Case Study
A 10-Year-Old Boy with Uncontrolled Type 1Diabetes

A Focus on Clinical Challenges and Recommendations

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Disclosure

I have received educational, research grants, lecture honorarium , travel supports to attend scientific meetings From Novonordisks, Pooyesh darou, Vitan pharmed, Orchidpharmed and Eli-lilly.

The CME responsibility is not Cobel Darou.

The content is prepared on my own, with review and approval by CD.

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I will receive speakership fee for this lecture from Cobel Darou.

Introduction

Overview of Type 1Diabetes (T1D)

Autoimmune condition common in children.

Challenges of managing hypoglycemia and uncontrolled diabetes:

Risk of complications and treatment discontinuation. Impact on quality of life.

Objective

Discuss Ramin's case and explore solutions.

Patient Overview

Name:

Ramin

Age:

10 years

Diagnosis:

Type 1 Diabetes (since age 6)

Current Issue:

Any time hypoglycemia and Uncontrolled glucose level despite medication.

Family and Patient Concerns

- Difficulty managing blood sugar levels.
- Difficulty managing Hypoglycemia episodes.
- Emotional burden on Ramin and his family.
- Challenges balancing school, activities, and diabetes care.

Clinical History

1. Diagnosed with T1D at age 6.
2. Past episodes of DKA.
3. No other significant medical history at diagnosis.

Current Medications

Current Basal Insulin:

Glargine 100 (switched brands multiple times).

Mealtime Insulin:

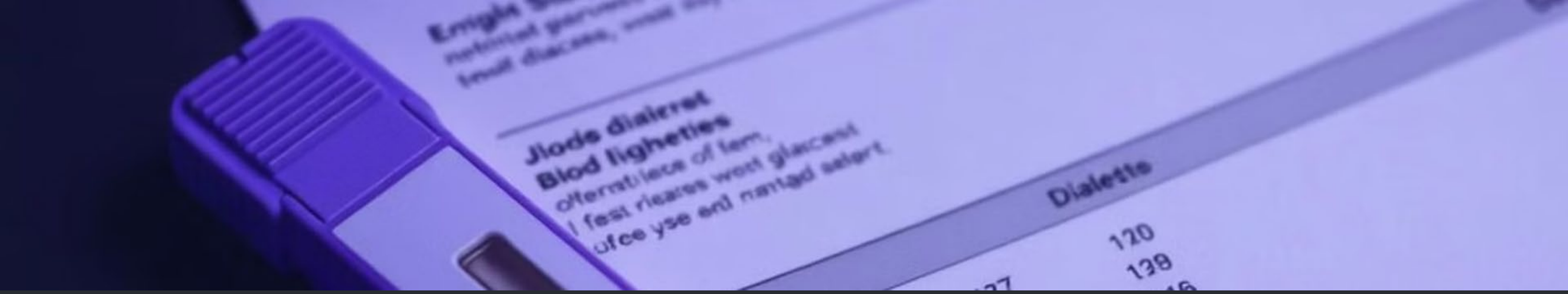
Rapid-acting analog (Glulisine)

Frequency of administration:

1 basal dose and 3-4 bolus doses daily.

Comorbidities

Suspected anxiety due to Hypoglycemia espisodes
And chronic illness.



Laboratory Test Results

HbA1c

9.2%

target <7.5% for children

Fasting Glucose Levels

Elevated consistently

Self-Monitoring of Blood Glucose (SMBG)

1 Patient checks blood glucose 4-5 times/day.

2 Average morning glucose: 210mg/dL

target: <130 mg/dL

3 Significant spikes post -breakfast and after meals.

Morning Glucose Levels

- Observation: Consistently above target, despite adjustments to nighttime insulin.

What Would You Recommend for Ramin?

1. Increase & divide Glargine 100
2. Switch to Toujeo
3. Adjust mealtime bolus insulin strategy
4. Introduce a CGM (continuous glucose monitor)
5. Focus on lifestyle and nutrition modifications

Recommended Actions

1 Address basal insulin stability

2 Explore activity and meal-timing solutions

Lifestyle and Nutrition Changes

Dietary Adjustments:

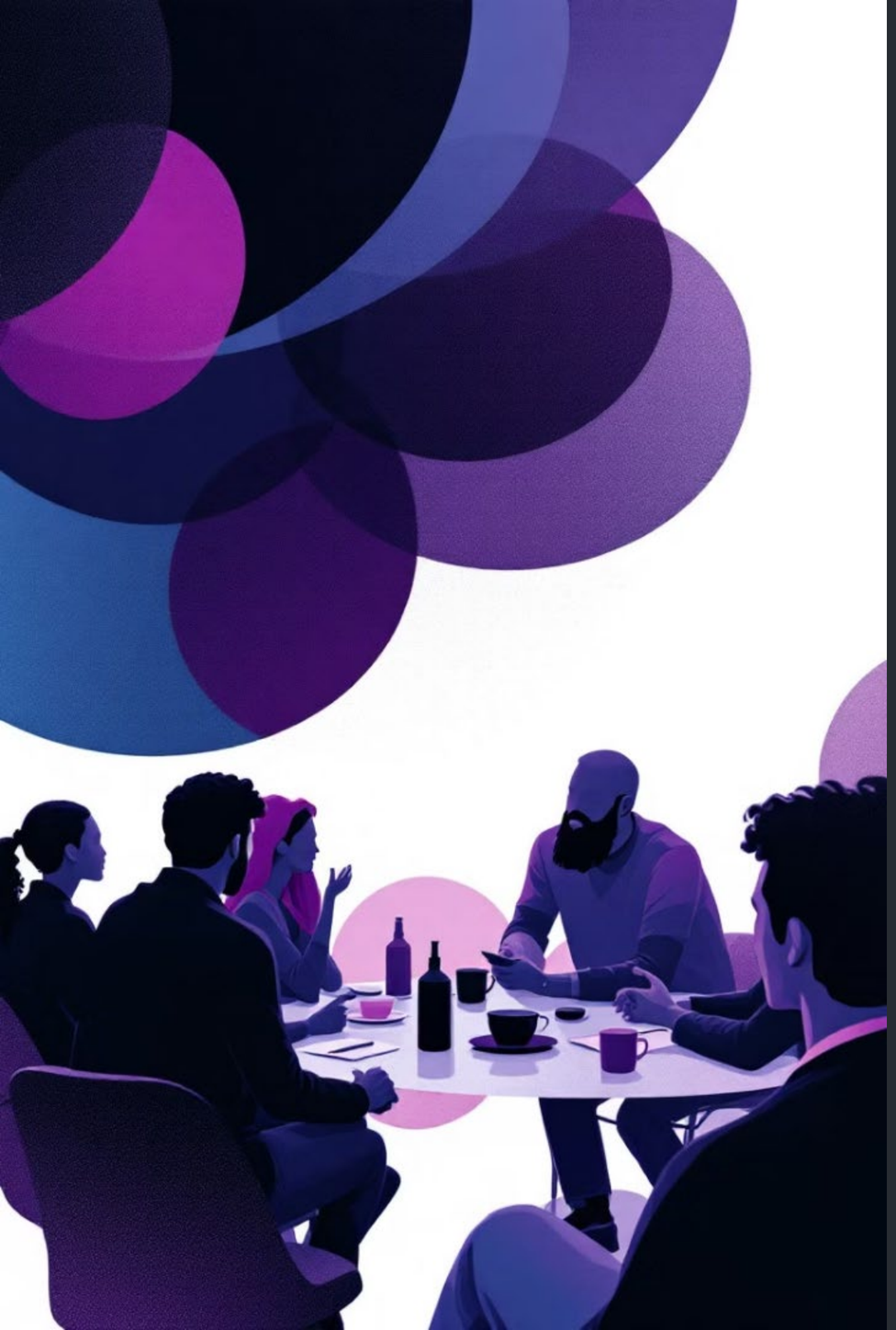
- Carbohydrate counting
- Avoid high-GI foods in the morning

Physical Activity:

- Regular exercise to improve insulin sensitivity

Sleep:

Ensure adequate rest to regulate glucose levels



Recommendations for Family Support

Parental Education:

- Importance of consistent monitoring
- Avoiding emotional tension around glucose fluctuations

Psychological Support:

- Engage with a counselor or diabetes educator
- Peer support for both Ramin and family

Medication Adjustment

Switch to Toujeo:

Dose to dose glargine 100
More stable basal coverage, fewer peaks

Continue Apidra :

Rapid-acting insulin to have flexibility of Apidra beside stability of Toujeo

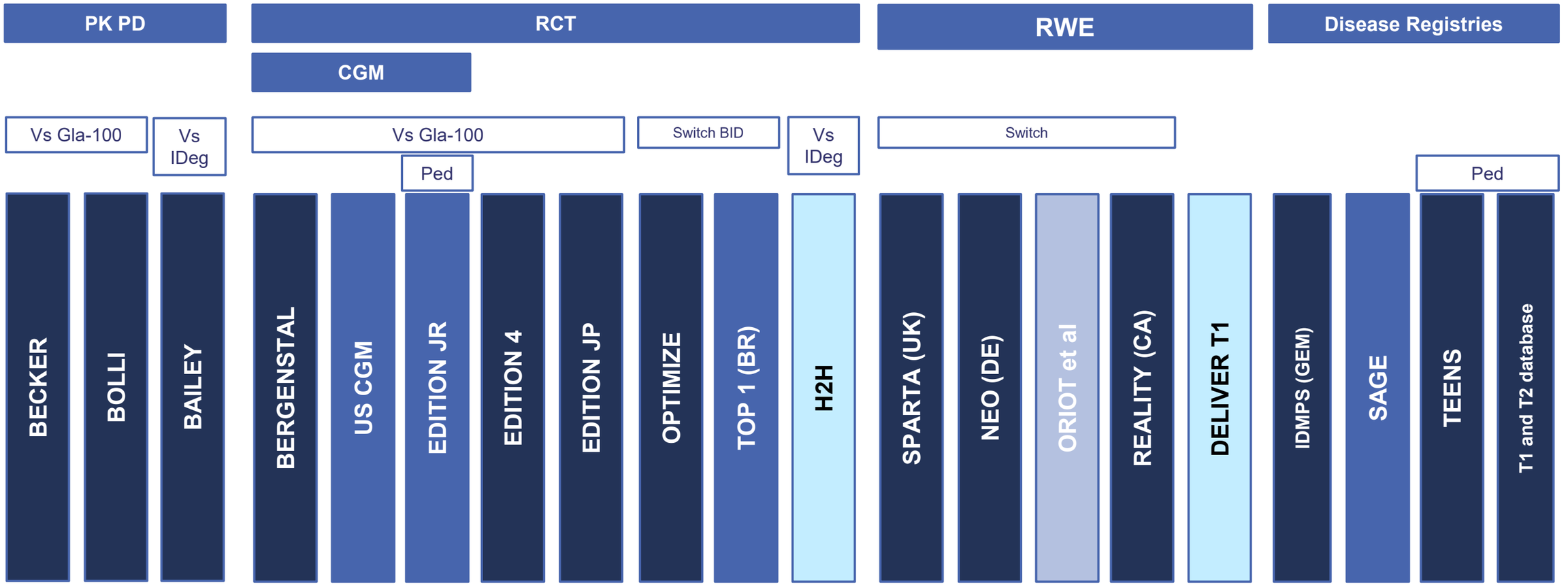
Expected Outcomes

1. Less hypoglycemia episodes
2. better glycemic control (target HbA1c: <7.5%)
3. Better physical and emotional well-being

Monitoring and Follow-Up

1. Regular reviews with endocrinologist
2. Data from SMBG or CGM used for fine-tuning
3. Ongoing family engagement

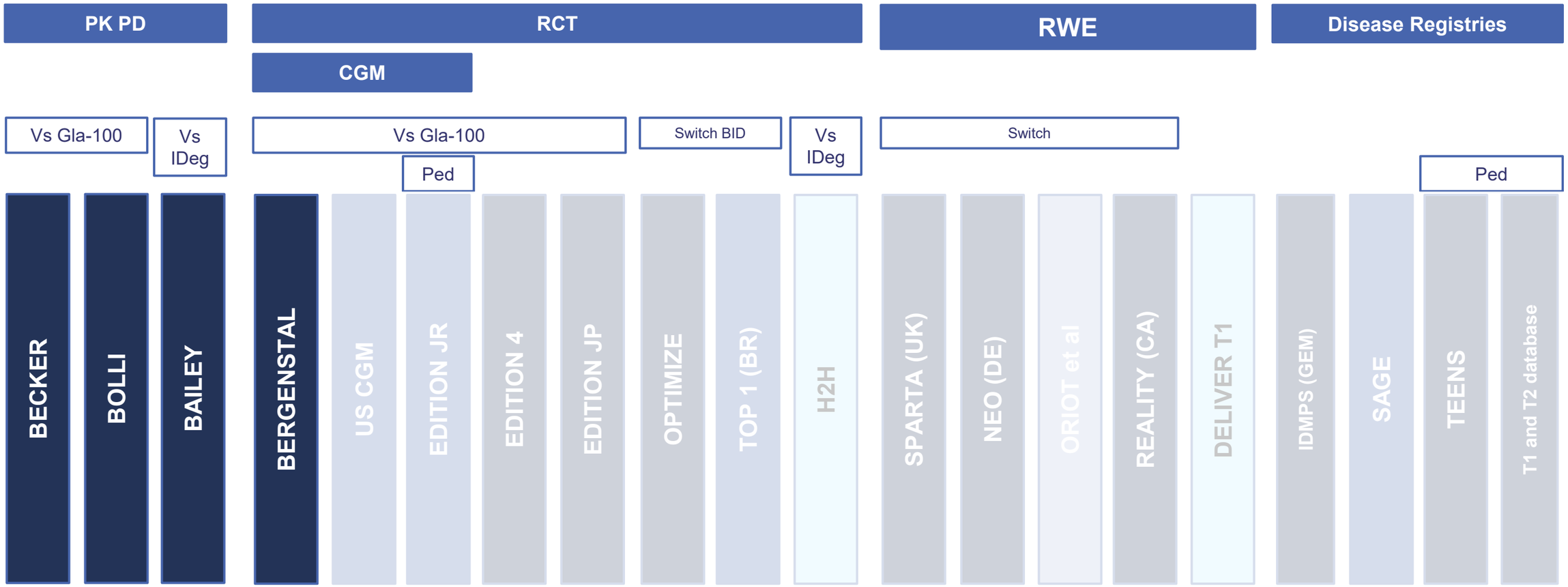
Comprehensive set of RCT and complimentary RWE also in T1DM with Gla-300



Becker RH et al. Diabetes Care. 2015;38:637-43; Porcellati F, et al. Diabetes Care 2018;DOI:10.2337/dc18-0706 [Epub ahead of print]; Bailey TS et al. Diabetes Metab. 2018;44:15–21; Bergenstal RM, et al. Diabetes Care 2017;40:554–60; Home PD et al. Diabetes Obes Metab 2018;20:121–8; Matsuhisa M et al. Diabetes Res Clin Pract 2016;122:133–40; Mathieu C, et al. Poster presented at ADA 78th Scientific Sessions 2018; 99-LB; Pang T, et al. Diabet Med. 2018 Oct 25. doi: 10.1111/dme.13847. [Epub ahead of print]; Fritsche A, et al. ADA 78th Scientific Sessions 2018; 1031-P; Oriot P, et al. Expert Rev Endocrinol Metab 2018;13:167–71; Abitbol A, et al. ADA 78th Scientific Sessions 2018; 1052-P; Aschner P, et al. Poster presented at ADA 78th Scientific Sessions 2018; Aschner P, et al. ADA 78th Scientific Sessions 2018; 1026-P; Laffel L et al ISPAD 2017 PO; Anderson BJ et al Diabetes Care Volume 40, August 2017

Maintaining a stable glycemic profile with Gla-300

Comprehensive set of RCT and complimentary RWE also in T1DM with Gla-300



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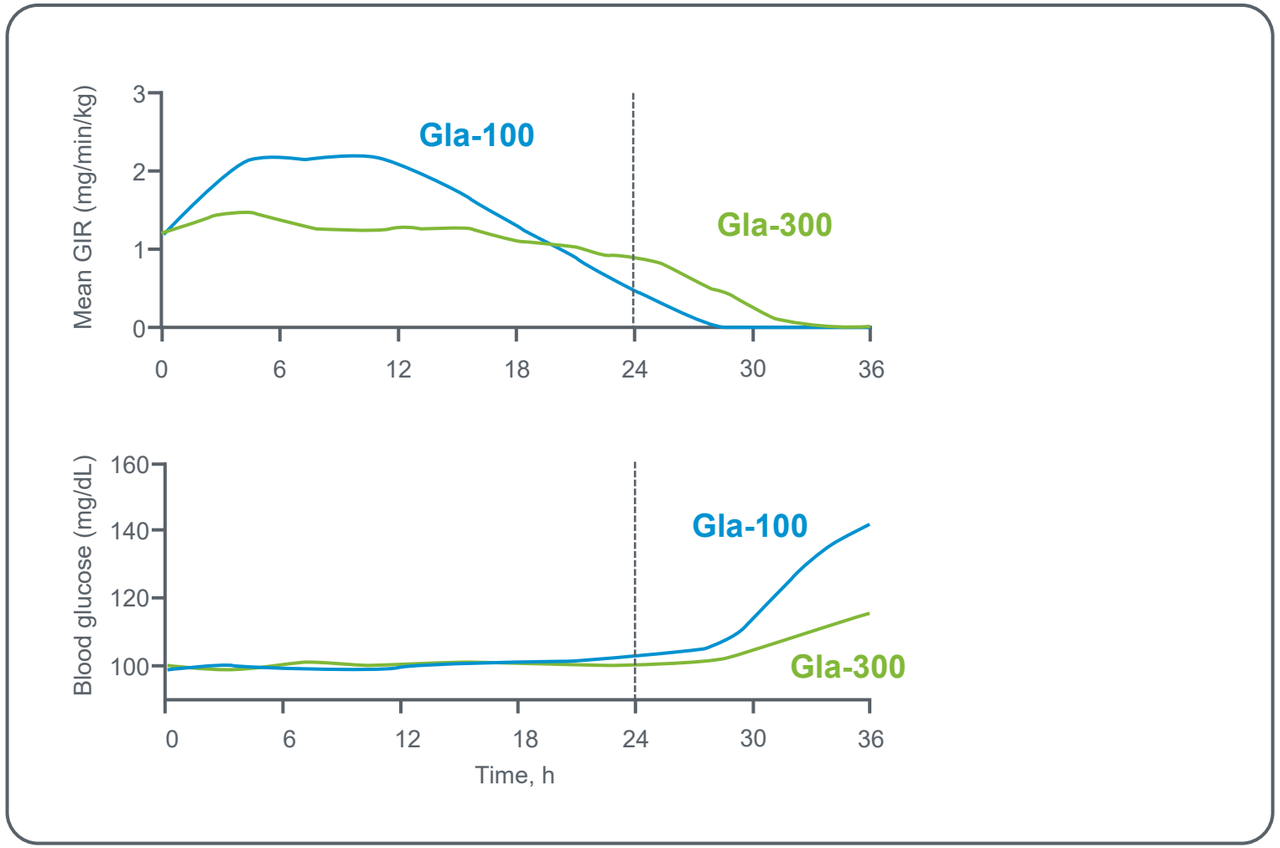
Anderson BJ et al Diabetes Care Volume 40, August 2017

More stable glucose-lowering (PD) profile with Gla-300 vs Gla-100

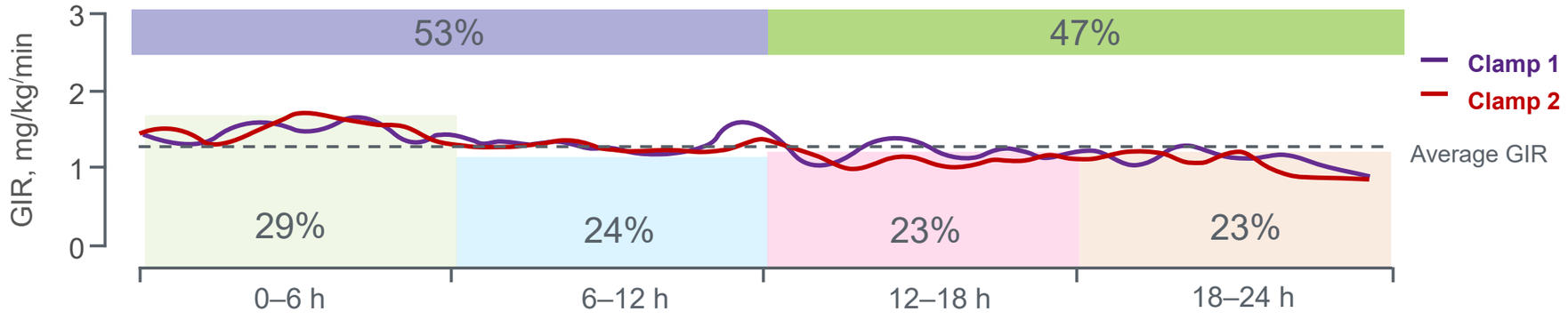


GIR, glucose infusion rate

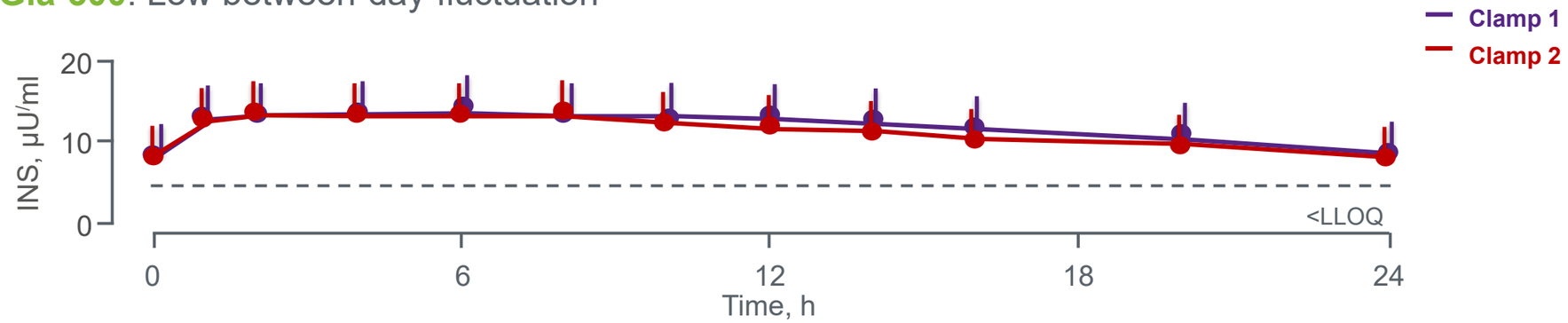
A randomized, double-blind, crossover euglycemic clamp study designed to assess the PK/PD profiles of Gla-300 vs Gla-100 at steady state in patients with T1DM

Low within-day and between-day fluctuation with Gla-300

Gla-300: Low within-day distribution of GIR-AUC as 6- and 12-hour fractions of total AUC



Gla-300: Low between-day fluctuation



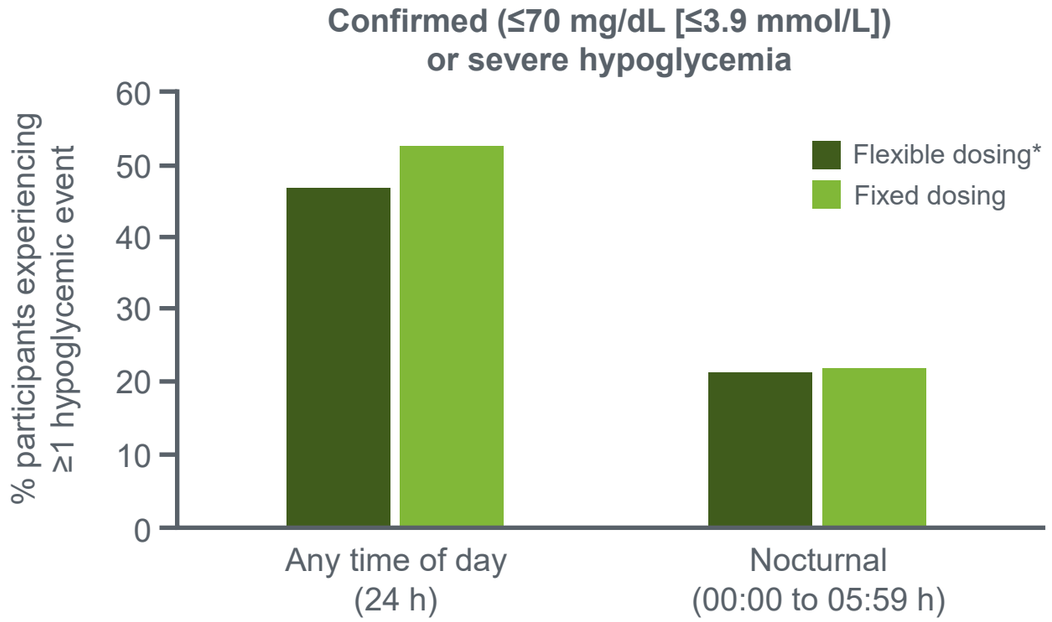
- AUC, area under the curve; GIR, glucose infusion rate; INS, serum insulin concentration; LLOQ, lower limit of quantification
- A double-blind, randomized, two-treatment, two-period, crossover euglycemic clamp study designed to characterise the variability in exposure and metabolic effect of Gla-300 at steady state in people with T1DM

Adapted from Becker RH et al. Diabetes Obes Metab. 2015;17:261–7 (main article and Supplementary Table 1)

Gla-300 can be administered using flexible dosing without compromising glycemic control and hypoglycemia vs fixed dosing

- Pooled EDITION 1 and 2 sub-studies in T2DM (Months 6–9)

HbA1c,%	Flexible dosing n=99	Fixed dosing n=95
Month 6, mean (SD)	7.30 (0.93)	7.30 (0.96)
Month 6–9, LS mean change (SE)	0.05 (0.06)	0.00 (0.07)
LS mean difference (95% CI)	0.05 (–0.13 to 0.23)	



Gla-300 may allow more freedom in timing injections (6-hour injection window [± 3 hours]) to deal with the situational variability experienced in daily life such as timing of the evening meal or bedtime, as required by work or family activities, or by travel

*Flexible dosing: Once-daily injection intervals of 24 ± 3 h

Adapted from Riddle MC, et al. Diabetes Technol Ther 2016;18:252–7

Glycemic stability: Summary

Gla-300 has a more stable glucose-lowering profile compared to Gla-100 in PD studies[1,2]

Gla-300 provides evenly-distributed 24 hr coverage as a result of low fluctuations in insulin exposure, which is also reproducible from day-to-day[3]

This stability is reflected in CGM studies, which show that Gla-300 offers significant improved glycemic control vs Gla-100, with less glycemic variability and nocturnal hypoglycemia[4]

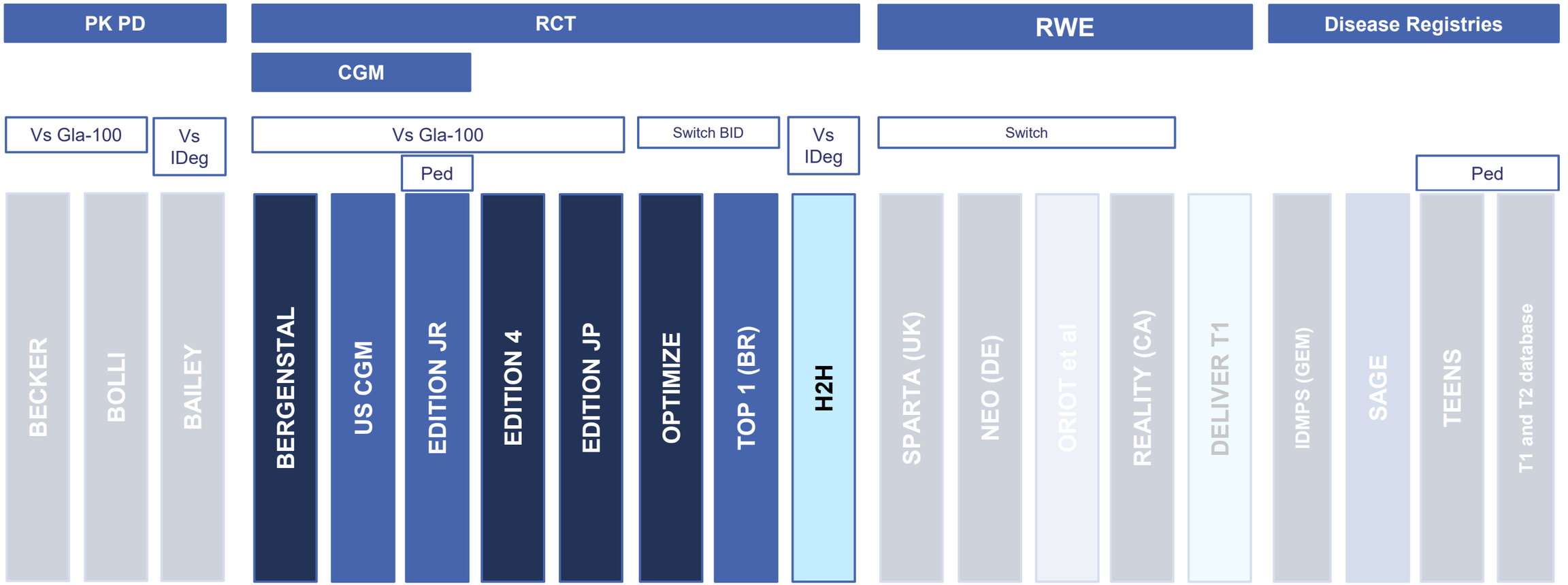
The glucose-lowering effect of Gla-300 is more stable then Gla-100 on average over 24 hrs[5]

Gla-300 can be flexibly administered (morning or evening) without jeopardizing glycemic control[6]

1. Becker RH et al. Diabetes Care. 2015;38:637–43; 2. Bailey TS et al. Diabetes Metab. 2018;44:15–21;
3. Becker RH, et al. Diabetes Obes Metab 2015;17:261–7; 4. Bergenstal RM, et al. Diabetes Care 2017;40 544–60;
5. Porcellati F, et al. Diabetes Care 2018; DOI: 10.2337/dc18-0706; 6, Riddle MC, et al. Diabetes Technol Ther 2016;18:252–7

Comparable glycemic control with lower rates of hypoglycemia during the titration period for Gla-300 vs Gla-100 across RCTs in patients with T1DM

Comprehensive set of RCT and complimentary RWE also in T1DM with Gla-300



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Comparable glycemic control between Gla-300 and Gla-100 over a 12 month period in adult patients (≥18 yrs) with T1DM

HbA1c over 12 months

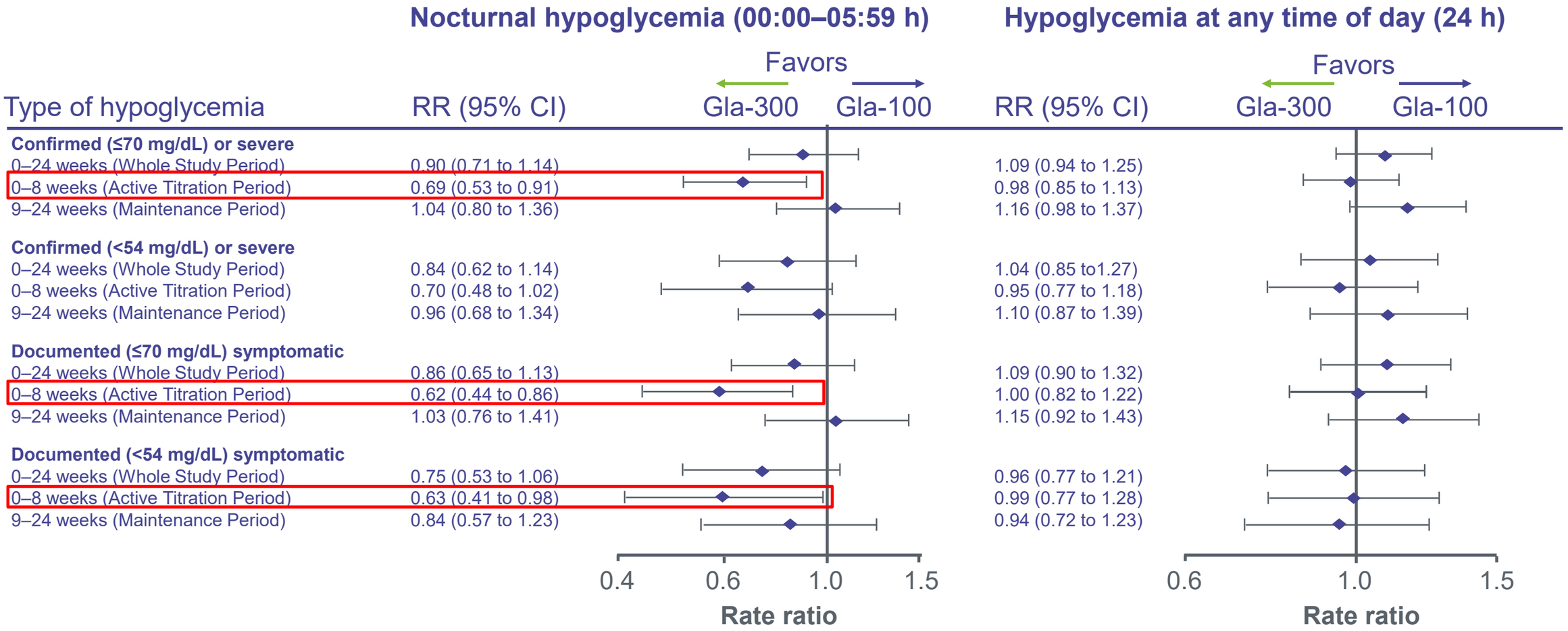
Mean HbA1c decreased similarly from baseline to month 12 in the Gla-300 and Gla-100 groups. LS mean difference in change from baseline (Gla-300 vs Gla-100) was 0.02 (95% CI: -0.13 to 0.17) %-units

CI, Confidence interval

EDITION 4 was a 6-month plus 6 months extension, multicenter, randomized, open-label phase 3 study designed to assess glycemic control and hypoglycemia with Gla-300 vs Gla-100 in patients with T1DM

Home PD, et al. Diabetes Obes Metab 2017;20:121–8

31% reduction in nocturnal confirmed (≤ 70mg/dL) or severe hypoglycemia rates during the titration period with Gla-300 vs Gla-100



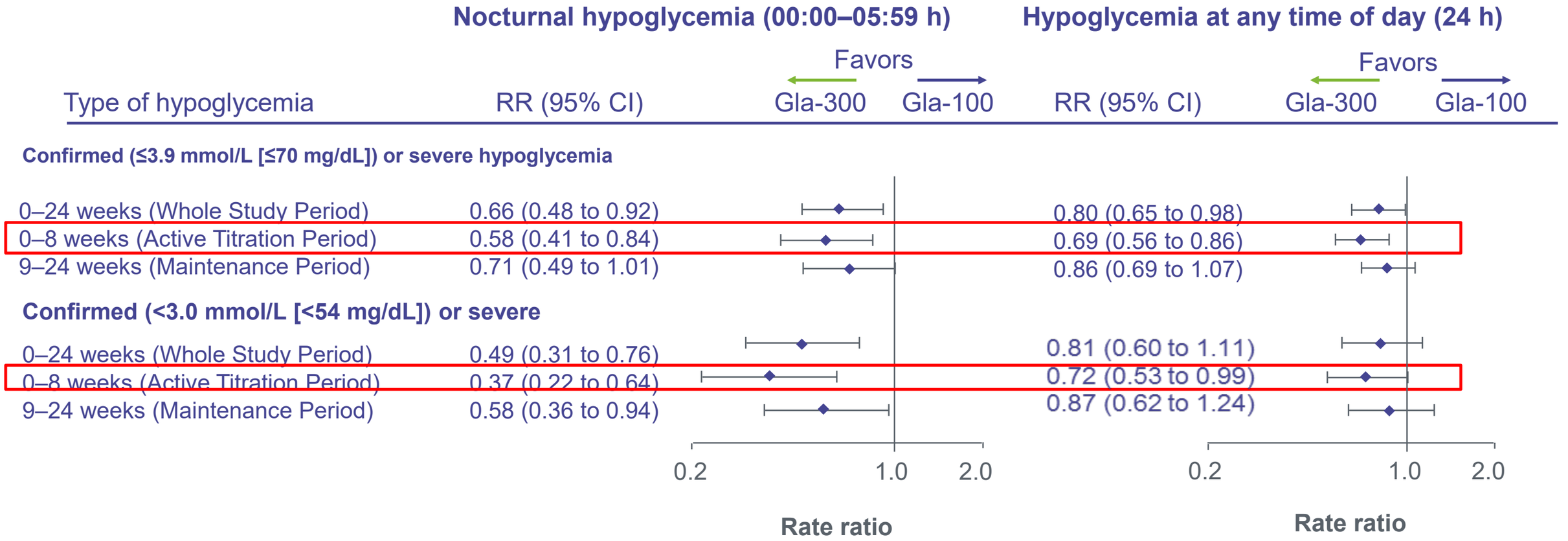
38% reduction in nocturnal documented symptomatic hypoglycemia rates during the titration period vs Gla-100

RR, rate ratio

EDITION 4 was a 6-month plus 6 months extension, multicenter, randomized, open-label phase 3 study designed to assess glycemic control and hypoglycemia with Gla-300 vs Gla-100 in patients with T1DM

Home PD, et al. Diabetes Care 2015;38:2217–25

42% reduction in nocturnal confirmed (≤ 70mg/dL) or severe hypoglycemia rates during the titration period vs Gla-100



31% reduction in any time of day (24 h) hypoglycemia rates during the titration period vs Gla-100

EDITION JP 1 was a multicenter, randomized, open-label phase 3 study to evaluate the efficacy and safety of Gla-300 vs Gla-100 in adults with T1DM in Japan

Adapted from Matsuhisa M, et al. Diabetes Obes Metab 2016;18:375–83

Summary of Gla-300 RCT data

Gla-300 offers improvements in glycemic control for uncontrolled T1DM patients who switch from once or twice daily basal* as part of basal–bolus regime [1,2]

Switching to Gla-300 from a twice-daily BI does not increase the hypoglycemia event rates in this challenging to treat patient population[1]

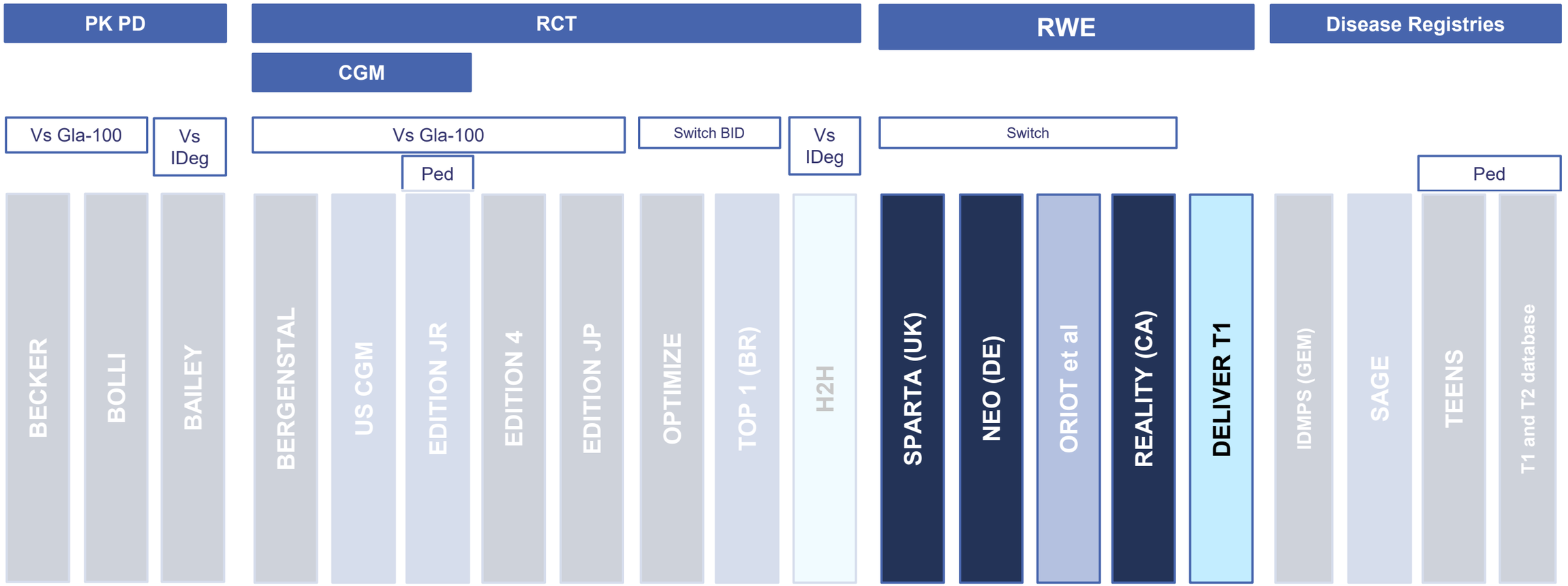
There is a significantly lower rate of nocturnal hypoglycemia during the titration period for patients with T1DM receiving Gla-300 vs Gla-100[2,3]

*Versus first generation basal insulin

1. Mathieu C, et al. Poster presented at ADA 78th Scientific Sessions 2018; 99-LB; 2. Home PD, et al. Diabetes Care 2015;38:2217–25; 3. Matsuhisa M, et al. Diabetes Obes Metab 2016;18:375–83

Comparable glycemic control with similar or lower rates of hypoglycemia after switching to Gla-300 in a real world setting for patients with T1DM

Comprehensive set of RCT and complimentary RWE also in T1DM with Gla-300



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Summary of Gla-300 in real-world evidence

Switching to Gla-300 leads to improved glycemic control in a real-world setting[1]

Switching to Gla-300 from any other BI* does not increase hypoglycemia event rates[2]

Patients who switch to Gla-300 could experience less nocturnal hypoglycemia in a real-world clinical setting[3]

*Versus first generation basal insulin

1. Pang T, et al. Diabet Med. 2018 Oct 25. doi: 10.1111/dme.13847. [Epub ahead of print]; 2. Fritsche A, et al. Poster presented at ADA 78th Scientific Sessions 2018; 1031-P; 3. Oriot P, et al. Expert Rev Endocrinol Metab 2018;13:167–71

Conclusion of Gla-300 evidence in patients with T1DM

Gla-300 has a more stable glucose-lowering profile compared to Gla-100 in PD and CGM studies[1,2,6]

Gla-300 offers comparable glycemic control and no increased risk of hypoglycemia for T1DM patients who switch from a once or twice-daily regime[3,5]

Patients who switch to Gla-300* could experience less nocturnal hypoglycemia in a real-world clinical setting[4]

*Versus first generation basal insulin

1. Becker RH et al. Diabetes Care. 2015;38:637–43; 2. Bailey TS et al. Diabetes Metab. 2018;44:15–21; 3. Mathieu C, et al. Poster presented at ADA 78th Scientific Sessions 2018; 99-LB; 4. Oriot P, et al. Expert Rev Endocrinol Metab 2018;13:167–71; 5. Home PD, et al. Diabetes Obes Metab 2017;20:121–8; 6. Bergenstal RM et al. Diabetes Care. 2017;40:554–60

Edition JUNIOR STUDY

EMERGING THERAPIES: DRUGS AND REGIMENS

Check for updates

Efficacy and Safety of Insulin Glargine 300 Units/mL (Gla-300) Versus Insulin Glargine 100 Units/mL (Gla-100) in Children and Adolescents (6–17 years) With Type 1 Diabetes: Results of the EDITION JUNIOR Randomized Controlled Trial

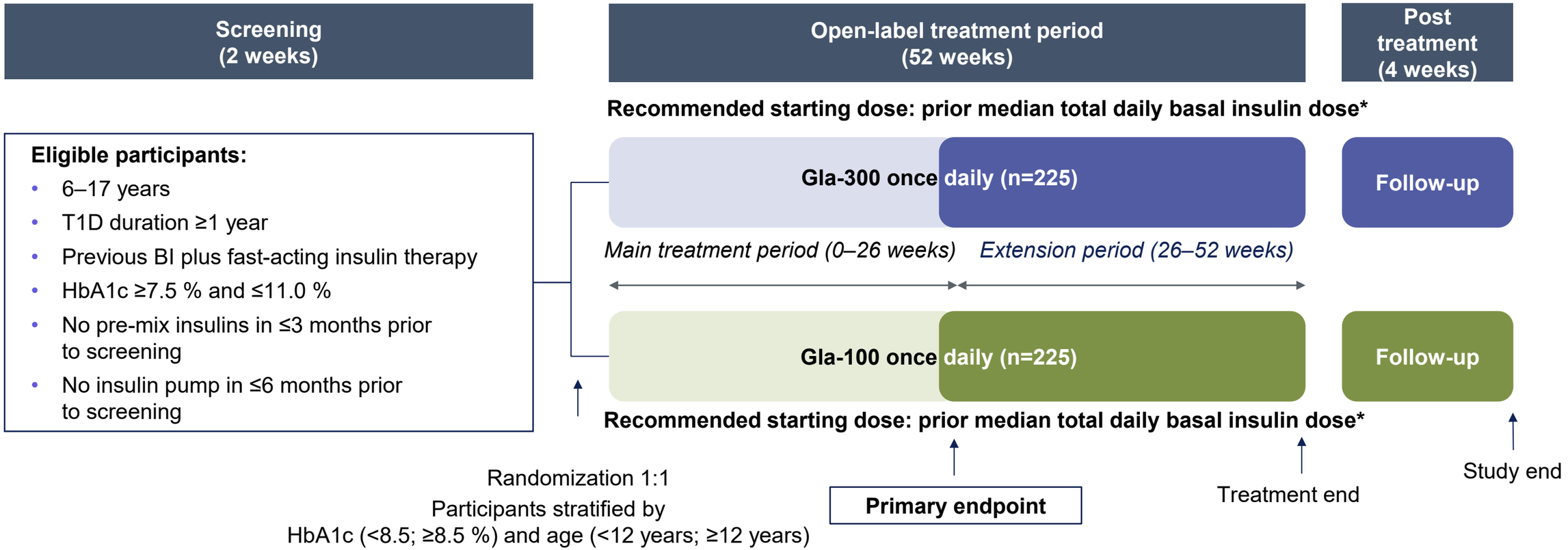
Thomas Danne,[1] William V. Tamborlane,[2] Oleg A. Malievsky,[3] Denise R. Franco,[4] Tomoyuki Kawamura,[5] Marek Demissie,[6] Elisabeth Niemoeller,[6] Harmonie Goyeau,[7] Marek Wardecki,[8] and Tadej Battelino[9]

Diabetes Care 2020;43:1512–1519 | https://doi.org/10.2337/dc19-1926

Edition junior

EDITION JUNIOR: Study design

Participants: Insulin-treated children and adolescents (6–17 years) with T1D confirmed by symptoms at diagnosis and/or antibody testing and/or clinical features (e.g. history of DKA)

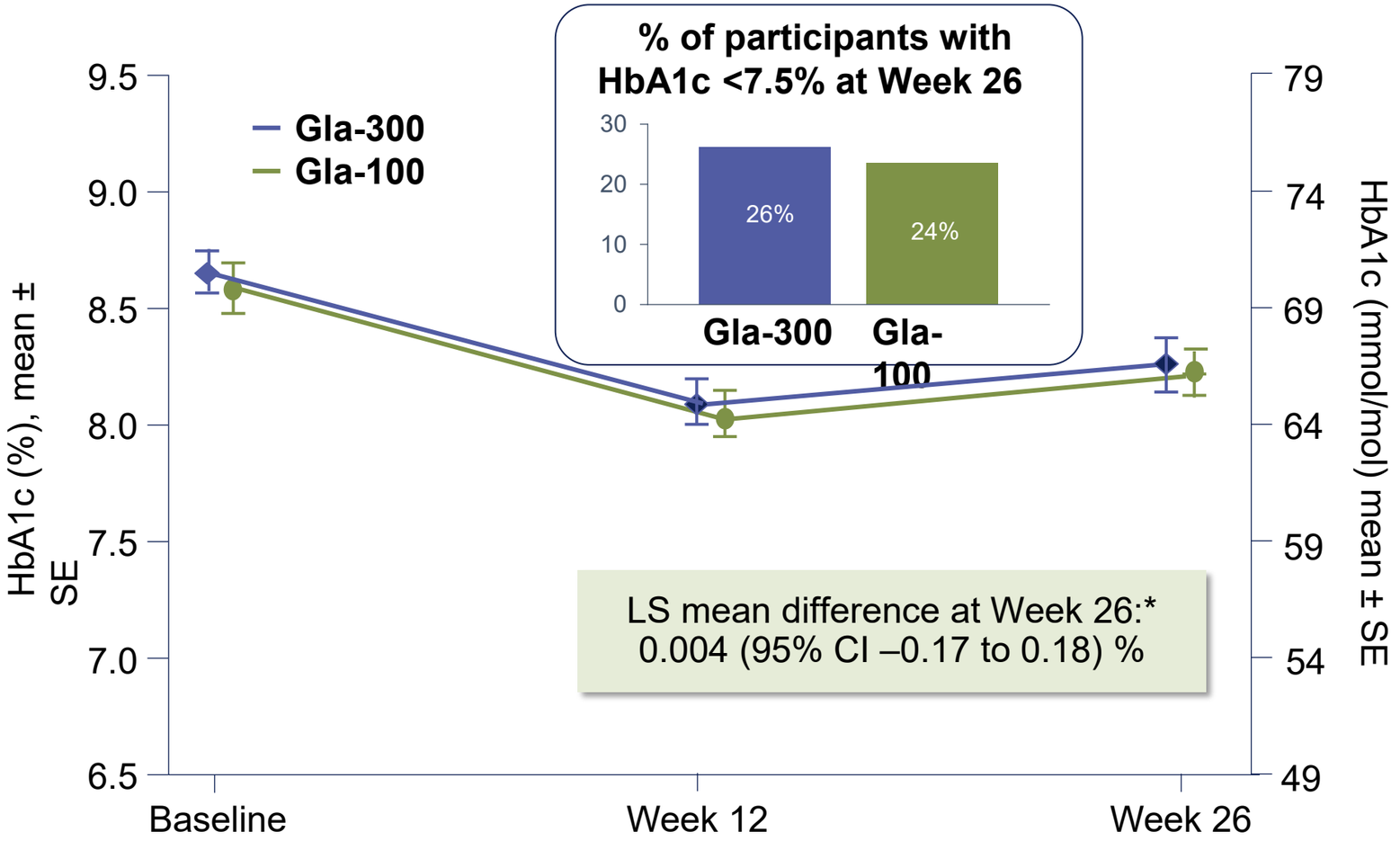


*Starting dose equal to the median (middle value out of three) total daily basal insulin dose from the previous 3 days. 20% reduction (from median) in total daily basal insulin dose if switching from twice-daily injections (e.g. NPH or insulin detemir)

DKA, diabetic ketoacidosis; Gla-100; insulin glargine 100 U/mL; Gla-300, insulin glargine 300 U/mL; NPH, neutral protamine Hagedorn

Danne T, Diabetes Care 2020;43:1512–9; https://clinicaltrials.gov/ct2/show/results/NCT02735044 (Last accessed September 2020)

Gla-300 met the primary endpoint of non-inferiority to Gla-100 for reduction in HbA1c at week 26



Gla-300 was non-inferior to Gla-100 in HbA1c change from baseline to Week 26 (the upper bound of the 95% CI was lower than the predefined non-inferiority margin of 0.3%)

Hba1c (%)	Gla-300 n=233	Gla-100 n=230
Baseline mean (SD)	8.65 (0.88)	8.61 (0.87)
Change from baseline to Week 26*		
LS Mean (SE) change	-0.40 (0.06)	-0.40 (0.06)
Combined LS Mean difference vs. Gla-100 (95% CI)	0.004 (-0.17 to 0.18)	
p-value for the superiority test	0.965	

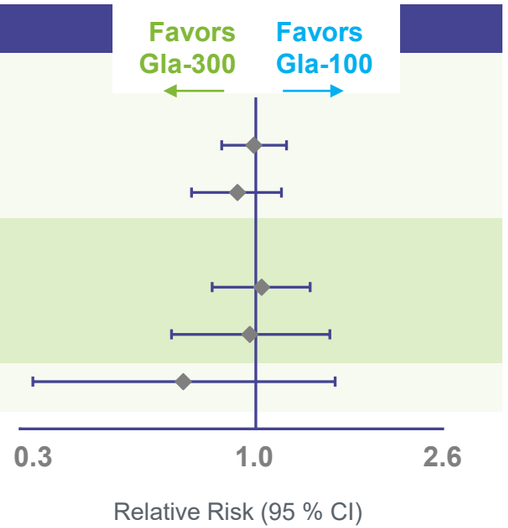
ITT population
*Multiple imputation analysis followed by analysis of covariance (ANCOVA) model (ITT estimate)
CI, confidence interval; Gla-100; insulin glargine 100 U/mL; Gla-300, insulin glargine 300 U/mL; ITT, intent-to-treat; LS, least squares; SE, standard error

Danne T, Diabetes Care 2020;43:1512–9

Rates of severe hypoglycemia were numerically lower in the Gla-300 vs the Gla-100 group

EDITION JUNIOR – 6 M

Hypoglycemia category	Number of events (event rate*) Gla-300 N=233	Number of events (event rate*) Gla-100 N= 228	Hypoglycemia Anytime (24 h) & Nocturnal (00:00–05:59 h) Relative Risk (95%CI)
			Gla-300 vs Gla-100
Anytime hypoglycemia (24 h)			
Severe and/or documented ≤70 mg/dL (≤3.9 mmol/L)	10341 (90.26)	10077 (90.02)	0.99 (0.84–1.17)
<54 mg/dL (<3.0 mmol/L)	1481 (12.93)	1565 (13.98)	0.91 (0.72–1.14)
Nocturnal hypoglycemia (00:00–05:59 h)			
≤70 mg/dL (≤3.9 mmol/L)	933 (8.14)	875 (7.82)	1.03 (0.80–1.32)
<54 mg/dL (<3.0 mmol/L)	124 (1.08)	119 (1.06)	0.97 (0.65–1.46)
Severe hypoglycemia (24 h)	21 (0.18)	30 (0.27)	0.69 (0.32–1.50)



*Annualized rates (events per participant-year) during the 6-month main treatment period (safety population)

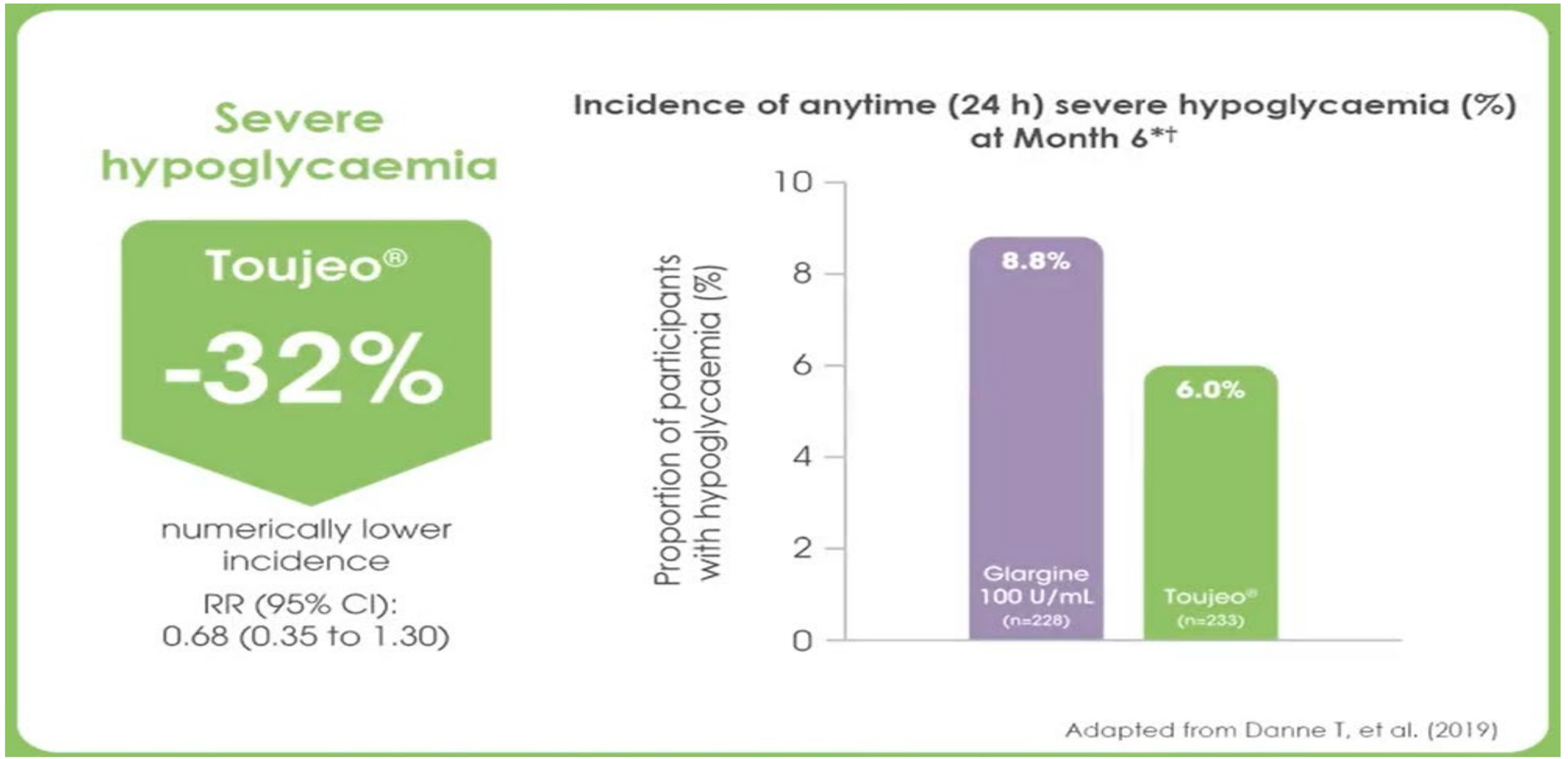
Gla-300 showed a similar rate of anytime and nocturnal hypoglycaemia vs Gla-100 in children/adolescents (6-17 years) with T1D

Safety population. CI, confidence interval. T1D, type 1 diabetes. RR based on negative binomial model with actual treatment groups (HOE901-U300 , Lantus), randomization strata of screening HbA1c (<8.5 or ≥8.5 %), randomization strata of age group at screening visit (<12 years and ≥12 years) as fixed effects, and logarithm of the treatment-emergent period as offset.

Severe hypoglycemia: an event in which the child/adolescent having altered mental status and cannot assist in their care, is semiconscious or unconscious, or in coma ± convulsions and may require parenteral therapy (glucagon or glucose).

Danne T, et al. Diabetes Care 2020;43:1512–1519

Severe Hypoglycemia



Hyperglycemia summary

Hyperglycemia with ketosis	Gla-300 (N=233)		Gla-100 (N=228)	
	Incidence, n (%)	Events (rate)	Incidence, n (%)	Events (rate)
Total patient-years		114.57		111.95
TEAE of hyperglycemia with ketosis during the main 6-month treatment period				
Any hyperglycemia with ketosis	**15 (6.4)**	34 (0.30)	**27 (11.8)**	46 (0.41)
Ketosis				
Diabetic ketoacidosis				
Hyperglycemia with k				
Any hyperglycemia w mmol/L and SMPG ≥				

Type of event	HOE901-U300 (N=233) N	HOE901-U300 (N=233) n(%)	Lantus (N=228) N	Lantus (N=228) n(%)	RR versus Lantus[a] RR vs Lantus	RR versus Lantus[a] 95% CI
Any hyperglycemia with ketosis						
6-month TEAE period	233	15 (6.44 %)	228	27 (11.84 %)	0.54	(0.30 to 0.99)
12-month TEAE period	233	22 (9.44 %)	228	36 (15.79 %)	0.60	(0.36 to 0.98)

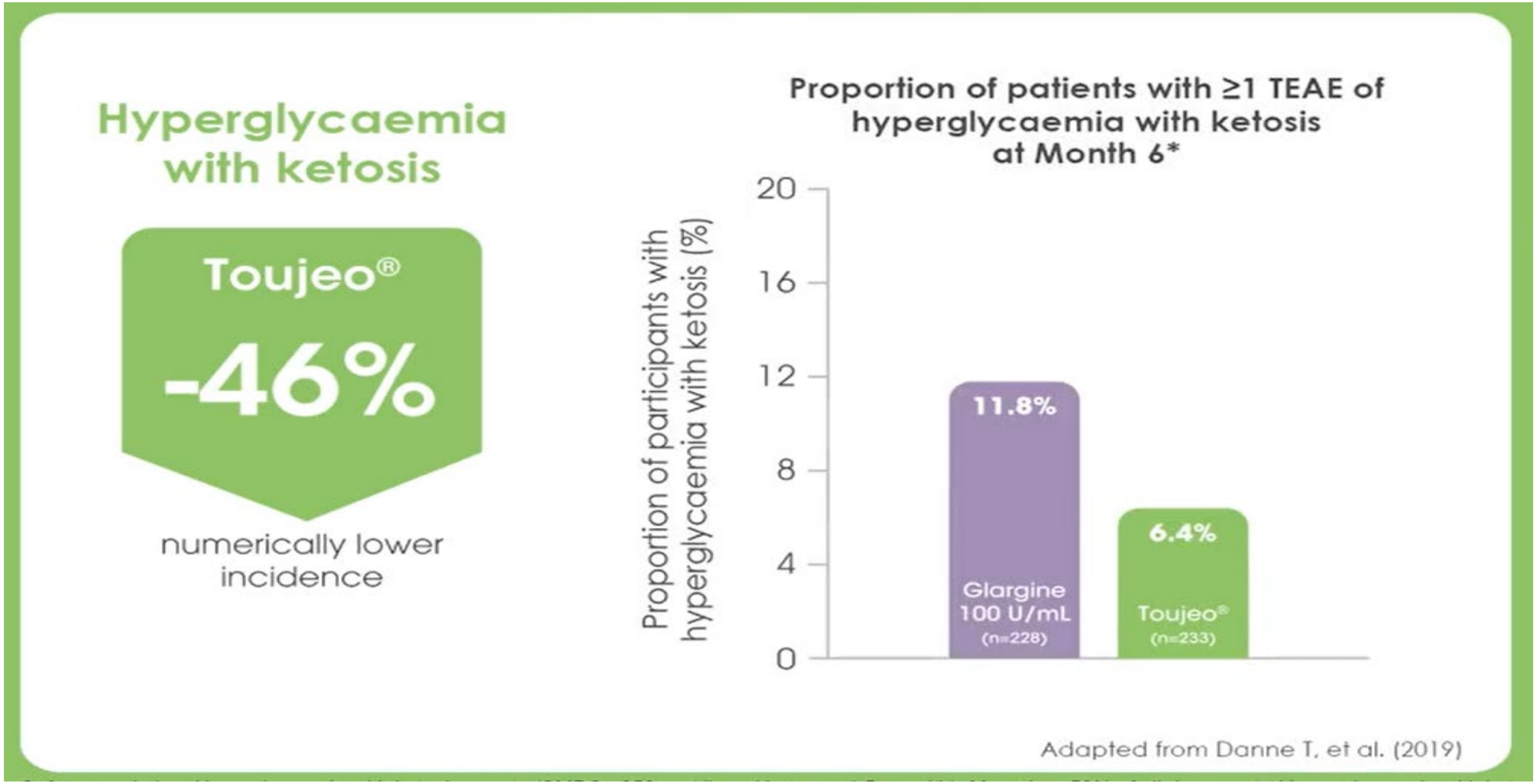
Proportion of individuals with ≥1 hyperglycemia and ketosis event was numerically lower in the Gla-300 (6.4%) vs Gla-100 group (11.8%) during the main 6-month treatment period

*Number of events and event rate per patient-years, linked to hyperglycemia with ketosis. More than 50% of all documented ketone values ≥1.5 mmol/L were reported by two individuals; **One individual reported 161 events; †One individual reported 69 events

Gla-100; insulin glargine 100 U/mL; Gla-300, insulin glargine 300 U/mL; SMPG, self-monitored plasma glucose; TEAE, treatment emergent adverse event

Danne T, Diabetes Care 2020;43:1512–9 (incl. Supplement)

Hyperglycemia with Ketosis



Similar AE profiles with Gla-300 and Gla-100 at Month 6

Number and percentage with at least one TEAE, n (%)	Gla-300 n=233	Gla-100 n=228
TEAE	152 (65.2)	150 (65.8)
Treatment-emergent SAE	17 (7.3)	21 (9.2)
TEAE leading to permanent treatment discontinuation	2 (0.9)	2 (0.9)
TEAE leading to death	1 (0.4)	0

The proportion of patients with ≥1 TEAE considered related to study treatment were low and comparable between the two treatment groups, Gla-300: n=14 (6.0%) Gla-100: n=19 (8.3%)

Safety population. SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Danne T, et al. Diabetes Care 2020;43:1512–1519

Conclusion:

- Gla-300 provided similar glycemic control to Gla-100 in children and adolescents with T1D.
- Both insulins had similar safety profiles but lower incidence and rates of severe hypoglycemia and lower incidence of hyperglycemia with ketosis were observed with Gla-300.

Danne T, et al. Diabetes Care 2020;43:1512–1519

Conclusion:

Gla-300 showed a lower risk for severe hypoglycemia compared with Gla-100 in a broad spectrum of patients with T1D, especially during the titration phase

Gla-300 provides effective and similar glycemic control versus Gla-100 in patients with T1D

Danne T, et al. Pediatr Diabetes 2019;20 (Suppl 28):P236. Poster presented at 45th Annual Conference for the International Society for Pediatric and Adolescents Diabetes (ISPAD) Boston 2019 – P236

Summary

1. Challenges: Uncontrolled glucose levels and hypoglycemia episodes in T1D
2. Solution: Multidisciplinary approach
3. Smart choice of Basal and prandial Insulins and Medication adjustment
4. Lifestyle changes and Family support

TOUJEO® (insulin glargine 300 units/ml) - Abbreviated Prescribing Information

NAME AND PRESENTATION: Toujeo 300 units/ml, solution for injection in a prefilled pen. 1 ml of solution contains 300 units of insulin glargine. Each SoloStar prefilled pen contains 1.5 ml of solution for injection (equivalent to 450 units). **THERAPEUTIC INDICATIONS:** Treatment of diabetes mellitus in adult, adolescents and children from the age of 6 years. **POSOLOGY AND METHOD OF ADMINISTRATION:** Toujeo is a basal insulin for once-daily administration at any time of the day, preferably at the same time every day. When needed, patients can administer Toujeo up to 3 hours before or after their usual time of administration. The dose regimen (dose and timing) should be adjusted according to individual response. In type 1 diabetes mellitus, Toujeo is to be used once-daily and must be combined with short-/rapid-acting insulin to cover mealtime insulin requirements. In patients with type 2 diabetes mellitus, the recommended daily starting dose is 0.2 units/kg. Toujeo can also be given together with other anti-hyperglycaemic medicinal products. **Switch:** When switching from insulin glargine 100 units/ml to Toujeo, this can be done on a unit-to-unit basis. When switching from a treatment regimen with an intermediate or long-acting insulin to a regimen with Toujeo, a change of the dose of the basal insulin may be required and the concomitant anti-hyperglycaemic treatment may need to be adjusted. Close metabolic monitoring is recommended during the switch and in the initial weeks thereafter. For switch details see full SmPC. **Special populations:** Toujeo can be used in elderly people, renal and hepatic impaired patients, and children and adolescents from the age of 6 years. **Renal impairment & hepatic impairment:** insulin requirements may be diminished. **Elderly:** progressive deterioration of renal function may lead to a steady decrease in insulin requirements. **Children:** Toujeo can be used in adolescents and children from the age of 6 years based on the same principles as for adult patients, and the safety and efficacy of Toujeo in children below 6 years of age have not been established. **Method of administration:** For subcutaneous use only. Toujeo must not be administered intravenously or in insulin infusion pumps. Toujeo SoloStar prefilled pen has been specifically designed for Toujeo, therefore no dose re-calculation is required. Toujeo must not be drawn from the cartridge of the SoloStar pre-filled pen into a syringe or severe overdose can result. Injection sites must be rotated within a given injection area from one injection to the next, in order to reduce the risk of lipodystrophy and cutaneous amyloidosis. For administration details see full SmPC. **CONTRA-INDICATIONS:** Hypersensitivity to the active substance or to any of the excipients listed in the full SmPC. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE:** In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded • Toujeo is not the insulin of choice for the treatment of diabetic ketoacidosis. The prolonged effect of insulin glargine may delay recovery from hypoglycemia. If pioglitazone is used in combination with insulin, especially in patients with risk factors for development of cardiac heart failure, patients should be observed for signs and symptoms of heart failure, weight gain and oedema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. For further details on special warnings and precautions for use see full SmPC. **DRUG INTERACTIONS:** Substances that may enhance or reduce the blood-glucose-lowering activity and increase susceptibility to hypoglycaemia are detailed in the full SmPC. **PREGNANCY AND LACTATION:** There is no clinical experience with use of Toujeo in pregnant women. For insulin glargine no clinical data on exposed pregnancies from controlled clinical studies are available. A large amount of data on pregnant women indicate no specific adverse effects on pregnancy and no specific malformative nor feto/neonatal toxicity of insulin glargine. The use of Toujeo may be considered during pregnancy if clinically needed. **EFFECTS ON ABILITY TO DRIVE:** Patients should be advised to take precautions to avoid hypoglycaemia whilst driving. **UNDESIRABLE EFFECTS: Very common:** Hypoglycemia. Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement. **Common:** Injection site reactions. Injection site reactions include redness, pain, itching, hives, swelling, or inflammation. Lipodystrophy and cutaneous amyloidosis with not known frequency. For uncommon, rare & very rare adverse events please consult the full SmPC. **OVERDOSAGE:** Mild episodes of hypoglycaemia can usually be treated with oral carbohydrates. More severe episodes may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. **PHARMACOLOGICAL PROPERTIES:** ATC Code: A10A E04. **MARKETING AUTHORIZATION HOLDER:** Sanofi-Aventis Deutschland GmbH, D 65926 Frankfurt am Main, Germany. **LEGAL CATEGORY:** Medicinal product subject to medical prescription. **DATE of Abbreviated Prescribing Information:** Updated based on April 2021 based on last SmPC related to version 5 CCDS. Before prescribing the product always refer to your full local prescribing information as this information may vary from country to country.

APIDRA® Abbreviated Prescribing Information

1. NAME AND PRESENTATION: Apidra 100 U/ml, solution for injection of insuline glulisine is available in a pre-filled disposable pens of 3ml for Solostar. **2.THERAPEUTIC INDICATIONS:** Treatment of adults, adolescents and children, 6 years or older with diabetes mellitus, where treatment with insulin is required. **3. POSOLOGY AND METHOD OFADMINISTRATION:** Apidra in pre-filled pen is only suitable for subcutaneous injections. Apidra should be given by subcutaneous injection shortly (0-15 min) before or soon after meals. Apidra could be used in regimens that include an intermediate or long acting insulin or basal insulin analogue and with oral hypoglycemic agents. The dosage of Apidra should be individually adjusted. When administered as a subcutaneous injection, Apidra® must not be mixed with other medicinal products except NPH human insulin. Injection sites must be rotated within a given injection area from one injection to the next, in order to reduce the risk of lipodystrophy and cutaneous amyloidosis. For administration details see full SmPC. Patients must be educated to use proper injection techniques and insulin. label must always be checked before each injection to avoid medication errors between Apidra and other insulins. **Renal impairment & hepatic impairment: i**nsulin requirements may be reduced. **Elderly:** deterioration of renal function may lead to a decrease in insulin requirements. **4. CONTRA-INDICATIONS:** Hypersensitivity to insulin glulisine or to any of the excipients. Hypoglycemia. **5. SPECIAL WARNINGS AND PRECAUTIONS FOR USE:** Transferring a patient to a new type or brand of insulin should be done under strict medical supervision. Changes in strength, brand, type, source and/or method of manufacture may result in the need for a change in dose. In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Concomitant oral antidiabetic treatment may need to be adjusted. Adjustment of dosage may be necessary if patients undertake increased physical activity or change their usual meal plan. Conditions which may take the early warning symptoms of hypoglycemia are detailed in the full SmPC. If pioglitazone is used in combination with insulin, especially in patients with CHF risk factors, patients should be observed for signs and symptoms of heart failure, weight gain and edema. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. **6. DRUG INTERACTIONS:** Substances that may enhance or reduce the blood-glucose-lowering activity and increase susceptibility to hypoglycemia are detailed in the full SmPC. **7. PREGNANCY AND LACTATION:** No adequate data are available. Pregnant and Breast-feeding mothers may require adjustments in insulin dose and diet. **8. ABILITY TO DRIVE:** The patient's ability to concentrate and react may be impaired as a result of hypoglycemia or hyperglycemia or, for example, as a result of visual impairment. Patients should be advised to take precautions to avoid hypoglycemia whilst driving. **9. UNDESIRABLE EFFECTS:** Hypoglycemia is the most frequent undesirable effect of insulin therapy. Injection site reactions and local hypersensitivity reactions. Lipodystrophy and cutaneous amyloidosis may occur at the injection site and delay local insulin absorption. Continuous rotation of the injection site within the given injection area may help to reduce or prevent these reactions For uncommon & rare adverse events, consult the full SmPC. **10. OVERDOSAGE:** Mild hypoglycemic episodes can be treated by oral administration of glucose or sugary products. Severe hypoglycemic episodes can be treated by glucagon (0.5 to 1 mg) given intramuscularly or subcutaneously or by glucose given intravenously.**11. PHARMACODYNAMIC PROPERTIES:** ATC code: A10AB06. **12. MARKETING AUTHORIZATION HOLDER:**Sanofi_-Aventis Deutschland GmbH, D-65926 Frankfurt am Main.Abbreviated Prescribing Information, **Date of Revision of API**: based on the EU SmPC as of Jun 2021 on last SmPC related to CCDS V12.

Always refer to the full Summary of Product Characteristics (SmPC) before prescribing

Thank you