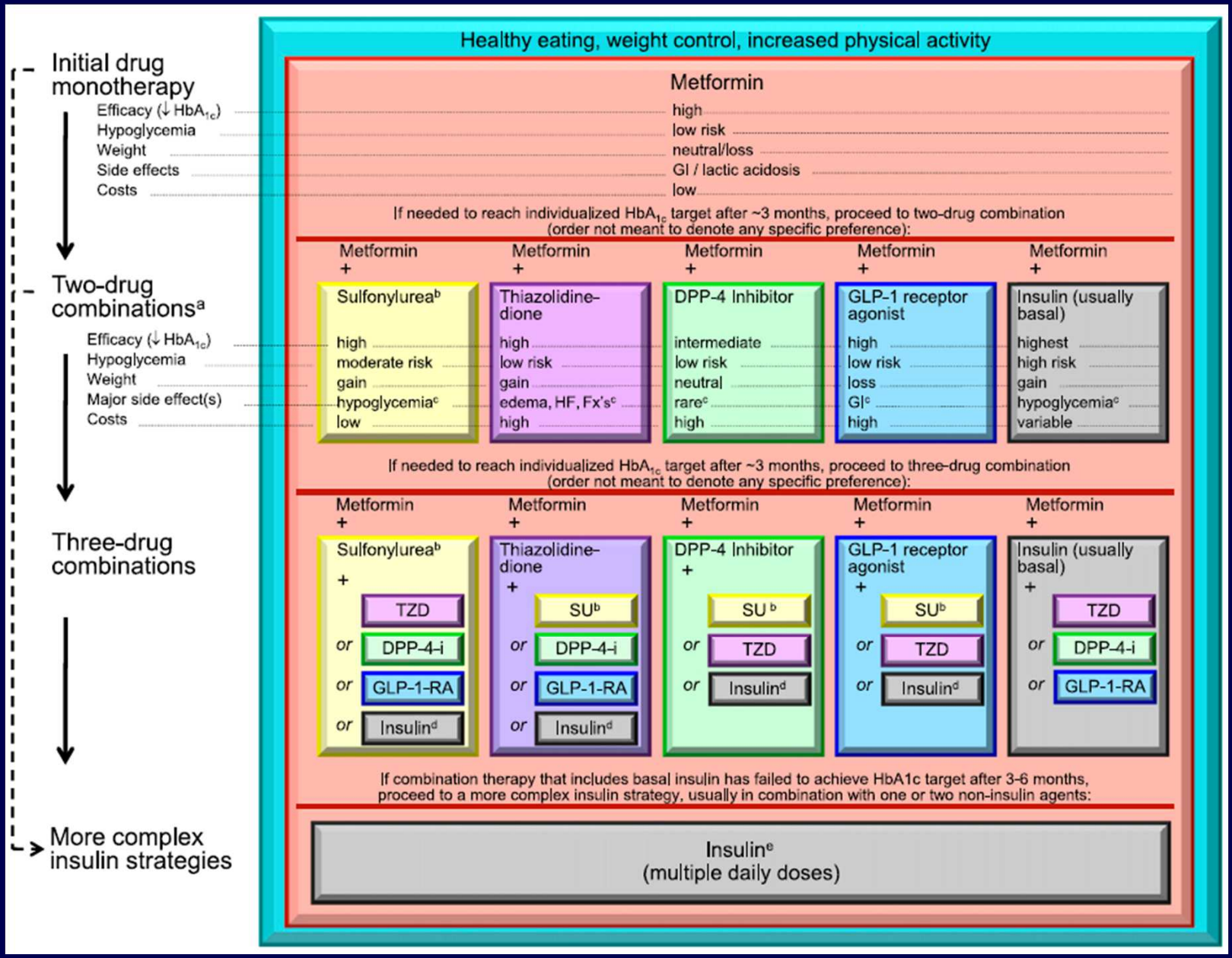
Les traitements du diabète : quelle place pour les nouvelles molécules?

François Jornayvaz

05.06.2014

Prise en charge médicamenteuse du DM2



Diabetes Care/Diabetologia, avril 2012

Traitement du diabète de type 2

- En premier lieu, **mesures hygiéno-diététiques** :
  - Perte pondérale, viser 7% du poids actuel
  - Activité physique (modérée type marche à pied), environ 150 minutes/semaine (en min 3 séances)

- Puis : **thérapeutique médicamenteuse** :
  - Choix
  - Recommandations
  - Evidence du bénéfice
  - Effets secondaires

Effet des antidiabétiques sur l'HbA1c

Table 1—*Summary of glucose-lowering interventions*

Intervention	Expected decrease in A1C with monotherapy (%)	Advantages	Disadvantages
Tier 1: well-validated core			
Step 1: initial therapy			
Lifestyle to decrease weight and increase activity	1.0–2.0	Broad benefits	Insufficient for most within first year
Metformin	1.0–2.0	Weight neutral	GI side effects, contraindicated with renal insufficiency
Step 2: additional therapy			
Insulin	1.5–3.5	No dose limit, rapidly effective, improved lipid profile	One to four injections daily, monitoring, weight gain, hypoglycemia, analogues are expensive
Sulfonylurea	1.0–2.0	Rapidly effective	Weight gain, hypoglycemia (especially with glibenclamide or chlorpropamide)
Tier 2: less well validated			
TZDs	0.5–1.4	Improved lipid profile (pioglitazone), potential decrease in MI (pioglitazone)	Fluid retention, CHF, weight gain, bone fractures, expensive, potential increase in MI (rosiglitazone)
GLP-1 agonist	0.5–1.0	Weight loss	Two injections daily, frequent GI side effects, long-term safety not established, expensive
Other therapy			
α-Glucosidase inhibitor	0.5–0.8	Weight neutral	Frequent GI side effects, three times/day dosing, expensive
Glinide	0.5–1.5[a]	Rapidly effective	Weight gain, three times/day dosing, hypoglycemia, expensive
Pramlintide	0.5–1.0	Weight loss	Three injections daily, frequent GI side effects, long-term safety not established, expensive
DPP-4 inhibitor	0.5–0.8	Weight neutral	Long-term safety not established, expensive

[a]Repaglinide more effective in lowering A1C than nateglinide. CHF, congestive heart failure; GI, gastrointestinal; MI, myocardial infarction.

Diabetes Care, 2009

Utilisation de la metformine

TITRATION OF METFORMIN

1. Begin with low-dose metformin (500 mg) taken once or twice per day with meals (breakfast and/or dinner) or 850 mg once per day.
2. After 5–7 days, if gastrointestinal side effects have not occurred, advance dose to 850, or two 500 mg tablets, twice per day (medication to be taken before breakfast and/or dinner).
3. If gastrointestinal side effects appear as doses advanced, decrease to previous lower dose and try to advance the dose at a later time.
4. The maximum effective dose can be up to 1,000 mg twice per day but is often 850 mg twice per day. Modestly greater effectiveness has been observed with doses up to about 2,500 mg/day. Gastrointestinal side effects may limit the dose that can be used.
5. Based on cost considerations, generic metformin is the first choice of therapy. A longer-acting formulation is available in some countries and can be given once per day.

Diabetes Care, Jan.2009

Metformine et procédure avec produit de contraste :

Discontinuer la metformine le jour de l'examen et reprendre le ttt 48 heures plus tard si la fonction rénale le permet.

Metformine au long cours et déficit en vitamine B12 :

Peut causer une neuropathie. Pas de recommandations claires à l'heure actuelle.

Sulfonylurées

Tableau 2. Propriétés pharmacocinétiques des principales sulfonylurées de seconde génération disponibles en Suisse

a Courte : < 12 heures ; Intermédiaire : 12-24 heures ; Longue : > 24 heures.

b Dose quotidienne avec la formule MR : 30-120 mg.

Principe actif	Dose quotidienne (mg)	Durée d'action[a]	Méta-bolites actifs	Voie d'élimination principale	
Glibenclamide	2,5-15	Intermédiaire à longue	Oui	Bile ≈ 50%	= Daonil, …
Glimépiride	1-6	Intermédiaire	Oui	Urine ≈ 80%	= Amaryl, …
Gliclazide	40-320[b]	Intermédiaire	Non	Urine ≈ 65%	= Diamicron, …
Glibornuride	12,5-75 mg	Intermédiaire	Non	Urine ≈ 65%	= Glutril

Revue Médicale Suisse, 2006

Diabète et conduite automobile

Selon directives de la SSED, 2011

3. Obligation médicale d'informer

insuline, sulfonylurées, glinides

Lors d'un traitement associé à un risque d'hypoglycémie, le médecin traitant est tenu de fournir des informations sur ces directives aux détenteurs d'un permis de conduire et d'expliquer au patient comment il doit évaluer sa capacité à conduire. Le fait que ces informations ont été fournies devrait être documenté dans le dossier médical. Le médecin n'est pas obligé de signaler à l'autorité de surveillance les personnes qui ne sont pas aptes à conduire avec sûreté, mais il a le droit de le faire (art. 14 paragraphe 4 LCR).

Tableau 2. Recommandations aux patients diabétiques avant de conduire un véhicule

- Ne pas prendre le volant avec une glycémie < 5 mmol/l
- Si la glycémie est < 5 mmol/l, prendre 15-20 g de glucides et contrôler la glycémie 20 minutes plus tard
- Si la glycémie est entre 5 et 7 mmol/l, prendre 10 g de glucides
- Manger à intervalles réguliers, faire une pause toutes les 60 à 90 minutes et contrôler la glycémie. Reprendre 10 g de glucides si celle-ci est entre 5 et 6 mmol/l
- Après une hypoglycémie, attendre 30 minutes avant de reprendre la route
- Toujours prévoir des aliments en suffisance dans le véhicule pour corriger une hypoglycémie

Rev Med Suisse, 2011

Extrait de la brochure :
www.associationdudiabete.ch

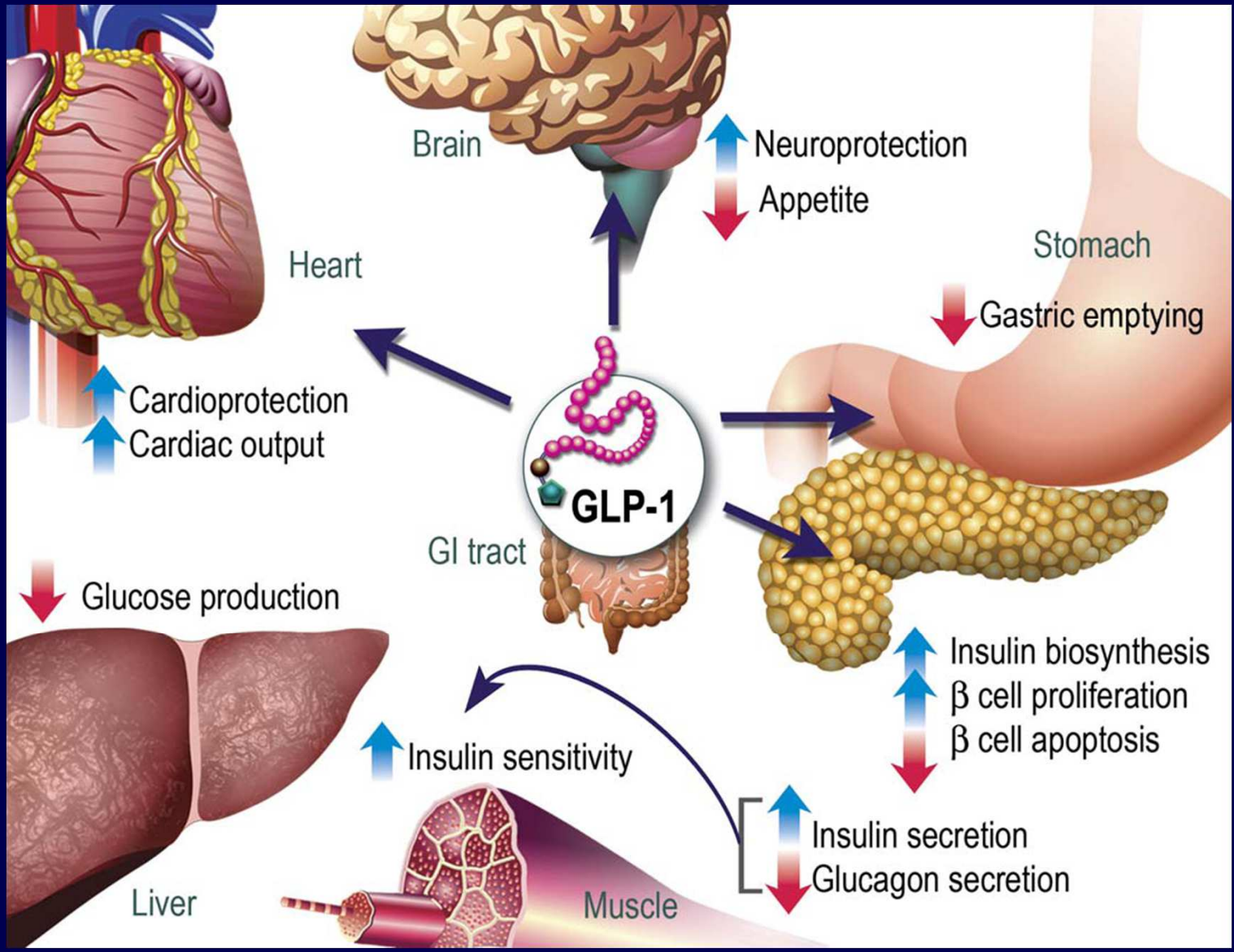
Glitazones

- **Cette classe thérapeutique n'a plus le vent en poupe et ne devrait être prescrite que dans des situations particulières. En plus des risques d'insuffisance cardiaque et d'ostéoporose :**

  - Rosiglitazone (Avandia) : retirée du marché fin 2010 pour augmentation de la mortalité CV.

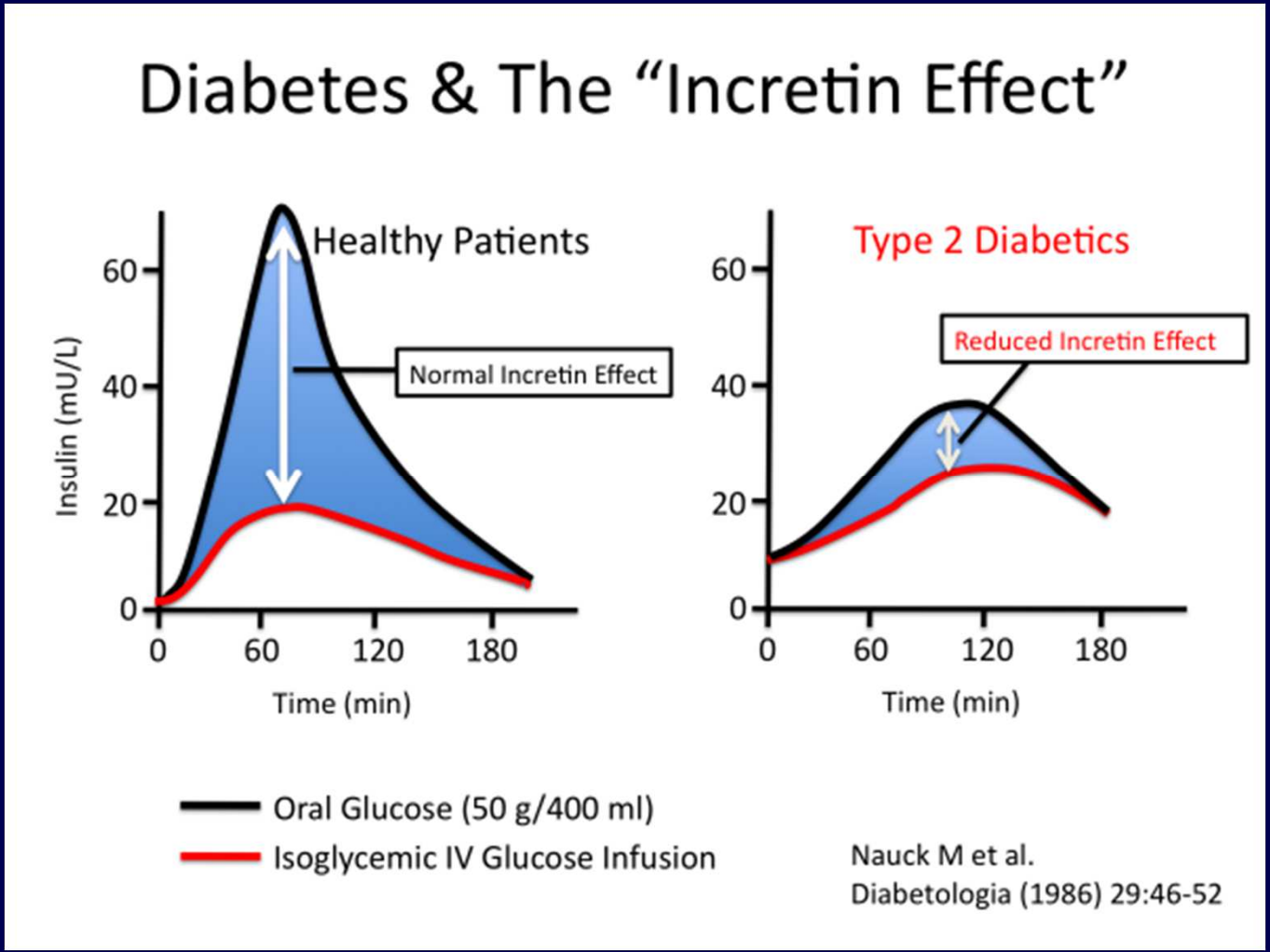
  - Pioglitazone (Actos) : risque accru de cancer de la vessie (essentiellement lié à la durée et à la dose cumulée). Retirée du marché en France.

Physiologic role of GLP-1



Drucker DJ, Cell Metab 2006

L’effet incrétine est diminué dans le DM2



Analogue GLP-1 : exenatide (Byetta)

- **Injection sc 5-10 µg 2x/j à n'importe quelle heure, avant les repas.**
- **Prise en charge de remboursement : patients avec DM2 avec contrôle insuffisant sous ADO (metformine ou sulfonylurée en monothérapie ou association de metformine et sulfonylurée), BMI > 28 kg/m^2.**

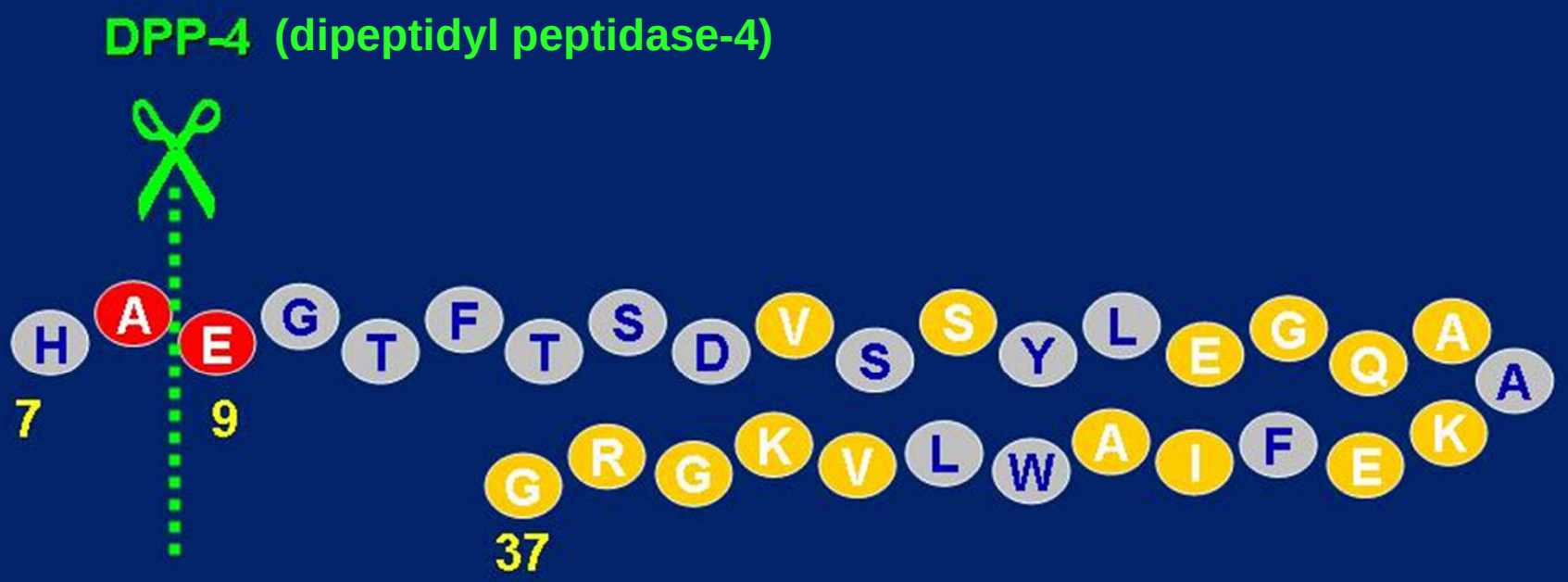
Analogue GLP-1 : exenatide (Bydureon)

- **Injection sc 2 mg 1x/sem à n'importe quelle heure, sans lien avec les repas.**
- **Prise en charge de remboursement : patients avec DM2 avec contrôle insuffisant sous ADO (metformine ou sulfonylurée en monothérapie ou association de metformine et sulfonylurée), BMI > 28 kg/m^2.**

Analogue GLP-1 : liraglutide (Victoza)

- **Injection sc 0.6, 1.2 ou 1.8 mg 1x/j à n'importe quelle heure, indépendamment des repas.**
- **Prise en charge de remboursement : patients avec DM2 avec contrôle insuffisant sous ADO (metformine ou sulfonylurée en monothérapie ou association de metformine et sulfonylurée), BMI > 28 kg/m^2.**

GLP-1 is Rapidly Degraded by the DPP-4 Enzyme



$T_{½}$ = 1–2 minutes

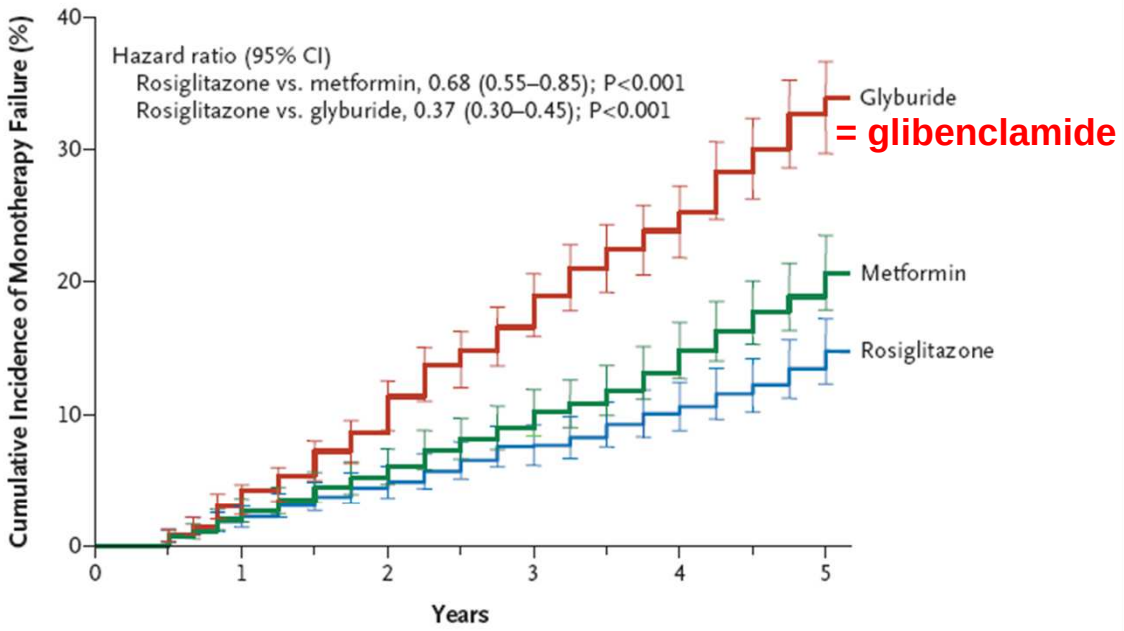
*Amino acids shown in gold are homologous with the structure of glucagon

Les inhibiteurs de l'enzyme DPP-4

- **Sitagliptine** (Januvia, Xelevia) : 100 mg 1x/j (25 ou 50 mg 1x/j selon IR)
- **Vildagliptine** (Galvus) : 50 mg 2x/j (1x/j si IR)
- **Saxagliptine** (Onglyza) : 5 mg 1x/j (2.5 mg 1x/j si IR)
- **Linagliptine** (Trajenta) : 5 mg 1x/j (Pas d'ajustement si IR)
- **Alogliptine** (Vipidia) : 25 mg 1x/j (12.5 ou 6.25 mg 1x/j selon IR)

Formes combinées avec metformine disponibles

Durabilité : l'étude ADOPT



No. at Risk						
Rosiglitazone	1393	1207	1078	957	844	324
Metformin	1397	1205	1076	950	818	311
Glyburide	1337	1114	958	781	617	218

Figure 2. Kaplan–Meier Estimates of the Cumulative Incidence of Monotherapy Failure at 5 Years.

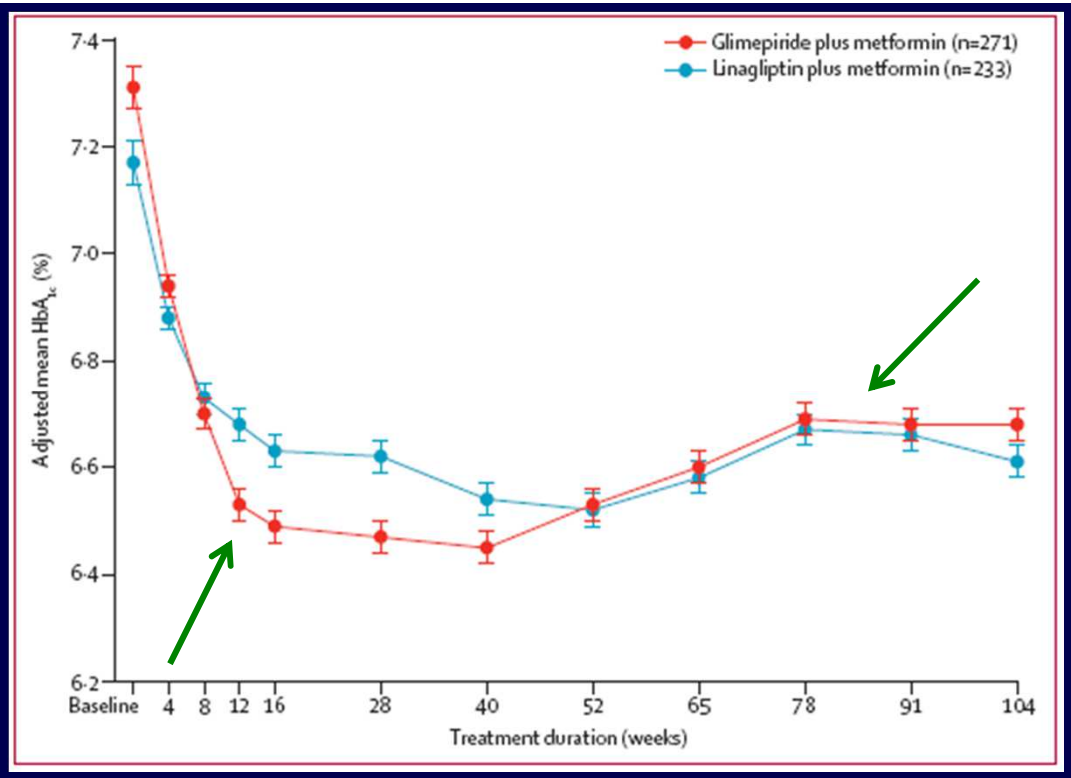
Treatment was considered to have failed if a patient had a confirmed or adjudicated level of fasting plasma glucose of more than 180 mg per deciliter. Risk reduction is listed for comparisons of pairwise groups from a baseline covariate-adjusted Cox proportional-hazards model. Gray's estimates of cumulative incidence adjusted for all deaths were smaller than Kaplan–Meier estimates of treatment failure: 10% in the rosiglitazone group, 15% in the metformin group, and 25% in the glyburide group. I bars indicate 95% CIs.

Kahn SE et al, N Engl J Med 2006;355:2427-43

Durabilité de la linagliptine

2-year efficacy and safety of linagliptin compared with glimepiride in patients with type 2 diabetes inadequately controlled on metformin: a randomised, double-blind, non-inferiority trial

Baptist Gallwitz, Julio Rosenstock, Thomas Rauch, Sudipta Bhattacharya, Sanjay Patel, Maximilian von Eynatten, Klaus A Dugi, Hans-Juergen Woerle



Gallwitz B et al, Lancet 2012; 380:475-83

Inhibiteurs DPP4 et études cardiovasculaires

	TECOS[1]	SAVOR-TIMI53[2]	EXAMINE[3]	CARMELINA[4]	CAROLINA[5]
DPP4 inhibitor	Sitagliptin	Saxagliptin	Alogliptin	Linagliptin	Linagliptin
Comparator	Placebo	Placebo	Placebo	Placebo	SU (active)
No. of patients	14,000	16,500	5,400	8,300	6,000
Trial initiation	Nov 2008	May 2010	Sept 2009	2013	Oct 2010
Background diabetes therapy per protocol	Any	Any	Any	Any	Predominantly on metformin background
Key inclusion criteria	Preexisting cardiovascular disease	High risk for CV events	History of ACS	Previous vascular complications and albuminuria; evidence of renal-related end-organ damage	Previous vascular complications; evidence of end-organ damage; ≥ two specified traditional CV risk factors

1,3,4,5. Primary endpoint: Cardiovascular (CV) death, nonfatal myocardial infarction (MI), nonfatal stroke, hospitalization due to unstable angina pectoris.
2. Primary endpoint: Major adverse cardiovascular events (CV death, nonfatal MI, nonfatal stroke).
Source: 1. ClinicalTrials.gov NCT00790205; 2. NCT01107886; 3. NCT00968708; 4. Data on file; 5. NCT01243424.

SAVOR-TIMI 53 STUDY

Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus

BACKGROUND

The cardiovascular safety and efficacy of many current antihyperglycemic agents, including saxagliptin, a dipeptidyl peptidase 4 (DPP-4) inhibitor, are unclear.

METHODS

We randomly assigned 16,492 patients with type 2 diabetes who had a history of, or were at risk for, cardiovascular events to receive saxagliptin or placebo and followed them for a median of 2.1 years. Physicians were permitted to adjust other medications, including antihyperglycemic agents. The primary end point was a composite of cardiovascular death, myocardial infarction, or ischemic stroke.

Scirica BM, N Engl J Med 2013

SAVOR-TIMI 53 STUDY

Table 2. Prespecified Clinical End Points.*

End Point	Saxagliptin (N=8280)	Placebo (N=8212)	Hazard Ratio (95% CI)	P Value
	no. (%)			
Cardiovascular death, myocardial infarction, or stroke: primary efficacy end point	613 (7.3)	609 (7.2)	1.00 (0.89–1.12)	0.99
Cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, heart failure, or coronary revascularization: secondary efficacy end point	1059 (12.8)	1034 (12.4)	1.02 (0.94–1.11)	0.66
Death from any cause	420 (4.9)	378 (4.2)	1.11 (0.96–1.27)	0.15
Death from cardiovascular causes	269 (3.2)	260 (2.9)	1.03 (0.87–1.22)	0.72
Myocardial infarction	265 (3.2)	278 (3.4)	0.95 (0.80–1.12)	0.52
Ischemic stroke	157 (1.9)	141 (1.7)	1.11 (0.88–1.39)	0.38
Hospitalization for unstable angina	97 (1.2)	81 (1.0)	1.19 (0.89–1.60)	0.24
Hospitalization for heart failure	289 (3.5)	228 (2.8)	1.27 (1.07–1.51)	0.007
Hospitalization for coronary revascularization	423 (5.2)	459 (5.6)	0.91 (0.80–1.04)	0.18
Doubling of creatinine level, initiation of dialysis, renal transplantation, or creatinine >6.0 mg/dl (530 μmol/liter)	194 (2.2)	178 (2.0)	1.08 (0.88–1.32)	0.46
Hospitalization for hypoglycemia	53 (0.6)	43 (0.5)	1.22 (0.82–1.83)	0.33

CONCLUSIONS

DPP-4 inhibition with saxagliptin did not increase or decrease the rate of ischemic events, though the rate of hospitalization for heart failure was increased. Although saxagliptin improves glycemic control, other approaches are necessary to reduce cardiovascular risk in patients with diabetes. (Funded by AstraZeneca and Bristol-Myers Squibb; SAVOR-TIMI 53 ClinicalTrials.gov number, NCT01107886.)

Scirica BM, N Engl J Med 2013

EXAMINE STUDY

Alogliptin after Acute Coronary Syndrome in Patients with Type 2 Diabetes

BACKGROUND

To assess potentially elevated cardiovascular risk related to new antihyperglycemic drugs in patients with type 2 diabetes, regulatory agencies require a comprehensive evaluation of the cardiovascular safety profile of new antidiabetic therapies. We assessed cardiovascular outcomes with alogliptin, a new inhibitor of dipeptidyl peptidase 4 (DPP-4), as compared with placebo in patients with type 2 diabetes who had had a recent acute coronary syndrome.

METHODS

We randomly assigned patients with type 2 diabetes and either an acute myocardial infarction or unstable angina requiring hospitalization within the previous 15 to 90 days to receive alogliptin or placebo in addition to existing antihyperglycemic and cardiovascular drug therapy. The study design was a double-blind, noninferiority trial with a prespecified noninferiority margin of 1.3 for the hazard ratio for the primary end point of a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

White WB, N Engl J Med 2013

EXAMINE STUDY

Table 3. Major Safety End Points.

End Point	Placebo (N=2679)	Alogliptin (N=2701)	Hazard Ratio for Alogliptin Group (95% CI)	P Value*
	no. (%)			
Primary end point†	316 (11.8)	305 (11.3)	0.96 (≤1.16)‡	0.32
Components of primary end point				
Death from cardiovascular causes	111 (4.1)	89 (3.3)	0.79 (0.60–1.04)	0.10
Nonfatal myocardial infarction	173 (6.5)	187 (6.9)	1.08 (0.88–1.33)	0.47
Nonfatal stroke	32 (1.2)	29 (1.1)	0.91 (0.55–1.50)	0.71
Principal secondary end point§	359 (13.4)	344 (12.7)	0.95 (≤1.14)‡	0.26
Other end points				
Death from any cause	173 (6.5)	153 (5.7)	0.88 (0.71–1.09)	0.23
Death from cardiovascular causes¶	130 (4.9)	112 (4.1)	0.85 (0.66–1.10)	0.21

CONCLUSIONS

Among patients with type 2 diabetes who had had a recent acute coronary syndrome, the rates of major adverse cardiovascular events were not increased with the DPP-4 inhibitor alogliptin as compared with placebo. (Funded by Takeda Development Center Americas; EXAMINE ClinicalTrials.gov number, NCT00968708.)

White WB, N Engl J Med 2013

Médicaments agissant sur le sytème incrétine, pancréatite et cancer pancréatique

Pancreatic Safety of Incretin-Based Drugs — FDA and EMA Assessment

Amy G. Egan, M.D., M.P.H., Eberhard Blind, M.D., Ph.D., Kristina Dunder, M.D., Pieter A. de Graeff, M.D., B. Timothy Hummer, Ph.D., Todd Bourcier, Ph.D., and Curtis Rosebraugh, M.D., M.P.H.

… the FDA and the EMA have explored multiple streams of data pertaining to a pancreatic safety signal associated with incretin-based drugs. …assertions concerning a causal association between incretin-based drugs and pancreatitis or pancreatic cancer, as expressed recently in the scientific literature and in the media, are inconsistent with the current data… Ongoing strategies include systematic capture of data on pancreatitis and pancreatic cancer from cardiovascular outcome trials and ongoing clinical trials, which should facilitate meta-analyses, and accumulation of further knowledge regarding these signals in the future…

N Engl J Med, février 2014

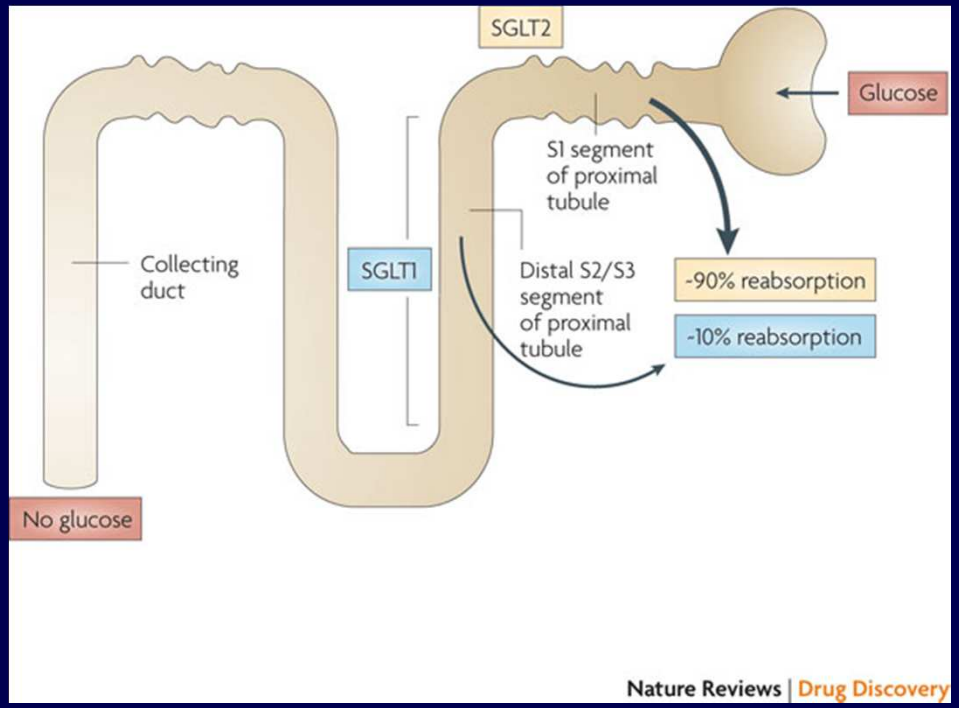
Les inhibiteurs du SGLT2

Table 1. SGLT-2 Inhibitors Currently in Development[8–15]

Stage in Development	Trade Name/Code Name	Manufacturer
Phase 1	GSK-1614235/DSP-3235/KPA-3235	GlaxoSmithKline, Dainippon Sumitomo Pharma (under license from Kissei Pharmaceutical Company)
Phase 2	PF-04971729	Pfizer
	LX-4211[a]	Lexicon Pharmaceutical
	BI-44847	Boehringer Ingelheim (under license from Ajinomoto)
	Ipragliflozin	Astellas Pharma, Kotobuki Pharmaceutical Company
Phase 3	Dapagliflozin	AstraZeneca, Bristol-Myers Squibb
	Empagliflozin, Canagliflozin	Boehringer Ingelheim, Eli Lilly, Johnson and Johnson, Mitsubishi Tanabe Pharma
	Tofogliflozin	Chugai Pharmaceutical, Roche

[a]SGLT-1 and SGLT-2 inhibitor.

Riser Taylor and Harris, Pharmacotherapy 2013



Les inhibiteurs du SGLT2 - CANAGLIFLOZINE

- **Avantages :**
  - **Réduction de l'HbA1c (-0.70 à -0.95%).**
  - **Faible risque d'hypoglycémie.**
  - **Perte pondérale (jusqu'à -2.3 kg comparé au placebo; effet plateau).**
  - **Diminution de la TA systolique (0.9-4.9 mmHg).**
  - **Peu d'interactions médicamenteuses.**

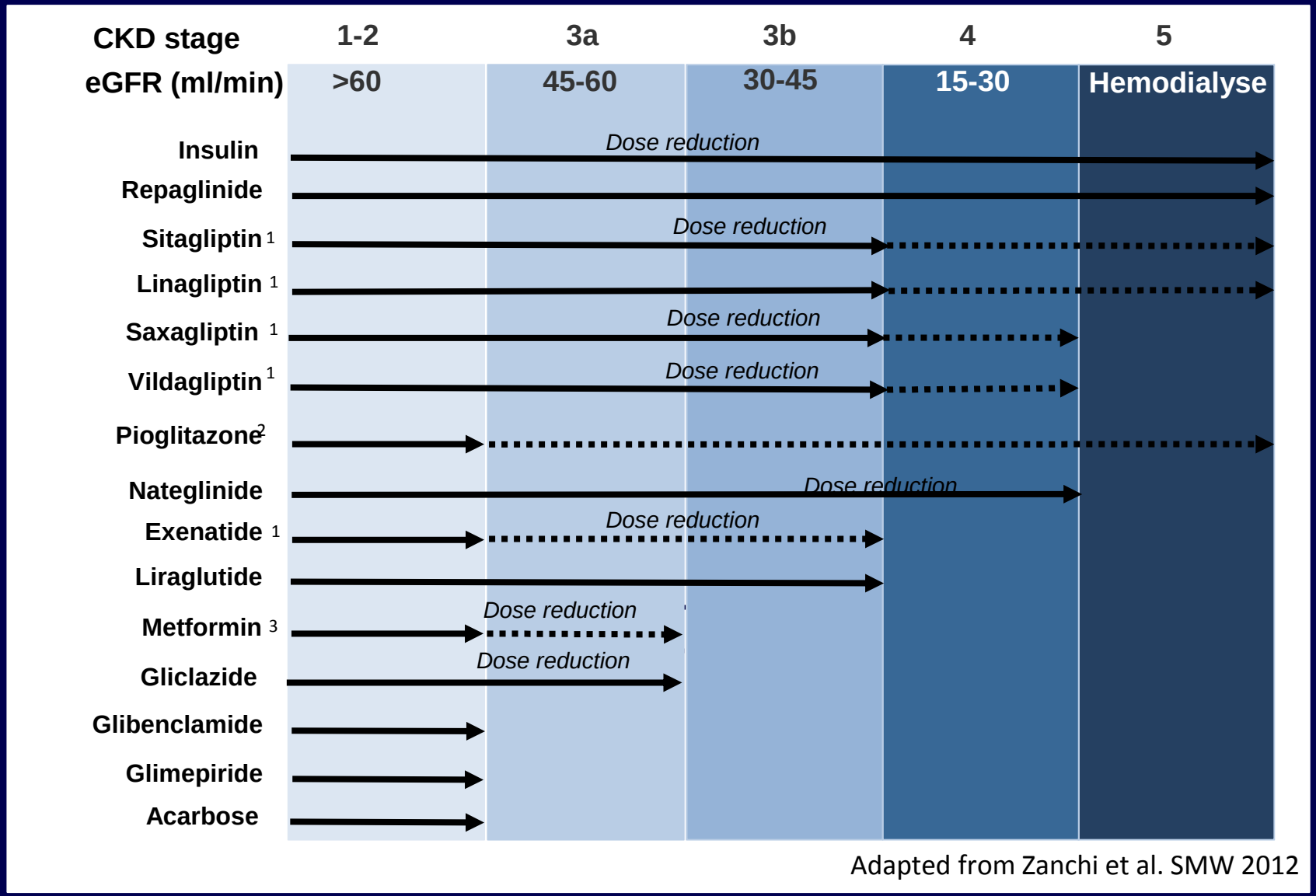
- **Désavantages :**
  - **Risque d'infection mycotique>urinaire (inf. mycotiques : env. 10% contre 3% avec placebo chez femmes; env. 4% contre 0.6% avec placebo chez hommes, surtout si non circoncis).**
  - **Effets à long terme inconnus (CANVAS : étude cardiovasculaire).**

Les inhibiteurs du SGLT2

- **Canagliflozine (Invokana) : *selon le compendium***

  - **Débuter à 100 mg/j, év. augmenter à 300 mg/j.**
  - **Inefficace si eGFR<45 ml/min (baisser la dose si eGFR<60 ml/min).**
  - **Pas d'ajustement dans l'insuffisance hépatique légère ou modérée.**
  - **Une prise avant le petit-déjeuner.**
  - **Monothérapie si intolérance à la metformine.**
  - **Admis en association avec metformine, SU, insuline (pas pioglitazone, DPP4 inhibiteurs et GLP-1 agonistes).**
  - **Risque d'hyperkaliémie (mécanisme?) : CAVE chez patients sous IEC/sartans ou diurétiques d'épargne potassique.**

Antidiabétiques oraux et insuffisance rénale



Adapted from Zanchi et al. SMW 2012

Prix des traitements journaliers

MEDICAMENT	DOSAGE	PRIX PAR JOUR
Glucophage Metfin	1000 mg 2x/j 1000 mg 2x/j	0.42 CHF 0.31 CHF
Diamicron MR Gliclazide MR	60 mg 1x/j 30 mg 2x/j	0.61 CHF 0.49 CHF
Januvia/Xelevia	100 mg 1x/j	2.16 CHF
Galvus	50 mg 2x/j	2.37 CHF
Onglyza	5 mg 1x/j	1.91 CHF
Trajenta	5 mg 1x/j	1.95 CHF
Jentadueto	2.5/1000 mg 2x/j	2.05 CHF
Invokana	100 mg 1x/j	2.15 CHF
Victoza	1,8 mg 1x/j	7.53 CHF
Byetta	10 µg 2x/j	4.66 CHF
Bydureon	2 mg 1x/sem	5.31 CHF

Source : Compendium Suisse des Médicaments, mai 2014

L'étude GRADE

The Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study

- **Aim:** The **GRADE** Study is a clinical trial that will compare commonly used diabetes medications (**glimepiride, sitagliptin, liraglutide, insulin glargine**), when **combined with metformin**, on glycemia-lowering effectiveness and patient-centered outcomes (**primary outcome: time to HbA1c ≥7% = time to primary failure**).

- Other long-term metabolic outcomes include the need for the addition of basal insulin after a confirmed A1C >7.5%.

- The four drugs will also be compared with respect to selected microvascular complications, cardiovascular disease risk factors, adverse effects, tolerability, quality of life, and cost-effectiveness.

Nathan DM et al, Diabetes Care 2013;36:2254-61

Evolution du patient diabétique de type 2

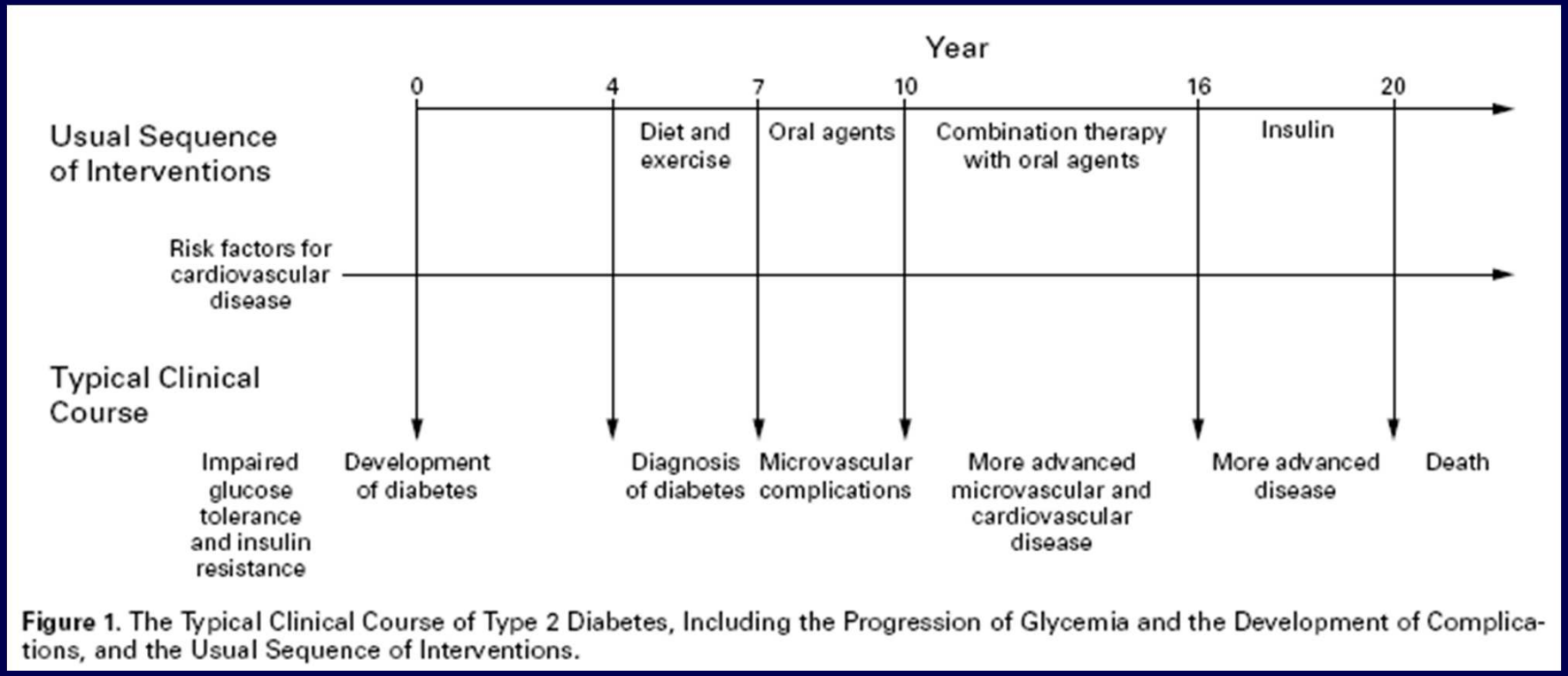
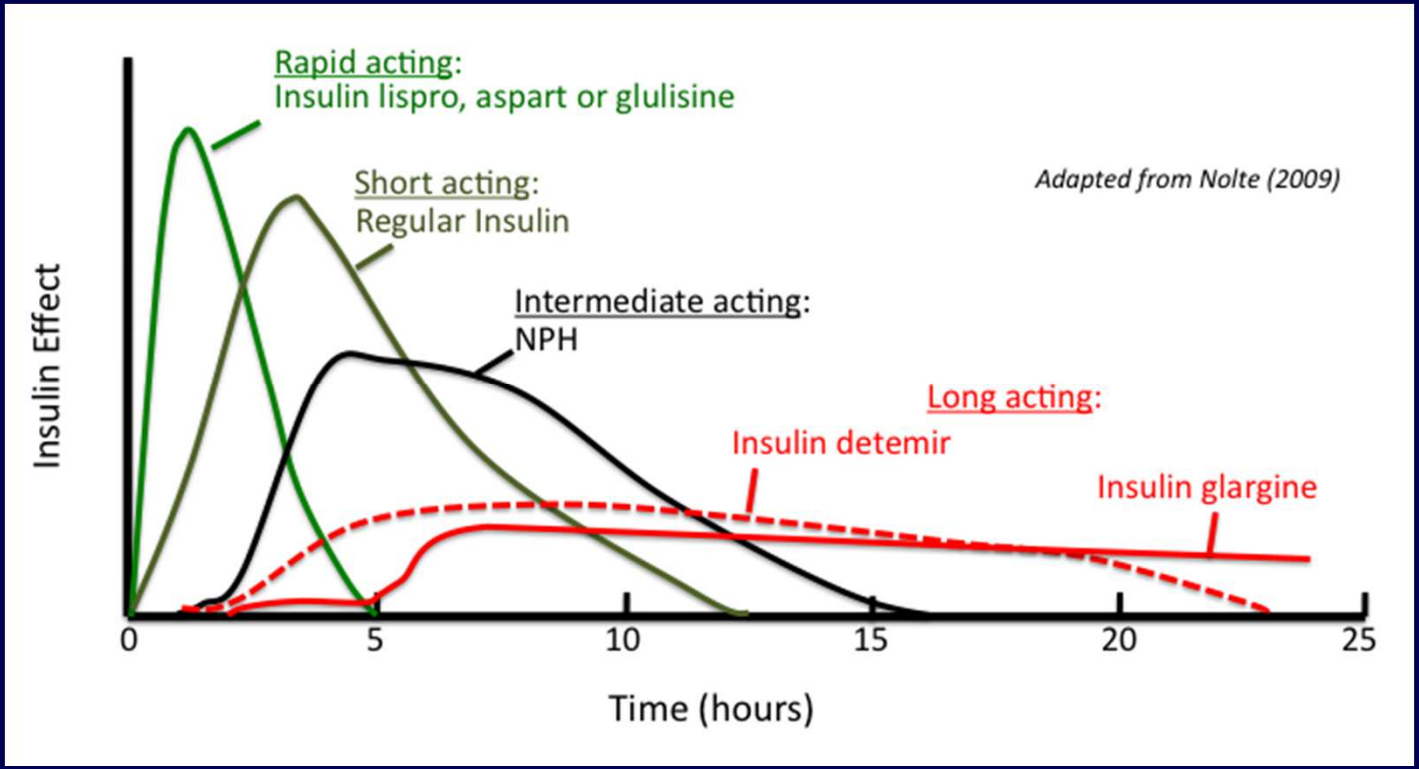


Figure 1. The Typical Clinical Course of Type 2 Diabetes, Including the Progression of Glycemia and the Development of Complications, and the Usual Sequence of Interventions.

NEJM, 2002

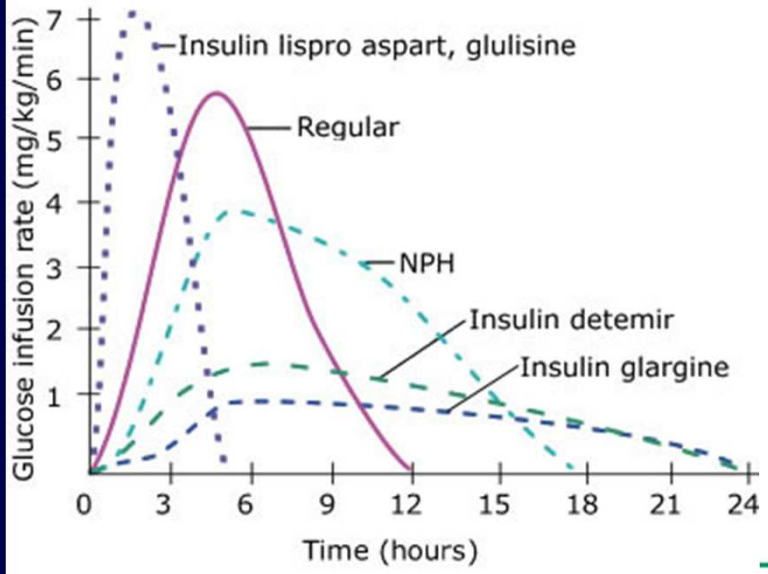
Profil des insulines



- **Rapides** : aspart (Novorapid), lispro (Humalog) et glulisine (Apidra)
- **NPH** : Insulatard et Huminsulin Basal
- **Determir** : Levemir
- **Glargine** : Lantus
- **Degludec** : Tresiba (profil plat, action plus longue que la glargine)

Profil des insulines

Activity Profiles of Different Types of Insulin



Pharmacokinetics of the most commonly used insulin insulin preparations

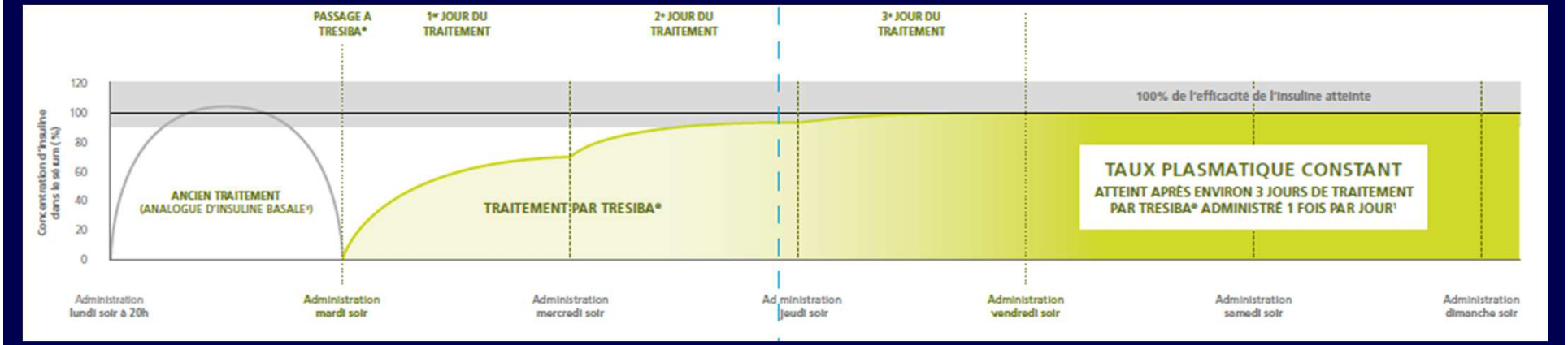
Insulin type	Onset of action	Peak effect	Duration of action
Lispro, aspart, glulisine	5 to 15 minutes	45 to 75 minutes	Two to four hours
Regular	About 30 minutes	Two to four hours	Five to eight hours
NPH	About two hours	4 to 12 hours	18 to 28 hours
Insulin glargine	About two hours	No peak	20 to >24 hours
Insulin detemir	About two hours	Three to nine hours	6 to 24 hours*
NPL	About two hours	Six hours	15 hours
Insulin degludec	About two hours	No peak	>40 hours

NPH: neutral protamine hagedorn; NPL: neutral protamine lispro.
* Duration of action is dose-dependent. At higher doses (≥0.8 units/kg), mean duration of action is longer and less variable (22 to 23 hours).

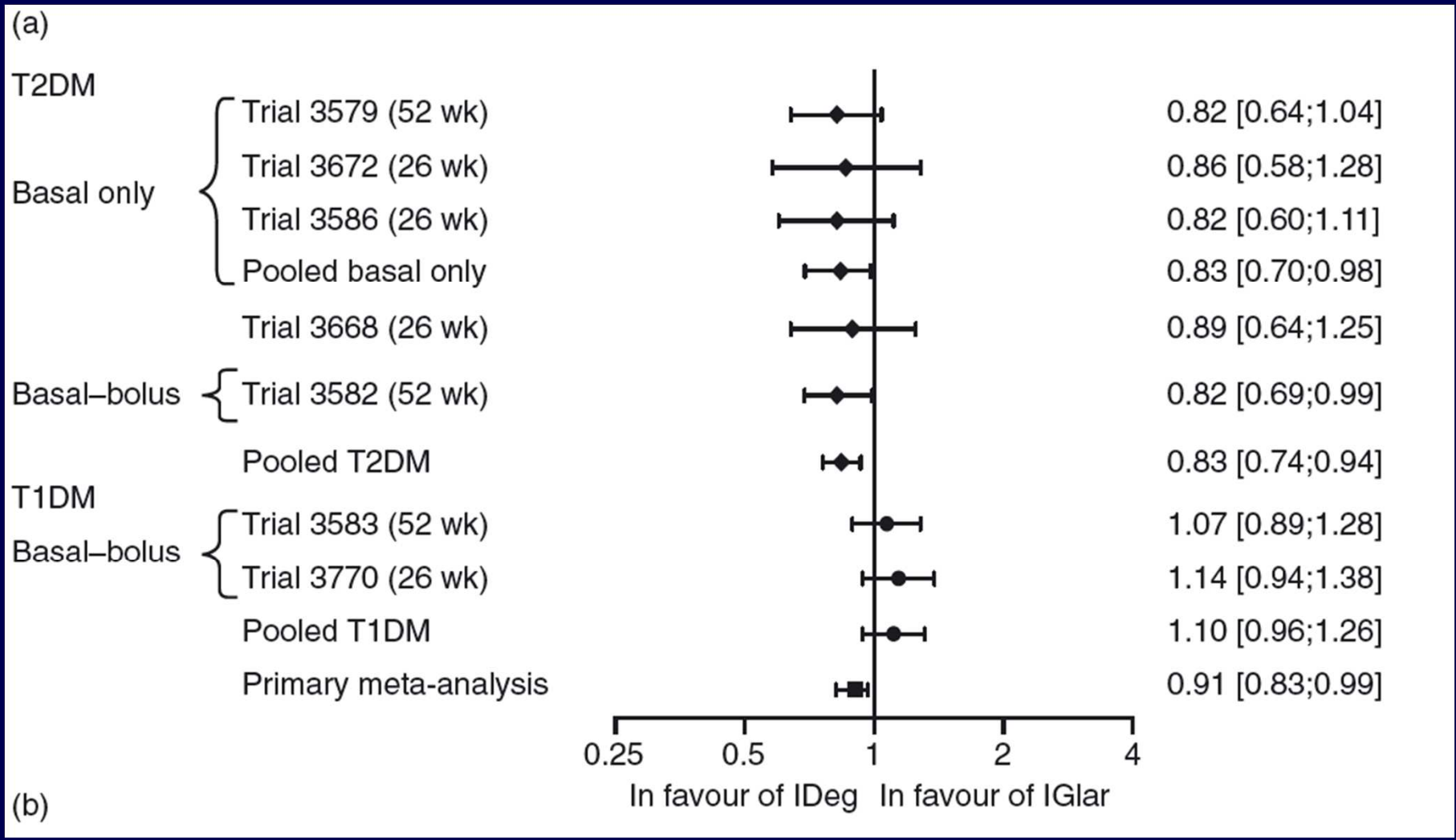
UpToDate®

L’insuline degludec

- **En pratique, comment l’introduire :**
  - Si switch depuis une autre insuline, réduire la dose de 20-30% (en cas de contrôle satisfaisant).
  - Au vu de la très longue durée d’action (environ 42 heures), le plateau est atteint après 3 jours, dès lors le contrôle glycémique est souvent suboptimal avant 3 jours.
  - Dès lors, il ne faut modifier le dosage qu’après 3 jours au plus tôt.

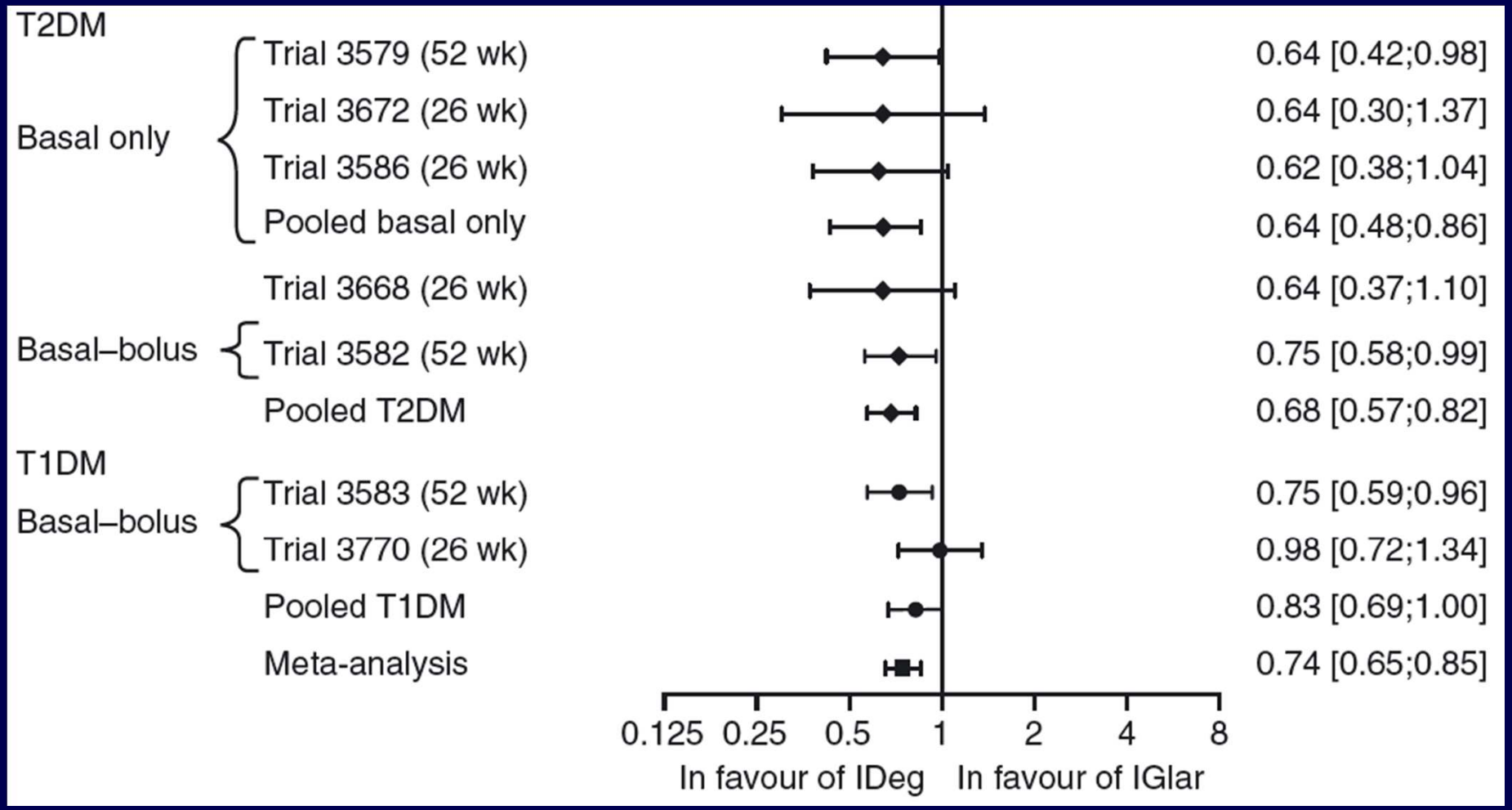


Insuline degludec : hypoglycémies totales



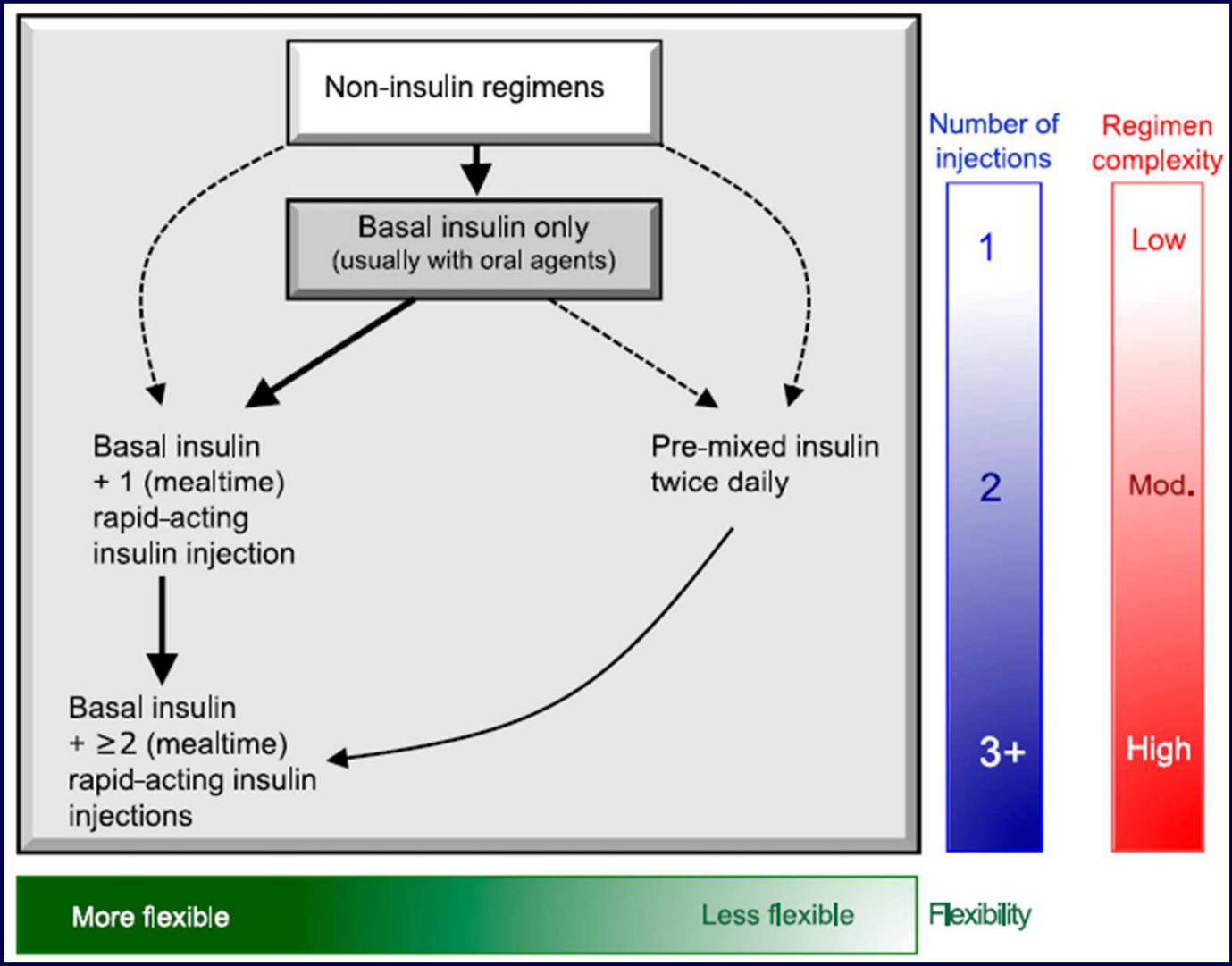
Diabetes, Obesity and Metabolism 15: 175–184, 2013

Insuline degludec : hypoglycémies nocturnes



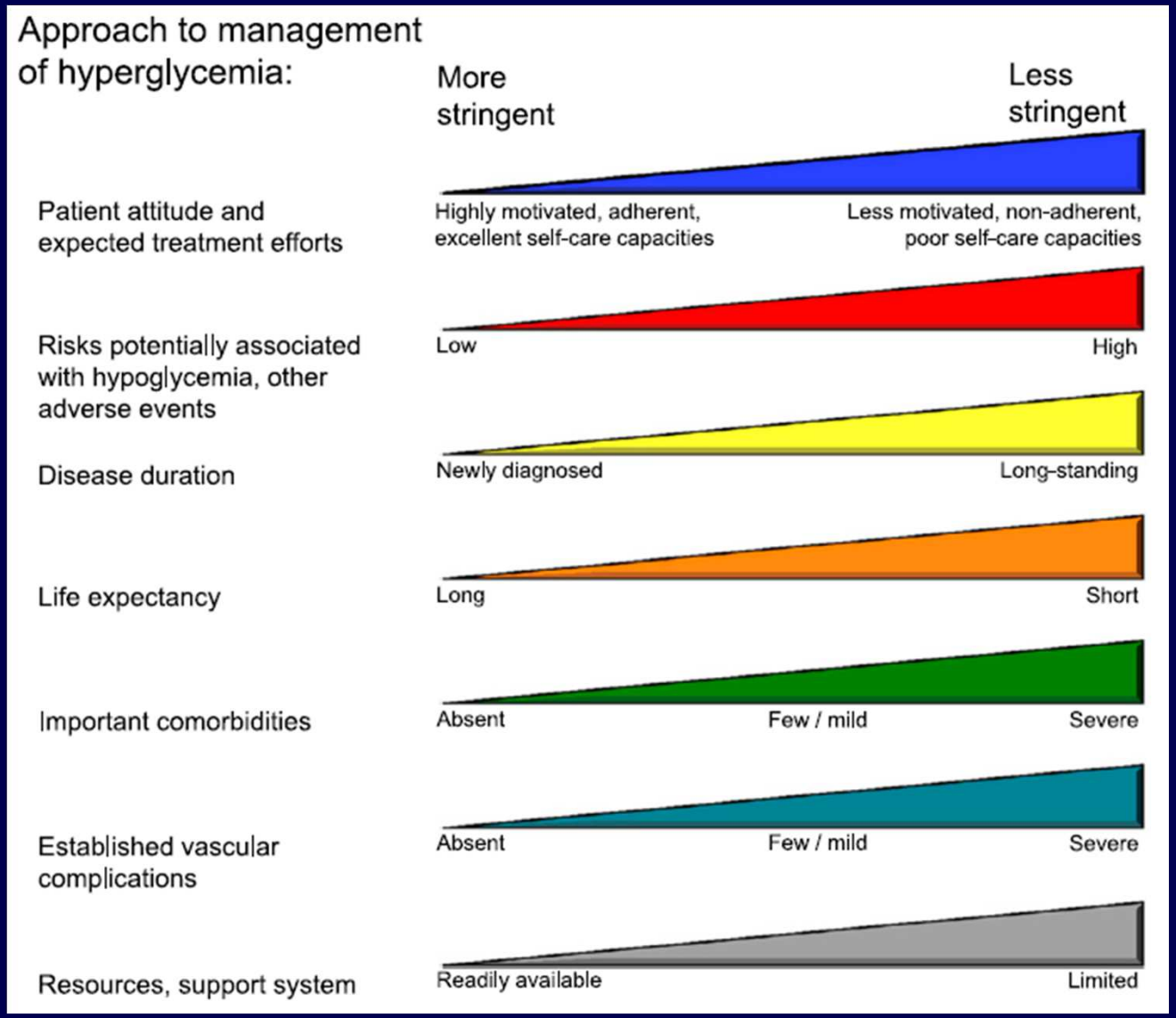
Diabetes, Obesity and Metabolism 15: 175–184, 2013

Traitement par insuline



Diabetes Care/Diabetologia, avril 2012

Prise en charge de l'hyperglycémie



Diabetes Care/Diabetologia, avril 2012

Choix du traitement : résumé

1) Adaptation du style de vie + metformine

2) Ajout sulfonylurée (préférence pour le gliclazide) et/ou inhibiteur DPP-4/SGLT2

3) Ajout de l'insuline

4) Considérer analogue du GLP-1 si BMI > 28 kg/m^2

CONCLUSIONS

- La tendance du traitement est d'éviter les effets secondaires au prix d'un contrôle raisonnable individualisé.
- Les gliptines et inhibiteurs SGLT2 sont une alternative aux sulfonylurées particulièrement chez les patients à risque d'hypoglycémies (conduite…) et de prise pondérale.
- Les gliptines sont cependant coûteuses et leur sécurité à long terme n'est pas clairement établie. Il en va de même pour les inhibiteurs SGLT2.
- La place des analogues du GLP-1 se situe chez les patients obèses avec échec de ttt par ADO (metformine + sulfonylurée +/- autre ttt) en alternative à l'insuline pour diminuer le risque d'hypoglycémie et la prise de poids.

Merci de votre attention!

Buts glycémiques

Table 9—Summary of glycemic recommendations for many nonpregnant adults with diabetes	
A1C	<7.0%*
Preprandial capillary plasma glucose	70–130 mg/dL* (3.9–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (<10.0 mmol/L)

• *Goals should be individualized based on:
  • duration of diabetes
  • age/life expectancy
  • comorbid conditions
  • known CVD or advanced microvascular complications
  • hypoglycemia unawareness
  • individual patient considerations
• More or less stringent glycemic goals may be appropriate for individual patients
• Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals	

†Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

Diabetes Care, Jan 2014

Qui dépister?

Table 4—Criteria for testing for diabetes in asymptomatic adult individuals

1. Testing should be considered in all adults who are overweight (BMI ≥25 kg/m^{2}*) and have additional risk factors:
   - physical inactivity
   - first-degree relative with diabetes
   - high-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - women who delivered a baby weighing >9 lb or were diagnosed with GDM
   - hypertension (≥140/90 mmHg or on therapy for hypertension)
   - HDL cholesterol level <35 mg/dL (0.90 mmol/L) and/or a triglyceride level >250 mg/dL (2.82 mmol/L)
   - women with polycystic ovarian syndrome
   - A1C ≥5.7%, IGT, or IFG on previous testing
   - other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
   - history of CVD
2. In the absence of the above criteria, testing for diabetes should begin at age 45 years.
3. If results are normal, testing should be repeated at least at 3-year intervals, with consideration of more frequent testing depending on initial results (e.g., those with prediabetes should be tested yearly) and risk status.

*At-risk BMI may be lower in some ethnic groups.

Diabetes Care, Jan 2014

Diagnostic de diabète et pré-diabète

Table 2—Criteria for the diagnosis of diabetes

A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
Two-hour PG ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR
In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

Table 3—Categories of increased risk for diabetes (prediabetes)*

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)
OR
2-h PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)
OR
A1C 5.7–6.4%

*For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at higher ends of the range.

Diabetes Care, Jan 2014