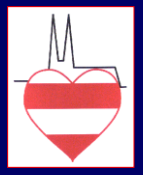
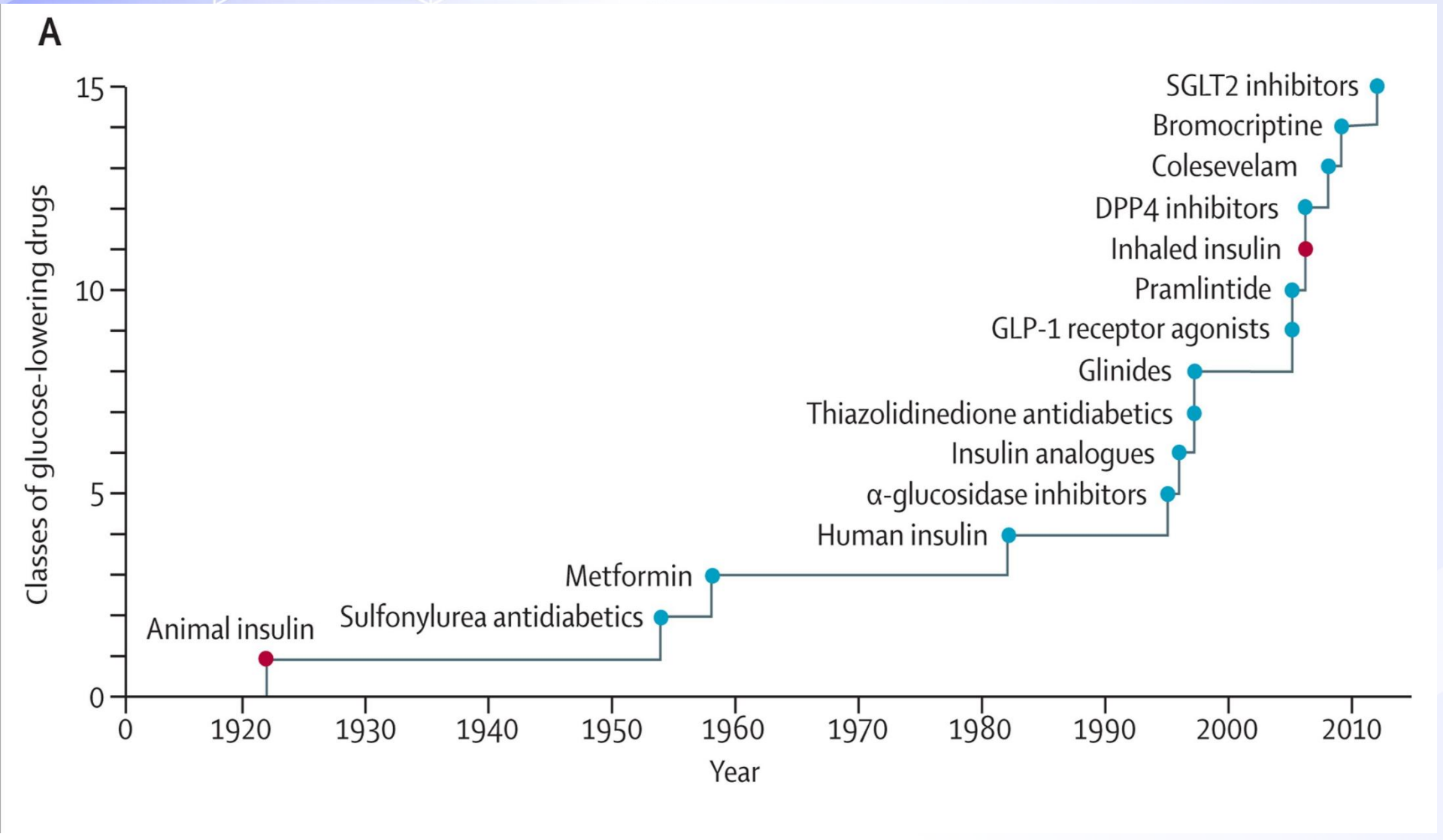
# Perorální antidabetika a KV riziko


## Špinar J.

### Interní kardiologická klinika

# Vývoj léků snižující glukózu



## ADA/EASD doporučení: úvodní farmakologická léčba

- **Metformin (MET) zůstává optimálním lékem pro monoterapii** u většiny pacientů

- Dvojkombinační terapie je doporučena, **pokud je hodnota HbA1c ≥ 9 % (≥75 mmol/mol)** pro efektivnější dosažení cílových hodnot

- Pokud jsou hodnoty glykémie ≥ 16,7-19,4 mmol/l a/nebo je hodnota HbA1c ≥10–12 % (≥ 86-108 mmol/mol), je **preferovaným úvodním režimem bazální inzulín + prandiální inzulín**

Inzucchi SE et al *Diabetologia* 2015;10.1077/s00125-014-3460-0

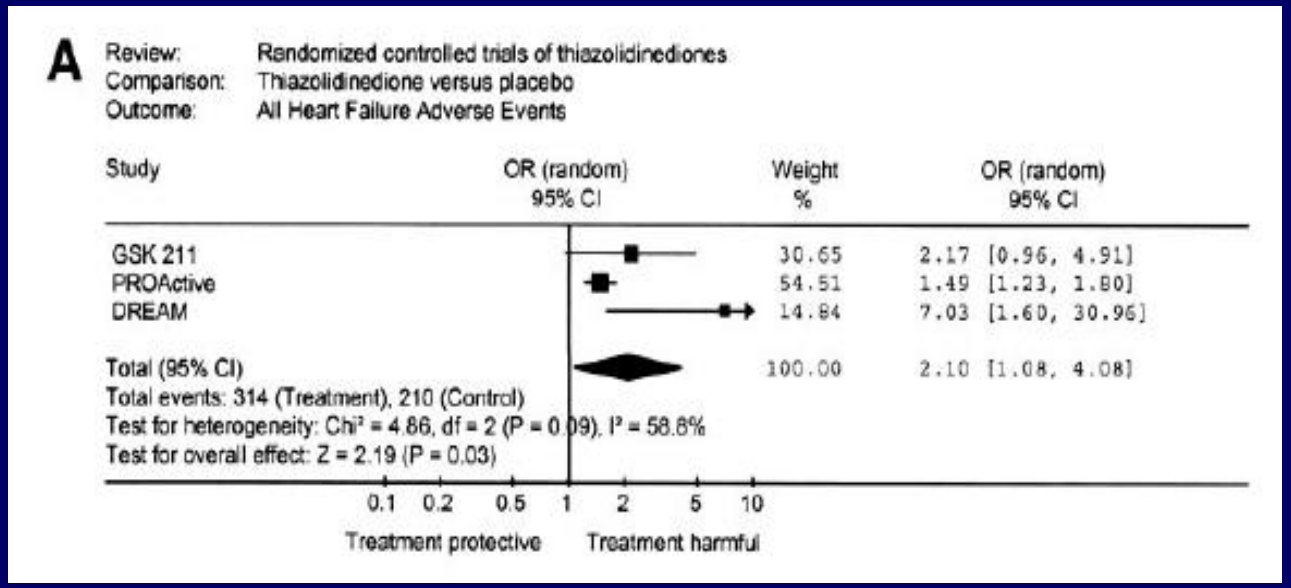
# Sulfonylurea

- Výhody : účinnost,
  bezpečnost (více jak 50. leté zkušenosti)
  cena
- Nevýhody : vzestup hmotnosti
  hypoglykemie
  časnější selhání (ADOPT)

Dnes není doporučována 1. generace SU

Z 2. generace doporučovány modernější preparáty
gliclazid (ADVANCE) a glimepirid
Registr PROSPERO – zvýšená mortalita prokázána pro glipizid.

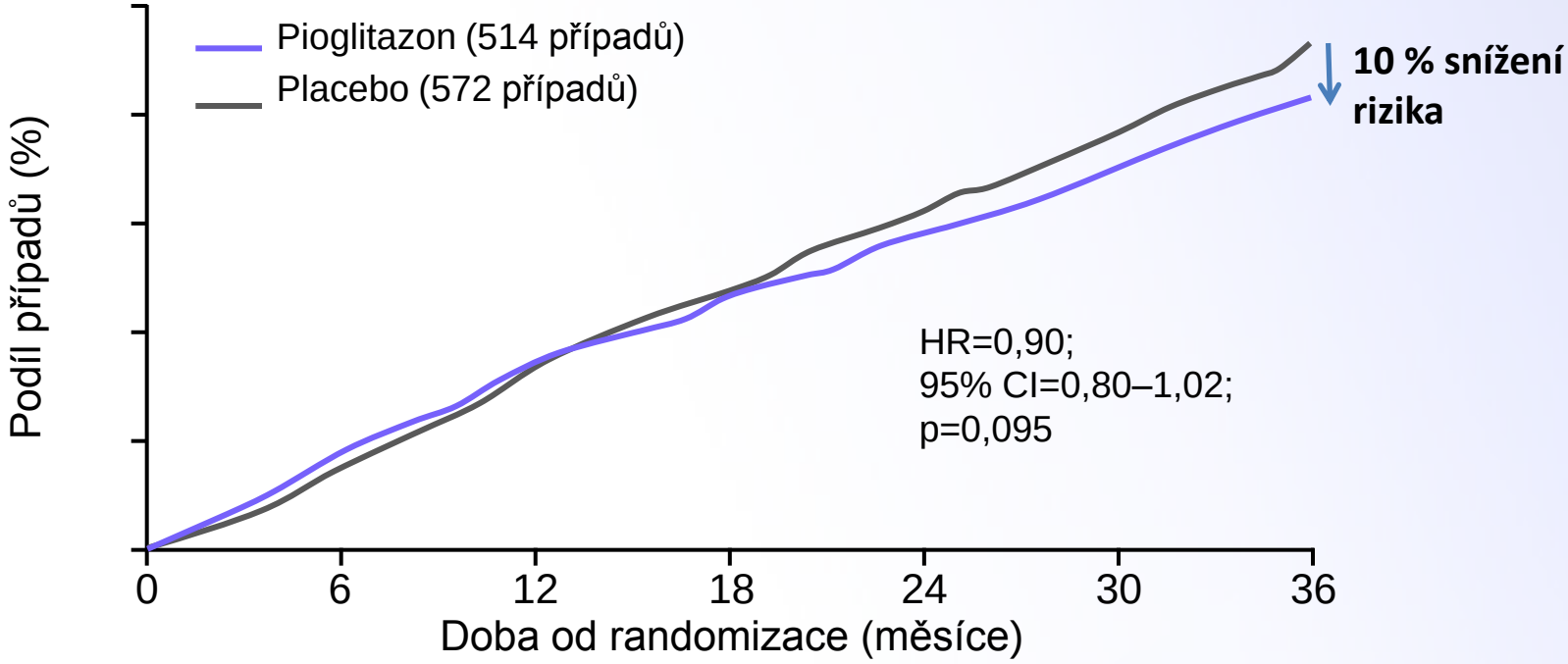
# Thiazolidindiony (glitazony)




**CONCLUSIONS — Analýza potvrdila zvýšené riziko srdečního selhání po TZD.** Autoři odhadují počet nemocných s novým výskytem ChSS po TZD více jak 50 během 2,2 let. **Existující doporučení by měla být revidována a toto riziko zavzít do charakteristiky TZD**

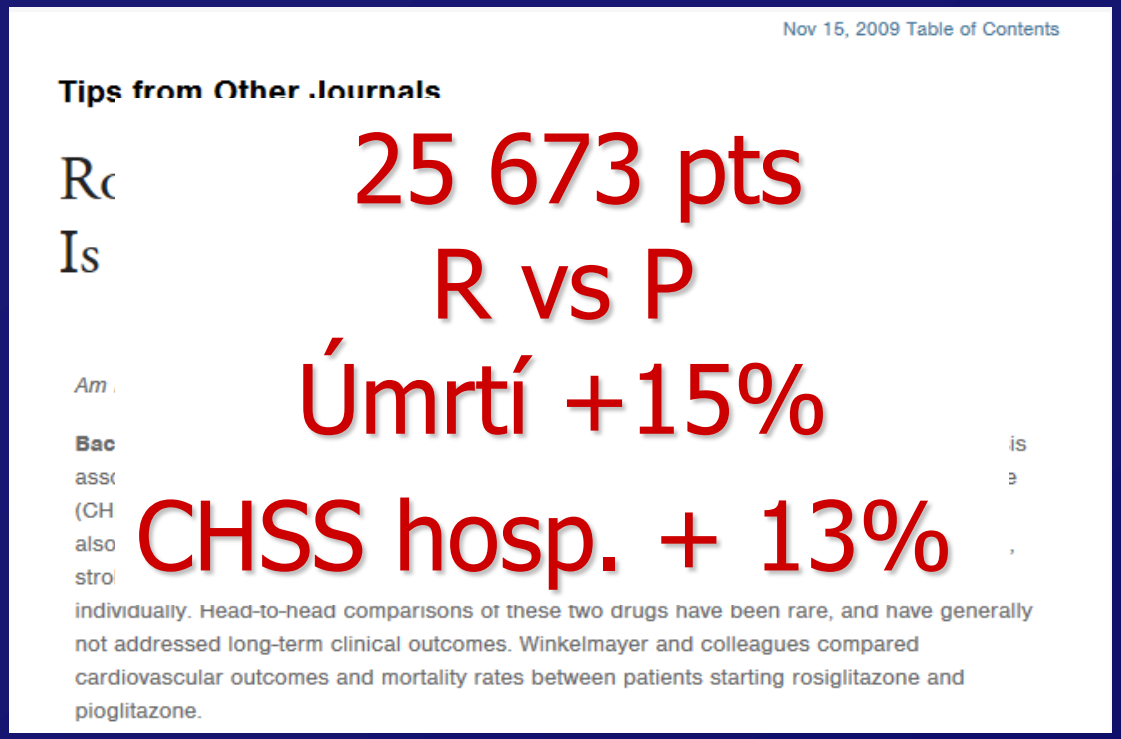
*Singh S. et al. Diabetes Care 2007;* **30:2148–2153**

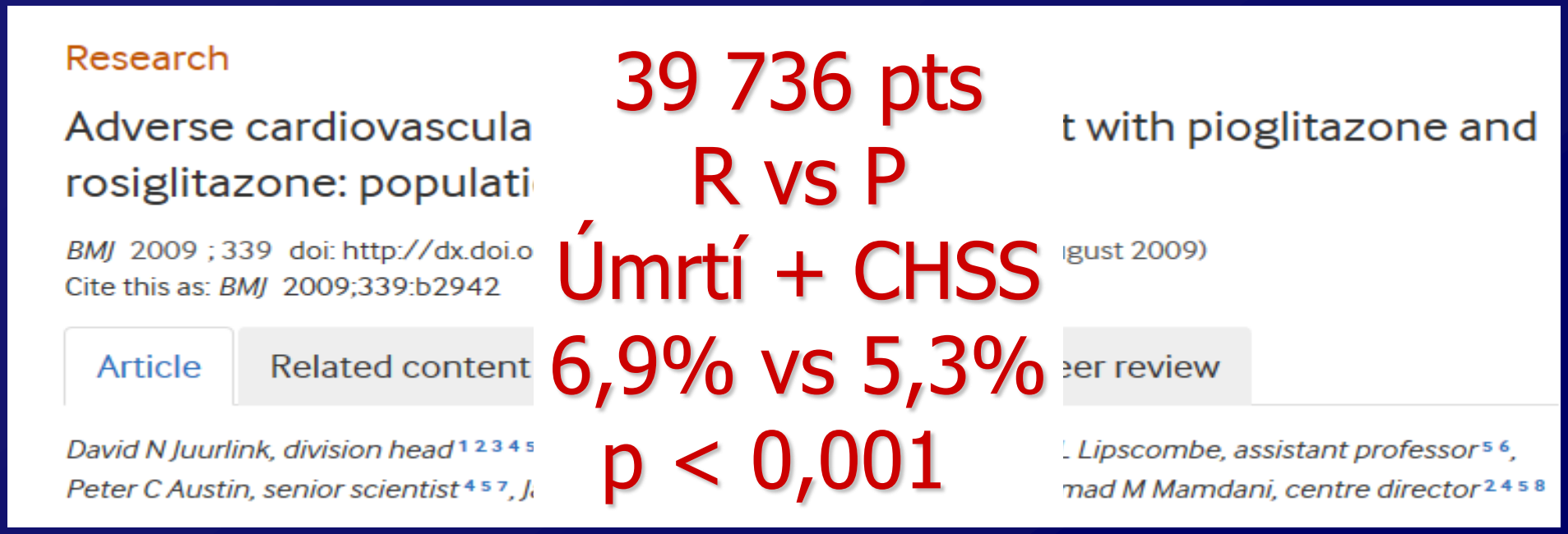
# Studie PROactive : primární složený cílový ukazatel



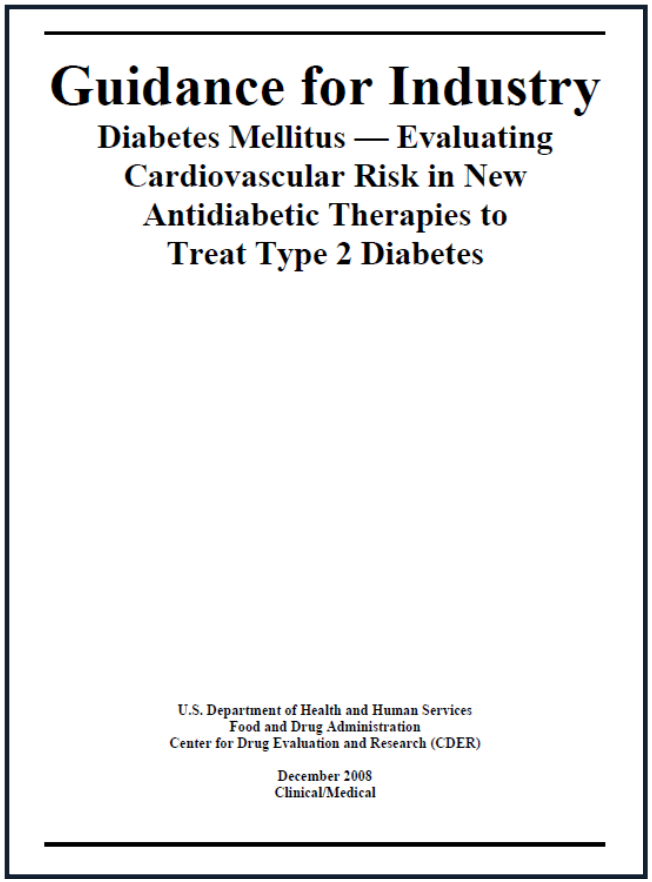

Doba do primárního cílového ukazatele (úmrtí z jakékoli příčiny, nefatální infarkt myokardu včetně klinicky němého infarktu myokardu, mrtvice, ACS, amputace nohy, koronární revaskularizace nebo revaskularizace nohy[1])

Dormandy et al. *Lancet.* 2005;366:1279–1289


Nov 15, 2009 Table of Contents
Tips from Other Journals
25 673 pts
R vs P
Úmrtí +15%
CHSS hosp. + 13%
individually. Head-to-head comparisons of these two drugs have been rare, and have generally not addressed long-term clinical outcomes. Winkelmayer and colleagues compared cardiovascular outcomes and mortality rates between patients starting rosiglitazone and pioglitazone.


Research
39 736 pts
R vs P
Úmrtí + CHSS
6,9% vs 5,3%
p < 0,001
Article
Related content

# FDA požadavky na kardiovaskulární cíle s novými perorálními antidiabetiky



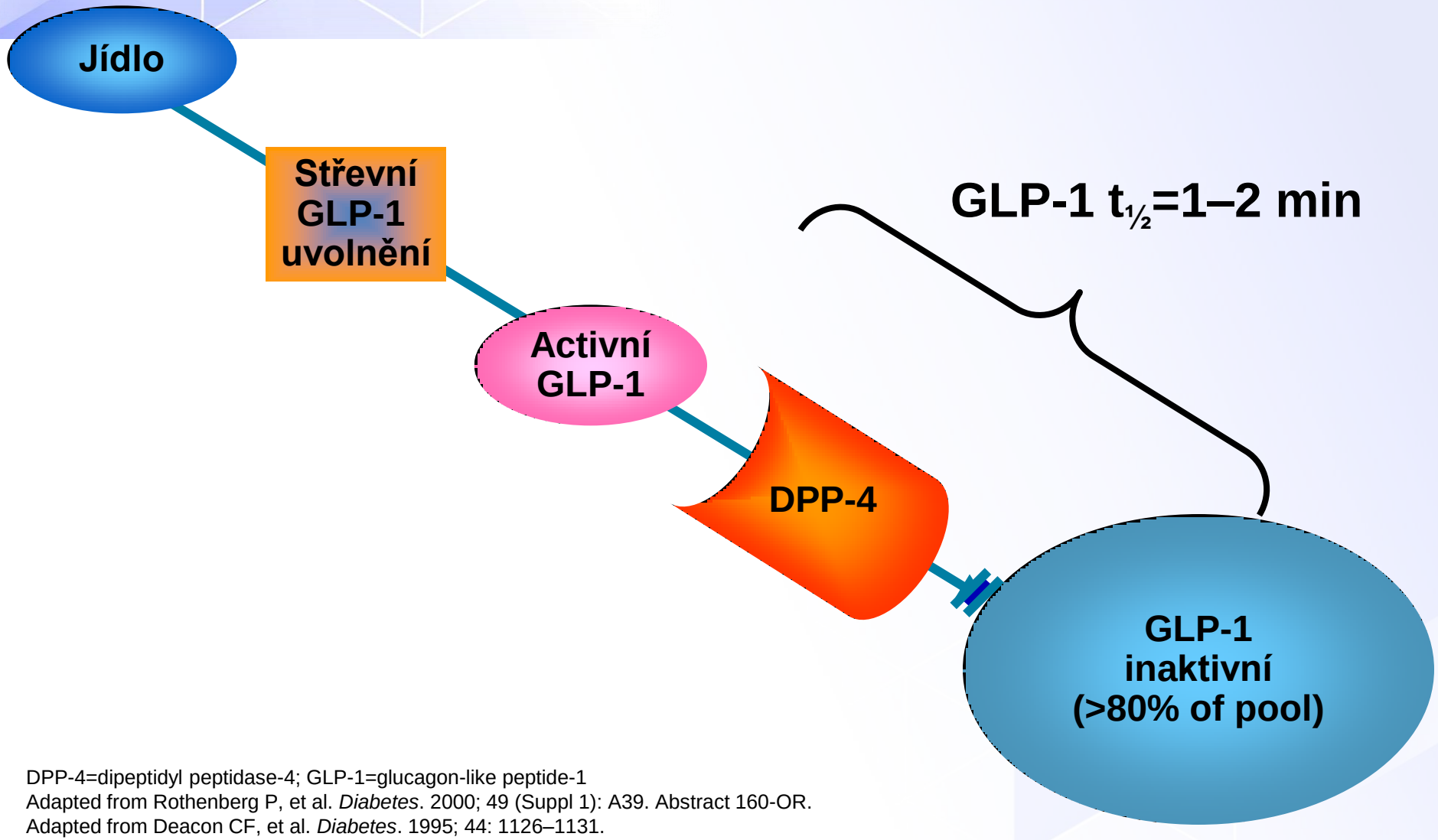

2008 FDA doporučení pro perorální antidiabetika zdůrazňují nutnost kardiovaskulární bezpečnosti (účinnosti) před samotným snížením glykémie.

FDA Guidance for Industry. Diabetes mellitus – evaluating cardiovascular risk in new antidiabetic therapies to treat type 2 diabetes. Available from: www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071627.pdf [Accessed Jan 2014]

# Studie s novým léky

- ***GLP-1 agonisté:*** *EXLIXA (lixisenatid); LEADER (liraglutid); EXSCEL (exenatid); REWIND (dulaglutid) a FREEDOM (ITCA650 exenatid SC pump)*
- ***DPP-4 inhibitory:*** *EXAMINE (alogliptin); SAVOR-TIMI 53 (saxagliptin); TECOS (sitagliptin) and CAROLINA (linagliptin)*
- ***SGLT2 inhibitory:*** *DECLARE-TIMI58 (dapaglifozin); CANVAS (canagliflozin); a EMPA-REG (empagliflozin)*

# Inhibice DPP-4 zvyšuje aktivitu GLP-1




DPP-4=dipeptidyl peptidase-4; GLP-1=glucagon-like peptide-1
Adapted from Rothenberg P, et al. *Diabetes*. 2000; 49 (Suppl 1): A39. Abstract 160-OR.
Adapted from Deacon CF, et al. *Diabetes*. 1995; 44: 1126–1131.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus

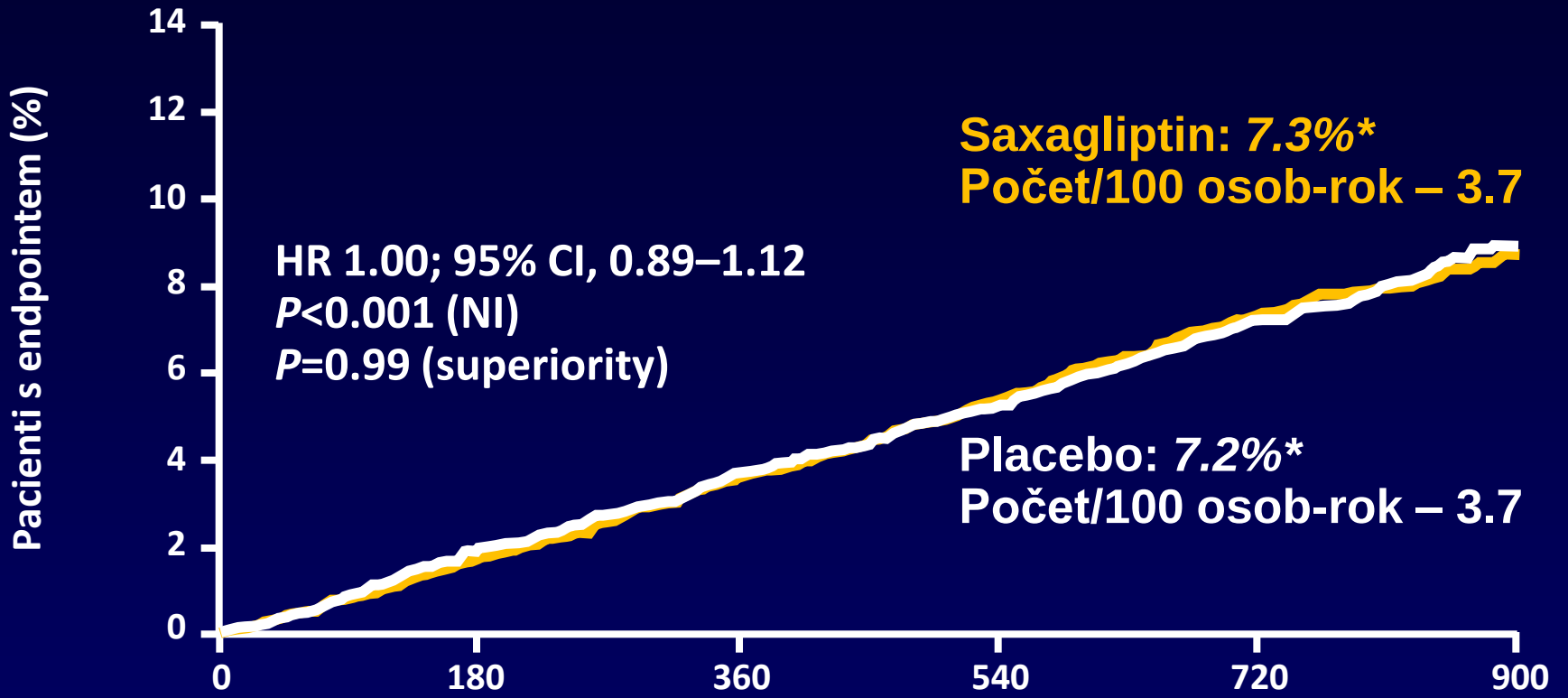
Benjamin M. Scirica, M.D., M.P.H., Deepak L. Bhatt, M.D., M.P.H., Eugene Braunwald, M.D., P. Gabriel Steg, M.D., Jaime Davidson, M.D., Boaz Hirshberg, M.D., Peter Ohman, M.D., Robert Frederich, M.D., Ph.D., Stephen D. Wiviott, M.D., Elaine B. Hoffman, Ph.D., Matthew A. Cavender, M.D., M.P.H., Jacob A. Udell, M.D., M.P.H., Nihar R. Desai, M.D., M.P.H., Ofri Mozenson, M.D., Darren K. McGuire, M.D., Kausik K. Ray, M.D., Lawrence A. Leiter, M.D., and Itamar Raz, M.D., for the SAVOR-TIMI 53 Steering Committee and Investigators*

## Zpráva ze sjezdu ESC 2013

## Studie SAVOR-TIMI 53 a EXAMINE byly prezentovány na ESC 2013 – nová data pro DPP-4 inhibitory

**prof. MUDr. Jindřich Špinar, CSc.**
*Interní kardiologická klinika LF MU a FN Brno*

# Primární cíl – KV úmrtí, nefatální IM, nefatální ischemická CMP




| | | | | | | |
|---|---|---|---|---|---|---|
| **Placebo** | 8212 | 7983 | 7761 | 7267 | 4855 | 851 |
| **Saxagliptin** | 8280 | 8071 | 7836 | 7313 | 4920 | 847 |

*K-M event rates are presented after 2 yrs.

HR: hazard ratio; K-M: Kaplan-Meier; Pbo: placebo; Saxa: saxagliptin

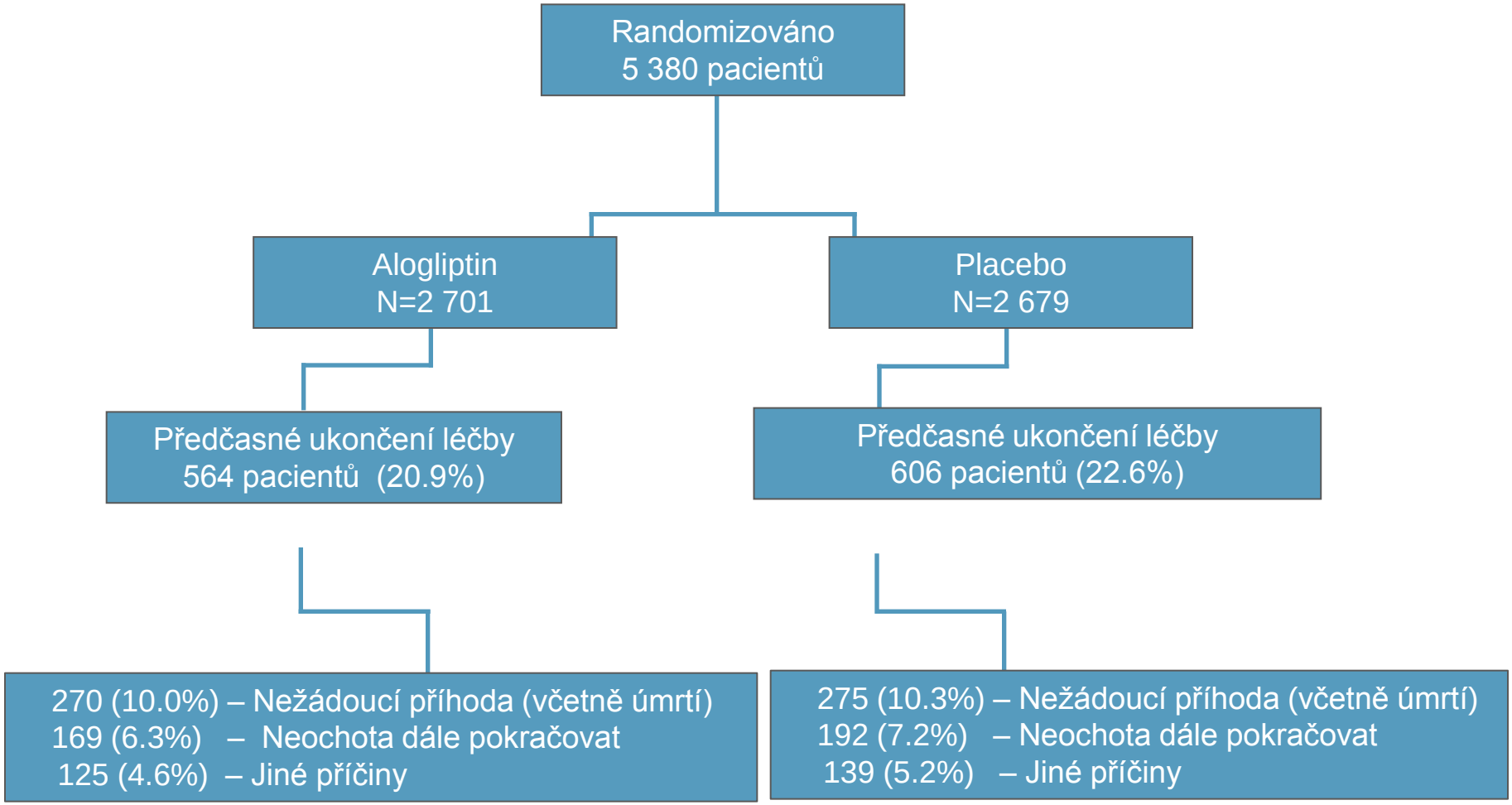
Scirica BM, et al. *N Engl J Med.* 2013.10.1056/NEJMoa1307684.

# Jednotlivé součásti sekundárního cíle

| Účinnost | Saxagliptin n (%)* (N = 8,280) | Placebo n (%)* (N = 8,212) | HR (95% CI) | *P* value |
|---|---|---|---|---|
| **KV úmrtí** | 269 (3.2) | 260 (2.9) | 1.03 (0.87–1.22) | 0.72 |
| **IM** | 265 (3.2) | 278 (3.4) | 0.95 (0.80–1.12) | 0.52 |
| **Ischemická CMP** | 157 (1.9) | 141 (1.7) | 1.11 (0.88–1.39) | 0.38 |
| **Hosp pro NAP** | 97 (1.2) | 81 (1.0) | 1.19 (0.89–1.60) | 0.24 |
| **Hosp pro SS** | 289 (3.5) | 228 (2.8) | 1.27 (1.07–1.51) | 0.007 |
| **Hosp pro koron. revasc.** | 423 (5.2) | 459 (5.6) | 0.91 (0.80–1.04) | 0.18 |

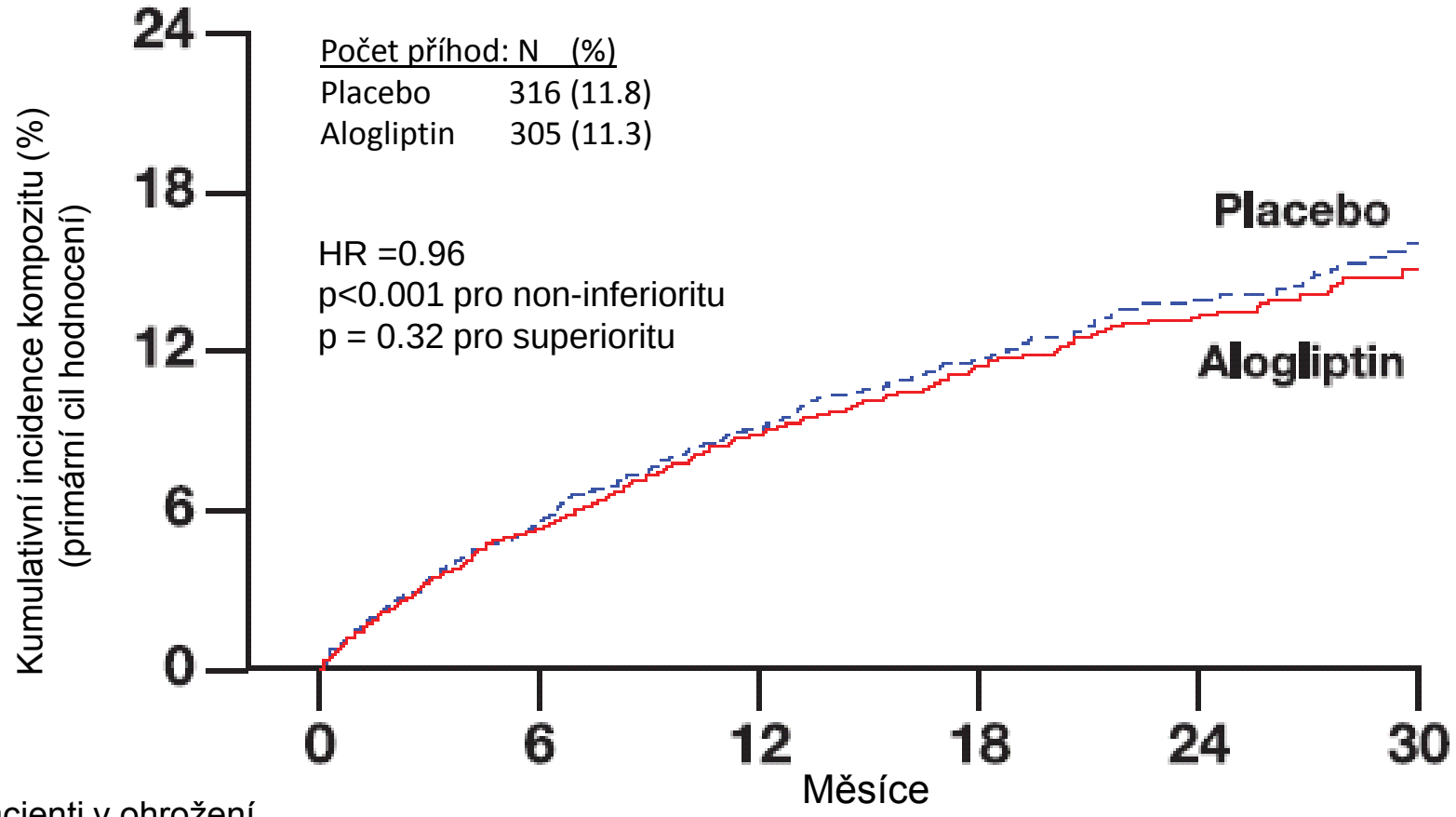
Scirica BM, et al. *N Engl J Med.* 2013.10.1056/NEJMoa1307684.

# EXAMINE: Uspořádání studie a rozdělení pacientů




White WB, et al. *N Engl J Med* 2013;369:1327–1335

# EXAMINE : Alogliptin + standardní léčba ve srovnání s placebem + standardní léčbou nezvyšuje výskyt MACE




| Pacienti v ohrožení | | | | | | |
|---|---|---|---|---|---|---|
| Placebo (n): | 2679 | 2299 | 1891 | 1375 | 805 | 286 |
| Alogliptin (n): | 2701 | 2316 | 1899 | 1394 | 821 | 296 |

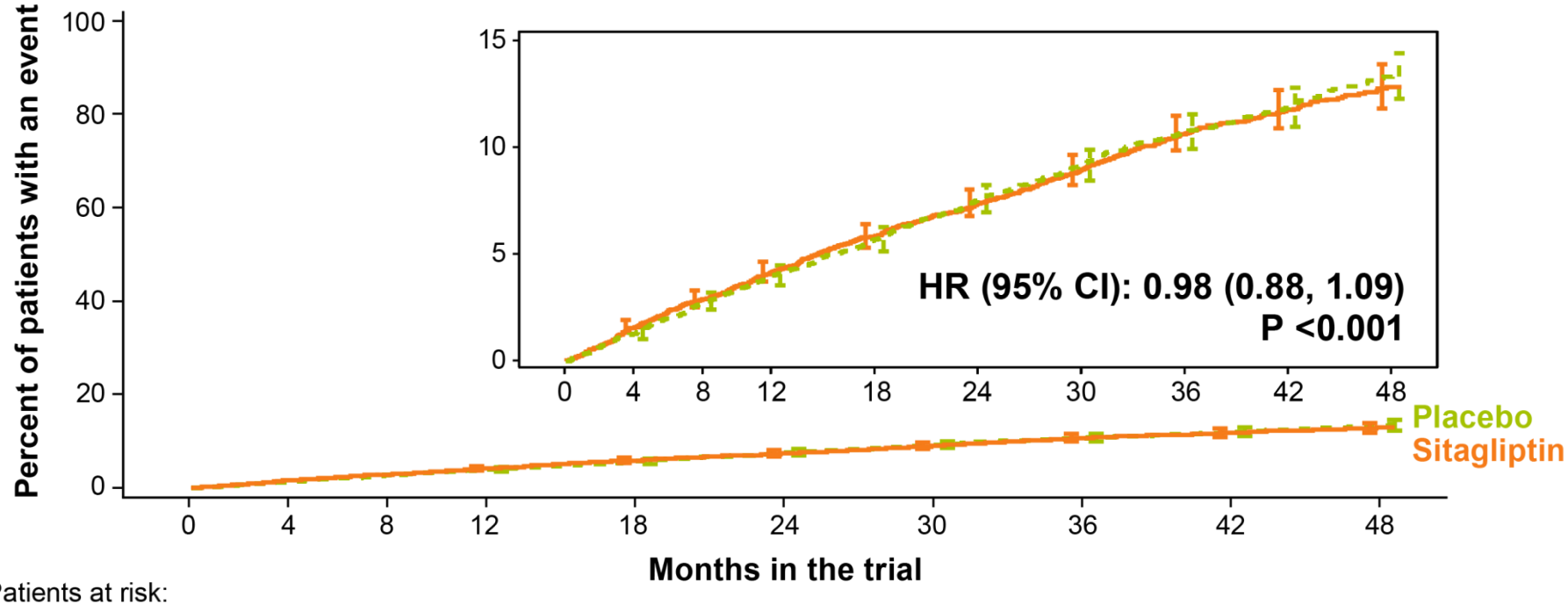
MACE: závažné kardiovaskulární příhody (CV úmrtí, nefatální infarkt myokardu, nefatální mozková mrtvice)

White WB, et al. *N Engl J Med* 2013;369:1327–1335

# Trial Evaluating Cardiovascular Outcomes With Sitagliptin (TECOS)

# Primární KV výsledky*

## PP Analýza pro non- inferioritu




Patients at risk:

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Sitagliptin | 7,257 | 6,857 | 6,519 | 6,275 | 5,931 | 5,616 | 3,919 | 2,896 | 1,748 | 1,028 |
| Placebo | 7,266 | 6,846 | 6,449 | 6,165 | 5,803 | 5,421 | 3,780 | 2,743 | 1,690 | 1,005 |

** KV úmrtí, nefatální IM, nefatální CMP, hospitalizace pro NAP*

*Green JB et al. NEJM 2015; DOI: 10.1056/NEJMoa1501352*

# Antidiabetic drugs and heart failure outcomes

## Dipeptidyl peptidase-4 inhibitors

| Medication | Placebo controlled RCT | No of patients | Patients with HF | Median follow-up (years) | HF outcome |
|---|---|---|---|---|---|
| **Saxagliptin** | **SAVOR-TIMI 53** | 8280 | 13% | 2.1 | Hospitalization for HF* **1.27 (1.07–1.51)** |
| Alogliptin | **EXAMINE** | 2701 | 28% | 1.5 | Hospitalization for HF* 1.07 (0.79–1.46) |
| Sitagliptin | **TECOS** | 7257 | 18% | 3.0 | Hospitalization for HF* 1.00 (0.83–1.20) |
| Vildagliptin | **VIVIDD** | 254 | All patients NYHA class I-III HF and EF <40% | 1.0 | No effect on LVEF but demonstrated an increase in LV volumes |

# ELIXA

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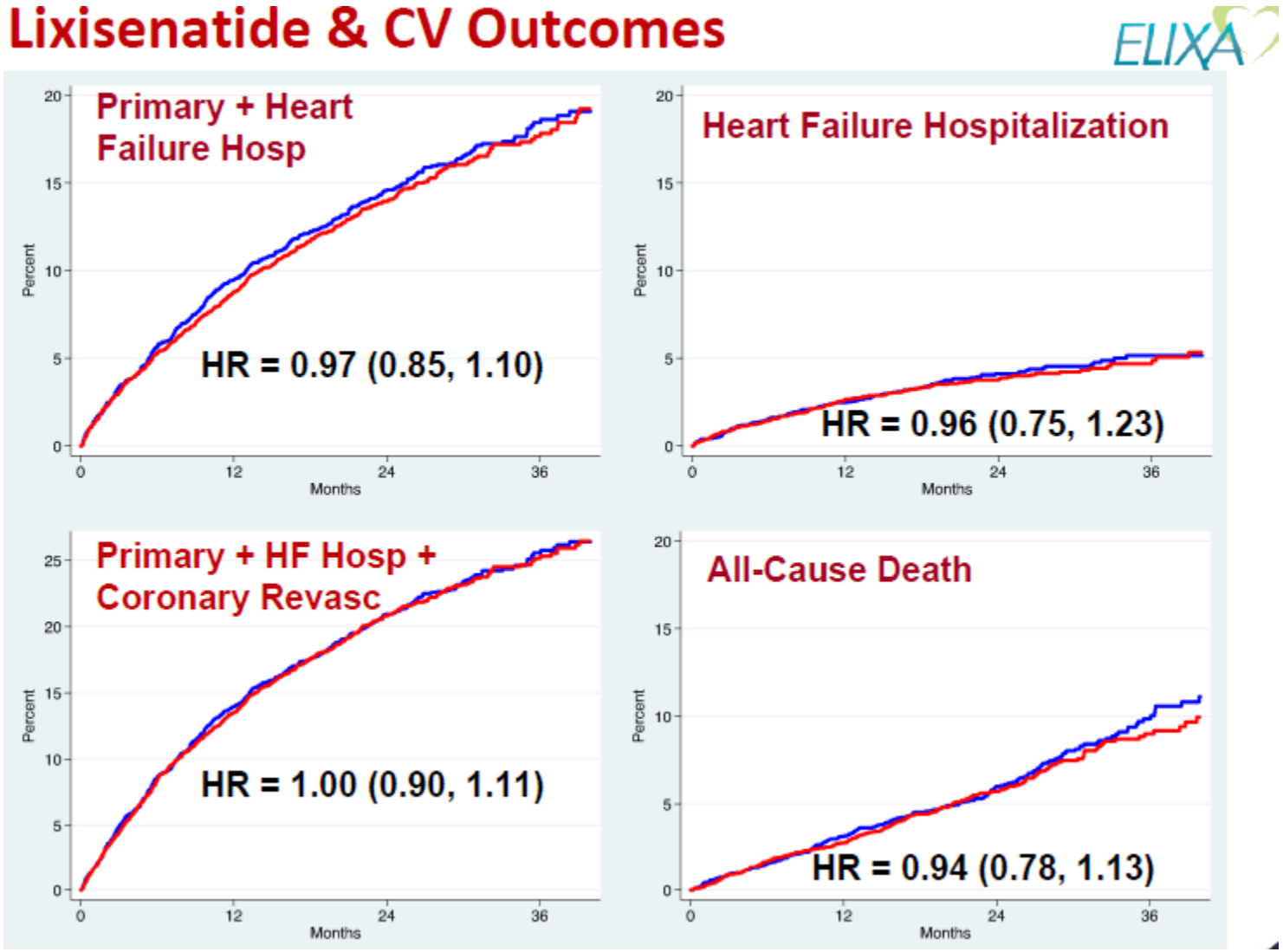
## ELIXA Trial Shows CV Safety of Lixisenatide

**STUDY NAME: The ELIXA Trial - SESSION NAME: Hot Line III - Diabetes Mellitus/Pharmacology**

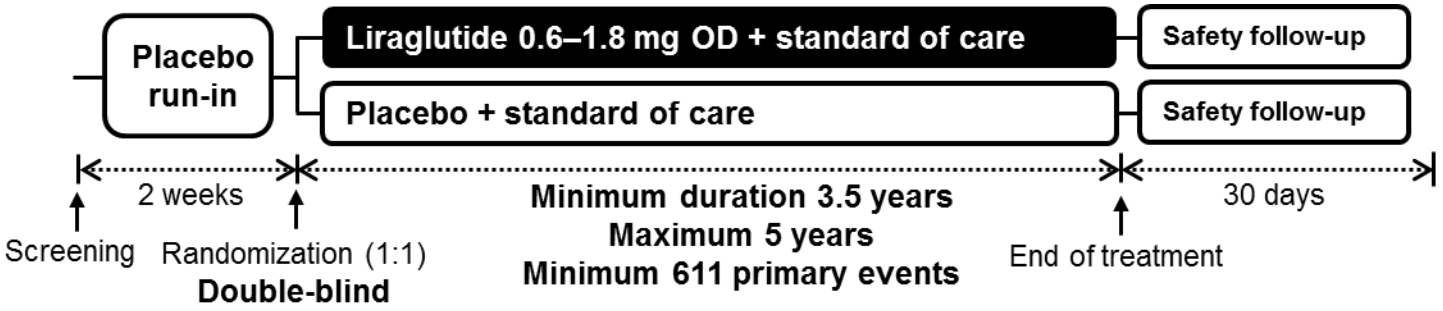
31 Aug 2015

In patients with type 2 diabetes and acute coronary syndrome, the glucose-lowering medication lixisenatide did not increase or decrease the rate of cardiovascular (CV) events compared to

# Lixisenatide + standardní léčba ve srovnání s placebem + standardní léčbou nezvyšuje výskyt MACE



# LEADER: Study design




**Key inclusion criteria**

- T2DM, $HbA_{1c}$ ≥7.0%
- Antidiabetic drug naïve; OADs and/or basal/premix insulin
- Age ≥50 years and established CV disease or chronic renal failure
  **or**
- Age ≥60 years and risk factors for CV disease

**Key exclusion criteria**

- T1DM
- Use of GLP-1RAs, DPP-4i, pramlintide, or rapid-acting insulin
- Familial or personal history of MEN-2 or MTC

CV: cardiovascular; DPP-4i, dipeptidyl peptidase-4 inhibitor; GLP-1RA: glucagon-like peptide-1 receptor agonist; $HbA_{1c}$: glycated hemoglobin; MEN-2: multiple endocrine neoplasia type 2; MTC: medullary thyroid cancer; OAD: oral antidiabetic drug; OD: once daily; T2DM: type 2 diabetes mellitus.

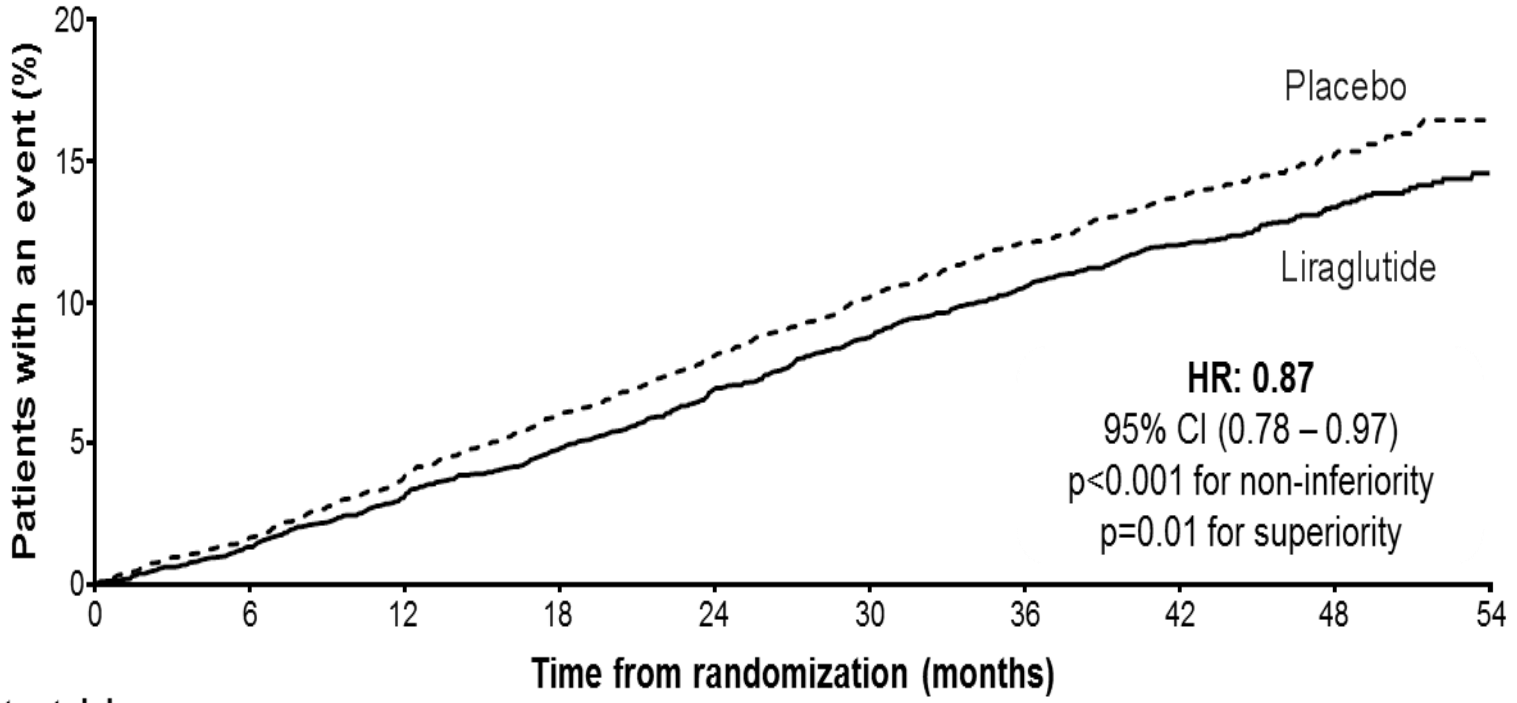
Presented at the American Diabetes Association 76th Scientific Sessions, Session 3-CT-SY24. June 13 2016, New Orleans, LA, USA.

LEADER®
Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results

# LEADER

## Primary outcome

### CV death, non-fatal myocardial infarction, or non-fatal stroke




**Patients at risk**

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Liraglutide | 4668 | 4593 | 4496 | 4400 | 4280 | 4172 | 4072 | 3982 | 1562 | 424 |
| Placebo | 4672 | 4588 | 4473 | 4352 | 4237 | 4123 | 4010 | 3914 | 1543 | 407 |

*–The primary composite outcome in the time-to-event analysis was the first occurrence of death from cardiovascular causes, non-fatal –myocardial infarction, or non-fatal stroke. The cumulative incidences were estimated with the use of the Kaplan–Meier method, and the –hazard ratios with the use of the Cox proportional-hazard regression model. The data analyses are truncated at 54 months, because less –than 10% of the patients had an observation time beyond 54 months. CI: confidence interval; CV: cardiovascular; HR: hazard ratio.*

*–Presented at the American Diabetes Association 76th Scientific Sessions, Session 3-CT-SY24. June 13 2016, New Orleans, LA, USA.*

# Albiglutide and cardiovascular outcomes in patients with type 2 diabetes and cardiovascular disease (Harmony Outcomes): a double-blind, randomised placebo-controlled trial

*Adrian F Hernandez, Jennifer B Green, Salim Janmohamed, Ralph B D'Agostino Sr, Christopher B Granger, Nigel P Jones, Lawrence A Leiter, Anne E Rosenberg, Kristina N Sigmon, Matthew C Somerville, Karl M Thorpe, John J V McMurray, Stefano Del Prato, for the Harmony Outcomes committees and investigators**

*Lancet* 2018; 392: 1519–29
Published Online
October 2, 2018

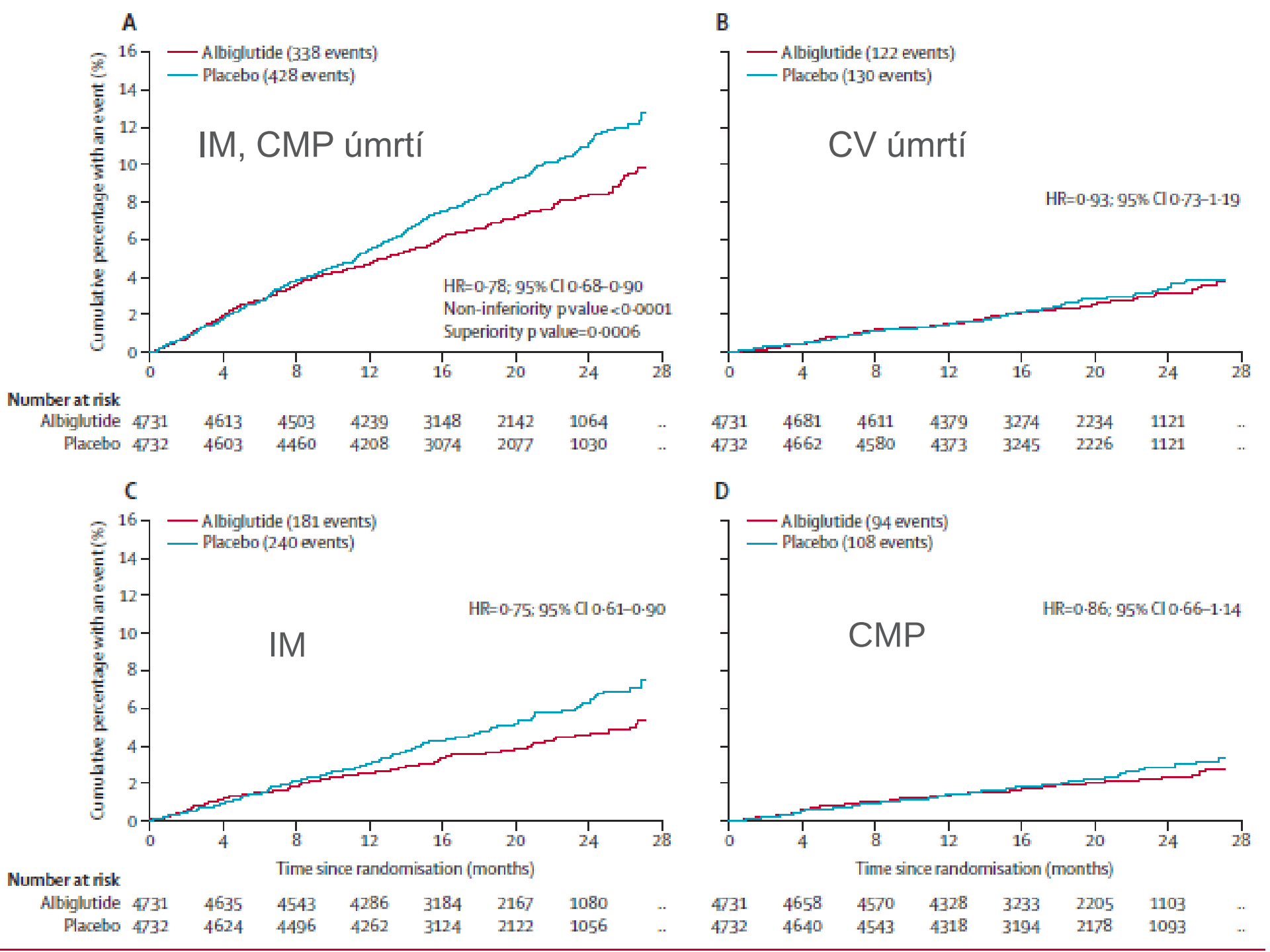
## Summary

**Background** Glucagon-like peptide 1 receptor agonists differ in chemical structure, duration of action, and in their effects on clinical outcomes. The cardiovascular effects of once-weekly albiglutide in type 2 diabetes are unknown. We aimed to determine the safety and efficacy of albiglutide in preventing cardiovascular death, myocardial infarction, or stroke.

***9 463 nemocných***

***Albiglutid*** ***Placebo***

***Průměr sledování 1,6 let***


A
Albiglutide (338 events)
Placebo (428 events)
IM, CMP úmrtí
HR=0·78; 95% CI 0·68–0·90
Non-inferiority p value <0·0001
Superiority p value=0·0006
Cumulative percentage with an event (%)
B
Albiglutide (122 events)
Placebo (130 events)
CV úmrtí
HR=0·93; 95% CI 0·73–1·19
C
Albiglutide (181 events)
Placebo (240 events)
IM
HR=0·75; 95% CI 0·61–0·90
D
Albiglutide (94 events)
Placebo (108 events)
CMP
HR=0·86; 95% CI 0·66–1·14
Time since randomisation (months)
Number at risk
Albiglutide 4731 4613 4503 4239 3148 2142 1064 .. 4731 4681 4611 4379 3274 2234 1121 ..
Placebo 4732 4603 4460 4208 3074 2077 1030 .. 4732 4662 4580 4373 3245 2226 1121 ..
Albiglutide 4731 4635 4543 4286 3184 2167 1080 .. 4731 4658 4570 4328 3233 2205 1103 ..
Placebo 4732 4624 4496 4262 3124 2122 1056 .. 4732 4640 4543 4318 3194 2178 1093 ..

# T2DM treatment and HF outcomes

## Glucagon-like peptide-1 receptor agonists

**Results of RTCs with GLP-1 receptor agonists suggest a neutral effect on the risk of HF hospitalization**

| Medication | Placebo controlled RCT | No of patients | Patients with HF | Median follow-up | HF outcome |
|---|---|---|---|---|---|
| Lixisenatide | ELIXA[1] | 6068 | 22% | 2.1 years | Hospitalization for HF* 0.96 (0.75-1.23) |
| Liraglutide | LEADER[2] | 9340 | 18% | 3.8 years | Hospitalization for HF* 0.97 (0.73 – 1.05) |
| Semaglutide | SUSTAIN-6[3] | 3297 | 24% | 2.1 years | Hospitalization for HF* 1.11 (0.77 – 1.61) |
| Exenatide | EXSCEL[4] | 14 752 | 16% (mostly HFpEF or HFmrEF) | 3.2 years | Hospitalization for HF* 0.94 (0.78 – 1.13) |

*Data presented as HR with 95% confidence interval

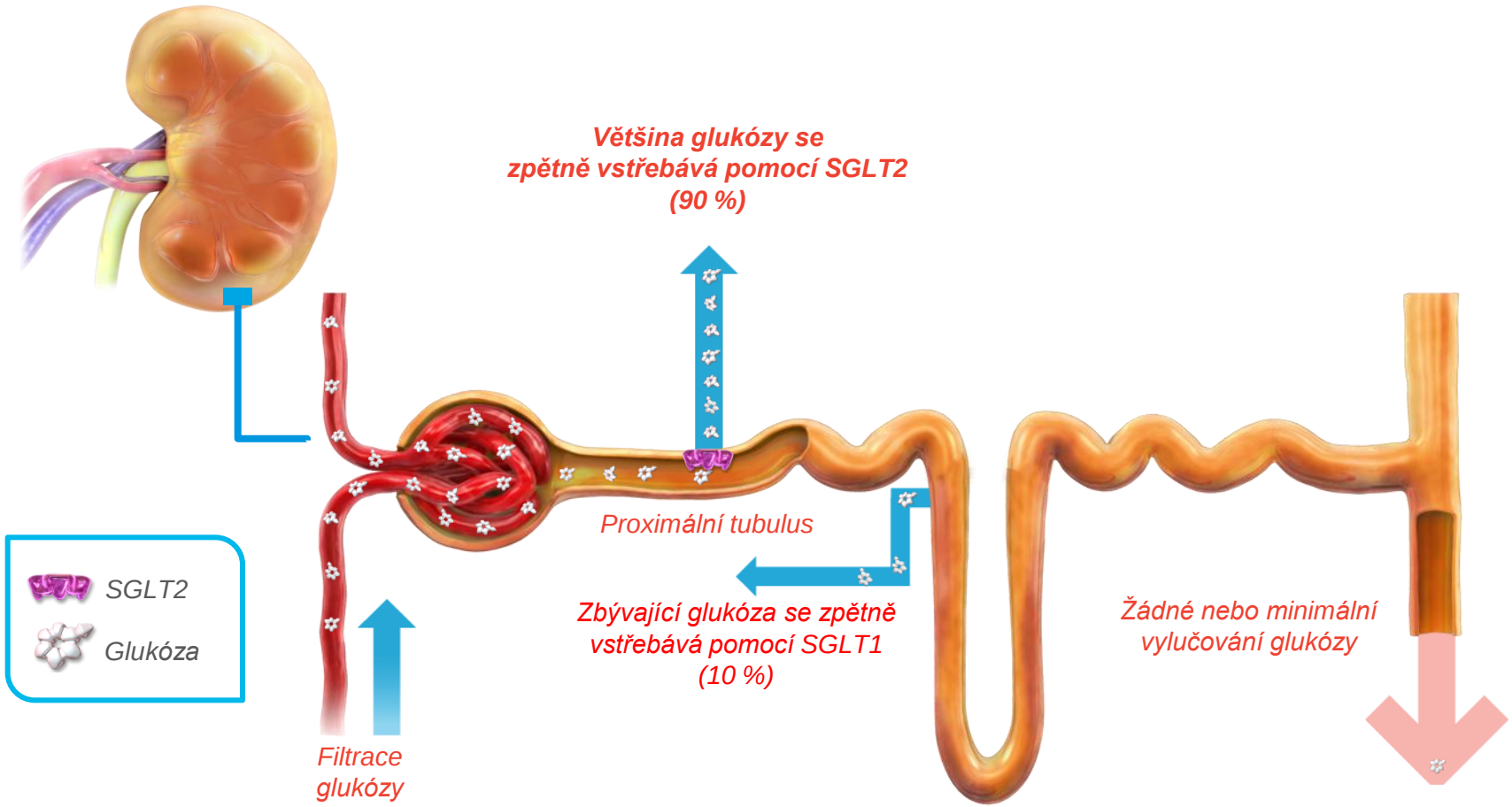
# *GLP1 novinky*

***Dulaglutid (Trulicity) – aplikace 1x týdně***
***Program AWARD***

***Fixní kombinace***
***analoga GLP1 + dlouhodobě působící inzulin***
***v předplněném peru***

***Xulotophy : Inzulin degludek + liraglutid***
***Suliqua : inzulin glargin + lixisenatid***
***1 denně***

# Normální transport glukózy v ledvinách[1–3]




SGLT, sodíko-glukózový kotransportér.


1. Wright EM. *Am J Physiol Renal Physiol* 2001;**280**:F10–18; 2. Lee YJ, *et al. Kidney Int Suppl* 2007;**106**:S27–35;
2. Hummel CS, *et al. Am J Physiol Cell Physiol* 2011;**300**:C14–21.

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ORIGINAL ARTICLE

## 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

September 17, 2015 | DOI: 10.1056/NEJMoa1504720

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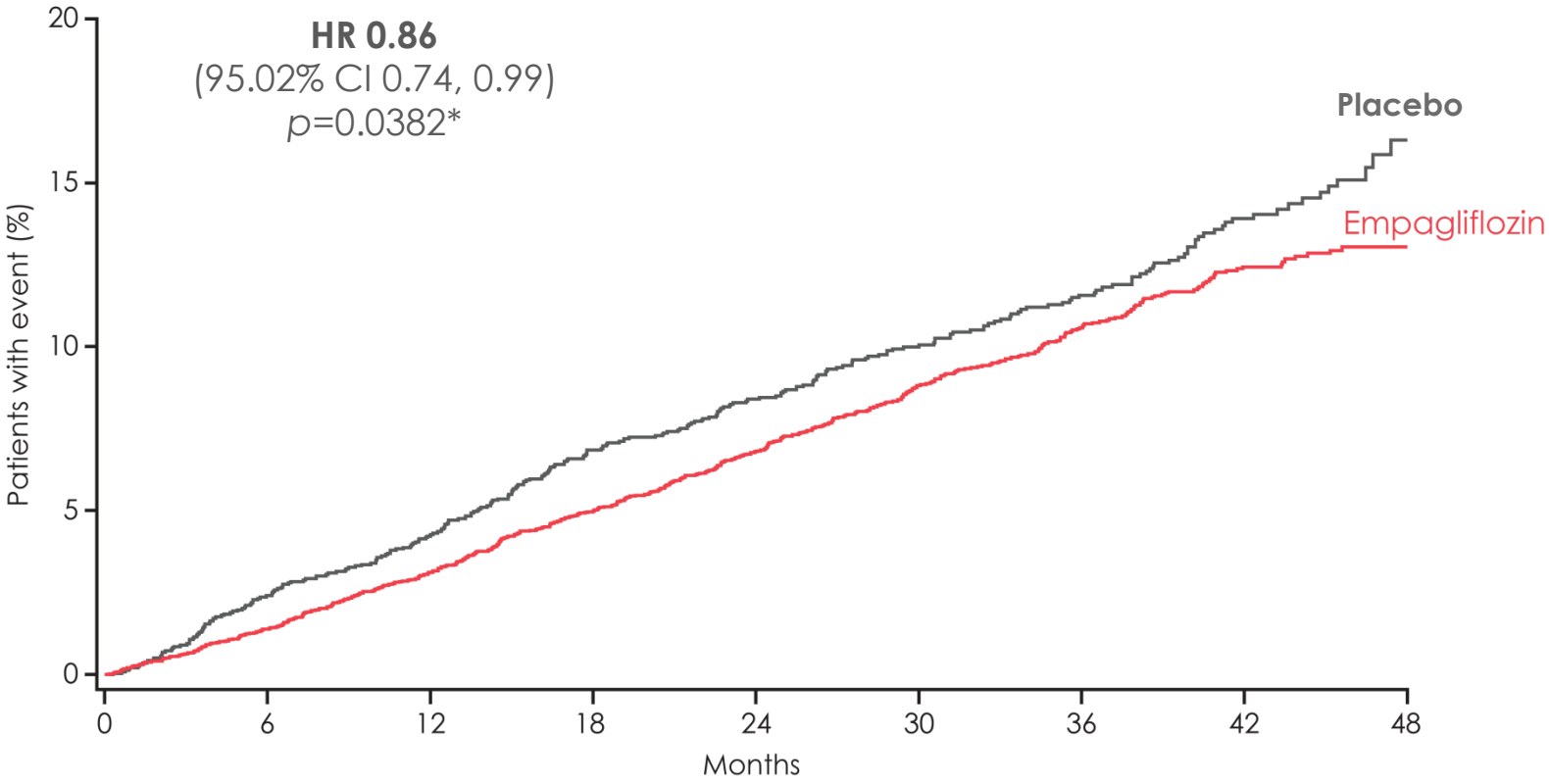
# Primární cíl: 3P-MACE
# **empagliflozin snížil riziko o 14%**




| No. of patients | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Empagliflozin | 4687 | 4580 | 4455 | 4328 | 3851 | 2821 | 2359 | 1534 | 370 |
| Placebo | 2333 | 2256 | 2194 | 2112 | 1875 | 1380 | 1161 | 741 | 166 |

–***Cumulative incidence function. MACE, Major Adverse Cardiovascular Event; HR, hazard ratio.***
**** Two-sided tests for superiority were conducted (statistical significance was indicated if p≤0.0498)***

Zinman B et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes.N Engl J Med. 2015 Sep 17. [Epub ahead of print]

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# CANVAS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# 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*

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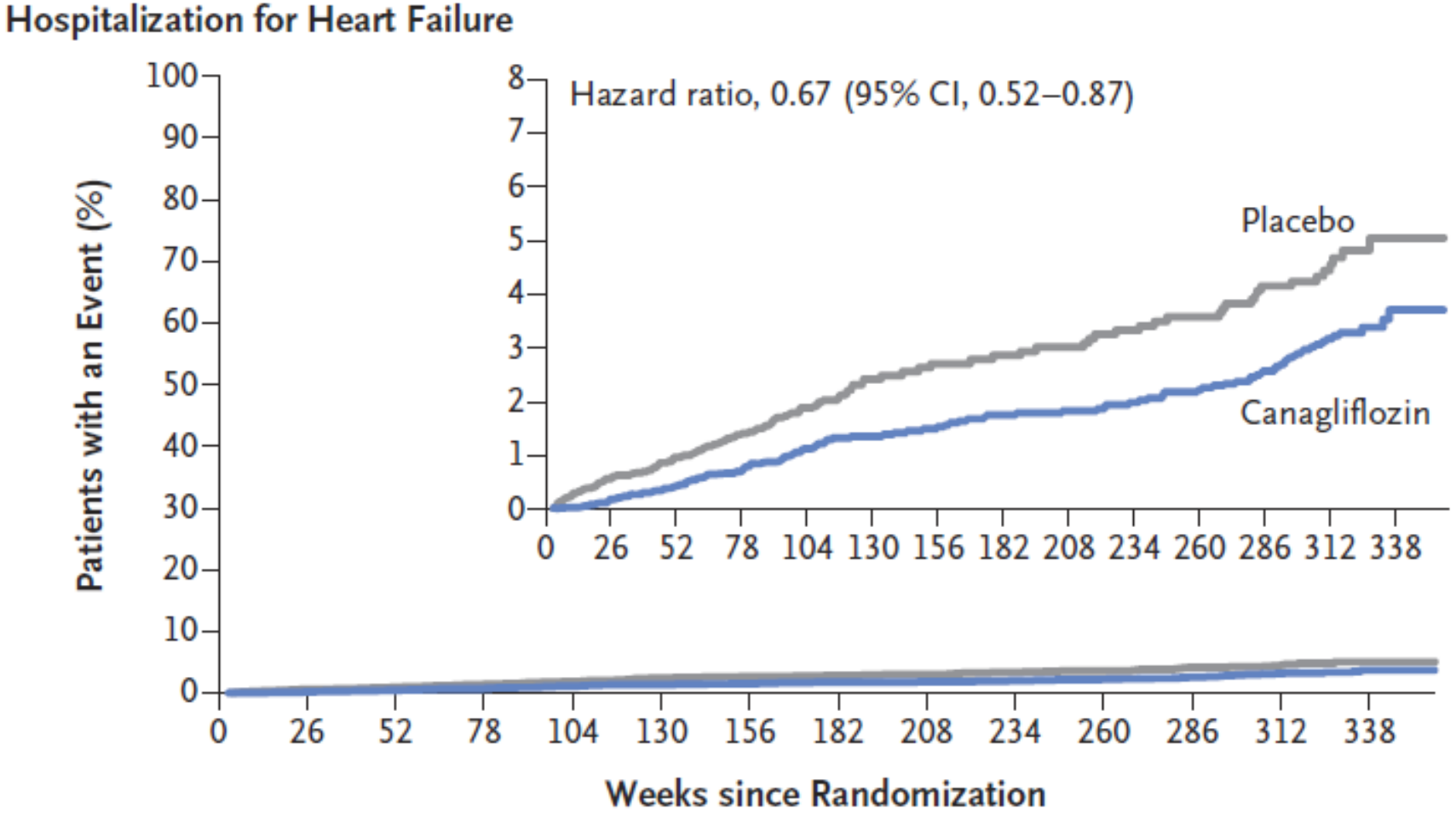
# CANVAS

## hospitalizace pro srdeční selhání




EMPA-REG OUTCOME®

# CANVAS

## Canagliflozin and the Risk of Leg and Foot Amputations

Jun 4, 2016

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*FDA issues alert about interim safety results from ongoing clinical trial, but study of potential canagliflozin amputation risk is ongoing.*

The FDA has not determined whether canagliflozin increases the risk of leg and foot amputations. They are currently investigating this new safety issue and will update the public when they have more information.

7 z 1000 pts/rok na 100mg canagliflozinu
5 z 1000 pts/rok na 300mg canagliflozinu
3 z 1000 pts/rok na placebu

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# CREDENCE

ORIGINAL ARTICLE FREE PREVIEW

## Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

Vlado Perkovic, M.B., B.S., Ph.D., Meg J. Jardine, M.B., B.S., Ph.D., Bruce Neal, M.B., Ch.B., Ph.D., Severine Bompoint, B.Sc., Hiddo J.L. Heerspink, Pharm.D., Ph.D., David M. Charytan, M.D., Robert Edwards, M.P.H., Rajiv Agarwal, M.D., George Bakris, M.D., Scott Bull, Pharm.D., Christopher P. Cannon, M.D., George Capuano, Ph.D., et al., for the CREDENCE Trial Investigators*

**SGLT2 inhibition lowers risk of kidney failure in patients with T2DM and kidney disease**


## Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

LITERATURE - PERKOVIC V, JARDINE MG, NEAL B ET AL., - NEW ENGL J MED. 2019. APRIL 14, DOI: 10.1056/NEJMOA1811744

Presented during *ISN-WCN 2019* in Melbourne, Australia on April 15, 2019.

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# CREDENCE

## Main results

- The primary composite outcome was seen significantly less f… than in the placebo group (43.2 vs 61.2 per 10… P=0.00001).
- The e… 0.66, 95%CI: 0.54-0.86, P=0… …ling of serum creatinine (HR: 0.60, 95%…
- Th… dialysis, kidney transplantation or renal death was also reduced (HR: 0… …54-0.97).

NEFROPROTEKCE

Rates of adverse events and serious adverse events were similar between groups. No significant difference was seen in the risk of lower-limb amputation (12.3 vs. 11.2 per 1000 PY with canagliflozin vs. placebo, HR: 1.1, 95%CI: 0.79-1.56) and fractures (HR: 0.98, 95%CI: 0.70-1.37).

???

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes

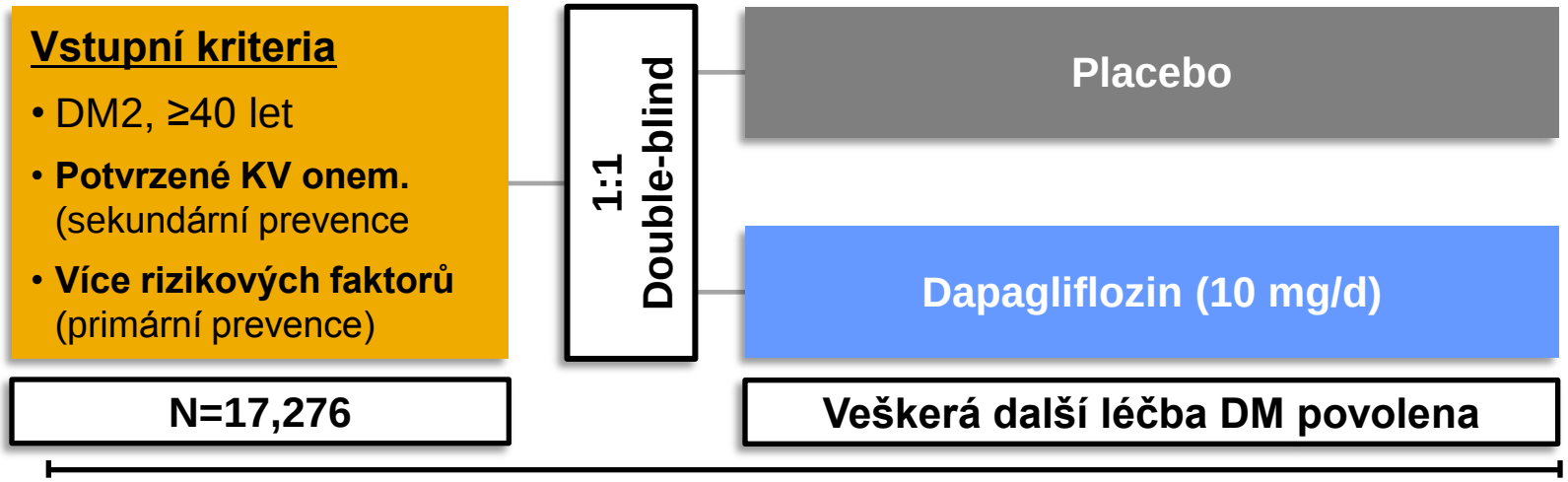
S.D. Wiviott, I. Raz, M.P. Bonaca, O. Mosenzon, E.T. Kato, A. Cahn, M.G. Silverman, T.A. Zelniker, J.F. Kuder, S.A. Murphy, D.L. Bhatt, L.A. Leiter, D.K. McGuire, J.P.H. Wilding, C.T. Ruff, I.A.M. Gause-Nilsson, M. Fredriksson, P.A. Johansson, A.-M. Langkilde, and M.S. Sabatine, for the DECLARE–TIMI 58 Investigators*

## ABSTRACT

**BACKGROUND**

The cardiovascular safety profile of dapagliflozin, a selective inhibitor of sodium–glucose cotransporter 2 that promotes glucosuria in patients with type 2 diabetes, is undefined.

# DECLARE
## (Dapagliflozin Effects on CardiovascuLAR Events)

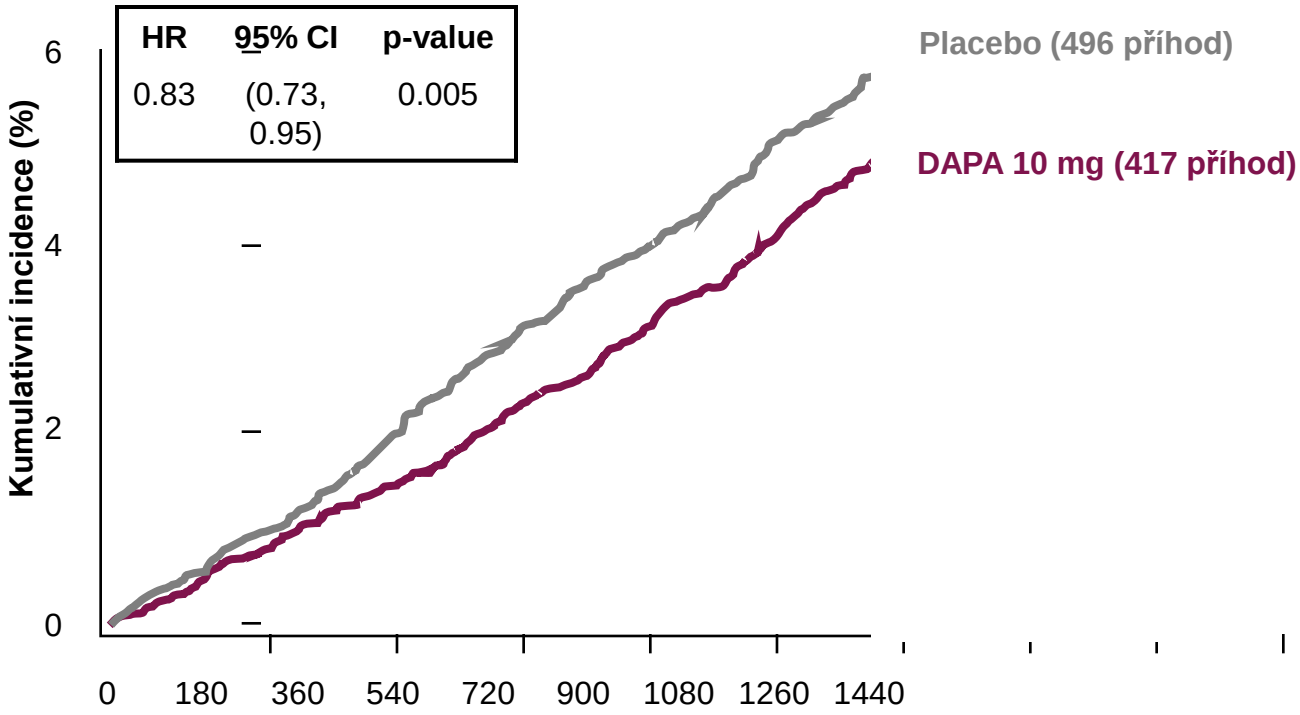



**Doba trvání:** 1,390 příhods
**Cíl: superiorita**

**Primární cíl**

•Kombinovaný: KV úmrtí, IM, Ischemická CMP

# Primární cíl: hospitalizace pro srdeční selhání a KV úmrtí

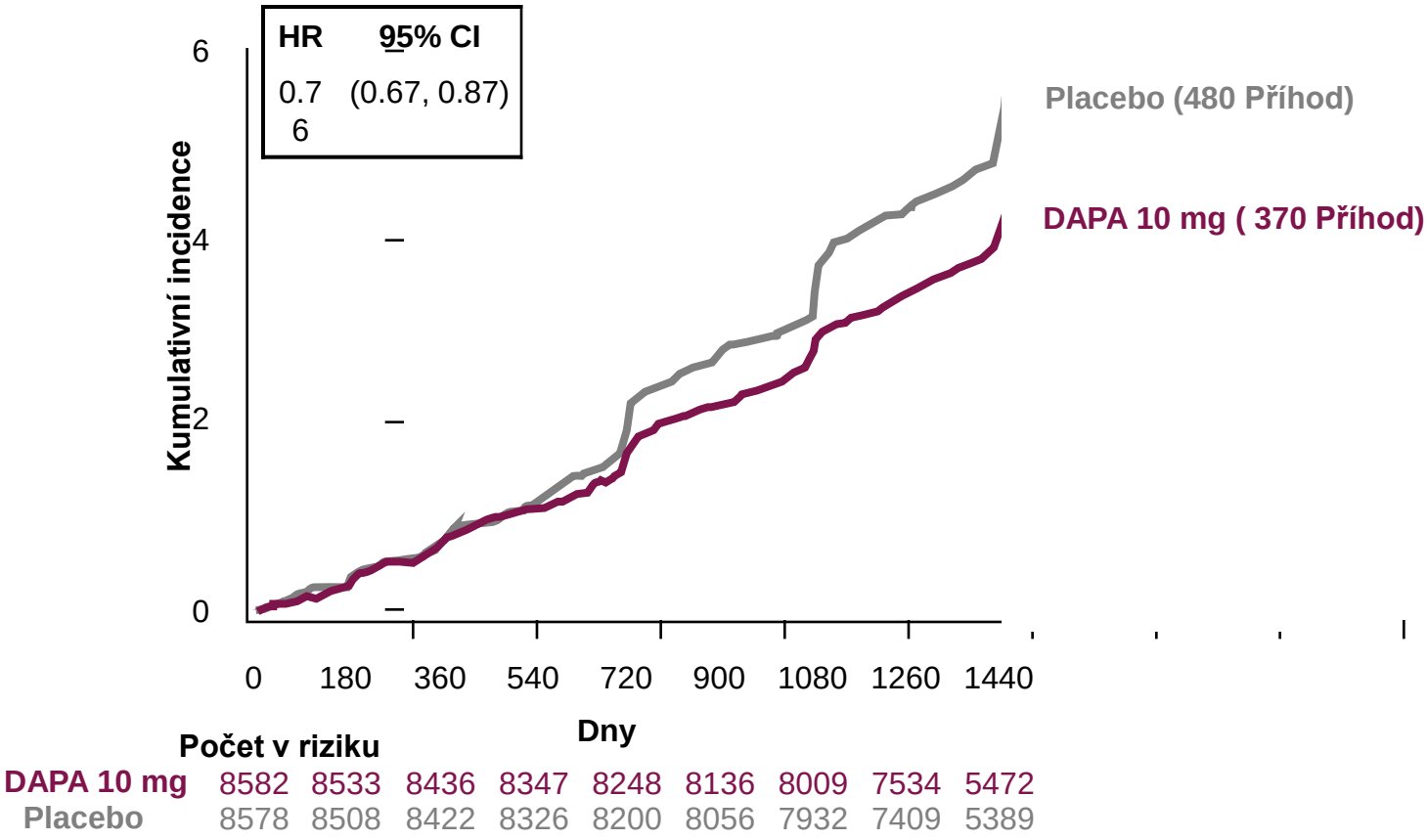



**Počet pts v riziku**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **DAPA 10 mg** | 8582 | 8517 | 8415 | 8322 | 8224 | 8110 | 7970 | 7497 | 5445 |
| **Placebo** | 8578 | 8485 | 8387 | 8259 | 8127 | 8003 | 7880 | 7367 | 5362 |

Wiviott SD et al. Online ahead of print. *New Engl J Med.* 2018.

# Sekundární cíl: Renální kompozitní cíl




Wiviott SD et al. Online ahead of print. *New Engl J Med.* 2018.

Circulation

ORIGINAL RESEARCH ARTICLE

# Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus

## Systematic Review and Meta-Analysis of Cardiovascular Outcomes Trials

**Zelniker T.A. et all: Circulation 2019; 139: 2022-2031**

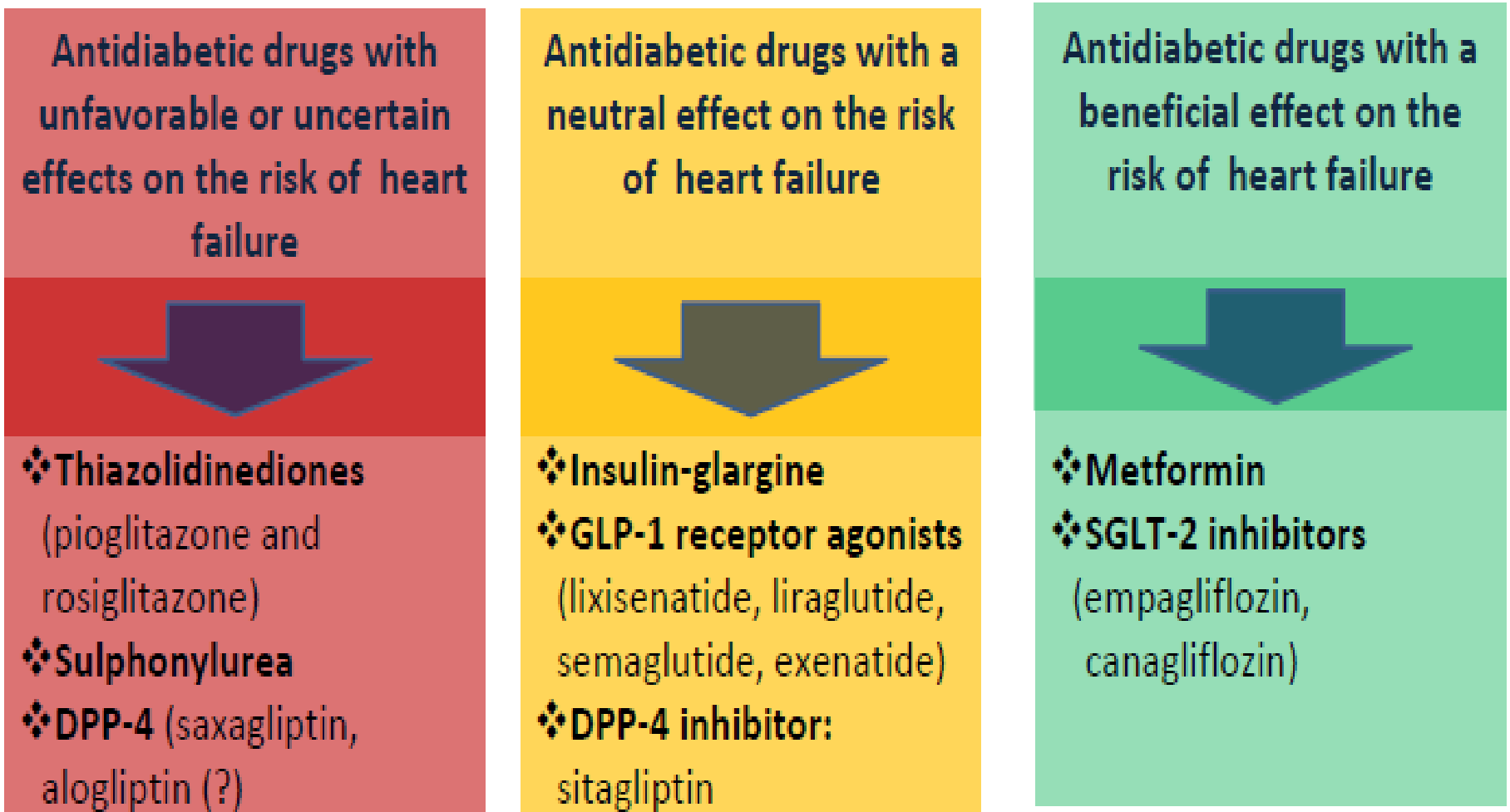
**RESULTS:** In total, data from 8 trials and 77 242 patients, 42 920 (55.6%) in GLP1-RA trials, and 34 322 (44.4%) in SGLT2i trials, were included. Both drug classes reduced MACE in a similar magnitude with GLP1-RA reducing the risk by 12% (hazard ratio [HR], 0.88; 95% CI, 0.84–0.94; *P*<0.001) and SGLT2i by 11% (HR, 0.89; 95% CI, 0.83–0.96; *P*=0.001). For both drug

SGLT2i reduced hospitalization for heart failure by 31% (HR, 0.69; 95% CI, 0.61–0.79; *P*<0.001), whereas GLP1-RA did not have a significant effect (HR, 0.93; 95% CI, 0.83–1.04; *P*=0.20).

**CONCLUSIONS:** In trials reported to date, GLP1-RA and SGLT2i reduce atherosclerotic MACE to a similar degree in patients with established atherosclerotic cardiovascular disease, whereas SGLT2i have a more marked effect on preventing hospitalization for heart failure and progression of kidney disease.

**Zelniker T.A. et all: Circulation 2019; 139: 2022-2031**

# Antidiabetic drugs and the risk of heart failure




Seferovic P et al. EJHF 2018;20:853-872

# DĚKUJI ZA POZORNOST