# Stratégie thérapeutique, diabète de type 2

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# Stratégie thérapeutique

- 1 Diététique & activité physique
- 2 traitement oraux
- 3 insuline seule ou en combinaison

- Education comment, dans quel cadre, combien, quel programme, quand?
- Médicaments: quand, quelle stratégie d'escalade?
- Insuline: quand, comment, pourquoi?

# Diététique

- 1/ Réduction Lipides et AGS (charcuterie, viande, fromages, huiles, fritures)
- 2/ Augmentation fibres, 20g/1000 Cal (céréales complètes, crudités, légumes verts, légumineuses, fruits (pruneaux abricots)
- 3/Objectif perte de 5% du poids?

En suis-je capable?
Est-ce que je me représente bien ce que cela signifie?

# Activité physique

- Pour être motivant le docteur doit être motivé,
- Pour être cru, le docteur doit être crédible,
- Et vous, que devriez-vous faire? Que faites-vous?

# Reduction in Weight and Cardiovascular Disease Risk Factors in Individuals With Type 2 Diabetes

One-year results of the Look AHEAD trial

| Characteristic | Intervention assignment | | P value |
|---|---|---|---|
| | ILI | DSE | |
| *n* | 2,570 | 2,575 | |
| Age (years) | 58.6 ± 6.8 | 58.9 ± 6.9 | 0.12† |
| History of cardiovascular disease‡ | 371 (14.4) | 351 (13.6) | 0.40* |
| Metabolic syndrome | 2,406 (93.6) | 2,431 (94.4) | 0.32* |
| Use of insulin | 381 (14.8) | 408 (15.8) | 0.31* |
| BMI ($kg/m^2$) | | | |
| Women | 36.3 ± 6.2 | 36.6 ± 6.0 | 0.15† |
| Men | 35.3 ± 5.7 | 35.1 ± 5.2 | 0.41† |

**Table 2—*Changes in measures of diabetes control, blood pressure control, measures of lipid/lipoproteins control, albumin-to-creatinine ratio, and prevalence of metabolic syndrome among participants seen at year 1***

| Measure | ILI | DSE | *P* value |
|---|---|---|---|
| *n* | 2,496 | 2,463 | |
| Use of diabetes medicines (%) | | | |
| Baseline | 86.5 ± 0.7 | 86.5 ± 0.7 | 0.93* |
| Year 1 | 78.6 ± 0.8 | 88.7 ± 0.6 | <0.001* |
| Change | −7.8 ± 0.6 | 2.2 ± 0.5 | <0.001† |
| Fasting glucose (mg/dl) | | | |
| Baseline | 151.9 ± 0.9 | 153.6 ± 0.9 | 0.21‡ |
| Year 1 | 130.4 ± 0.8 | 146.4 ± 0.9 | <0.001‡ |
| Change | −21.5 ± 0.9 | −7.2 ± 0.9 | <0.001‡ |
| A1C (%) | | | |
| Baseline | 7.25 ± 0.02 | 7.29 ± 0.02 | 0.26‡ |
| Year 1 | 6.61 ± 0.02 | 7.15 ± 0.02 | <0.001‡ |
| Difference | −0.64 ± 0.02 | −0.14 ± 0.02 | <0.001‡ |

# Long-term Effects of a Lifestyle Intervention on Weight and Cardiovascular Risk Factors in Individuals With Type 2 Diabetes Mellitus

*Four-Year Results of the Look AHEAD Trial*

Arch Intern Med. 2010;170(17):1566-1575

**Table 2. Proportion of DSE and ILI Participants Who Initiated or Maintained Use of Medication for Diabetes, Hypertension, or Lowering Lipid Levels**

| | Use of Medication at Follow-up by Group | | | | | |
|---|---|---|---|---|---|---|
| | No Use at Baseline | | | Continued Use From Baseline | | |
| | DSE | ILI | *P* Value | DSE | ILI | *P* Value |
| Diabetes medication | | | | | | |
| No. at baseline[a] | 348 | 354 | | 2208 | 2202 | |
| Follow-up year, % | | | | | | |
| 1 | 33.1 | 10.4 | <.001 | 97.5 | 89.4 | <.001 |
| 2 | 46.3 | 17.4 | <.001 | 96.3 | 88.2 | <.001 |
| 3 | 58.6 | 27.3 | <.001 | 95.4 | 89.2 | <.001 |
| 4 | 66.8 | 41.8 | <.001 | 96.0 | 90.6 | <.001 |
| Insulin | | | | | | |
| No. at baseline[a] | 2167 | 2190 | | 408 | 380 | |
| Follow-up year, % | | | | | | |
| 1 | 3.7 | 1.7 | <.001 | 91.6 | 80.6 | <.001 |
| 2 | 6.7 | 3.1 | <.001 | 86.4 | 76.1 | <.001 |
| 3 | 8.9 | 4.3 | <.001 | 86.3 | 77.7 | .004 |
| 4 | 11.5 | 6.9 | <.001 | 88.0 | 77.4 | <.001 |

# An intensified lifestyle intervention programme may be superior to insulin treatment in poorly controlled Type 2 diabetic patients on oral hypoglycaemic agents: results of a feasibility study

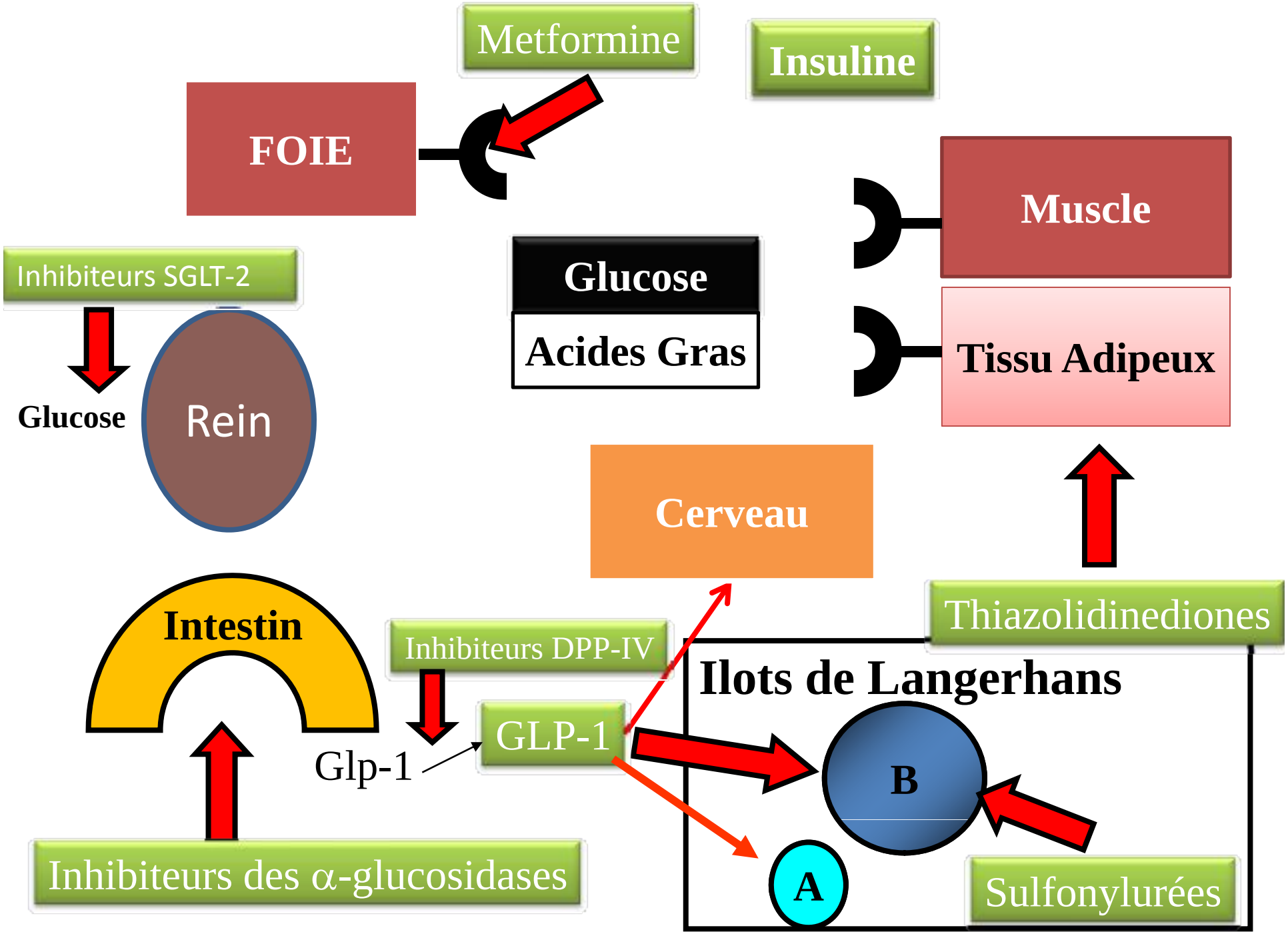
A. M. Aas*†, I. Bergstad*†, P. M. Thorsby†‡, Ø. Johannesen§, M. Solberg¶ and K. I. Birkeland†‡§

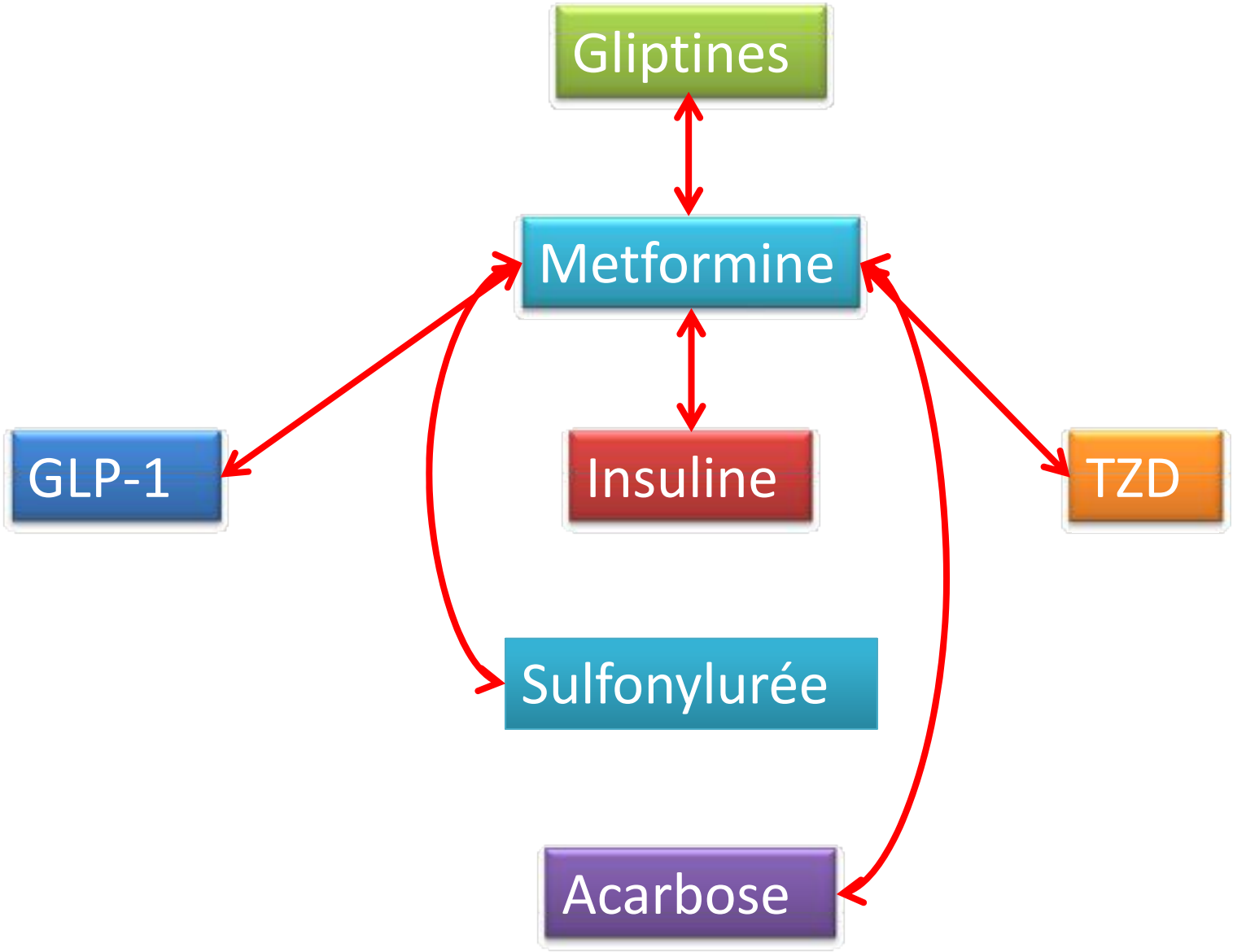
**Table 1** Median (25th–75th centiles) for baseline characteristics

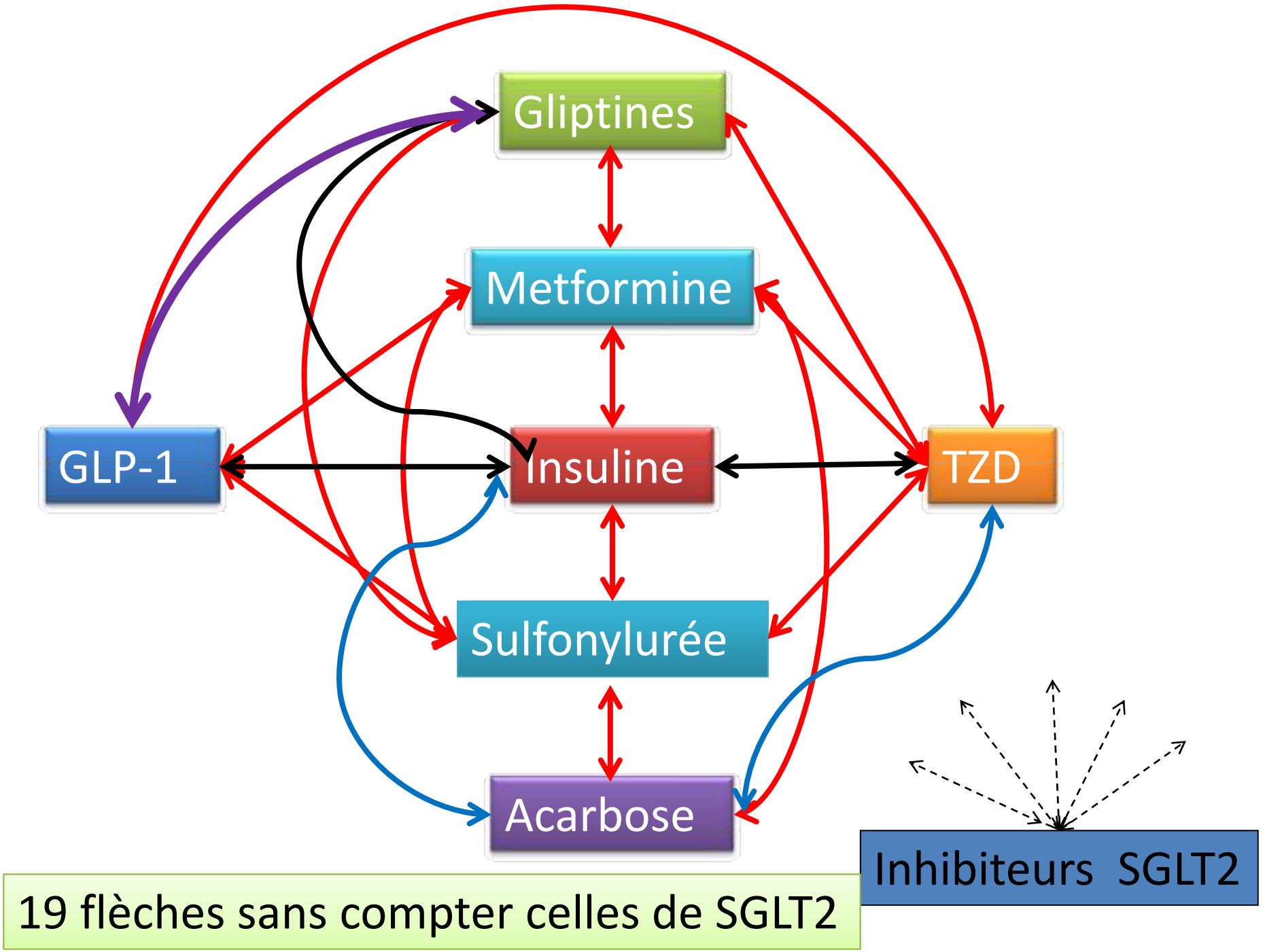
| | All randomized $n = 38$ |
|---|---|
| Age (years) | 57 (47–67) |
| Sex (male/female) | 24/14 |
| Diabetes duration (years) | 6 (4–11) |
| $HbA_{1c}$ (%) | 9.0 (8.1–9.8) |
| Fasting blood glucose (mmol/l) | 11.8 (9.6–14.3) |
| BMI ($kg/m^2$) | 30 (28–34) |

| | Lifestyle group<br>$n = 9$ | Lifestyle + insulin<br>$n = 10$ | Insulin group<br>$n = 9$ | $P^*$ |
|---|---|---|---|---|
| $HbA_{1c}$ (%) | | | | |
| Pre-study | 8.3 (8.0–9.4) | 9.2 (7.7–9.7) | 9.8 (8.7–10.1) | |
| 1 year | 7.4 (7.2–8.4) | 7.6 (7.2–8.2) | 7.7 (7.5–8.8) | |
| Δ 1 year | −1.2 (−1.3–0.3) | −1.0 (−2.3–0.6) | −1.5 (−2.4–0.1) | 0.743 |

| | Lifestyle group<br>$n = 9$ | Lifestyle + insulin<br>$n = 10$ | Insulin group<br>$n = 9$ | $P^*$ |
|---|---|---|---|---|
| Body weight (kg) | | | | |
| Pre-study | 93.9 (88.3–100.6) | 86.3 (77.1–99.5) | 89.7 (75.3–97.2) | |
| 1 year | 91.3 (86.3–97.5) | 89.0 (79.5–105.3) | 87.5 (80.8–101.0) | |
| Δ 1 year | −3.0 (−5.4–1.4)[a] | 3.5 (1.6–5.0)[b] | 4.9 (1.5–8.4)[b] | 0.004 |


Metformine
Insuline
FOIE
Muscle
Inhibiteurs SGLT-2
Glucose
Acides Gras
Tissu Adipeux
Glucose
Rein
Cerveau
Thiazolidinediones
Intestin
Inhibiteurs DPP-IV
Ilots de Langerhans
GLP-1
Glp-1
B
A
Inhibiteurs des α-glucosidases
Sulfonylurées


Gliptines
Metformine
GLP-1
Insuline
TZD
Sulfonylurée
Acarbose


Gliptines
Metformine
GLP-1
Insuline
TZD
Sulfonylurée
Acarbose
Inhibiteurs SGLT2
19 flèches sans compter celles de SGLT2

The NEW ENGLAND JOURNAL of MEDICINE

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# Effects of Intensive Glucose Lowering in Type 2 Diabetes

The Action to Control Cardiovascular Risk in Diabetes Study Group*

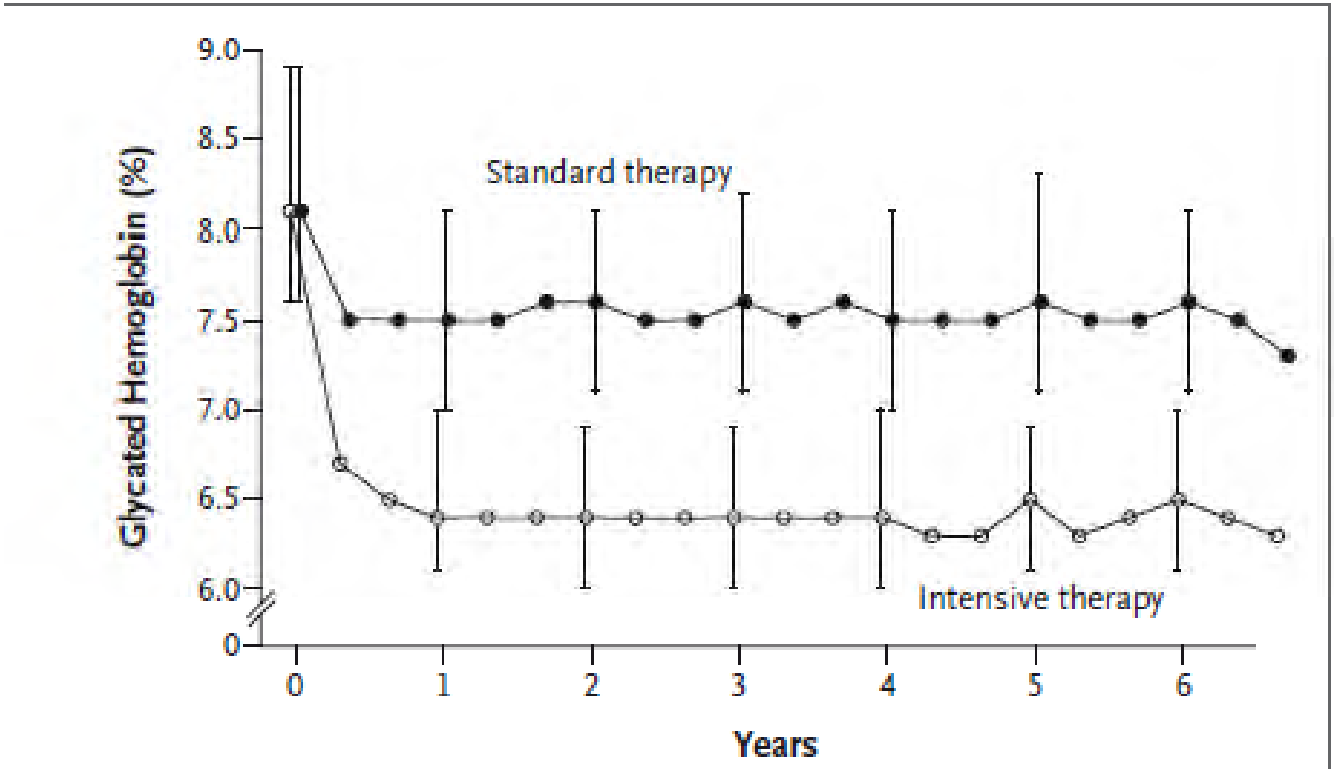


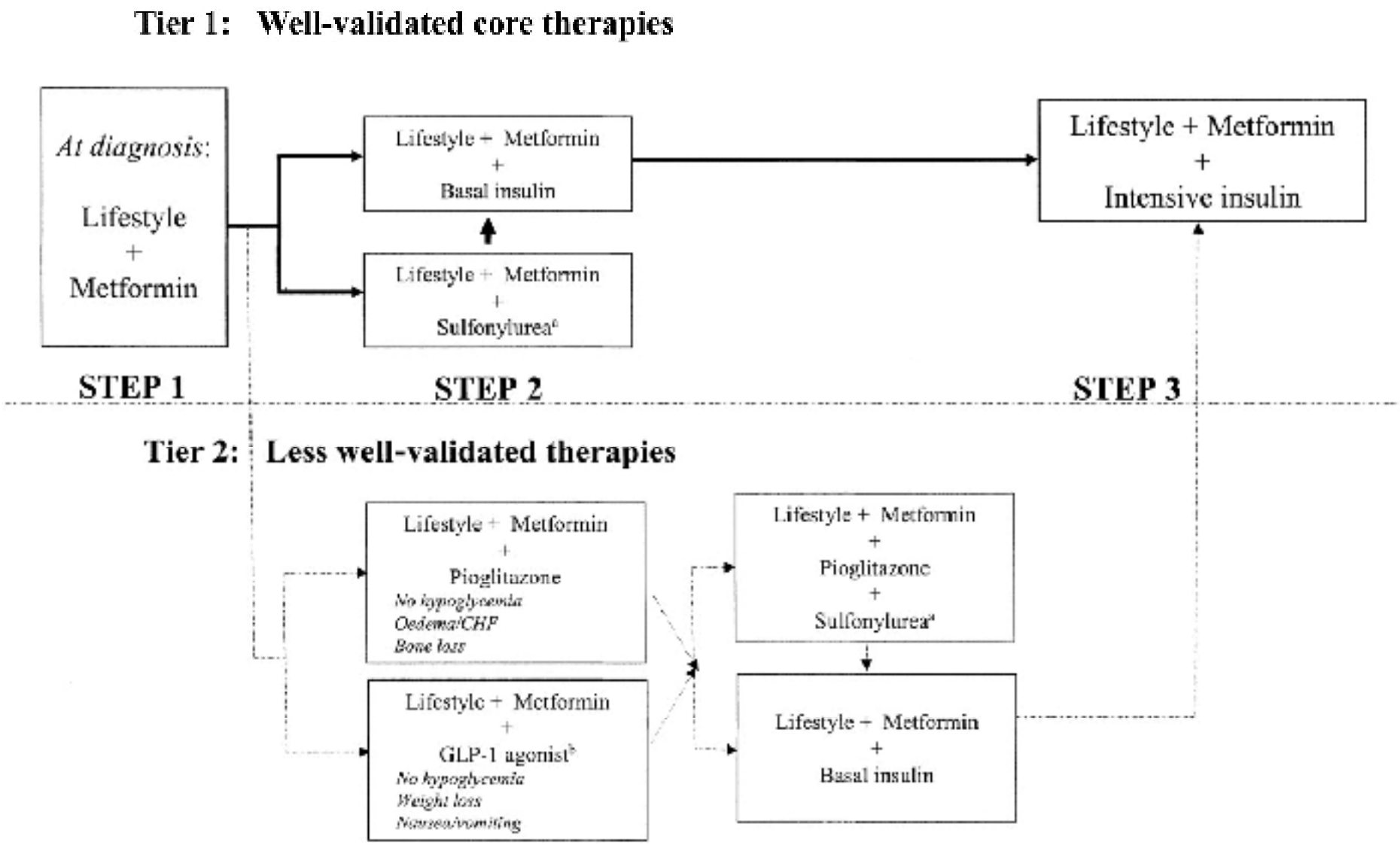
**Table 2. Prescribed Glucose-Lowering Drugs.***

| Drug Class and Name | Intensive Therapy (N = 5128) | | Standard Therapy (N = 5123) | |
|---|---|---|---|---|
| | *no. of patients (%)* | *person-years* | *no. of patients (%)* | *person-years* |
| **Single class** | | | | |
| Metformin | 4856 (94.7) | 14,444 | 4452 (86.9) | 12,693 |
| Secretagogue† | 4443 (86.6) | 12,021 | 3779 (73.8) | 10,059 |
| Glimepiride | 4010 (78.2) | 9,142 | 3465 (67.6) | 8,955 |
| Repaglinide | 2574 (50.2) | 4,447 | 908 (17.7) | 1,293 |
| Thiazolidinedione‡ | 4702 (91.7) | 12,844 | 2986 (58.3) | 6,719 |
| Rosiglitazone | 4677 (91.2) | 12,639 | 2946 (57.5) | 6,563 |
| α-Glucosidase inhibitor§ | 1191 (23.2) | 941 | 263 (5.1) | 200 |
| Incretin¶ | 911 (17.8) | 566 | 251 (4.9) | 175 |
| Exenatide | 622 (12.1) | 415 | 204 (4.0) | 155 |
| Any insulin | 3965 (77.3) | 11,902 | 2837 (55.4) | 7,842 |
| Any bolus insulin | 2834 (55.3) | 6,806 | 1794 (35.0) | 4,336 |
| **Combination of classes** | | | | |
| No. of classes without insulin | | | | |
| 1 or 2 | 2798 (54.6) | 2,011 | 3224 (62.9) | 6,612 |
| 3 | 3030 (59.1) | 3,681 | 1681 (32.8) | 2,545 |
| 4 or 5 | 539 (10.5) | 332 | 109 (2.1) | 67 |
| No. of classes with insulin | | | | |
| 0 | 916 (17.9) | 829 | 892 (17.4) | 1,495 |
| 1 or 2 | 3311 (64.6) | 6,603 | 2375 (46.4) | 5,284 |
| 3 | 2668 (52.0) | 4,126 | 834 (16.3) | 1,027 |
| 4 or 5 | 526 (10.3) | 344 | 64 (1.2) | 36 |

ACCORD NEJM 2010

# Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy

A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes



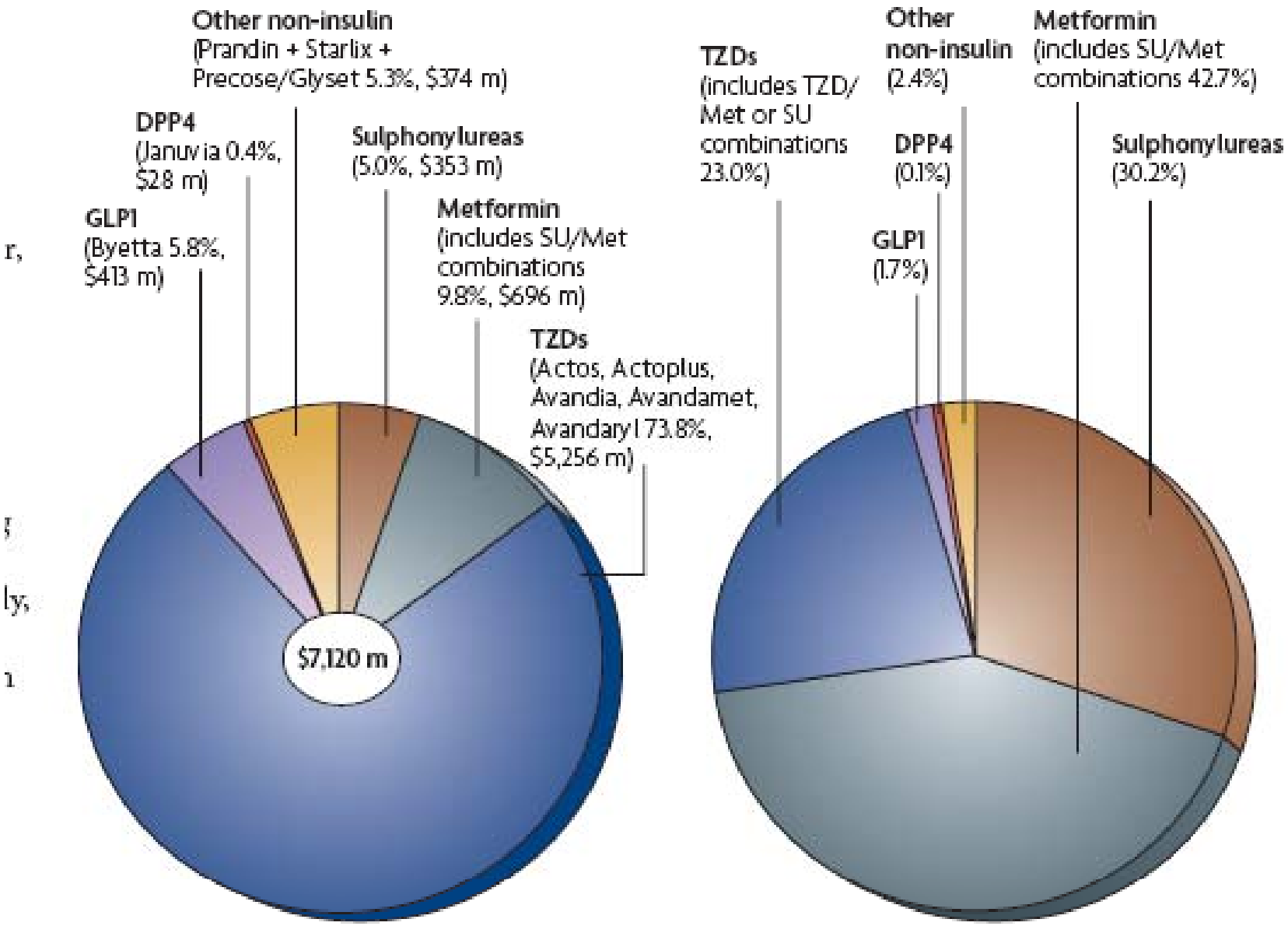



Figure 1 | **US non-insulin antidiabetes sales and prescriptions, 2006.** Metformin (Met)

# Coût pour 30 jours

(sous réserve d'erreurs de ma part, source: Vidal)

- Daonil® 5mg*3/j: 5
- Glucophage® 1000mg*2/j : 9,06
- Diamicron® 30mg*2/j: 14,33
- Novonorm® 2mg* 3/j: 15,98
- Glucor ® 100mg*3/j: 19,33
- Actos 30mg/j ® : 29,53
- Insulatard ® 40U/j: 33,43
- Januvia ® 100 mg/j: 47,88
- Lantus ® 40 U/j: 53
- Victoza ® 1,2 mg/j: 110

# Traitement du diabète de type 2, les choix en 2010

1. Insuline:
    1. Basale
    2. Mélanges
    3. Bolus
    4. Basale-bolus
    5. Pompe.
2. Chirurgie bariatrique
3. Sulfonylurées et glinides
4. Metformine
5. ~~Thiazolidinediones~~
6. Acarbose
7. Orlistat (Xénical ®)
8. Agonistes GLP-1
9. Inhibiteurs DPP-IV
10. ~~Benfluorex (Médiator®)~~
11. ~~Rimonabant~~

# Cas clinique N°1

- Patient âgé de 60 ans, diabète de type 2 depuis 10 ans, macroangiopathie, IMC 29 kg/m². HbA1c 8,2%. Bon contrôle des fdr vasculaires.
- Traitement actuel
  - Metformine dose maximale
  - Gliclazide dose max.
- 1/Et après?
- 2/ Et après après?

# Cas clinique N°1

- Options:
  - 1 Insuline basale
  - 2 Insuline bolus
  - 3 Insuline basale bolus
  - Trithérapie
    - 4 Inhibiteur DPP4
    - 5 IAG
    - 6 Pioglitazone
    - 7 Agoniste GLP-1
  - 8 Chirurgie bariatrique

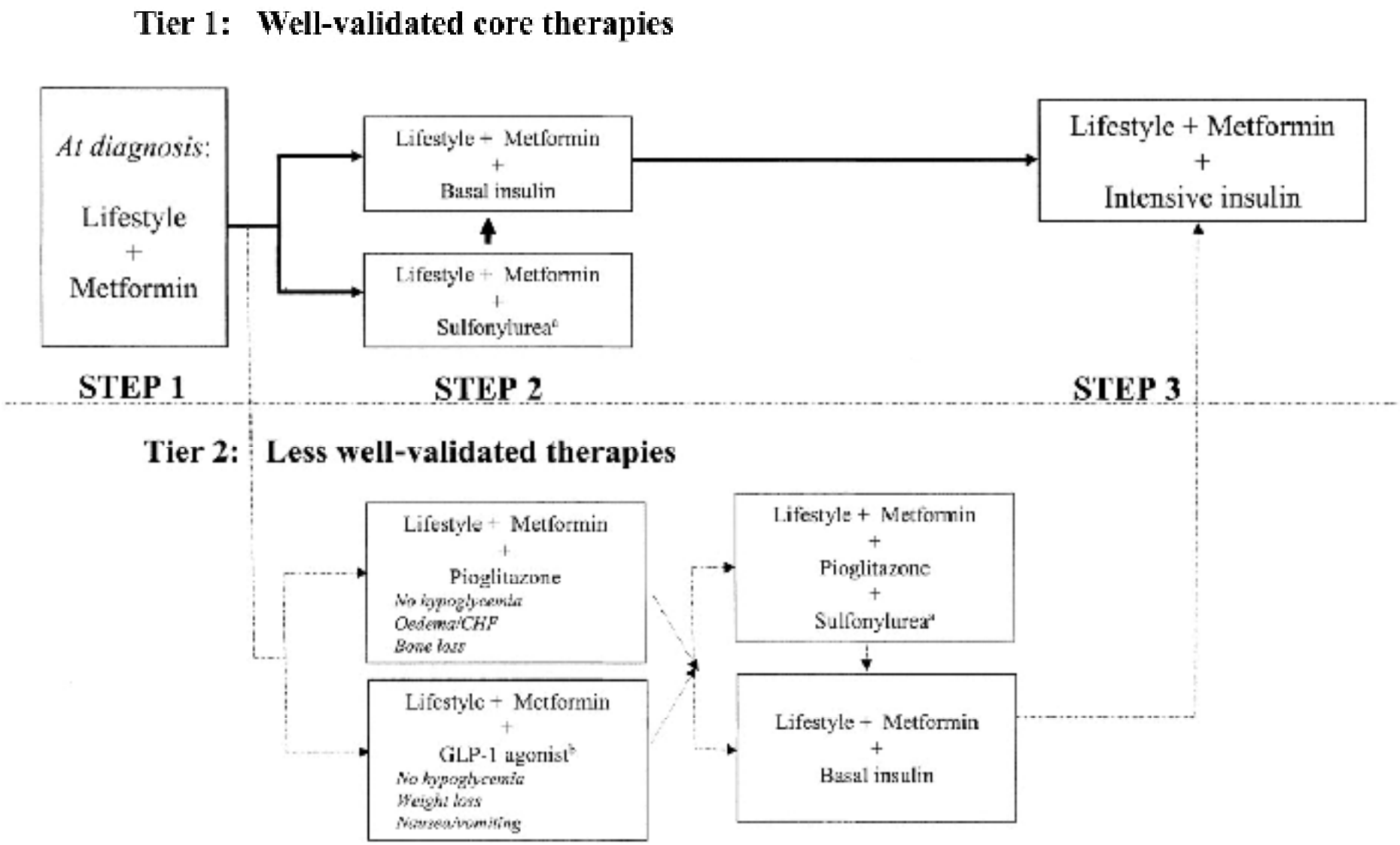
| | Avantage | Inconvénient |
|---|---|---|
| Insuline basale | Coût, expérience | Éducation, poids, hypo |
| Insuline bolus | Coût, expérience, plus de chance d'arriver à cible | Education, hypo, poids |
| Insuline Basale bolus | Coût, expérience, plus de chance d'arriver à cible | Education, hypo, poids |
| GLP1 | Poids, début simple injection | Manque d'expérience, pas très puissant, piqure |
| I. DPP4 | Simplicité, peu d'effets indésirables | Manque d'expérience, pas très puissant |
| IAG | Expérience, peu d'effets indésirables | Effets indésirables! |
| Pioglitazone | Efficace (parfois très), seul ayant bénéfice CV | Poids, os, anémie (cancer vessie) |
| Chirurgie bariatrique | Traitement radical | Pas d'expérience, lourd, engagement à vie, augmentation suicide, etc. |

| | Metformin (MET) | DPP4 Inhibitor | GLP-1 Agonist (Incretin Mimetic) | Sulfonylurea (SU) | Glinide** | Thiazolidinedione (TZD) |
|---|---|---|---|---|---|---|
| **BENEFITS** | | | | | | |
| Postprandial Glucose (PPG) - lowering | Mild | Moderate | Moderate to Marked | Moderate | Moderate | Mild |
| Fasting glucose (FPG) - lowering | Moderate | Mild | Mild | Moderate | Mild | Moderate |
| Nonalcoholic fatty liver disease (NAFLD) | Mild | Neutral | Mild | Neutral | Neutral | Moderate |
| **RISKS** | | | | | | |
| Hypoglycemia | Neutral | Neutral | Neutral | Moderate | Mild | Neutral |
| Gastrointestinal Symptoms | Moderate | Neutral | Moderate | Neutral | Neutral | Neutral |
| Risk of use with renal insufficiency | Severe | Reduce Dosage | Moderate | Moderate | Neutral | Mild |
| Contraindicated in Liver Failure or Predisposition to Lactic Acidosis | Severe | Neutral | Neutral | Moderate | Moderate | Moderate |
| Heart failure / Edema | Contra-indicated in CHF | Neutral | Neutral | Neutral | Neutral | Mild / Moderate<br>Contraindicated in class 3,4 CHF |
| Weight Gain | Benefit | Neutral | Benefit | Mild | Mild | Moderate |
| Fractures | Neutral | Neutral | Neutral | Neutral | Neutral | Moderate |
| Drug-Drug interactions | Neutral | Neutral | Neutral | Moderate | Moderate | Neutral |

Consensus AACE

# Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy

A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes



afssaps
Agence française de sécurité sanitaire des produits de santé

HAS
HAUTE AUTORITÉ DE SANTÉ

| Seuil de prescription | Stratégie thérapeutique | Objectif |
|---|---|---|
| **HbA1c > 6 %** | ***Etape 1***<br>Mesures hygiéno-diététiques (MHD) | **HbA1c < 6 %** |
| *Si malgré étape 1*<br>**HbA1c >6%**<br>(à la phase précoce du diabète)<br>*Si malgré étape 1,*<br>**HbA1c > 6,5%** | ***Etape 2***<br>MONOTHERAPIE+MHD : **Metformine** *voire IAG*<br><br>MONOTHERAPIE au choix + MHD<br>**Metformine** ou **IAG ou SU ou Glinides** | **maintenir**<br>**l'HbA1c < 6.5 %** |
| ***Si malgré étape 2,***<br>**HbA1c > 6.5 %** | ***Etape 3***<br>BITHERAPIE + MHD | **ramener**<br>**l'HbA1c < 6.5 %** |
| ***Si malgré étape 3,***<br>**HbA1c > 7 %** | ***Etape 4***<br>**TRITHERAPIE + MHD** ou **INSULINE ± ADO + MHD** | **ramener**<br>**l'HbA1c < 7 %** |
| ***Si malgré étape 4,***<br>**HbA1c > 8 %** | *Etape 5*<br>**INSULINE ± ADO + MHD** ; **INSULINE FRACTIONNEE + MHD** | **ramener**<br>**l'HbA1c < 7 %** |

# Caïssa, la déesse des échecs

Diabetologia (2010) 53:1258–1269
DOI 10.1007/s00125-010-1702-3

FOR DEBATE

# Is the ADA/EASD algorithm for the management of type 2 diabetes (January 2009) based on evidence or opinion? A critical analysis

G. Schernthaner · A. H. Barnett · D. J. Betteridge · R. Carmena · A. Ceriello · B. Charbonnel · M. Hanefeld · R. Lehmann · M. T. Malecki · R. Nesto · V. Pirags · A. Scheen · J. Seufert · A. Sjohölm · A. Tsatsoulis · R. DeFronzo

| Intervention | Main advantages | Main disadvantages |
|---|---|---|
| Metformin | •Reduces macrovascular risk<br>•Weight loss<br>•Low risk of hypoglycaemia<br>•Improved multiple cardiovascular risk factors/markers (lipids, CRP, PAI-1, thrombocyte hyperactivity)<br>•Drug costs<br>•FDCs available (with sulfonylureas, thiazolidinediones, DPP-IV inhibitors) | •Gastrointestinal side effects<br>•Potential cardiovascular safety issues in combination with sulfonylureas<br>•Lactic acidosis (rare in patients without contraindications) |
| Sulfonylureas | •Reduces microvascular risk (glibenclamide)<br>•Reduces nephropathy (gliclazide)<br>•Drug costs<br>•FDCs available (with metformin, thiazolidinediones) | •Rapid secondary failure (vs metformin or thiazolidinediones)<br>•Weight gain (varies between different agents)<br>•Moderate risk of hypoglycaemia (varies between different agents)<br>•Potential cardiovascular safety issues, especially in combination with metformin |
| Thiazolidinediones | •More sustained glucose control (vs metformin or sulfonylureas)<br>•Reduced macrovascular risk (pioglitazone only)<br>•Low risk of hypoglycaemia<br>•Reduced atherosclerosis progression (coronary IVUS [pioglitazone only], CIMT)<br>•Improved multiple cardiovascular risk factors/markers (lipids, blood pressure, CRP, adiponectin, PAI-1, MMP-9)<br>•Reduced microalbuminuria<br>•FDCs available (with metformin, glimepiride) | •Weight gain<br>•Peripheral oedema<br>•Uncertain macrovascular risk profile with rosiglitazone<br>•Increased incidence of CHF (but no increased macrovascular/ mortality consequences)<br>•Increased risk of distal fractures in women<br>•Drug costs |
| Glinides | •Reduces postprandial blood glucose | •No outcomes data<br>•Hypoglycaemia (possibly similar risk to sulfonylureas)<br>•Weight gain<br>•Long term efficacy/safety data lacking (especially in combination with other oral agents)<br>•Drug costs |
| α-Glucosidase inhibitors | •Weight neutral<br>•Low risk of hypoglycaemia<br>•Serious side effects extremely rare | •No robust cardiovascular outcomes data<br>•Gastrointestinal side effects (leading to poor adherence)<br>•Glucose-lowering efficacy only modest |
| DPP-IV inhibitors | •Low risk of hypoglycaemia | •No outcomes data |

| | | |
|---|---|---|
| DPP-IV inhibitors | •Low risk of hypoglycaemia (except in combination with a sulfonylurea)<br>•Weight-neutral<br>•FDCs available (with metformin) | •No outcomes data<br>•Limited long-term clinical experience at present<br>•Possible link to pancreatitis<br>•Drug costs |
| Insulin | •Glucose-lowering efficacy (potentially limitless with uptitration)<br>•Reduces microvascular risk | •Most effective insulin strategy remains undetermined<br>•Moderate to high risk of hypoglycaemia<br>•Weight gain<br>•Frequent blood glucose monitoring<br>•May involve frequent injections<br>•Drug costs (esp. analogues) |
| GLP-1 receptor agonists | •Low risk of hypoglycaemia (except in combination with a sulfonylurea)<br>•Weight loss<br>•Lowers blood pressure<br>•Potential beta cell protective effect | •No outcomes data<br>•Gastrointestinal side effects<br>•Limited long-term clinical experience at present<br>•Antibody formation (exenatide only)<br>•Possible interaction with other drugs due to delayed gastric emptying<br>•Possible link to pancreatitis<br>•Drug costs |

**Consensus guidelines, algorithms and care of the individual patient with type 2 diabetes**

J. J. Nolan

**From authority recommendations to fact-sheets—a future for guidelines**

I. Mühlhauser

**The American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) algorithm for managing glycaemia in patients with type 2 diabetes mellitus: comparison with the ADA/EASD algorithm**

H. W. Rodbard · P. S. Jellinger

**The combinatorics of medications precludes evidence-based algorithms for therapy**

D. Rodbard

**Should the algorithm for the treatment of type 2 diabetes be evidence-based?**

P.-J. Guillausseau

**Guidelines: we'll always need them, we sometimes dislike them, and we have to make them better**

R. Kahn

# Autosurveillance des glycémies

- Recommandations du groupe « NICE » (2008): seulement dans le contexte d'un programme structuré, pour les patients traités par insuline ou les patients à risque d'hypoglycémie.
- Efficacité démontrée (↘0,4% A1c) seulement dans le contexte d'une prise en charge plus globale
- En dehors de ce contexte, efficacité douteuse : étude DiGEM (BMJ 2008, Health Technol Ass 2009)
- Problèmes
  - Conséquences thérapeutiques?
  - Dépression.
  - Le docteur ne regarde pas.