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In besten Händen.

Antidiabetika in der Kardiologie: Zeit für einen Paradigmenwechsel?

Barmelweid Kolloquium 23.08.2018

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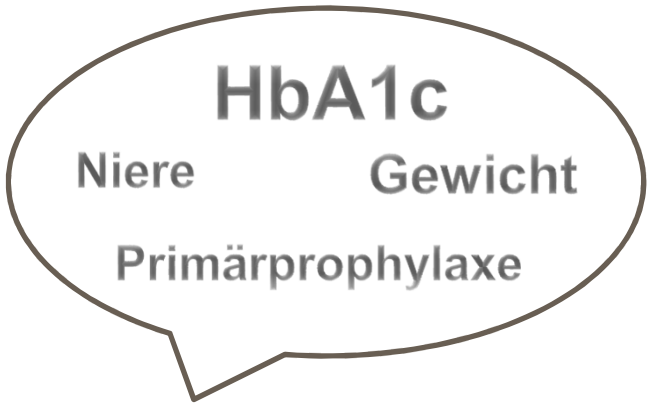
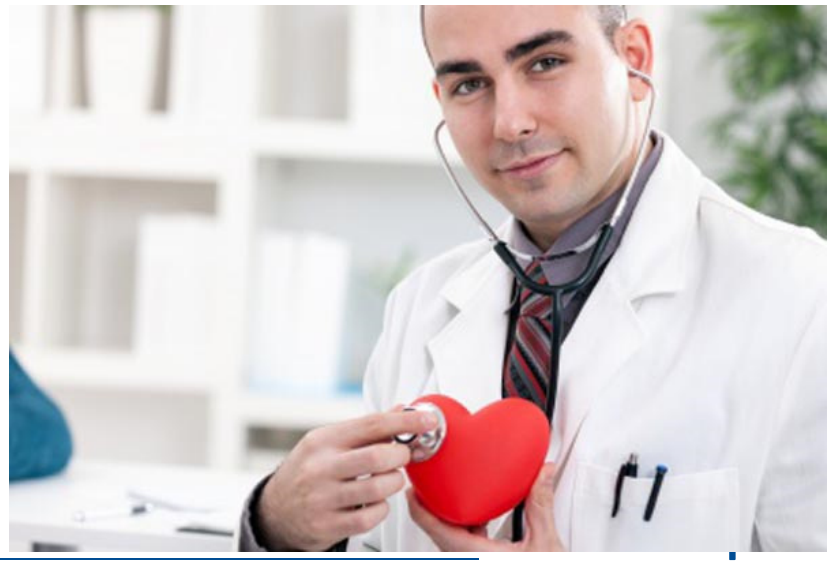
Bariatrisches Referenzzentrum

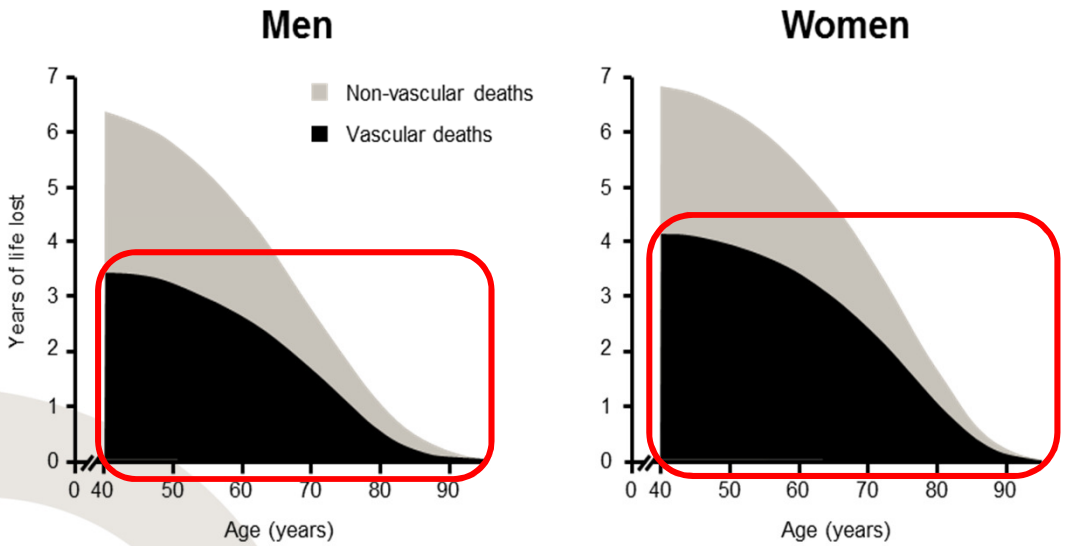
Diabetes und Herz:
verschiedene Fachrichtungen – verschiedene Interessen?





Kardiovaskuläre Komplikationen bei Typ 2 Diabetes

Years of life lost in people with diabetes* compared with non-diabetes peers[1]



Mortality risk associated with diabetes (n=820,900)[1]

Seshasai et al. *N Engl J Med* 2011;364:829-41;

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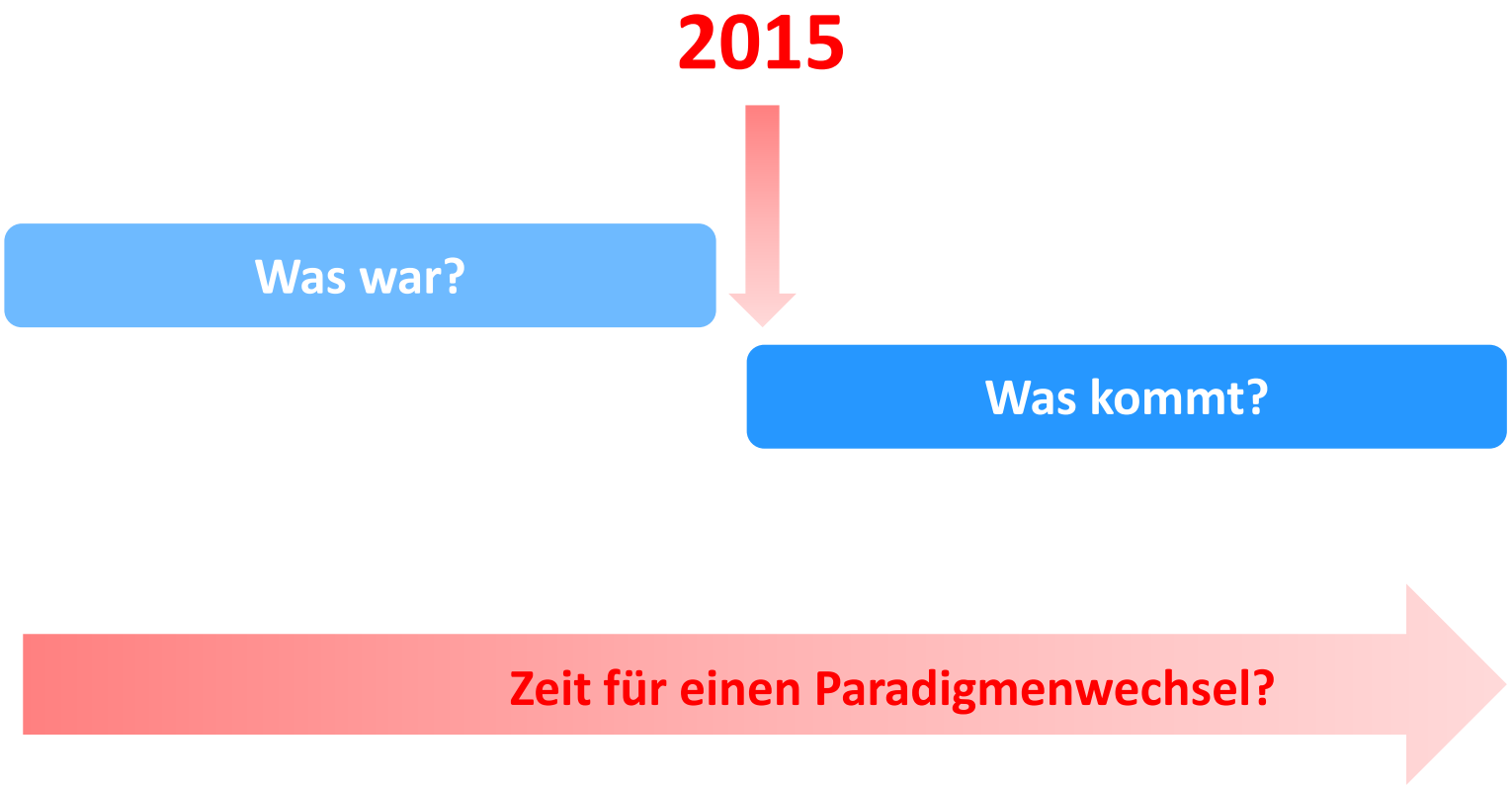
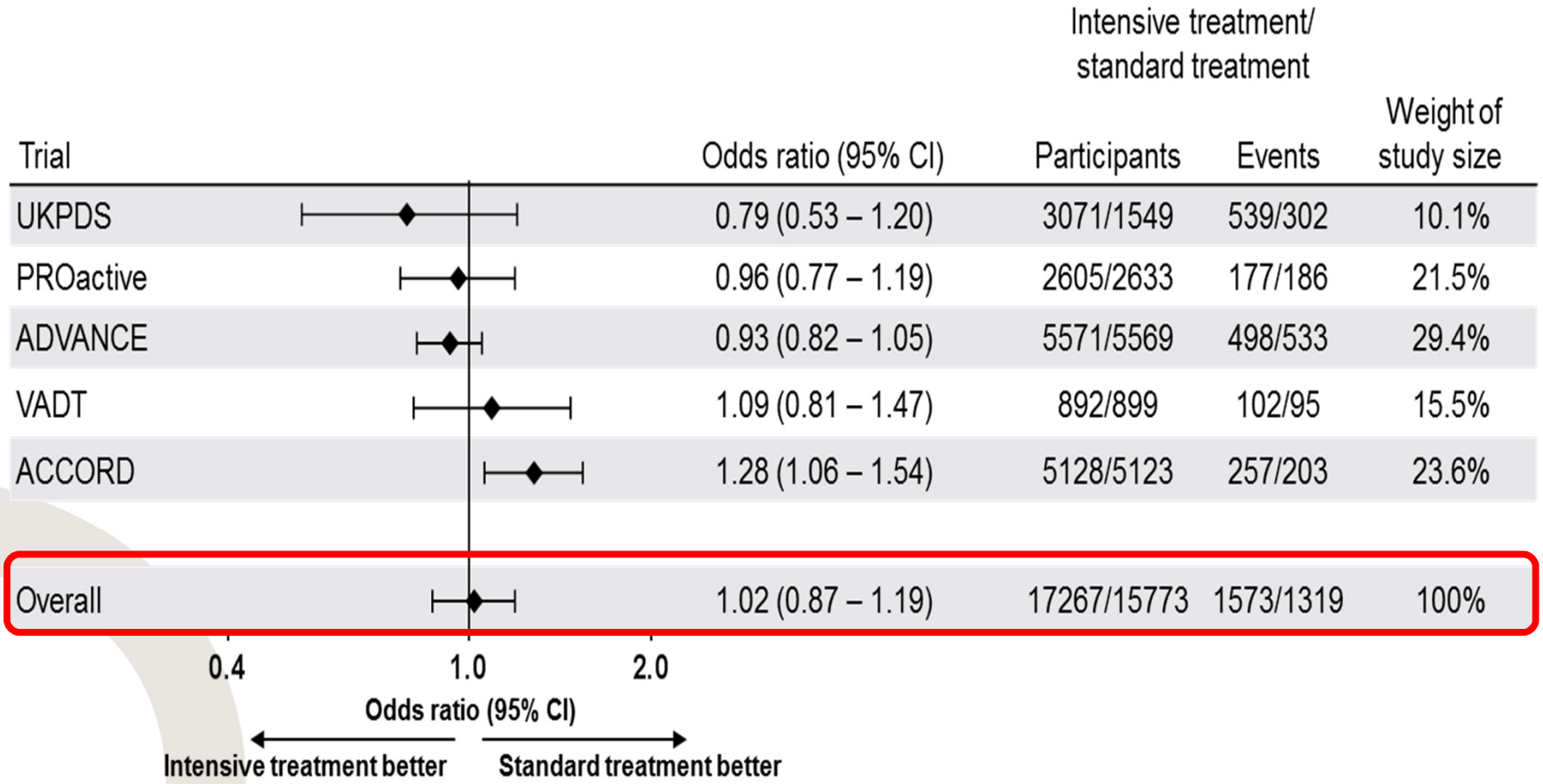
Diabetes und Herz – Beginn einer neuen Ära?



Intensive vs Standard glucosesenkende Therapie

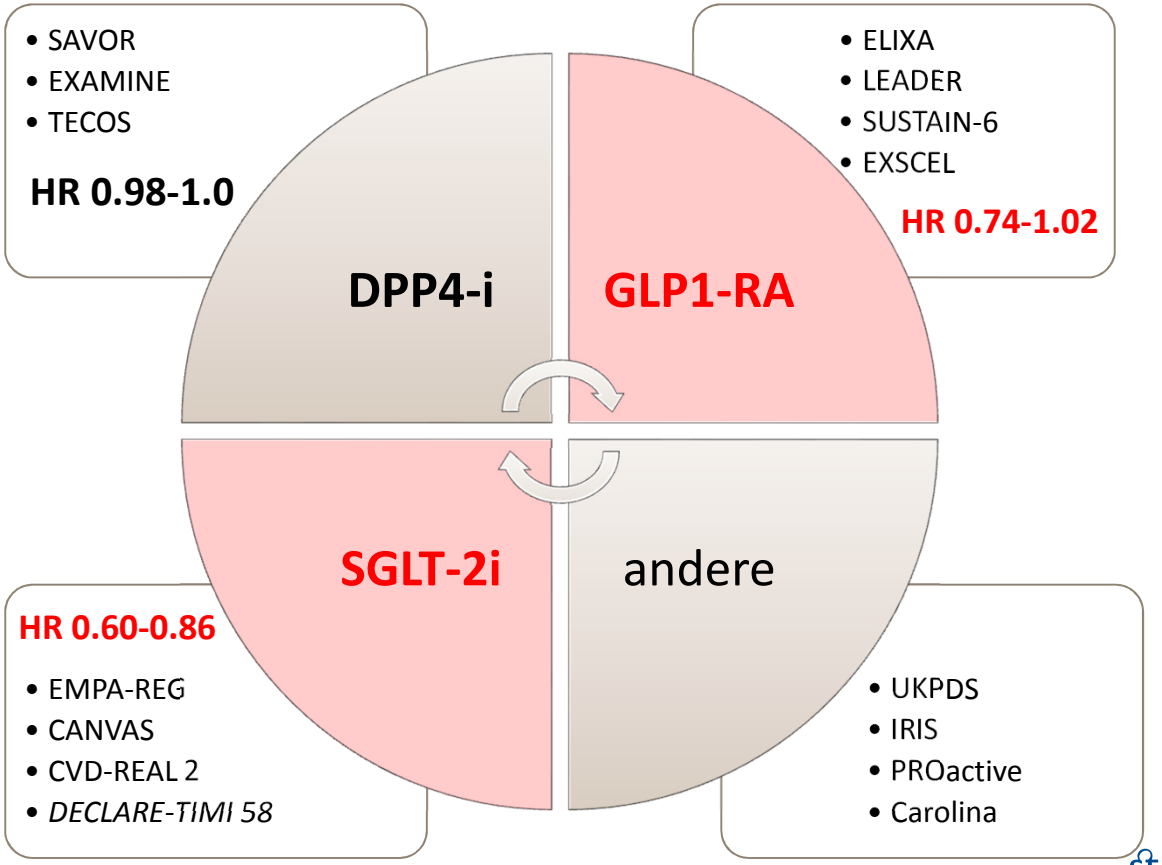
Studienlage vor 2015



Ray KK et al *Lancet* 2009;373:1765–1772.

Neue Antidiabetika und das CV-Risiko

Studienlage nach 2015



Antidiabetika in der Kardiologie

GLP1-REZEPTORAGONISTEN

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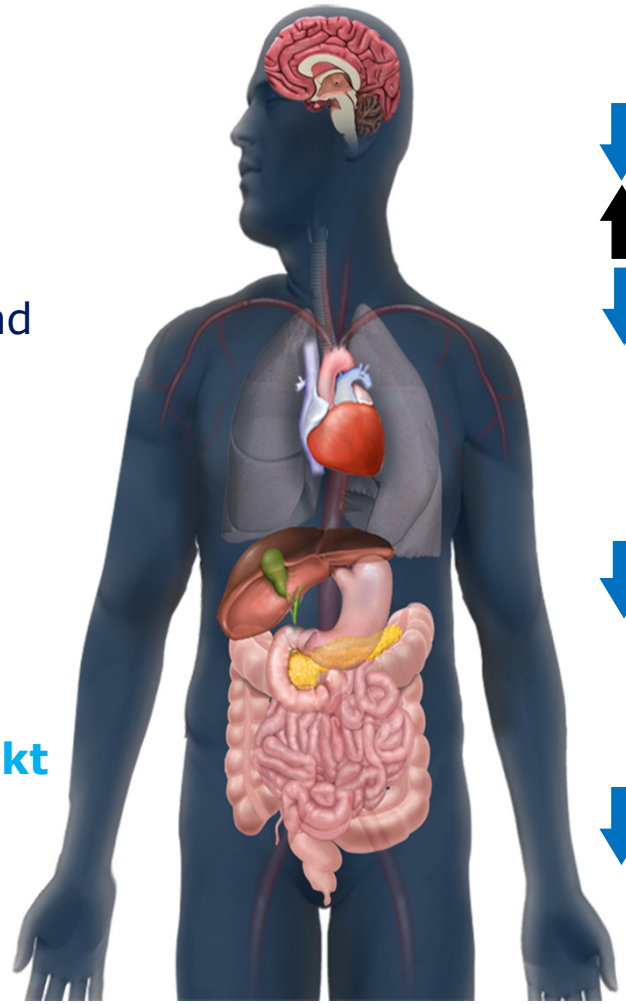
GLP1-RA- Wirkung auf die menschliche Physiologie



Pankreas

↑ Insulinsekretion (glukoseabhängig) und Beta-Zell-Sensitivität

↑ Insulinsynthese

↓ Glukagonsekretion (glukoseabhängig)

Gastrointestinal Trakt

↓ Verminderte Motilität

Gehirn

↓ Körpergewicht:

↑ Sättigungsgefühl

↓ Energieaufnahme

Kardiovaskuläres System

↓ Systolischer Blutdruck

Leber

↓ Hepatische Glukoseausschüttung

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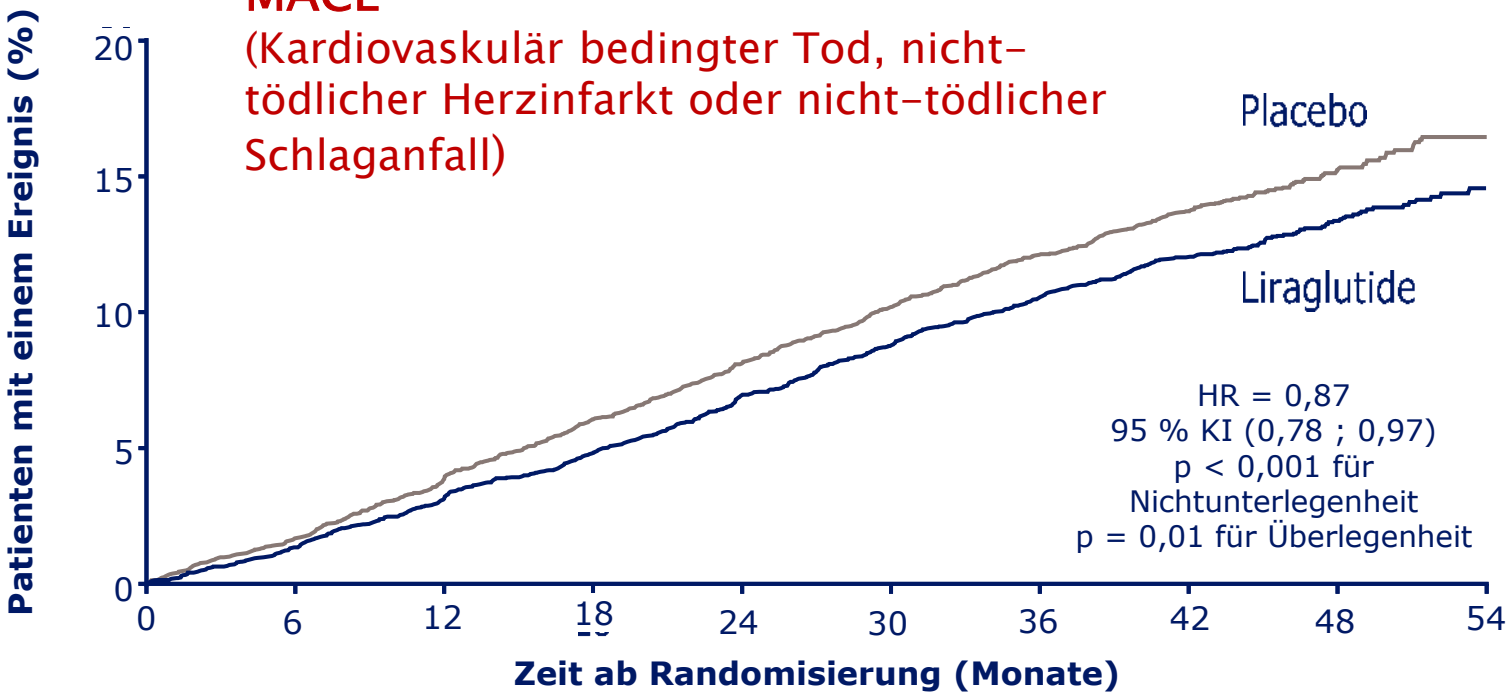
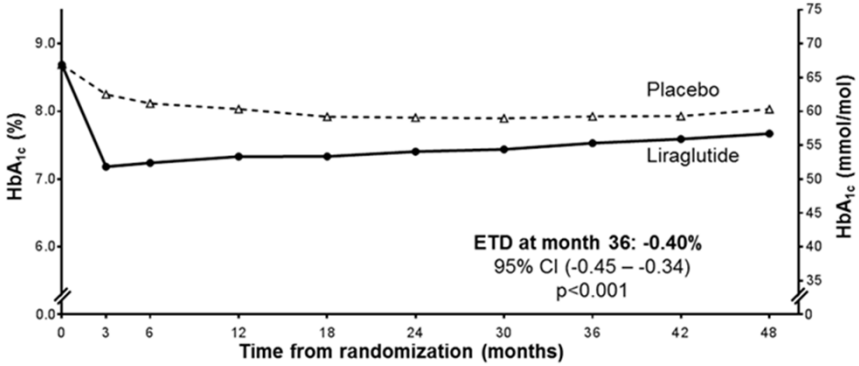
GLP1-Analoga

LEADER

MACE

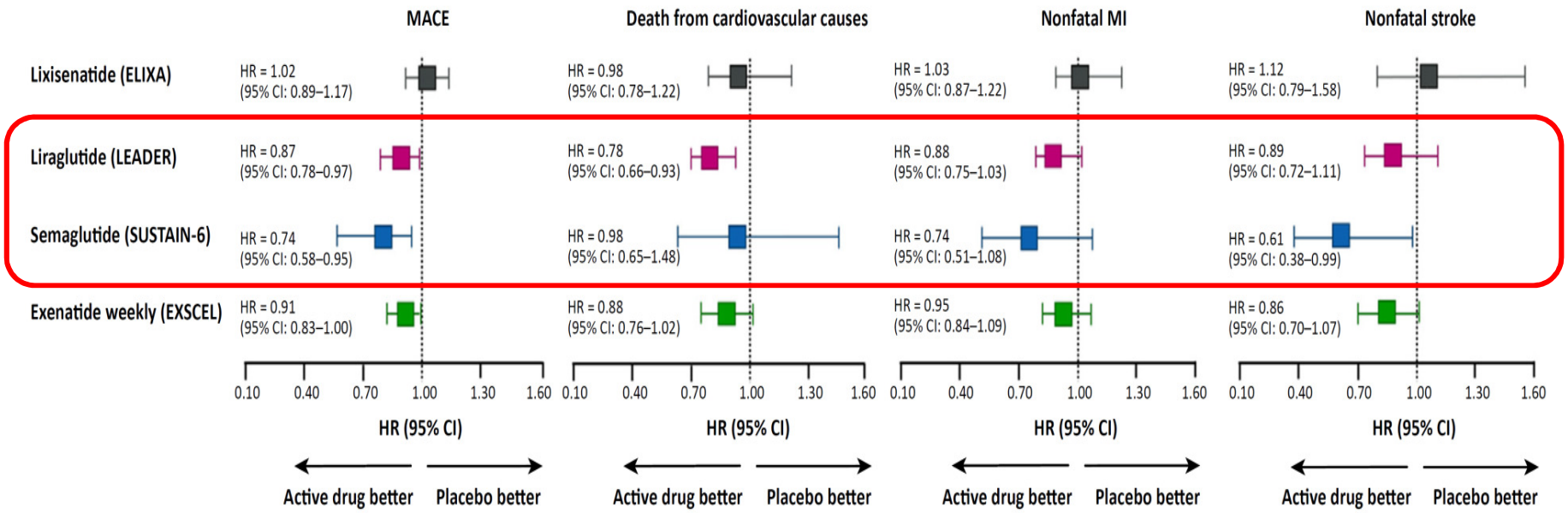
(Kardiovaskulär bedingter Tod, nicht-tödlicher Herzinfarkt oder nicht-tödlicher Schlaganfall)





Marso et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med 2016;375(4)

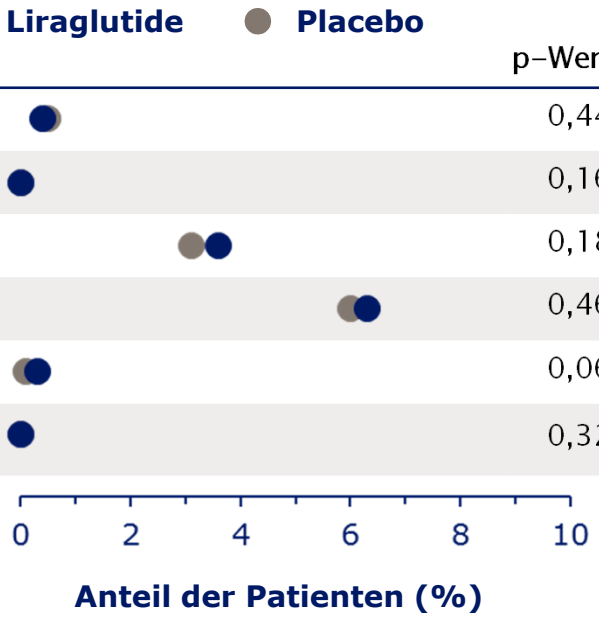
GLP1-Analoga
CV-Outcome Studienlage-Klasseneffekt?



Lim S *et al.* Glucagon-like Peptide-1 Receptor Agonists and Cardiovascular Events: Class Effects versus Individual Patterns.*Trends Endocrinol Metab* 2018 ;29:238-248.

GLP1-RA
Unerwünschte Wirkungen

	Liraglutide		Placebo		p-Wert
	n	%	n	%	
Akute Pankreatitis	18	0,4	23	0,5	0,44
Chronische Pankreatitis	0	0	2	< 0,1	0,16
Benigne Neoplasie	168	3,6	145	3,1	0,18
Maligne Neoplasie	296	6,3	279	6,0	0,46
Pankreaskarzinom	13	0,3	5	0,1	0,06
Medulläres Schilddrüsenkarzinom	0	0	1	< 0,1	0,32



Häufig: Gastrointestinale Nebenwirkungen (bis zu 15%)

Semaglutide: Retinopathie

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Antidiabetika in der Kardiologie

SGLT2-INHIBITOREN

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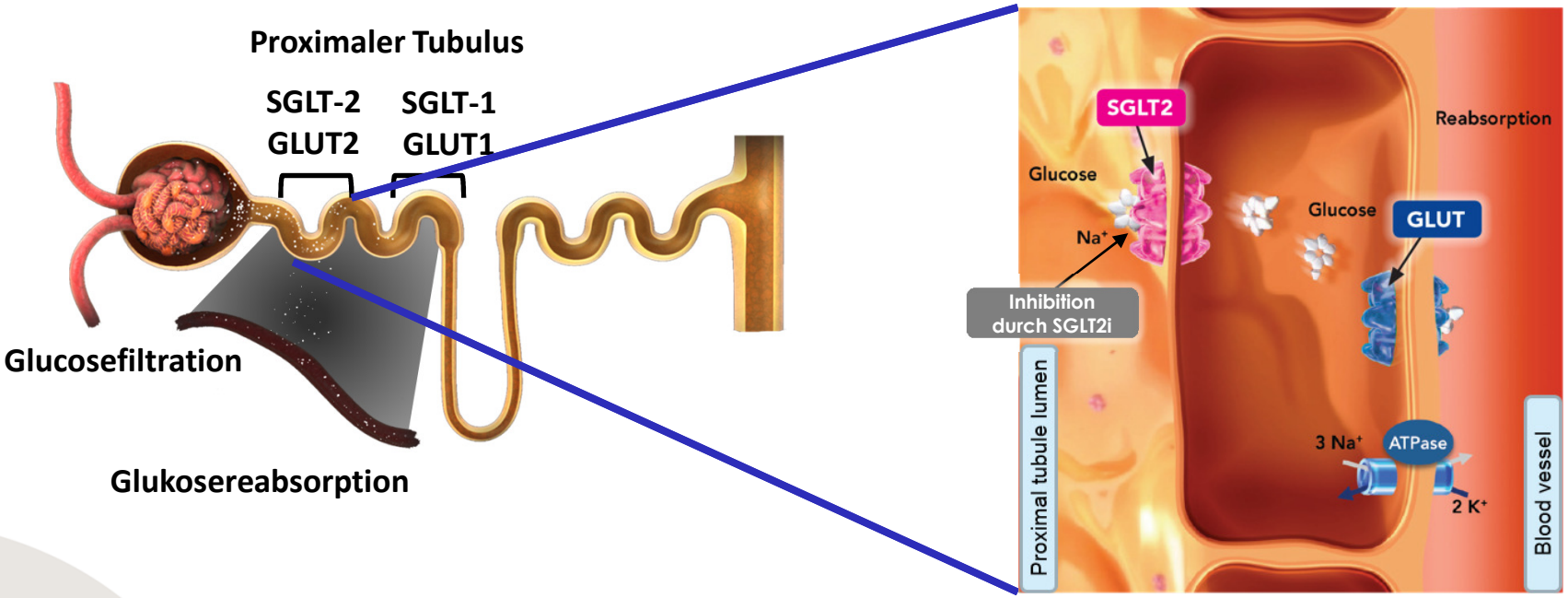
SGLT2-Wirkmechanismus



↑ Renale Glukoseausscheidung (insulinunabhängig)

↓ HbA1C
↓ Gewicht
↓ Systolischer Blutdruck

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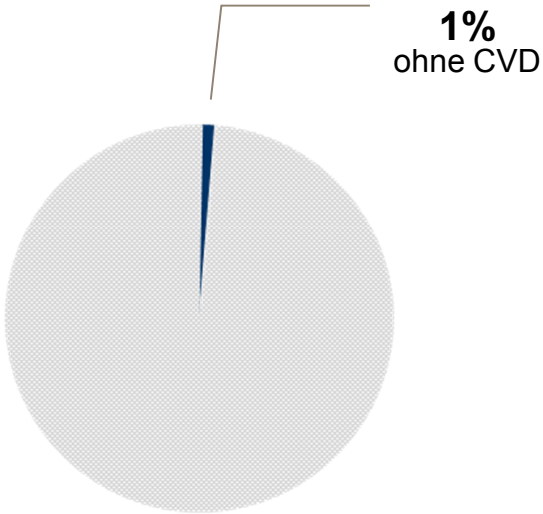
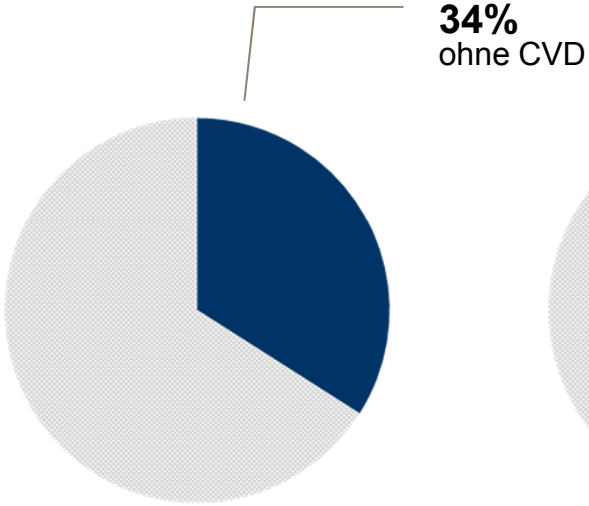
SGLT2-Inhibitoren
CV Outcome Studien

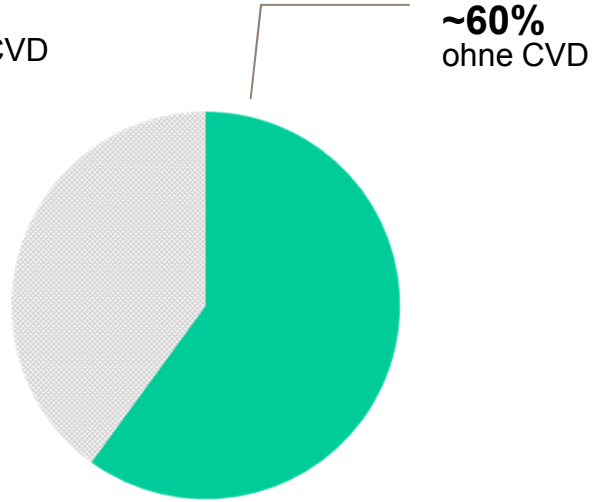
EMPA-REG OUTCOME
(N=7,020)



CANVAS
(N=10,142)



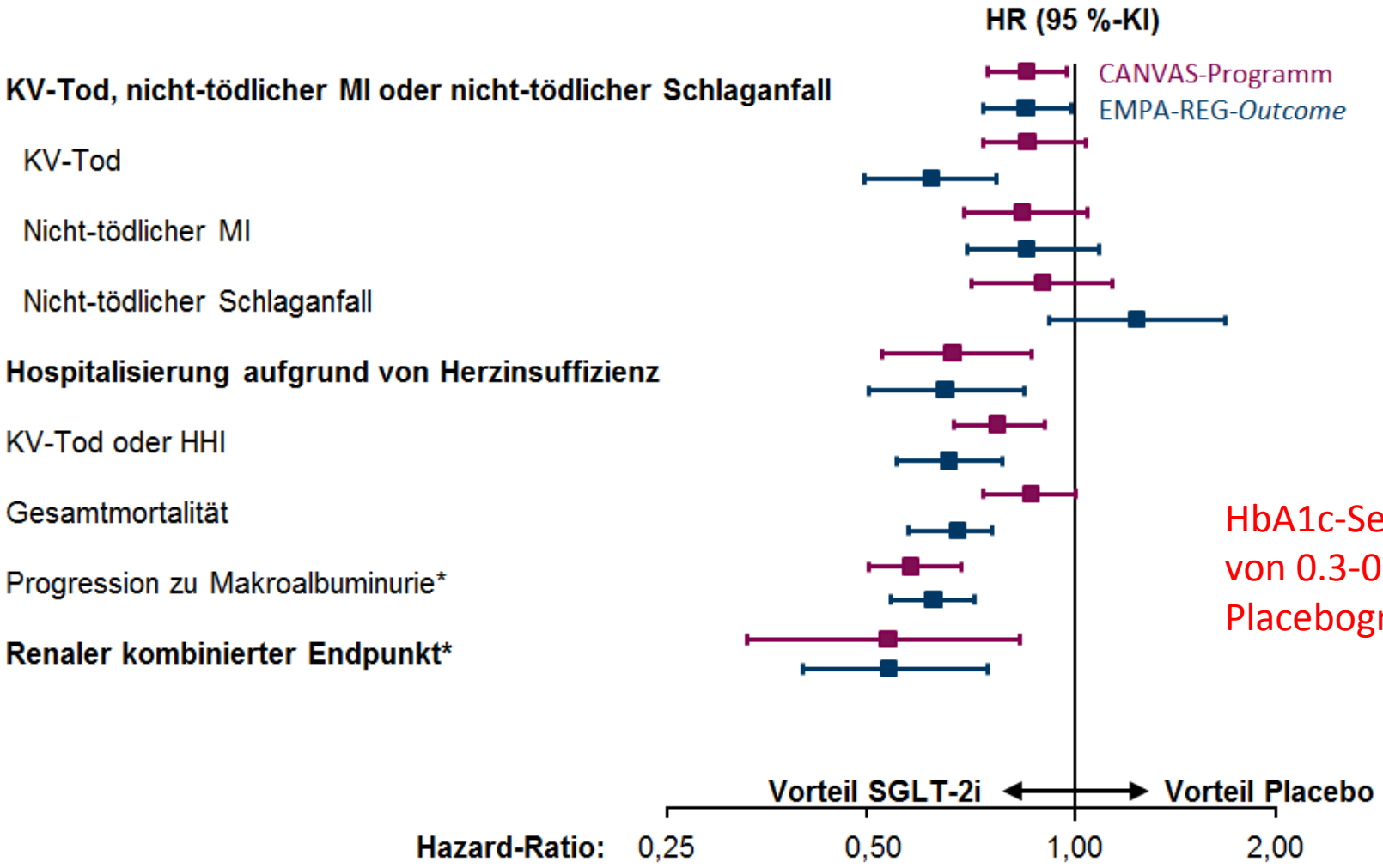
DECLARE
(N=17,160)



Zinman B, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med 2015;373:2117–2128; 2. Neal B, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med 2017 377:644-57; 3. Sattar N. Revisiting the links between glycaemia, diabetes and cardiovascular disease. Diabetologia (2013) 56:686–695; 4. Raz I, et al. DECLARE-TIMI 58: Participants' baseline characteristics. *Diabetes Obes Metab* 2018. http://dx.doi.org/10.1111/dom.13217.

CANVAS-Studienprogramm und EMPA-REG:

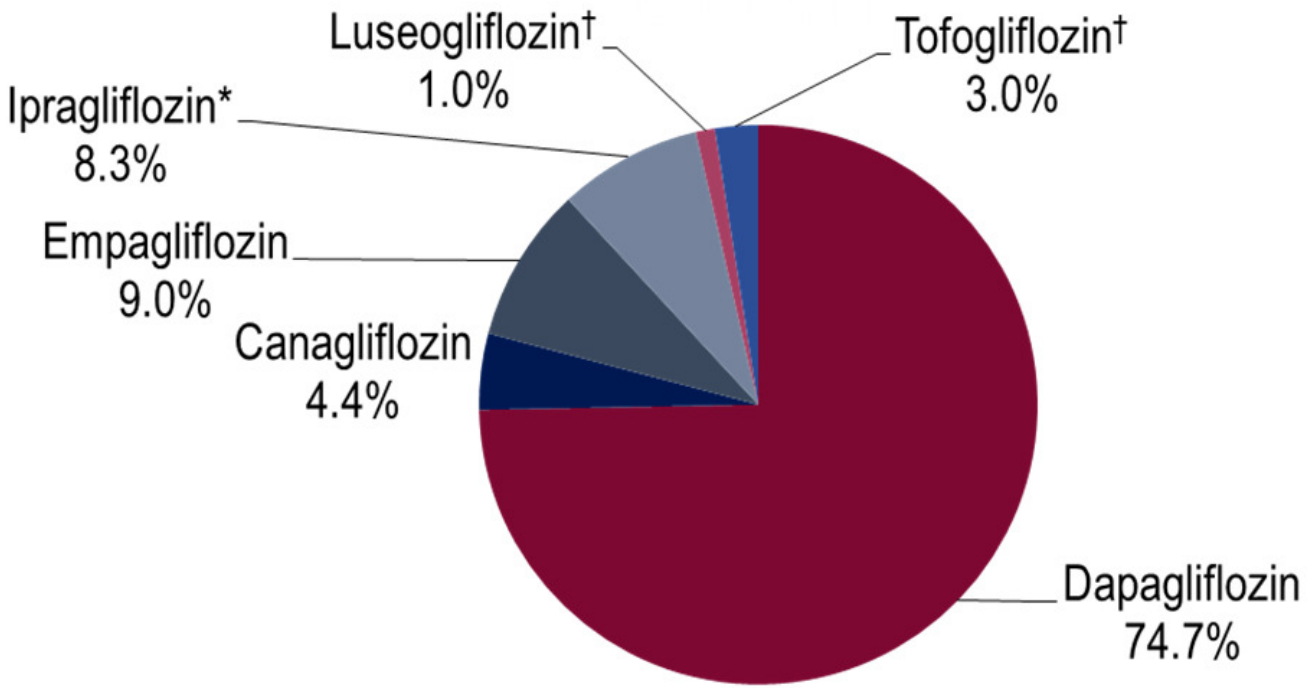
Wichtigste Ergebnisse im Vergleich



HbA1c-Senkung von 0.3-0.4% vs Placebogruppe

Modifiziert nach: 1. Neal B, et al. N Engl J Med 2017.; 2. Wanner C, et al. N Engl J Med 2016; 375:323-34; 3. Präsentiert auf den American Diabetes Association 77th Scientific Sessions San Diego, CA, June 9–13, 2017.

SGLT2-i: Klasseneffekt?
CVD-Real 2



- Multinationale Studie
- N>400.000 Patienten
- 87% der Patienten ohne vorbestehende CVD

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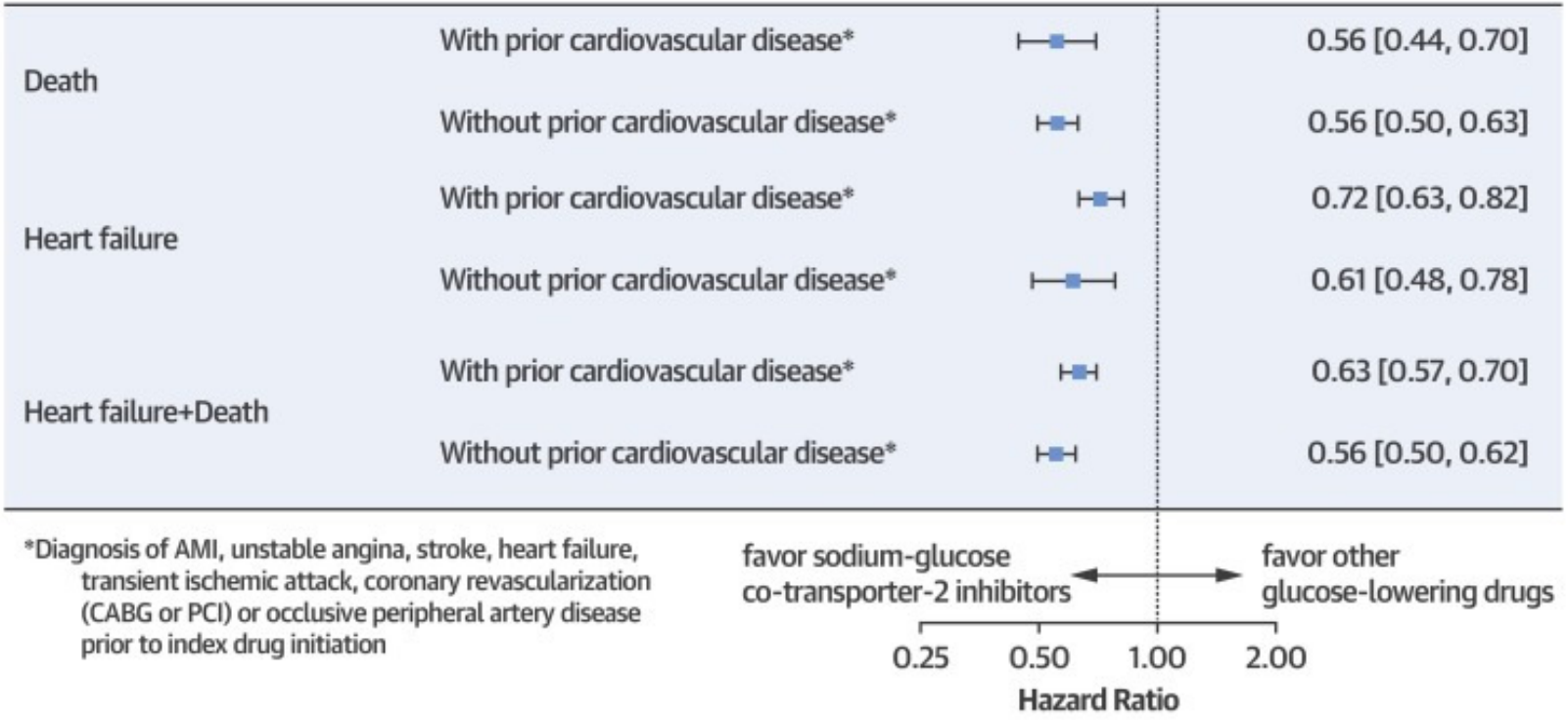
Kosiborod M et al., Lower Cardiovascular Risk Associated with SGLT-2i in >400,000 Patients: The CVD-REAL 2 Study. J Am Coll Cardiol. 2018 Mar 7. doi: 10.1016/j.jacc.2018.03.009.

CVD-Real2
Ergebnisse

CENTRAL ILLUSTRATION: Sodium-Glucose Co-Transporter-2 Inhibitors in Patients With and Without Cardiovascular Disease



Cavender, M.A. et al. J Am Coll Cardiol. 2018;71(22):2497-506.

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SGLT2-i
Unerwünschte Wirkungen

UA	Canagliflozin	Dapagliflozin	Empagliflozin
Urogenitalinfekte	x	x	x
Ketoazidose	x	x	x
Hypotonie	x	x	x
Amputationen	X		
Frakturen	x		

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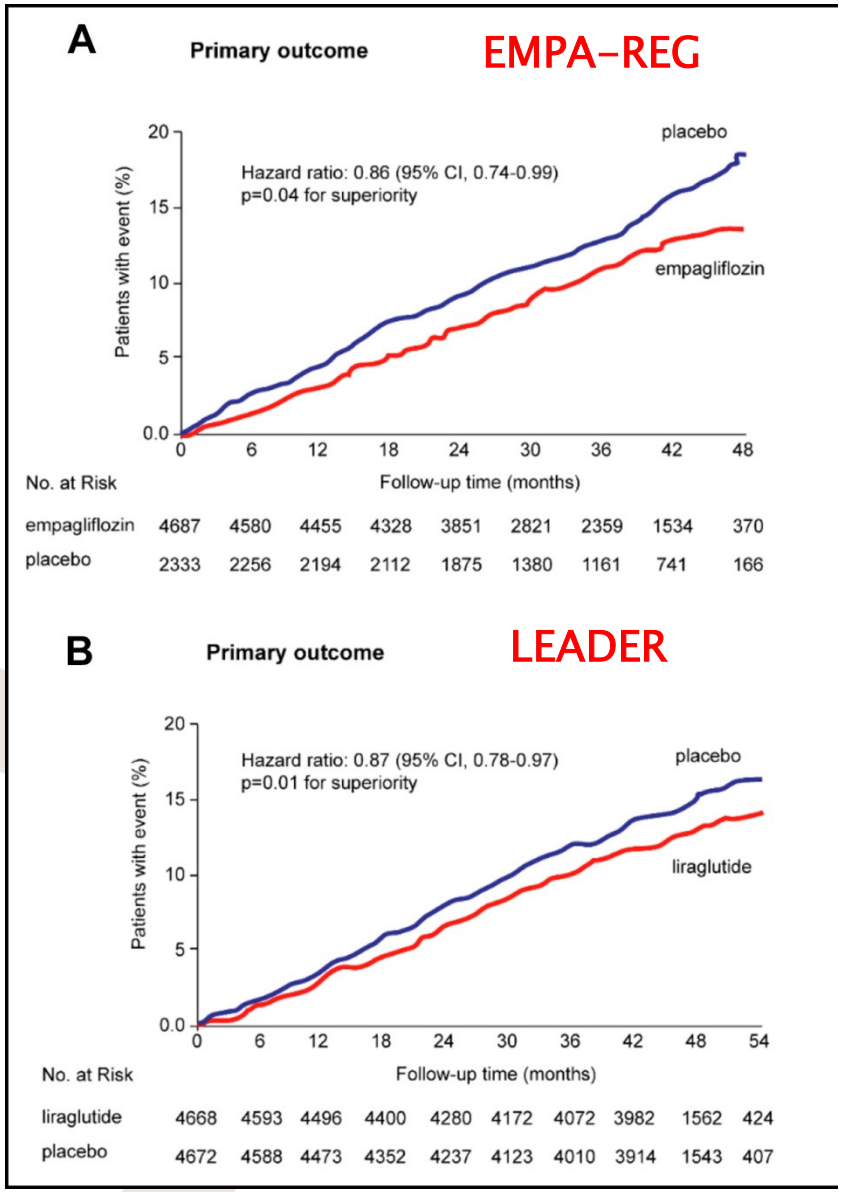
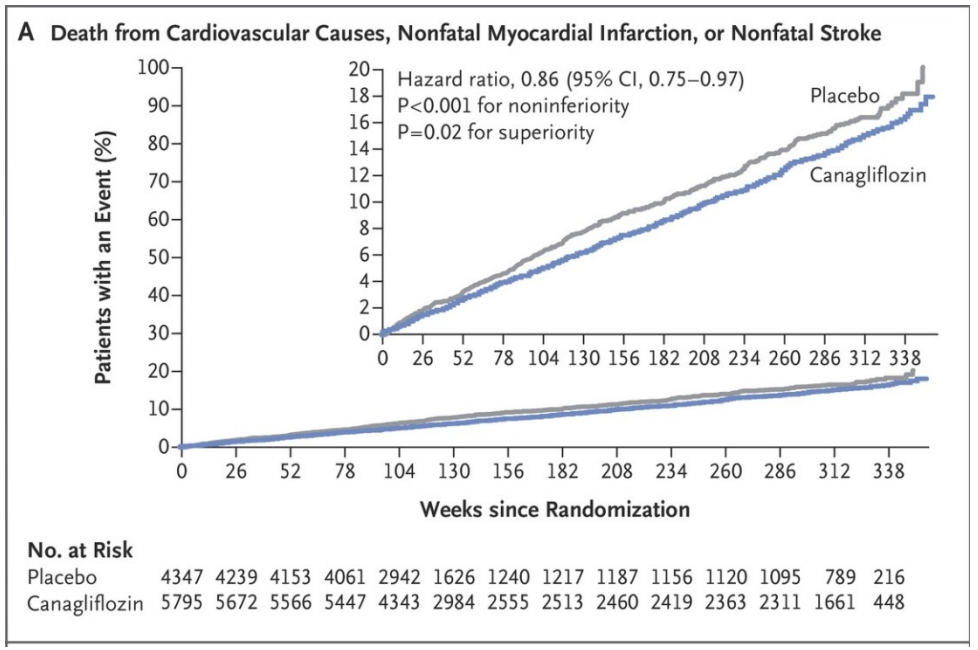
Neue Antidiabetika
CV-Outcome im Vergleich

Trial	EMPA-REG	CANVAS	LEADER
	Empagliflozin	Canagliflozin	Liraglutide
Vorherige CVD (%)	99	65	81
3 pt MACE	**0.86**	**0.86**	**0.87**
CV-Tod	0.62	0.87	0.78
Herzinsuffizienz	0.65	0.67	0.87
Gesamtmortalität	0.68	0.87	0.85
Gewichtsverlust	**k.A.**	**-1.6 kg**	**-2.3 kg**

EMPA-REG vs LEADER vs CANVAS



CANVAS



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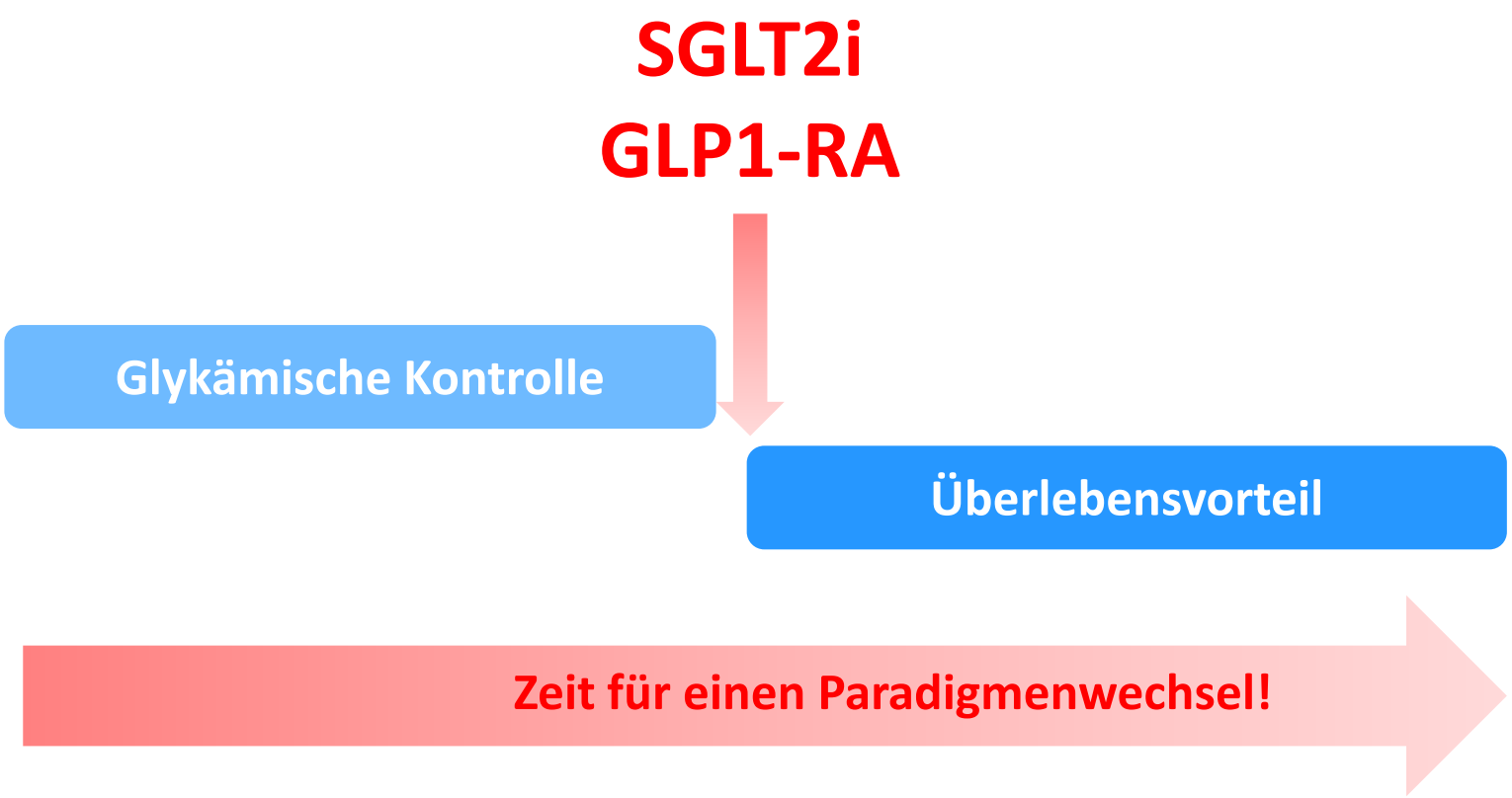
In besten Händen.

Diabetes und Herz – Beginn einer neuen Ära?

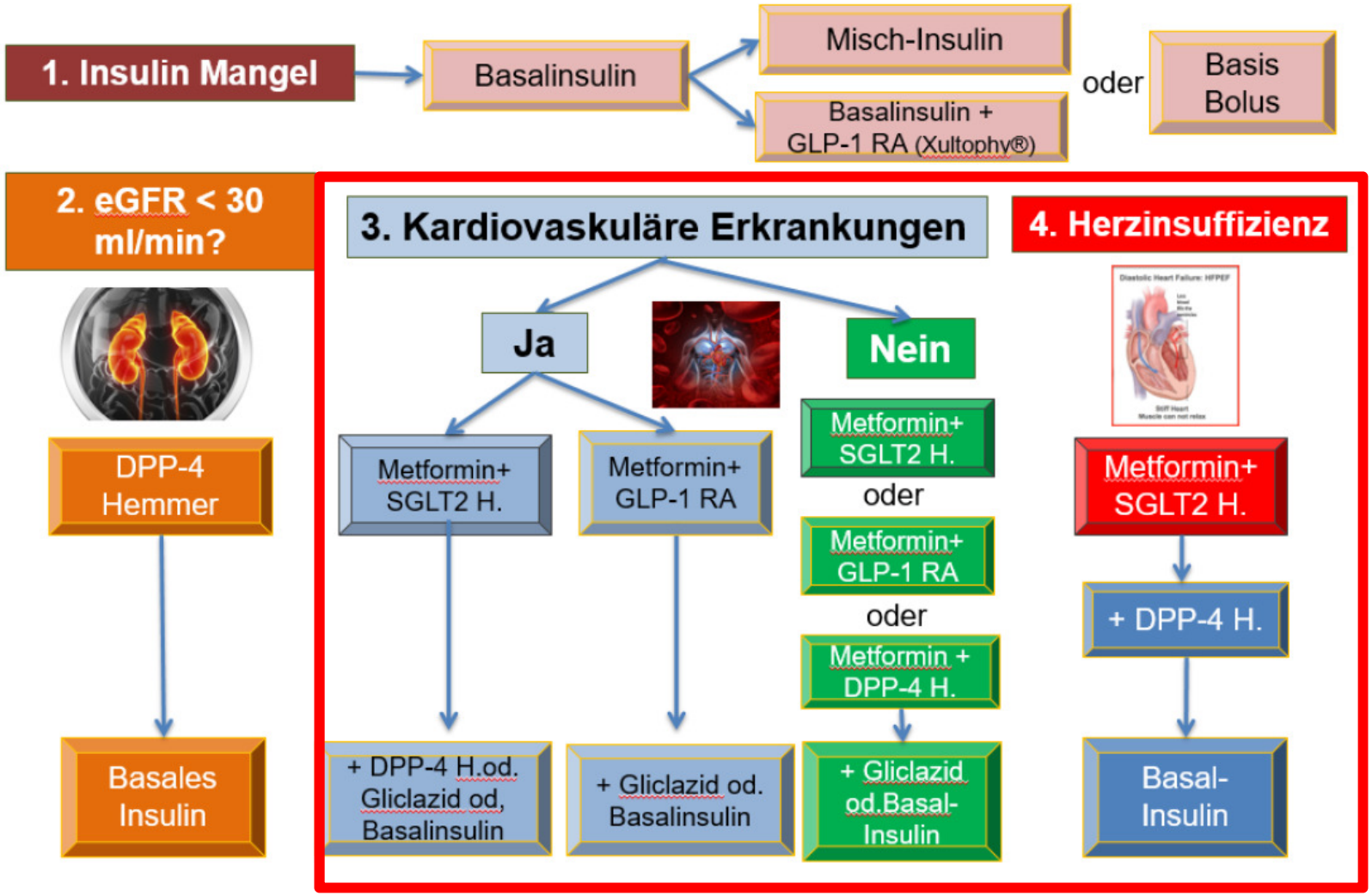


Zeit für einen Paradigmenwechsel?

News > Medscape Medical News > Conference News > ADA 2018

New ADA/EASD Guidance on Diabetes: Assess CV Status First

Flow Chart Schweizerische Empfehlungen 2016



Flow Chart erstellt durch R. Lehmann, Vorsitzender der Arbeitsgruppe **revidiert März 2017**

ESC-Guidelines

Recommendations	Class	Level
Metformin is recommended as first-line therapy, if tolerated and not contra-indicated, following evaluation of renal function.	I	B
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
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
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
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

Diabetologie und Kardiologie:

Verschiedene Fachrichtungen – Ein gemeinsames Interesse!