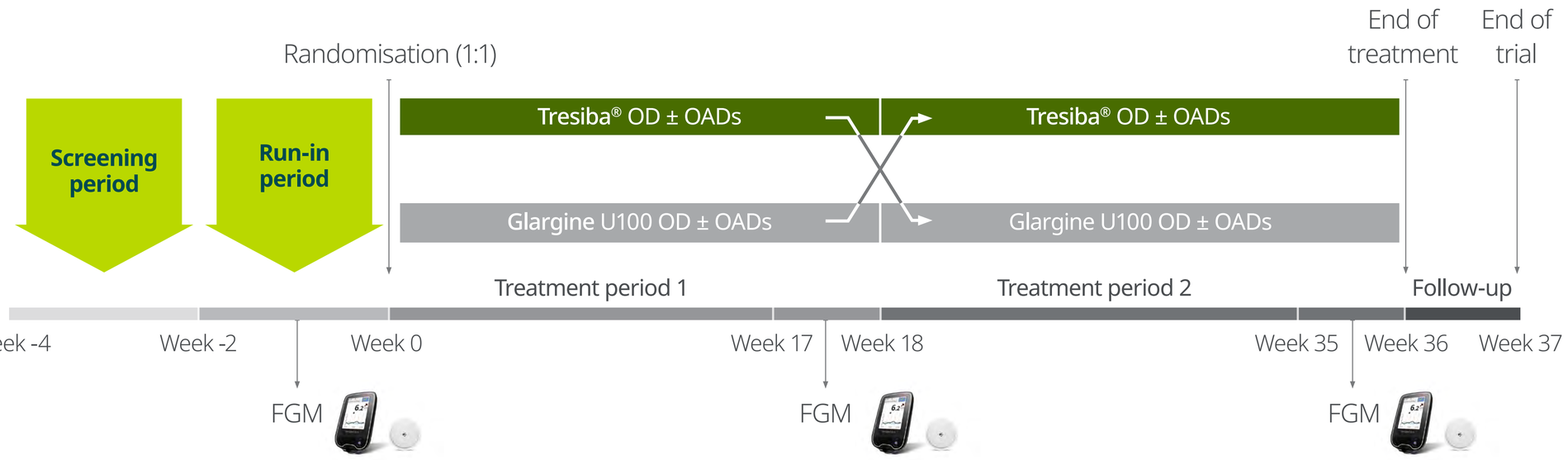
Exploratory endpoints

- 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[16]

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)

Exploratory endpoints

- 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.[16]

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[21]*

Hypos impact patient behaviour[22]

- Reducing insulin dose[22]
- Skipping injections[22]
- Avoiding physical exercise[22]

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[21]*

Hypos impact patient behaviour[22]

- Reducing insulin dose[22]
- Skipping injections[22]
- Avoiding physical exercise[22]

* 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).[21]

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[23†]

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[24‖]

✔ **Without compromising glycaemic control[1-3,23,24]**

Reassurance from consistently few hypos

* Real-world evidence studies.

† (p=0.002).[23]
Data from the extension trial set.[23]
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.[23]

‡ (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]

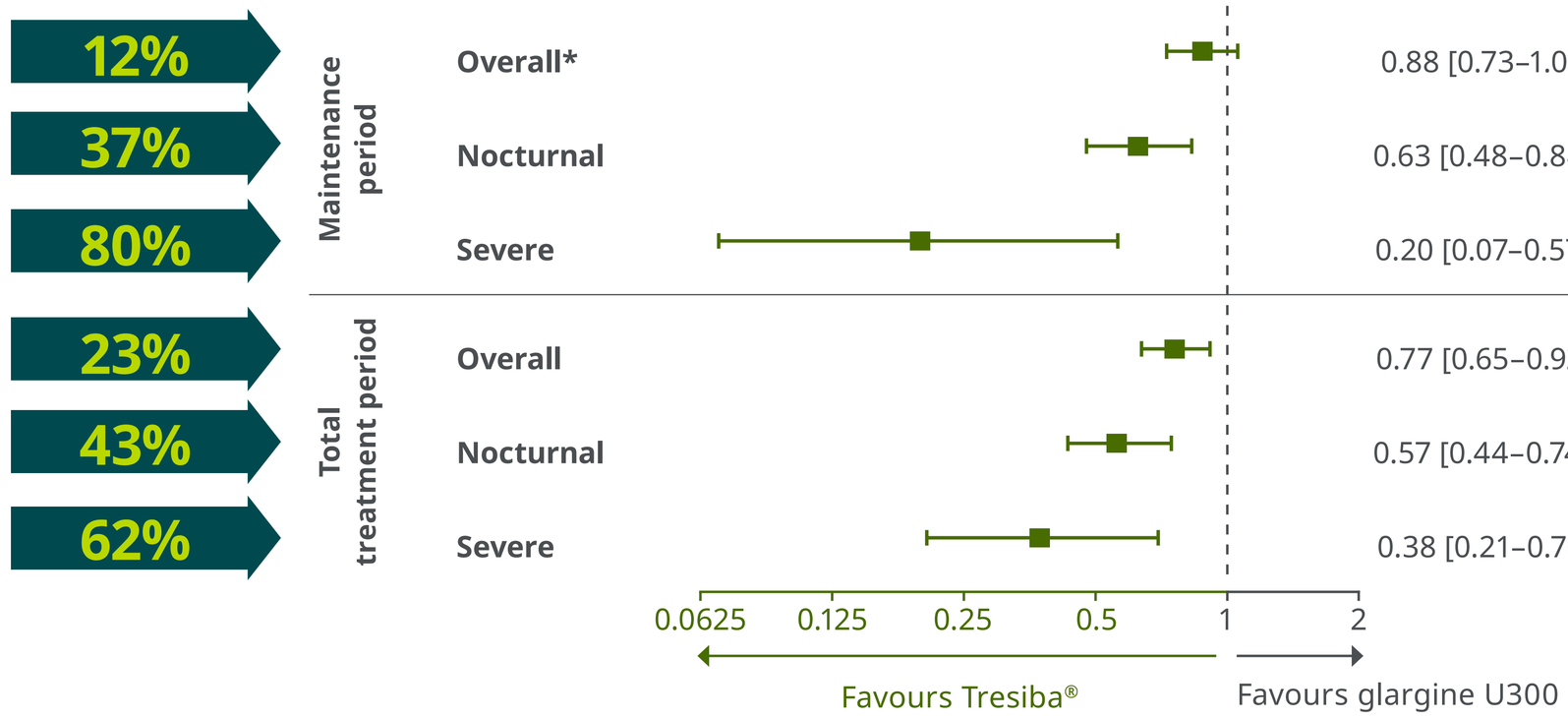
‖ (p<0.001).[24]
ReFLeCT was a prospective, real-world study.[24]
In the ReFLeCT study, in patients with type 2 diabetes, overall hypoglycaemia was defined as any event recorded as hypoglycaemia in patients' diaries irrespective of symptoms, blood glucose or time of day.[24]

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

Based on CONCLUDE, which would you choose?[25]

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).[25]



✔ **Without compromising glycaemic control[25†]**

Based on CONCLUDE, which would you choose?[25]

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).[25]

12%

37%

maintenance period

Rate of hypoglycaemia	Rate ratio [95% CI]
Overall*	0.88 [0.73–1.06]
Nocturnal	0.63 [0.48–0.84]

* Primary endpoint of the study was not met.[25]

† *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).[25]

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.[25]

Secondary endpoints should not be interpreted independently of the primary endpoint.[25]

Overall symptomatic hypoglycaemia was defined as severe or BG-confirmed.[25]

Nocturnal symptomatic hypoglycaemia was defined as severe or BG-confirmed, occurring between the times of 00:01 and 05:59.[25]

Severe hypoglycaemia was defined as an event requiring third-party assistance as per the ADA definition.[25,26]

BG-confirmed events were defined as BG <3.1 mmol/L (<56 mg/dL), with symptoms.[25]

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

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).

CONCLUDE – designed to demonstrate TRESIBA® safety profile[25,26]

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

Trial completers

Glargine U300 ± OADs — **n=706**

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.[25,26]
Overall symptomatic hypoglycaemia was defined as severe or BG-confirmed.[25]
Nocturnal symptomatic hypoglycaemia was defined as severe or BG-confirmed, occurring between the times of 00:01 and 05:59.[25]
Severe hypoglycaemia was defined as an event requiring third-party assistance as per the ADA definition.[25,27]
BG-confirmed events were defined as BG <3.1 mmol/L (<56 mg/dL), with symptoms.[25]
* 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.[25]
† Primary and secondary endpoints related to hypoglycaemia were assessed during the maintenance period.[25]
ADA (American Diabetes Association). BG (blood glucose). OADs (oral anti-diabetic drugs).

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.

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-d
insulin or
glargine U3

Consider

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
?

* 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.[13,28]

† ADA-recommended FPG goal is 4.4–7.2 mmol/L (80–130 mg/dL) for many adults with diabetes.[29]

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

Patient models and examples for illustration only.

TRESIBA® is available in FlexTouch®

Easy to use[30-34]

- **≥85%** of patients rated FlexTouch® easier to use than SoloSTAR®* or KwikPen®[34†]

Confidence in insulin delivery[30-32,35,36]

- **96%** felt confident in managing daily injections with FlexTouch®[36‡]

Preferred by patients[30-32,36]

- **100%** of patients would recommend FlexTouch®[36‡]

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

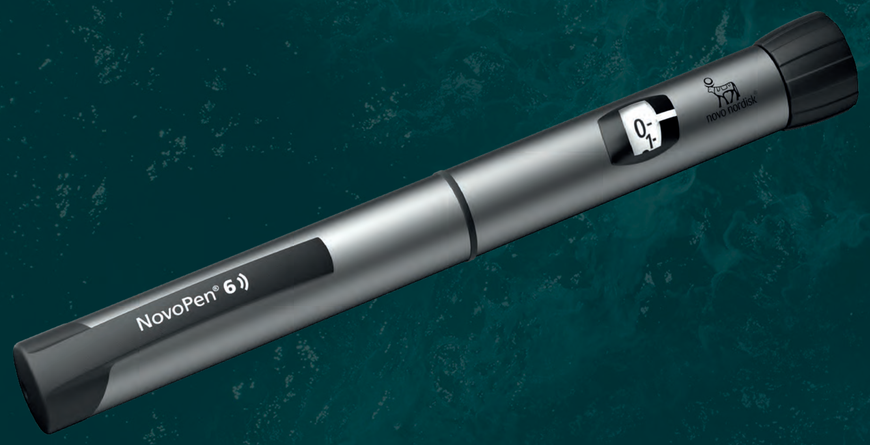
- **Pen delivers the same dose in half the volume of U100[12]**
- **Patients who need higher doses can inject up to 160 units in one injection[12]**
- **2-unit dose adjustments[12]**

* Glargine U100 units/mL. † In two usability studies (n=59) and n=79.[34]
‡ Randomised study, N=222.[36]

Smart ways to use TRESIBA®

NovoPen® 6 | NovoPen Echo® Plus | Dialoq®

NovoPen® 6 can help improve patients' Time in Range (TiR)[37]



~2 hours
more **TiR** every day
after using NovoPen® 6[37]*

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

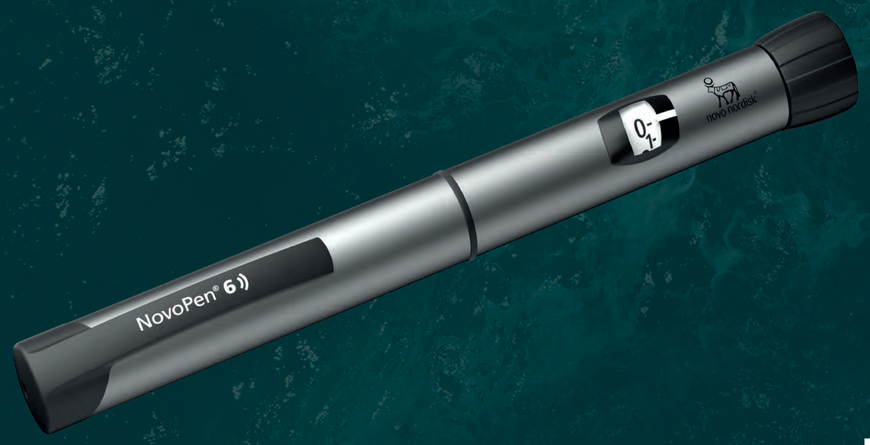
Study subjects not limited to patients using Tresiba.®

NP6 NPE+ Dialoq

Smart ways to use TRESIBA®

NovoPen® 6 | NovoPen Echo® Plus | Dialoq®

NovoPen® 6 can help improve patients' Time in Range (TiR)[37]



~2 hours
more **TiR** every day
after using NovoPen® 6[37]*

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).[37]

† Self-reported diabetes information can often be unreliable.[38] Automatic logging may be more reliable than manual logging.

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

TiR (Time in Range).

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

* 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®

The TRESIBA® label now includes controlled clinical trial data on its use in pregnant women with diabetes*[12]

- **TRESIBA®** is the first and only new-generation basal insulin with evidence from controlled clinical trial data supporting its use in pregnant women with diabetes*[12,39]
- In the **EXPECT** trial, when used in combination with NovoRapid® (insulin aspart) as a mealtime insulin, **TRESIBA®** demonstrated non-inferior HbA_{1C} to insulin detemir† during pregnancy in women with type 1 diabetes[40]
- Pregnancy outcomes and safety profiles for both women with type 1 diabetes and their fetuses/ infants were comparable between insulin degludec and insulin detemir[40]

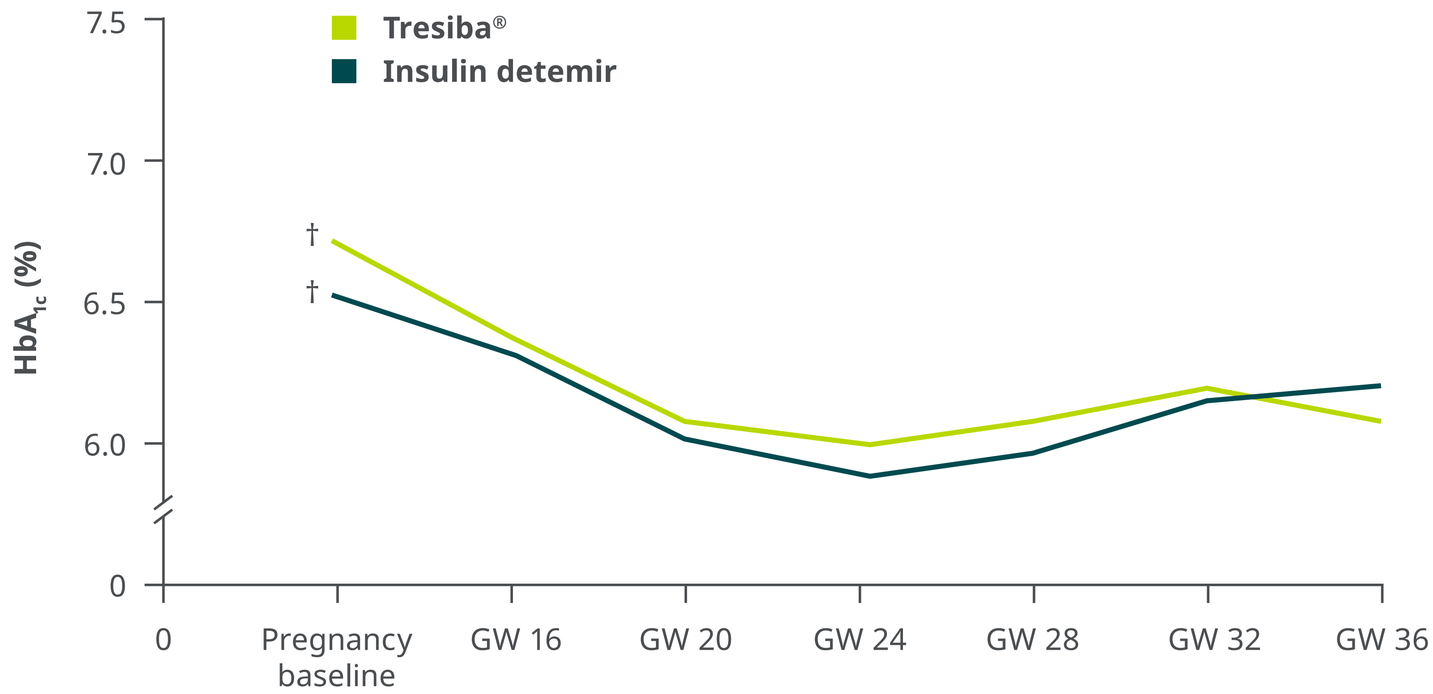
EXPECT results | Study design

The image shown is a model and not a real patient.

* As per, ADA Standards of Medical Care in Diabetes – 2022: Management of Diabetes in Pregnancy: Insulins studied in randomised controlled trials (RCTs) are preferred over those studied in cohort studies, which are preferred over those studied in case reports only[41]

† Levemir® (insulin detemir) in combination with NovoRapid® (insulin aspart) is a well-established treatment that has been widely used in clinical practice and is indicated for use during pregnancy.[42,43]

HbA_{1C} during pregnancy in the EXPECT trial[40]



Safety outcomes[40]

- There was no clinically relevant difference in the risk of hypoglycaemia between treatment groups
- No adverse events led to participant discontinuation in the TRESIBA® treatment group

6.3%

6.2% ETD: –0.11% (95% CI: –0.31, 0.08); **non-inferiority confirmed***

Last planned visit (estimated mean)

* p<0.0001.
† Observed data (pregnancy baseline to GW 36)

CI: confidence interval; ETD: estimated treatment difference; GW: gestational week

aspart) is a well-established treatment that has been widely used in clinical practice and is indicated for use during pregnancy.[42,43]

Study design | Pregnant | Planning to become pregnant

EXPECT study design[40]

EXPECT was a randomised, open-label, parallel-group, multicentre, multinational, treat-to-target, active-controlled trial.

Study aim:

The primary analysis aimed to assess the non-inferiority (margin 0.4%) of TRESIBA® to insulin detemir on the last planned HbA_{1C} measurement before delivery in pregnant women with type 1 diabetes (>16 weeks' gestation) using ANCOVA.

Inclusion criteria:

- ≥18 years of age with type 1 diabetes for ≥1 year
- An HbA_{1C} at screening of ≤8.0% and receiving insulin treatment for ≥90 days
- Pregnant from gestational week 8 to 14 or planning to become pregnant within 52 weeks

Treatment details:

Participants (N=225) were randomised 1:1 to receive either TRESIBA® once daily or insulin detemir once/twice daily, both with insulin aspart, 2–4 times daily with meals.

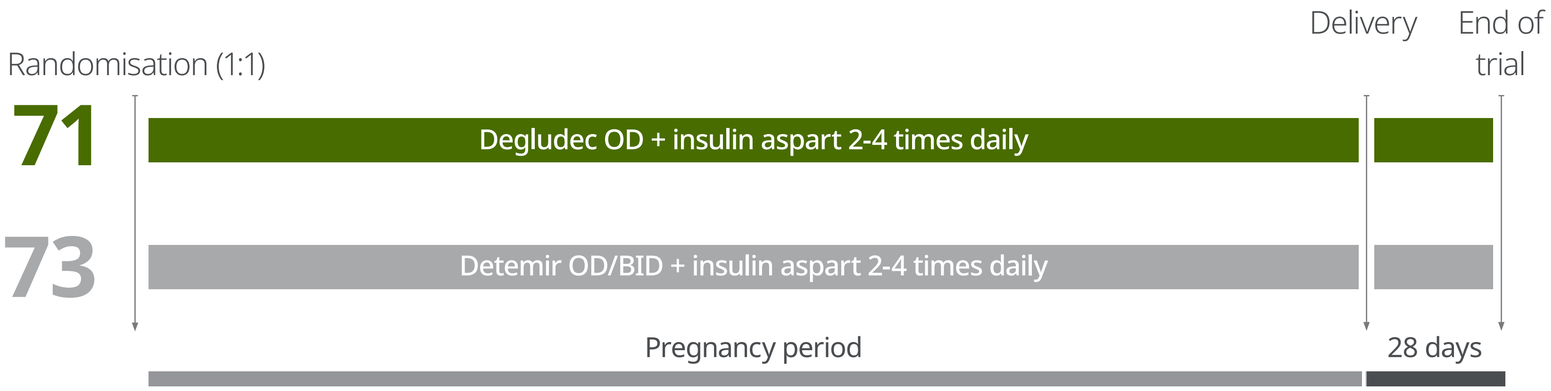
Participants received treatment throughout pregnancy and 28 days after delivery. Non-pregnant women received treatment for up to 52 weeks during the conception period.

During the trial, 188 women (degludec: n=92; detemir: n=96) were pregnant with a singleton fetus.

Study design | Pregnant | Planning to become pregnant

Study participants who were pregnant at randomisation[40]

Pregnant with one living fetus (GW 8 to 14)

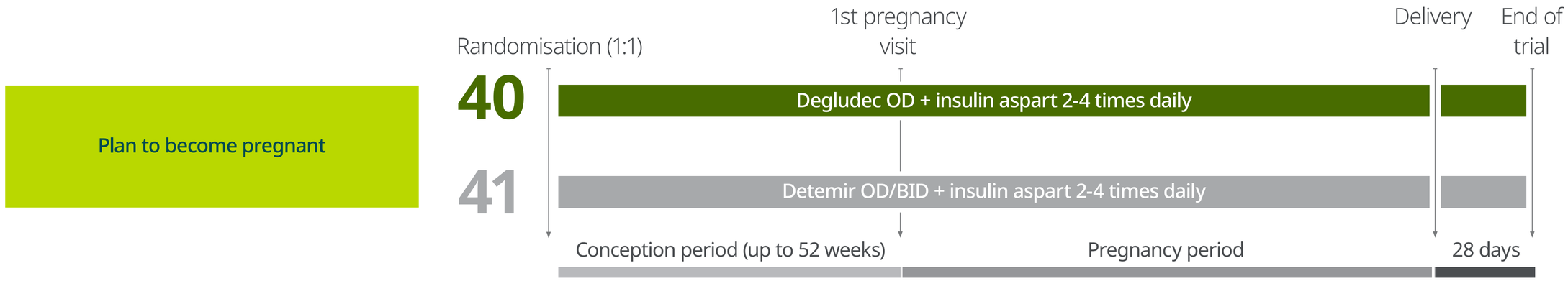


Exclusion criteria:[40]

- Proteinuria (urine protein to creatinine ratio ≥300 mg/g at screening)
- Being treated with IVF or other medical infertility treatment
- Receiving any concomitant medication contraindicated in pregnancy according to local label

aspart) is a well-established treatment that has been widely used in clinical practice and is indicated for use during pregnancy.[42,43]

Study participants who at randomisation were planning to become pregnant[40]



Exclusion criteria:[40]

- Proteinuria (urine protein to creatinine ratio ≥300 mg/g at screening)
- Being treated with IVF or other medical infertility treatment
- Receiving any concomitant medication contraindicated in pregnancy according to local label

aspart) is a well-established treatment that has been widely used in clinical practice and is indicated for use during pregnancy.[42,43]

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[16]

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

To help reassure patients of **few hypos**[1-3,23*]

* Compared with glargine U100 or glargine U300.[1-3,23]

HQ22TSM00023. Approval date: Sept 2022.

References

1. Wysham C, Bhargava A, Chaykin L, de la Rosa R, Handelsman Y, Troelsen L, Kvist K, Norwood P. Effect of insulin degludec vs insulin glargine U100 on hypoglycemia in patients with type 2 diabetes: The SWITCH 2 Randomized Clinical Trial. *JAMA* 2017; 318(1):45–56.
2. Marso SP, McGuire DK, Zinman B, Poulter NR, Emerson SS, Pieber TR, Pratley RE, Haahr P-M, Lange M, Brown-Frandsen K, Moses A, Skibsted S, Kvist K, Buse JB for the DEVOTE Study Group. Efficacy and safety of degludec versus glargine in type 2 diabetes. *New England Journal of Medicine* 2017; 377(8):723–732.
3. Tibaldi J, Hadley-Brown M, Liebl A, Haldrup S, Sandberg V, Wolden ML, Rodbard HW. A comparative effectiveness study of degludec and insulin glargine 300 U/mL in insulin-naïve patients with type 2 diabetes. *Diabetes, Obesity and Metabolism* 2019; 21:1001–1009.
4. Curtis B, Lage MJ. Glycemic control among patients with type 2 diabetes who initiate basal insulin: a retrospective cohort study. *Journal of Medical Economics* 2014; 17(1):21–31.
5. Farsaei S, Radfar M, Heydari Z, Abbasi F, Qorbani M. Insulin adherence in patients with diabetes: risk factors for injection omission. *Primary Care Diabetes*. 2014; 8(4):338–345.
6. Fidler C, Elmelund Christensen T, Gillard S. Hypoglycemia: An overview of fear of hypoglycemia, quality-of-life, and impact on costs. *Journal of Medical Economics*. 2011; 14(5):646–655.
7. Peyrot M, Barnett AH, Meneghini LF, Schumm-Draeger P-M. Insulin adherence behaviours and barriers in the multinational global attitudes of patients and physicians in insulin therapy study. *Diabetic Medicine* 2012; 29(5):682–689.
8. British Geriatric Society. Good Practice Guide. Diabetes. Available at https://www.bgs.org.uk/resources/diabetes Diabetes UK. Facts and Stats. Available at: https://diabetes-resources-production.s3-eu-west-1.amazonaws.com/diabetes-storage/migration/pdf/DiabetesUK_Facts_Stats_Oct16.pdf
9. American Diabetes Association. Microvascular complications and foot care. Sec. 9. In Standards of Medical Care in Diabetes – 2015. *Diabetes Care* 2015; 38(Suppl. 1): S58–S66.
10. Yang Y et al. Diabetes mellitus and risk of falls in older adults: a systematic review and meta-analysis. *Age Ageing*. 2016; 45(6): 761–767.
11. Diabetes UK. Facts and Stats. Available at: www.diabetes-resources-production.s3-eu-west-1.amazonaws.com/diabetes-storage/migration/pdf/DiabetesUK_Facts_Stats_Oct16.pdf
12. Tresiba (Summary of Product Characteristics). Bagsværd, Denmark: Novo Nordisk A/S; January 2022.
13. Haahr H, Heise T. A Review of the Pharmacological Properties of Insulin Degludec and Their Clinical Relevance. *Clinical Pharmacokinetics* 2014; 53(9):787–800.
14. Vora J, Cariou B, Evans M, Gross JL, Harris S, Landstedt-Hallin L, Mithal A, Rodriguez MR, Meneghini L. Clinical use of insulin degludec. *Diabetes Research and Clinical Practice* 2015; 109(1):19–31.
15. Vora J, Heise T. Variability of glucose-lowering effect as a limiting factor in optimizing basal insulin therapy: a review. *Diabetes, Obesity & Metabolism* 2013; 15(8):701–712.
16. Goldenberg RM, Aroda VR, Billings LK, Christiansen ASL, Donatsky AM, Rizi EP, Podgorski G, Raslova K, Klonoff DC, Bergenstal RM. Effect of insulin degludec versus insulin glargine U100 on time in range: SWITCH PRO, a crossover study of basal insulin-treated adults with type 2 diabetes and risk factors for hypoglycaemia. *Diabetes, Obesity and Metabolism* 2021. doi: 10.1111/dom.14504.
17. Siegelaar SE, Holleman F, Hoekstra JBL, DeVries JH. Glucose variability; does it matter? *Endocrine Reviews* 2010; 31(2):171−182.
18. Runge AS, Kennedy L, Brown AS, Dove AE, Levine BJ, Koontz SP, Iyengar VS, Odeh SA, Close KL, Hirsch IB, Wood R. Does Time-in-Range matter? Perspectives from people with diabetes on the success of current therapies and the drivers of improved outcomes. *Clinical Diabetes* 2018; 36(2):112–119.
19. Battelino T, Danne T, Bergenstal RM, Amiel SA, Beck R, Biester T et al. Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations from the International Consensus on Time in Range. *Diabetes Care* 2019; 42(8):1593–1603.

20. Beck RW, Riddlesworth T, Ruedy K, Ahmann A, Haller S, Kruger D, McGill JB, Polonsky W, Price D, Aronoff S, Aronson R, Toschi E, Kollman C, Bergenstal R for the DIAMOND Study Group. Continuous Glucose Monitoring versus usual care in patients with type 2 diabetes receiving multiple daily insulin injections: A randomized trial. *Annals of Internal Medicine* 2017; 167(6):365–374.

21. Khunti K, Alsifri S, Aronson R, Cigrovski Berkovic´ M, Enters-Weijnen C, Forsén T, Galstyan G, Geelhoed-Duijvestijn P, Goldfracht M, Gydesen H, Kapur R, Lalic N, Ludvik B, Moberg E, Pedersen-Bjergaard U, Ramachandran A on behalf of the HAT Investigator Group. Rates and predictors of hypoglycaemia in 27 585 people from 24 countries with insulin-treated type 1 and type 2 diabetes: the global HAT study. *Diabetes, Obesity & Metabolism* 2016; 18(9):907–915.

22. Khunti K, Alsifri S, Aronson R, Cigrovski Berkovic´ M, Enters-Weijnen C, Forsén T, Galstyan G, Geelhoed-Duijvestijn P, Goldfracht M, Gydesen H, Kapur R, Lalic N, Ludvik B, Moberg E, Pedersen-Bjergaard U, Ramachandran A on behalf of the HAT Investigator Group. Impact of hypoglycaemia on patient-reported outcomes from a global, 24-country study of 27,585 people with type 1 and insulin-treated type 2 diabetes. *Diabetes research and clinical practice* 2017; 130:121–129.

23. Rodbard HW, Cariou B, Zinman B, Handelsman Y, Philis-Tsimikas A, Skjøth TV, Rana A, Mathieu C on behalf of the BEGIN Once Long Trial Investigators. Comparison of insulin degludec with insulin glargine in insulin-naive subjects with Type 2 diabetes: a 2-year randomized, treat-to-target trial. *Diabetic Medicine* 2013; 30(11):1298–1304.

24. Fadini GP, Feher M, Hansen TK, de Valk HW, Koefoed MM, Wolden M, Zimmermann E, Jendle J. Switching to degludec from other basal insulins is associated with reduced hypoglycemia rates: a prospective study. *Journal of Clinical Endocrinology and Metabolism* 2019; 104(12):5977–5990.

25. Philis-Tsimikas A, Klonoff DC, Khunti K, Bajaj HS, Leiter LA, Hansen MV, Troelsen LN, Ladelund S, Heller S, Pieber TR on behalf of the CONCLUDE Study Group. Risk of hypoglycaemia with insulin degludec versus insulin glargine U300 in insulin-treated patients with type 2 diabetes: the randomised, head-to-head CONCLUDE trial. *Diabetologia* 2020; 63(4):698–710.

26. Philis-Tsimikas A, Stratton I, Troelsen LN, Bak BA, Leiter LA. Efficacy and safety of degludec compared to glargine 300 units/mL in insulin-experienced patients with type 2 diabetes: trial protocol amendment (NCT03078478). *Journal of Diabetes Science and Technology* 2019; 13(3):498–506.

27. Seaquist ER, Anderson J, Childs B, Cryer P, Dagogo-Jack S, Fish L, Heller SR, Rodriguez H, Rosenzweig J, Vigersky R. Hypoglycemia and diabetes: a report of a workgroup of the American Diabetes Association and the Endocrine Society. *Diabetes Care* 2013; 36:1384–1395.

28. Heise T, Korsatko S, Nosek L, Coester HV, Deller S, Roepstorff C, Segel S, Kapur R, Haahr H, Hompesch M. Steady state is reached within 2–3 days of once-daily administration of degludec, a basal insulin with an ultralong duration of action. *Journal of Diabetes* 2016; 8(1):132–138.

29. American Diabetes Association. Standards of medical care in diabetes–2020. *Diabetes Care* 2020; 43(Suppl. 1):S1–S212.

30. Oyer D, Narendran P, Qvist M, Niemeyer M, Nadeau DA. Ease of use and preference of a new versus widely available prefilled insulin pen assessed by people with diabetes, physicians and nurses. *Expert Opinion on Drug Delivery* 2011; 8(10):1259–1269.

31. Bailey T, Thurman J, Niemeyer M, Schmeisl G. Usability and preference evaluation of a prefilled insulin pen with a novel injection mechanism by people with diabetes and healthcare professionals. *Current Medical Research and Opinio*n 2011; 27(10):2043–2052.

32. Bailey T, Campos C. FlexTouch® for the delivery of insulin: technical attributes and perception among patients and healthcare professionals. *Expert Review of Medical Devices* 2012; 9(3):209–217.

33. Hemmingsen H, Niemeyer M, Hansen MR, Bucher D, Thomsen NB. A prefilled insulin pen with a novel injection mechanism and a lower injection force than other prefilled insulin pens. *Diabetes Technology & Therapeutics* 2011; 13(12):1207–1211.

34. Nadeau D, Campos C, Niemeyer M, Bailey T. Healthcare professional and patient assessment of a new prefilled insulin pen versus two widely available prefilled insulin pens for ease of use, teaching and learning. *Current Medical Research and Opinion* 2012; 28(1):3–13.

35. Wielandt JO, Niemeyer M, Hansen MR, Bucher D, Thomsen NB. FlexTouch: a prefilled insulin pen with a novel injection mechanism with consistent high accuracy at low- (1 U), medium- (40 U), and high- (80 U) dose settings. *Journal of Diabetes Science and Technology* 2011; 5(5):1195–1199.

36. Philis-Tsimikas A, Brod M, Niemeyer M, Ocampo Francisco AM, Rothman J. Insulin degludec once-daily in type 2 diabetes: simple or step-wise titration (BEGIN: once simple use). *Advances in Therapy* 2013; 30(6):607–622.

37. Adolfsson P, Hartvig NV, Kaas A, Møller JB, Hellman J. Increased Time in Range and fewer missed bolus injections after introduction of a smart connected insulin pen. *Diabetes Technology & Therapeutics* 2020; 22(10):709–718.

38. Kalergis M, Nadeau J, Pacaud D, Yared Z, Yale JF. Accuracy and reliability of reporting self-monitoring of blood glucose results in adults with type 1 and type 2 diabetes. *Canadian Journal of Diabetes* 2006; 30(3):241–247.

39. Toujeo® Summary of Product Characteristics, November 2021.

40. Mathiesen ER *et al*. Maternal efficacy, safety, and pregnancy outcomes with degludec versus detemir in the treatment of pregnant women with type 1 diabetes: an international, multicentre, randomised trial. Presented at the European Association for the Study of Diabetes 57th Annual Meeting, 27 September–1 October 2021, Virtual Meeting.

41. American Diabetes Association. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes – 2022. Diabetes Care 2022;45(Suppl. 1):S232–S243.

42. Levemir® Summary of Product Characteristics, April 2021.

43. Levemir Insulin Detemir [rDNA origin] Injection Prescribing information. Available at: LEVEMIR® (insulin detemir injection), for subcutaneous use (fda.gov). August 2022.