Tresiba®

L’efficacité sans compromis

Pr Samia Zekri

Symposium Novo nordisk

Congrès national de la SAMEV – Hôtel Mercure – Alger, le 19 Mai 2023

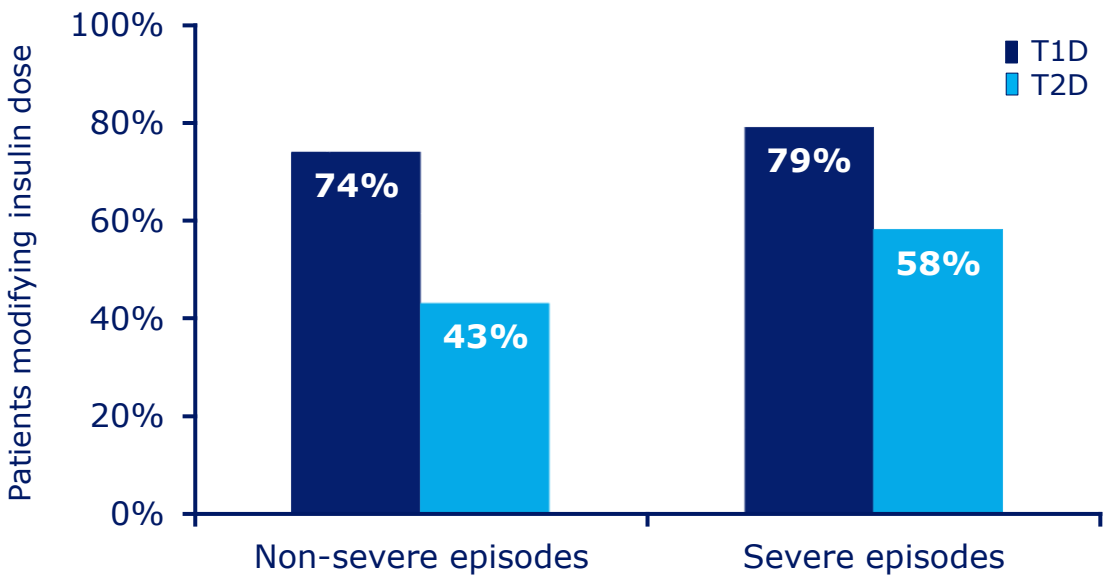
Introduction

- Peu de nos patients atteignent la cible glycémique
- Le frein principal de cette situation est représenté par la crainte des hypoglycémies.
- Degludec analogue d’insuline basale de nouvelle génération apporte t- elle une valeur ajoutée à la prise en charge des patients vivants avec un diabète ?

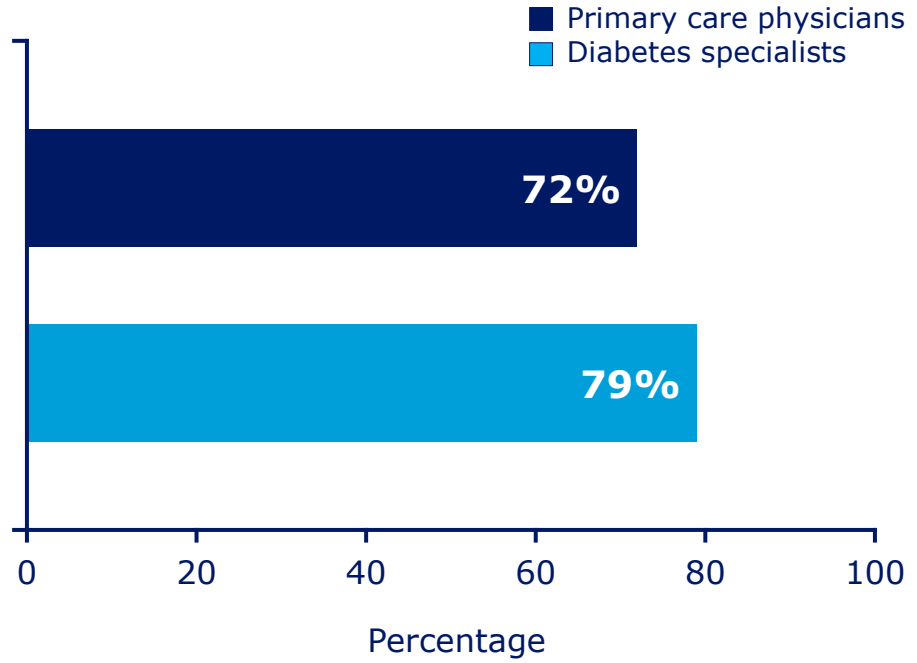
Les défis de l’équilibre glycémique

La peur de l'hypoglycémie est en contradiction avec le succès du traitement, aussi bien pour les patients que pour les cliniciens

Pourcentage de patients diminuant leur dose d'insuline suite à un événement hypoglycémiant



Je traiterais mes patients plus agressivement s'il n'y avait aucune inquiétude concernant l'hypoglycémie



- Total patient sample, n=335 (T1D, n=202; T2D, n=133)
- T1D, type 1 diabetes; T2D, type 2 diabetes

Leiter *et al. Can J Diabetes* 2005;29:186–92

GAPP™ (A global internet survey of patient and physician beliefs regarding insulin therapy): n=1250 physicians

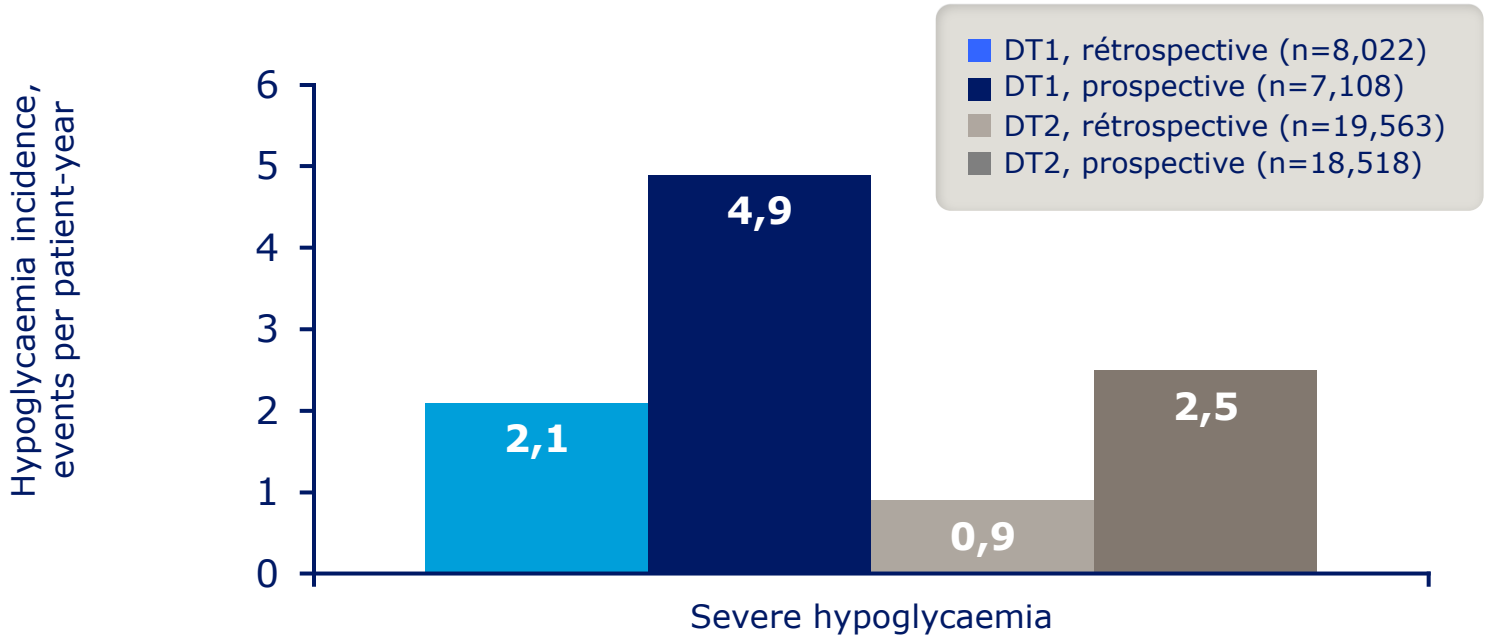
Peyrot *et al. Diabet Med* 2012;29:682–9

Les taux d'hypoglycémie sont plus élevés que prévu

Résultats de HAT study

HAT study

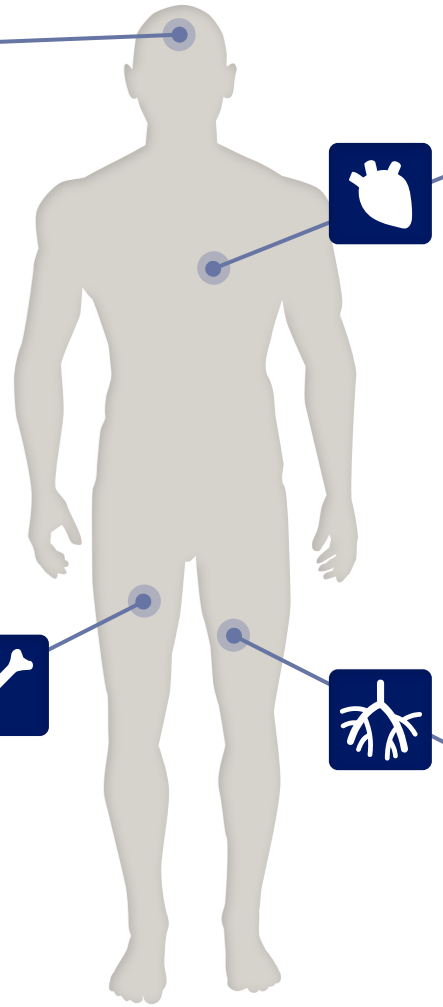
- Rétrospective non interventionnelle, mondiale, de 6 mois et étude prospective de 1 mois sur les événements hypoglycémiques autodéclarés par le patient
- n=27,585 (DT1: 8,022; DT2: 19,563)



Les données prospectives suggèrent des taux d'hypoglycémie plus élevés que précédemment observés chez DT1 et DT2, en particulier dans les évènements graves

- HAT, Hypoglycaemia Assessment Tool; T1D, type 1 diabetes; T2D, type 2 diabetes
- Khunti *et al. Diabetes Obes Metab* 2016: 2016;18:907–15; Khunti *et al.* Poster presented at the 10th International Diabetes Federation-Western Pacific Region Congress, 21–24 November 2014, Singapore

Les conséquences de l'hypoglycémie



Cerveau

Dysfonctionnement cognitif
convulsions, comas
Effets psychologiques

Coeur

Infarctus du myocarde
Arythmies cardiaques

Appareil locomoteur

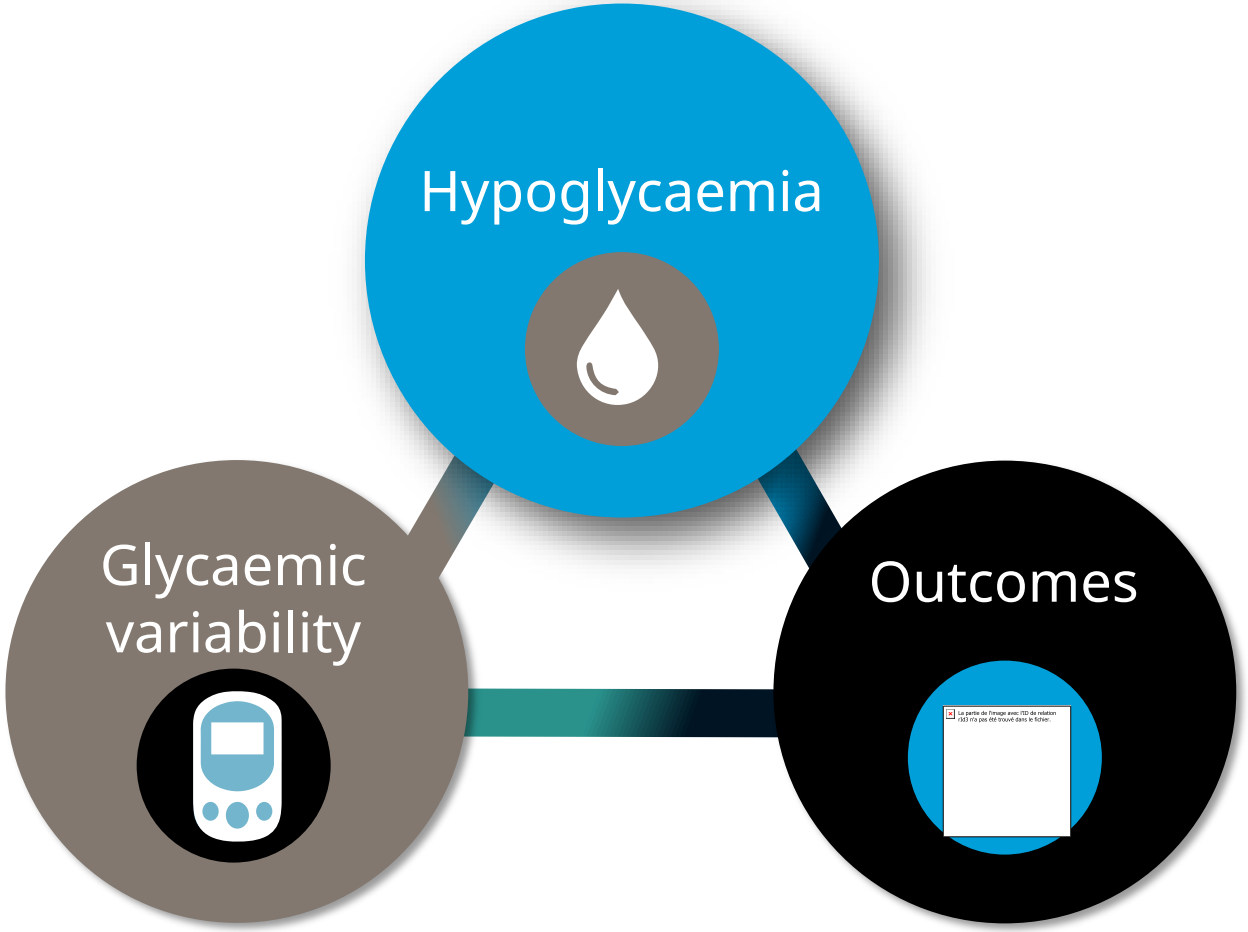
Chutes, accidents, accidents de conduite
Fractures
Luxations

Circulation

Inflammation
Anomalies de la coagulation sanguine
Changements hémodynamiques
Dysfonction endothéliale

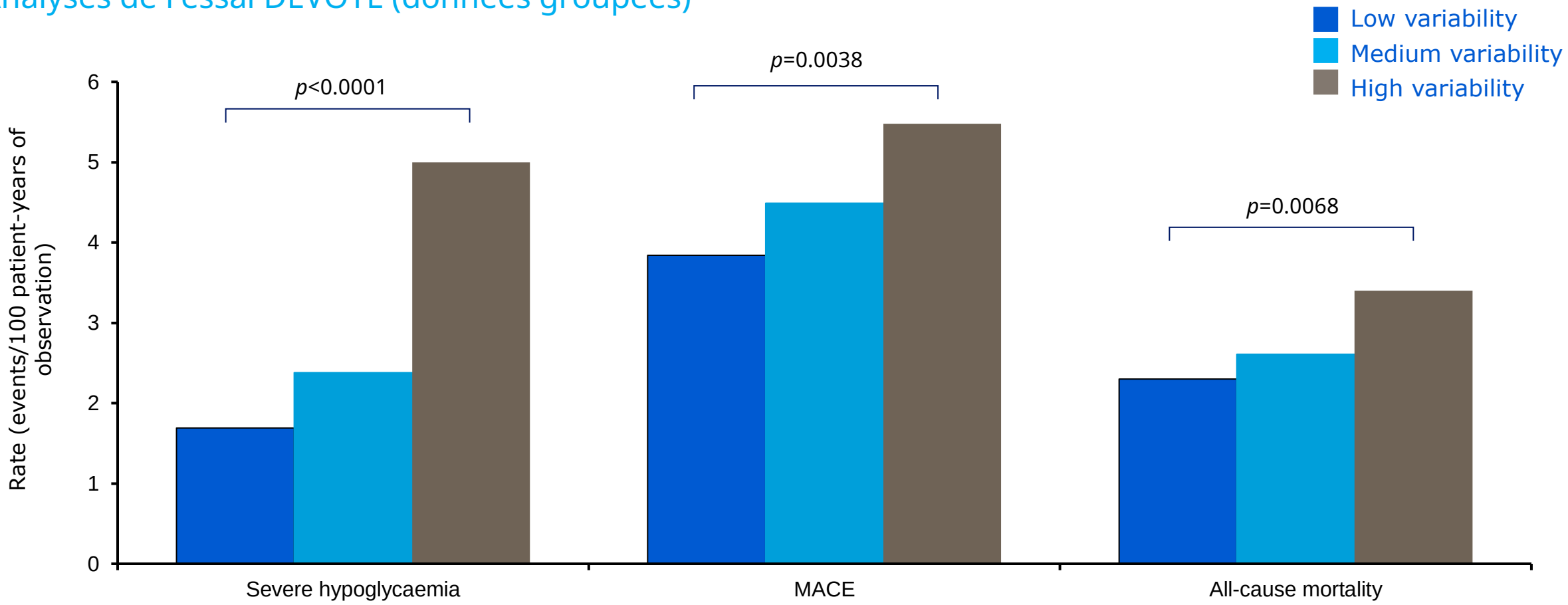
- Desouza *et al. Diabetes Care* 2010;33:1389–94; Frier *et al. Diabetes Care* 2011;34(Suppl. 2):S132–7; Frier. *Nat Rev Endocrinol* 2014;10:711–22; Gjedde *et al. Diabetes* 2015;64(Suppl. 1):A91

Relations entre variabilité glycémique, hypoglycémies, et complications cardio-vasculaires du diabète



L'augmentation de la variabilité de la glycémie à jeun accroît considérablement le risque d'hypoglycémie, de MACE et de mortalité toutes causes confondues.

Analyses de l'essai DEVOTE (données groupées)



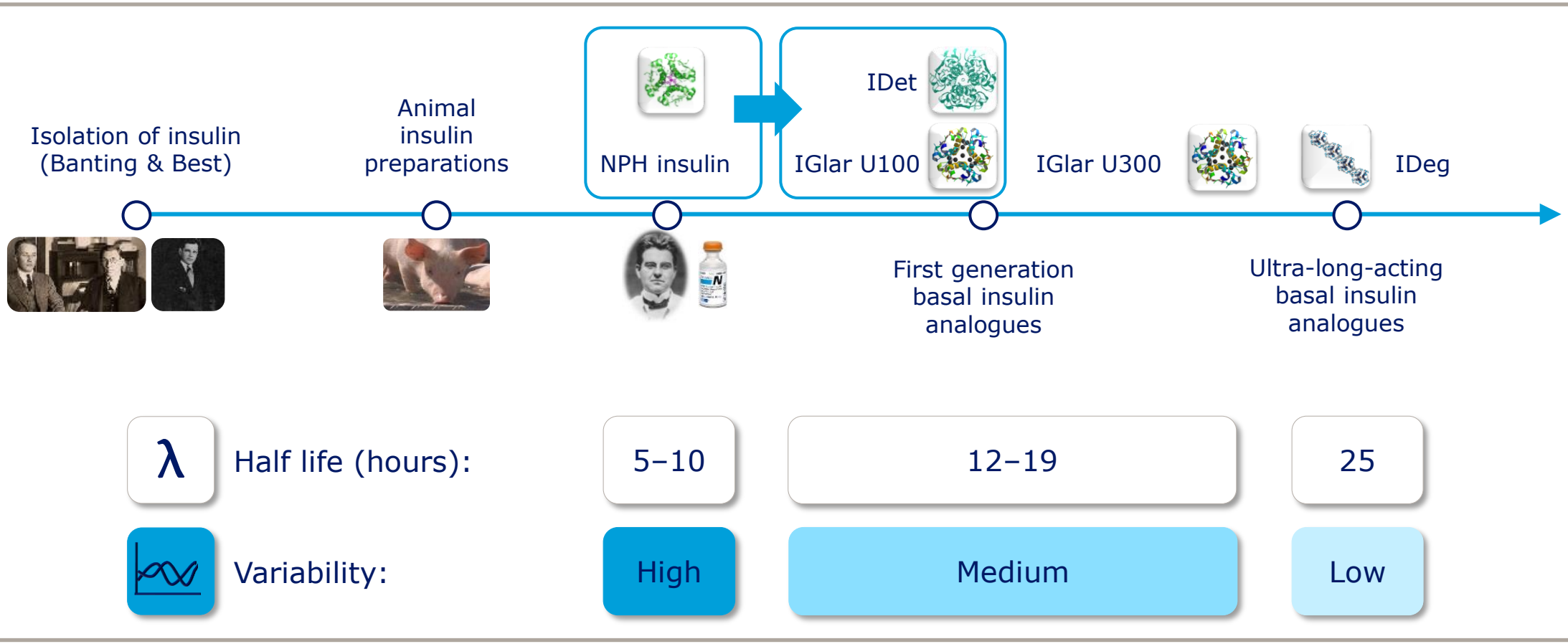
Variabilité définie à partir des mesures de la glycémie à jeun 3 jours avant chaque contact mensuel

MACE, major adverse cardiovascular event
Adapted from Zinman et al. Diabetologia 2018;61:48–57

Besoin en innovation

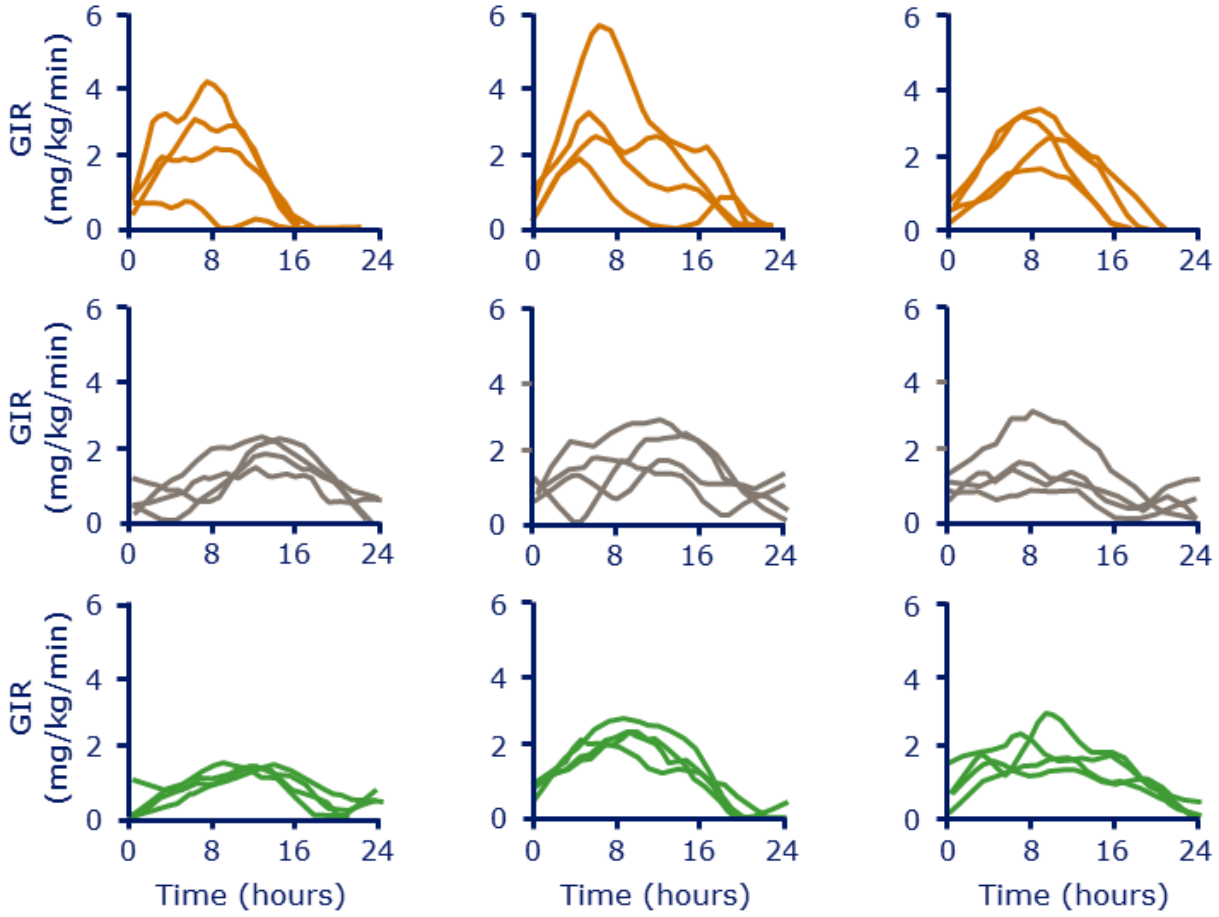
La quête de l'insuline basale idéale

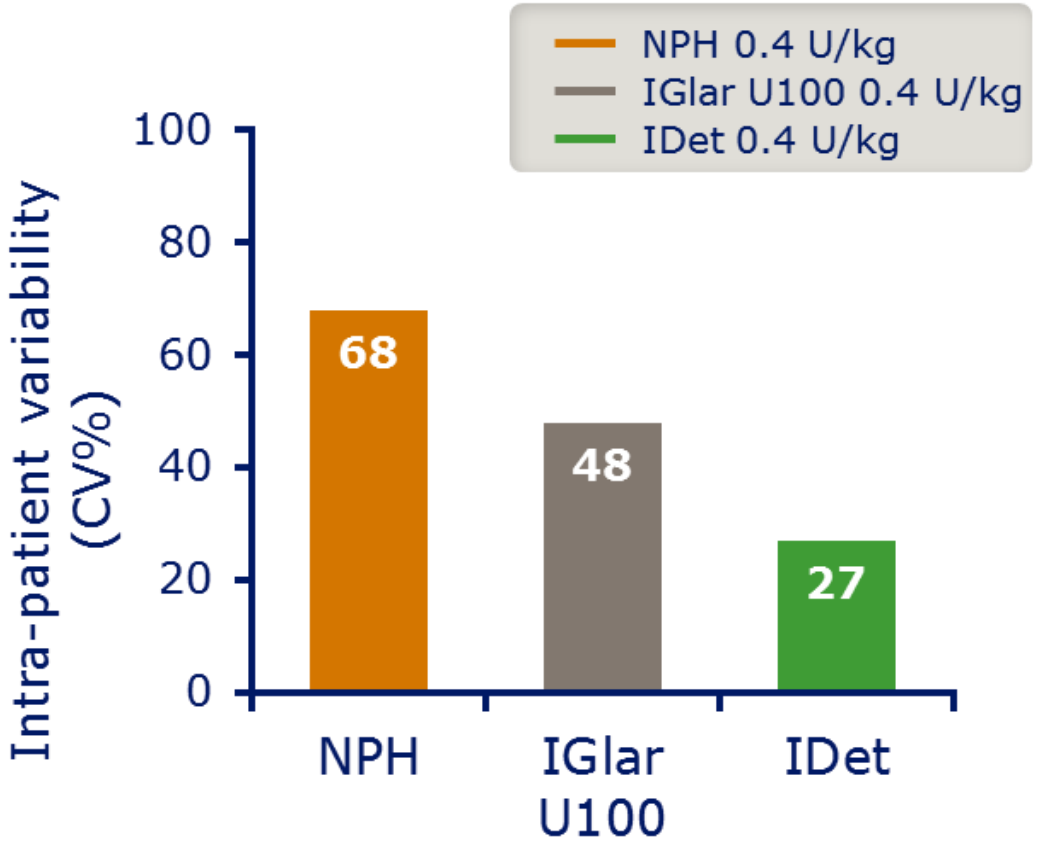
De la NPH aux insulines basales analogues



IDeg, insulin degludec; IDet insulin detemir; IGlar, insulin glargine; NPH, neutral protamine Hagedorn
NPH SmPC. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000441/WC500033307.pdf;
IDet SmPC. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000528/WC500036662.pdf;
IGlar U100 SmPC. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000284/WC500036082.pdf;
IGlar U300 SmPC. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000309/WC500047935.pdf;
IDeg SmPC. http://ec.europa.eu/health/documents/community-register/2013/20130121124987/anx_124987_en.pdf. All accessed December 2016

Variabilité quotidienne de l'effet de l'insuline plus faible avec les analogues de l'insuline basale de première génération par rapport à la NPH

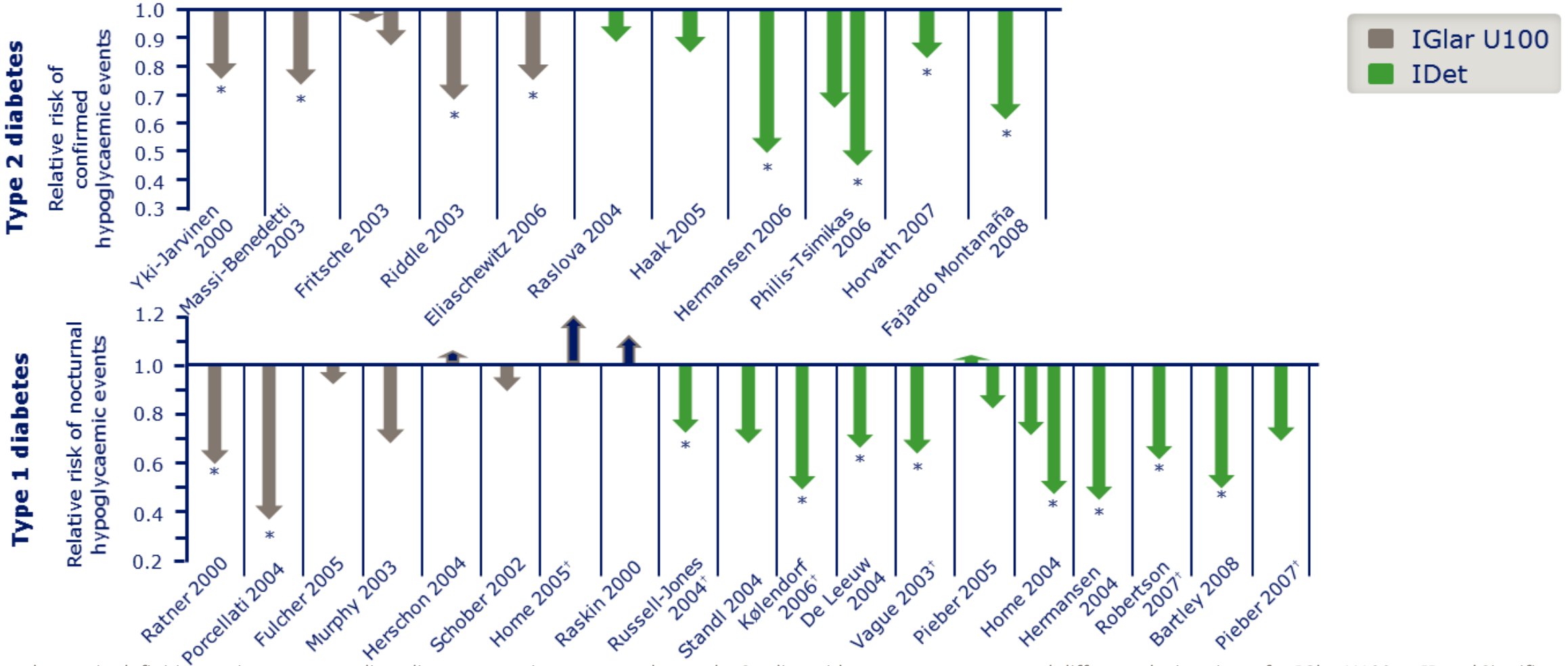




CV, coefficient of variation; GIR, glucose infusion rate

Heise *et al. Diabetes* 2004;53:1614–20.

Réduction du risque d'hypoglycémie avec les analogues de l'insuline basale de première génération par rapport à la NPH



Hypoglycaemia definition varies across studies; direct comparisons cannot be made. Studies with two arrows compared different dosing times for IGlar U100 or IDet. *Significant difference; †Not treat-to-target. Devries et al. Diabetes Metab Res 2007;23:441–54; Fajardo Montanaña et al. Diabet Med 2008;25:916–23; Horvath et al. Cochrane Database Syst Rev 2007;18:CD005613; Robertson et al. Diabet Med 2007;24:27–34; Bartley et al. Diabet Med 2008;25:442–9;
Pieber et al. Diabet Med 2007;24:635–42.

Objectifs du développement d'une nouvelle insuline basale

- Contrôle glycémique
- Administration une fois par jour
- Faible risque d'hypoglycémie
- Flexibilité de l’horaire d’injection

→

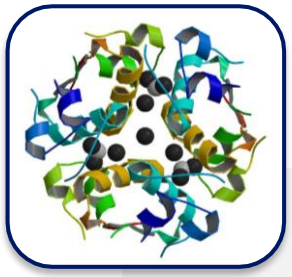
Efficacité
(effet hypoglycémiant)

Profil glycémique plat

Faible variabilité

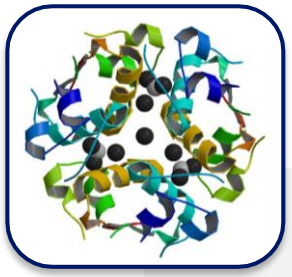
Longue durée d'action

IGlar U100, IGlar U300 et l’insulin degludec



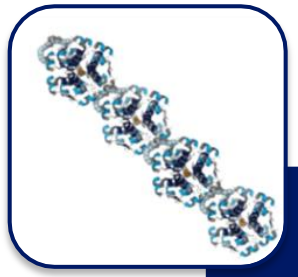
IGlar U100

- Première génération d’insuline basale
- Précipite en microcristaux
- Demi vie ~12 heures



IGlar U300

- Ultra-concentration d’insuline basale de première génération
- Précipite en microcristaux
- Demi vie ~19 heures



Insulin degludec

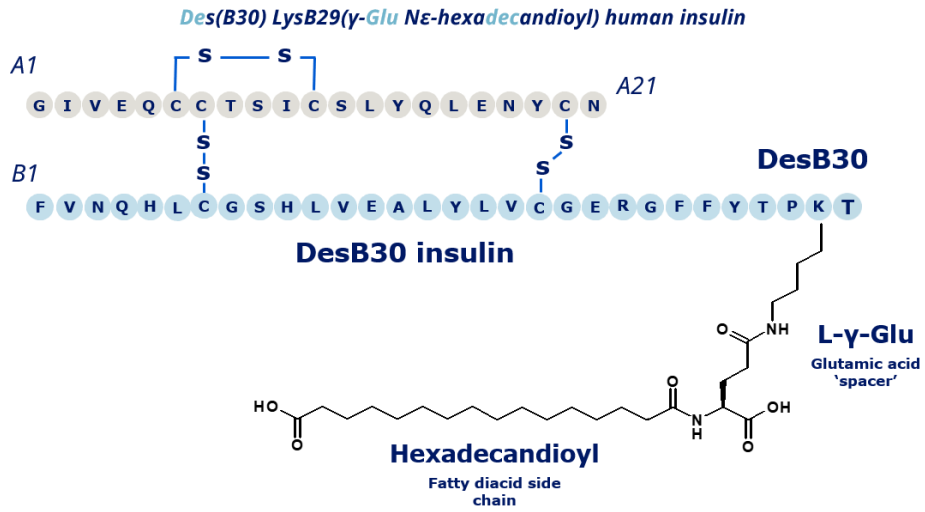
- Nouvelle generation d’insuine basale à ultra longue durée d’action
- Formation de multihexamères
- Demi vie ~25 heures

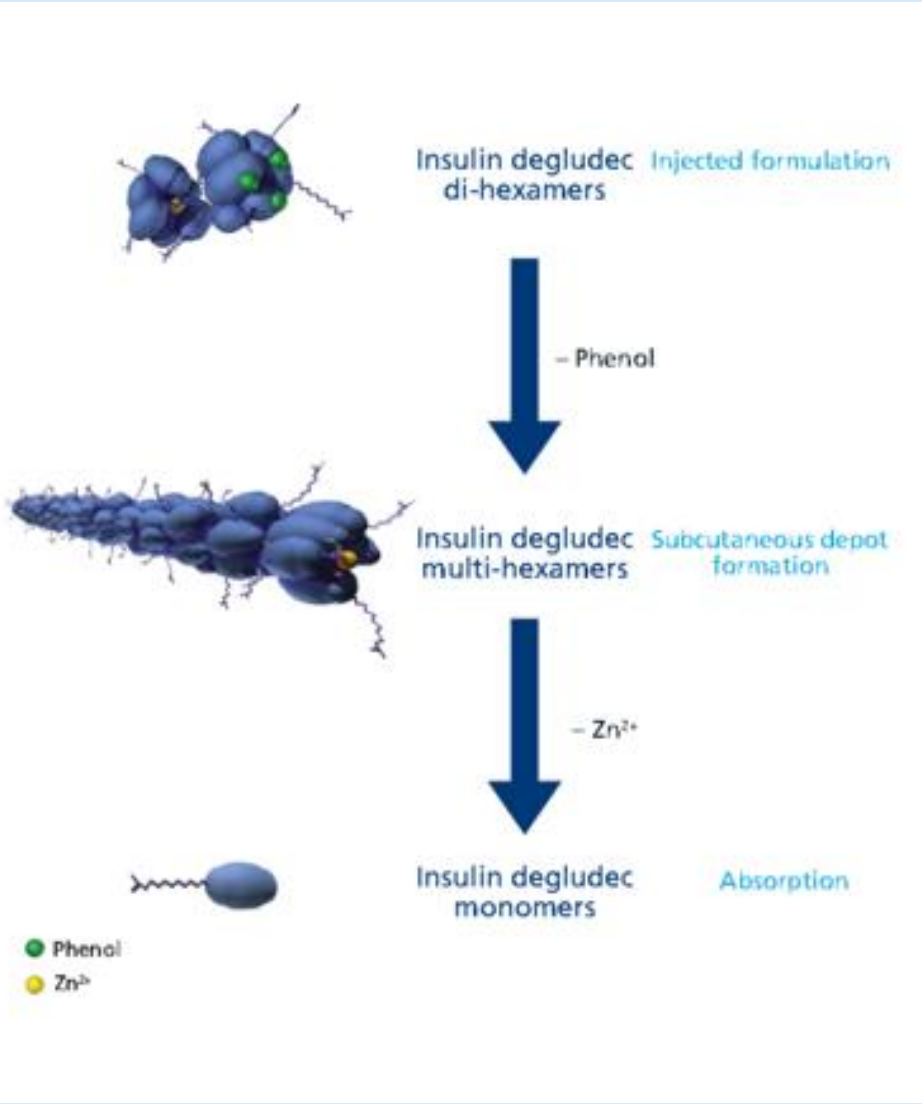
Glargine U100 image data on file; IGlar U300 optical microscopy images obtained from European patent application http://worldwide.espacenet.com/publicationDetails/originalDocument?CC=EP&NR=2387989A2&KC=A2&date=&FT=D&locale=en_EP.
IGlar U100, insulin glargine 100 units/mL; IGlar U300, insulin glargine 300 units/mL.
1. Jonassen I et al. *Pharm Res*. 2012;29:2104–14; 2. Heise T et al. *Expert Opin Drug Metab Toxicol*. 2015;11:1193–201;
3. Heise T et al. *Diabetes Obes Metab*. 2012;14:859–64.

Insuline degludec Structure moléculaire innovante

Degludec

Rationally designed, beyond sequence modification



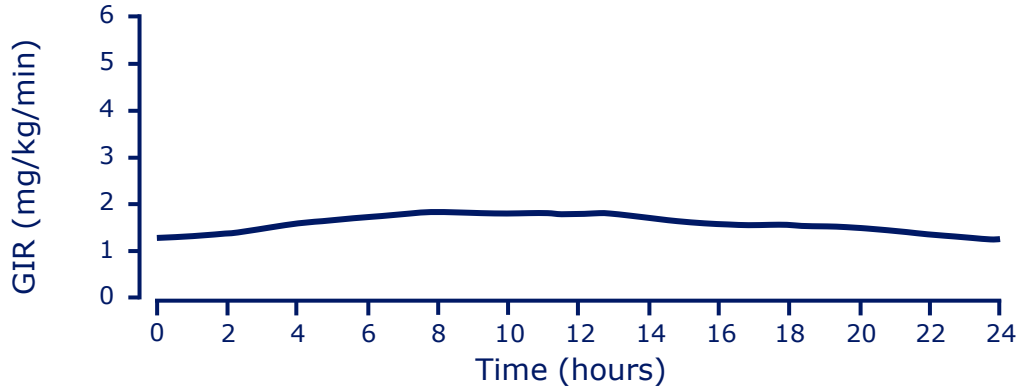


Caractéristiques pharmacologiques de Tresiba®

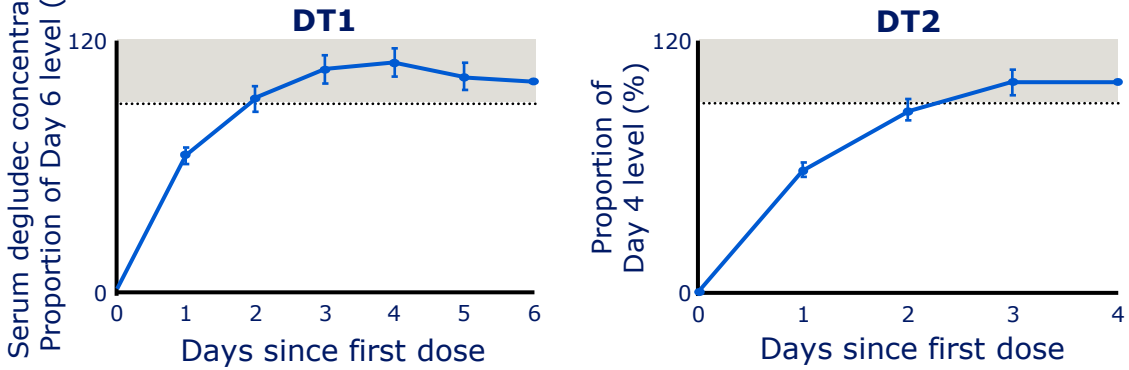
Demi-vie deux fois plus longue avec l'insuline degludec en comparaison à la glargine U100

	Degludec			Glargine U100		
	0.4 U/kg	0.6 U/kg	0.8 U/kg	0.4 U/kg	0.6 U/kg	0.8 U/kg
Half-life (hours)	25.9	27.0	23.6	11.5	12.9	11.9
Mean half-life	**25.4**			**12.1**		

Profil temps-action plat à l'état d'équilibre



La concentration de degludec atteint l'état d'équilibre clinique en 2 ou 3 jours

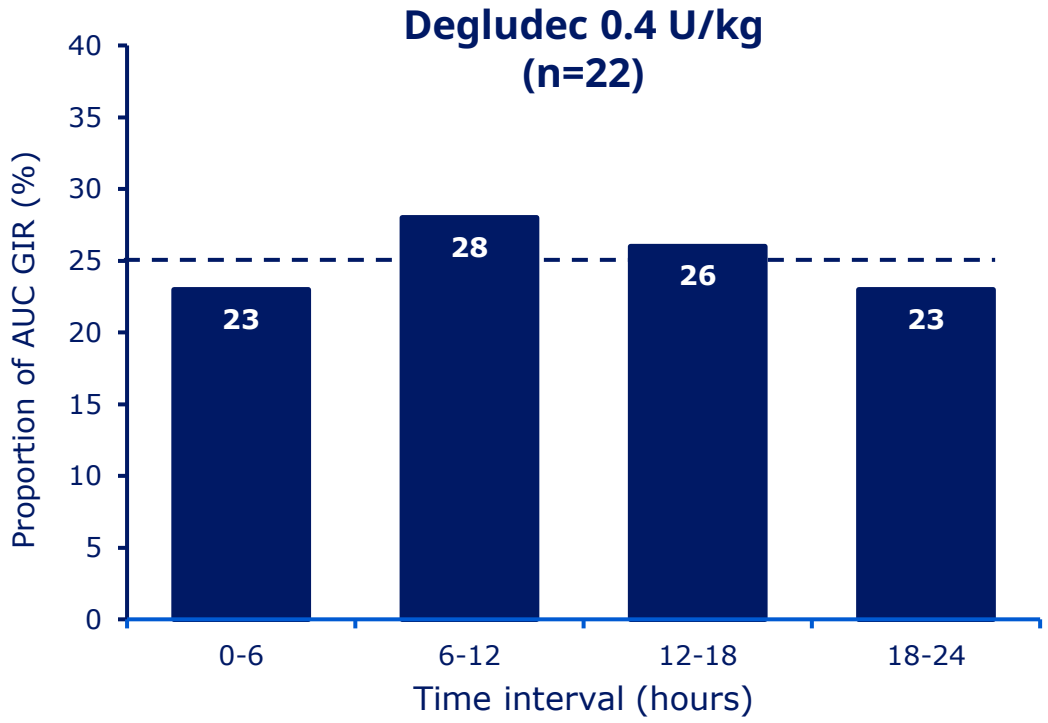


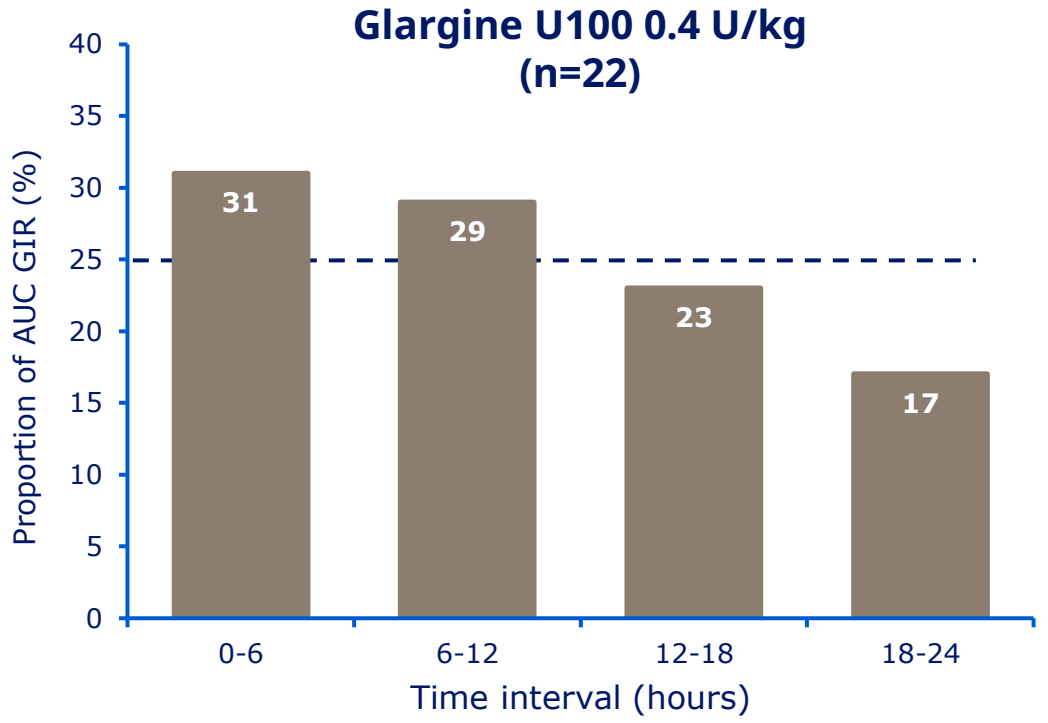
GIR, glucose infusion rate; glargine U100, insulin glargine 100 units/mL; T1D, type 1 diabetes; T2D, type 2 diabetes

Heise et al. Diabetes 2011;60(Suppl. 1):LB11; Heise et al. Expert Opin Drug Metab Toxicol 2015;11:1193–201; Heise et al. Diabetes 2012;61(Suppl. 1):A259; Heise et al. J Diabetes Sci Technol 2018;12:356-363

La variabilité d'effet glycémique intra-journalière est moindre avec Tresiba® qu'avec glargine U100

L'effet hypoglycémiant total était plus uniformément réparti sur un intervalle de 24 heures avec degludec qu'avec la glargine U100





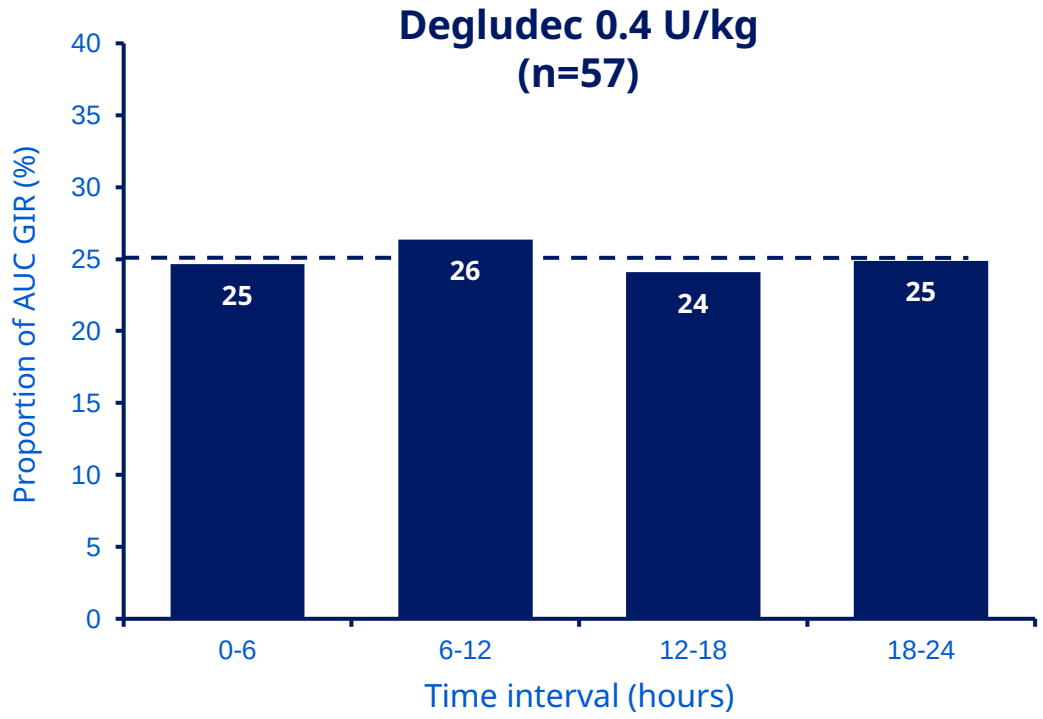
Proportion of effect in 6-hour time intervals across one dosing interval (%); patients with T1D (n=66)[1]

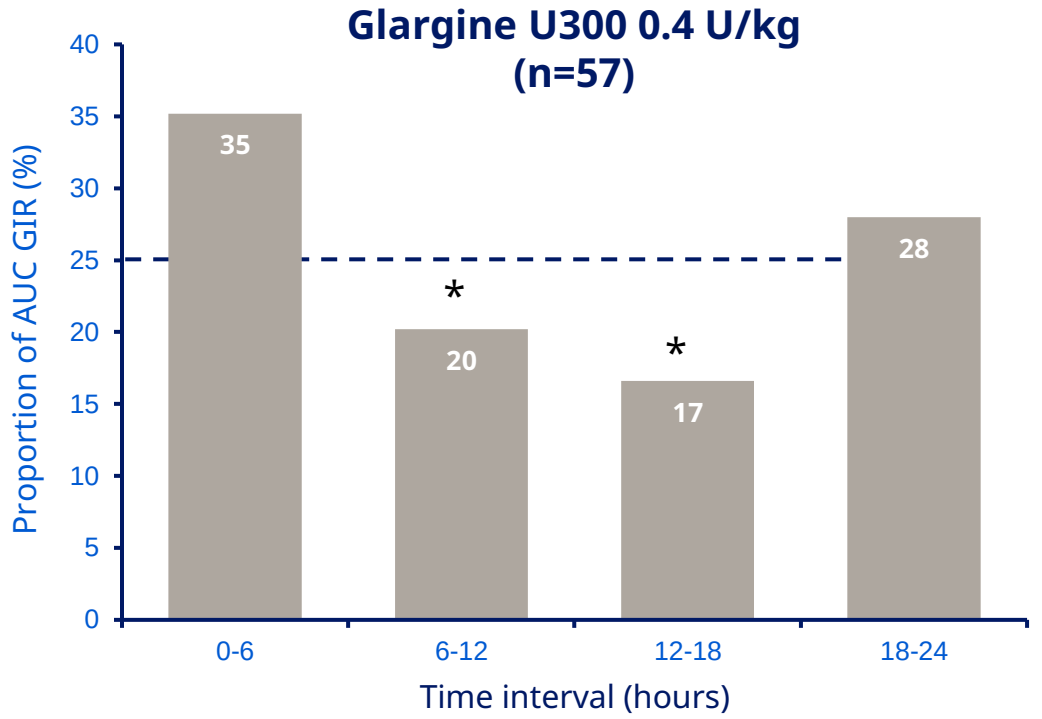
AUC, area under the curve; GIR, glucose infusion rate; glargine U100, insulin glargine 100 units/mL; T1D, type 1 diabetes

Heise et al. Expert Opin Drug Metab Toxicol 2015;11:1193–201

La variabilité d'effet glycémique intra-journalière est moindre avec Tresiba® qu'avec glargine U300

Degludec a présenté une variabilité intra-journalière de l'effet hypoglycémiant moindre d'environ 40 % à celle de la glargine U300.†**



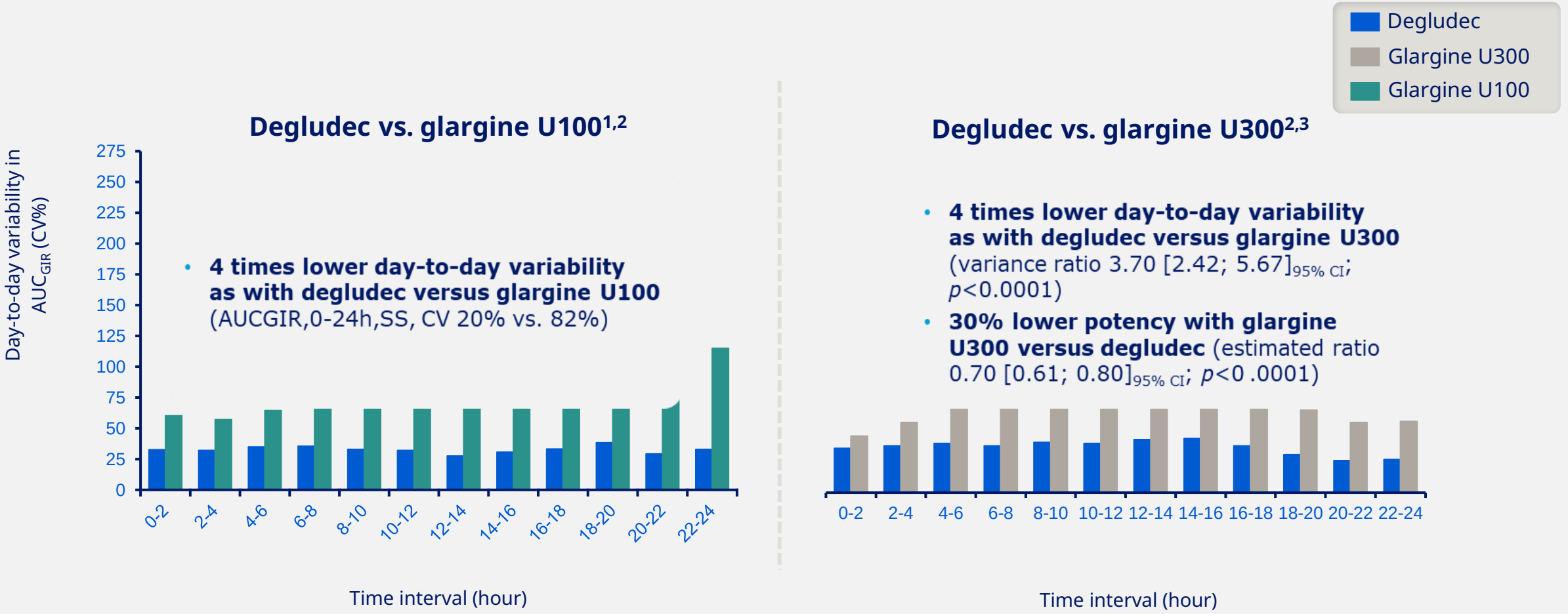


*Proportion of effect in 6-hour time intervals across one dosing interval (%); *p<0.0001 compared with the 0–6 hour and 18–24 hour interval; **calculated at relative fluctuations and given in geometric means. †post hoc analysis[1]*

AUC, area under the curve; GIR, glucose infusion rate; glargine U300, insulin glargine 300 units/mL

Heise et al. Diabetes Obes Metab 2017;19:1032–9

Lower day-to-day variability in glucose-lowering effect for degludec versus glargine U100 and U300



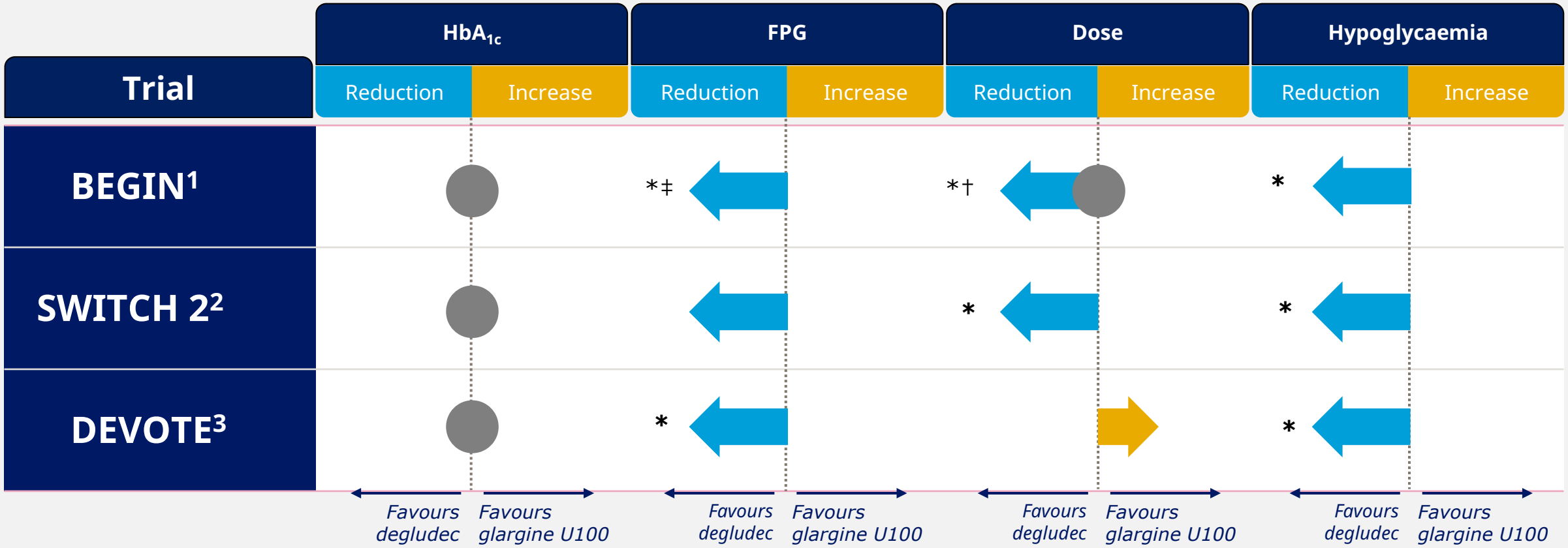
AUC, area under the curve; CV, coefficient of variation; GIR, glucose infusion rate; glargine U100, insulin glargine 100 units/mL; glargine U300, insulin glargine 300 units/mL

1. Heise *et al. Diabetes Obes Metab* 2012;14:85–64; 2. Heise *et al. J Diabetes Sci Technol* 2018;12:356-363; 3. Heise *et al. Diabetes Obes Metab* 2017;19:1032–9

Programme de developpement de phase 3 de Tresiba®

Novo Nordisk®

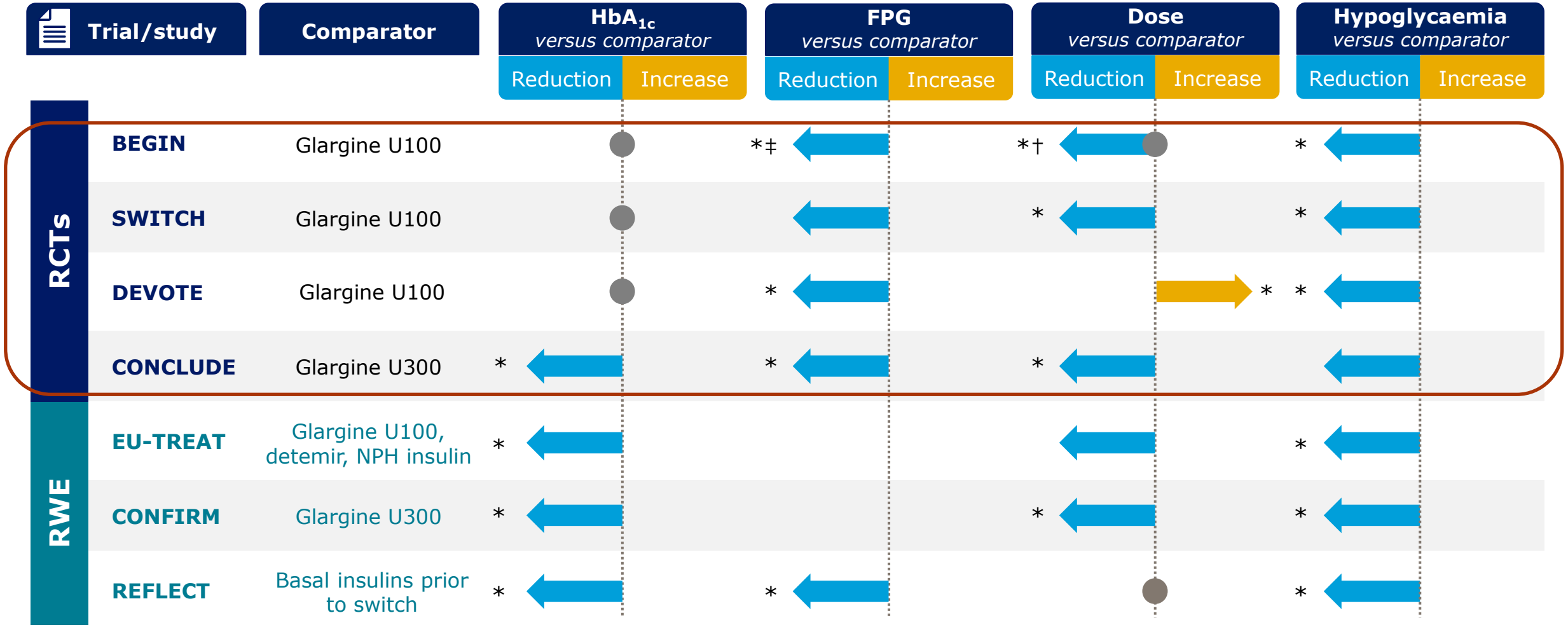
Degludec vs. glargine U100 chez des patients diabétiques de type 2



*Significant difference, †Insulin-naïve: significantly reduced dose, basal–bolus: no difference; ‡ Insulin-naïve: significant reduction, basal–bolus: not significant
FPG, fasting plasma glucose; glargine U100/U300, insulin glargine 100/300 units/mL; RCTs, randomised controlled trials; T2D, type 2 diabetes
1. Ratner et al. Diabetes Obes Metab 2013;15:175–84; 2. Wysham et al. JAMA 2017;318:45–56 3. Marso et al. N Engl J Med 2017;377:723–32

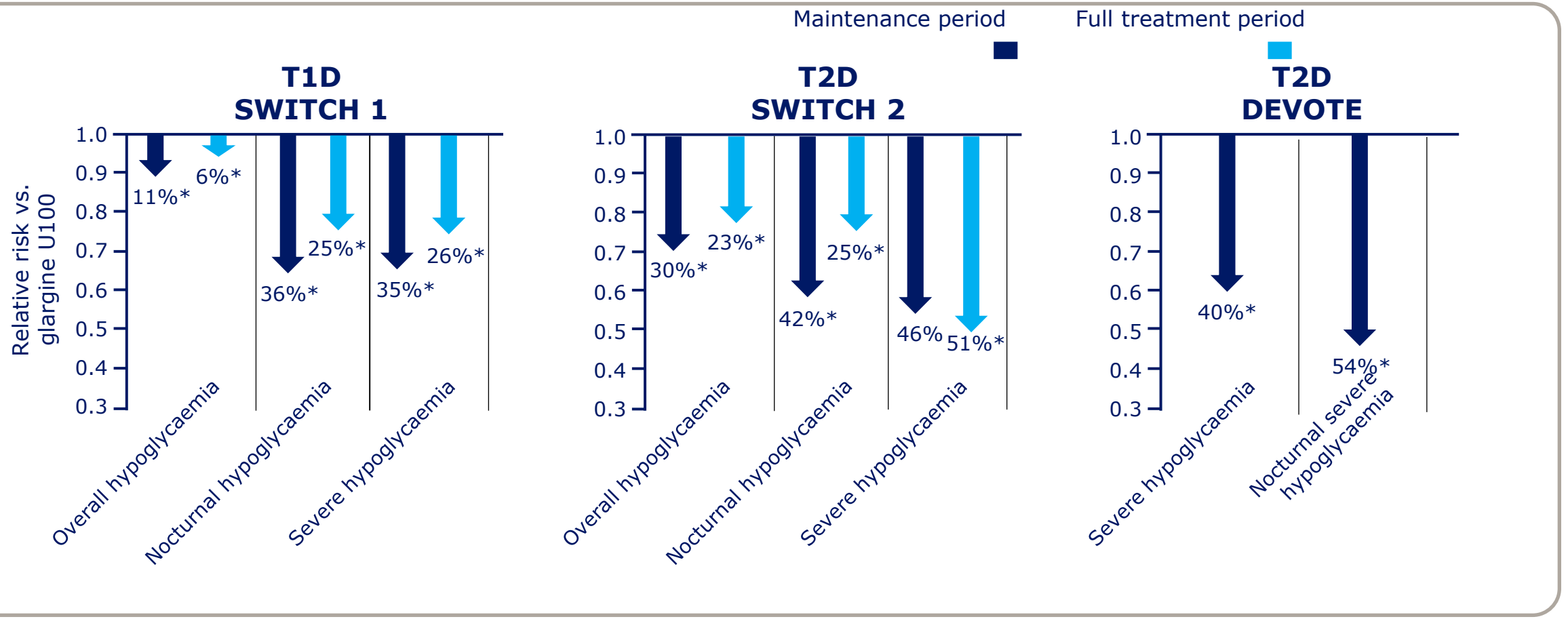
Tresiba®,
Quels bénéfices *vs* insuline glargine ?

Évidences cliniques – Preuves Cliniques Tresiba® à travers les RCTs et les RWE



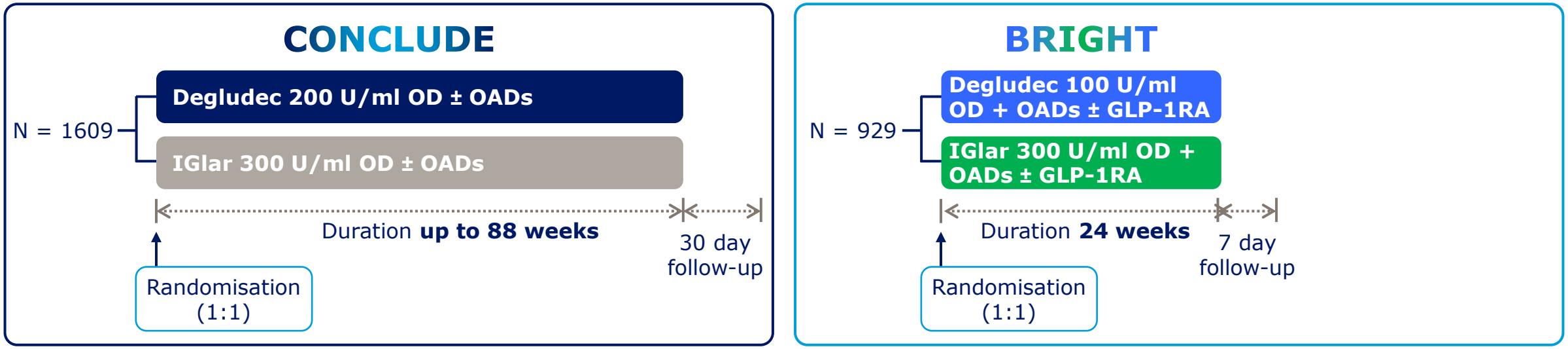
*Significant difference. †Insulin-naïve: significantly reduced dose, basal–bolus: no difference. ‡Insulin-naïve: significant reduction, basal–bolus: not significant. FPG, fasting plasma glucose; glargine U100/U300, insulin glargine 100/300 units/mL; NPH, neutral protamine Hagedorn; RCTs, randomised controlled trials; RWE, real-world evidence; T2D, type 2 diabetes

Études comparatives vs iGlar U100:
Réduction significative du risque d'hypoglycémies avec Tresiba® vs iGlar U100



- *Significant difference. Overall hypoglycaemia: severe or BG-confirmed hypoglycaemia; nocturnal hypoglycaemia, severe or BG-confirmed hypoglycaemia occurring between 00:01 am and 05:59 am, both inclusive; severe hypoglycaemia, an episode requiring third-party assistance and external adjudication BG, blood glucose; glargine U100, insulin glargine 100 units/mL; T1D, type 1 diabetes; T2D, type 2 diabetes
- Lane *et al. JAMA* 2017;318:33–44; Wysham *et al. JAMA* 2017;318:45–56; Marso *et al. N Engl J Med* 2017;377:723–32

Études comparatives vs iGlar U300:
CONCLUDE vs BRIGHT



	CONCLUDE[1]	BRIGHT[2]
Patient /population	Insulino-experimenté	Insulino-naïf
Critères d'inclusion/ D'exclusion	Patients inclus présentant au moins un critère de risque d'hypoglycémie	Exclusion des patients ayant présenté des épisodes d'hypoglycémies répétées et/ou non sensibilisé au risqué d'hypoglycémie
Administration	Randomisation selon administration le matin ou le soir	Administration du soir (18:00-20:00 hrs)
Objectif SMPG de titration	4.0-5.0 mmol/L	4.4-5.6 mmol/L
Objectif principal	épisodes d'hypoglycémie symptomatique sévères ou confirmés par le BG pendant la période d'entretien	Variation de l'HbA1c entre le début et la fin de l'étude

EOT, end of treatment; OAD, oral antidiabetes drug; OD, once daily; SMPG, self-measured plasma glucose

1. Philis-Tsimikas et al. J Diabetes Sci Technol 2019;13:498–506. 2. Rosentock et al, Diabetes Care, 2018, 41: 2147-2154

CONCLUDE and BRIGHT

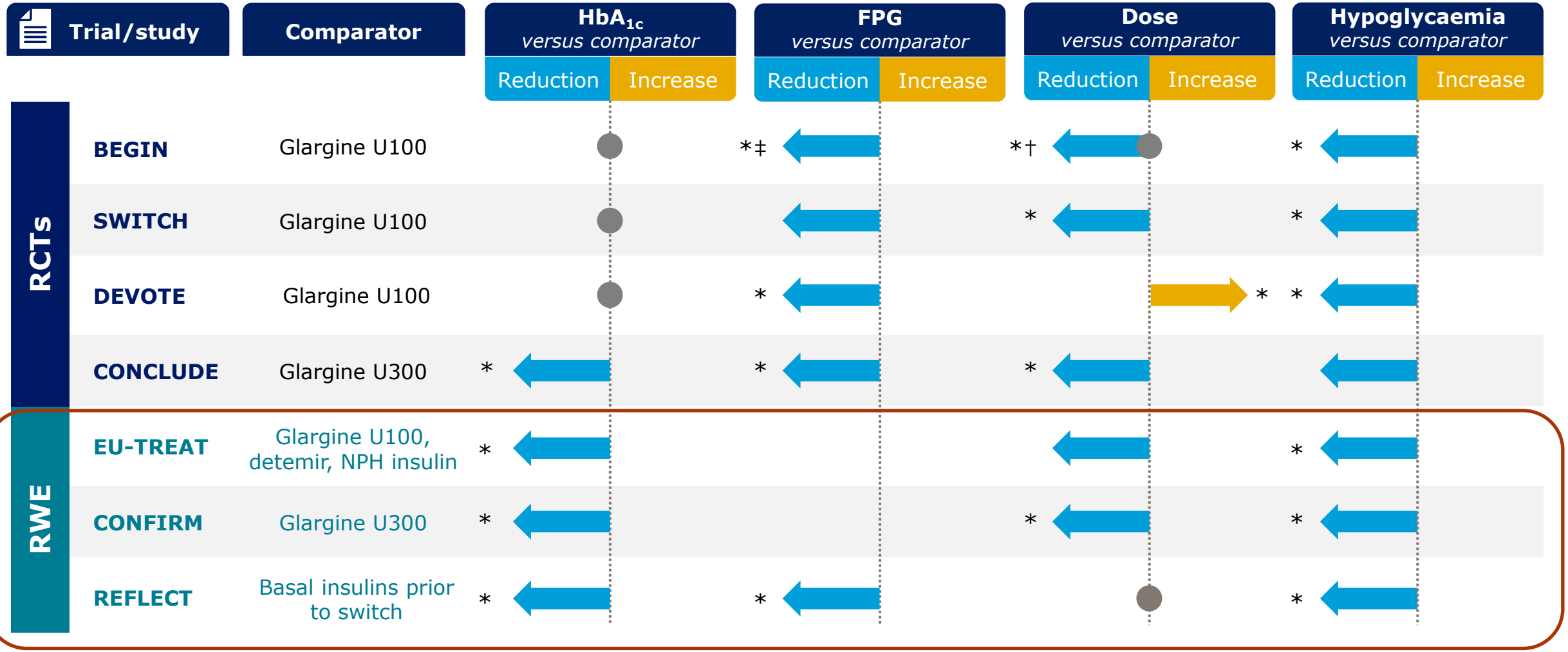
Comparatif des résultats

Endpoints		CONCLUDE[1]	BRIGHT[2]
HbA_{1c}		**Lower with degludec vs glargine U300**	Similar reduction
Dose		**12% lower for degludec vs glargine U300**	**20% lower for degludec vs glargine U300**
FPG		**Lower with degludec vs glargine U300**	**Lower with degludec vs glargine U300**
Rate of hypoglycaemia	**Titration period***	• **Overall symptomatic hypoglycaemia: Lower with degludec vs glargine U300** • Other definitions: comparable	**Lower with glargine U300 vs degludec**
	Maintenance period†	• Overall symptomatic hypoglycaemia: comparable • **Other definitions: Lower with degludec vs glargine U300**	Comparable
	Total treatment period‡	**Lower with degludec vs glargine U300**	Comparable
Proportion of patients with hypoglycaemia	**Titration period***	Comparable	**Lower with glargine U300 vs degludec§**
	Maintenance period†	**Lower with degludec vs glargine U300**	Comparable
	Total treatment period‡	**Lower with degludec vs glargine U300**	Comparable

*Titration period: 12 weeks in BRIGHT and 16 weeks in CONCLUDE; †Maintenance period: 12 weeks in BRIGHT and 36 weeks in CONCLUDE; ‡Total treatment period: 24 weeks in BRIGHT and up to 88 weeks in CONCLUDE; §Anytime hypoglycaemia (nocturnal hypoglycaemia was comparable)

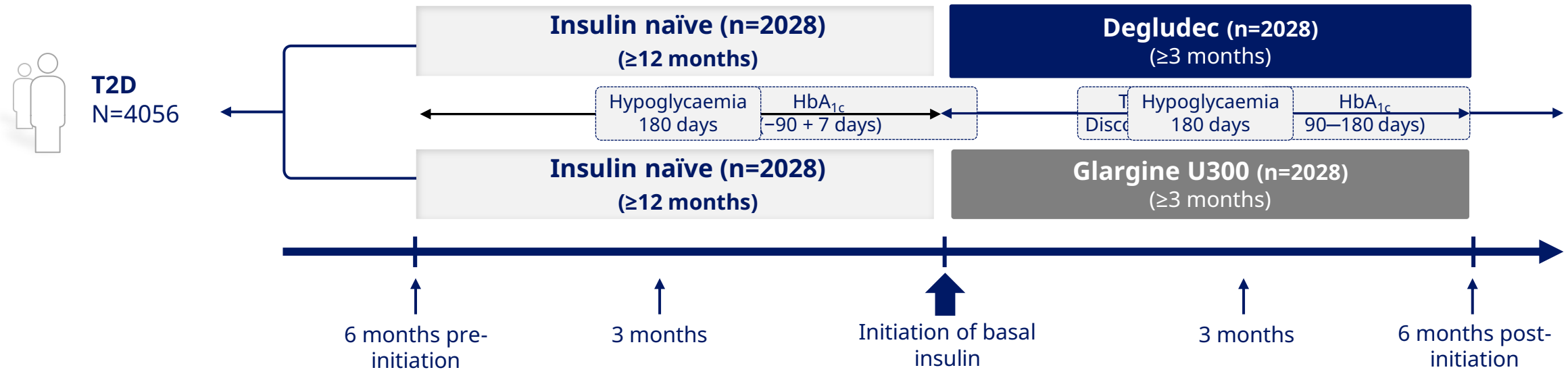
1. Philis-Tsimikas et al. *Diabetologia*. 2020. DOI: 10.1007/s00125-019-05080-9; 2.Rosenstock et al. *Diabetes Care*. 2018;41:2147–2154

Totality of Evidence - Consistency across degludec clinical trial programme of RCTs and RWE



*Significant difference. †Insulin-naïve: significantly reduced dose, basal–bolus: no difference. ‡Insulin-naïve: significant reduction, basal–bolus: not significant. FPG, fasting plasma glucose; glargine U100/U300, insulin glargine 100/300 units/mL; NPH, neutral protamine Hagedorn; RCTs, randomised controlled trials; RWE, real-world evidence; T2D, type 2 diabetes

CONFIRM: design de l'étude



Primary endpoint

- Change in mean HbA_{1c} from the initiation date until 180-day follow-up

Secondary endpoints

- Change in rate of overall hypoglycaemic episodes from the initiation date until 180-day follow-up
- Change in the proportion of patients with ≥1 hypoglycaemic episodes from the initiation date until 180-day follow-up
- Time-to-discontinuation of first prescribed basal insulin

Exploratory endpoint

- Mean basal insulin dose (units/day) at 180-day follow-up

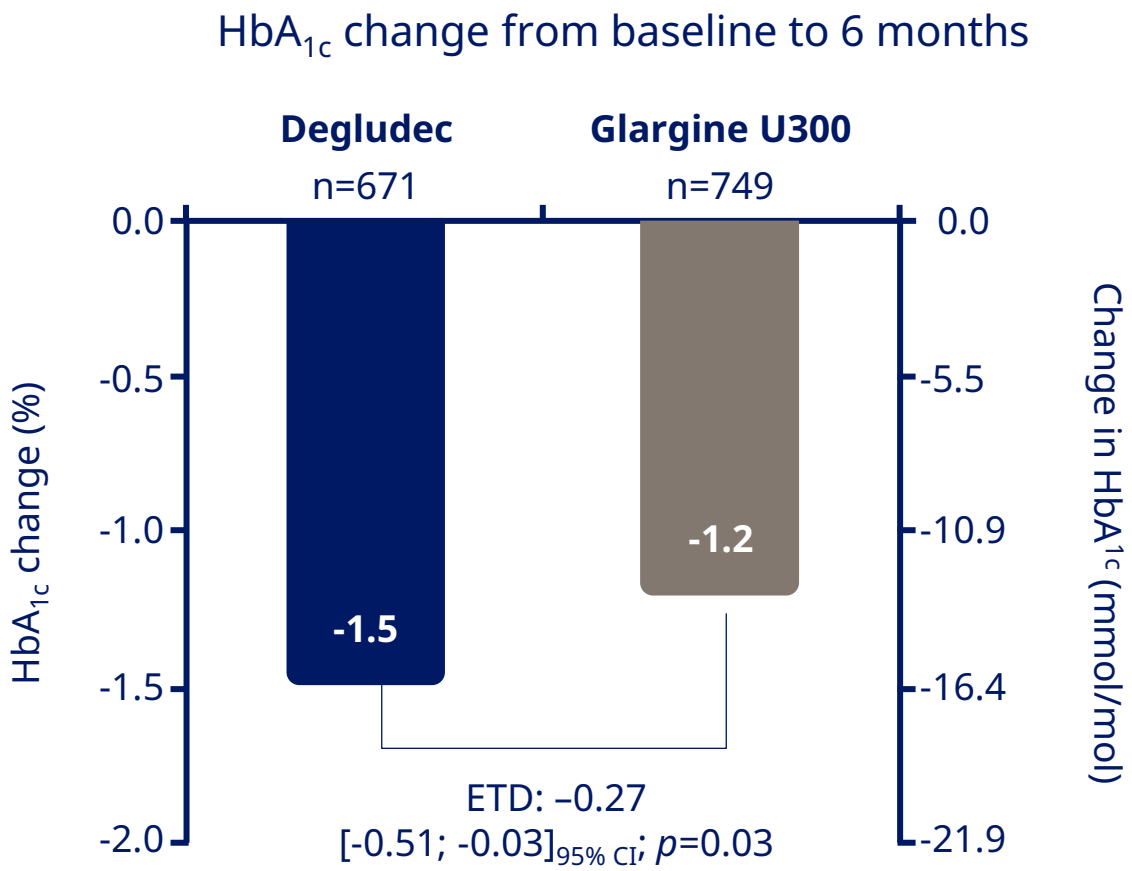
Hypoglycaemia definition

- Captured during hospital/clinic visit
- Defined according to International Classification of Diseases clinical modification codes 9/10[1]

- *Glargine U300, insulin glargine 300 units/mL; T2D, type 2 diabetes*
- *Tibaldi et al. Diabetes Obes Metab 2019; 21(4): 1001-1009*

CONFIRM: contrôle glycémique

Tresiba provided a **greater reduction in HbA_{1c}** when compared with glargine U300 (ETD –0.3%, *p*=0.03)

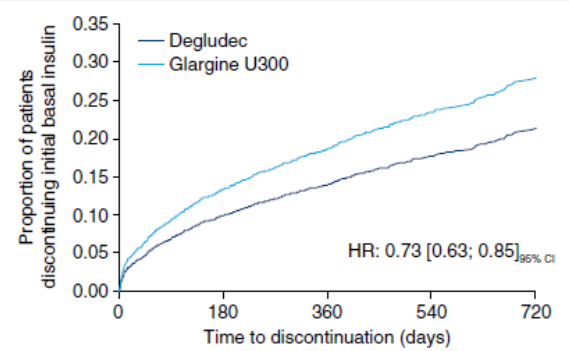


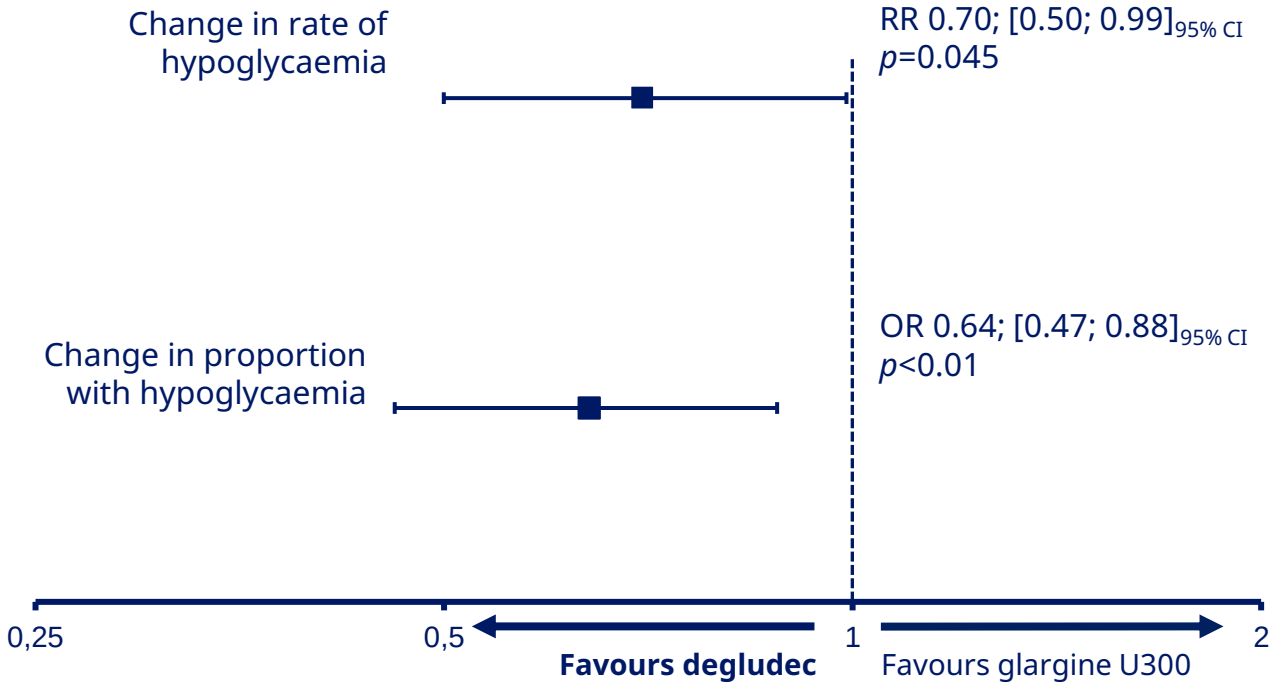
- *HbA1c values were estimated using repeated-measure analysis of covariance (ANCOVA) with treatment as factor, baseline vs. follow-up and patient as random effect. Results are presented as means with associated ETDs and p-value*
- *CI, confidence interval; ETD, estimated treatment difference; Glargine U300, insulin glargine 300 units/mL; HbA1c, glycated haemoglobin*
- *Tibaldi et al. Diabetes Obes Metab 2019; 21(4): 1001-1009*

CONFIRM: Hypoglycémie

The change in the rates of hypoglycaemia demonstrated a **30% lower rates** of hypoglycaemia with **Tresiba** vs glargine U300 (*p*=0.045)

The change in the proportion of patients experiencing ≥1 episode of hypoglycaemia was **significantly lower** with **Tresiba** vs glargine U300 (*p*<0.01)





- *Hypoglycaemia rate ratio was estimated using repeated-measure negative binomial regression. The likelihood of having ≥1 hypoglycaemic event was estimated using repeated-measure logistic regression. Robust standard errors was used to adjust for the potential dependence between repeated measures on individuals*
- *CI, confidence interval; Glargine U100, insulin glargine 100 units/mL; OR, odds ratio; RR, rate ratio*
  Tibaldi et al. Diabetes Obes Metab 2019; 21(4): 1001-1009

Continuous glucose monitoring-based time-in-range using insulin glargine 300 units/ml versus insulin degludec 100 units/ml in type 1 diabetes: The head-to-head randomized controlled InRange trial

Tadej Battelino

Diabetes Obes Metab. 2023;25:545–555.

Aim: To use continuous glucose monitoring (CGM)-based time-in-range (TIR) as a primary efficacy endpoint to compare the second-generation basal insulin (BI) analogues insulin glargine 300 U/ml (Gla-300) and insulin degludec 100 U/ml (IDeg-100) in adults with type 1 diabetes (T1D).

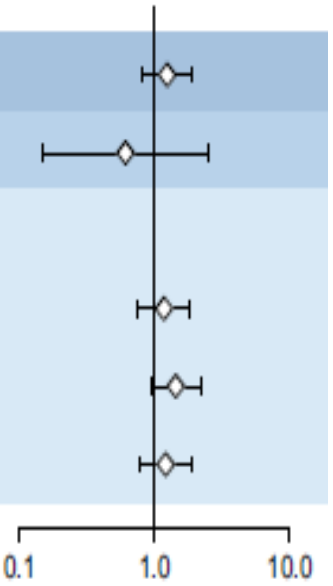
Materials and Methods: InRange was a 12-week, multicentre, randomized, active-controlled, parallel-group, open-label study comparing glucose TIR and variability between Gla-300 and IDeg-100 using blinded 20-day CGM profiles. The inclusion criteria consisted of adults with T1D treated with multiple daily injections, using BI once daily and rapid-acting insulin analogues for at least 1 year, with an HbA1c of 7% or higher and of 10% or less at screening.

Conclusions: Using clinically relevant CGM metrics, InRange shows that Gla-300 is non-inferior to IDeg-100 in people with T1D, with comparable hypoglycaemia and safety profiles.

Efficacy endpoint (ITT population)	Gla-300 (N = 172)	IDeg-100 (N = 171)
Time in glucose range ≥ 70 to ≤ 180 mg/dl (≥ 3.9 to ≤ 10 mmol/L) (%)		
Baseline (after optimization of previous insulin therapy), mean (SD)	51.19 (12.38)	52.37 (14.24)
Week 12		
LS mean [95% CI]	52.74 [51.06, 54.42]	55.09 [53.34, 56.84]
Non-inferiority LS mean difference [95% CI][a]	3.16 [0.88, 5.44]	
Non-inferiority *P* value	*P* = .0067	
LS mean difference [95% CI]	−2.35 [−4.75, 0.05]	
Superiority *P* value[b]	*P* = .0548	

(B) Nocturnal (00:00 AM-05:59 AM) hypoglycaemia

Any hypoglycaemia	113 (65.7)	104 (60.8)	1.23 [0.79, 1.92]
Severe hypoglycaemia	3 (1.7)	5 (2.9)	0.59 [0.14, 2.52]
Documented hypoglycaemia			
<70 mg/dl	109 (63.4)	102 (59.6)	1.17 [0.76, 1.81]
<70 mg/dl and ≥54 mg/dl	97 (56.4)	81 (47.4)	1.44 [0.94, 2.20]
<54 mg/dl	72 (41.9)	64 (37.4)	1.20 [0.78, 1.86]



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

Elisabeth R. Mathiesen,[1,2] Rosa Corcoy,[3] Fidelma Dunne,[4] Magnus Ekelund,[5] Denice S. Feig,[6] Moshe Hod,[7] Ting Jia,[5] Balamurali Kalyanam,[8] Soumitra Kar,[8] Alexandra Kautzky-Willer,[9] Peter Damm,[1,2] on behalf of the EXPECT study group

Insulin degludec (degludec) was non-inferior to insulin detemir (detemir) with respect to HbA_{1c} prior to delivery, with comparable maternal and pregnancy safety profiles in pregnant women with type 1 diabetes and their fetuses/infants.

Aim

- Poor glycaemic control in women with type 1 diabetes is related to poor pregnancy outcomes.[1]
- Degludec has a well-established efficacy and safety profile outside pregnancy; however, information on degludec in pregnancy is limited.
- The EXPECT trial evaluated the efficacy and safety of degludec versus detemir in pregnant women with type 1 diabetes.

Methods

- EXPECT was a randomised, open-label, parallel-group, multicentre, multinational, treat-to-target, active-controlled trial.
- Inclusion criteria: ≥18 years of age with type 1 diabetes for ≥1 year, HbA_{1c} at screening ≤8.0% (64 mmol/mol), and insulin treatment for ≥90 days prior to screening. Participants were pregnant from gestational week 8 to 14 or planning to become pregnant within 52 weeks.
- Exclusion criteria: proteinuria (urine protein-to-creatinine ratio ≥300 mg/g at screening), being treated with IVF or other medical infertility treatment, or receipt of any concomitant medication contraindicated in pregnancy according to local label.
- Eligible women were randomised 1:1 to either degludec once daily or detemir once or 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.
- Primary analysis aimed to assess the non-inferiority (margin 0.4%) of degludec to detemir with respect to the last planned HbA_{1c} measurement prior to delivery (>16 weeks' gestation) using ANCOVA.

Key results

Figure. HbA_{1c} during pregnancy

Key result

*p<0.0001; †observed data (pregnancy baseline to GW 36).
Abbreviations: degludec, insulin degludec; detemir, insulin detemir; GW, gestational week.

Table 1. Maternal safety endpoints (pregnancy period)

	Degludec				Detemir			
	n/N	%	Events	Rate	n/N	%	Events	Rate
Overall hypoglycaemia	89/91	97.8	5431	11,845	91/94	96.8	5982	13,401
Nocturnal hypoglycaemia	71/91	78.0	712	1553	69/94	73.4	759	1700
Adjudicated severe hypoglycaemia	6/91	6.6	8	–	3/94	3.2	4	–
	n/N		%		n/N		%	
Pre-eclampsia[a]	12/86		14.0		7/85		8.2	
Adverse events	78/91		85.7		76/94		80.9	
Serious adverse events	38/91		41.8		32/94		34.0	

[a]Non significant in *post hoc* analysis. Estimated odds ratio: 1.86 (95% CI: 0.63;5.48). •For women with liveborn infants. Assessed over pregnancy period among all randomised women who received ≥1 dose. Rate of events is per 100 years of exposure. Hypoglycaemia is based on American Diabetes Association (ADA) classification. Nocturnal, episodes occurring between 00:01 and 05:59 (both inclusive); severe, episodes requiring third-party assistance. n, number of women with ≥1 event; N, total number of women in treatment group and analysis set. Abbreviations: degludec, insulin degludec; detemir, insulin detemir.

Table 2. Pregnancy outcomes

	Degludec		Detemir		
	n	%	n	%	
All fetuses/infants	92	100.0	96	100.0	
Left the study due to withdrawn consent	1	1.1	4	4.2	
Early fetal loss (<20 weeks' gestation)	5	5.4	7	7.3	
Perinatal mortality	0	–	0	–	
Neonatal mortality	0	–	0	–	
Liveborn infants	86	93.5	85	88.5	
Fetuses/infants with major abnormalities (EUROCAT classified)	8	8.7	8	8.3	
Pre-term delivery (<37 weeks' gestation)	29	33.7	19	22.4	Non significant in *post hoc* analysis[a]
Infants born large for gestational age	55	64.0	43	50.6	Non significant in *post hoc* analysis[a]
Infants with neonatal hypoglycaemia (during first 24 h after birth)[b]	20	23.3	19	22.4	Similar in both treatment groups (summary statistics)
Adverse events (after delivery)	54	59.3	57	60.6	

[a]*Post hoc* analysis, estimated odds ratios (95% CI): pre-term delivery, 1.54 (0.75;3.15); large for gestational age (birth weight >90th percentile), 1.65 (0.87;3.15). [b]Defined as blood glucose <1.7 mmol/L (<31 mg/dL). Assessed in all randomised women who were pregnant during trial; %, percentage based on all fetuses/infants; n, number of women and each woman is linked with a single fetus/infant; neonatal mortality, death of infant between ≥7 completed days after delivery and <28 completed days after delivery; perinatal mortality, death of fetus/infant between ≥20 completed gestational weeks before delivery and <7 completed days after delivery.
Abbreviations: degludec, insulin degludec; detemir, insulin detemir; EUROCAT, European Concerted Action on Congenital Abnormalities and Twins.

- Overall, 111 women were randomised to degludec (pregnant n=71, non-pregnant n=40) and 114 were randomised to detemir (pregnant n=73, non-pregnant n=41).
- Mean (standard deviation) baseline characteristics in all women who were pregnant during the trial were similar between groups, including age: 30.7 (5.1) versus 30.9 (5.2) years; diabetes duration: 14.2 (8.3) versus 14.0 (8.5) years; and HbA_{1c}: 6.6 (0.6) % versus 6.5 (0.8)%.
- Estimated mean HbA_{1c} prior to delivery, was 6.23% in the degludec group and 6.34% in the detemir group. The estimated treatment difference was –0.11% (95% CI: –0.31;0.08), confirming non-inferiority (margin 0.4%), p<0.0001 (Figure).
- Maternal safety outcomes were generally comparable between treatment groups (Table 1).
  - There was no clinically relevant difference in the risk of hypoglycaemia between treatment groups
  - No adverse events led to participant discontinuation in the degludec treatment group
- Over the trial, 188 women (degludec n=92, detemir n=96) with singleton pregnancies were included. There were 171 liveborn infants (degludec, n=86; detemir, n=85), with no perinatal or neonatal deaths (Table 2).
- Pregnancy outcomes were comparable between treatment groups (Table 2).

Conclusions

- In pregnant women with type 1 diabetes, degludec was non-inferior to detemir with respect to HbA_{1c} prior to delivery.
- Pregnancy outcomes and safety profiles for both women with type 1 diabetes and their fetuses/infants were comparable between degludec and detemir.

Author affiliations [1]Center for Pregnant Women with Diabetes, Departments of Endocrinology and Obstetrics, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [2]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark; [3]Universitat Autònoma de Barcelona, Barcelona, Spain; [4]National University of Ireland Galway, Galway, Ireland; [5]Novo Nordisk A/S, Søborg, Denmark; [6]University of Toronto, Toronto, Ontario, Canada; [7]Tel Aviv University, Tel Aviv, Israel; [8]Novo Nordisk Service Centre India Private Ltd, Bangalore, India; [9]Medical University of Vienna, Vienna, Austria

Acknowledgements This trial was sponsored by Novo Nordisk A/S and is registered with ClinicalTrials.gov (NCT03377699). The authors acknowledge the medical writing assistance of Ashfield MedComms, an Ashfield Health company, funded by Novo Nordisk A/S. Presented at the European Association for the Study of Diabetes 57th Annual Meeting, 27 September–1 October 2021, Virtual Meeting.

Reference (1) Jensen DM *et al. Diabetes Care* 2004;27:2819–23

Tresiba®

En conclusion

- Efficacité , puissance d’action, sécurité, flexibilité et constance des résultats aussi bien dans les RCT que dans les RWE.
- Ideg peut être prescrit chez le nourrisson dès l’âge de 1 an, également chez la femme enceinte.
- Figure dans la liste des médicaments essentiels de l’OMS
- ASMR IV - HAS
- ETP