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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*

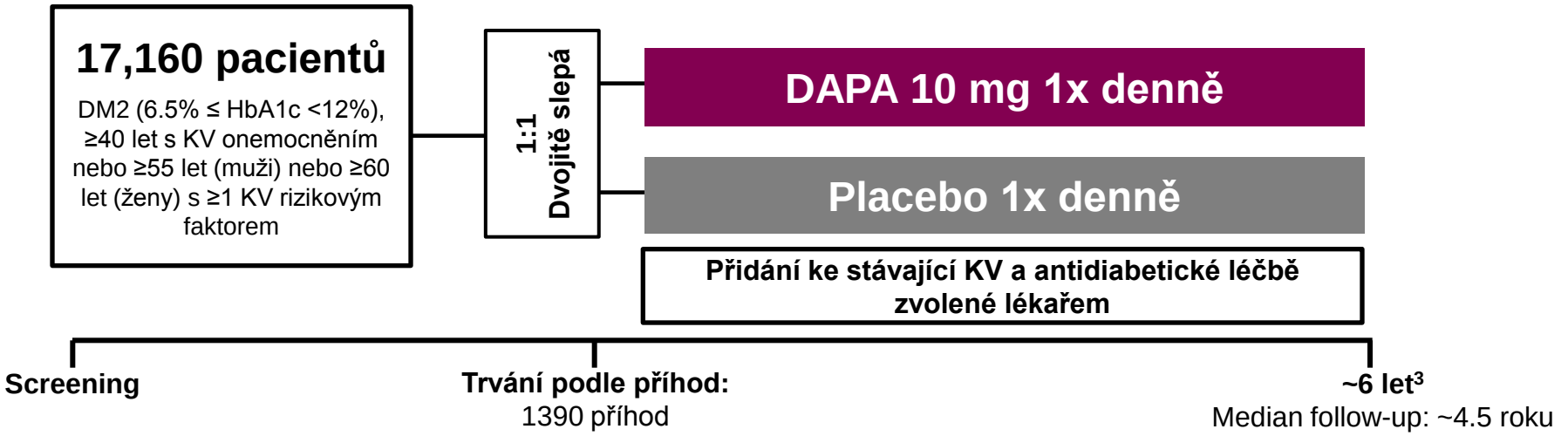
ABSTRACT

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-TIMI 58: Multicentrická randomizovaná dvojitě zaslepená placebem kontrolovaná kardiovaskulární studie fáze 3

Design studie[1,2]



Primární parametry[1,2]

- Složený parametr KV úmrtí, IM nebo CMP
- Složený parametr KV úmrtí nebo hospitalizace pro srdeční selhání

Sekundární parametr[2]

- Renální složený parametr
- Úmrtí ze všech příčin

Posouzení zaslepení[4]

- KV příhody
- Malignity
- Hepatální příhody
- Potenciální příhody DKA

Komise pro monitorování dat[4]

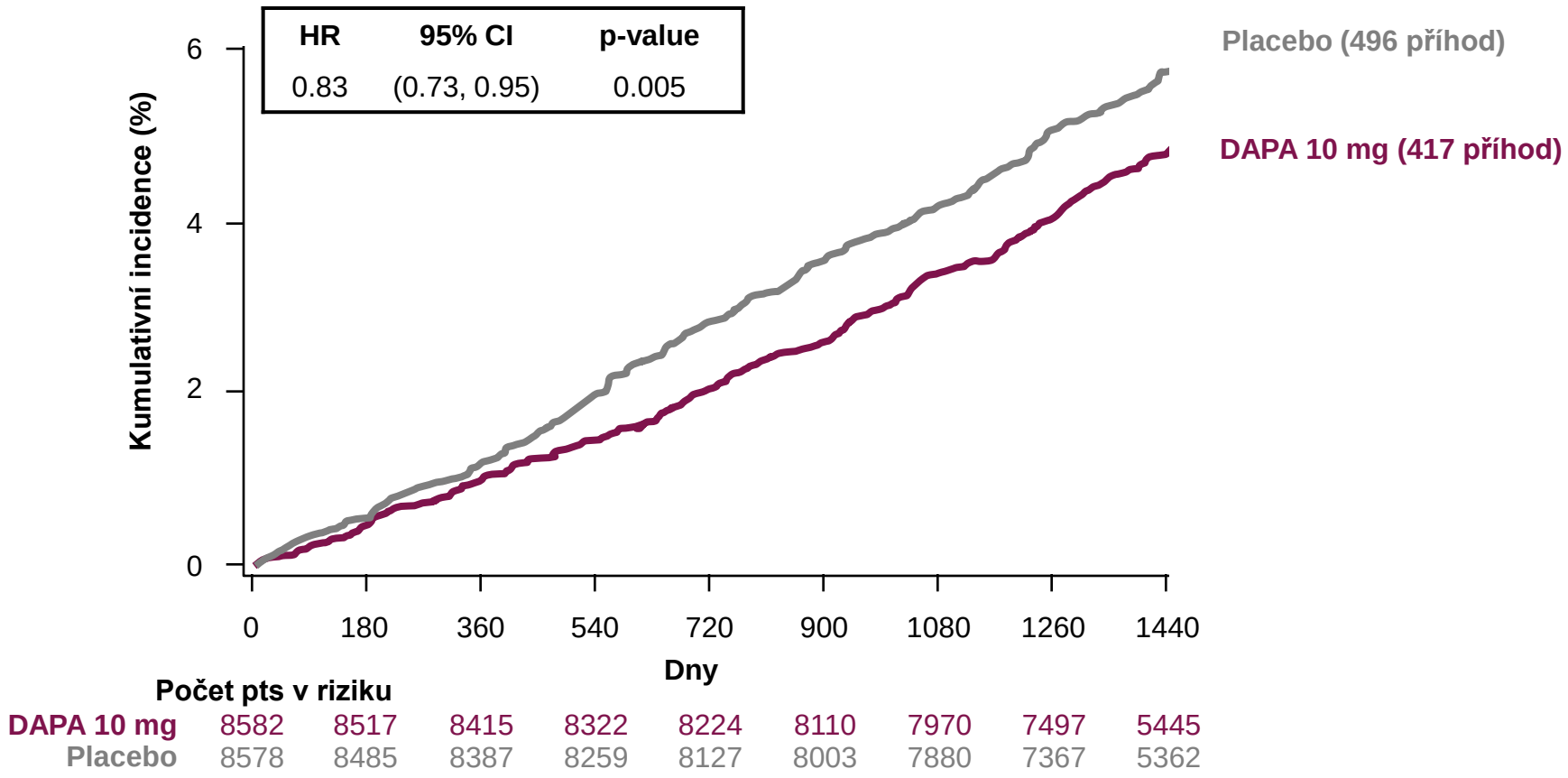
- Periodické review bezpečnosti
- Dvě plánovaná review účinnosti
- Posouzení karcinomu močového měchýře každých 8 případů
  8 events

KV, kardiovaskulární; CMP, cévní mozková příhoda; DAPA, dapagliflozin; DKA, diabetiická ketoacidóza; HbA1c, glykovaný hemoglobin; IM, infarkt myokardu; DM2, diabetes 2. typu.

1. Raz I et al. Poster presented at: 77th Scientific Sessions of the American Diabetes Association; June 9-13, 2017; San Diego, CA. Poster 1245-P; 2. Raz I et al. Poster presented at: 53rd Annual Meeting of the European Association for the Study of Diabetes; September 11–15, 2017; Lisbon, Portugal. Poster 1129; 3. Study NCT01730534. ClinicalTrials.gov website. Accessed December 13, 2017; 4. In House Data, AstraZeneca Pharmaceuticals LP. CSP D1693C00001; 5. AstraZeneca Pharmaceuticals LP. H1 2017 results. Published July 27, 2017. 2. Raz I et al. Article doi: 10.1111/dom.13217

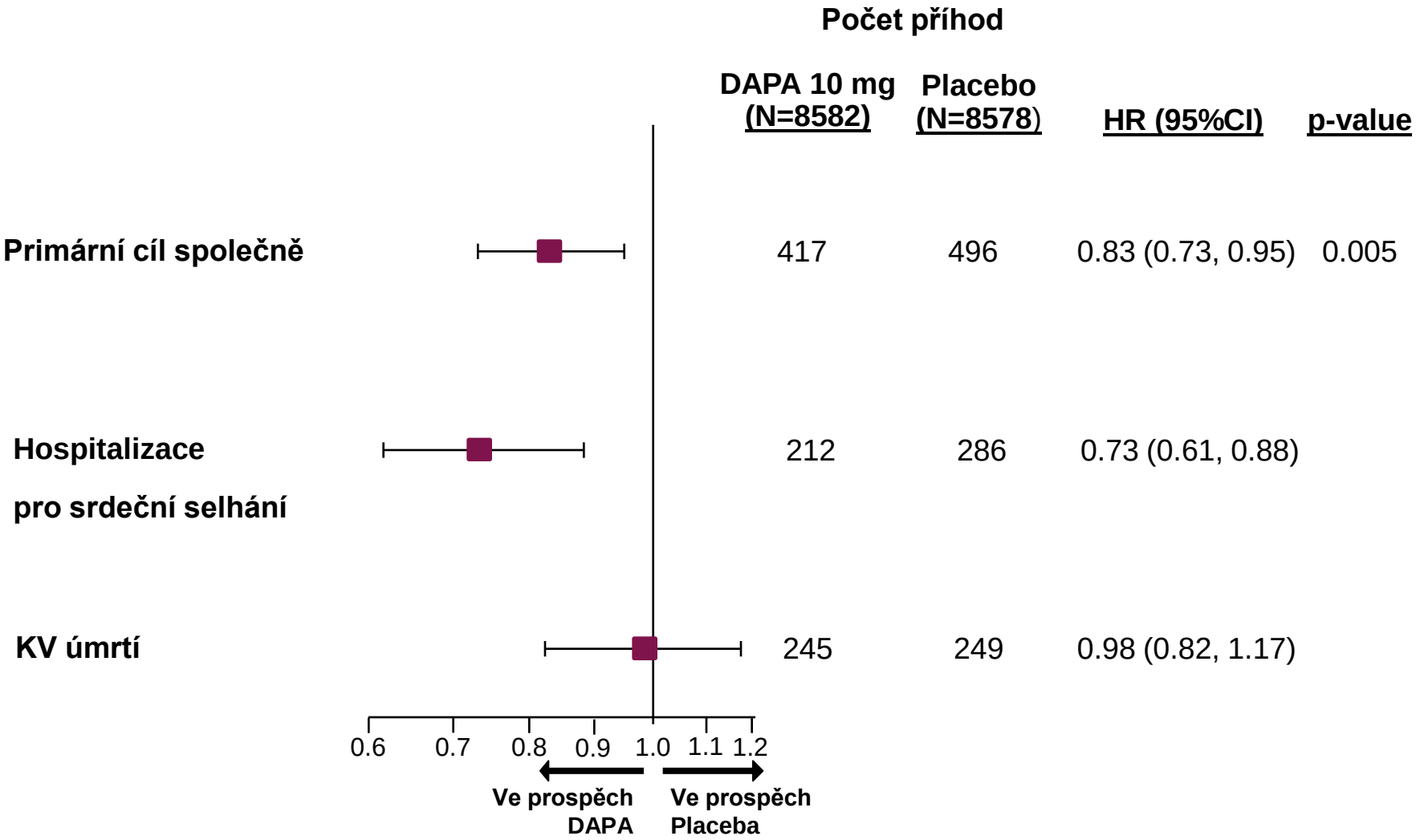
Obr. 1

Primární cíl: hospitalizace pro srdeční selhání a KV úmrtí



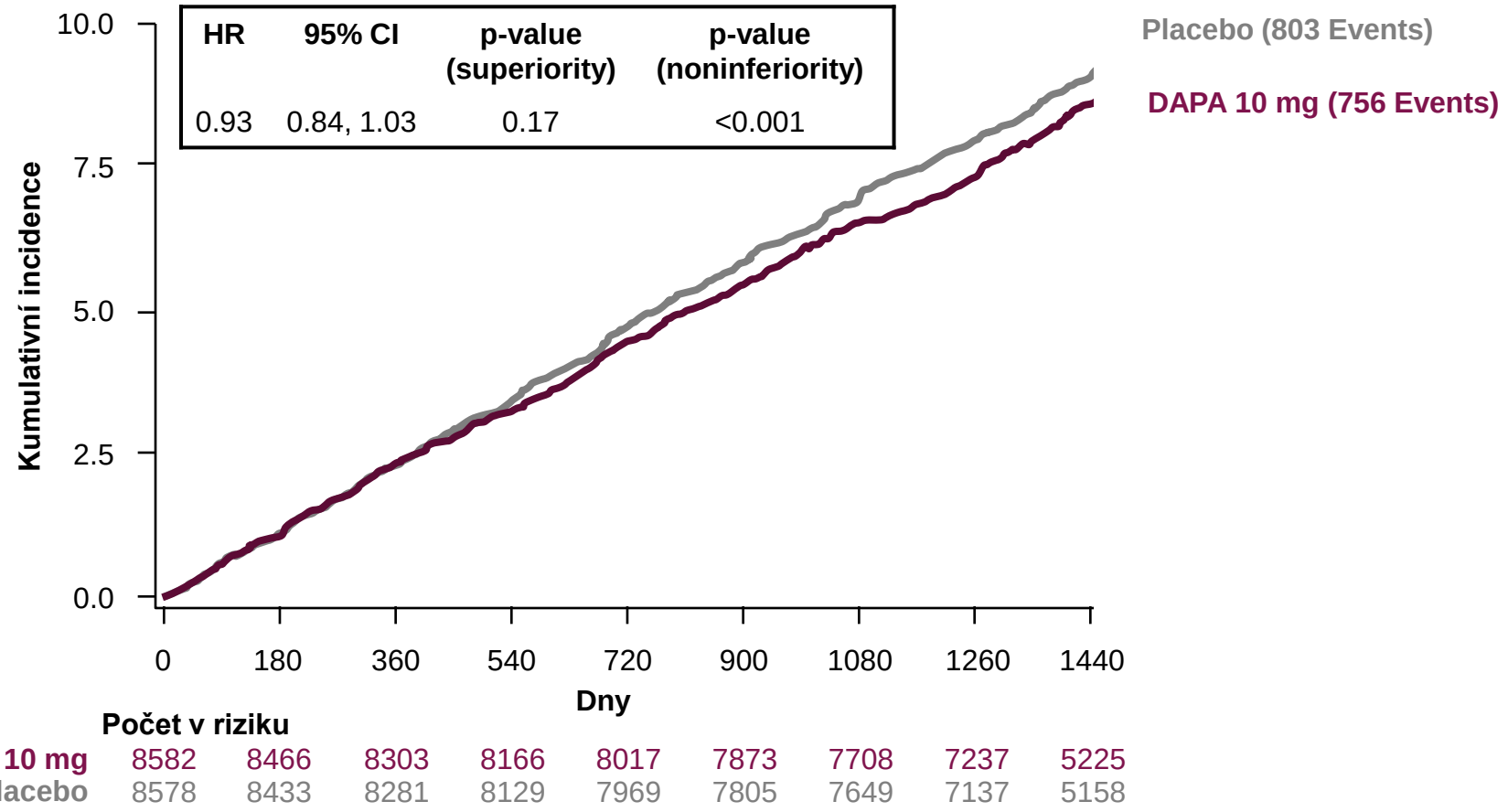
Wiviott SD et al. Online ahead of print. *New Engl J Med.* 2018.

Primární cíl:
Hospitalizace pro srdeční selhání a KV úmrtí a jednotlivé komponenty



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

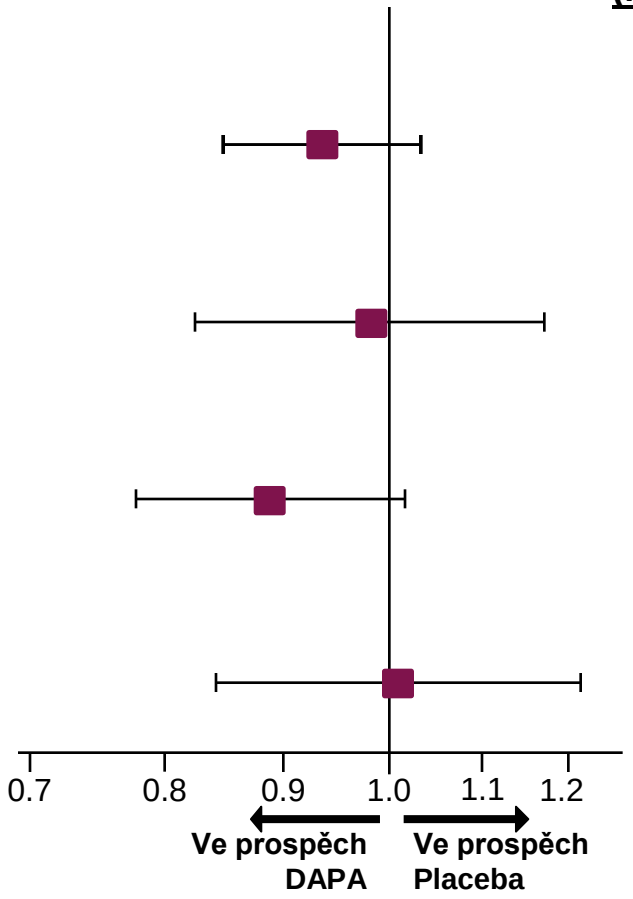
Primární cíl: MACE



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

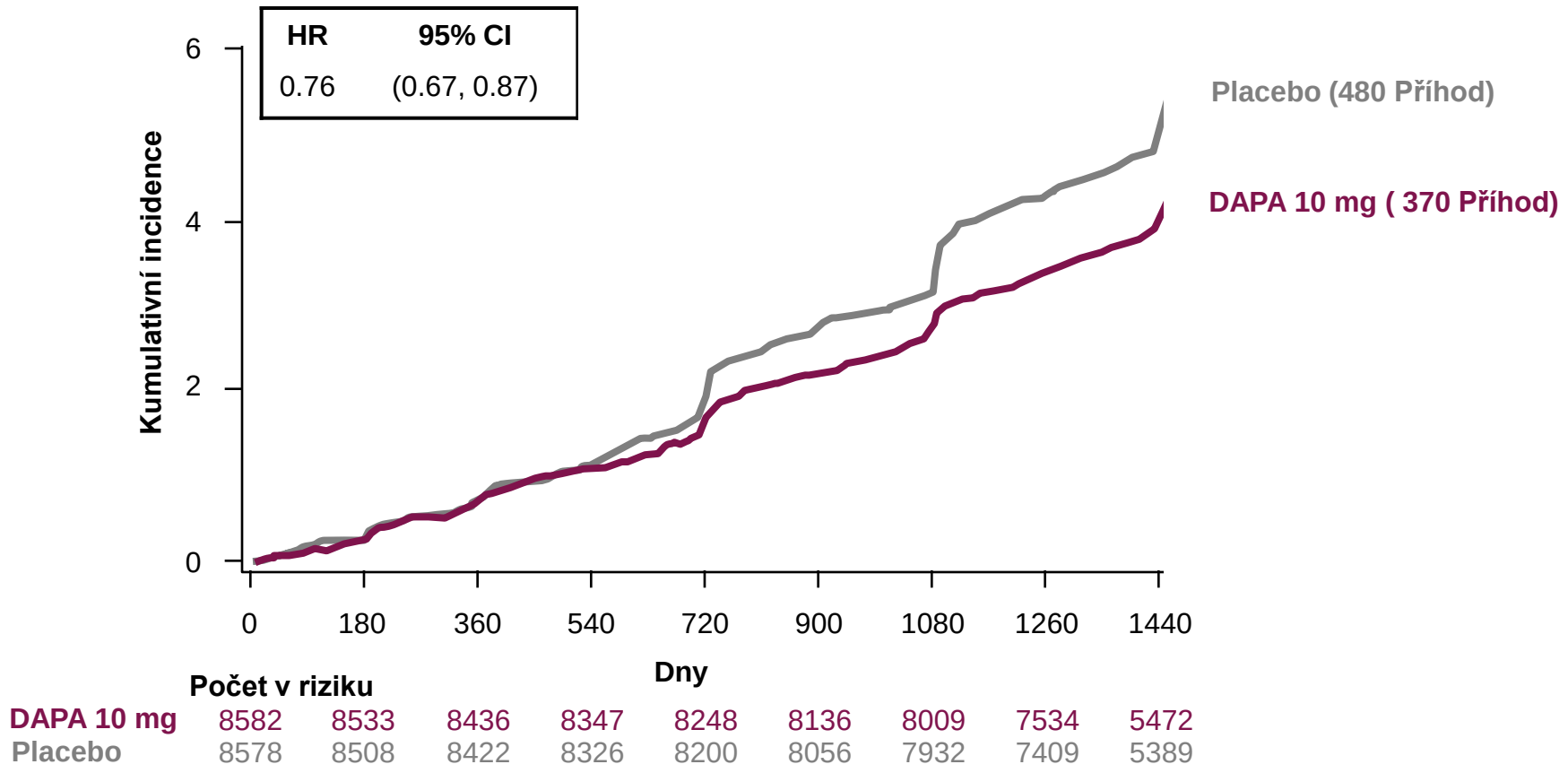
Primární cíl:
Složený MACE a jednotlivé cíle

	Počet příhod			
	DAPA 10 mg (N=8582)	Placebo (N=8578)	HR (95%CI)	p-value[a]
MACE	756	803	0.93 (0.84,1.03)	0.17
KV úmrtí	245	249	0.98 (0.82,1.17)	
Infarkt myokardu	393	441	0.89 (0.77,1.01)	
CMP	235	231	1.01 (0.84,1.21)	



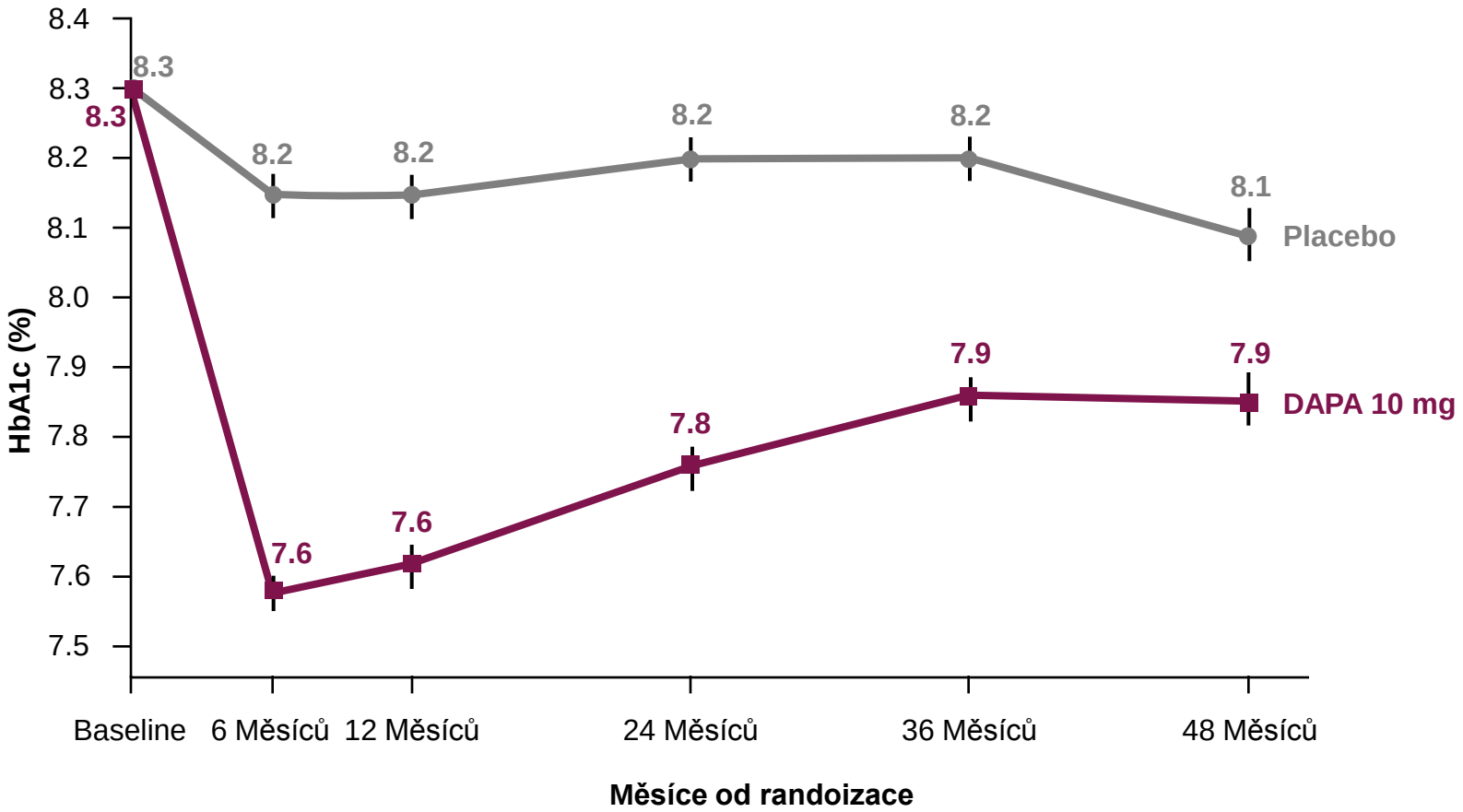
Wiviott SD et al. Online ahead of print. *New Engl J Med.* 2018.

Sekundární cíl: Renální kompozitní cíl



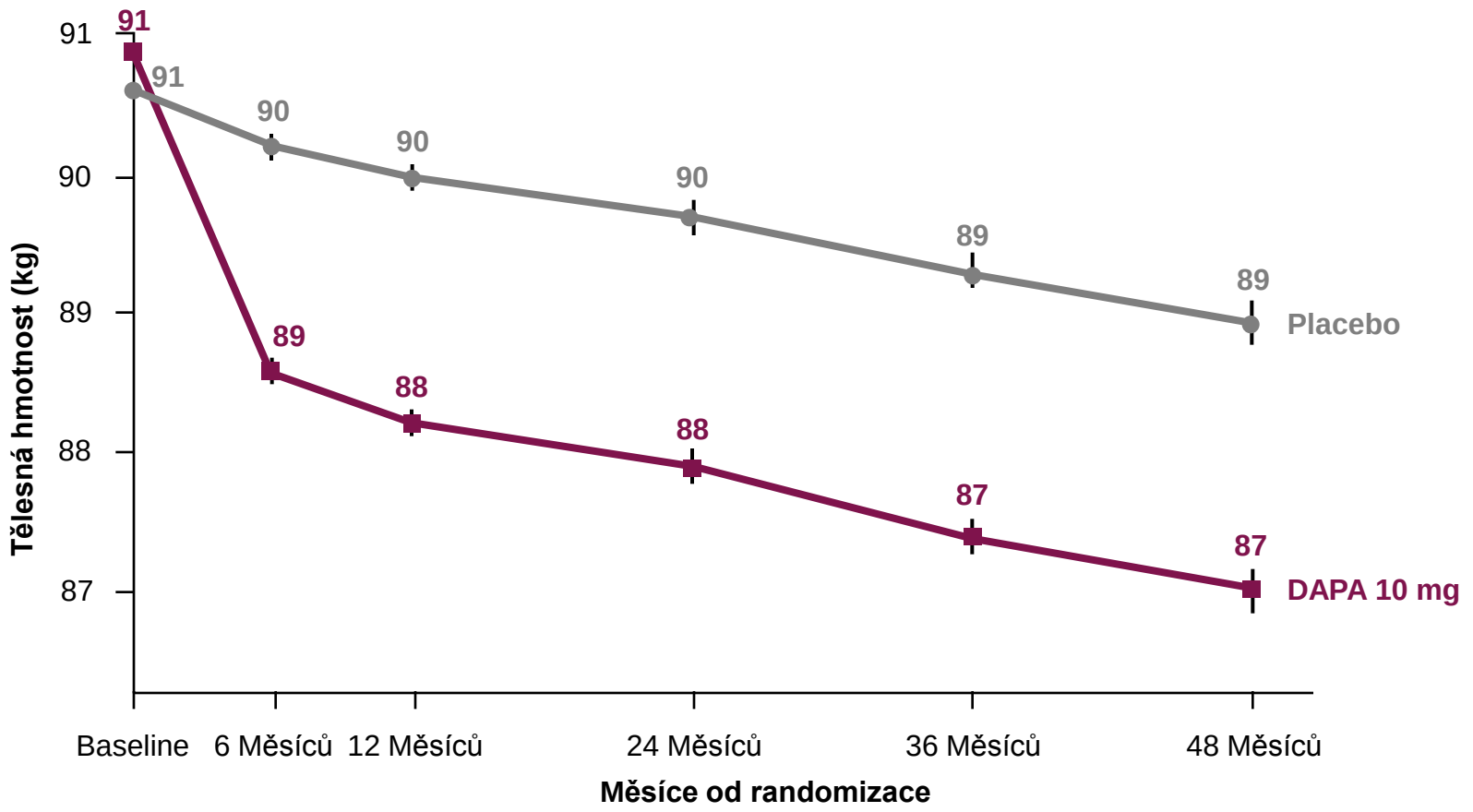
Wiviott SD et al. Online ahead of print. *New Engl J Med.* 2018.

Pokles glykovaného hemoglobinu



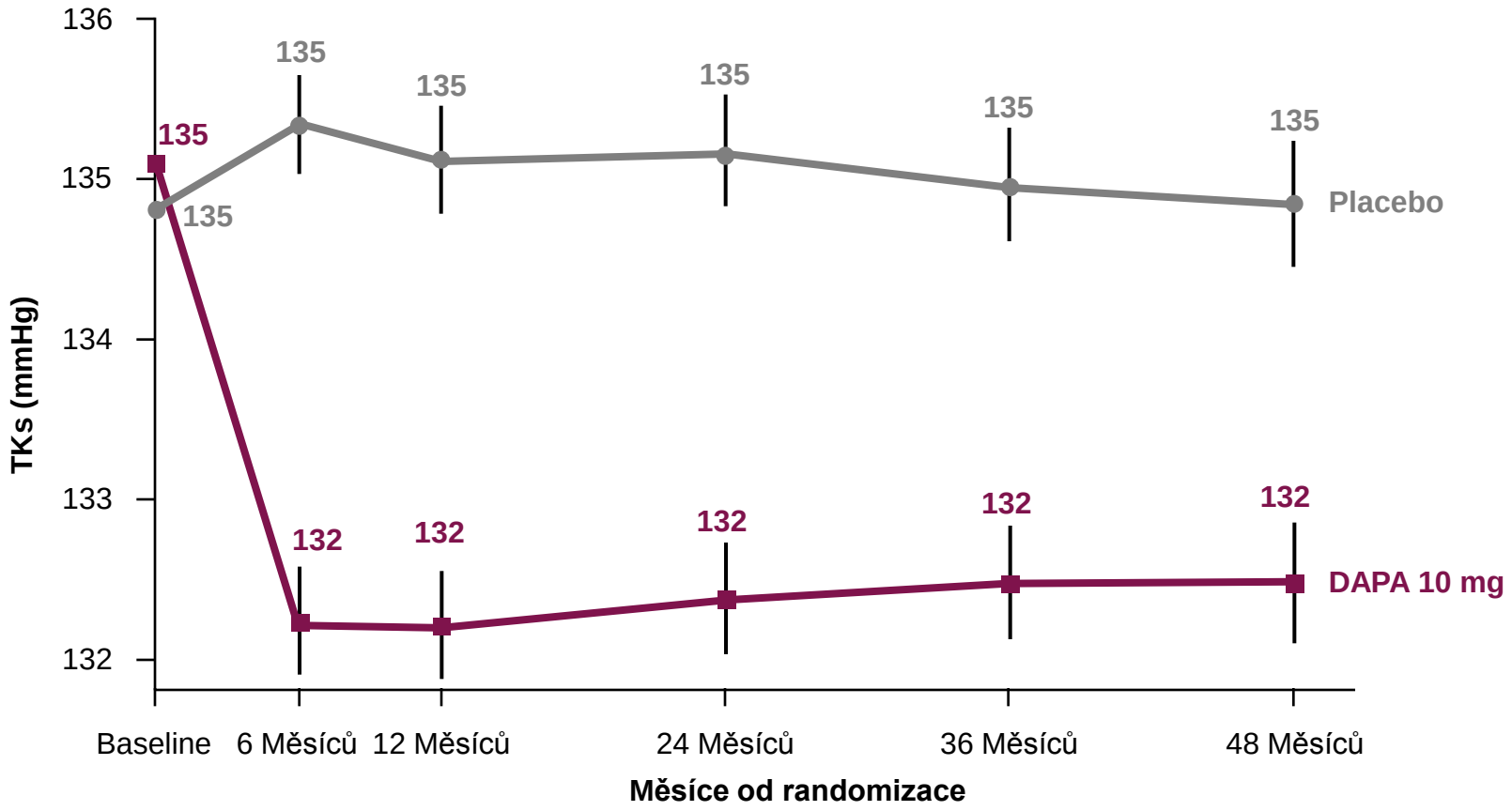
Wiviott SD et al. Online ahead of print. *New Engl J Med.* 2018.

Pokles hmotnosti



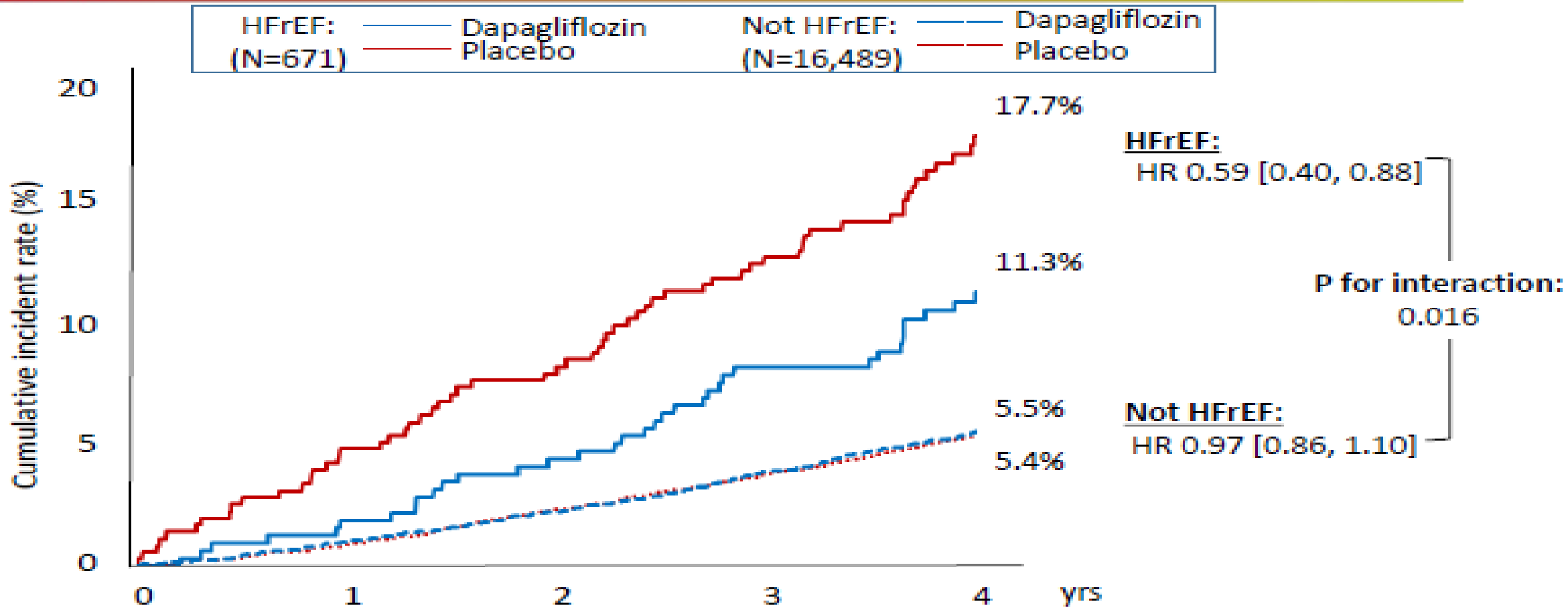
Wiviott SD et al. Online ahead of print. *New Engl J Med.* 2018.

Pokles systolického krevního tlaku



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

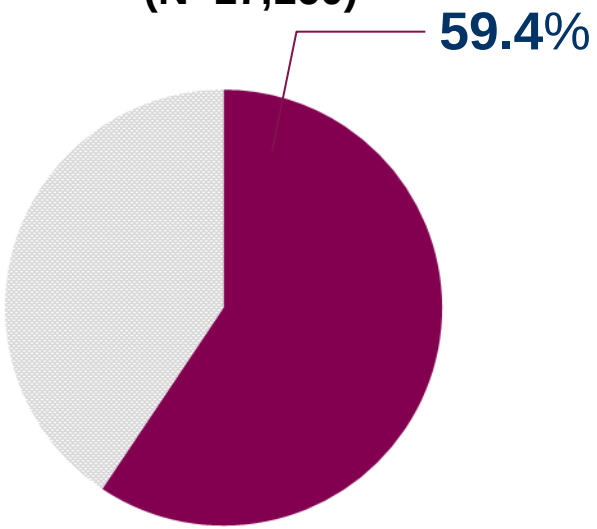
All Cause Mortality
by HFrEF vs not HFrEF subgroups



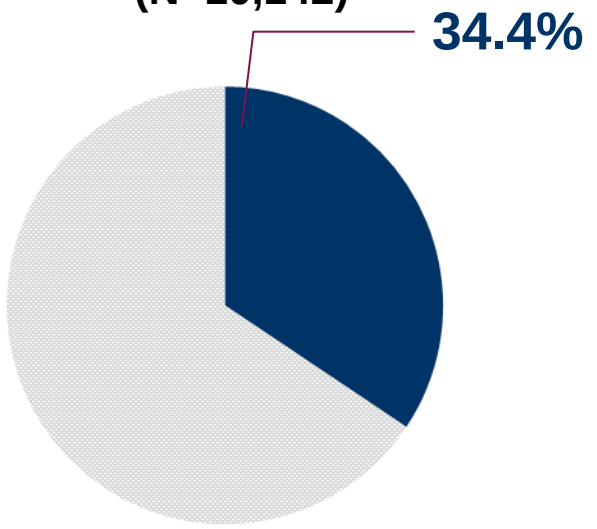
DECLARE měl největší počet nemocných v primární prevenci

U pacientů s DM 2. typu většina nemá potvrzené KV onemocnění[1]

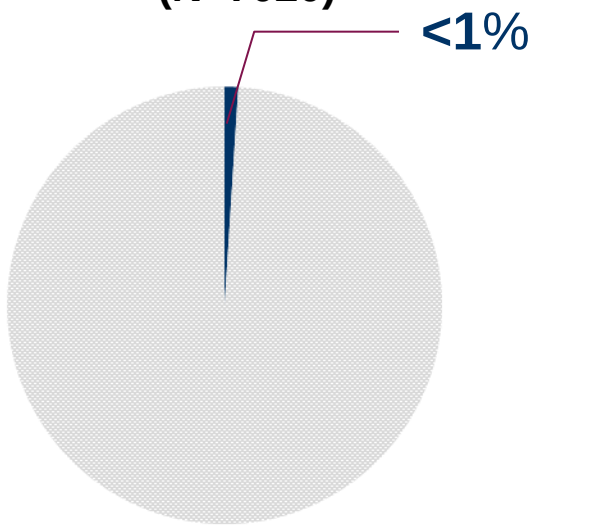
DECLARE-TIMI 58[2]
(N=17,160)



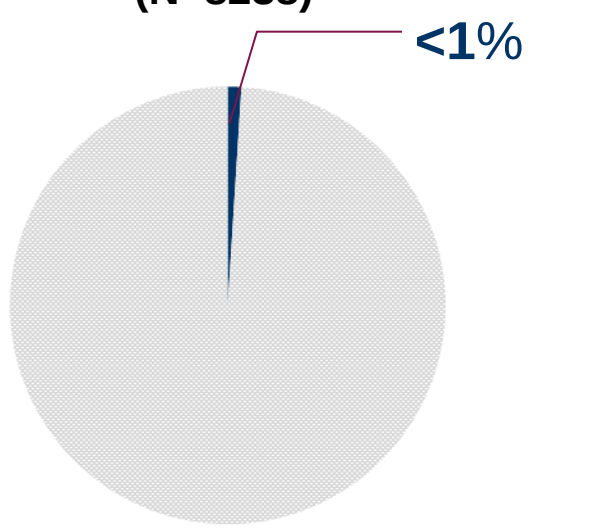
CANVAS Program[3]
(N=10,142)



EMPA-REG OUTCOME[4]
(N=7020)



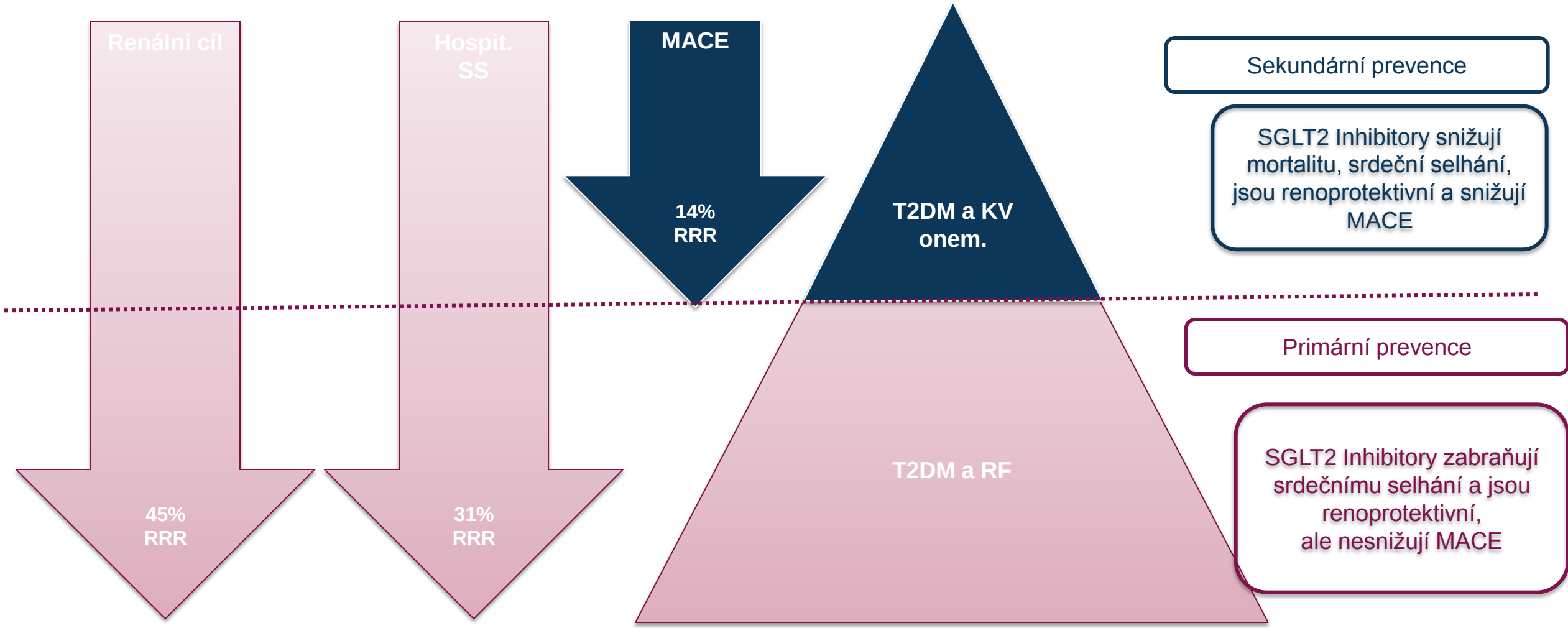
VERTIS-CV[5]
(N=8238)



CV, cardiovascular; eCVD, established CV disease; SGLT2i, sodium glucose co-transporter 2 inhibitor; T2D, type 2 diabetes

1. Einarson TR, et al. *Cardiovasc Diabetol* 2018;17:83; 2. Raz I, et al. *Diabetes Obes Metab* 2018;20:1102–1110; 3. Neal B, et al. *N Engl J Med* 2017;377:644–657; 4. Zinman B, et al. *N Engl J Med* 2015;373:2117–2128;
5. Cannon CP et al. Poster presented at: American College of Cardiology 67th Annual Scientific Session; March 10-12, 2018; Orlando, FL; *J Am Coll Cardiol.* 2018;71:A1825.

Kardiorenální prospěch SGLT2



[a]Composite of worsening eGFR, end-stage renal disease, or renal death.
ASCVD, atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; hHF, hospitalization for heart failure; MACE, major cardiovascular adverse event; RRR, relative risk reduction; SGLT2, sodium-glucose cotransporter 2; T2D, type 2 diabetes.

Zelniker TA et al. *Lancet. 2019;393:31-39*; Verma S et al. *Lancet.* 2019; 393:3-5.

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

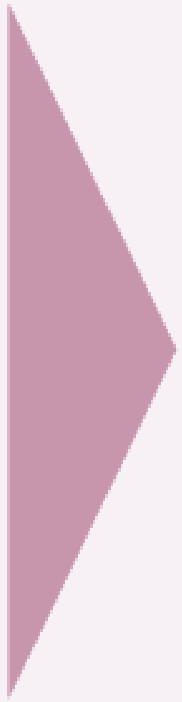
Recommendations for Adults With Type 2 Diabetes Mellitus Referenced studies that support recommendations are summarized in Online Data Supplement 10.		
COR	**LOE**	**Recommendations**
I	A	1. For all adults with T2DM, a tailored nutrition plan focusing on a heart-healthy dietary pattern is recommended to improve glycemic control, achieve weight loss if needed, and improve other ASCVD risk factors (S4.2-1, S4.2-2).
I	A	2. Adults with T2DM should perform at least 150 minutes per week of moderate-intensity physical activity or 75 minutes of vigorous-intensity physical activity to improve glycemic control, achieve weight loss if needed, and improve other ASCVD risk factors (S4.2-3, S4.2-4).
IIa	B-R	3. For adults with T2DM, it is reasonable to initiate metformin as first-line therapy along with lifestyle therapies at the time of diagnosis to improve glycemic control and reduce ASCVD risk (S4.2-5–S4.2-8).
IIb	B-R	4 For adults with T2DM and additional ASCVD risk factors who require glucose-lowering therapy despite initial lifestyle modifications and metformin, it may be reasonable to initiate a sodium-glucose cotransporter 2 (SGLT-2) inhibitor or a glucagon-like peptide-1 receptor (GLP-1R) agonist to improve glycemic control and reduce CVD risk (S4.2-9–S4.2-14).

SGLT2 inhibitory
posun v indikacích

současnost

budoucnost?

SGLT2 inhibitory
prospěšné v prevenci SS
u nemocných s DM



SGLT2 inhibitor
prospěšné v léčbě SS
u nemocných bez DM

Děkuji za pozornost