Diabetes mellitus novidades na terapêutica…

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Agenda: novidades na terapêutica e não só...

- Contexto histórico
- Classificação atual da diabetes mellitus
- Nova Classificação
- A evolução do octeto sinistro: novos intervenientes
- Novos aliados na terapêutica: aGLP1 e iSGLT2
- Mensagem final

Contexto Historico

- Papiro de Ebers 1550 a.c.

A diabetes é tão antiga como a Humanidade…

Século II

- Areteu da Capadócia

  Diabetes "sifão"

  …"**curta será a vida** do homem em quem esta doença se desenvolva"

- Thomas Willis 1679 acrescentou "mellitus"

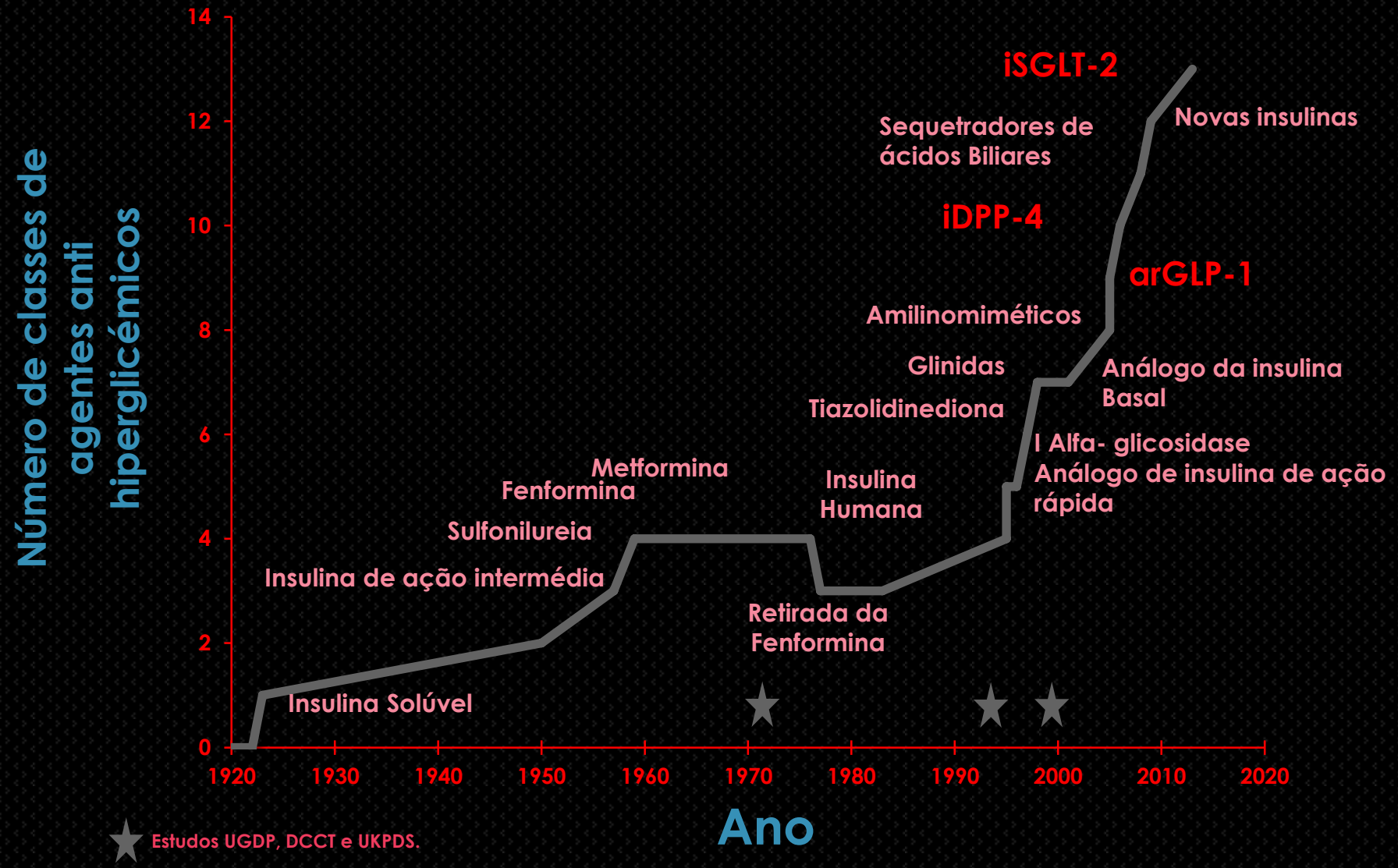
Século XX

- 1921 Banting e Best

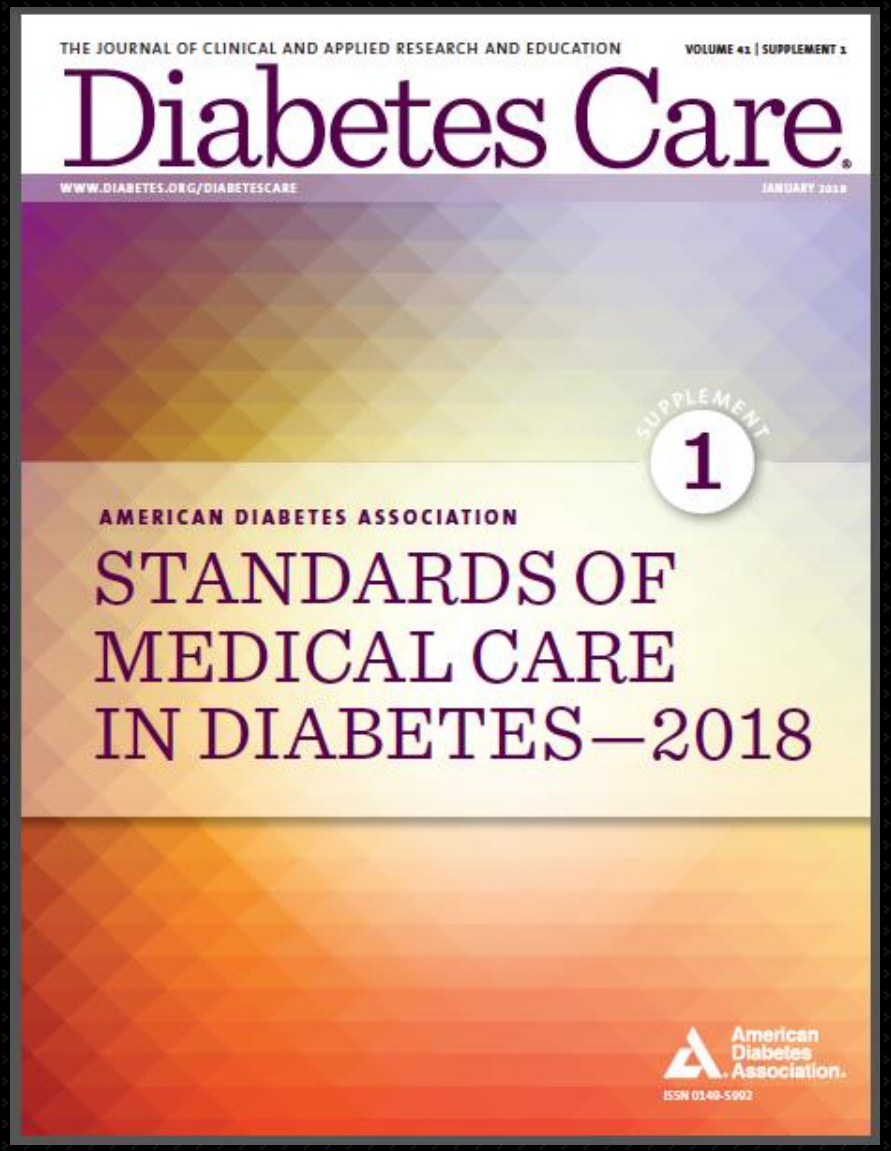
Ao longo do séc XX

- 1936 – percepção de diferentes "insulino sensibilidades"
- Décadas 40 / 50 biguanidas e sulfunilureias
- **1959** – identificação de diabetes tipo 1 (insulino dependente) e tipo 2 (não insulino dependente).
- 1998 - UKPDS

Evolução terapêutica antihiperglicémica



Classificação atual



Classificação Diabetes

Tipo1	• Destruição auto imune da célula beta • Insulino carência absoluta
Tipo2	• Insulino resistência importante • Deficiência secundária da célula beta
Gestacional	• Diabetes diagnosticada no 2º ou 3º trimestres da gravidez • Potencialmente reversível
Outros	• Diabetes secundária • MODY (maturity onset od diabetes of the young)

Diabetes Care Volume 41, Supplement 1, January 2018

Diabetes mellitus tipo1

Table 2.1—Staging of type 1 diabetes (4,5)

	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• New-onset hyperglycemia • Symptomatic
Diagnostic criteria	• Multiple autoantibodies • No IGT or IFG	• Multiple autoantibodies • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	• Clinical symptoms • Diabetes by standard criteria

Diabetes Care Volume 41, Supplement 1, January 2018

Critérios de Diagnóstico de Diabetes

Table 2.2—Criteria for the diagnosis of diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG ≥200 mg/dL (11.1 mmol/L) during 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

A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

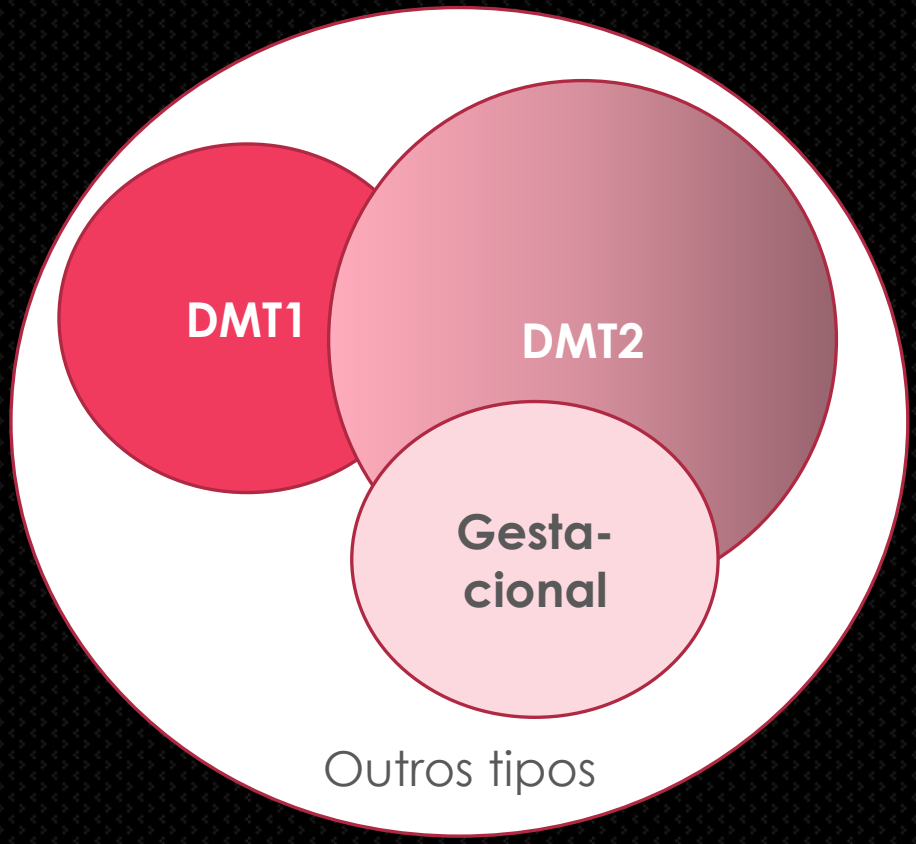
OR

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, results should be confirmed by repeat testing.

Diabetes Care Volume 41, Supplement 1, January 2018

Na pratica clínica....



Nova Classificação

Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables

Emma Ahlqvist, Petter Storm, Annemari Käräjämäki*, Mats Martinell*, Mozhgan Dorkhan, Annelie Carlsson, Petter Vikman, Rashmi B Prasad, Dina Mansour Aly, Peter Almgren, Ylva Wessman, Nael Shaat, Peter Spégel, Hindrik Mulder, Eero Lindholm, Olle Melander, Ola Hansson, Ulf Malmqvist, Åke Lernmark, Kaj Lahti, Tom Forsén, Tiinamaija Tuomi, Anders H Rosengren, Leif Groop

Introdução

- Nova classificação permite organizar sub tipos de diabetes com intenção de definir abordagens terapêuticas;
- Identificação dos doentes com risco mais elevado de complicações;

Memória Metabólica

www.thelancet.com/diabetes-endocrinology Published online March 1, 2018 http://dx.doi.org/10.1016/S2213-8587(18)30051-2

Métodos

- Utilizaram 5 cohorts dos países escandinavos:
  - Swedish All New Diabetics in Scania (ANDIS) -> 2008-2016
  - Scania Diabetes Registry (SDR),
  - All New Diabetics in Uppsala (ANDIU),
  - Diabetes Registry Vaasa (DIREVA),
  - Malmö Diet and Cancer Cardiovascular Arm (MDC-CVA)
- Cerca de 15 000 doentes que foram avaliados na altura do diagnóstico

www.thelancet.com/diabetes-endocrinology Published online March 1, 2018 http://dx.doi.org/10.1016/S2213-8587(18)30051-2

Métodos

- Idade do diagnóstico
- IMC
- HbA1C
- Anticorpos glutamato descarboxilase
- Modelo homeostático de insulino resistência (HOMA2-B) e função célula beta HOMA2-IR), através do doseamento do péptido C;

- Colheita de amostra de sangue (glicemia, HbA1C, pep C, transaminases, ureia e creatinina) e amostra de DNA:

www.thelancet.com/diabetes-endocrinology Published online March 1, 2018 http://dx.doi.org/10.1016/S2213-8587(18)30051-2

Métodos e resultados

- Identificação de 5 clusters :

Cluster	N (%)	Characteristics	Name
1	577 (6.4)	Early disease onset (at a young age), essentially corresponds with type 1 diabetes and LADA, relatively low BMI, poor metabolic control, insulin deficiency (impaired insulin production), GADA+	Severe autoimmune diabetes (SAID)
2	1575 (17.5)	Similar to cluster 1 but GADA–, high HbA_{1c}, highest incidence of retinopathy	Severe insulin-deficient diabetes (SIDD)
3	1373 (15.3)	Insulin resistance, high BMI, highest incidence of nephropathy	Severe-insulin resistant diabetes (SIRD)
4	1942 (21.6)	Obesity, younger age, not insulin resistant	Mild obesity-related diabetes (MOD)
5	3513 (39.1)	Older age, modest metabolic alterations	Mild age-related diabetes (MARD)

DM T1

DM T2

www.thelancet.com/diabetes-endocrinology Published online March 1, 2018 http://dx.doi.org/10.1016/S2213-8587(18)30051-2

Resultados

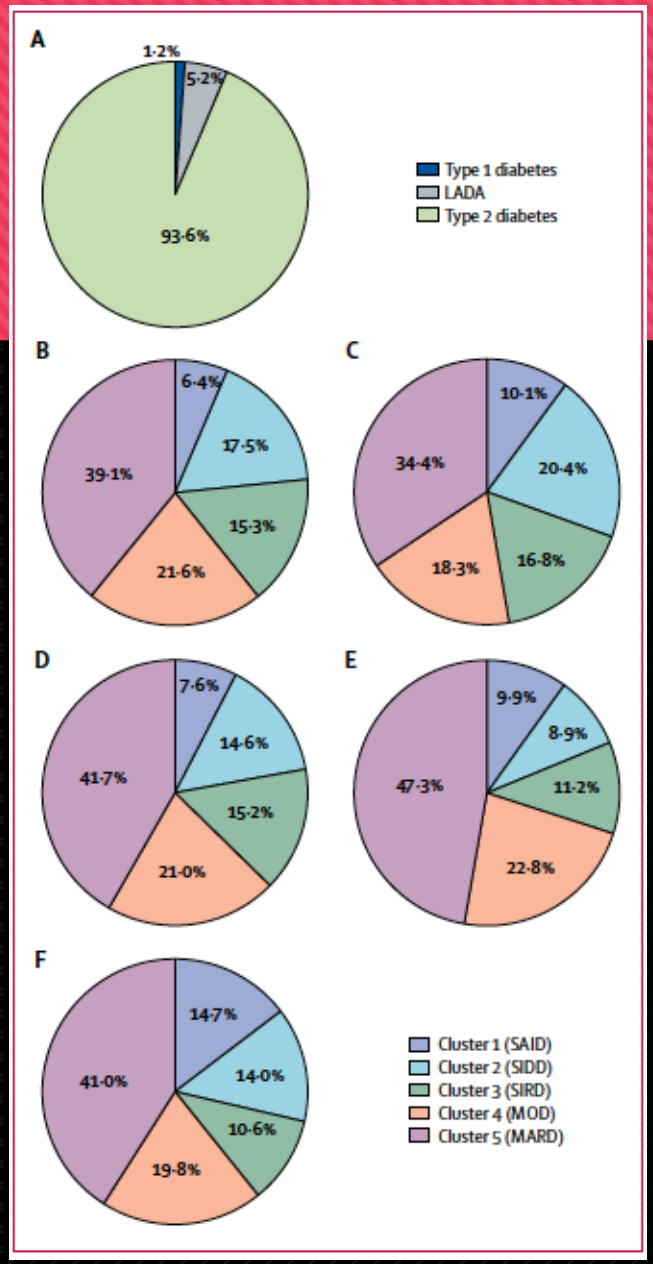


Figure 1: Patient distribution according to method of classification
(A) Distribution of ANDIS patients (n=8980) according to traditional classification. (B) Distribution of ANDIS patients (n=8980) according to k-means clustering. (C) Distribution of patients in the Scania Diabetes Registry (n=1466) according to k-means clustering. (D) Distribution of patients in the All New Diabetics in Uppsala cohort (n=844) according to k-means clustering. (E) Distribution of DIREVA patients with newly diagnosed diabetes (n=878) according to k-means clustering. (F) Distribution of DIREVA patients with longer-term diabetes (n=2607) according to k-means clustering. LADA=latent autoimmune diabetes in adults. SAID=severe autoimmune diabetes. SIDD=severe insulin-deficient diabetes. SIRD=severe insulin-resistant diabetes. MOD=mild obesity-related diabetes. MARD=mild age-related diabetes. ANDIS=All New Diabetics in Scania. DIREVA=Diabetes Registry Vaasa.

www.thelancet.com/diabetes-endocrinology Published online March 1, 2018 http://dx.doi.org/10.1016/S2213-8587(18)30051-2

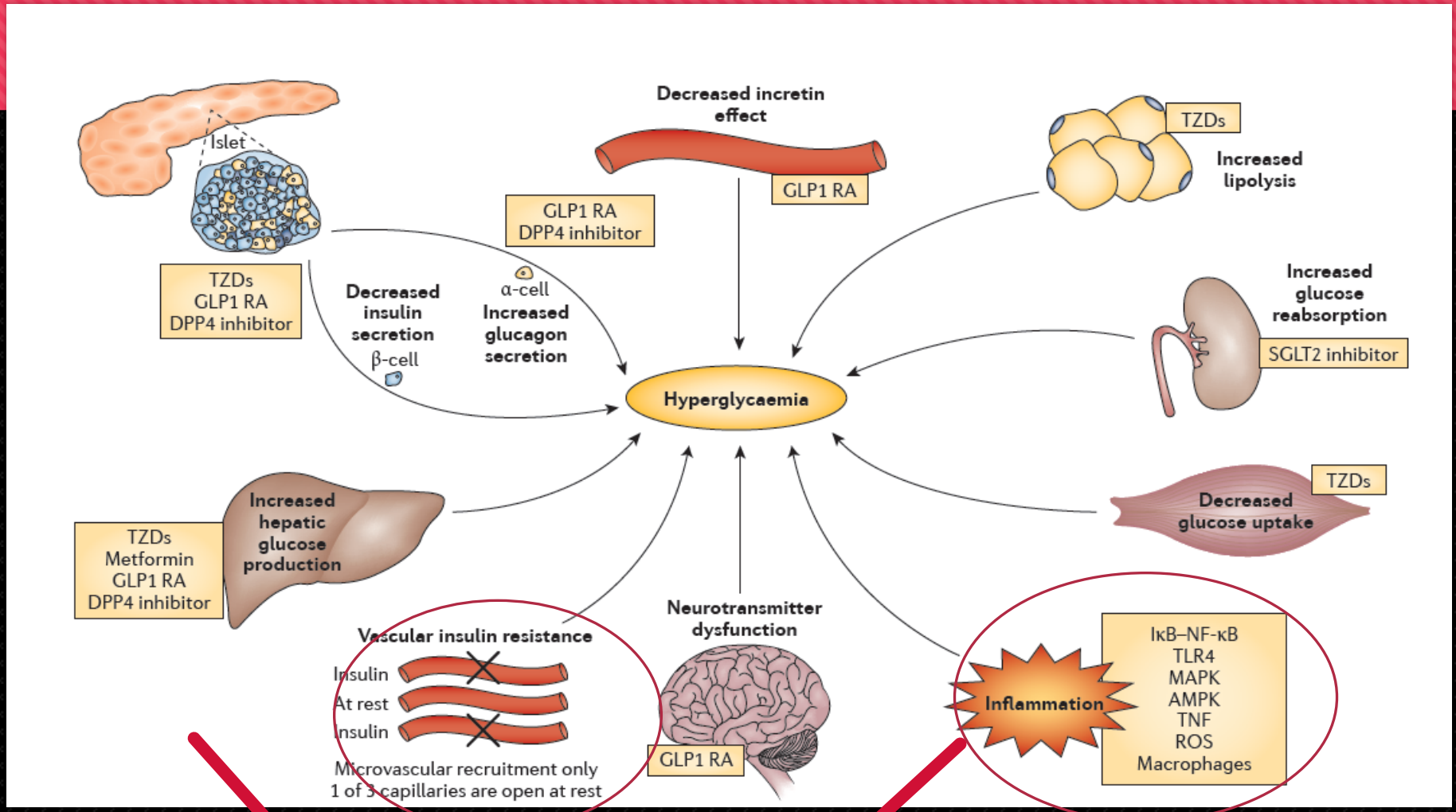
Conclusões

- Ainda faltam biomarcadores, genótipos e scores de risco genético;
- Utilização de 6 items em vez de 1 (glicémia) é melhor e mais adequado para personalização da terapêutica;

- Várias questões a colocar (onde ficou a diabetes gestacional??); Aplicável a todas as populações? Estamos a sub diagnosticar os DMT1?

www.thelancet.com/diabetes-endocrinology Published online March 1, 2018 http://dx.doi.org/10.1016/S2213-8587(18)30051-2

Ao octeto sinistro associam-se mais dois mecanismos fisiopatológicos:



Bloqueio da insulino vasodilatação

Activação das vias inflamatórias

Ambos justificam os fenómenos de insulino resistência do músculo.

Type 2 diabetes mellitus

Ralph A. DeFronzo[1], Ele Ferrannini[2], Leif Groop[3], Robert R. Henry[4], William H. Herman[5], Jens Juul Holst[6], Frank B. Hu[7], C. Ronald Kahn[8], Itamar Raz[9], Gerald I. Shulman[10], Donald C. Simonson[11], Marcia A. Testa[12] and Ram Weiss[13]

NATURE REVIEWS | DISEASE PRIMERS

Novos fármacos

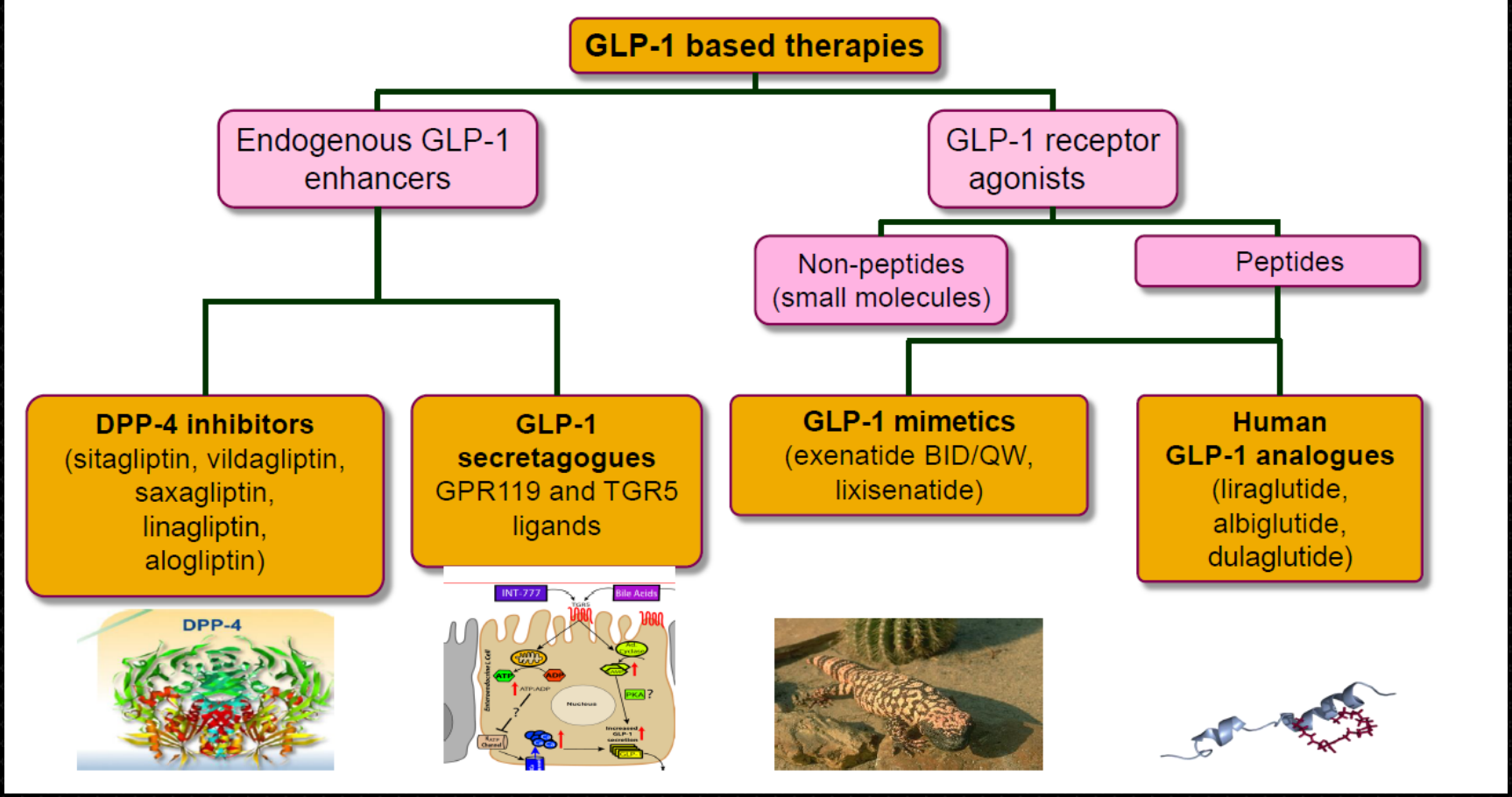
Quais são e mais valias?

Novos fármacos

Análogos GLP-1

Inibidores Sódio Glucose Transportadores

a GLP1



Gorgojo-Martinez JJ. Hipertens Riesgo Vasc. 2014;31:45-57.

a GLP1 em Portugal

- **Liraglutide** (2014) – 1,2 a 1,8 mg/d (TFG > 30 ml/mn)
- **Exenatide OW** (2015) – 2m /sem (TGF > 50 ml/mn)
- **Dulaglutide OW** (2017) 75 a 150 mg/sem (TFG > 15 ml/mn)

DMT2
+
IMC >35

Adaptado RCM Victoza ®, Bydureon ® e Trulicity ®.

a GLP1 em Portugal

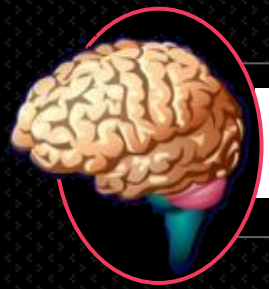
Classe	Composto(s)	Mecanismo celular	Ações fisiológicas primárias	Vantagens	Desvantagens
Agonistas dos recetores do GLP-1	· Exenatido · Exenatido de libertação prolongada · Liraglutido · Albiglutide* · Dulaglutide* · Lixisenatide*	Ativam os recetores da GLP-1	· ↑ Secreção da insulina (dependente da glicose) · ↓ Secreção do glucagon (dependente da glicose) · Atraso do esvaziamento gástrico · ↑ Saciedade	· Sem hipoglicemia · Redução de peso · ↓ Picos pós-prandiais da glicose · ↓ Alguns fatores de risco cardio-vasculares	· Efeitos secundários gastrointestinais (náuseas/vómitos) · ↑ Frequência cardíaca · Pancreatite aguda? · Hiperplasia das células C tiroideias/carcinoma medular da tiróide em animais · Injetável · Requer formação

Revista Portuguesa de Diabetes. 2015; 10 (1): 40-48.

GLP-1 apresenta uma variedade de ações em múltiplos tecidos-alvo implicados na DMT2

↑Ação cronotrópica e inotrópica

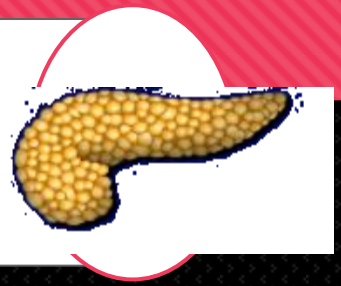
Efeito antiapoptótico no músculo cardíaco



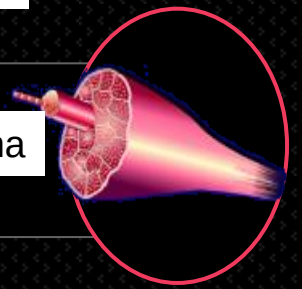
Neuroproteção
Indução de saciedade

Atraso no esvaziamento gástrico

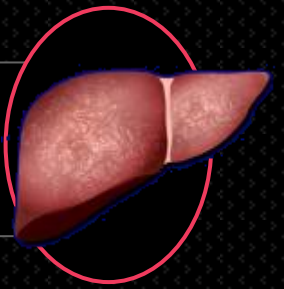
↑Libertação de insulina
↑Inibição do glucagon
↑Proliferação das células β
↓Apoptose das células β



Sensibilidade à Insulina



Inibição do *output* de glicose



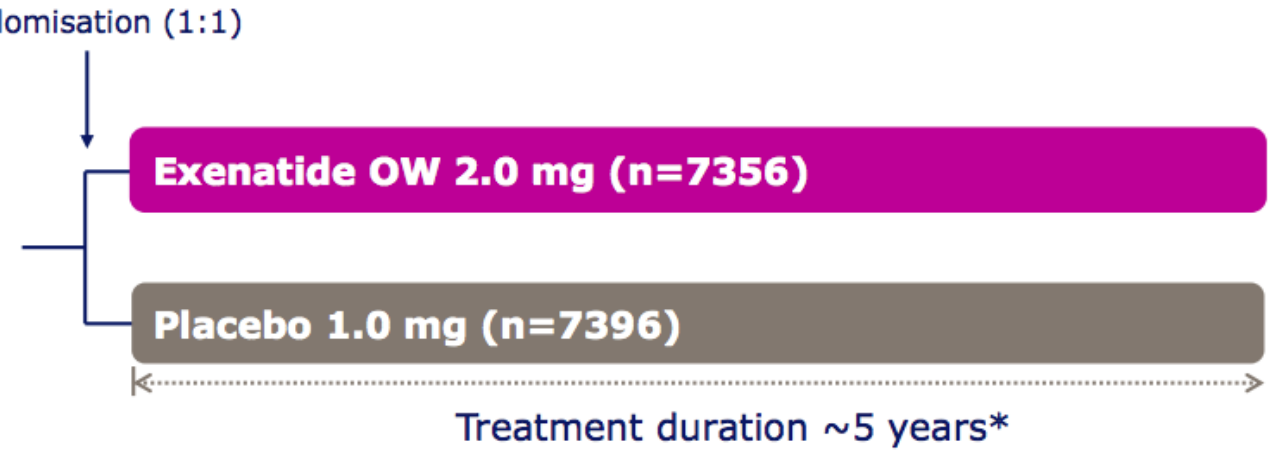
- GLP-1: peptídeo-1 similar ao glucagon.
- Deacon C, et al. Front Biosci. 2008;13:1780–94; Drucker D. Cell Metab. 2006;3:153–65; Ahern B. Horm Metab Res. 2004;36:842–5.

EXSCEL: Study Design

Exenatide Study of Cardiovascular Event Lowering Trial

14780 patients with T2D

- HbA_{1c} ≥6.5 and ≤10.5%
- Currently being treated with at least 1 OAD or insulin
- No prior treatment with GLP-1RA



Trial information

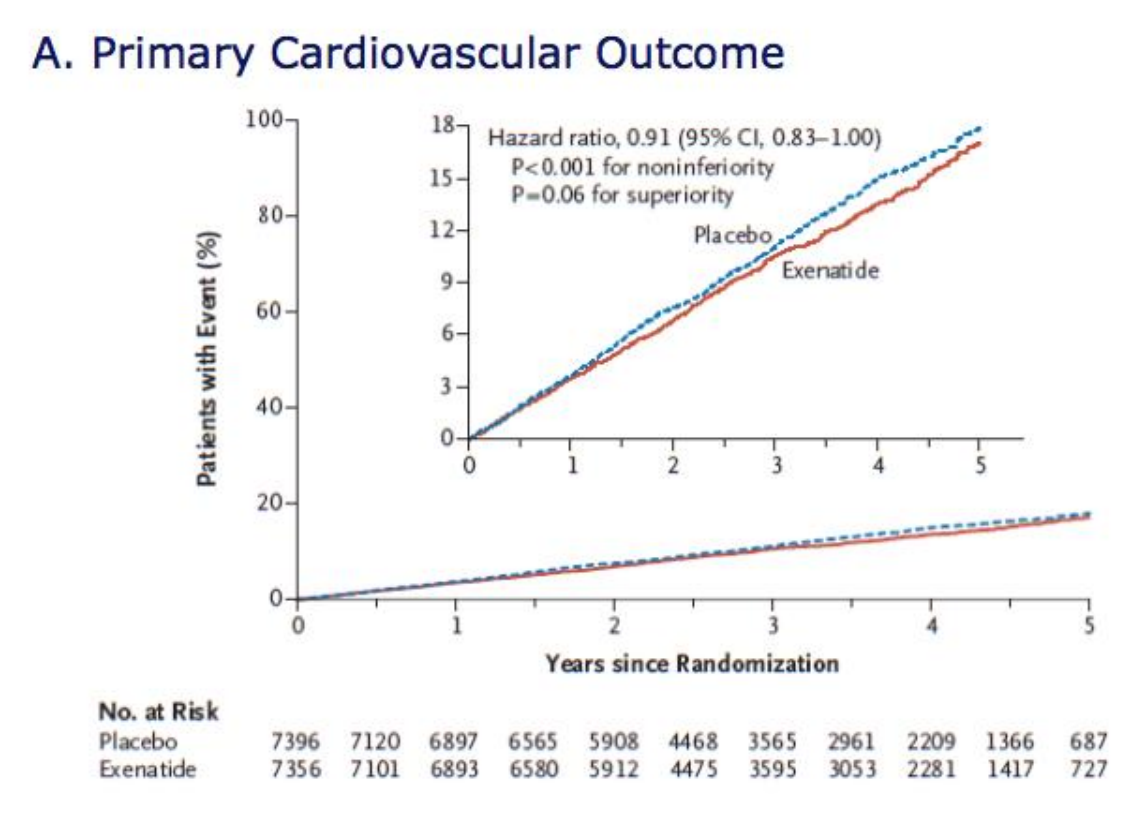
- Phase III/IV randomised, double-blind, placebo-controlled, parallel-group, multicentre, multinational, trial to evaluate CV outcomes after treatment with exenatide OW in patients with T2D
- Primary outcome: a composite endpoint of cardiovascular death, non-fatal MI, or non-fatal stroke

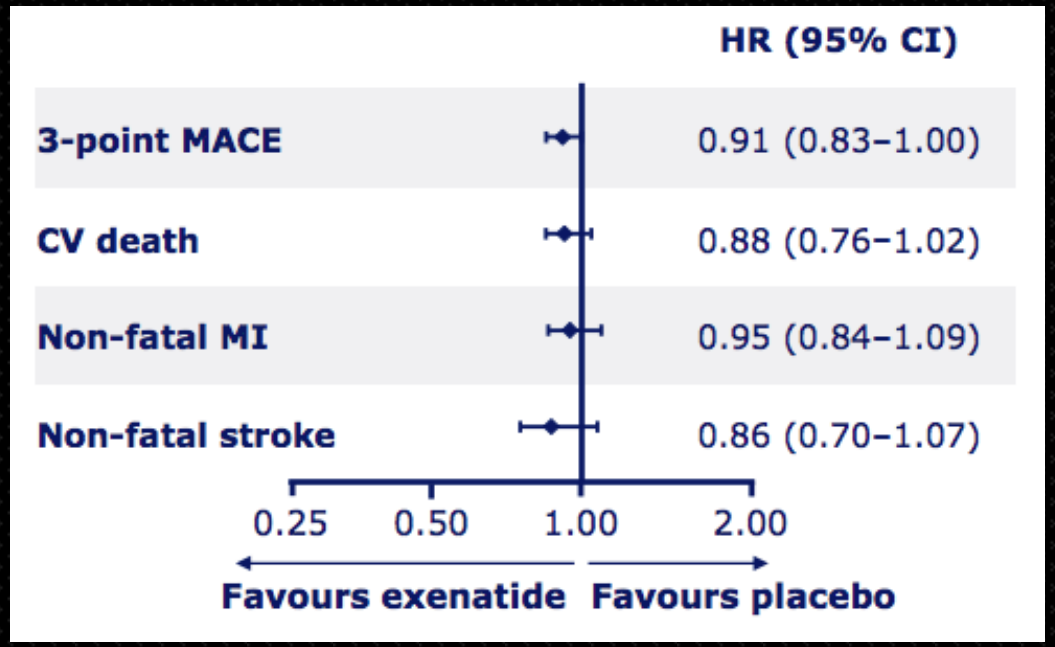
*Until 1360 confirmed primary composite cardiovascular endpoints occur

CV, cardiovascular; GLP-1RA, glucagon-like peptide-1 receptor agonist; MI, myocardial infarction; OAD, oral antidiabetic drug; OW, once-weekly; T2D, type 2 diabetes

www.ClinicalTrials.gov (NCT01144338). Holman *et al. Am Heart J* 2016;174:103–10

EXSCEL
Exenetide Study Cardiovascular Event Lowering

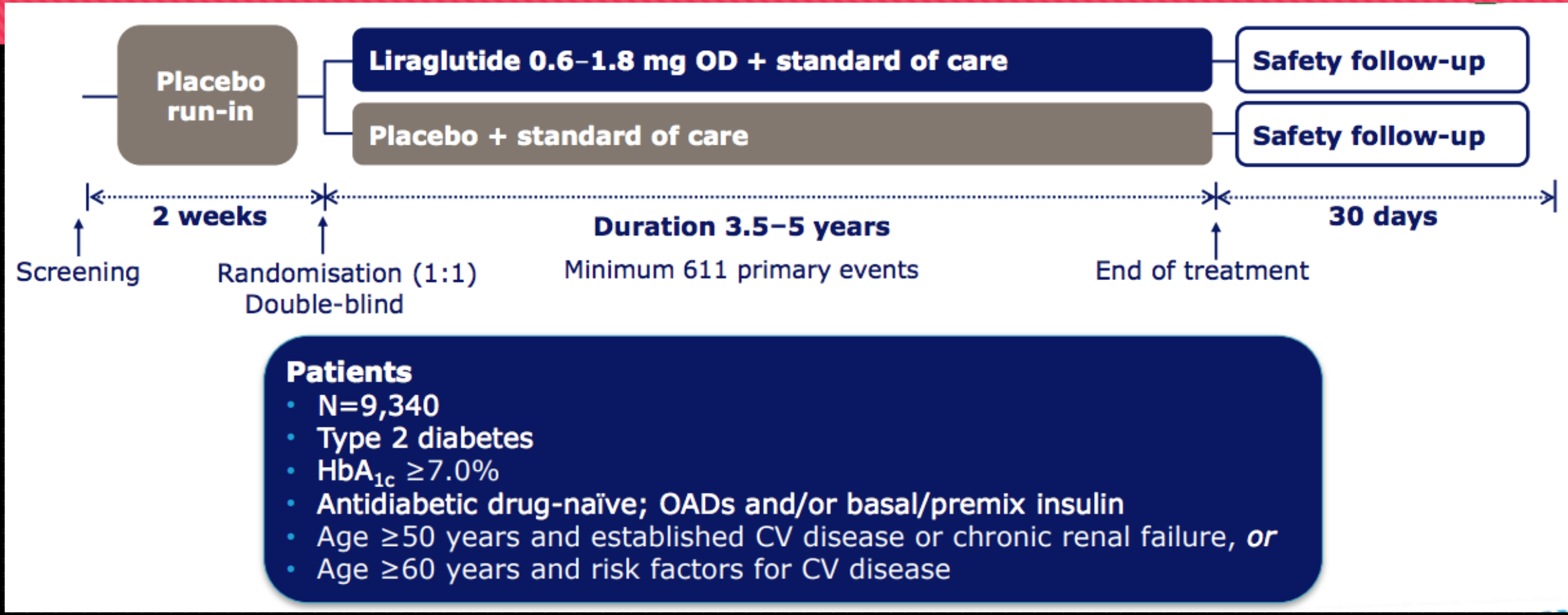




The primary composite outcome was the first occurrence of death from CV causes, non-fatal MI, or non-fatal stroke.
CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MACE, major adverse cardiovascular event; MI, myocardial infarction
Holman *et al. N Engl J Med* 2017 [epub ahead of print]

LEADER: Study Design

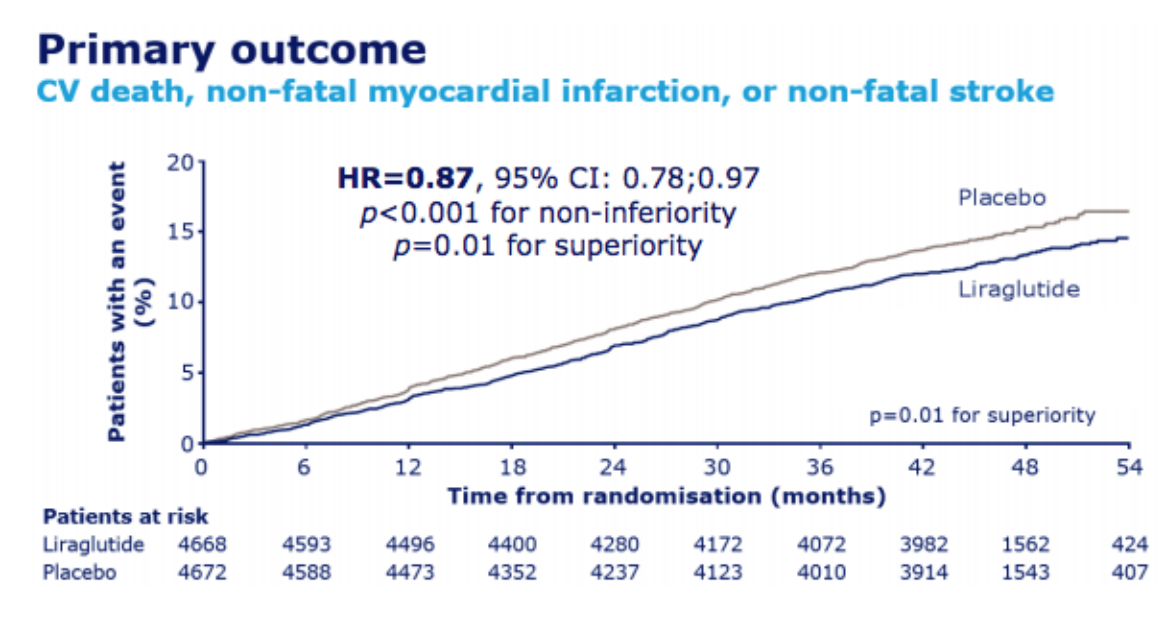
Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results

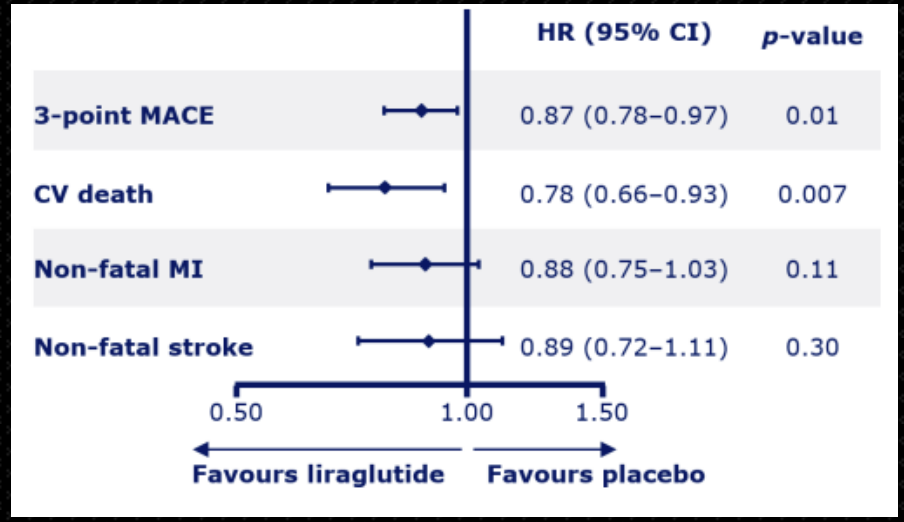


CV, cardiovascular; OAD, oral antidiabetic drug; OD, once daily

Marso *et al. N Engl J Med* 2016;375:311–22

LEADER
Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Results

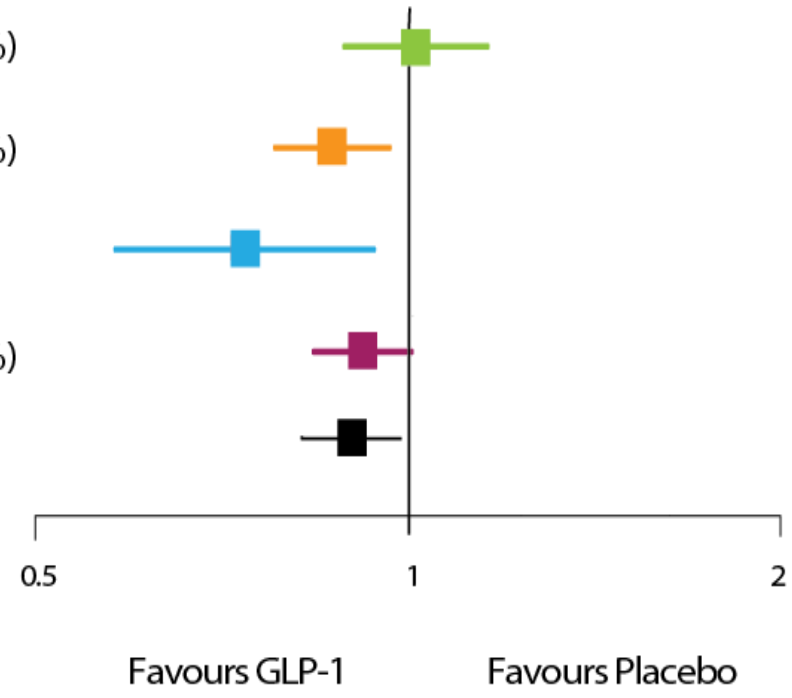




CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MACE, major adverse cardiovascular event; MI, myocardial infarction
Marso *et al. N Engl J Med* 2016;375:311–22

Meta-analysis: MACE-3 endpoint

Study name	GLP-1 Group	Placebo Group	Hazard ratio and 95% CI	Hazard ratio	Lower limit	Upper limit	p-Value
ELIXA	400/3034 (13.2%)	392/3034 (12.9%)		1.02	0.89	1.17	0.776
LEADER	608/4668 (13.0%)	694/4672 (14.9%)		0.87	0.78	0.97	0.015
SUSTAIN-6	108/1648 (6.6%)	146/1649 (8.9%)		0.74	0.58	0.95	0.016
EXSCEL	839/7356 (11.4%)	905/7396 (12.2%)		0.91	0.83	1.00	0.061
Overall				0.90	0.82	0.99	0.033



Test for heterogeneity
Q-test p value = 0.11
$I^2 = 50\%$

Bethel et al. TLDE 2017; in press

Uso de a GLP1 na DMT2

- Usar no início da doença
- Idealmente antes da insulinização;
- Em combinação com insulina basal;
- Utilização com TFG > 30 ml/mn;

- Controlo metabólico, com baixo risco de hipoglicémias;
- Perda ponderal entre 3 a 5 kgs;
- Redução perímetro abdominal/ gordura visceral;
- Redução PA sistólica e diastólica;

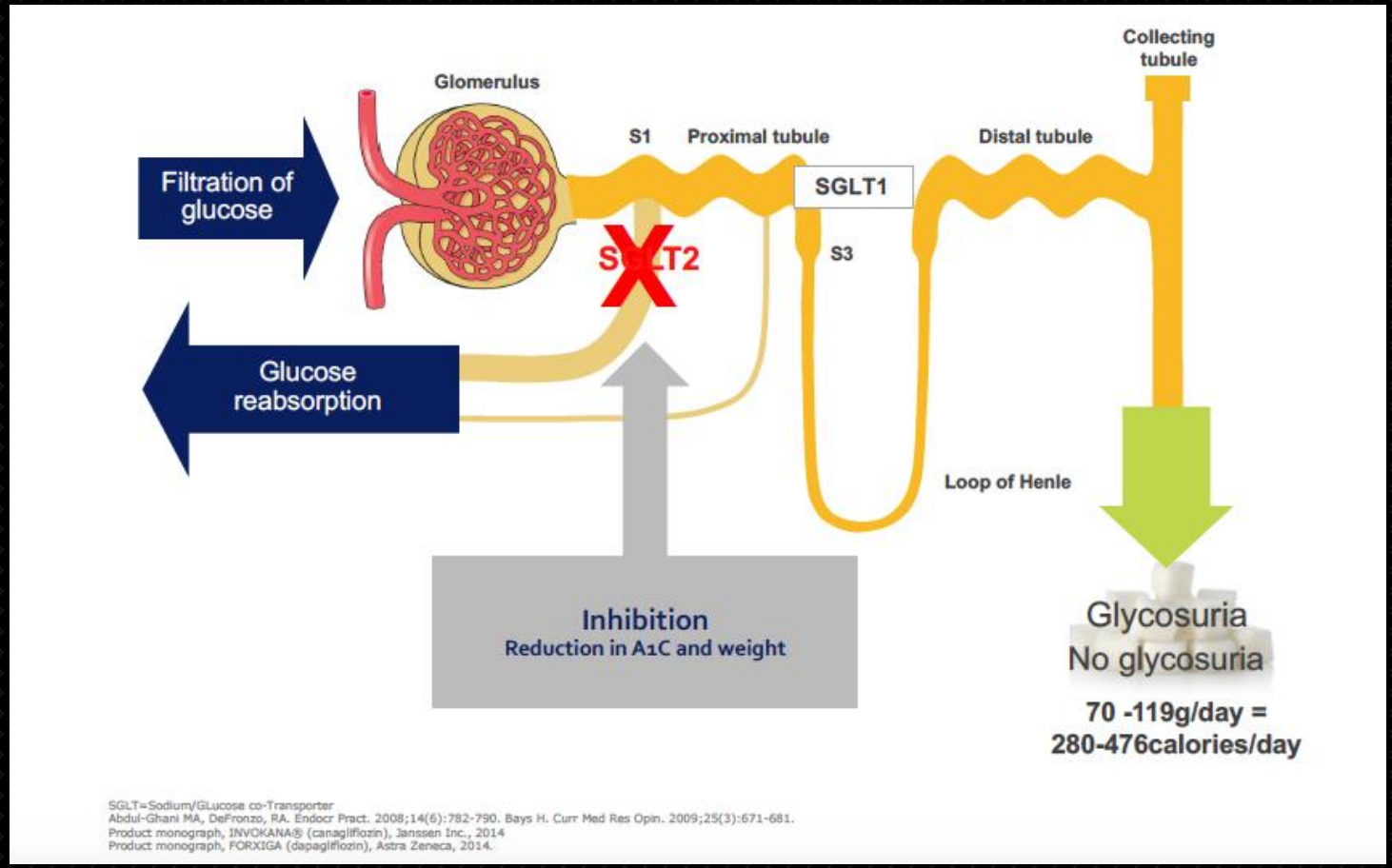
Diabetes Care Volume 40, Supplement 1, January 2017

Novos fármacos

Análogos GLP-1

Inibidores Sódio Glucose Transportadores

iSGLT2 Mecanismo de ação



SGLT=Sodium/Glucose co-Transporter
Abdul-Ghani MA, DeFronzo, RA. Endocr Pract. 2008;14(6):782-790. Bays H. Curr Med Res Opin. 2009;25(3):671-681.
Product monograph, INVOKANA® (canagliflozin), Janssen Inc., 2014
Product monograph, FORXIGA (dapagliflozin), Astra Zeneca, 2014.

- ✓ Controlo metabólico
- ✓ Perda ponderal
- ✓ Diminuição PA

Mecanismos envolvidos na proteção cardiovascular dos iSGLT2

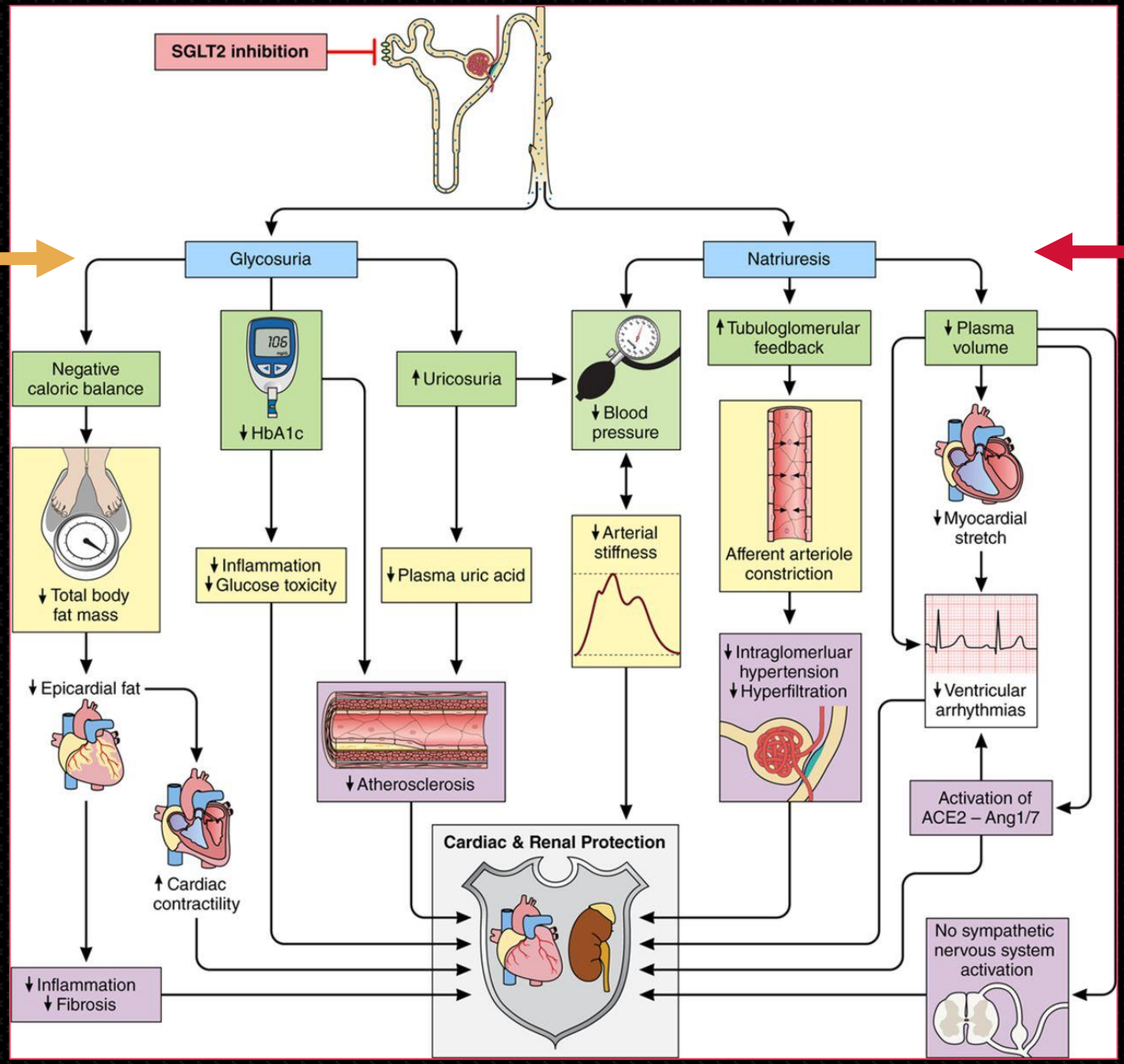
Efeitos não glicémicos: Natriurese

- Diminuição de PA: diminuição rigidez arterial;
- Aumento do feedback tubuloglomerular;
- Diminuição do volume plasmático

Efeitos glicémicos: Glicosúria

- Balanço calórico negativo: diminuição IMC, inflamação e da fibrose;
- Diminuição HbA1C : redução glucotoxicidade
- Uricosuria: redução acido úrico- diminuição aterosclerose;

Glic



Na

Mecanismos fisiológicos implicados na proteção cardiovascular e renal com inibição SGLT2.

Circulation. 2016; 134: 752-772.DOI: 10.1161/CIRCULATIONAHA-116-021887

Empa Reg

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D., Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

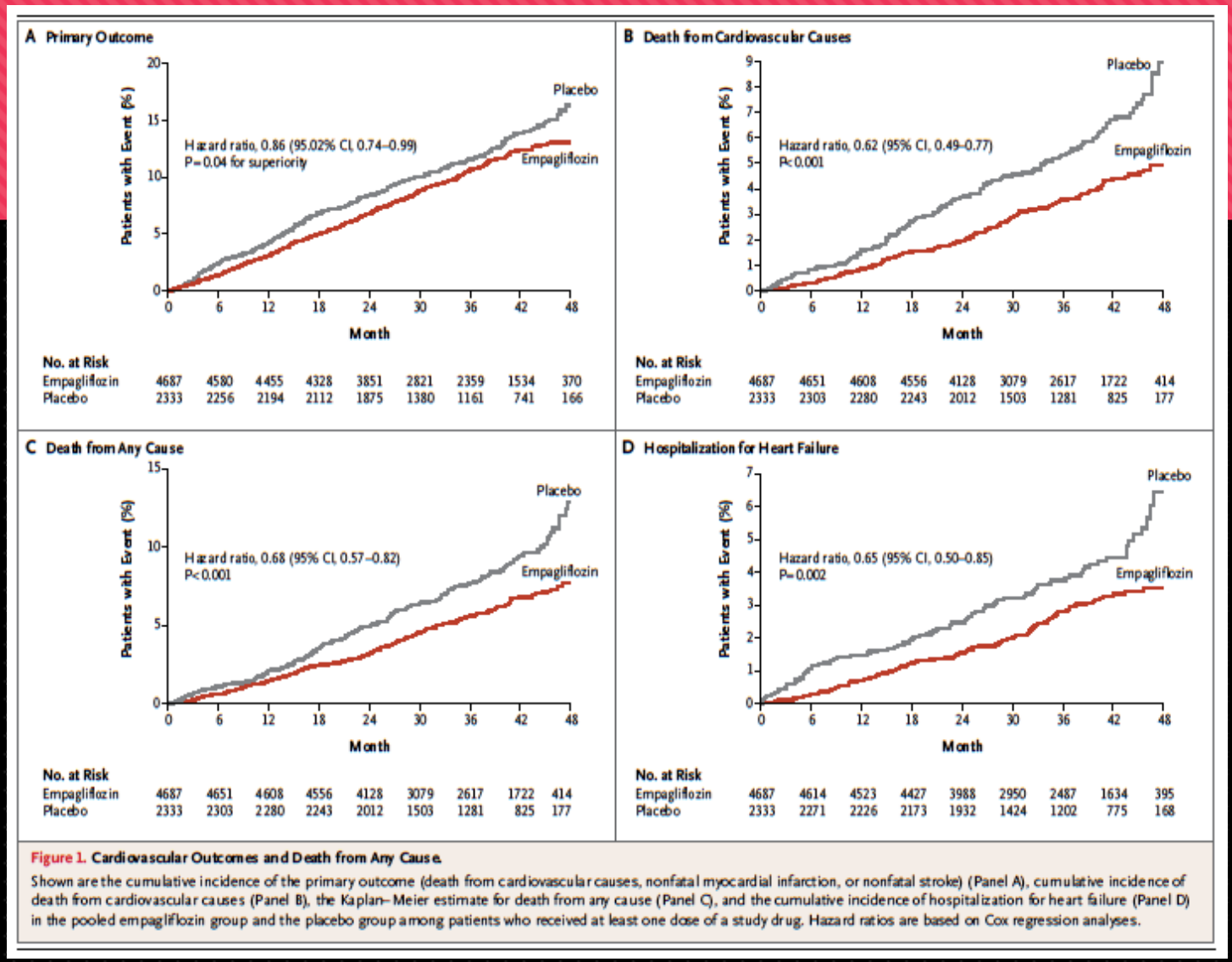


Figure 1. Cardiovascular Outcomes and Death from Any Cause.

Shown are the cumulative incidence of the primary outcome (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke) (Panel A), cumulative incidence of death from cardiovascular causes (Panel B), the Kaplan–Meier estimate for death from any cause (Panel C), and the cumulative incidence of hospitalization for heart failure (Panel D) in the pooled empagliflozin group and the placebo group among patients who received at least one dose of a study drug. Hazard ratios are based on Cox regression analyses.

N ENGL J MED 373;22 NEJM.ORG NOVEMBER 26, 2015

CANVAS

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes

Bruce Neal, M.B., Ch.B., Ph.D., Vlado Perkovic, M.B., B.S., Ph.D., Kenneth W. Mahaffey, M.D., Dick de Zeeuw, M.D., Ph.D., Greg Fulcher, M.D., Ngozi Erondu, M.D., Ph.D., Wayne Shaw, D.S.L., Gordon Law, Ph.D., Mehul Desai, M.D., and David R. Matthews, D.Phil., B.M., B.Ch., for the CANVAS Program Collaborative Group*

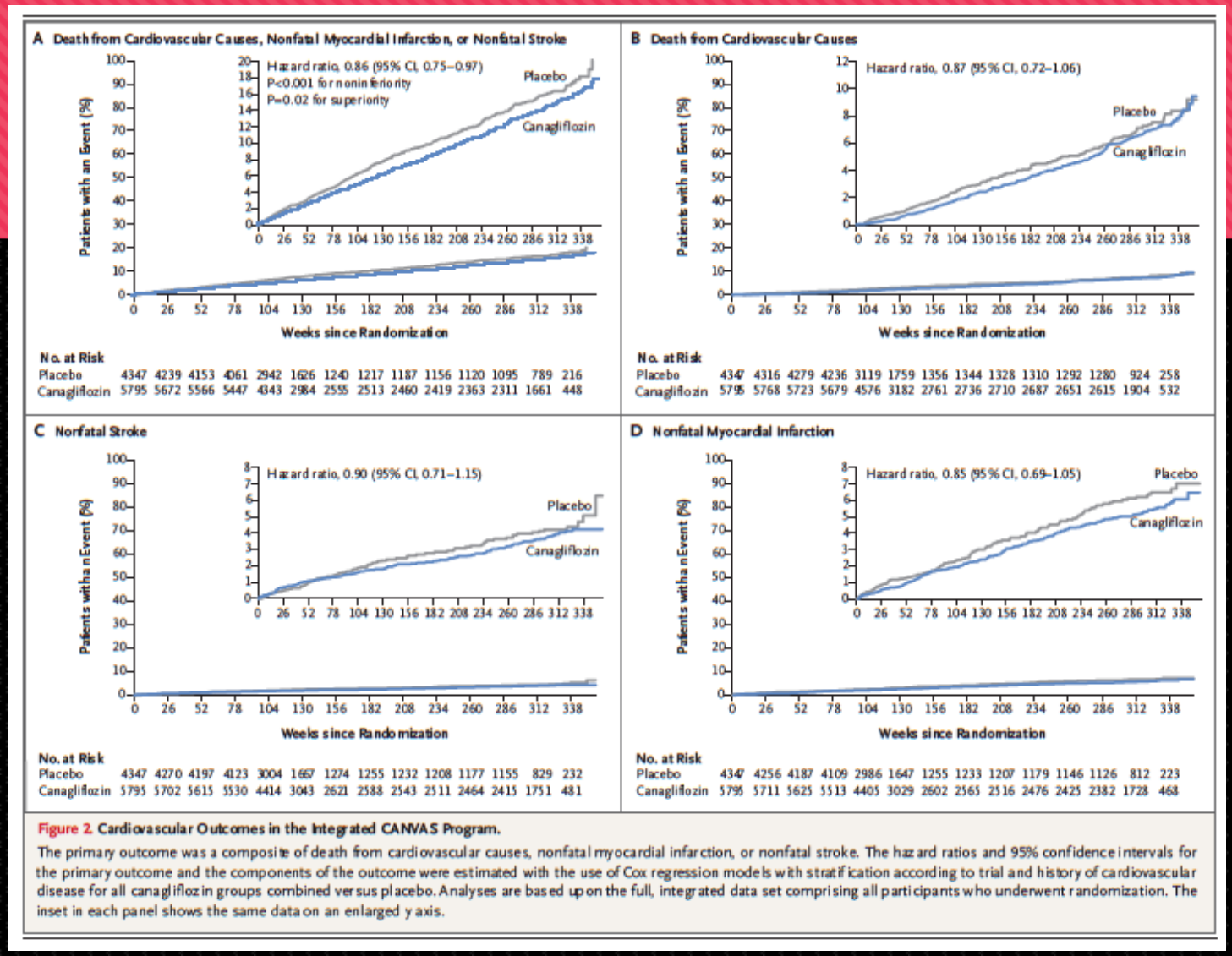


Figure 2. Cardiovascular Outcomes in the Integrated CANVAS Program.

The primary outcome was a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. The hazard ratios and 95% confidence intervals for the primary outcome and the components of the outcome were estimated with the use of Cox regression models with stratification according to trial and history of cardiovascular disease for all canagliflozin groups combined versus placebo. Analyses are based upon the full, integrated data set comprising all participants who underwent randomization. The inset in each panel shows the same data on an enlarged y axis.

CVDREAL

Key Unanswered Questions

- Are the observed benefits compound-specific, or do they represent a “class effect”?
- Will effects observed in those with established cardiovascular disease apply to a Type 2 diabetes population with a broader cardiovascular risk profile?
- Will the effects observed in EMPA-REG OUTCOME translate to real world clinical practice?

Study Objectives

Primary

- Compare risk of HHF in patients with Type 2 diabetes newly initiated on SGLT-2 inhibitors versus other glucose-lowering drugs (GLDs)

Secondary

- Compare risk of all-cause death between the two treatment groups
- Compare risk of HHF or all-cause death between the two treatment groups

CVDREAL

ACC.17

Data Sources: Health Records Across Six Countries

- Truven MarketScan Claims & Encounters and linked Medicare
- National full-population registries
- National full-population registries
- National full-population registries
- Clinical Practice Research Datalink (CPRD) and The Health Improvement Network (THIN)
- Diabetes Patienten Verlaufsdokumentation (DPV) initiative

Cohort 1
HHF

Cohort 2
All-cause death and composite HHF/all-cause death

CVDREAL

ACC.17

Conclusions

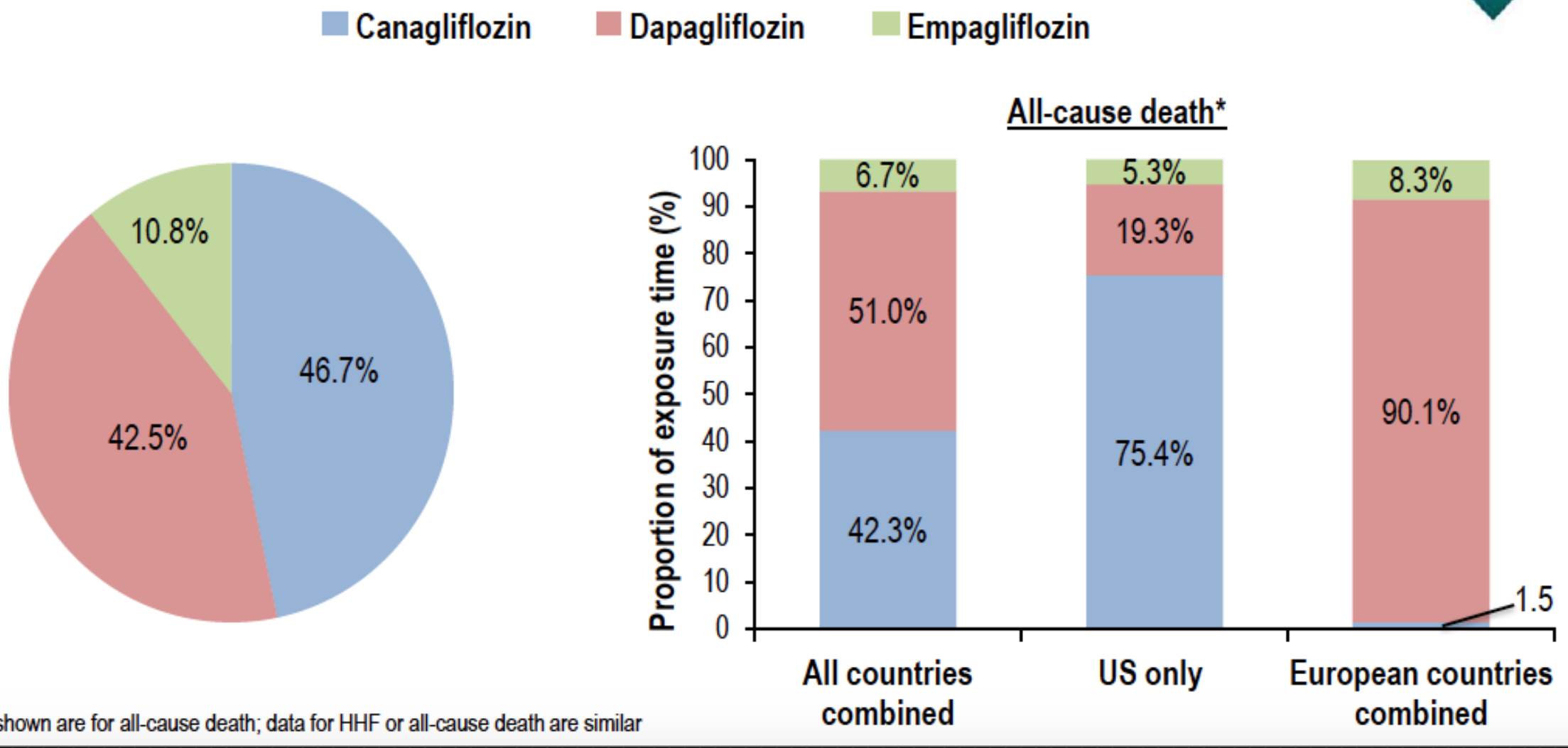
- In a large real-world study across six countries and a broad population of patients with Type 2 diabetes, treatment with SGLT-2 inhibitors versus other GLDs was associated with significant reductions in:
  - Hospitalization for heart failure
  - All-cause death
  - Hospitalization for heart failure or all-cause death

CVDREAL

ACC.17

Contribution of SGLT-2 inhibitor Class as a Proportion of Exposure Time in Propensity-Match Cohorts

Cohort 2: All-Cause Death and HHF or All-Cause Death Analyses (N=215,622)



*Data shown are for all-cause death; data for HHF or all-cause death are similar

iSGLT2 em Portugal

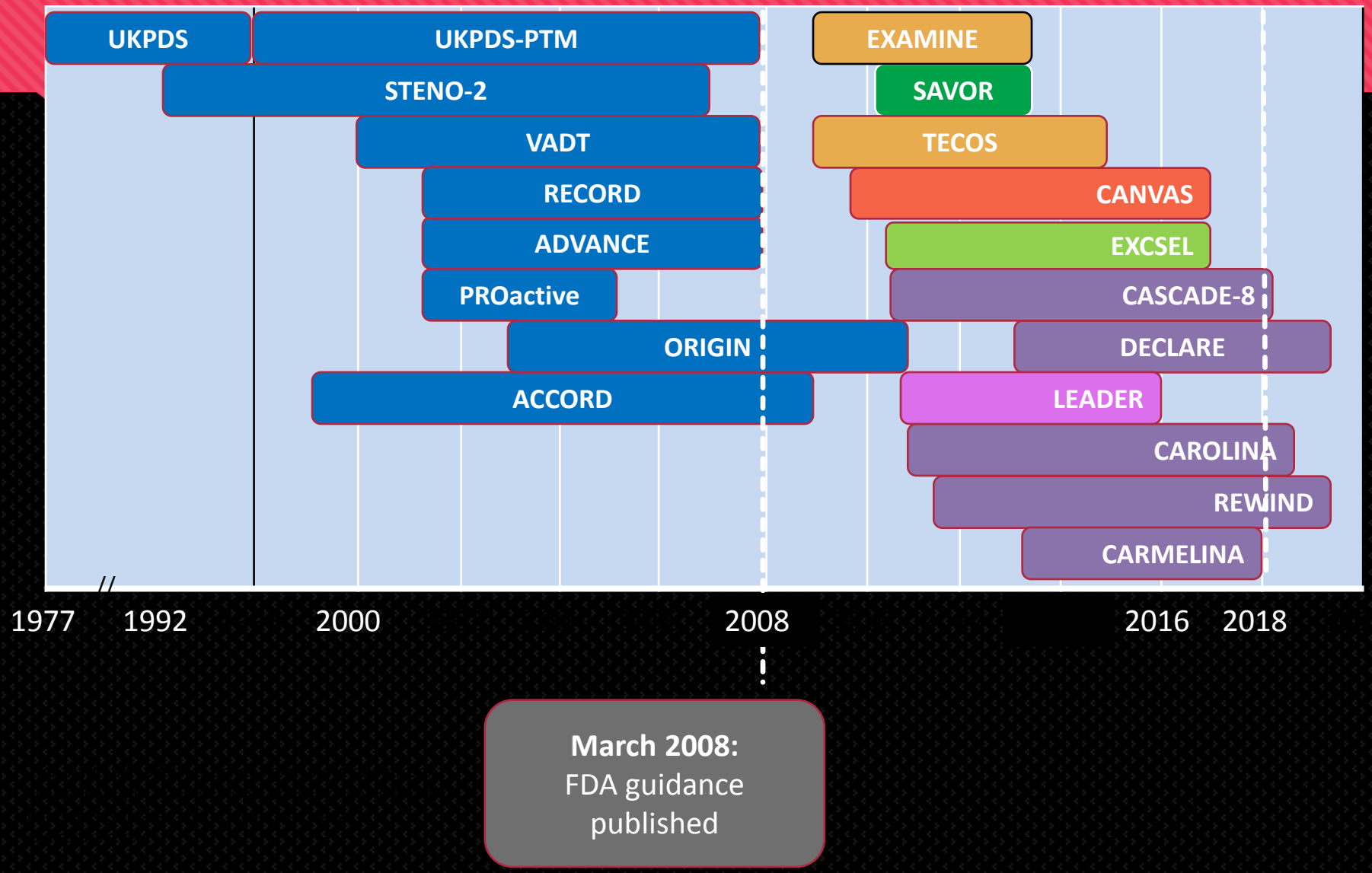
- Dapagliflozina 10 mg
- Dapagliflozina + metformina

- Empagliflozina 10 mg
- Empagliflozina 25 mg

- Canagliflozina 100 mg
- Canagliflozina 300 mg

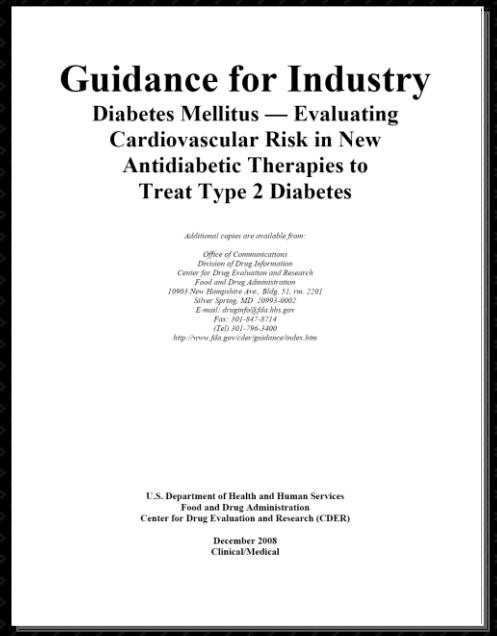
RCM Forxiga®, Xigduo®, Jardiance® e Invokane®;

Desde o UKPDS



Segurança cardiovascular FDA

Exigências regulamentares para todos os novos fármacos anti-diabéticos - 2008



Guidance for Industry

Diabetes Mellitus — Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes

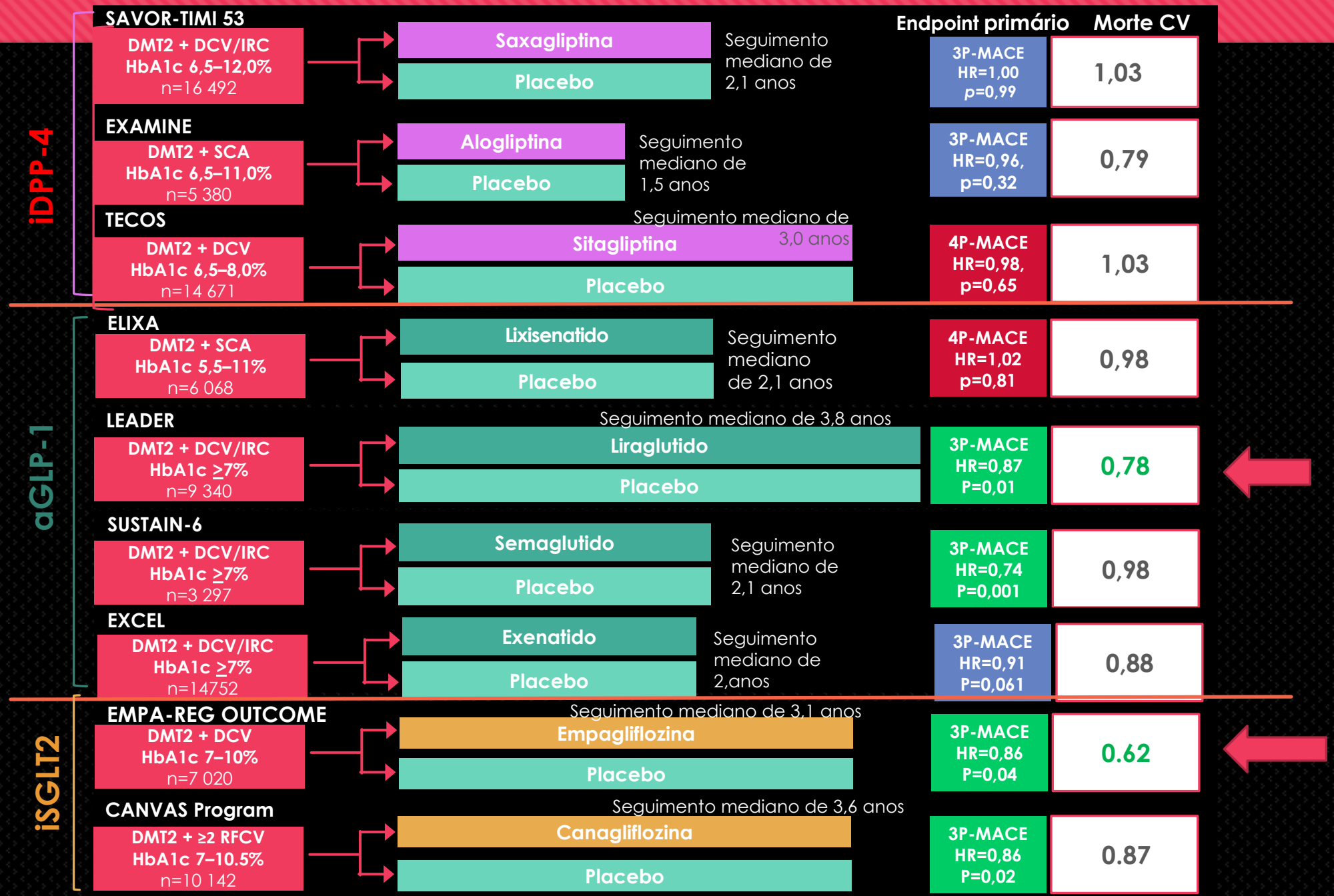
Additional copies are available from:

Office of Communications
Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 51, rm. 2201
Silver Spring, MD 20993-0002
E-mail: druginfo@fda.hhs.gov
Fax: 301-847-8714
(Tel) 301-796-3400
http://www.fda.gov/cder/guidance/index.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

December 2008
Clinical/Medical

Resumo dos ERCV concluídos relativamente aos mais recentes agentes para a DMT2



Prevenção do Risco Cardiovascular

European Heart Journal Advance Access published May 23, 2016

European Heart Journal
doi:10.1093/eurheartj/ehw106

JOINT ESC GUIDELINES

2016 European Guidelines on cardiovascular disease prevention in clinical practice

The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)

Recommendations for management of diabetes

Recommendations	Class[a]	Level[b]	Ref[c]
Lifestyle changes including smoking cessation, low fat diet, high fibre diet, aerobic physical activity, and strength training are recommended.	I	A	387
Reduction in energy intake is recommended to patients to help achieve lower weight or prevent weight gain.	I	B	387
A target HbA1c for the reduction in risk of CVD and microvascular complications in DM of <7.0% (<53 mmol/mol) is recommended for the majority of non-pregnant adults with either type 1 or type 2 DM.	I	A	388, 389
For patients with a long duration of DM, the elderly, frail, or those with existing CVD, a relaxing of the HbA1c targets (i.e. less stringent) should be considered.	IIa	B	389
A target HbA1c of ≤6.5% (≤48 mmol/mol) should be considered at diagnosis or early in the course of type 2 DM in patients, who are not frail and do not have CVD.	IIa	B	389
When screening for DM in individuals with or without CVD, assessment of HbA1c (which can be done non-fasting) or fasting blood glucose should be considered. An oral glucose tolerance test can be offered when there is still doubt.	IIa	A	390
Metformin is recommended as first-line therapy, if tolerated and not contra-indicated, following evaluation of renal function.	I	B	391
Avoidance of hypoglycaemia and excessive weight gain should be considered and individual approaches (with respect to both treatment targets and drug choices) should be considered in patients with advanced disease.	IIa	B	389, 392, 393
In patients with type 2 DM and CVD, the use of an SGLT2 inhibitor should be considered early in the course of the disease to reduce CV and total mortality.	IIa	B	394
Lipid lowering agents (principally statins) are recommended to reduce CV risk in all patients with type 2 or type 1 DM above the age of 40 years.	I	A	371, 372
Lipid lowering agents (principally statins) may be considered also in individuals below 40 years of age if at significantly elevated risk, based on the presence of micro-vascular complications or of multiple CV risk factors.	IIb	A	371, 372
In DM patients at very high-risk (see table 5), a LDL-C target <1.8 mmol/L (<70 mg/dL), or a reduction of at least 50% if the baseline LDL-C is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL), is recommended.[d] In DM patients with high-risk (see table 5), LDL-C target <2.6 mmol/L (<100mg/dL) or a reduction of at least 50% if the baseline LDL-C is between 2.6 and 5.1 mmol/L (100 and 200 mg/dL) is recommended.[d]	I	B	395
BP targets in type 2 DM are generally recommended to be <140/85 mmHg, but a lower target of <130/80 mmHg is recommended in selected patients (e.g. younger patients at elevated risk for specific complications) for additional gains on stroke, retinopathy and albuminuria risk. Renin-angiotensin-aldosterone system blocker is recommended in the treatment of hypertension in DM, particularly in the presence of proteinuria or micro- albuminuria. Recommended BP target in patients with type 1 DM is <130/80 mmHg.	I	B	396, 397
The use of drugs that increase HDL-C to prevent CVD in type 2 DM is not recommended.	III	A	386
Antiplatelet therapy (e.g. with aspirin) is not recommended for people with DM who do not have CVD.	III	A	398

BP = blood pressure; CV = cardiovascular; DM = diabetes mellitus; HbA1c = glycated haemoglobin; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; SGLT2 = Sodium-glucose co-transporter-2.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.
[d]Non-HDL-C is a reasonable and practical alternative target because it does not require fasting. Non HDL-C secondary targets of <2.6 and <3.3 mmol/L (<100 and <130 mg/dL) are recommended for very high, and high-risk subjects, respectively See section 3a.7.10 for more details.

http://eurheartj.oxfordjournals.org/content/ehj/early/2016/05/23/eurheartj.ehw106.full.pdf

Tratar diabetes...

- ✓ Tratar melhor de acordo com os FRCV;
- ✓ Ao longo da história da diabetes:
  - ✓ Na prevenção do evento CV;
  - ✓ Com segurança e benefício após evento CV;

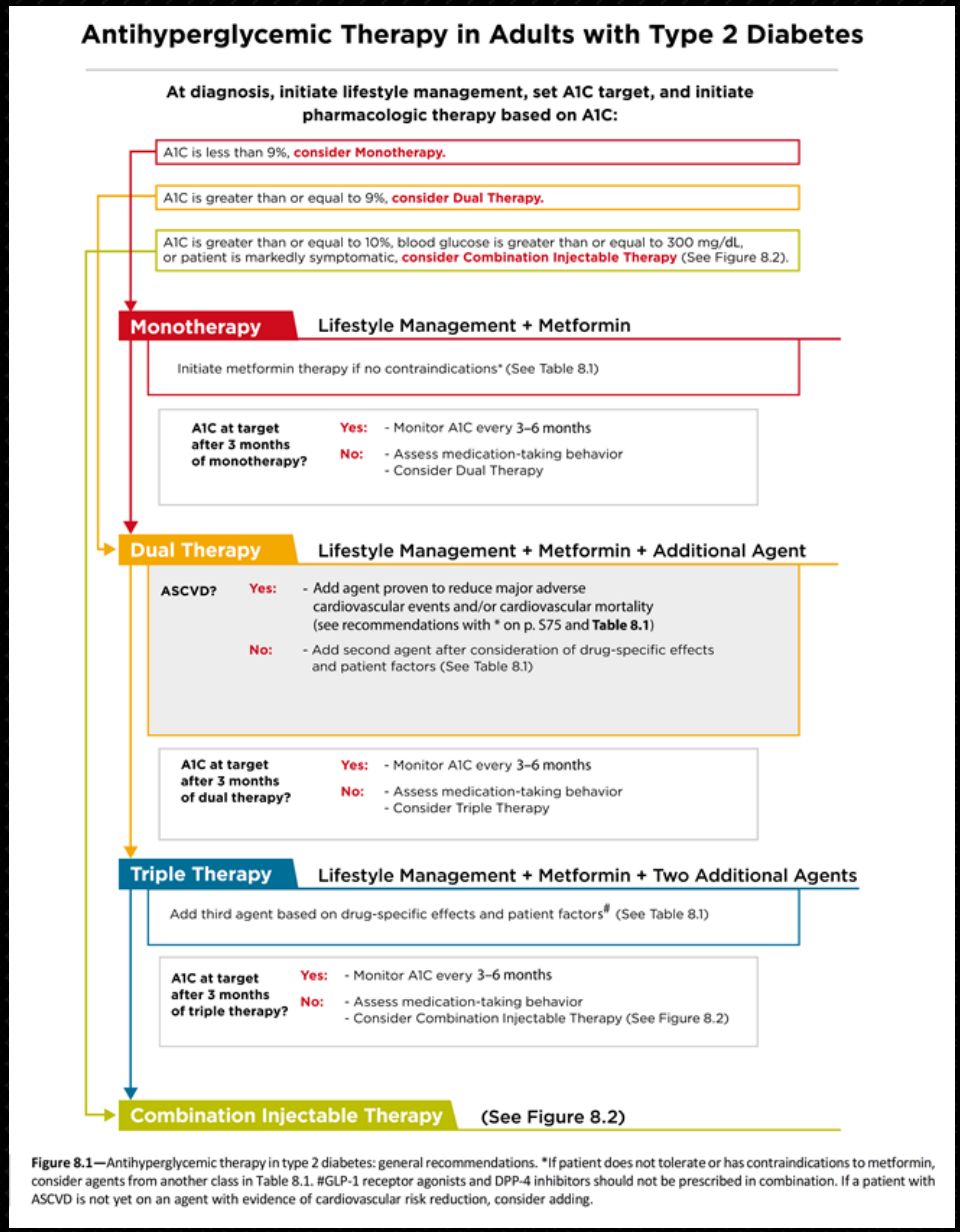


Figure 8.1—Antihyperglycemic therapy in type 2 diabetes: general recommendations. *If patient does not tolerate or has contraindications to metformin, consider agents from another class in Table 8.1. #GLP-1 receptor agonists and DPP-4 inhibitors should not be prescribed in combination. If a patient with ASCVD is not yet on an agent with evidence of cardiovascular risk reduction, consider adding.

ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular

American Diabetes Association. *Diabetes Care* 2018;41:S1

Metas 2020

PROGRAMA NACIONAL PARA A DIABETES

2017

4.4. Metas de Saúde a 2020

Diminuir o desenvolvimento de diabetes em 30.000 utentes de risco identificados através da avaliação do cálculo de risco de desenvolver a doença

Aumentar em 30.000 o número de novos diagnósticos de diabetes através do diagnóstico precoce em utentes

Diminuir a mortalidade prematura por diabetes ≤ 70 anos em Portugal em 5% até 2020

DGS desde 1899 Direção-Geral da Saúde

Programa Nacional para a Diabetes