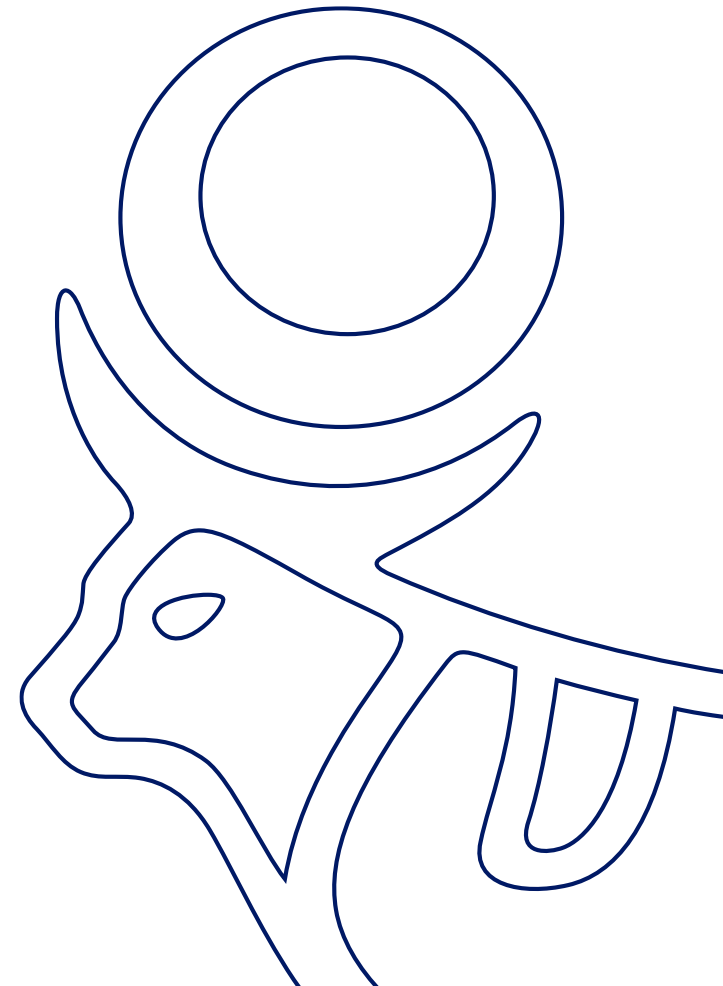


ABC of diabetes management

Treating to fail, fails the patient

Michelle Nel

24 May 2026



Novo Nordisk Disclaimer and Disclosure

- This educational event is funded by Novo Nordisk South Africa as part of their medical education program for healthcare professionals, aiming to foster scientific and clinical knowledge exchange.
- Novo Nordisk advocates for the use of their products strictly as per the approved local guidelines and package insert.

Considerations with insulin therapy: All in an instant

Food¹

Type, amount and timing of meals need to be considered when determining the appropriate insulin regimen

→ *Cultural influences?**

Succeeding on therapy^{3,4}

Timely initiation, rapid titration and appropriate intensification are key to good glycemic control

→ *Titration instructions? Overcoming barriers? Supporting adherence?**

Social determinants and cost⁶

People with limited access to healthcare, or who cannot afford insulin, may struggle to maintain adequate glycemic targets

→ *Are there issues impacting access to medication or administration of medication? Health literacy? Support?**

Physiology²

Insulin therapy aims to mimic the normal physiological response of the body to glucose intake

→ *Insulin-physiology match? Likely requirements? Concomitant medication management?**

Environment^{2,5}

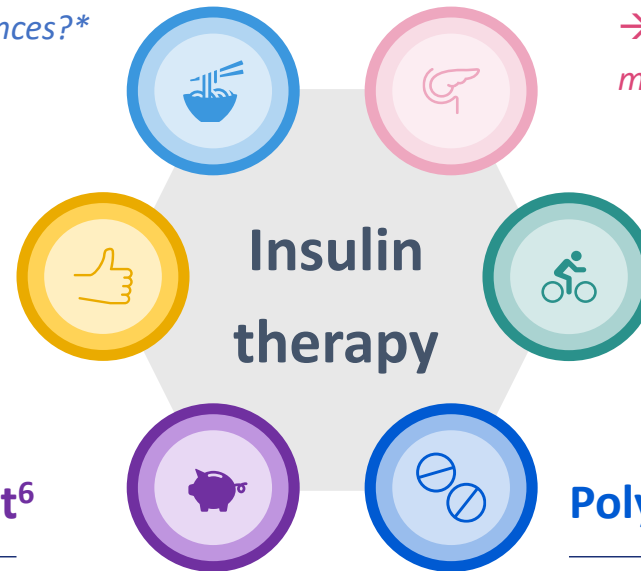
Environmental factors (e.g., physical activity, stress, illness) can affect blood glucose levels and insulin requirements

→ *How will dietary habits and activity level influence insulin requirements?**

Polypharmacy⁷

Concurrent use of other medications for optimal glycemic control is often required. Polypharmacy can increase the risk of drug interactions and adverse effects

→ *How will other medications impact insulin needs and vice versa?**

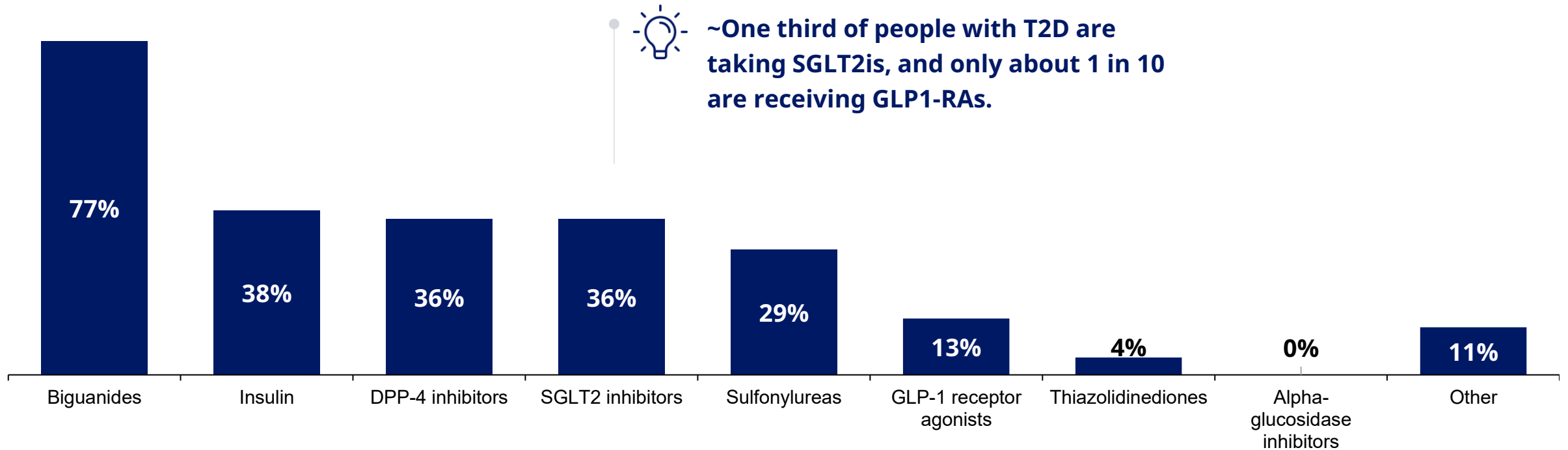


*Based on speaker's clinical experience.

1. Evert AB. Diabetes Spectr 2020;33:149–55; 2. Home PD. Diabetes Obes Metab 2015;17:1011–20; 3. Russell-Jones D et al. Diabetes Obes Metab 2018;20:488–96; 4. Swinnen SG et al. Diabetes Care 2009;32(Suppl 2):S253–9; 5. American Diabetes Association. Clin Diabetes 2018;36:202; 6. Zgibor JC, Songer TJ. Diabetes Spectr 2001;14:23–28; 7. Hoel RW et al. Mayo Clin Proc 2021;96:242–56.

Medication Data

Percentage of patients (N=3726) on glucose-lowering therapies



Medication Data

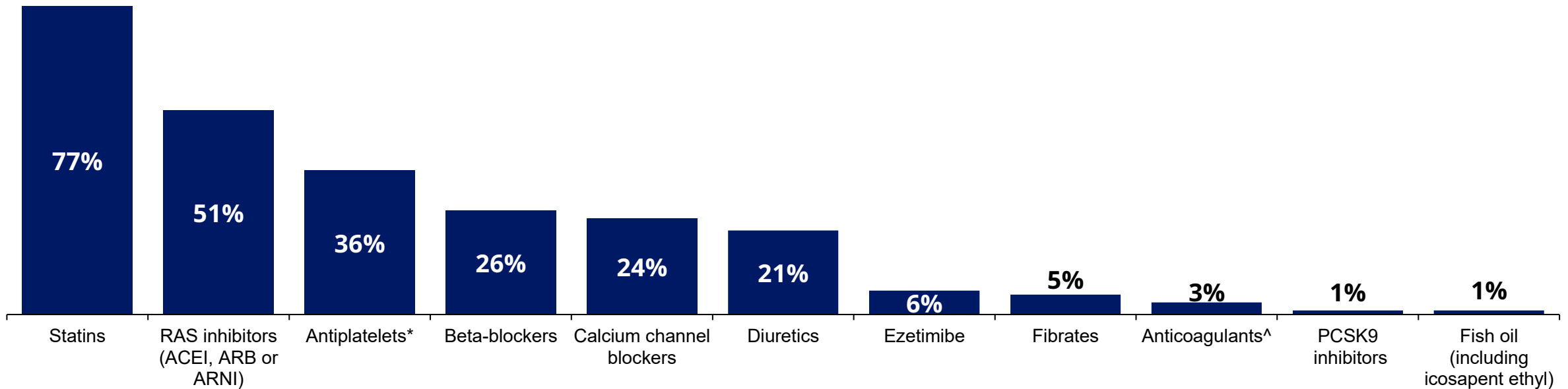
Percentage of patients (N=3726) on cardiovascular therapies

Statin therapy‡

Low intensity	2%
Moderate intensity	63%
High intensity	35%



Although most people with T2D are on statins, only about one-third are receiving high-intensity statins.



**BAMEAC
PACT-MEA**

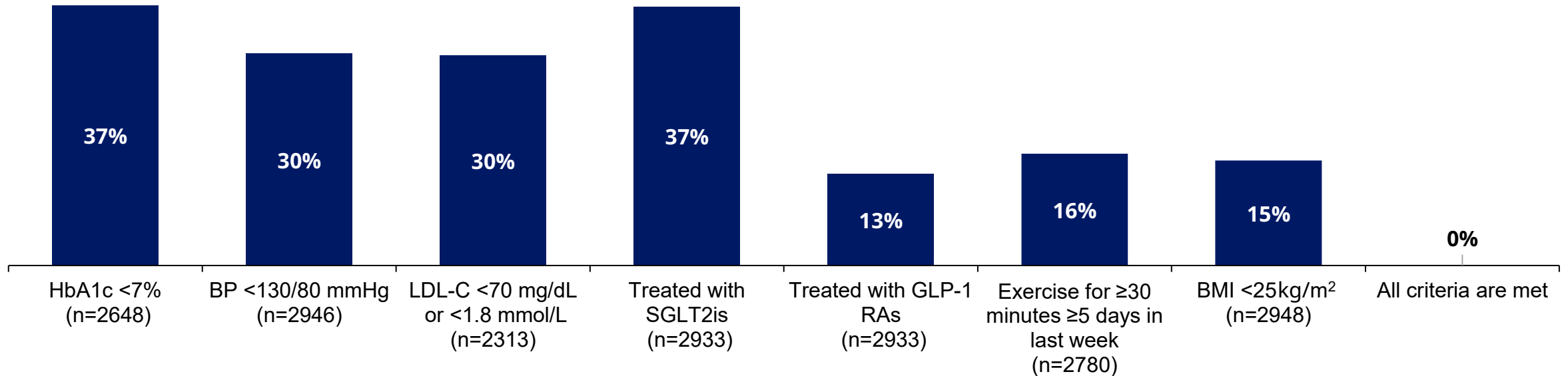
*Antiplatelet therapies include acetylsalicylic acid, clopidogrel, ticagrelor, prasugrel. ^Anticoagulant therapies include apixaban, rivaroxaban, edoxaban, dabigatran, warfarin. ‡Low intensity: lowers LDL-C by <30%, moderate intensity: lowers LDL-C by 30%-49%, high intensity: lowers LDL-C by ≥50%. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; LDL-C, low-density lipoprotein cholesterol; PCSK9, proprotein convertase subtilisin/kexin type 9; T2D, type 2 diabetes

Achievement of ESC 2021 guideline-recommended targets for risk factors by people with T2D at high/very high risk*

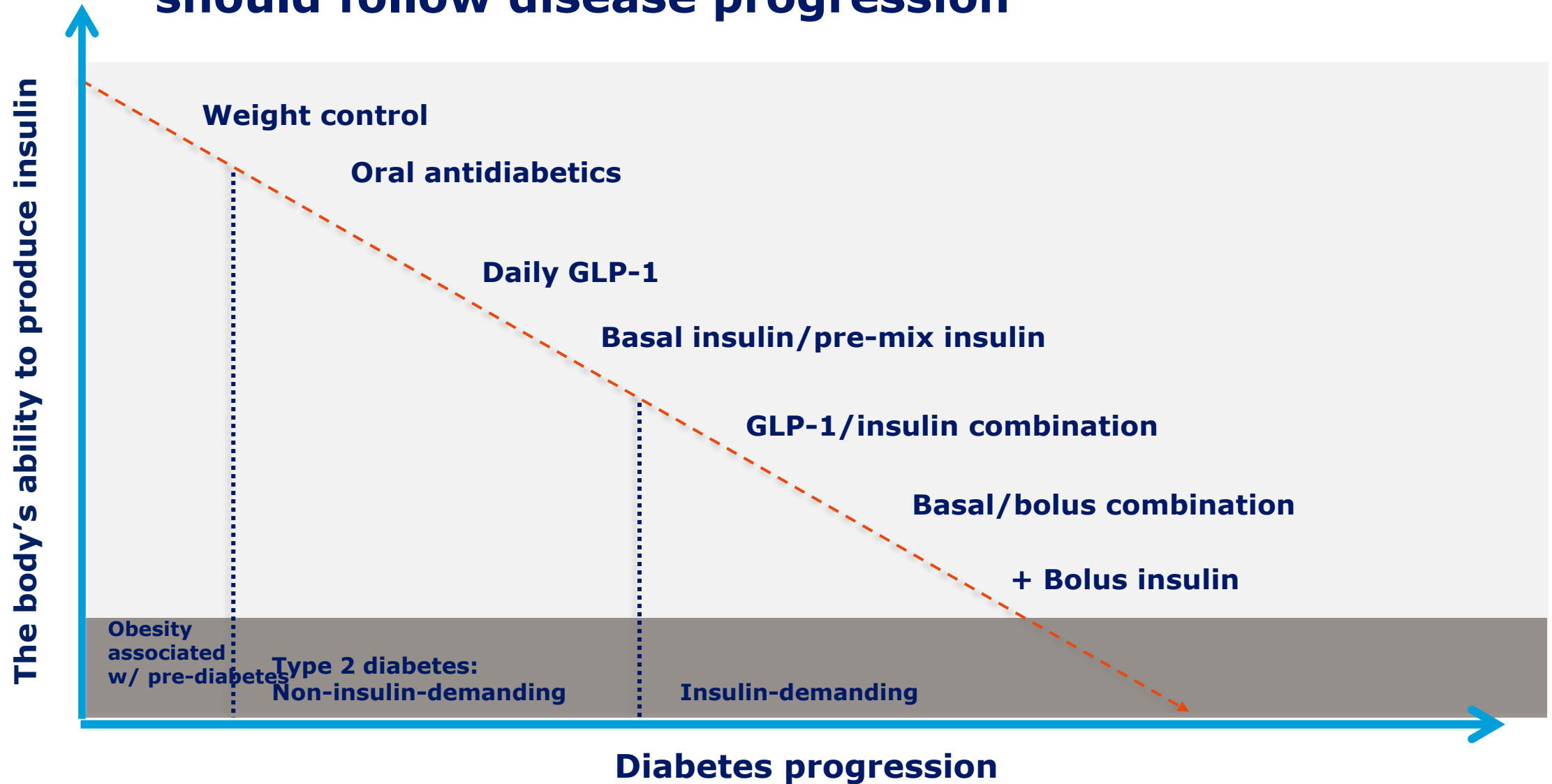


Fewer than 4 in 10 people with T2D achieved any one of the risk factor targets

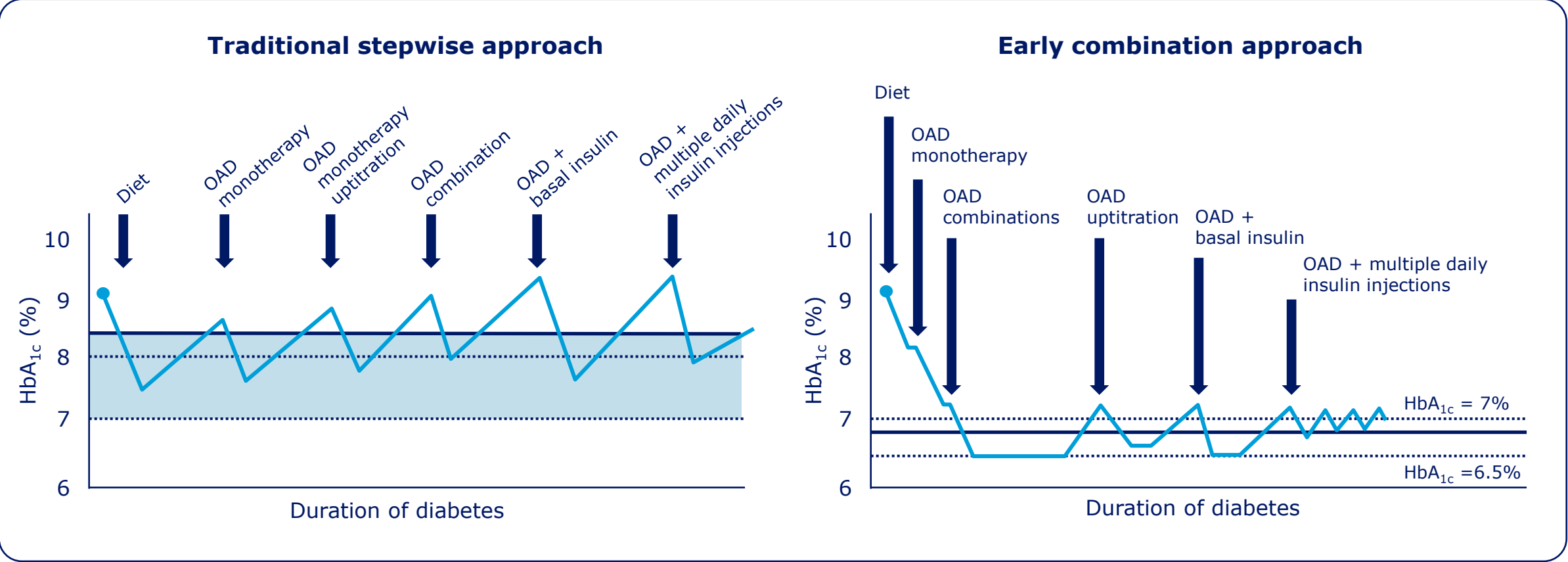
No patients met targets for all risk factors



Insulin initiation, optimisation and intensification should follow disease progression



Conventional treat-at-failure versus early intensive treatment as approaches to T2D management



OAD, oral anti-hyperglycaemic drug. Campbell IW. *Br J Cardiol.* 2000;7(10):625-631; Del Prato S, et al. *Int J Clin Pract.* 2005;59:1345-1355.

Glycaemic control matters



The importance of HbA_{1c} <7%

Reduces diabetes-related complications¹

HbA_{1c} <7% results in:



Reduced microvascular complications



Reduced long-term CVD rates if implemented in newly diagnosed patients



Reduction in diabetes-related mortality

Reduces total diabetes-related costs²

HbA_{1c} ≤7% continuously for 1 year results in . . .

Diabetes-related treatment costs

25%

. . . compared with patients above target HbA_{1c} ≤7%

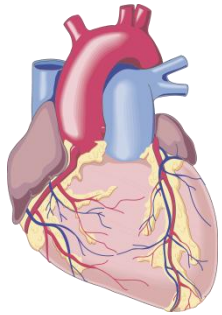
Which included:

- ✓ 22% lower diabetes medical costs
- ✓ 28% lower diabetes pharmacy costs

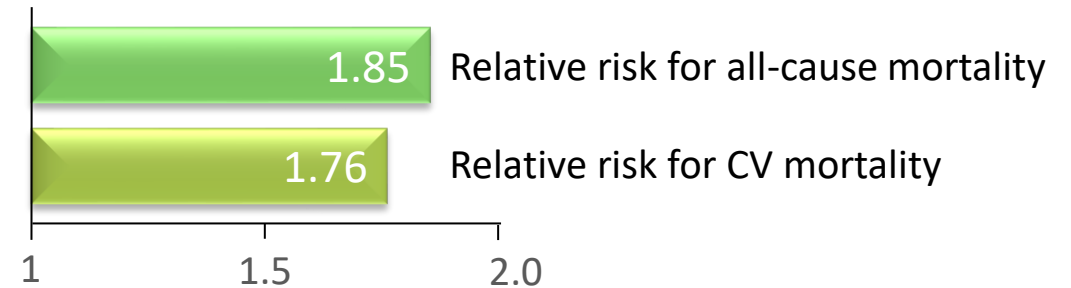
More than half of T2D patients on basal insulin are not at target HbA_{1c}³



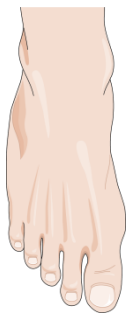
Morbidity and mortality in patients with T2DM



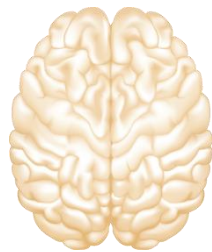
Patients with T2DM have double the risk of CV disease
Up to 75% will succumb to a cardiac related event
Heart disease by 2–4 fold²



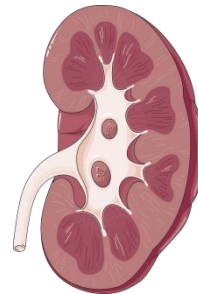
In the next 24 hours, 17,280 patients will develop diabetes...



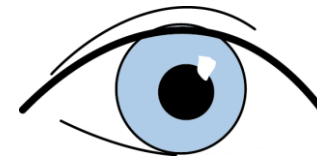
186 new patients will have an amputation²



Stroke by more than 2–4 fold²



40% of global diabetic have some degree of CKD
137 new patients will need dialysis²



62 new patients will have severe vision loss due to diabetes²



20 million people will suffer with DPN tonight³

How Well are we Doing Locally ?

211 patients with Diabetes¹

Beginning of Study

Average HbA1c 9.7%
13 % at Target (<7%)

End of Study

Average HbA1c 8.4%
30% at Target (< 7%)

261 patients with T2DM at CMJAH⁴

Average HbA1c 8.7%

15.5% at Target

599 diabetic patients from 12 PHCs in the Tshwane district (Gauteng, South Africa)²

The mean Hba1c was 8.68 %

Tertiary Referral Centre in Jhb (Only receives poorly controlled patients with T2DM)³

321 consecutive patients

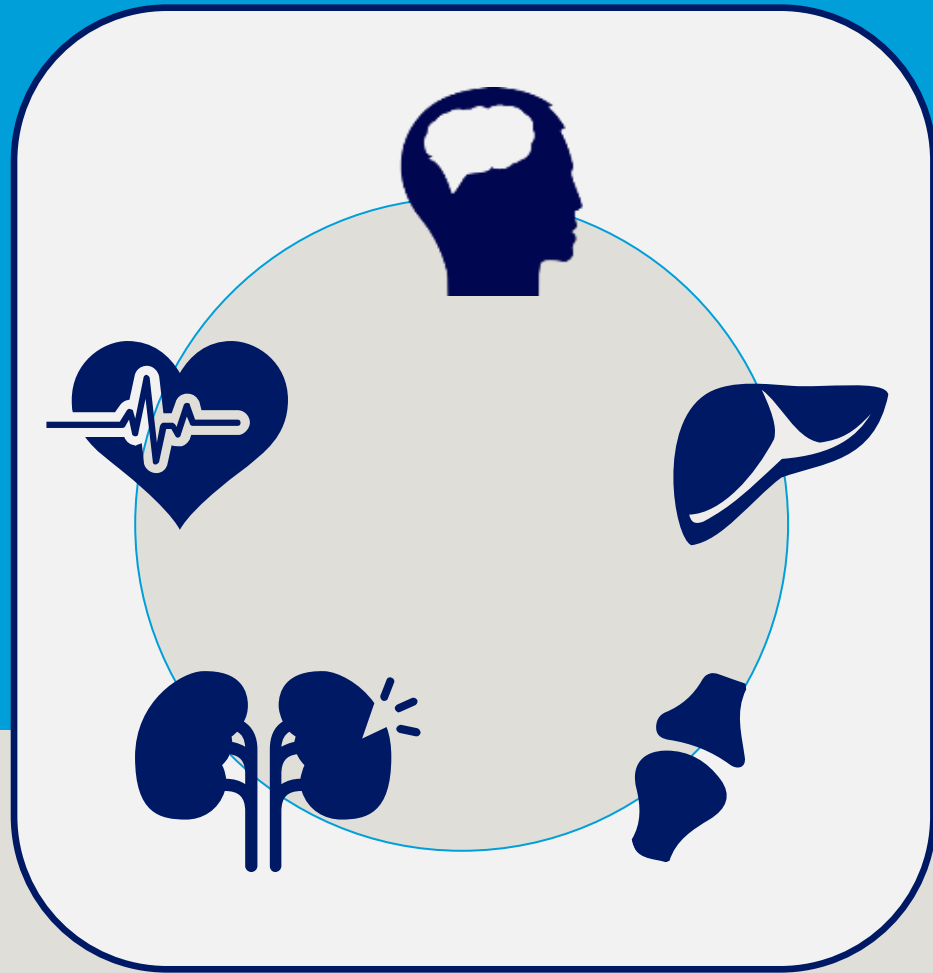
Average HbA1c 9.5%
15.3% at Target

1. Lara A. Motta, Mark D.S. Shephard, Julie Brink, Stefan Lawson, Paul Rheeder. *Primary Care Diabetes*. June 2017, Volume 11, Issue 3, Pages 248–253

4. Pinchevsky Y, Shukla V, Butlow N, Raal F. J, Chirwa T. *JEMDSA*. 20(2):81–6..

2. E Webb, P Rheeder. *Primary Care Diabetes*. December 2017, Volume 11, Issue 6, Pages 546–554

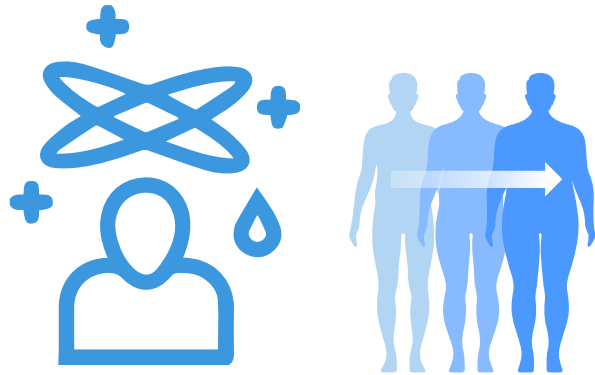
3. Bulbulia S, Bayat Z (Unpublished Data – submitted for publication)



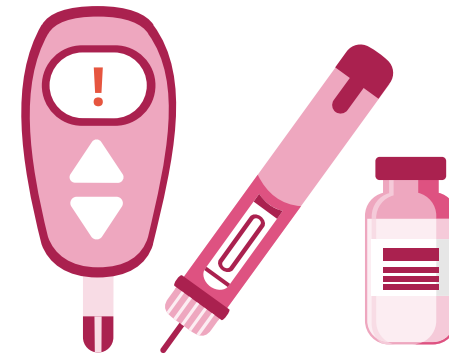
**Simplicity of
treatment improves
outcomes**

There are barriers to treatment intensification with insulin in T2D

Barriers to T2D treatment intensification with insulin include concerns about hypoglycaemia, weight gain and increasing complexity of treatment regimens.



Fear of **hypoglycaemia** and **weight gain** discourages up to **50%** of people with T2D from insulin intensification¹⁻³



Patients and physicians identify **complexity of treatment** and **fear of injections** as a burden^{1,4}

T2D, type 2 diabetes.

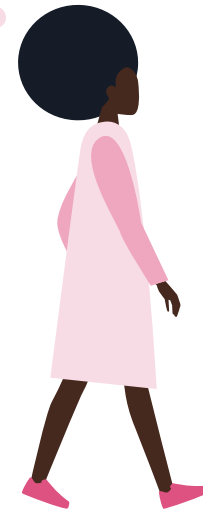
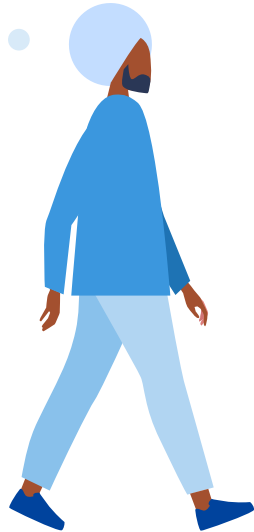
1. Peyrot M et al. *Diabet Med*. 2012;29:682-689; 2. Carver C. *Diabetes Educ*. 2006;32:910-7; 3. Sir George A. *The DAWN (Diabetes Attitudes, Wishes and Needs) study*. *Practical Diabetes International*. 2002;19:22-24a; 4. Wunna W, et al. *Postgrad Med J* 2020;97:384-90

Combination therapy may help overcome the barriers to treatment in T2D

Fewer injections

Fewer SMBG measurements

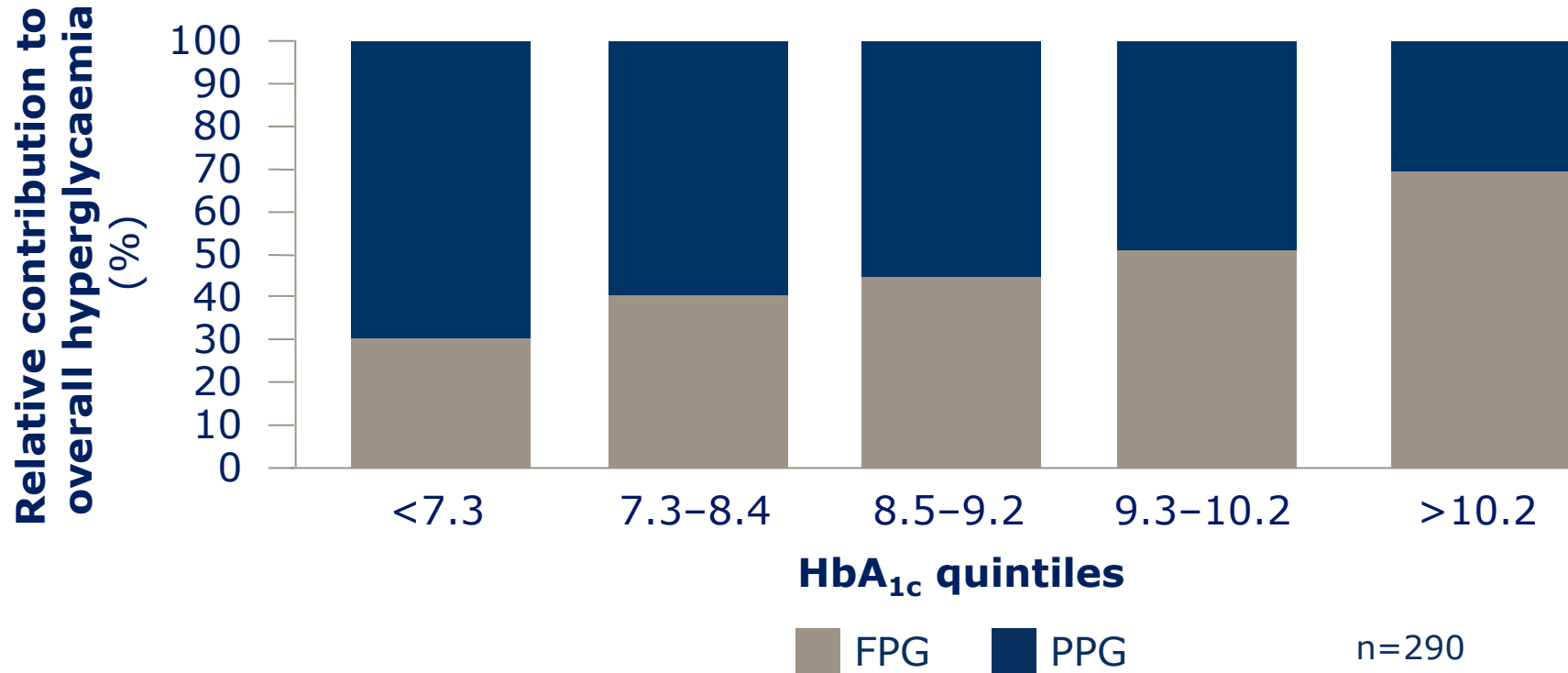
Less complex dosing schedule



Combination therapy has the potential to improve adherence and persistence¹

PPG control is vital to achieving HbA_{1c} targets¹

At every level of HbA_{1c}, PPG contributes to hyperglycaemia



- PPG has an increasing contribution to overall hyperglycaemia as patients approach HbA_{1c} targets
- **Postprandial hyperglycaemia is an independent risk factor for cardiovascular disease**
- **Postprandial hyperglycaemia is associated with:**
 - Macrovascular disease and retinopathy
 - Oxidative stress, inflammation and endothelial dysfunction

1. Adapted from Monnier et al. Diabetes Care 2003;26:881-5.

1. Ceriello et al. 2011 Guideline for Management of PostMeal Glucose in Diabetes. Available at: http://www.idf.org/webdata/docs/Guideline_PMG_final.pdf (accessed May 2013)

Efficacy, Safety and Flexibility

IDegAsp provides:



Similar glycaemic control among all the trials:



Lower insulin dose



Reduction in nocturnal, overall & severe hypoglycaemia vs. comparators

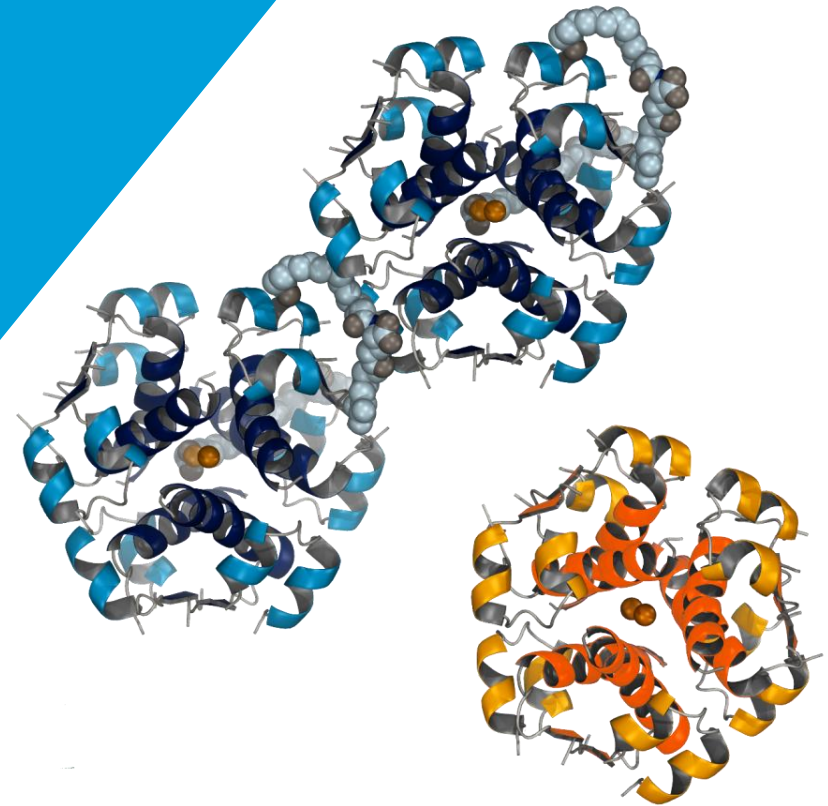
FPG and PPG control achieved with flexible dosing at the main meals

Simple intensification option and flexibility in dose timing vs. basal bolus

Comparators: BIAsp 30 (start twice daily, Intensify Premix I and ALL, China, Ramadan); Insulin degludec OD + IAsp (twice daily vs. basal bolus); IDet (BOOST T1); IGlax U100 + IAsp (step-by-step trial)

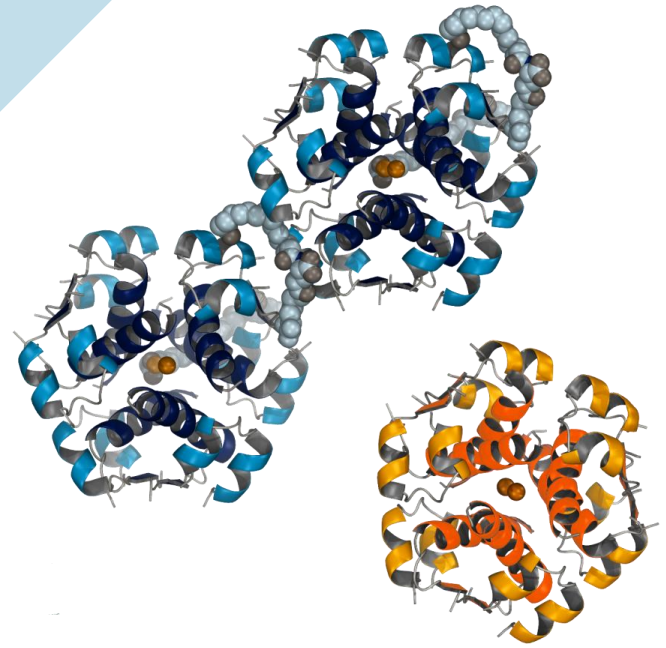
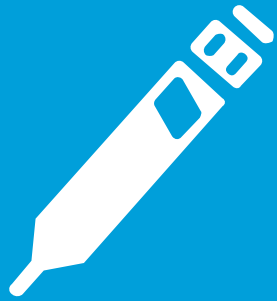
BIAsp, biphasic insulin aspart; BID, twice daily; FPG, fasting plasma glucose; IDegAsp, insulin degludec/insulin aspart; IDet, insulin detemir; IGlax U100, insulin glargine U100; OD, once daily; PPG, post prandial glucose; T2D, type 2 diabetes

Insulin degludec/ insulin aspart (IDegAsp)



Insulin-naïve T2D OD

BOOST JAPAN



Insulin-naïve T2D OD: study design

BOOST JAPAN



Inclusion criteria

- Type 2 diabetes ≥ 6 months
- Previously treated with ≥ 1 OAD for at least 12 weeks with at least recommended maintenance dose per local labelling
- HbA_{1c} 7.0–10.0%
- BMI ≤ 35 kg/m²
- Age ≥ 20 years

- Open-label
- Prior to randomisation, SUs, DPP-4 inhibitors and glinides were discontinued
- IDegAsp was administered with the largest meal of the day; the dosing time was chosen at the discretion of the patient*
- IGLar U100 was administered according to label (either before breakfast or at bedtime) at the discretion of the patient*

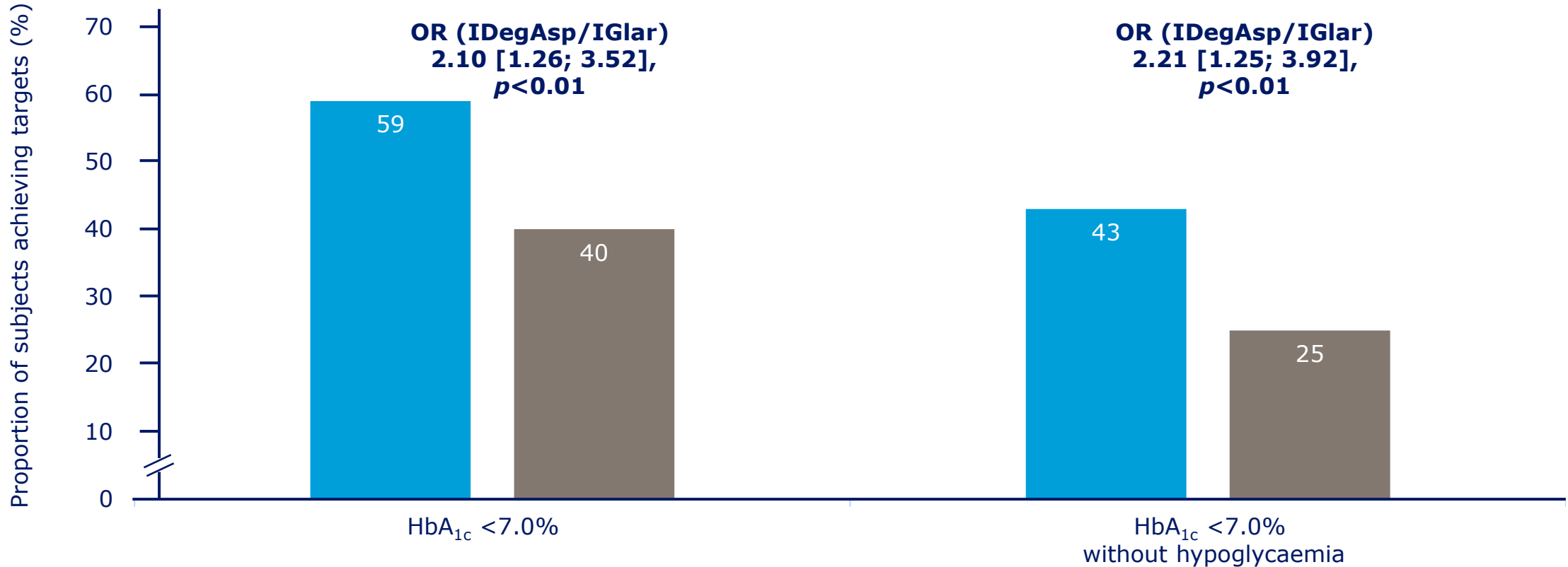
*Starting dose was 10U

BMI, body mass index; DPP-4, dipeptidyl peptidase 4; IDegAsp, insulin degludec/insulin aspart; IGLar U100, insulin glargine U100; OAD, oral antidiabetic drug; OD, once daily; SU, sulphonylurea; T2D, type 2 diabetes; U, units
Onishi *et al. Diabetes Obes Metab* 2013;15:826–32



Subjects achieving treatment targets

■ IDegAsp OD ■ IGlAr U100 OD



A significantly higher proportion of patients achieved a glycaemic target of HbA_{1c} < 7% which is two times higher with IDegAsp than with IGlAr U100

Conclusions

BOOST JAPAN

Week 26

IDegAsp

VS

**IGlar
U100**

HbA_{1c}

Superiority confirmed*

Total daily insulin dose

**Similar
(NS)**

Confirmed hypoglycaemia

**27% lower with IDegAsp
(NS)**

**Nocturnal-confirmed
hypoglycaemia**

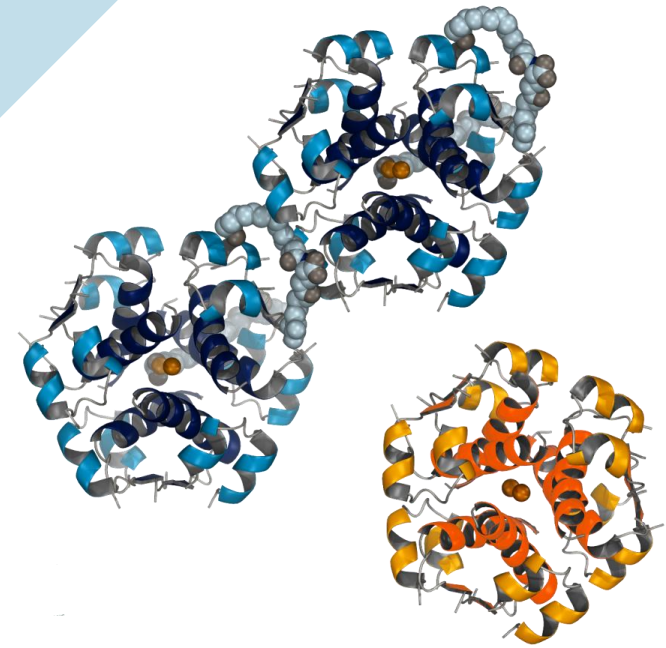
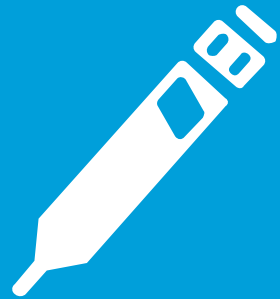
**25% lower with IDegAsp
(NS)**

* $p < 0.01$

IDegAsp, insulin degludec/insulin aspart; IGLar U100, insulin glargine U100; NS, not significant
Onishi *et al. Diabetes Obes Metab* 2013;15:826–32

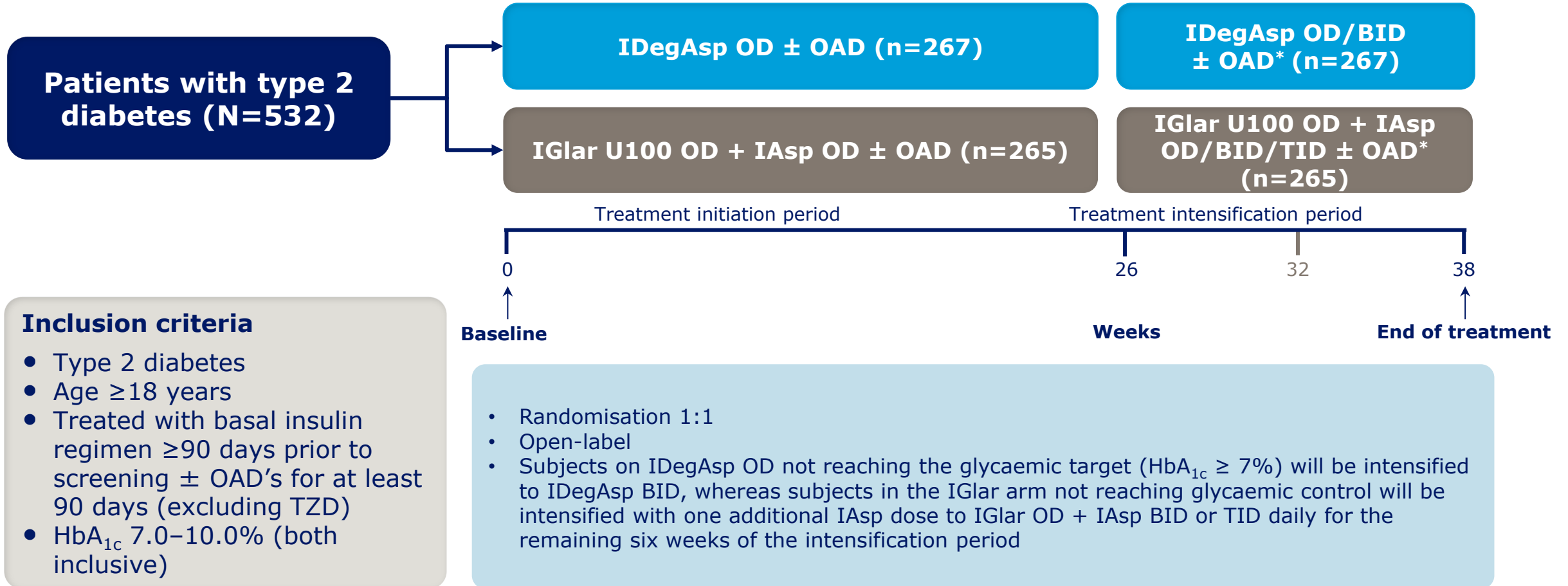


Insulin-experienced T2D OD/BID IDegAsp Step-by-Step Intensification Trial



Insulin-experienced T2D OD/BID: study design

IDegAsp Step-by-Step Intensification Trial

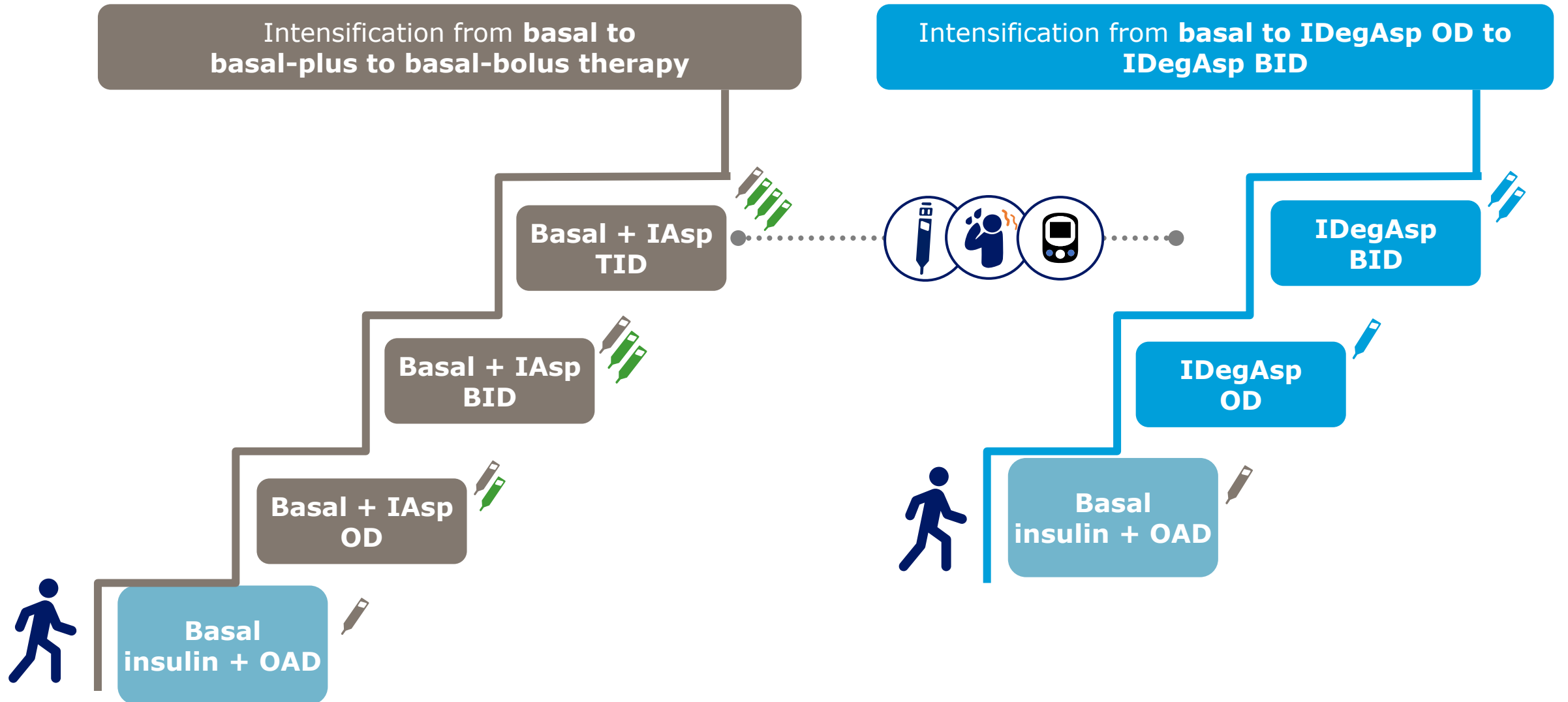


*Treatment intensification period was followed by 1 week washout period and then 30 day follow-up period; OADs included: metformin, DPP-4i, SGLT-2i, αGI (SU/glinides were discontinued at randomisation)

αGI, Alpha-glucosidase inhibitors; BID, twice daily; DPP-4i, dipeptidyl peptidase 4 inhibitors; IAsp, insulin aspart; IDegAsp, insulin degludec/insulin aspart; IGlar U100, insulin glargine U100; OAD: Oral anti-diabetic drug; OD, once daily; SGLT-2i, Sodium-glucose co-transporters inhibitors; SU, sulfonylureas; TID, thrice daily; TZD: Thiazolidinedione
 Philis-Tsimikas et al, *Diabetes Res Clin Pract*, 2019. 147:157-165. ClinicalTrials.gov Identifier: NCT02906917



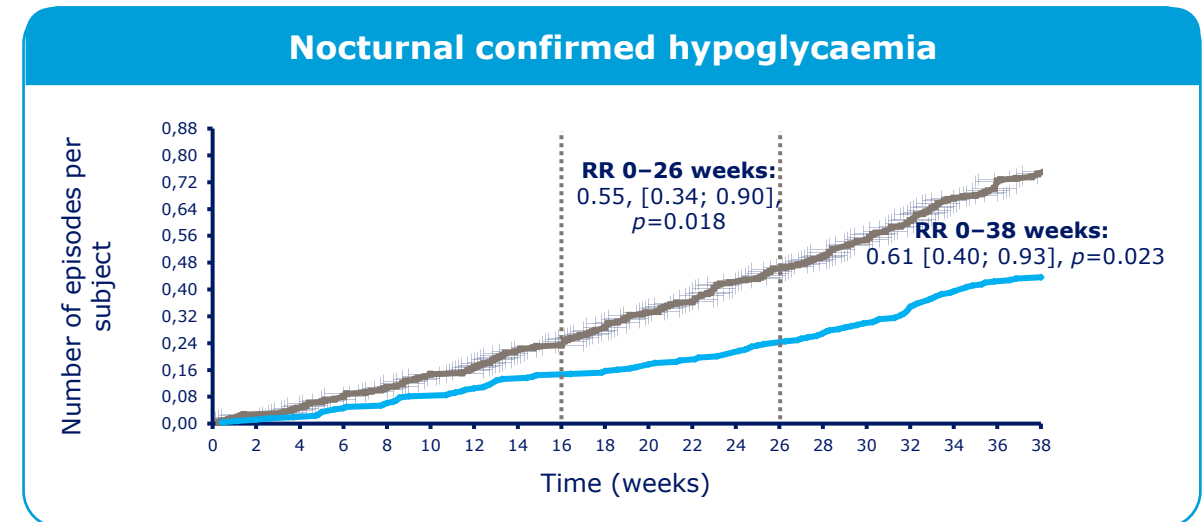
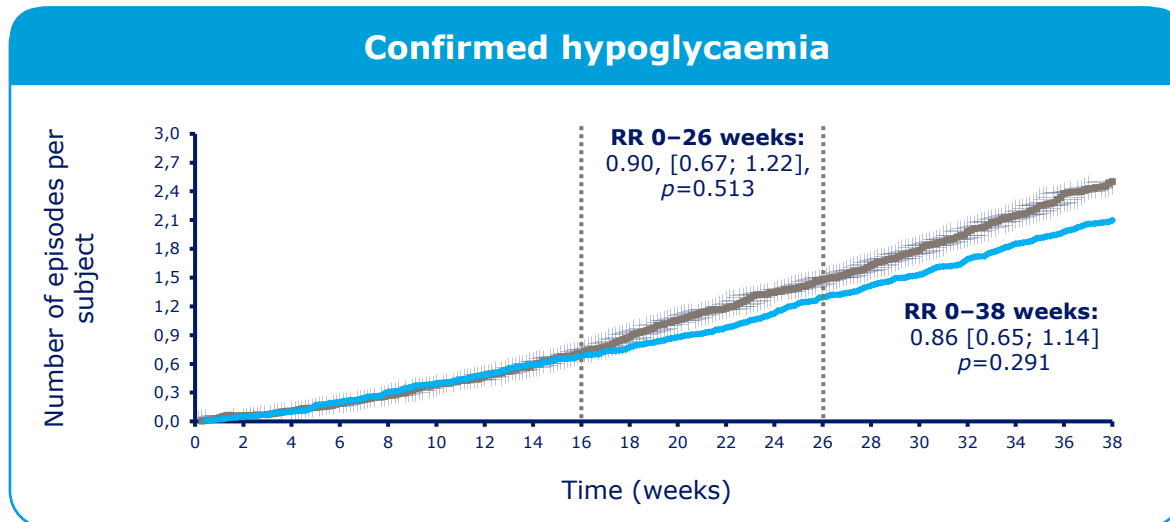
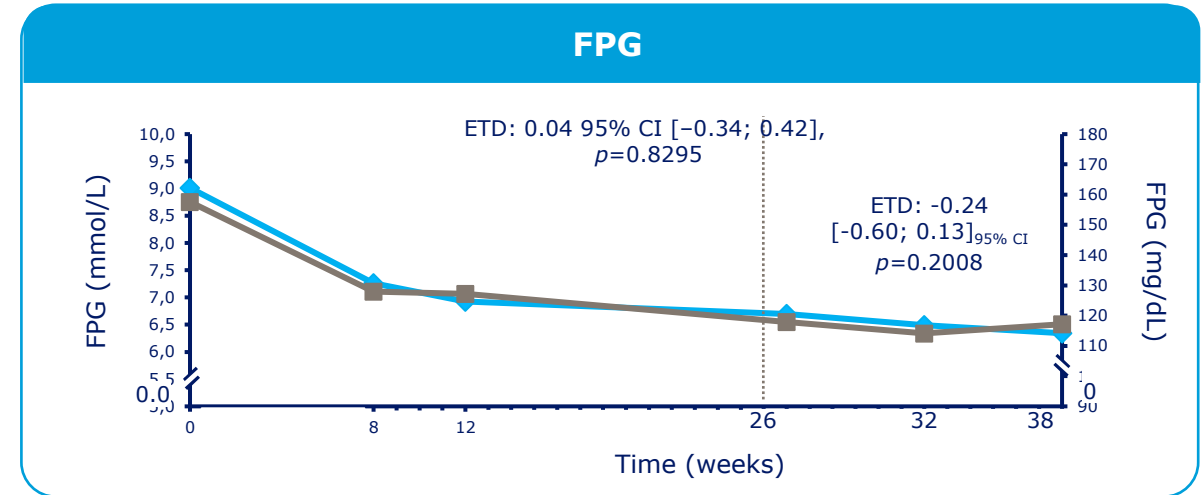
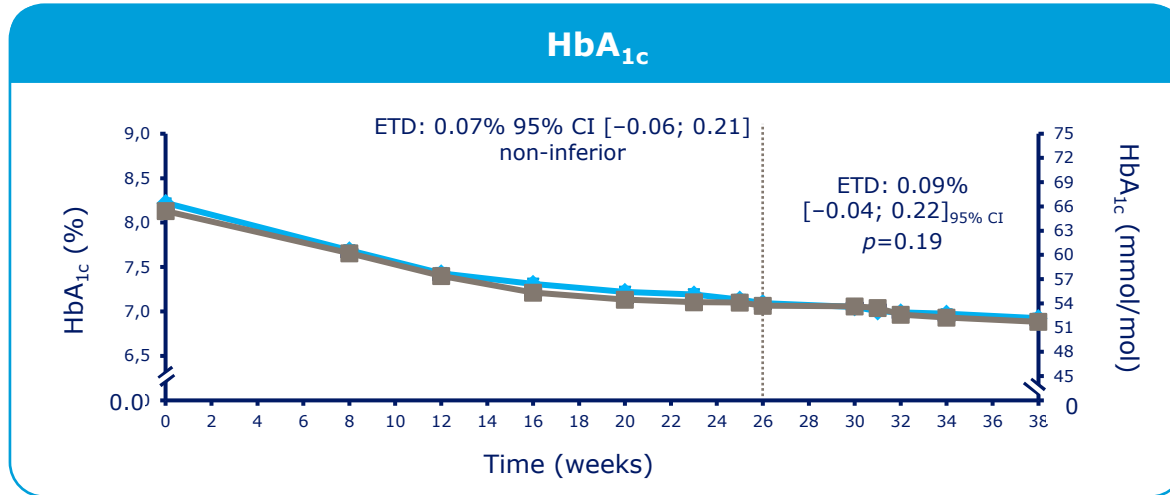
Basal insulin intensification approach



Insulin-experienced T2D OD/BID: results

IDegAsp Step-by-Step Intensification Trial

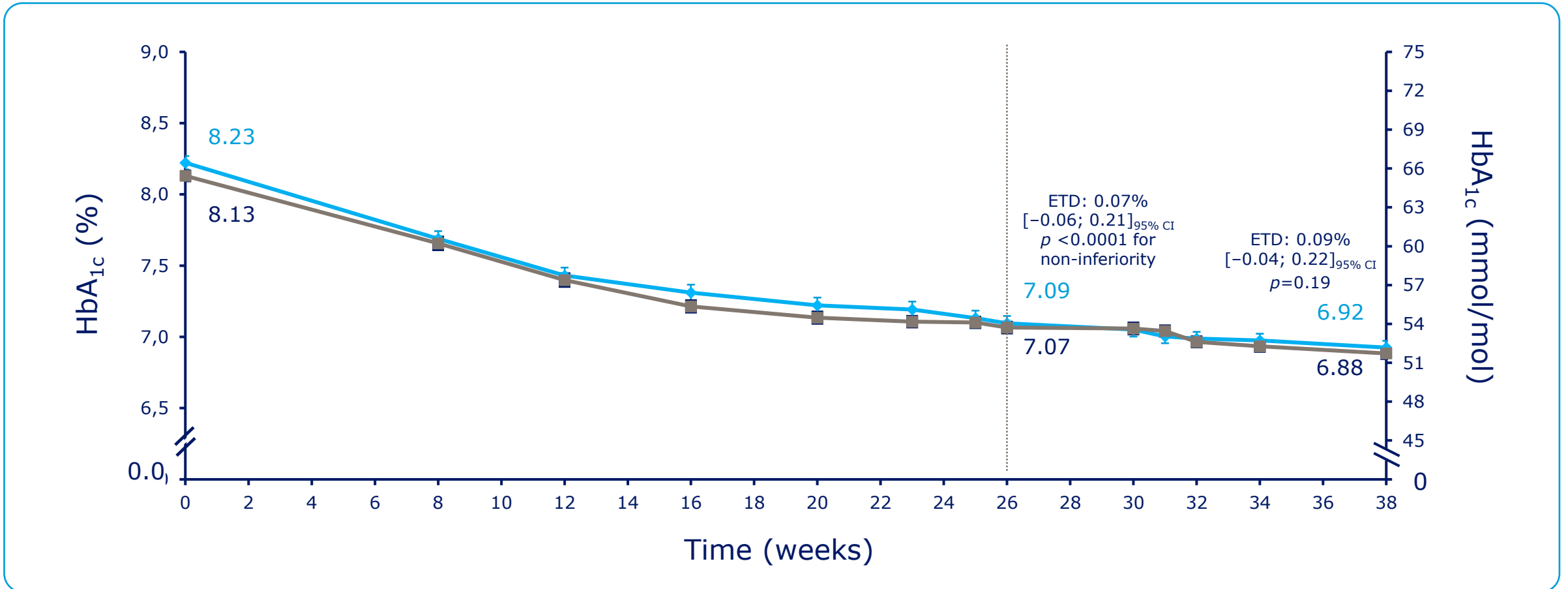
◆ IDegAsp ■ IGlar U100 + IAsp



HbA_{1c} over time

IDegAsp Step-by-Step Intensification Trial

◆ IDegAsp ■ IGlar U100 + IAsp



Full analysis set. Observed data. Error bars \pm standard error (mean). ANCOVA with multiple imputation by treatment arm. A penalty of 0.4% is added for treatment discontinued subjects, and subjects with missing values after 26 and 38 weeks, for IDegAsp arm. Covariate and fixed effects: Region, sex, previous insulin regimen, previous OAD treatment, age, baseline HbA_{1c}.

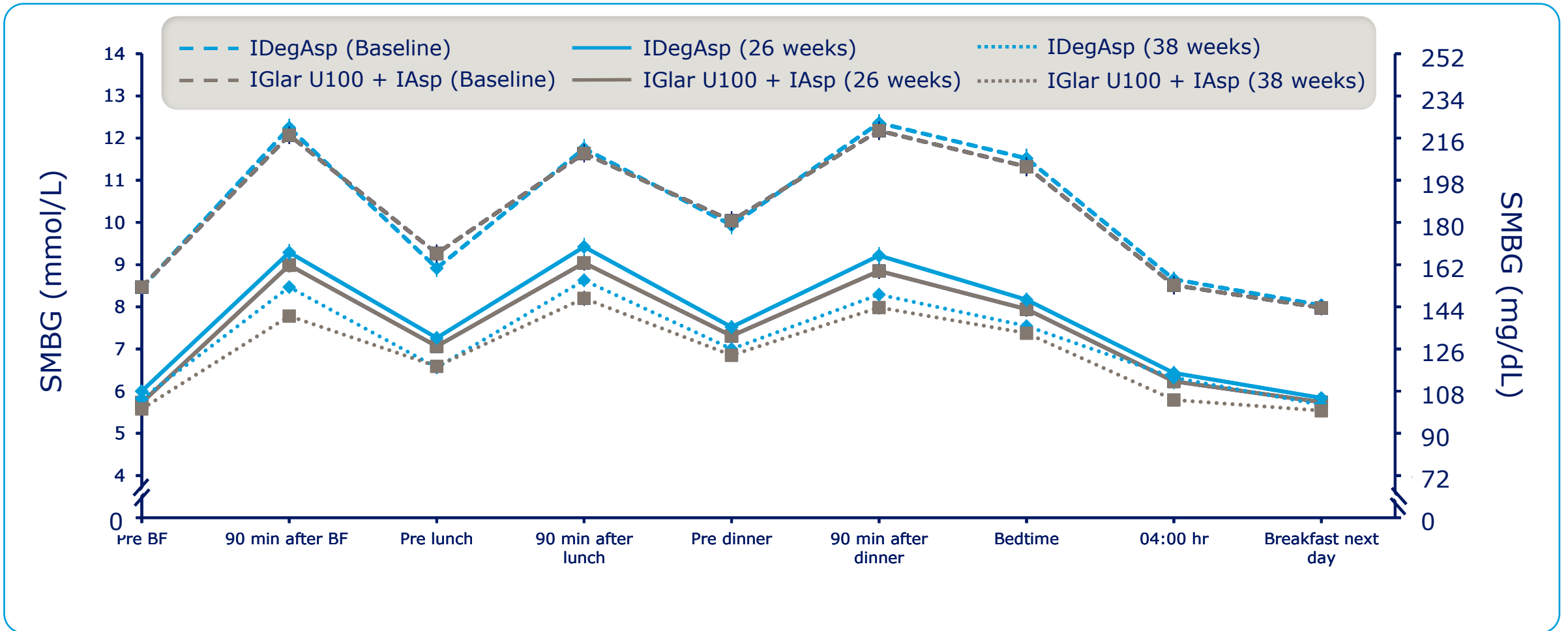
ANCOVA, analysis of covariance; BID, twice-daily; CI, confidence interval; ETD, estimated treatment difference; IAsp, insulin aspart; IDegAsp, insulin degludec/insulin aspart; IGlar U100, insulin glargine U100; OAD, oral antidiabetic drug; OD, once daily

Philis-Tsimikas et al, *Diabetes Res Clin Pract*, 2019. 147:157-165



9-point SMBG

IDegAsp Step-by-Step Intensification Trial



Significance level: Significantly higher pre-breakfast SMBG with IDegAsp OD compared with IGLar OD + Iasp ETD: 0.28 mmol/L, 95% CI: [0.05; 0.51]

OD at 26 weeks (ETD: 0.28 mmol/L, 95% CI: [0.05; 0.51]). Full analysis set. Observed data. Plot symbols arithmetic mean. Error bars \pm standard error (mean).

BF, breakfast; BID, twice-daily; IAsp, insulin aspart; IDegAsp, insulin degludec/insulin aspart; IGLar U100, insulin glargine U100; OD, once daily; SMBG, self-measured blood glucose

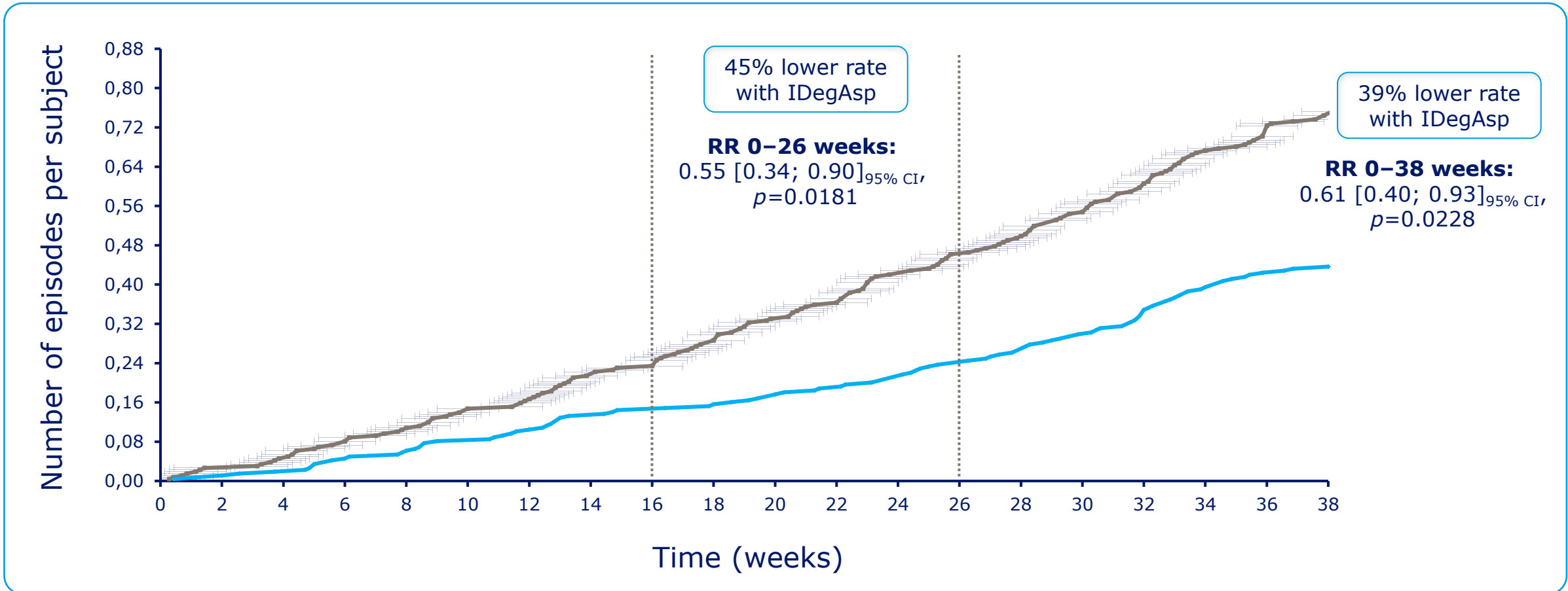
Novo Nordisk. NN5401-4266. Data on file (Data on the slide can only be presented with prior permission)



Nocturnal confirmed hypoglycaemia

IDegAsp Step-by-Step Intensification Trial

— IDegAsp (n=265)
— IGlAr U100 + IAsp (n=263)



Safety analysis set. Severe or BG-confirmed hypoglycaemia: subject unable to treat himself/herself and/or has a recorded plasma glucose value of <3.1 mmol/L (56mg/dL), with symptoms consistent with hypoglycaemia. The nocturnal period defined as the period between 00:01 and 05:59 a.m. (both inclusive)

BG, blood glucose; BID, twice-daily; CI, confidence interval; IAsp, insulin aspart; IDegAsp, insulin degludec/insulin aspart; IGlAr U100, insulin glargine U100; n, number of patients; RR, rate ratio

Philis-Tsimikas et al, *Diabetes Res Clin Pract*, 2019. 147:157-165

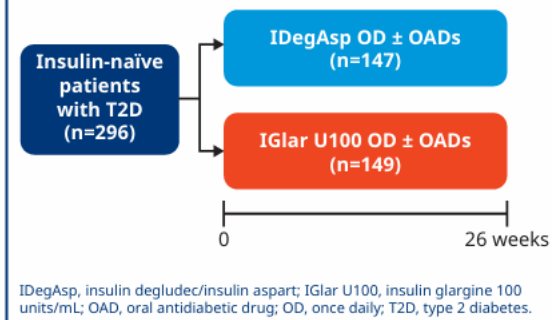


Time in range with IdegAsp in naïve T2D patients

Aim

- We used the concept of blood-glucose-monitored derived time in range (dTIR) to evaluate and compare treatment with insulin degludec/insulin aspart (IDegAsp) and insulin glargine 100 units/mL (IGlar U100) in insulin-naïve patients with type 2 diabetes (T2D).

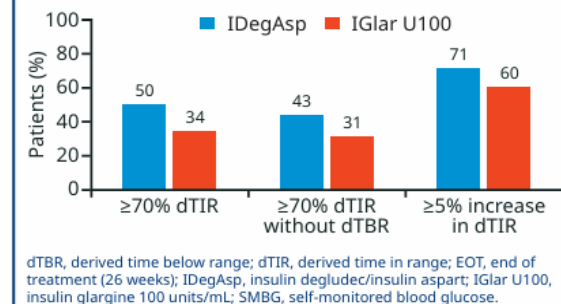
Figure 1: BOOST® Japan study design



Methods

- BOOST® Japan (NN5401-3896; NCT01272193) was a phase 3, open-label, treat-to-target trial of insulin-naïve Japanese adults with T2D who were randomised to either IDegAsp (n=147) or IGlar U100 (n=149)⁴ (Figure 1). Both insulins were titrated to a target pre-breakfast self-measured plasma glucose of 3.9 to <5.0 mmol/L (70 to <90 mg/dL).
- Data from this trial were evaluated post hoc. Nine-point SMBG profiles were taken at weeks 0, 12, 16 and 26, with time points before breakfast, at lunch, dinner, 90 min after each meal, bedtime and 04:00, and before breakfast the next day.⁴
- SMBG profiles with ≥ 6 readings were used to derive the proportion of available readings within (dTIR; 3.9–10 mmol/L [70–180 mg/dL]), below (derived time below range [dTBR]; <3.9 mmol/L [<70 mg/dL]) or above (derived time above range [dTAR]; >10 mmol/L [>180 mg/dL]) target range.

Figure 3: The percentages of patients achieving $\geq 70\%$ dTIR at EOT, $\geq 70\%$ dTIR without dTBR from baseline to EOT, and a $\geq 5\%$ increase in dTIR from baseline to EOT



Conclusions

- IDegAsp was associated with significantly greater dTIR versus IGlar U100 without an increase in dTBR in insulin-naïve patients with T2D.
- This highlights the clinical value of IDegAsp – a unique co-formulation that provides convenient dosing with the main meal.

1) Wilmot et al. *Diabet Med* 2021;38:e14433;

(2) diaTribeLearn. *Time in Range*. <https://diatribe.org/time-range/>;

(3) Beck et al. *Diabetes Care* 2019;42:400–5;

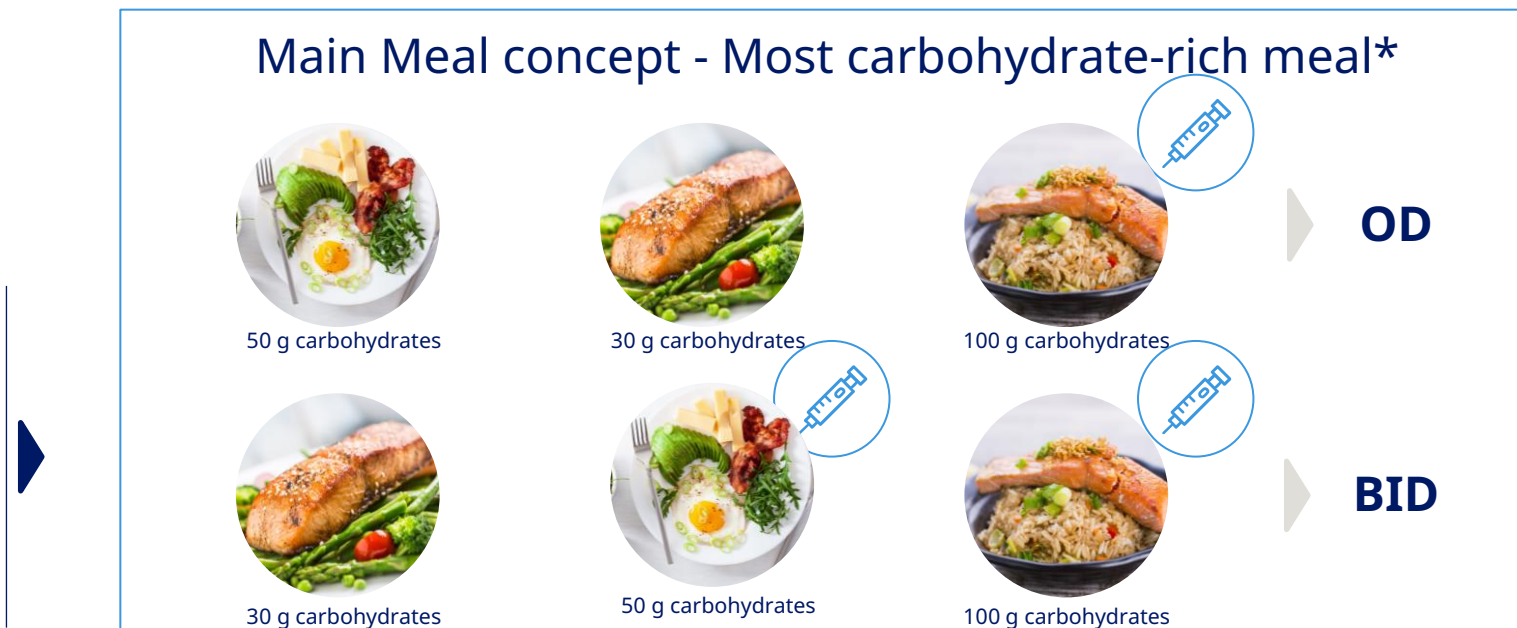
(4) Onishi et al. *Diabetes Obes Metab* 2013;15:826–32.



IDegAsp dosing based on meal content

Timing of IDegAsp dose

Main Meal Concept versus Adherence Strategy



*Main meal is the meal with the highest carbohydrate content in the meal and not the portion size of the complete meal
IDegAsp, insulin degludec/insulin aspart; OD, once daily; BID, twice daily. Mehta R, et al. *Diabetes Obes Metab.* 2020;10.1111/dom.14128.

Need for titration of insulin

- Active dose titration of basal and pre mix insulin is important for maintaining glycaemic control, teaching patient's self-titration based on fasting morning glucose readings (FPG) improves glycaemic control.
- It is important for patients to understand at the outset that the basal or pre mix insulin dose will need to be increased incrementally, determined by daily FPG levels and that achieving the optimal dose may take several weeks or months.

Titration for initiation with IDegAsp

- Recommended starting total daily dose : 10 units with meal
- Titration to Fasting blood glucose levels , as you would with a basal insulin. Only titrate one dose at a time. FBG must be at target before considering the second insulin dose based on HbA1c
- Once weekly titration
- For people at higher cardiovascular risk, less stringent FPG targets
- Use the lowest reading of the three FBG readings prior to weekly titration to adjust dose once weekly

Dose adjustment	Premeal blood glucose concentration
+8 U	>9.0 mmol/L (>162 mg/dL)
+6 U	8.1-9.0 mmol/L (145-162 mg/dL)
+4 U	7.1-8.0 mmol/L (127-144 mg/dL)
+2 U	5.1-7.0 mmol/L (91-126 mg/dL)
No change	4.0-5.0 mmol/L (71-90 mg/dl)
-2U	3.1-3.9 mmol/L (56-70 mg/dL)
-4 U	<3.1 mmol (<56 mg/dL)

Device-IDegAsp is delivered in the FlexTouch[®] pen

70/30 – 3 ml prefilled pen



Maximum dose/injection:
80 U

Injection sites:
Rotate frequently within the chosen area

Storage:
Opened pens – 2–8°C or room temperature for 4 weeks
Unopened pens – 2–8°C until expiry date

Needle:
Do not re-use needles



Dosing of IDegAsp in T2D

INITIATION

- Administer OD or BID with the main meal(s)
- Administer:
 - alone or
 - in combination with OADs or bolus insulin
- Recommended (total) daily starting dose 10 U
- Requires subsequent individual dosage adjustments

SWITCHING

Basal/Premix

OD

1:1

IDegAsp

OD/BID

Basal/Premix

≥BID

1:1

IDegAsp

BID/OD

Ind. req.

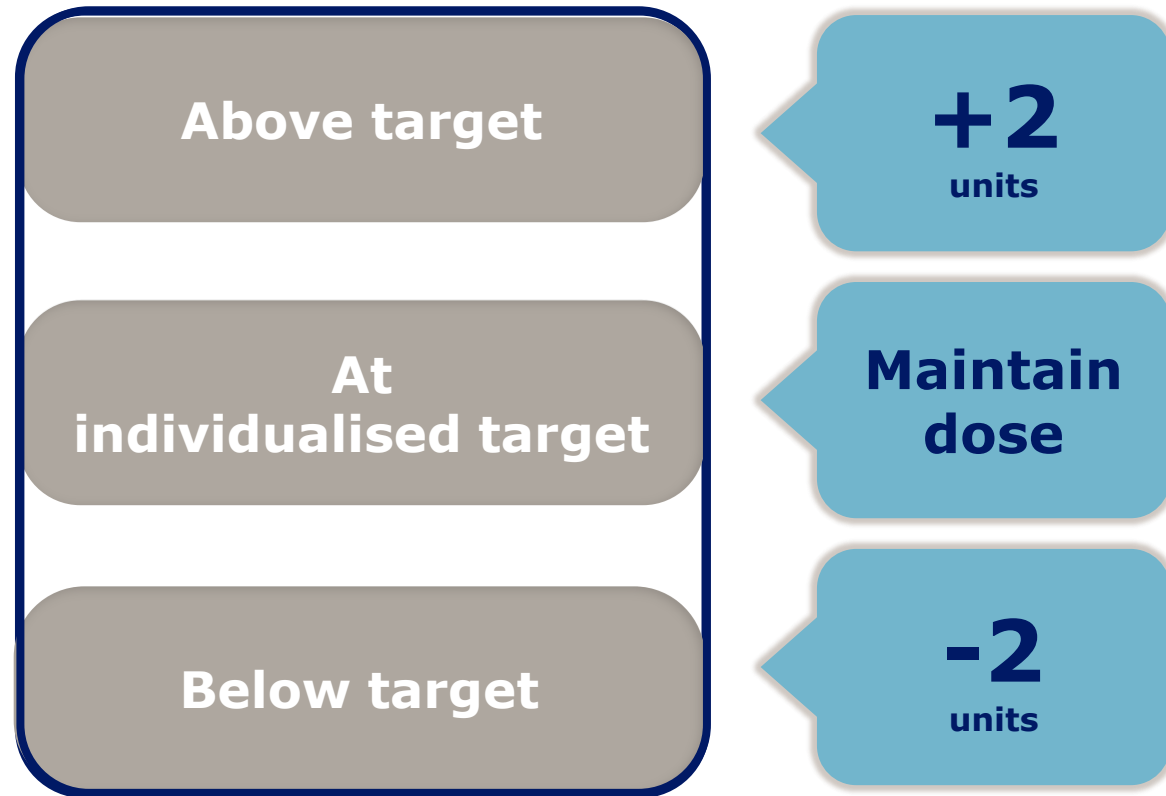
BB

IDegAsp

Recommend using close glucose monitoring for first few weeks



Suggested once-weekly titration schedule for IDegAsp in T2D



- Dose adjustments based on lowest of the 3 preceding FPG measurements
- FPG target should be individualised
- Do not increase dose if hypoglycaemia or symptoms suggestive of hypoglycaemia are present
- For twice-daily dosing, consider adjusting one dose at a time during weekly titration

FPG, fasting plasma glucose; IDegAsp, insulin degludec/insulin aspart; T2D, type 2 diabetes

1. Gerety *et al.* *Endocr Pract* 2016;22:546–54; 2. Endocrinologic and Metabolic Drug Advisory Committee. Insulin degludec and insulin degludec/insulin aspart treatment to improve glycemic control in patients with diabetes mellitus: NDAs 203314 and 203313 briefing document. Published November 8, 2012



Titration algorithms for IDegAsp

T1D	
Pre-breakfast plasma glucose ^a	Adjustment
mmol/L	U
<3.1 ^b	-4 (If dose >45 U, reduce by 10%)
3.1–3.8 ^b	-2 (If dose >45 U, reduce by 5%)
3.9–4.9	0
5.0–9.9	+2
10.0–14.9	+4
≥15.0	+6

T2D	
Pre-breakfast/pre-main evening meal plasma glucose ^{a*}	Adjustment
mmol/L	U
<3.1 ^b	-4 (If dose >45 U, reduce by 10%)
3.1–3.8 ^b	-2 (If dose >45 U, reduce by 5%)
3.9–4.9	0
5.0–6.9	+2
7.0–7.9	+4
8.0–8.9	+6
≥9.0	+8

^a Mean of 3 consecutive days measurements for up titration; ^b Reduction in dose is based on one measurement unless there is obvious explanation for the low value, such as a missed meal. *Pre-breakfast plasma glucose used for OD dosing and pre-breakfast and pre-evening meal plasma glucose used for BID dosing
 IDegAsp, insulin degludec/insulin aspart; T1D, type 1 diabetes; T2D, type 2 diabetes; U, units
 Fulcher *et al. Diabetes Care* 2014;37:2084–90; Kaneko *et al. Diabetes Res Clin Pract* 2015;107:139–47; Onishi *et al. Diabetes Obes Metab* 2013;15:826–32; Kumar *et al. Diabet Med* 2016 34(2), 180-188; Hirsch *et al. Diabetes Care* 2012;35:2174–81



Summary



HCP



Match **physiologic need** of people with diabetes in a way that is **feasible** and **sustainable**

Thank you

