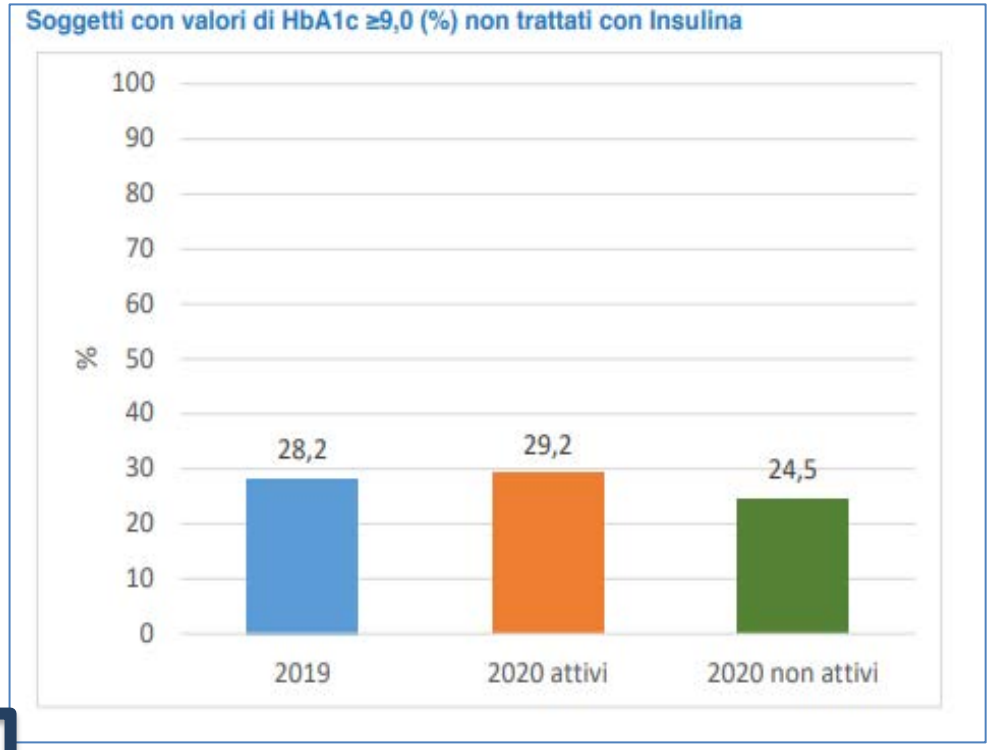
Si può impostare una terapia insulinica anche da remoto? Quali opportunità offrono le nuove combinazioni precostituite di insulina basale più GLP1-RA in quest'ambito?

Elisa Forte
Presidente AMD Regione Lazio

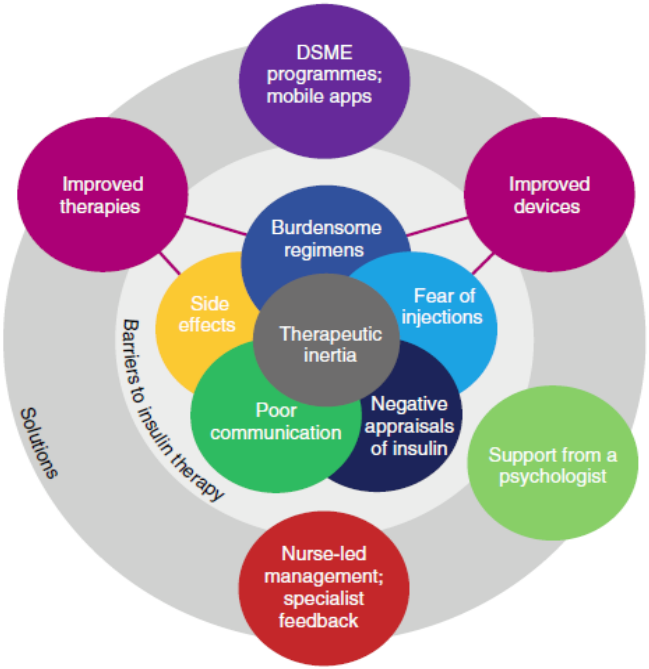
Annali AMD 2021

Trattamento	2019	2020 ATTIVI	2020 NON ATTIVI
Metformina	71,0	71,8	63,3
Sulfanilurea	14,0	12,9	13,0
Glinide	2,7	2,2	3,3
Glitazone	4,5	4,5	4,0
Acarbose	2,0	1,8	1,9
DPPIVi	21,9	22,5	26,0
GLP1-RA	10,9	15,7	9,8
SGLT2i	12,1	16,6	11,7
Insulina	32,8	34,6	37,2
Insulina basale	28,1	29,5	31,7
Insulina rapida	19,2	19,4	23,1



La percentuale di **soggetti non trattati con insulina, nonostante valori di HbA1c >9%**, indicatore di inerzia terapeutica, è invariata rispetto al 2018 (28.2%) e non modificata nemmeno rispetto ai dati 2016. Questo è un dato difficile da interpretare: nell'ultimo quinquennio non siamo infatti riusciti ad incidere su un aspetto importante dell'atteggiamento terapeutico dei diabetologi.

Identification of barriers to insulin therapy and approaches to overcoming them



- Fear of hypoglycaemia and weight gain
- Fear of injections
- Impact on daily life
- Negative appraisal of insulin
- Lack of HCP resources, assistance and education for patients
- Inerzia terapeutica

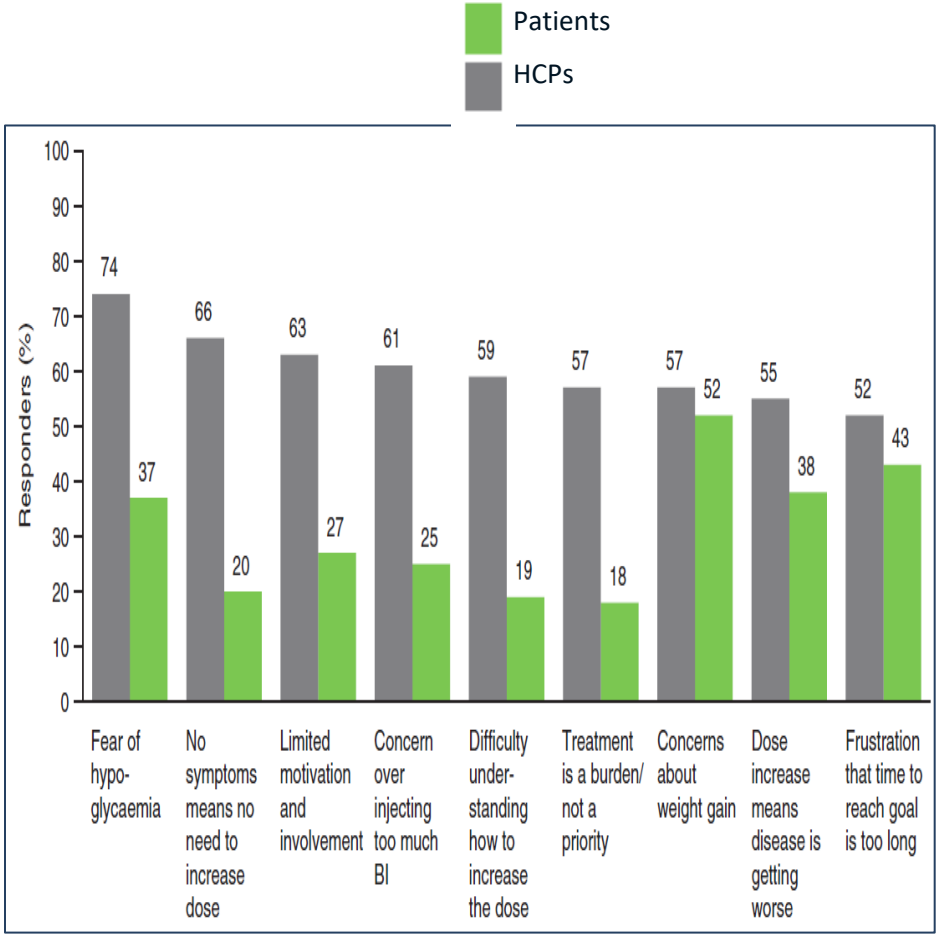
Russell-Jones D et al. Diabetes Obes Metab. 2018;20:488–496.

Barriers to self-titration identified by HCPs and patients

Results of a quantitative survey

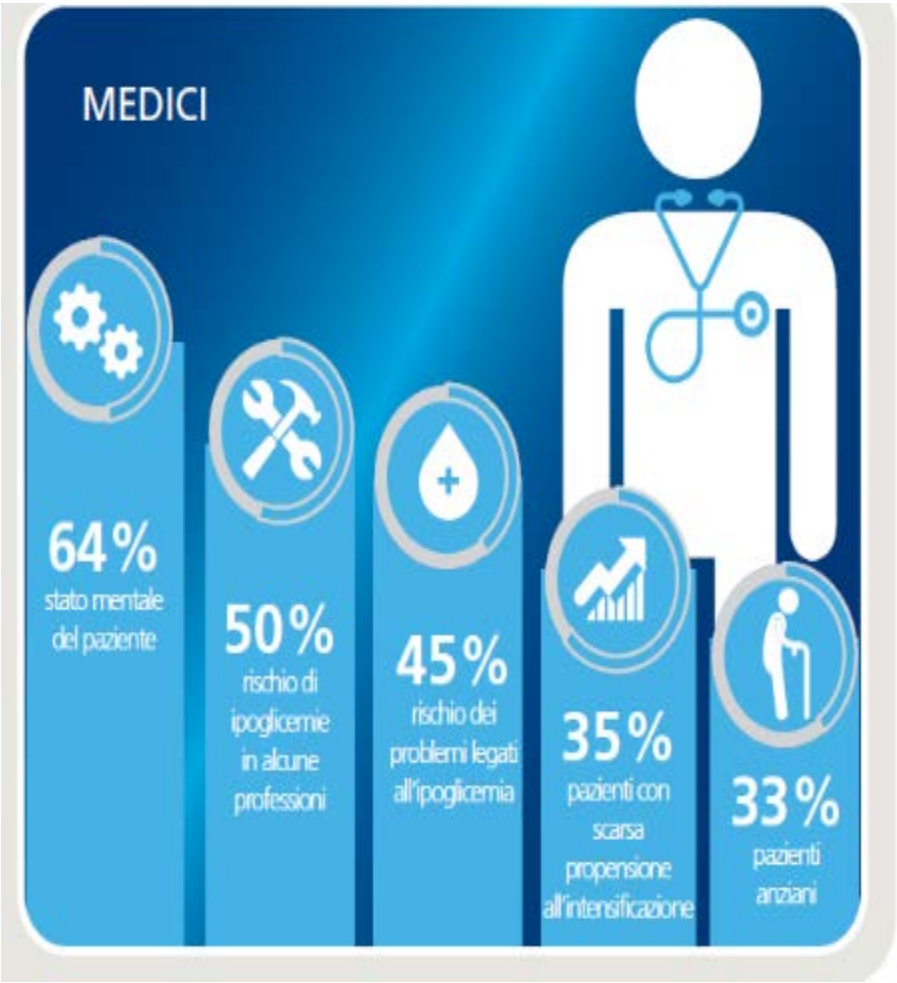
HCPs
- fear of hypoglycaemia
- failure to titrate in the absence of symptoms
- low patient motivation

Patients
- fear of hypoglycaemia
- weight gain
- perception that titration meant worsening disease
- frustration over the time to reach HbA1c goals

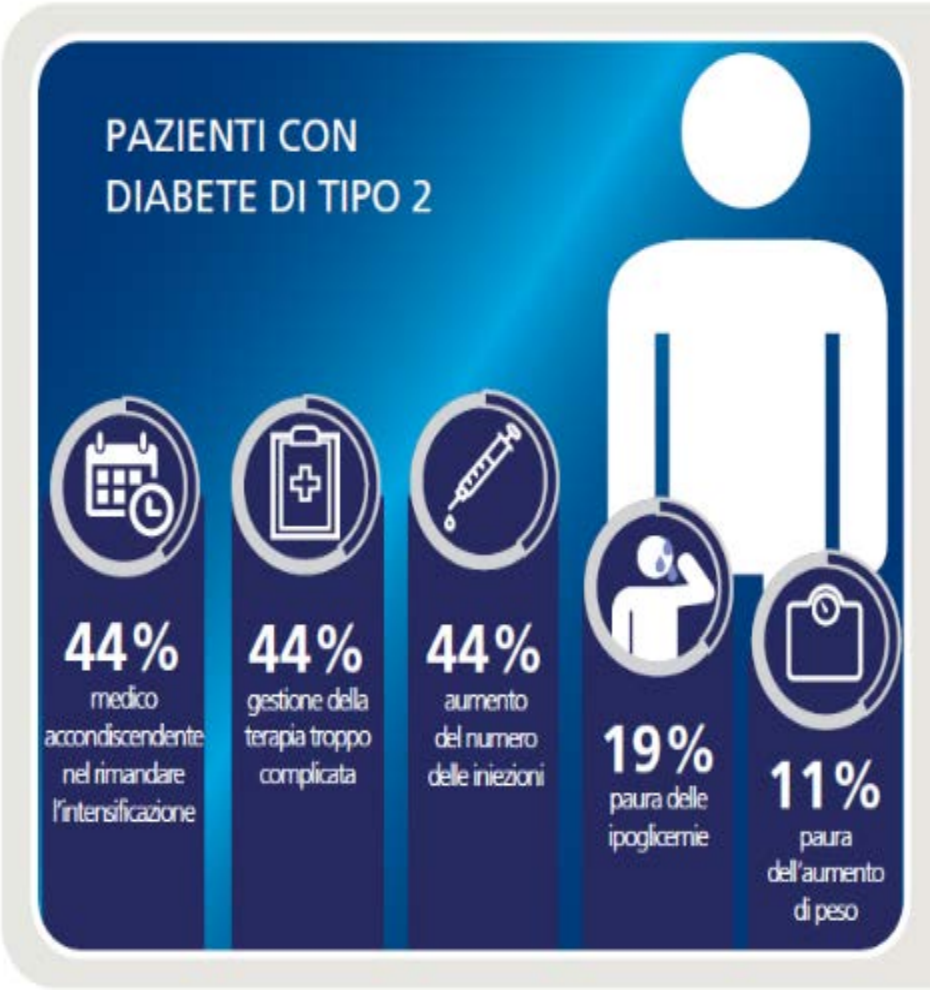


Berard L et al. Diabetes Obes Metab. 2018;20:301–308.

Barriers to intensification: What the physicians think

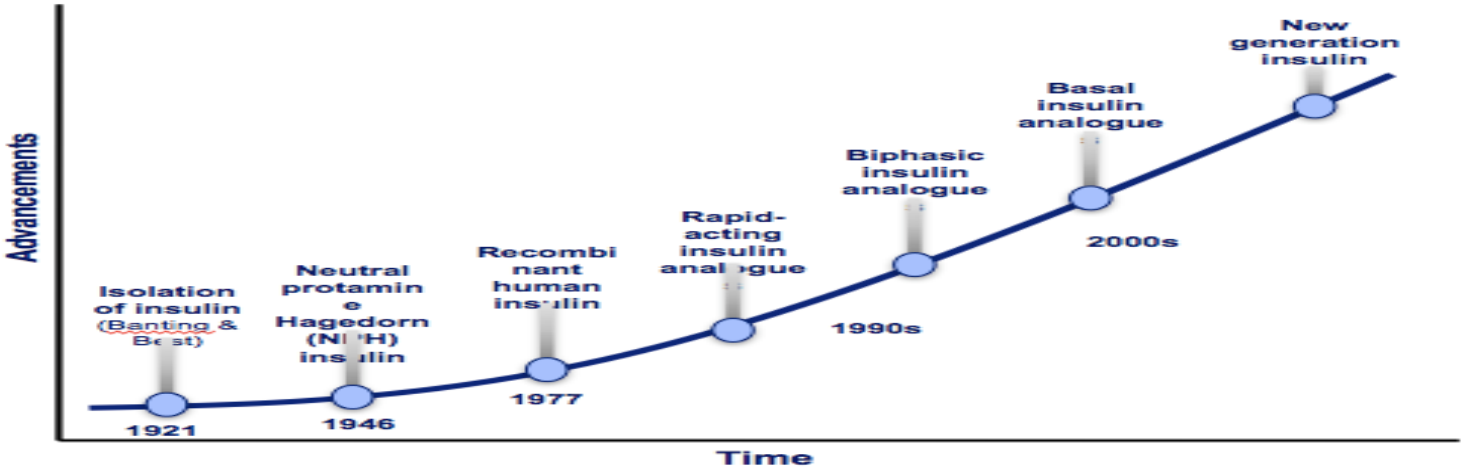


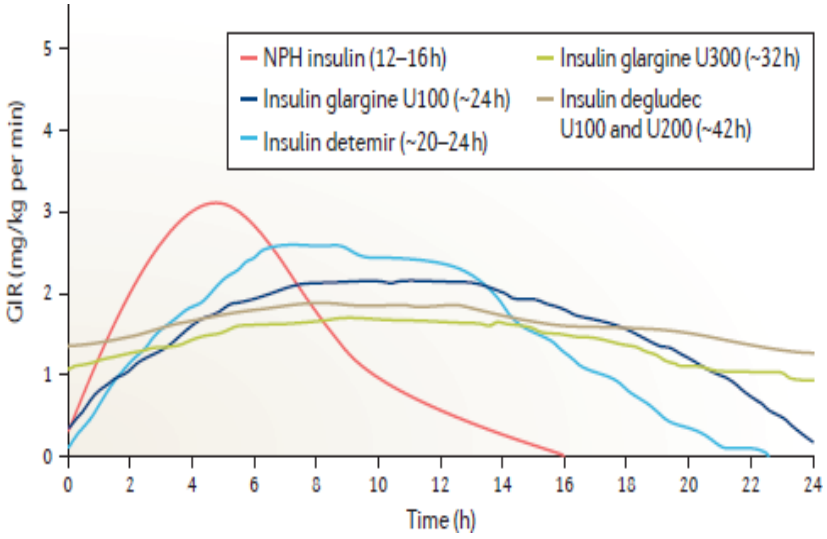
Barriers to intensification: What the PATIENTS think



Fonte: A. Nicolucci, M. Comaschi, S. Frontoni, K. Vaccaro
Perceptions of diabetes control among physicians and people with type 2 diabetes on basal insulin in Italy submitted
Data on file

L’evoluzione della terapia insulinica



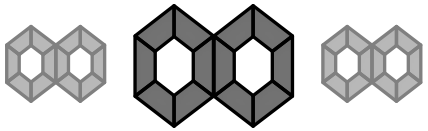


Hanefeld et al. Use of insulin in type 2 diabetes: what we learned from recent clinical trials on the benefits of early insulin initiation. Diabetes Metab, 2014

Unique properties of the liraglutide and insulin degludec combination

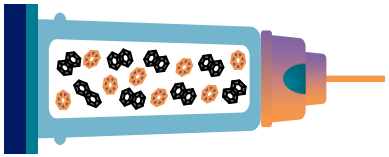
FORMULATION

Degludec dihexamers
(100 U/mL)



+

Liraglutide heptamers
(3.6 mg/mL)



3 mL pre-filled pen

PROPERTIES

- Once-daily administration, independent of meals, in a single pen device
- Glycaemic control throughout the day
  - FPG reduction
  - PPG coverage at all meals
- Steady titration resulting in a more favourable tolerability profile

Complementary actions of basal insulin and a GLP-1 RA target the underlying pathophysiology of type 2 diabetes

GLP-1 RA

Brain

- Decreased energy intake
- Increased satiety

Pancreas

- Glucose-dependent insulin and glucagon secretion
- Insulin synthesis

Gi tract

- Inhibits gastric emptying

Liver

- Inhibition of hepatic glucose production

Basal insulin

Liver

- Inhibition of hepatic glucose production

Adipose tissue

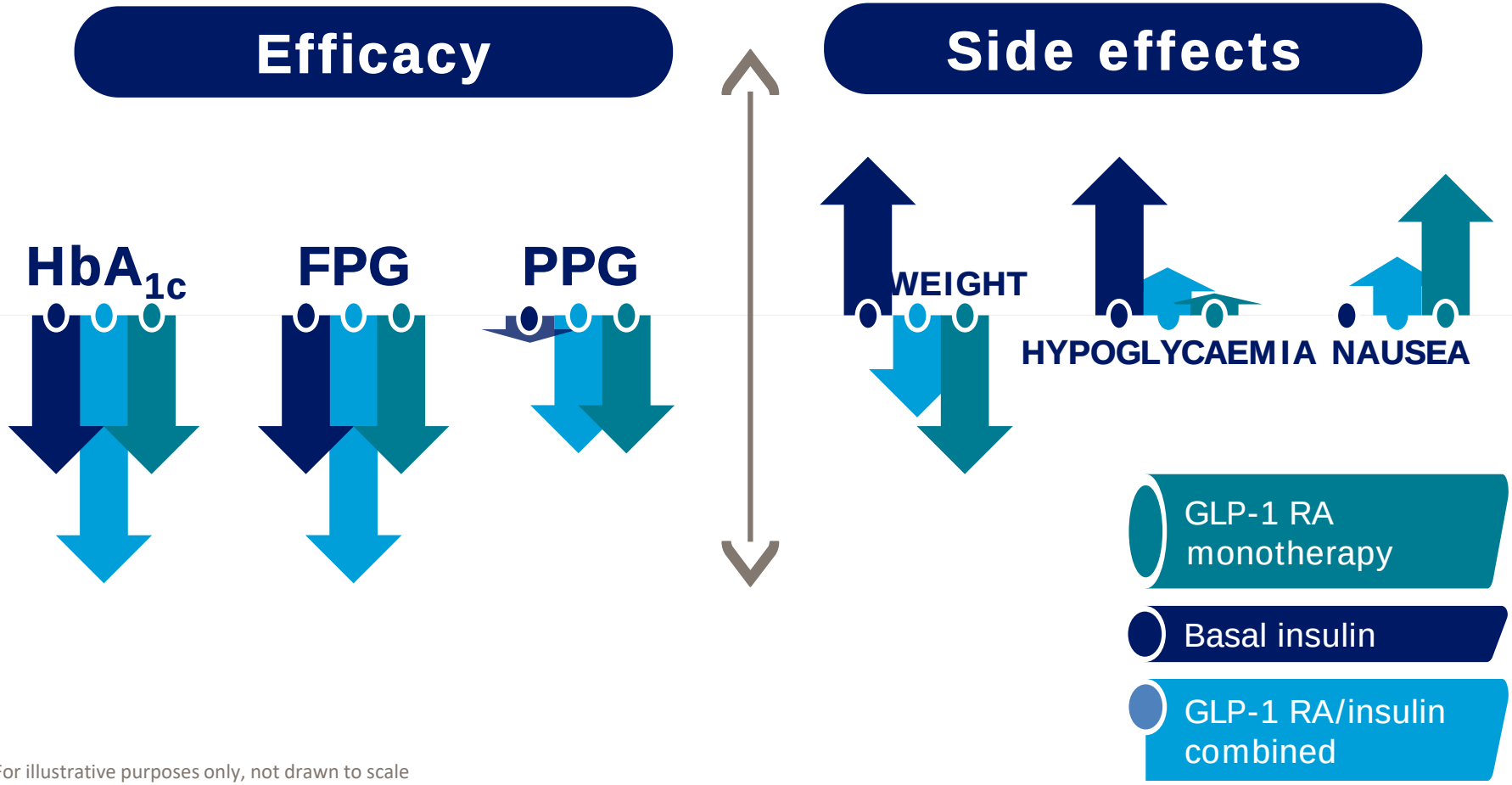
- Insulin receptor activation

Skeletal muscle

- Increased glucose disposal

1. Baggio & Drucker. *Gastroenterol* 2007;132:2131–57; 2. Niswender. *Postgrad Med* 2011;123:27–37

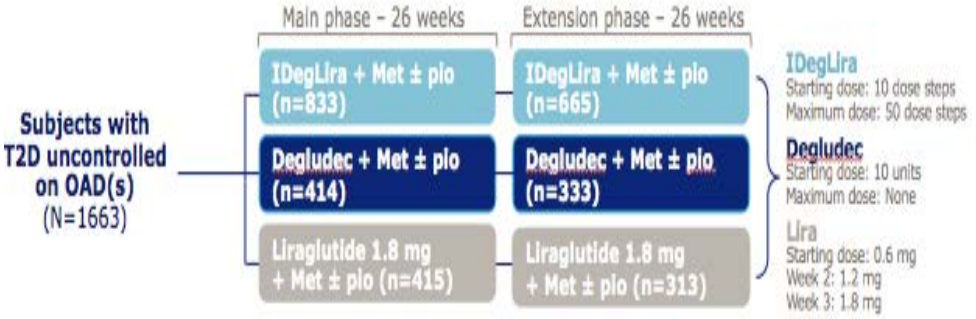
What can we expect when combining a GLP-1 RA and a basal insulin in one pen?



For illustrative purposes only, not drawn to scale

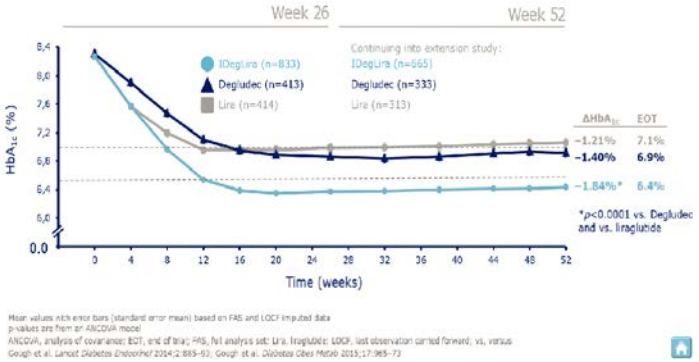
FPG, fasting plasma glucose; GLP-1 RA, glucagon-like peptide-1 receptor agonist; PPG, postprandial glucose

DUAL I and extension



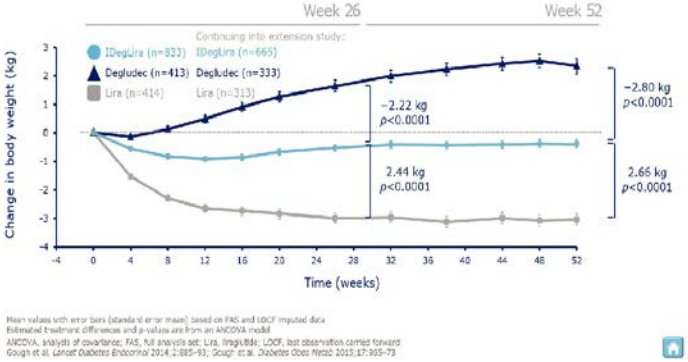
DUAL I and extension

HbA$_{1c}$ over time



DUAL I and extension

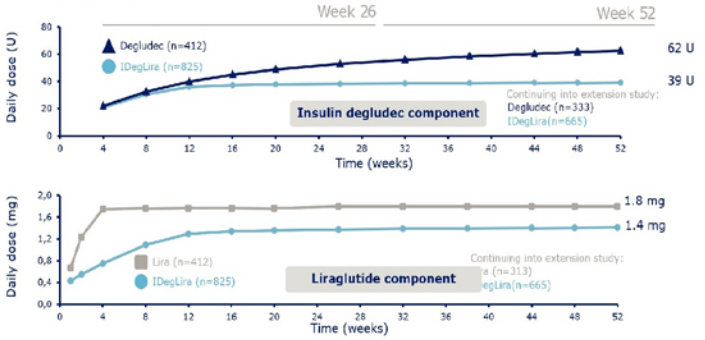
Change in body weight over time



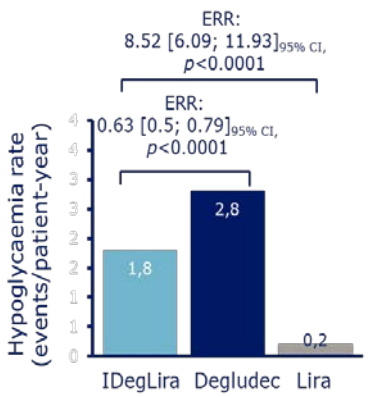
DUAL I and extension

Mean daily doses

After 52 weeks, 57% of subjects had reached the maximum dose of IDegLira, of whom 70% had an HbA$_{1c}$ <7%

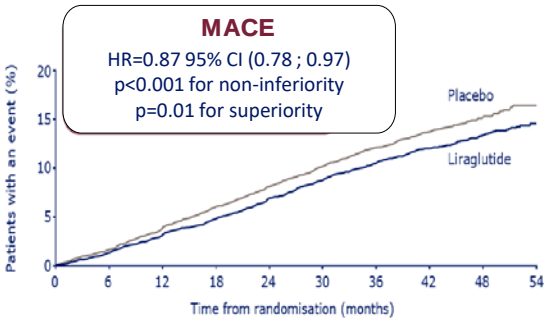


Confirmed hypoglycaemia



Cardiovascular safety

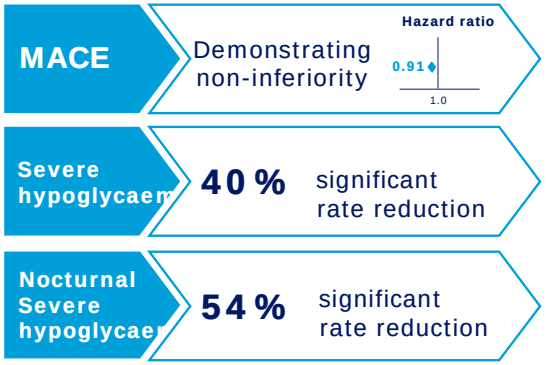
LEADER[1]



Subgroup analysis
Basal insulin users[5]

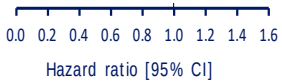
	N(%)	HR [95% CI]
Basal insulin users		
MACE	3159 (15.1)	0.84 [0.70; 1.00]
CV Death	3159 (6.0)	0.77 [0.57; 1.02]

DEVOTE[2]



Post hoc analysis
Liraglutide users[6]

Liraglutide vs. Non-Liraglutide	Liraglutide Y/N
	HR [95% CI]
MACE*	0.62 [0.42; 0.92]
CV death*	0.47 [0.23; 0.96]
Non-fatal stroke	0.56 [0.23; 1.37]
Non-fatal MI	0.82 [0.49; 1.37]
All cause death*	0.50 [0.29; 0.88]

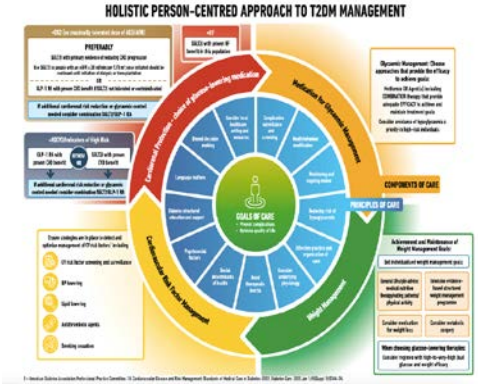


CV RISK MARKER S[3,4]

Patients uncontrolled on basal insulin (DUAL II, V and VII) IDegLira is associated with an overall improvement in CV risk markers

- *P<0.05
- %, proportion in % of subjects with a first event between randomization date and follow up date; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MACE, major adverse cardiovascular event; N, number of subjects; vs, versus; Y/N, yes/no
- 1. Marso et al. *N Engl J Med* 2017;377:723–32; 2. Marso et al. *N Engl J Med* 2017;377:723–32; 3. Vilsboll T et al. *EASD* 2017; OP #113; 4. Billings et al. *Diabetes Care* 2018;41(5):1009-1016; 5. Cornelis T et al. *ADA* 2018; 438-P; 6. Brown-Frandsen et al. *ADA* 2018; 1065-P

Management of hyperglycaemia in type 2 diabetes, September 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)



PLACE OF INSULIN[1]

- **Consider immediate start of insulin**
  - Severe hyperglycaemia
  - Acute glycaemic dysregulation
  - When T1D is suspected
- **If not already on GLP-1 RA, consider use of GLP-1 RA**
- **When not familiar with insulin use or when targets not reached, consider shared care with specialist team**

Consider adding insulin when personalised HbA_{1c} targets are not met with strategies described in Fig. 4

- Maintain cardiorenal protective agents
- Maintain metformin, SGLT2i and GLP-1 RA to avoid weight gain and limit insulin dose and hypoglycaemia risk
- Consider using combination products of basal insulin/GLP-1 RA

Start using basal insulin* (10 U or 0.1–0.2 U/kg per day) at bedtime or more flexibility with timing for longer-acting analogues

Titrate to FPG target but avoid overbasalisation of insulin (consider introduction of CGM)

When FPG is on target but HbA_{1c} or TIR is not

If not already on GLP-1 RA, consider use of GLP-1 RA

Intensify along the way and preferentially at each step

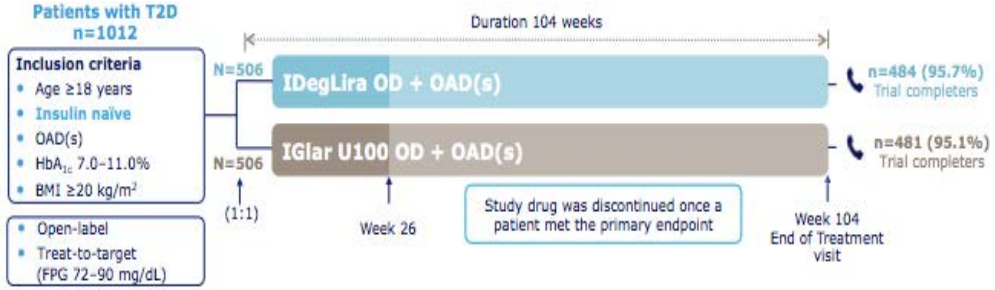
- Healthy behaviour
- Nutritional therapy
- DSMES: with additional focus on injection technique, hypoglycaemia, weight

ADD MEALTIME INSULIN UNDER FORM OF:

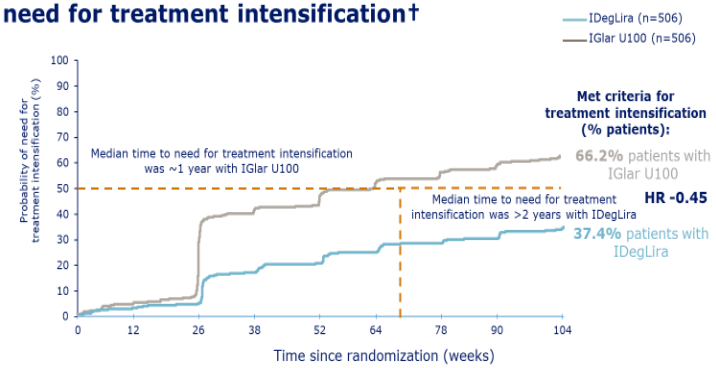
- Basal plus (progressive addition of boluses)
- Premixed insulins
- MDI (multiple daily injections)

Diabetologia
https://doi.org/10.1007/s00125-022-05787-2

DUAL VIII

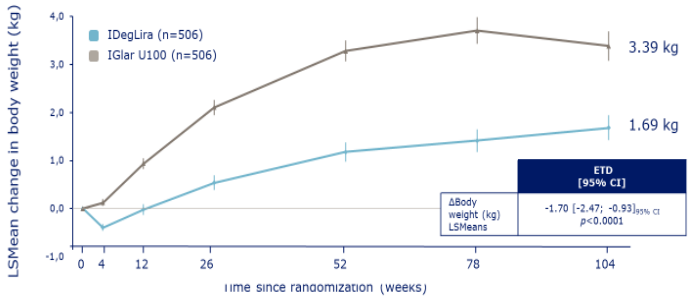


DUAL VIII: Primary outcome – time to meeting criteria for need for treatment intensification†



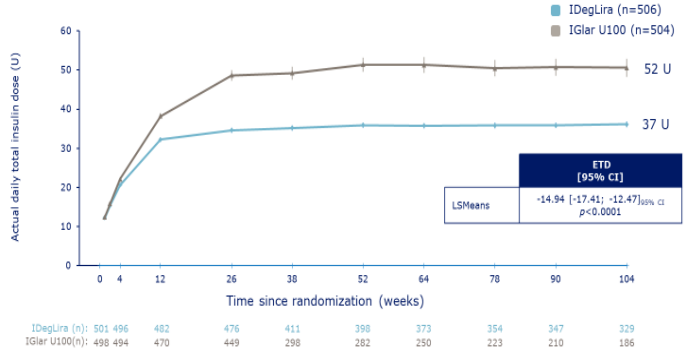
†HbA_{1c} ≥7% at two consecutive visits. Full analysis set. Treatment policy strategy. Kaplan–Meier curves. Test for no treatment difference is based on a stratified log-rank test (p-value: <0.0001) where treatment, baseline HbA_{1c} group and pre-trial OAD treatment group are included as strata in the model. Patients discontinuing treatment contribute to analyses as needing treatment intensification from time of discontinuation
IDegLira, insulin degludec/liraglutide; IGlar U100, insulin glargine 100 units/mL; n, number of patients
Aroda VR, et al. Lancet Diabetes Endocrinol. 2019;7(8):596-605

DUAL VIII: Body weight over time



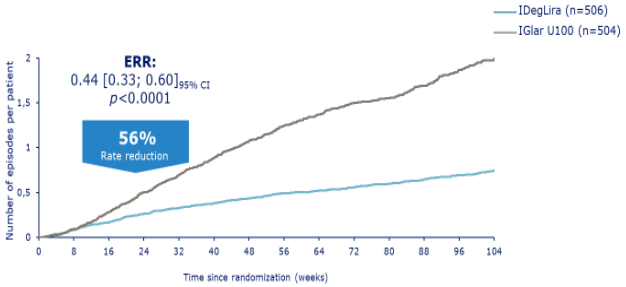
Full analysis set. Trial product strategy.
LSMeans from the MMRM model, error bars +/- standard error (of estimated LSMeans)
CI, confidence interval; ETD, estimated treatment difference; IDegLira, insulin degludec/liraglutide; IGlar U100, insulin glargine U100; LS, least squares; MMRM, mixed model repeated measurement
Aroda VR, et al. Lancet Diabetes Endocrinol. 2019;7(8):596-605

DUAL VIII: Insulin dose (U) over time



Safety analysis set. Observed data.
At week 104, 90 patients (27.36%) had max dose of IDegLira. 75.3% were at target <7%.
Mean (symbol) and mean +/- standard error to the mean (error bars). Number of patients contributing to the data points appears in the bottom panel.
IDegLira, insulin degludec/liraglutide; IGlar U100, insulin glargine U100; U, units
Aroda VR, et al. Lancet Diabetes Endocrinol. 2019;7(8):596-605

DUAL VIII: Cumulative severe or BG-confirmed symptomatic hypoglycemic episodes over time

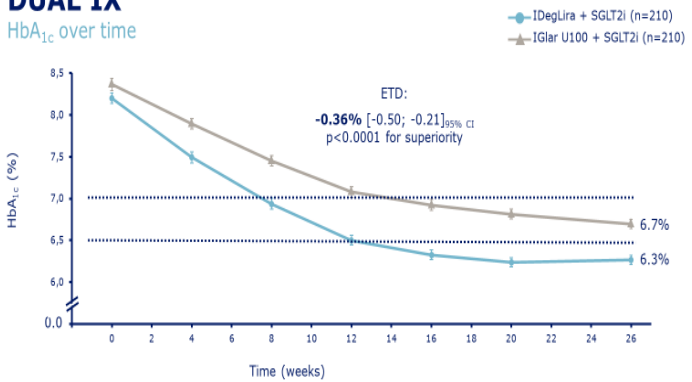


Safety analysis set. Observed data. ERR is estimated based on the trial product strategy (based on the FAS)
Severe or BG confirmed symptomatic: an episode that is severe according to the ADA classification or BG confirmed by a plasma glucose value < 3.1 mmol/L (56 mg/L) with symptoms consistent with hypoglycemia.
ADA: American Diabetes association; BG, Blood glucose; CI, confidence interval; conf., confirmed; ERR, estimated rate ratio; IDegLira, insulin degludec/liraglutide; IGlar U100, insulin glargine U100; symp., symptomatic
Aroda VR, et al. Lancet Diabetes Endocrinol. 2019;7(8):596-605

DUAL IX

DUAL IX

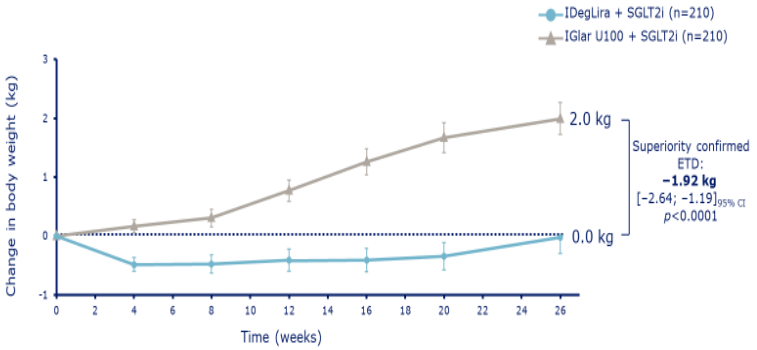
HbA$_{1c}$ over time



Mean observed values with error bars (standard error of the mean) based on full analysis set. ETD is based on FAS, and an ANCOVA model with treatment, pre-trial OAD and region as factors and corresponding baseline value as covariate. Missing data are imputed using unconditional MI including data obtained after premature treatment discontinuation. ---
ADA/EASD HbA$_{1c}$ target <7.0% and AACE HbA$_{1c}$ target ≤6.5%
AACE, American Association of Clinical Endocrinologists; ADA, American Diabetes Association; ANCOVA, analysis of covariance; CI, confidence interval; EASD, European Association for the Study of Diabetes; ETD, estimated treatment difference; FAS, full analysis set; IGlar U100, insulin glargine U100; MI, multiple imputation; OAD, oral anti-diabetic drug; SGLT2i, sodium-glucose co-transporter 2 inhibitor
Philis-Tsimikas et al. Diabetes Obes Metab. 2019. 21(6):1399-1408

DUAL IX

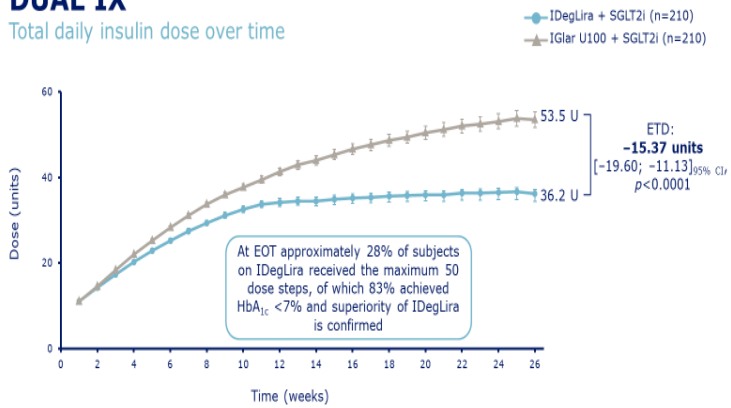
Change in body weight over time



Mean observed values with error bars (standard error of the mean) including data obtained after premature treatment discontinuation based on FAS. ETD based on FAS, and an ANCOVA model with treatment, pre-trial OAD and region as factors and corresponding baseline value as covariate
ANCOVA, analysis of covariance; CI, confidence interval; ETD, estimated treatment difference; FAS, full analysis set; IGlar U100, insulin glargine U100; OAD, oral anti-diabetic drug; SGLT2i, sodium-glucose co-transporter 2 inhibitor
Philis-Tsimikas et al. Diabetes Obes Metab. 2019. 21(6):1399-1408

DUAL IX

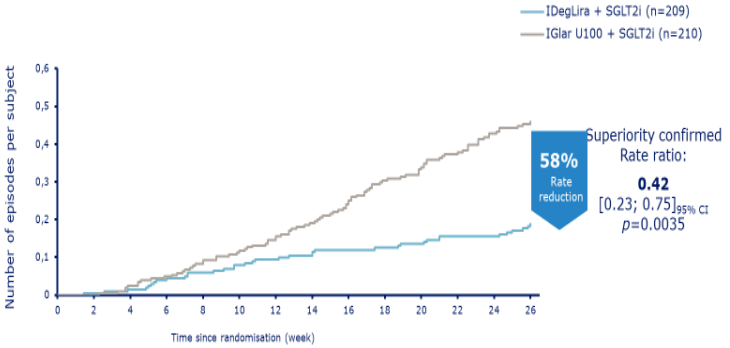
Total daily insulin dose over time



Insulin dose is based on retrieved data which may be any basal insulin, bolus insulin or premix, irrespective of randomised treatment. ETD is based on observed data for the full analysis set using ANCOVA model with treatment, pre-trial OAD and region as factors and corresponding baseline HbA$_{1c}$ as covariate. Mean observed values with error bars (standard error mean) based on full analysis set. ETD is based on observed data using ANCOVA model with treatment, pre-trial OAD and region as factors and corresponding baseline HbA$_{1c}$ as covariate.
ANCOVA, analysis of covariance; CI, confidence interval; EOT, end of trial; ETD, estimated treatment difference; OAD, oral anti-diabetic drug; SGLT2i, sodium-glucose co-transporter 2 inhibitor; U, units
Philis-Tsimikas et al. Diabetes Obes Metab. 2019. 21(6):1399-1408

DUAL IX

Severe or BG-confirmed symptomatic hypoglycaemia over time



Mean cumulative function based on safety analysis set. Severe or BG-confirmed symptomatic: an episode that is severe according to the ADA classification or BG-confirmed by a plasma glucose value <3.1 mmol/L (<56 mg/dL) with symptoms consistent with hypoglycaemia.
ADA, American Diabetes Association; BG, blood glucose; CI, confidence interval; IGlar U100, insulin glargine U100; SGLT2i, sodium-glucose co-transporter 2 inhibitor
Philis-Tsimikas et al. Diabetes Obes Metab. 2019. 21(6):1399-1408

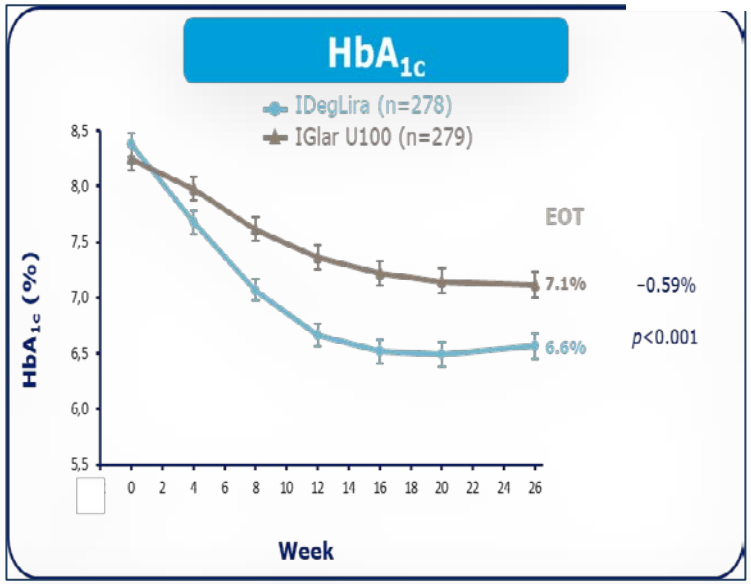
DUAL V

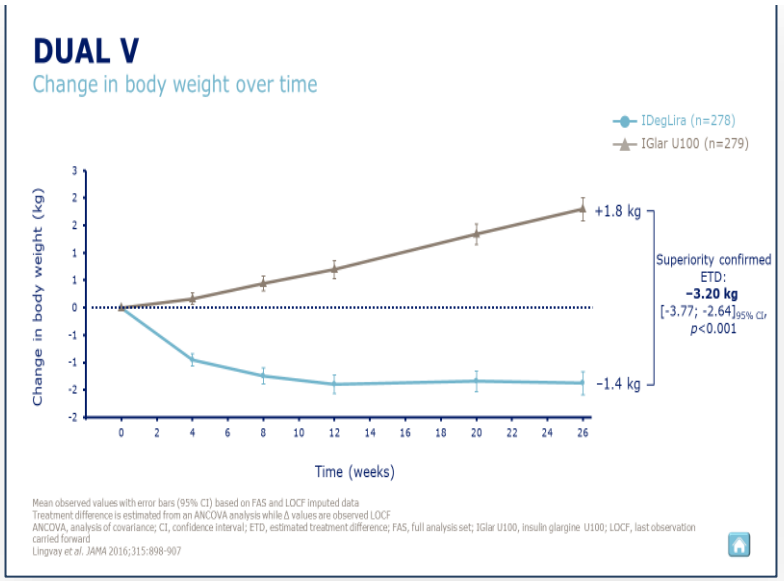
Subjects with T2D uncontrolled on basal insulin
(N=557)

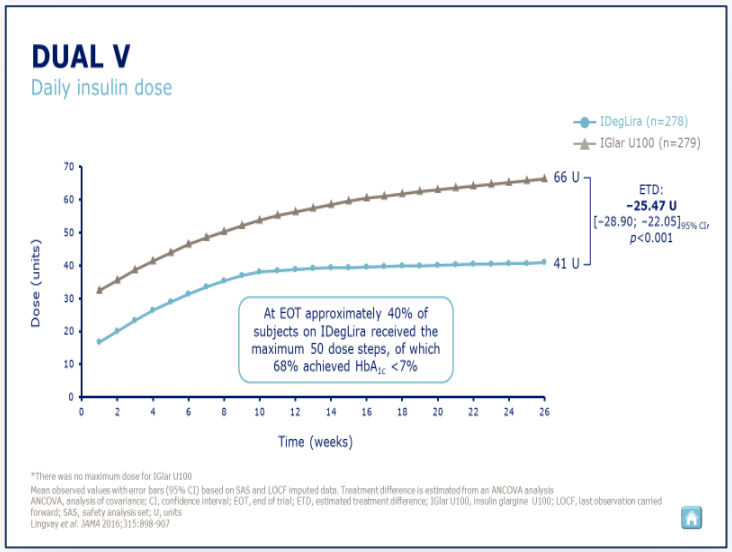
- **IDegLira + metformin** (n=278)
- **IGlar U100 + metformin** (n=279)

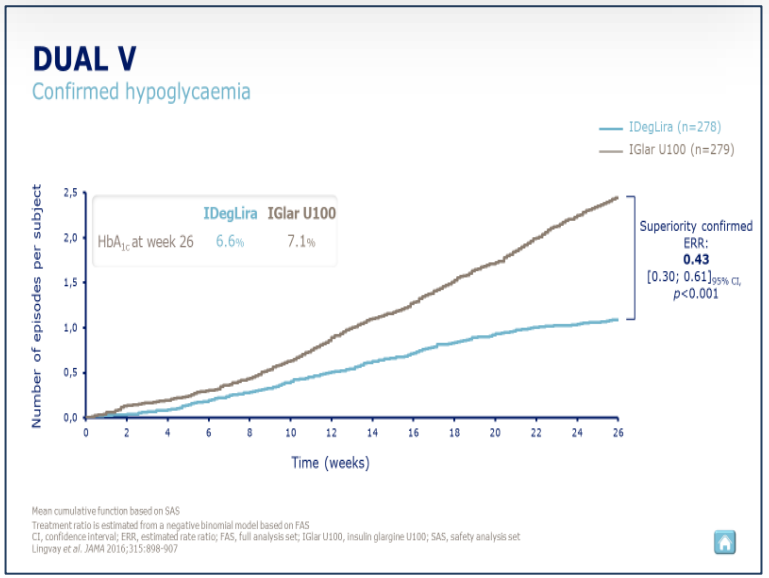
IDegLira
Starting dose: 16 dose steps
Maximum dose: 50 dose steps

IGlar U100
Starting dose: Pre-trial dose
Maximum dose: None









RWE Italiane

European Review for Medical and Pharmacological Sciences 2020; 24: 10671-10679

IDegLira fixed-ratio combination in the real world: a retrospective observational single-center Italian experience

C. DI LORETO, R. CELLENO, L. PIASTRELLA, P. DEL SINDACO

Servizio di Diabetologia – Distretto del Perugino – USL Umbria 1, "Poliambulatorio Europa", Perugia, Italy

Results: IDegLira results to be effective in reducing HbA1c and fasting plasma glucose, especially among GLP-1 RA and BOT subgroup. In BOT group, a statistical difference was noted from the first month of treatment, also for post-prandial glycemia. Obtained results were achieved at a moderate dose of IDegLira reported during the study, which also represents a significant reduction of the amount of basal insulin in BB patients

...unsatisfactory glycemic control, or who experienced side effects such as weight gain and hypoglycemia of other insulin therapies.

Key Words:
Insulin degludec, Liraglutide, IDegLira, Fixed-ratio combination, Diabetes, Basal bolus, Oral anti-diabetic therapy.

...into the circulation for a stable glucose-lowering effect[7]. Liraglutide is a GLP-1 analogue (administered subcutaneously) with a protracted action and a long plasma half-life. This improves glycemic control by lowering both fasting and postprandial blood glucose levels, stimulating insulin secretion and lowering inappropriately

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ORIGINAL RESEARCH

Real-World Evaluation of Glycemic Outcomes and Extra-Glycemic Parameters in Diabetic Patients Treated with the Combined Formulation Degludec–Liraglutide (Ideglira)

Luciano Zenari · Andrea Da Porto · Lorena De Moliner · Francesca Lugli · Valeria Guazzoni · Gloria Groppelli · Laura Molteni · Massimo Bracaccia · Vera Frison · Natalino Simioni · Barbara Bonsembiante · Cesare Miranda · Annunziata Lapolla

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ABSTRACT

Switch to IDegLira treatment is a valid option for patients failing to achieve glycemic control targets, patients with side effects such as weight gain and hypoglycemia

...ian patients with ... the encouraging ...d with IDegLira, ... Italy in January ...n Italian clinical ...ter, retrospective, ...ents with T2DM ...uary to December ... IDegLira therapy, ... with or without ... oral antidiabetic ...ding to the basal ...pid-acting insulin treatment; BB group).

Electronic supplementary material: The online version of this article (https://doi.org/10.1007/s13300-020-00945-4) contains supplementary material, which is available to authorized users.

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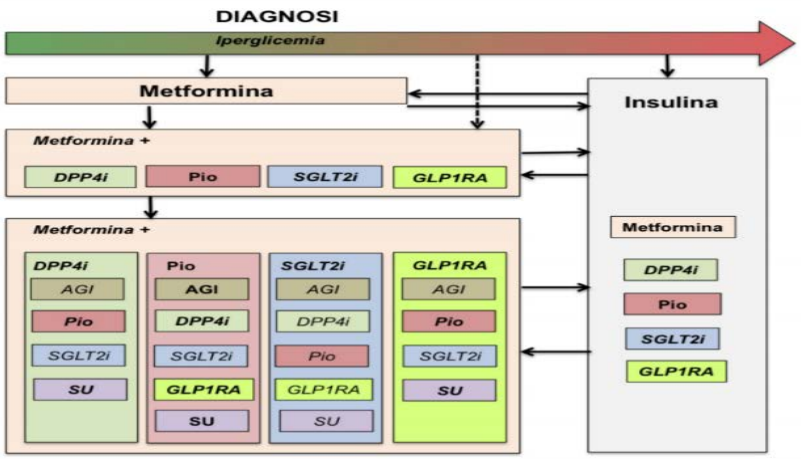


- **Sono disponibili associazioni precostituite di degludec e liraglutide (iDegLira**) e di glargine e lixisenatide (LixiLan)

- Nei trial clinici di confronto diretto con la sola insulina basale, con adeguata titolazione, queste associazioni producono una riduzione dell'emoglobina glicata più ampia, con effetti più favorevoli sul peso corporeo e con minor rischio di ipoglicemia
- Le associazione precostituite di insulina basale e GLP-1RA possono rappresentare un'alternativa all'insulina basale, oppure un'opzione per l'intensificazione della terapia con insulina basale, qualora non sia desiderata l'associazione con altri farmaci incretinici

Tabella 4.H4. Terapia insulinica nel diabete di tipo 2.

Iniziare la terapia insulinica secondo uno schema adeguato all'andamento delle glicemie del paziente.
Gli schemi possibili comprendono:
1. La somministrazione di sola insulina lenta, preferibilmente serale (schema più frequente)
2. La somministrazione di sola insulina rapida a uno o più pasti
3. La somministrazione di insulina lenta associata ad insulina rapida a uno o più pasti

In generale, è consigliabile iniziare con gli schemi più semplici possibili per poi aumentare il numero di somministrazioni se necessario.

Nel caso sia necessaria la sola insulina lenta e non si reputi utile una dose massimale di agonisti del recettore del GLP-1, considerare come opzione alternativa l'associazione precostituita di liraglutide e degludec o di lixisenatide e glargine.

Istruire il paziente adeguatamente sulla tecnica di iniezione al momento della prescrizione.

Verificare che il paziente sia ben addestrato all'automonitoraggio della glicemia e che sia in grado di riconoscere e trattare adeguatamente l'ipoglicemia.

Se non controindicata, associare all'insulina la metformina.
Anche l'associazione di inibitori DPP4, inibitori SGLT2 e agonisti GLP1, con o senza metformina, è vantaggiosa, in quanto consente di contrastare l'aumento di peso, ridurre il fabbisogno di insulina e, in qualche caso, di ridurre anche il numero di iniezioni necessarie.
Qualora si intenda associare all'insulina il pioglitazone, sorvegliare l'eventuale comparsa di edemi.
Qualora si intenda associare all'insulina l'acarbose, informare il paziente che eventuali ipoglicemie vanno corrette con glucosio e non con saccarosio.
La terapia combinata di insulina e sulfaniluree o glinidi è sconsigliabile per l'elevato rischio di ipoglicemia.

Titolare le dosi di insulina sulla base delle glicemie domiciliari del paziente, fino al raggiungimento degli obiettivi terapeutici. Per una titolazione efficace, si devono prevedere contatti frequenti, o in alternativa istruire il paziente ad effettuare una auto titolazione.

Nota 100

Inibitori DPPIV	Agonisti recettoriali GLP1	SGLT2-i	Associazioni precostituite	Associazioni precostituite	Associazioni precostituite
• Alogliptin • Linagliptin • Sitagliptin • Saxagliptin • Vildagliptin	• Dulaglutide • Exenatide • Exenatide LAR • Liraglutide • Lixisenatide • Semaglutide	• Canaglifozin • Dapaglifozin • Empaglifozin • Ertuglifozin	• Canaglifozin /metformina • Dapaglifozin /metformina • Empaglifozin /metformina • Ertuglifozin/ metformina	• Alogliptin/metformina • Alogliptin/pioglitazone • Linagliptin/metformina • Saxagliptin/ metformina • Sitagliptin/metformina • Vildagliptin/ metformina	• Degludec/liraglutide • Glargine/lixisenatide

Sono state inserite nella **Nota 100** le **associazioni precostituite insulina basale/GLP1** come **possibili** opzioni terapeutiche con associazioni di farmaci prima non rimborsabili : SGLT2

DUAL VII

Subjects with T2D uncontrolled on basal insulin
(N=506)

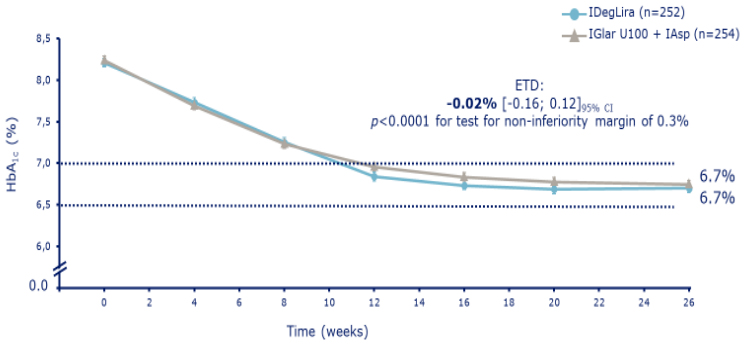
- **IDegLira + metformin (n=252)**
- **IGlar U100 + IAsp (≤4 times) + metformin (n=254)**

Starting dose: 16 dose steps
Maximum dose: 50 dose steps

IGlar U100
Starting dose: Pre-trial dose
Maximum dose: None

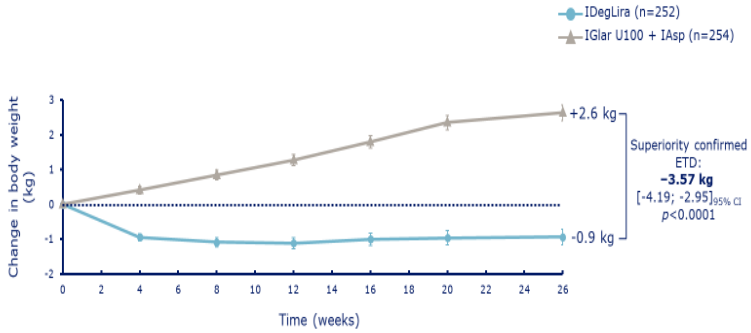
IAsp
Starting dose: 4 U*
Maximum dose: None

DUAL VII
HbA$_{1c}$ over time



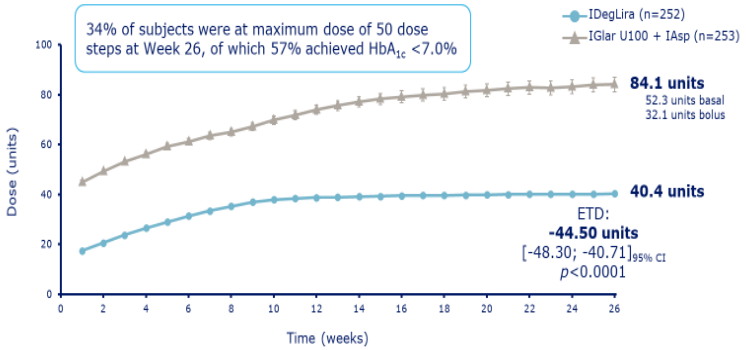
Mean observed values with error bars (standard error mean) based on full analysis set. ETD is based on LSMeans from full analysis set, using mixed model for repeated measurement. ---ADA/EASD HbA$_{1c}$ target <7.0% and AACE HbA$_{1c}$ target ≤6.5%
AACE, American Association of Clinical Endocrinologists; ADA, American Diabetes Association; CI, confidence interval; EASD, European Association for the Study of Diabetes; ETD, estimated treatment difference; IAsp, insulin aspart; IGlar U100, insulin glargine U100; LSMean, least square mean
Billings et al. *Diabetes Care* 2018;41(5):1009-1016

DUAL VII
Change in body weight over time



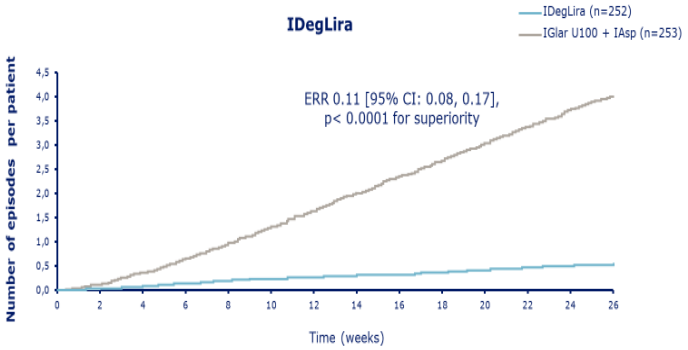
LSMean values with error bars (standard error mean) based on full analysis set, using MMRM. MMRM with treatment, region and visit as factors and baseline value as covariate. Interactions between visit and all other factors and covariate are included.
CI, confidence interval; ETD, estimated treatment difference; IAsp, insulin aspart; IGlar U100, insulin glargine U100; LSMean, least square mean; MMRM, mixed model for repeated measurement
Billings et al. Diabetes Care 2018;41(5):1009-1016

DUAL VII
Total daily insulin dose over time



Based on observed mean values at end of trial from the safety analysis set; Mean observed values with error bars (standard error mean) based on safety analysis set. ETD is based on observed data using MMRM with treatment, region and visit as factors and insulin dose at screening and baseline HbA1c as covariates;
CI, confidence interval; ETD, estimated treatment difference; IAsp, insulin aspart; IGlar U100, insulin glargine U100; MMRM, mixed model repeated measurement
Billings et al. Diabetes Care 2018;41(5):1009-1016

DUAL VII
Severe or BG-confirmed symptomatic hypoglycaemia



Mean cumulative function based on safety analysis set. Severe or BG-confirmed symptomatic: an episode that is severe according to the ADA classification or BG-confirmed by a plasma glucose value <3.1 mmol/L (<56 mg/dL) with symptoms consistent with hypoglycaemia
ADA, American Diabetes Association; BG, blood glucose; CI, confidence interval; IAsp, insulin aspart; IGlar U100, insulin glargine U100
Billings et al. *Diabetes Care* 2018;41(5):1009-1016

European Review for Medical and Pharmacological Sciences 2021; 25: 923-931

Real-word study on the effectiveness and safety of basal insulin IDegLira in type 2 diabetic patients previously treated with multi-injective insulin therapy

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Abstract. – **OBJECTIVE:** Achieving glycemic target is paramount to control diabetes mellitus (DM) and reduce micro vascular and mac-

Results: HbA1c (8.4 vs. 7.4%; p<0.0001) and body weight (94.1 vs. 93 kg; p<0.0001) were significantly lower after 6 months for patients on the degludec/liraglutide combination. A similar trend was observed in fasting glycemia levels (159 vs. 125 mg/dl; p<0.0001). An improved glycemic control was achieved with degludec/liraglutide despite a reduction in total daily insulin units (42 U at 6 months vs. 22 U at baseline; p<0.0001). In addition, higher scores in the DTSQ were registered after 6 months on degludec/liraglutide (mean score: 27 vs. 20; p<0.0001). The combination therapy also proved more convenient than basal-bolus therapy in terms of costs, with an average per-patient cost difference of €-0.41±0.59/die (p<0.0001).

combination therapy also proved more convenient than basal-bolus therapy in terms of costs, with an average per-patient cost difference of

in units (42 U at 6 months *vs.* 22 U at baseline, *p*<0.0001). In addition, higher scores in the DTSQ were registered after 6 months on degludec/liraglutide (mean score: 27 *vs.* 20; *p*<0.0001). The

management, recommend an add-on therapy for patients who do not achieve their glycemic target by means of metformin intake alone[6]. The

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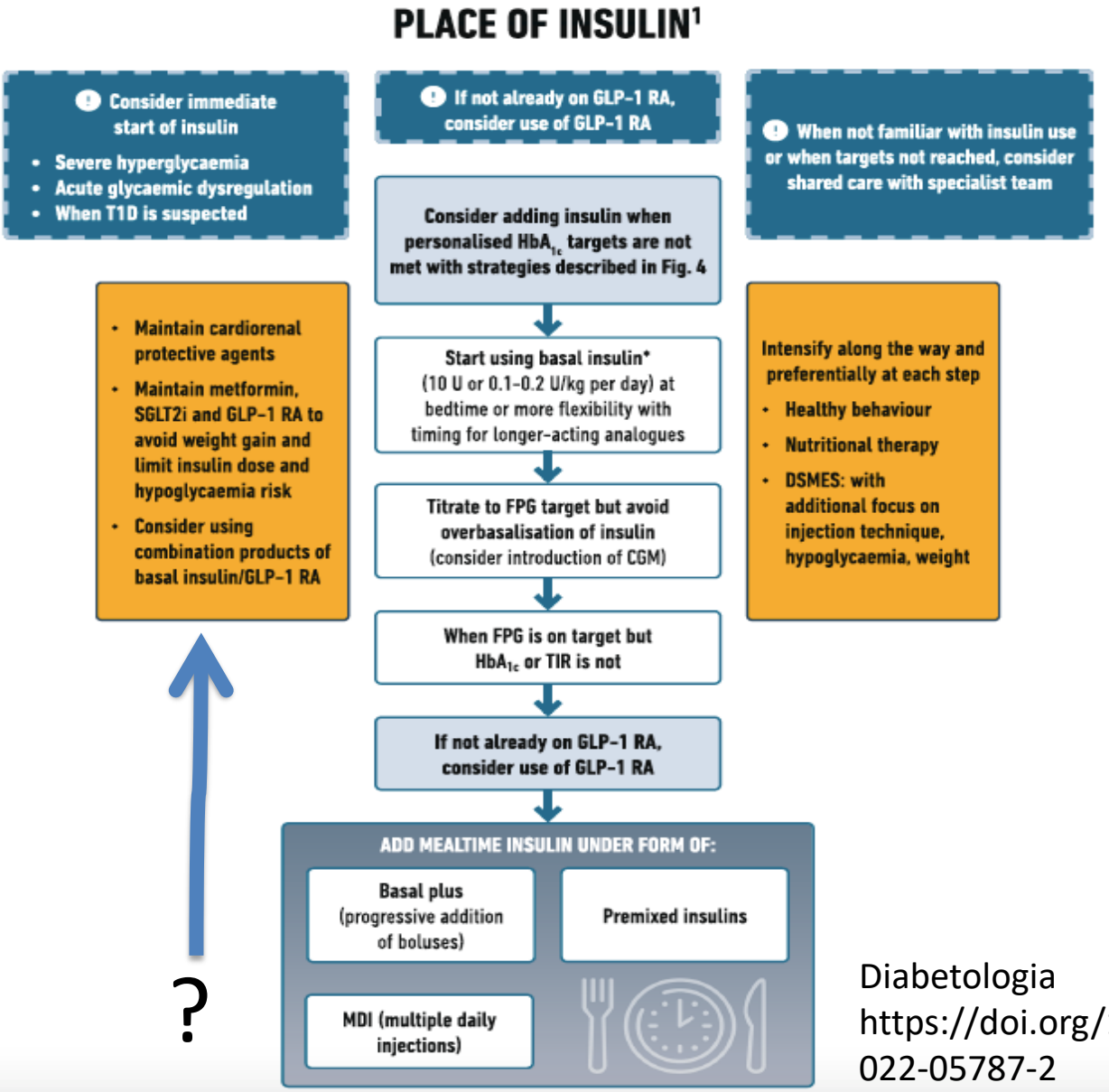
Management of hyperglycaemia in type 2 diabetes, September 2022.
A consensus report by the American Diabetes Association (ADA)
and the European Association for the Study of Diabetes (EASD)



Diabetologia
https://doi.org/10.1007/s00125-022-05787-2

Tabella 9: Indicatori di intensità/appropriatezza del trattamento. Confronto 2019 – 2020.

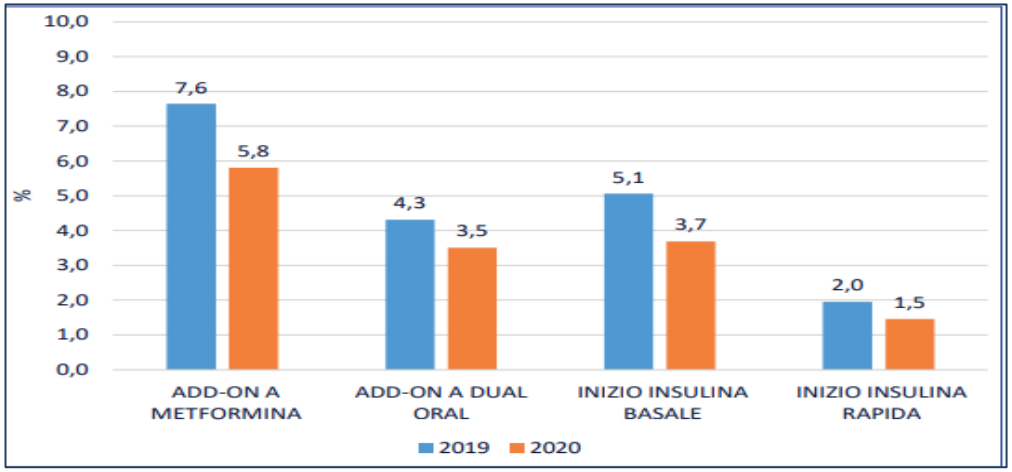
Indicatore	2019 (%)	2020 (%)
Soggetti non trattati con insulina nonostante valori di HbA1c ≥ 9,0% (%)	28,2	29,3
Soggetti con HbA1c ≥ 9,0% nonostante il trattamento con insulina (%)	16,5	18,4
Soggetti non trattati con ipolipemizzanti nonostante valori di C-LDL ≥ 130 mg/dl (%)	45,9	46,2
Soggetti con C-LDL ≥ 130 mg/dl nonostante il trattamento con ipolipemizzanti (%)	9,9	9,5
Soggetti non trattati con antiipertensivi nonostante valori di PA ≥ 140/90 mmHg (%)	26,7	27,1
Soggetti con PA ≥ 140/90 mmHg nonostante il trattamento con antiipertensivi (%)	48,2	51,1
Soggetti con evento CV pregresso (infarto e/o ictus) in terapia antiaggregante piastrinica (%)	75,1	72,7

È lievemente peggiorata dal 2018 anche la percentuale dei pazienti con HbA1c > 9% nonostante il trattamento con insulina . Oltre ad una quota di pazienti che "cronicamente" non è possibile riportare a target, potrebbero aprirsi nuovi spazi – in questa categoria di soggetti – per una rivalutazione critica degli schemi di terapia insulinica utilizzati nei DM2 (alcuni pazienti obesi, con secrezione residua non soppressa, potrebbero ad esempio beneficiare maggiormente dell'associazione di un GLP1-RA ad insulina basale rispetto a schemi basal-bolus, inefficaci in pazienti insulinoresistenti).

Si può impostare una terapia insulinica anche da remoto?

Tabella 12: Livelli medi di HbA1c al momento dell'intensificazione.

Tipo di intensificazione	2019	2020
Add-on a metformina	8,2±1,7	8,2±1,8
Add-on a dual oral	8,4±1,5	8,3±1,4
Inizio insulina basale	8,7±1,9	8,7±2,0
Inizio insulina rapida	9,2±2,3	9,3±2,5



La Monografia degli Annali AMD 2020 "Indicatori di inerzia clinica nel DM2" ci ha mostrato che l'inerzia nell'intensificazione della terapia con insulina basale è un fenomeno rilevante, di entità maggiore rispetto a quanto accade nel momento dell'add-on di altri farmaci ipoglicemizzanti, con potenziale danno per i pazienti con diabete, in termini di rischio di sviluppo di complicanze.

L'impatto della pandemia di COVID-19 sulla intensificazione con insulina basale si è rivelato maggiore rispetto a quanto accaduto per le altre forme di intensificazione terapeutica: la riduzione relativa del numero di soggetti in cui nel 2020 è stata intensificata la terapia mediante insulina basale è stata del 27,5% rispetto a quanto avvenuto nel 2019, essendosi ciò verificato nel 3,7% dei pazienti, contro il 5,1% del 2019 (figura 4). Durante il 2020 una quota rilevante di pazienti è stata visitata "da remoto", in particolare nei primi mesi di lockdown; l'inizio della terapia insulinica richiede una necessaria educazione terapeutica, che difficilmente può avvenire se non in presenza, e ciò potrebbe in parte spiegare l'entità della riduzione, che comunque si accompagna ad un calo generalizzato del numero di farmaci prescritti per la cura del diabete.

La complessità dell'educazione al trattamento insulinico

Ensuring that patients and/or caregivers understand correct insulin injection technique is important to optimize glucose control and insulin use safety. Thus, it is important that insulin be delivered into the proper tissue in the right way. (Hypoglycemia)

- Appropriate body areas, injection site rotation
- Appropriate care of injection sites to avoid infection or other complications
- Intramuscular
- Use of short needles (e.g., 4-mm pen needles)

To avoid

- lipohypertrophy.
- erratic insulin absorption
- increased glycemic variability
- unexplained hypoglycemic episodes

Standards of Medical Care in Diabetes—2020
Insulin Injection Technique

Quali opportunità offrono le nuove combinazioni precostituite di insulina basale più GLP1-RA in questo ambito ?

Rispetto ad altre basali

- Controllo glicemico globale (FPG e PPG)
- Maggiore riduzione e controllo durevole della HbA1c
- Sicurezza e tollerabilità sul lungo termine
- Rischio minimo di ipoglicemia
- Effetto favorevole sul peso
- Effetto favorevole sul rischio CV
- Semplicità di somministrazione

Rispetto allo schema bb

- Non-inferiorità di HbA_{1c}
- Minor numero di ipoglicemie e variabilità glicemica
- Effetto favorevole sul rischio CV
- 1 somministrazione giornaliera
- Riduzione significativa del peso
- Costi minori
- Maggiore aderenza alla terapia
- Migliore qualità della vita

Semplicità di trattamento

Efficacy and Safety of Basal Insulin/GLP-1 Receptor Agonist Used in Combination for Type 2 Diabetes Management

Management of type 2 diabetes is complex and multifactorial.

Utilizing combination products is a way to target several areas of the disease while decreasing the complexity and burden to the patient.

Basal insulin/glucagon-like peptide-1 (GLP-1) agonist combination products have the benefit of being highly efficacious while having favorable effects on weight, reduced gastrointestinal adverse effects, and low hypoglycemic risks compared to the individual agents used alone.

Journal of pharmacy practice Delilah McCarty, Volume 32, Issue 6
https://doi.org/10.1177/0897190018764984

Clinical Considerations When Initiating and Titrating Insulin Degludec/Liraglutide (IDegLira) in People with Type 2 Diabetes

Therapeutic inertia is a substantial obstacle to the initiation of insulin therapy in people with uncontrolled type 2 diabetes……As an injectable therapy that is simple to titrate, **IDegLira** has the potential to optimize the ability to achieve relevant glycemic targets, and offers a suitable treatment option for people with T2D requiring insulin therapy who are at risk of hypoglycemia or weight gain.

Harris Drugs 2020 Feb;80(2):147-165

Si può impostare una terapia insulinica anche da remoto?
Quali opportunità offrono le nuove combinazioni precostituite di insulina basale più GLP1-RA in questo ambito ?

Efficacia - Sicurezza – Durability - Semplicità !!!