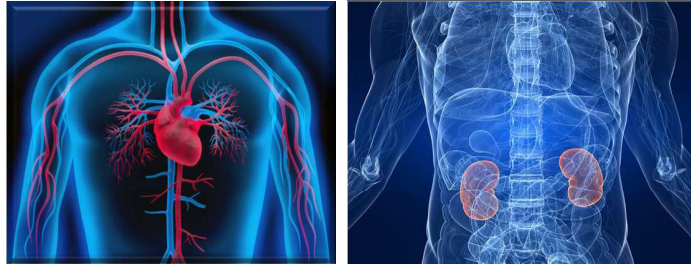


Moderne Therapie des Diabetes

Was können wir besser als vor 10 Jahren
und ist es das wert?



Peter Wiesli
Kantonsspital Frauenfeld



Effects of Intensive Glucose Lowering in Type 2 Diabetes
The Action to Control Cardiovascular Risk in Diabetes Study Group*

16% der Patienten Hypoglykämie Grad II-III

Table 3. Adverse Events, Clinical Measures, Tobacco Use, and Use of Nonglycemic Medication after Randomization.*

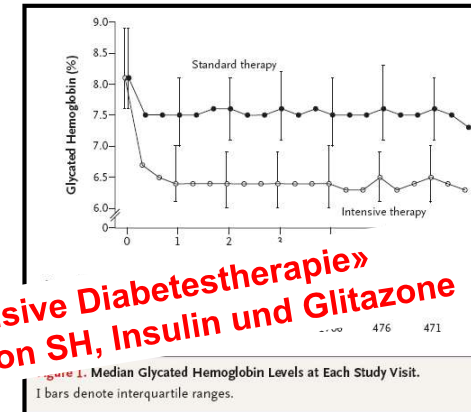
Variable	Intensive Therapy (N = 5128)	Standard Therapy (N = 5123)	P Value†
Adverse events			
Hypoglycemia — no. (%)			
Requiring medical assistance	538 (10.5)	179 (3.5)	<0.001
Requiring any assistance	830 (16.2)	261 (5.1)	<0.001
Fatal or nonfatal heart failure — no. (%)	152 (3.0)	124 (2.4)	0.10
Motor vehicle accident in which patient was driver — no./total no. (%)	9/5033 (0.2)	14/5036 (0.3)	0.40

ACCORD, N Engl J Med 2008; 358: 2545



Effects of Intensive Glucose Lowering in Type 2 Diabetes
The Action to Control Cardiovascular Risk in Diabetes Study Group*

Ziel
HbA1c 7-8%
HbA1c <6%

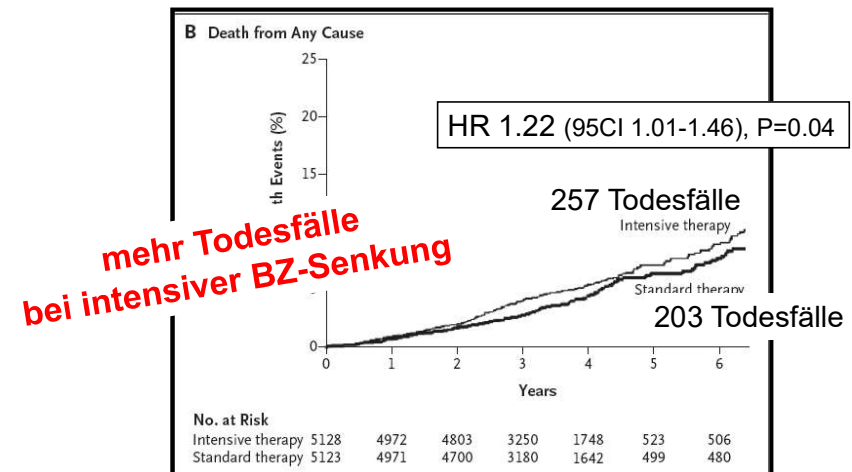


erreicht
HbA1c 7.5%
HbA1c 6.4%

«Intensive Diabetestherapie»
Kombination SH, Insulin und Glitazone

ACCORD, N Engl J Med 2008; 358: 2545

ACCORD: Vorzeitiger Abbruch



mehr Todesfälle
bei intensiver BZ-Senkung

ACCORD, N Engl J Med 2008; 358: 2545

Was können wir besser als vor 10 Jahren

Diabetestherapie 2019 vs 2009

Weniger Hypoglykämien
Gewichtsabnahme statt Gewichtszunahme
Nephroprotektion
Reduktion kv Ereignisse/Herzinsuffizienz
Reduktion Mortalität

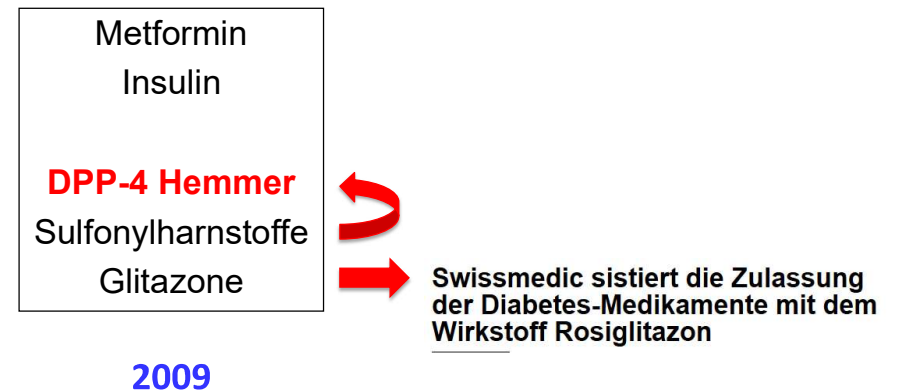
und ist es das wert?

DPP-4 Hemmer



Wirksubstanz	Name	Kombination Metformin	Kombination SGLT-2
Sitagliptin	Januvia Xelevia	Janumet Velmetia	Steglujan
Vildagliptin	Galvus	Galvumet	
Saxagliptin	Onglyza	Kombiglyze XR	Qtern
Linagliptin	Trajenta	Jentadueto	Glyxambi
Alogliptin	Vipidia	Vipdomet	

Moderne Therapie des Typ 2 Diabetes mellitus



DPP-4 Hemmer: Linagliptin

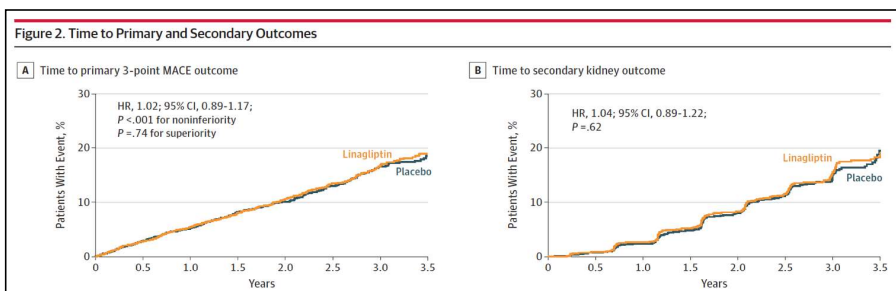
Research

JAMA | Original Investigation

Effect of Linagliptin vs Placebo on Major Cardiovascular Events in Adults With Type 2 Diabetes and High Cardiovascular and Renal Risk
The CARMELINA Randomized Clinical Trial

Hohes kardiales und renales Risiko (kv Erkrankung, Niereninsuff., Albuminurie)
6991 Patienten, 66y, eGFR 55, 80% UACR >30mg/g

DPP-4 Hemmer: Linagliptin



Kardiovaskuläre Sicherheit
aber kardiovaskulär oder renal KEINE Vorteile

Rosenstock et al, JAMA 2019; 32: 69

DPP-4 Hemmer: Linagliptin

Table 3. Adverse Events, Including Hypoglycemic Events, by Treatment Group^a

Adverse Events	No. (%) Linagliptin (n = 3494)	Placebo (n = 3485)
Any adverse events	2697 (77.2)	2723 (78.1)
Serious adverse events	1293 (37.0)	1343 (38.5)
Adverse events leading to study drug discontinuation	359 (10.3)	402 (11.5)
Hypersensitivity reactions ^b	114 (3.3)	109 (3.1)
Angioedema events with concomitant ACE inhibitor/ARB use at baseline	13 (0.5)	16 (0.6)
Pemphigoid	7 (0.2)	0 (0.0)
Skin lesions	5 (0.1)	1 (<0.1)
Acute pancreatitis (adjudication confirmed)	9 (0.3) ^c	5 (0.1)
Chronic pancreatitis (adjudication confirmed)	2 (0.1)	3 (0.1)
All cancers	116 (3.3)	134 (3.8)
Colon cancer	6 (0.2)	8 (0.2)
Pancreatic cancer (adjudication confirmed)	11 (0.3)	4 (0.1)
Gastric cancer	0	3 (0.1)
Hypoglycemic events		
Investigator-reported hypoglycemia	1036 (29.7)	1024 (29.4)
Confirmed hypoglycemic adverse events with plasma glucose <54 mg/dL (<3.0 mmol/L) or severe events ^d	557 (15.9)	572 (16.4)
Severe events ^d	106 (3.0)	108 (3.1)

Nebenwirkungen wie Placebo

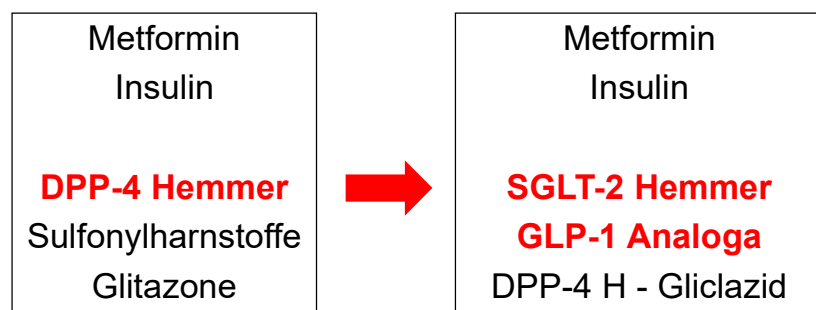
Pankreatitis (selten)

Pemphigoid (selten)



Rosenstock et al, JAMA 2019; 32: 69

Moderne Therapie des Typ 2 Diabetes mellitus



SGLT-2 Hemmer: Präparate

Wirksubstanz	Name	Kombination Metformin
Canagliflozin	Invokana	Vokanamet
Dapagliflozin	Forxiga	Xigduo XR
Empagliflozin	Jardiance	Jardiance Met
Ertugliflozin	Steglatro	Stegluromet

SGLT-2 Inhibitor Empagliflozin:

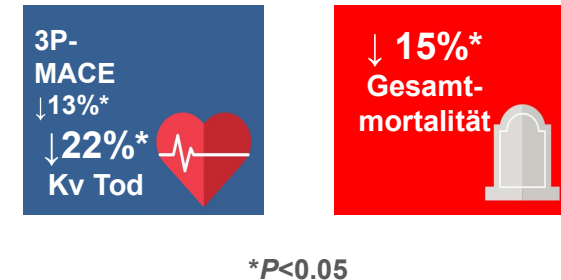
EMPA-REG OUTCOME = erste Endpunktstudie mit Nutzen



Zinman et al. N Engl J Med 2015;373:2117–28.

GLP-1 Rezeptoragonist Liraglutid:

LEADER= zweite Endpunktstudie mit Nutzen



Marso SP et al. N Engl J Med 2016;375:311–322.

GLP-1 Agonisten: kv Benefit



täglich				wöchentlich	
Lyxumia (Lixisenatid)	Byetta (Exenatid)	Victoza (Liraglutid)	Trulicity (Dulaglutid)	Bydureon (Exenatid)	Ozempic (Semaglutid)
1x täglich	2x täglich	1x täglich	1x Woche	1x Woche	1x Woche
					

Klinische Zeichen Insulinmangel

Polyurie, Polydipsie, Gewichtsabnahme
Ketonurie



Primär Insulintherapie



Beurteilung Diabetestyp und Management
nach Rekompensation

initial kein SGLT-2 Hemmer
evt nach Rekompensation (in Kombination mit Insulin)



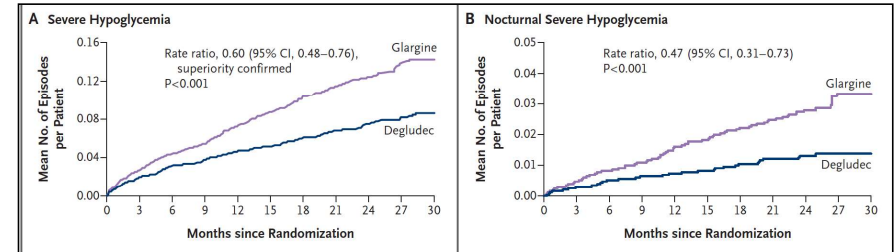
Basalinsuline

NPH	Detemir	Glargin100	Glargin100	Glargin300	Degludec
Insulatard	Levemir	Lantus	Abasaglar	Toujeo	Tresiba
					

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy and Safety of Degludec versus Glargine in Type 2 Diabetes



40% tiefere Rate
schwere Hypos

53% tiefer Rate
schwere nächtliche Hypos

Marso et al, N Engl J Med 2017; June 12

Schwere Niereninsuffizienz: eGFR <30

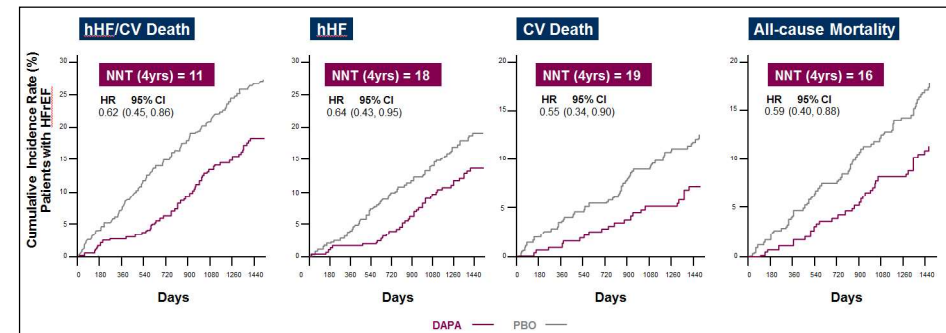
DPP-4 Hemmer

GLP-1 Analoga

Insulin



Dapagliflozin Patienten mit HFrEF



Benefit schon früh nach Beginn

Kato ET et al. Circulation 2019; in press

Dapagliflozin reduces death and hospitalisation in patients with heart failure

DAPA-HF trial presented in a Hot Line Session today at ESC Congress 2019 together with WCC

01 Sep 2019

Topic(s): *Diabetes and the Heart; Heart Failure;*

Paris, France – 1 Sept 2019: Dapagliflozin reduces death and hospitalisation in patients with heart failure and reduced ejection fraction with and without diabetes. The late breaking results of the DAPA-HF trial are presented in a Hot Line Session today at ESC Congress 2019 together with the World Congress of Cardiology(1).

Principal investigator Professor John McMurray of the University of Glasgow, UK said: "The most important finding of all is the benefit in patients without diabetes. This is truly a treatment for heart failure and not just a drug for diabetes."

He concluded: "The trial shows that dapagliflozin reduces death and hospitalisation, and improves health-related quality of life, in patients with heart failure and reduced ejection fraction, with and without diabetes. The clinical implications are potentially huge – few drugs achieve these results in heart failure and dapagliflozin does even when added to excellent standard therapy."



**SGLT-2 Hemmer bei Herzinsuffizienz (HFrEF):
Wirkung bei Patienten mit und ohne Diabetes**