

Neuigkeiten aus der Diabetologie anhand eines Fallberichtes



Prof. Dr. Burkhard L. Herrmann

Endokrinologie /// Diabetologie /// Innere Medizin

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Geringer Effekt der Flüssigmahlzeiten bei Typ-2-Diabetes mellitus

A Systematic Review and Meta-analysis of Randomized Controlled Trials

Nine trial comparisons ($N = 961$ [median follow-up **24 weeks**]) met eligibility criteria.



- 2,37 kg

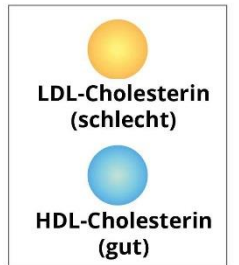
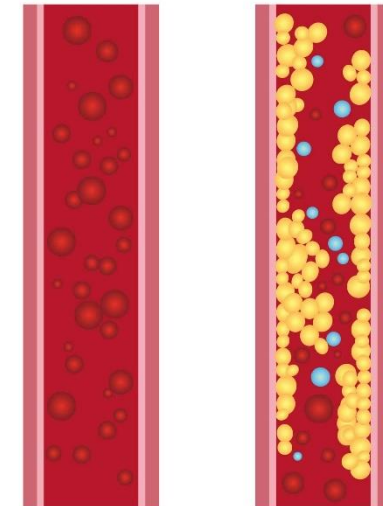


**RR [mmHg]
systol. -5 / -2 diastol.**

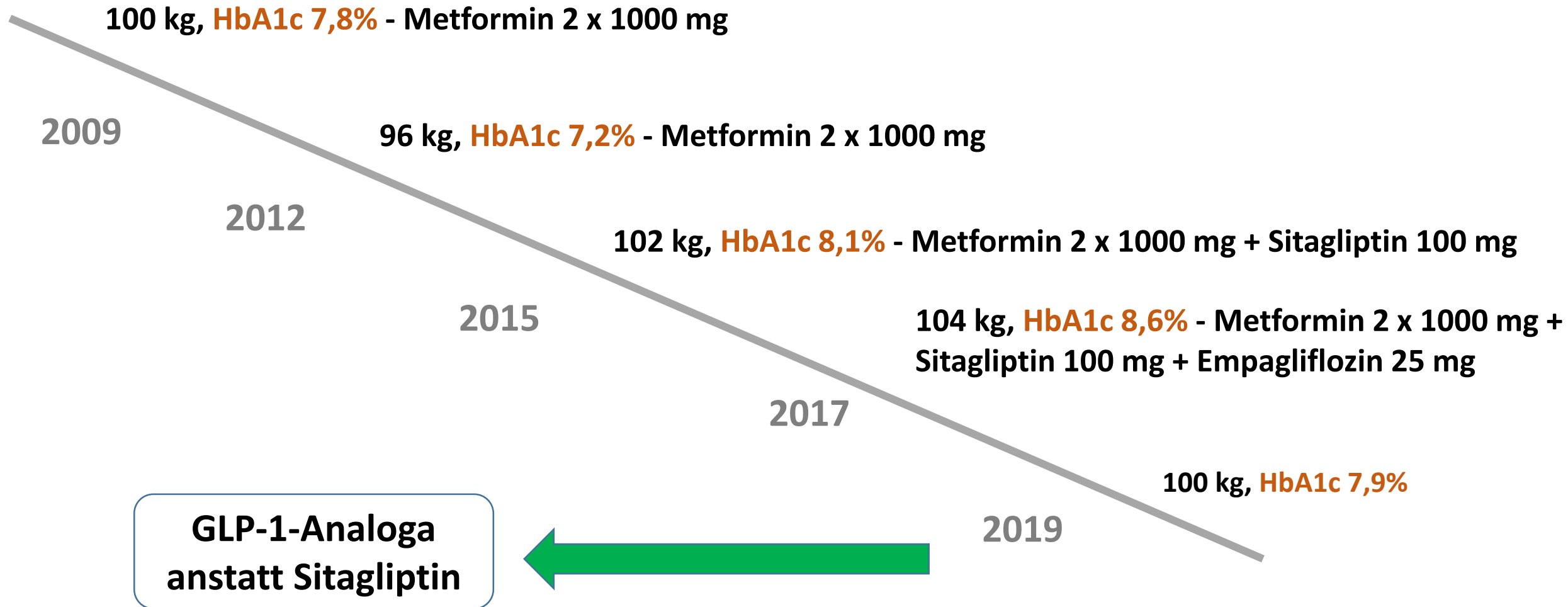


**HbA1c
-0,43%**

no change



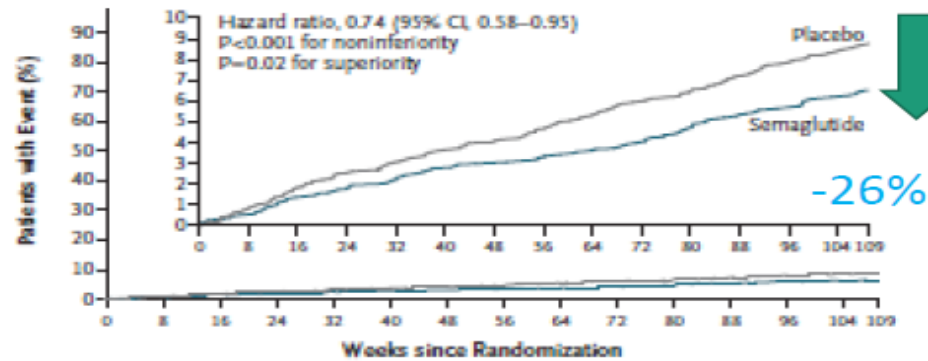
Diabetespatient, m, 183cm, geb. 13.6.1959



Semaglutide: Kardiovaskuläre Daten SUSTAIN-6 Studie

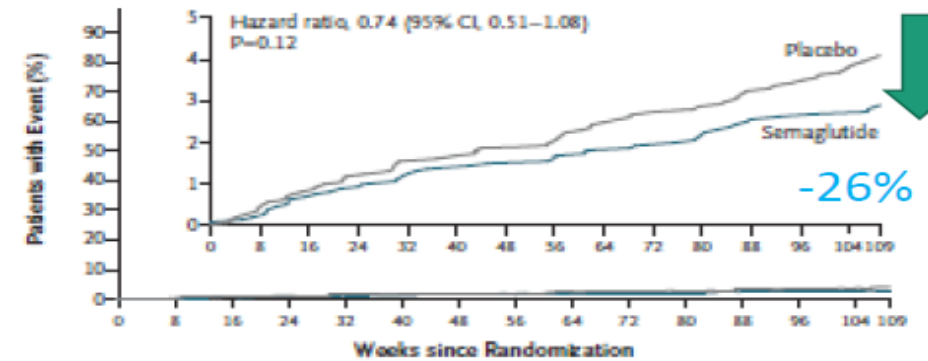
subcutan

Primärer Endpunkt (MACE-3)



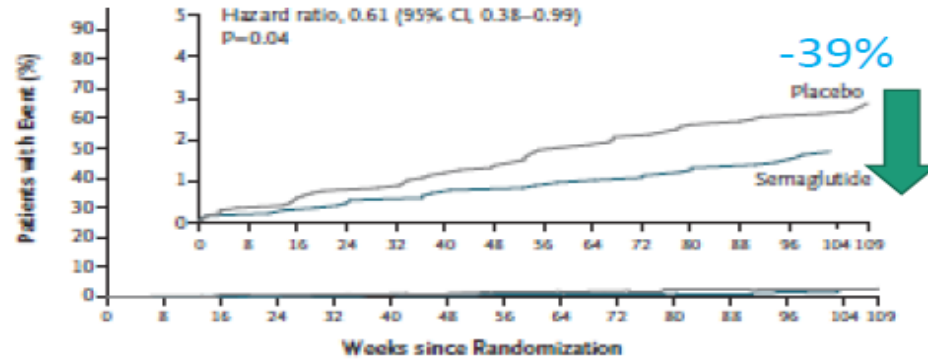
No. at Risk	0	8	16	24	32	40	48	56	64	72	80	88	96	104	109
Placebo	1649	1616	1586	1567	1534	1508	1479								
Semaglutide	1648	1619	1601	1584	1568	1543	1524								

Nicht-tödl. Myokardinfarkt



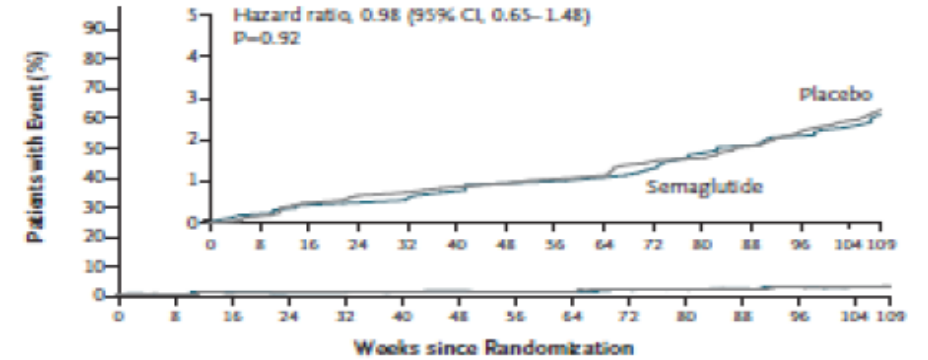
No. at Risk	0	8	16	24	32	40	48	56	64	72	80	88	96	104	109
Placebo	1649	1624	1598	1587	1562	1542	1516								
Semaglutide	1648	1623	1609	1595	1582	1560	1543								

Nicht-tödl. Schlaganfall



No. at Risk	0	8	16	24	32	40	48	56	64	72	80	88	96	104	109
Placebo	1649	1629	1611	1597	1571	1548	1528								
Semaglutide	1648	1630	1619	1606	1593	1572	1558								

Tod durch CV Ursachen



No. at Risk	0	8	16	24	32	40	48	56	64	72	80	88	96	104	109
Placebo	1649	1637	1623	1617	1600	1584	1566								
Semaglutide	1648	1634	1627	1617	1607	1589	1579								

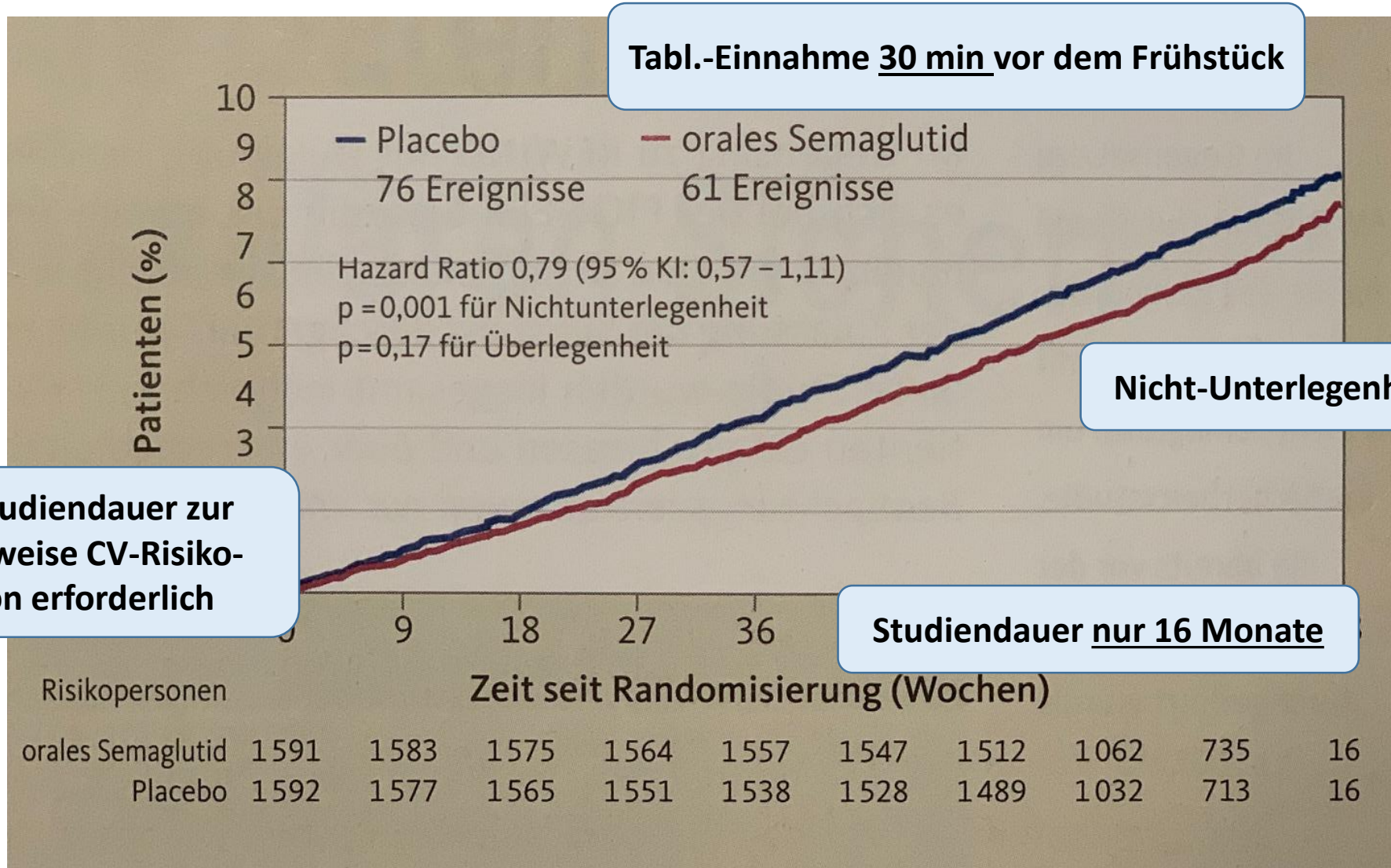
Diabetespatient, m, 183cm, geb. 13.6.1959



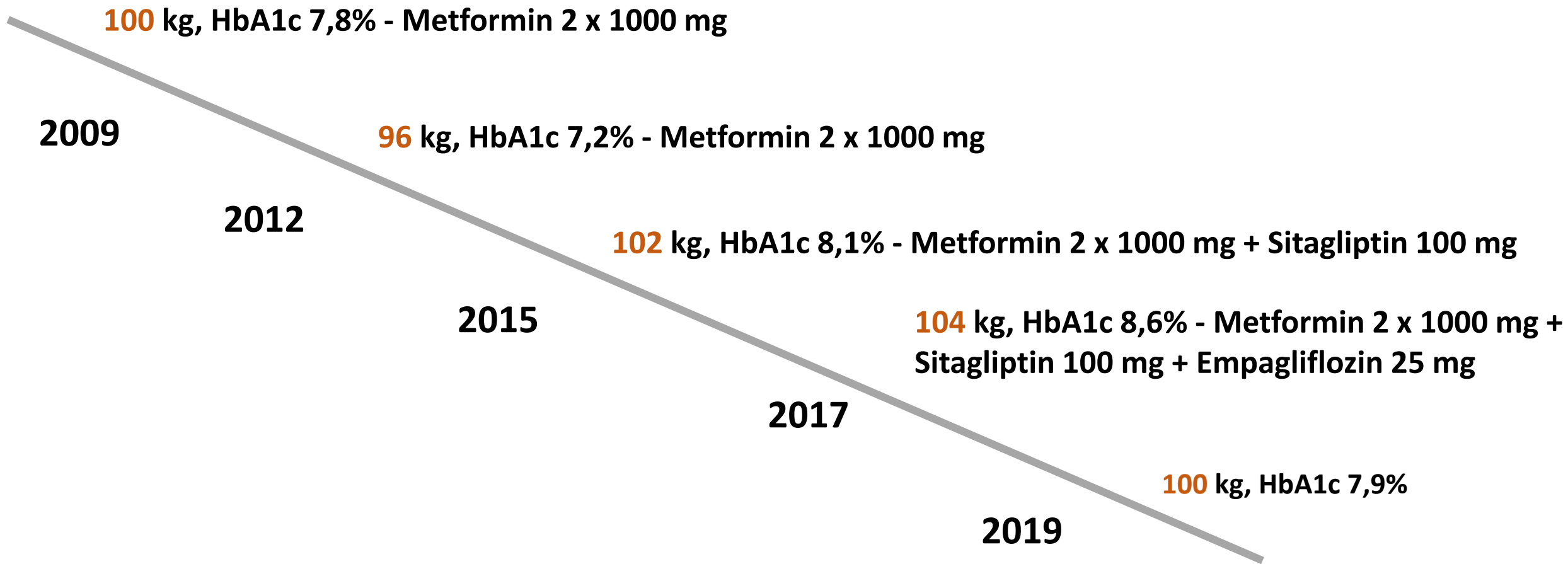
Semaglutid – ein GLP-Rezeptoragonist jetzt auch zur oralen Diabetesbehandlung

- **Injizierende Form** von **Semaglutid** bereits auf dem Markt.
- Der Zulassungsantrag für **orales Semaglutid** wurde im April 2019 bei der FDA und EMA eingereicht.
- Die günstigen Effekte von **1x wöchentlich s.c. Semaglutid** wie in der **SUSTAIN-6-Studie (2)** zeigten sich auch bei der **oralen Form von Semaglutid** wie Senkung von HbA1c und Gewicht (**PIONEER-6**).
- **Kardiovaskuläre (CV) Ereignisse** wurden mit der oralen Form **jedoch nicht in signifikantem** Ausmass gesenkt (um 21%, $p=0.17$).
- Gegenüber Plazebo bestand somit **nur eine Nicht-Unterlegenheit**.

Semaglutid – ein GLP-Rezeptoragonist jetzt auch zur oralen Diabetesbehandlung



Gewichtszunahme - Diabetespatient, m, 183cm, geb. 13.6.1959

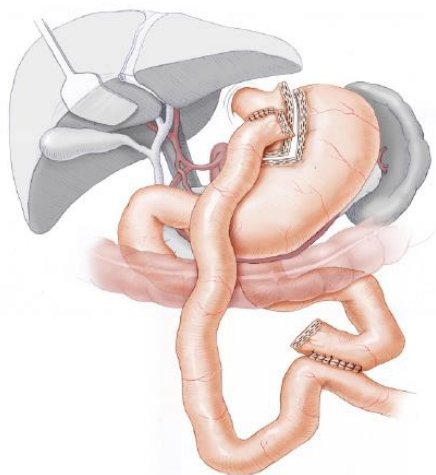




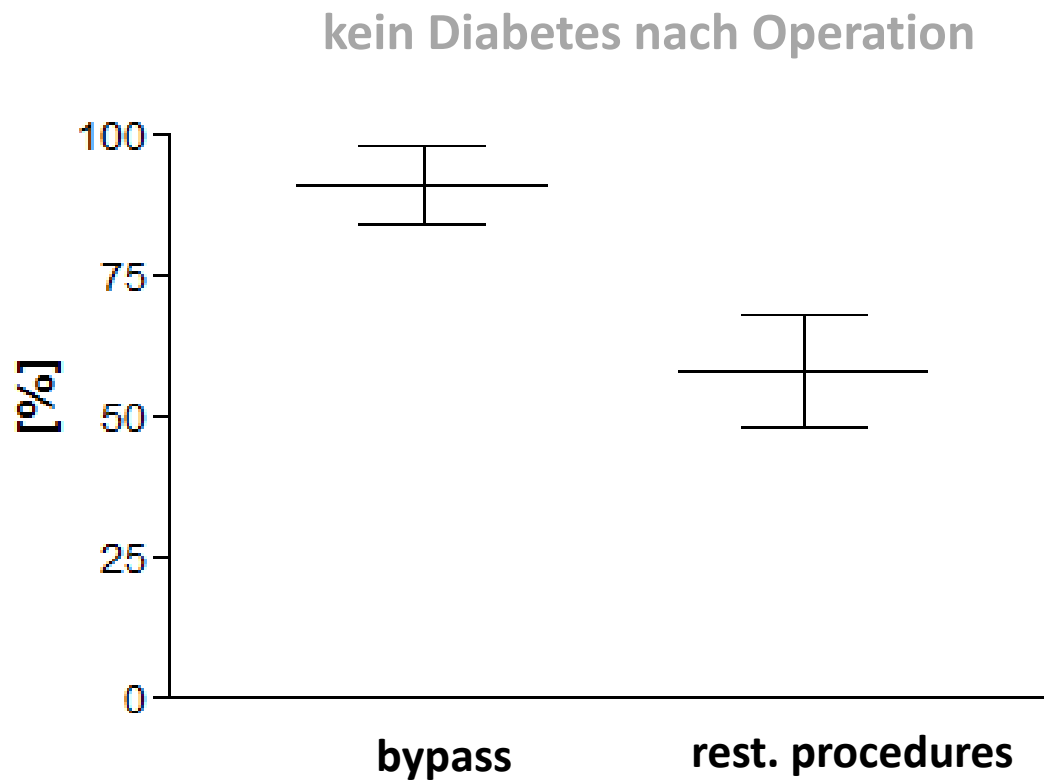
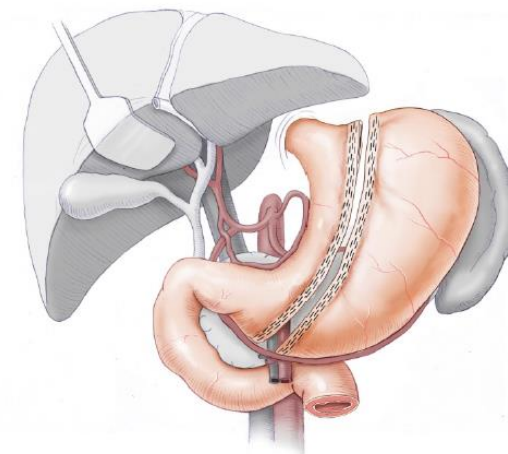
Blutzucker ↑

Magenoperationen heilt Typ 2 Diabetes mellitus

Magen-Bypass
(Roux-en-Y-Bypass)



Schlauchmagen (Sleeve)



Medikamentöse Adipositas-Therapie

Abdominelle Adipositas

	Erhöhtes Risiko	Abdominelle Adipositas
Männer	94 cm	102 cm
Frauen	80 cm	88 cm

Tab. 3

Indikationen zur zusätzlichen Pharmakotherapie der Adipositas

- Patienten mit BMI > 30, die mit Basisprogrammen keine ausreichende Gewichtsreduktion, d.h. keine Gewichtsabnahme von >5% innerhalb drei bis sechs Monaten erzielen konnten.
- Patienten mit BMI > 27, die zusätzlich gravierende Risikofaktoren und/oder Komorbiditäten aufweisen und bei denen die Basistherapie nicht erfolgreich war.

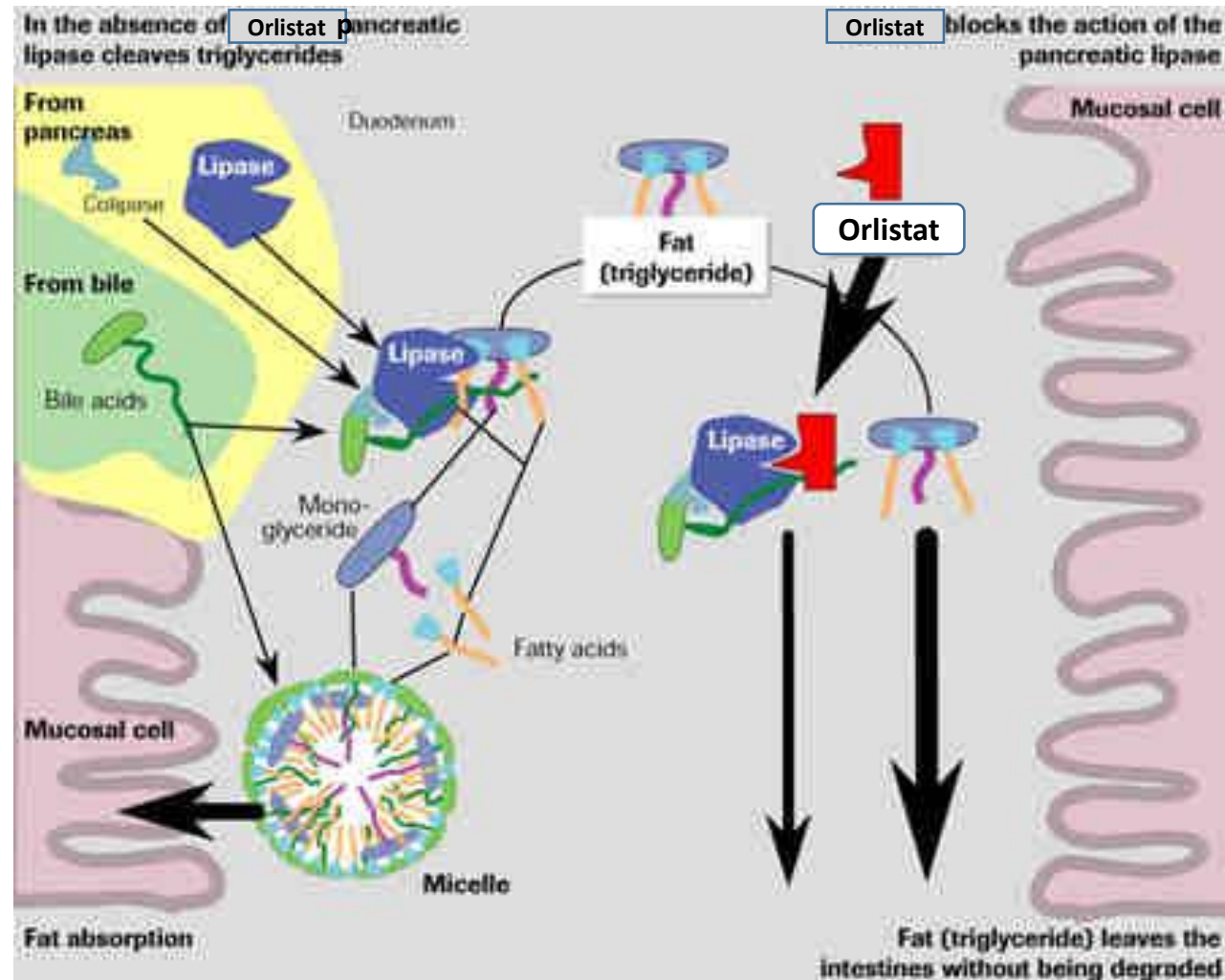
Tab. 4

Medikamentöse Adipositas-Therapie

Orlistat

Lorcaserin

Liraglutide



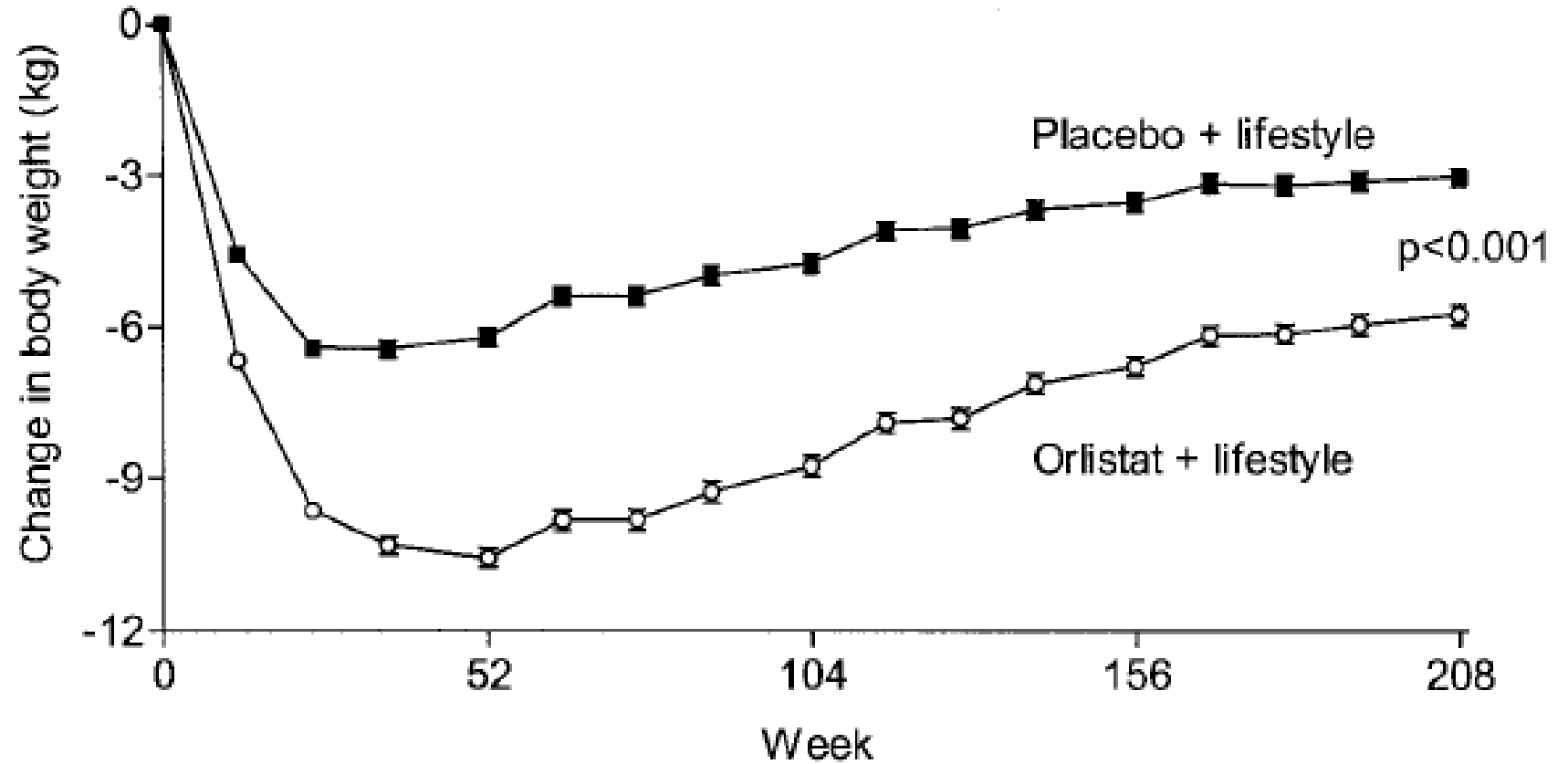
Medikamentöse Adipositas-Therapie

Orlistat

3 x120 mg

Lorcaserin

Liraglutide



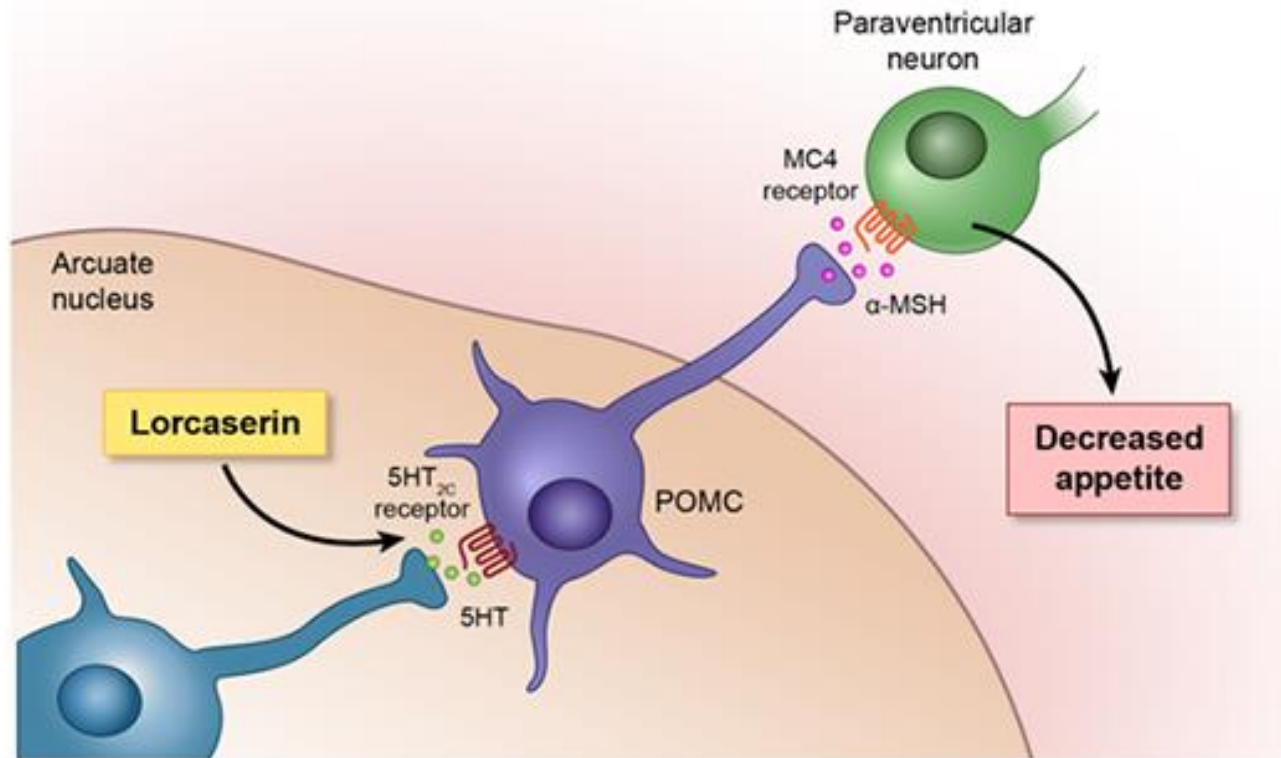
Medikamentöse Adipositas-Therapie

Orlistat

Lorcaserin

Liraglutide

Serotoninagonist zur Appetitzügelung

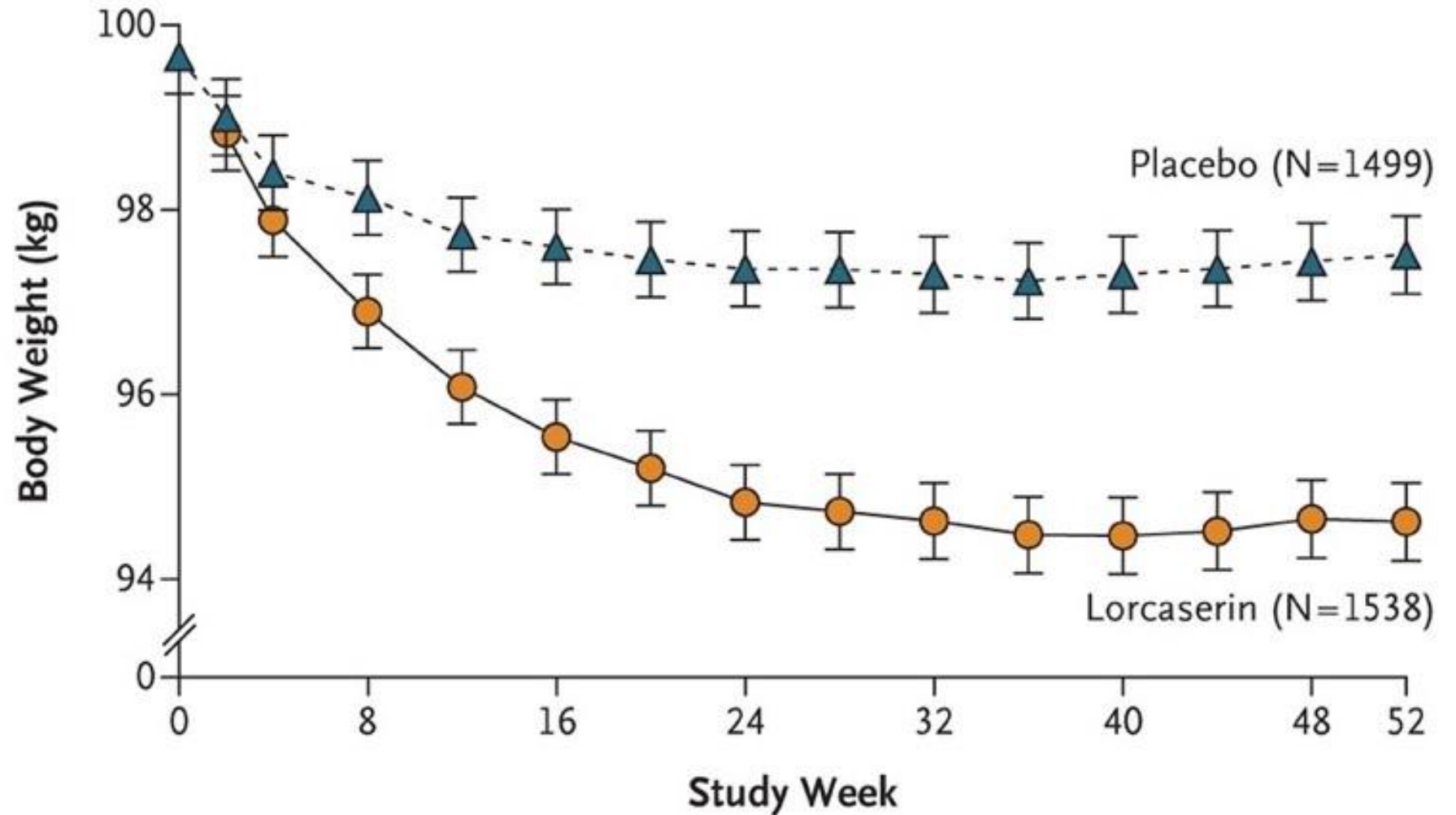


Medikamentöse Adipositas-Therapie

Orlistat

Lorcaserin
10 mg

Liraglutide



Medikamentöse Adipositas-Therapie

Orlistat

Lorcaserin

Liraglutide

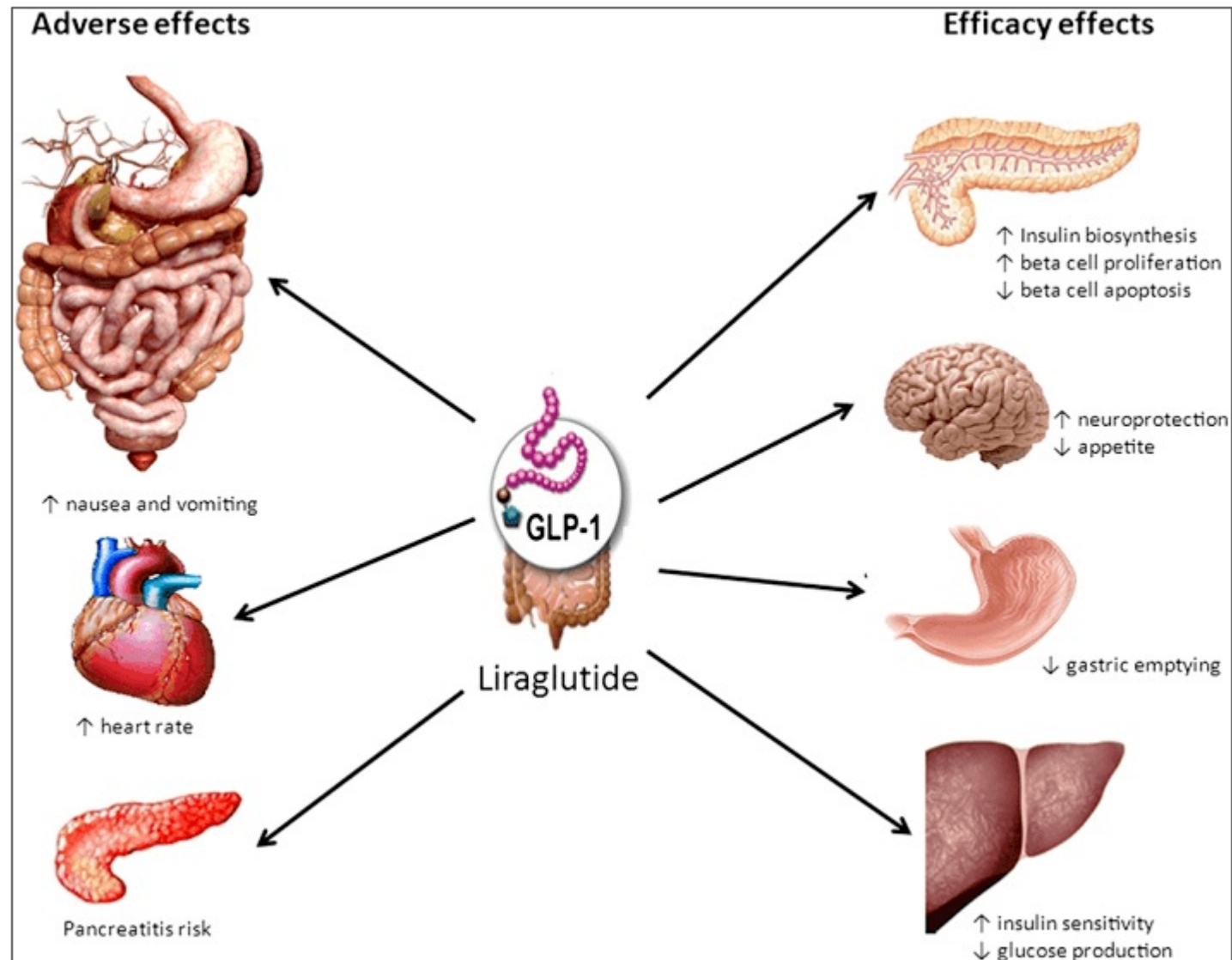


Figure 1

Effects of liraglutide (GLP-1 receptor agonist) – Efficacy and Adverse Effects Liraglutide causes a glucose dependent stimulation of insulin secretion, reduction in plasma glucagon concentrations, delayed gastric emptying, appetite suppression ...

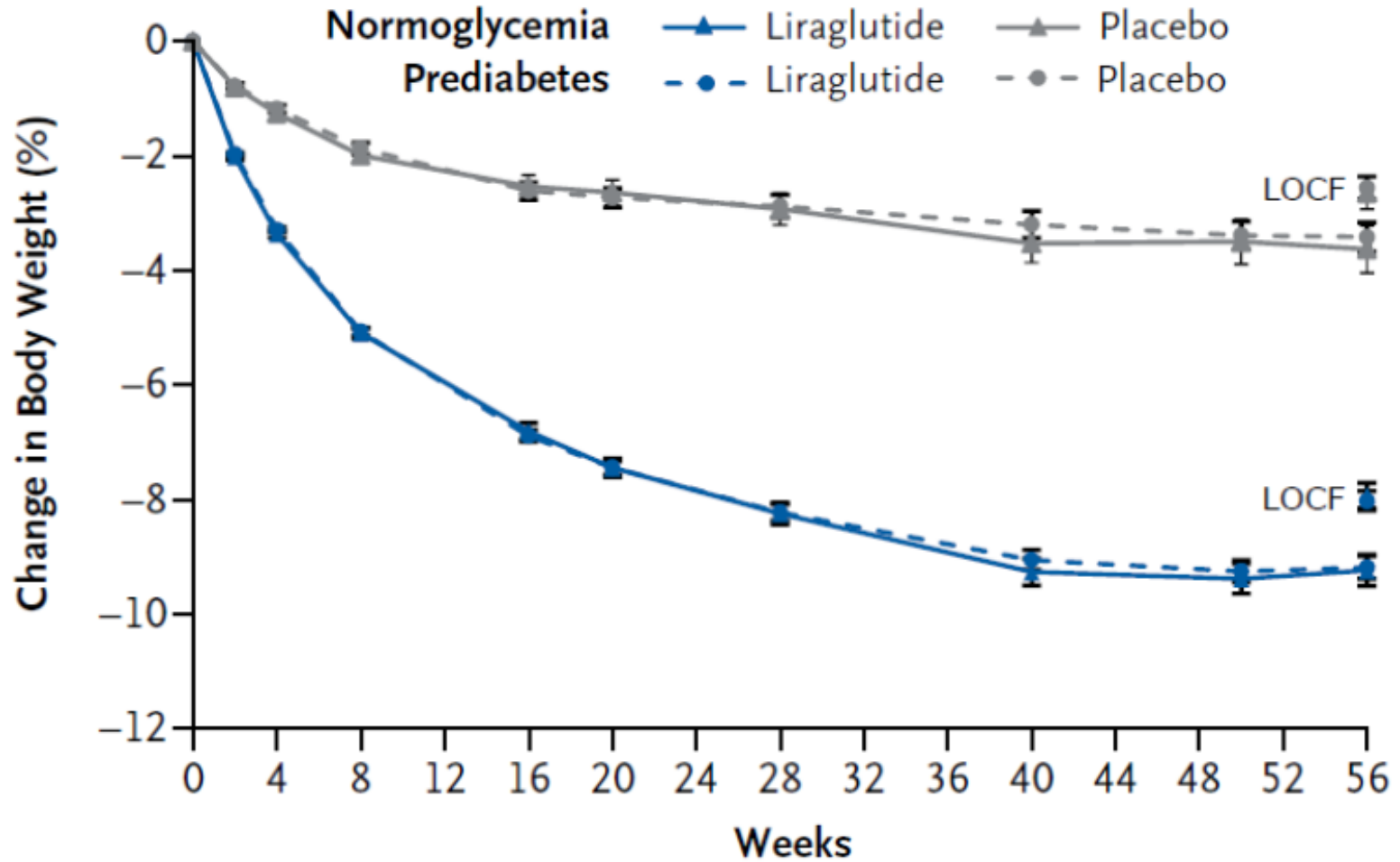
Medikamentöse Adipositas-Therapie

Orlistat

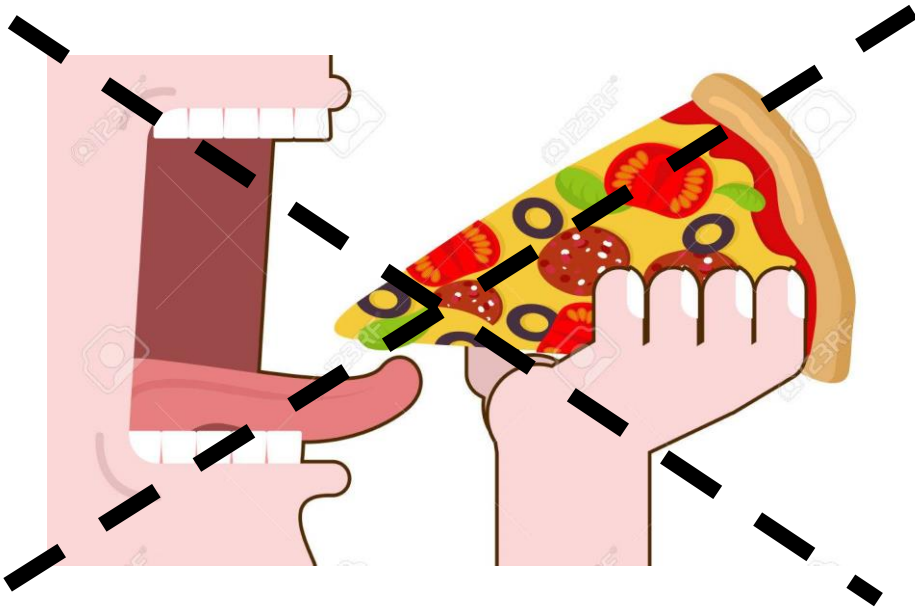
Lorcaserin

Liraglutide

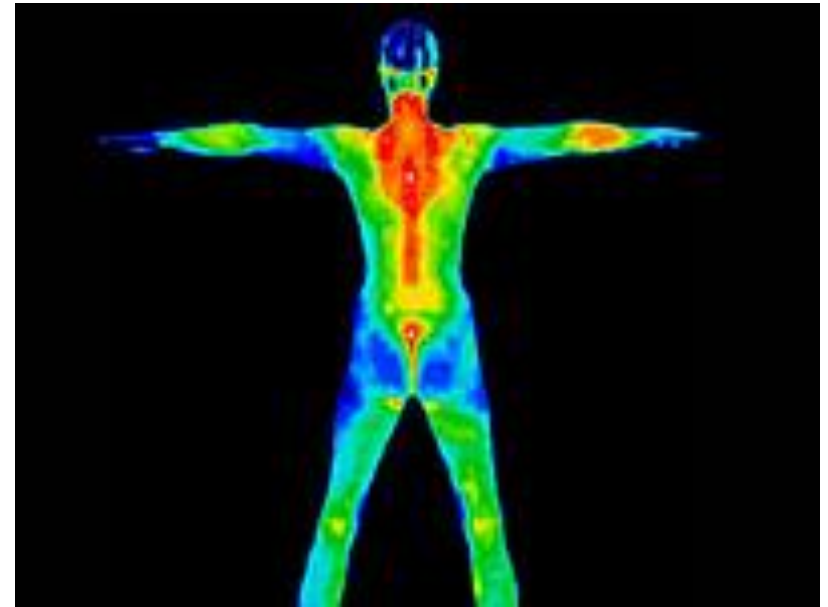
3 mg s.c.



Ziel

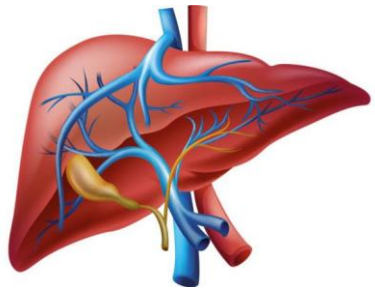


Nahrungsaufnahme ↓

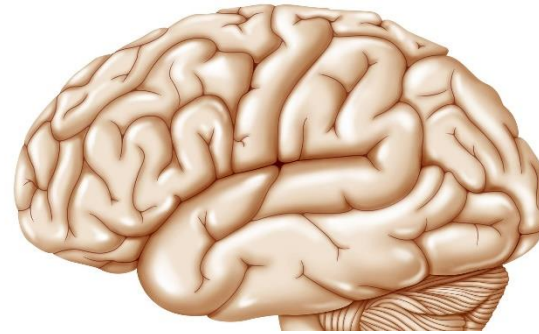


Energieumsatz ↑

Glucagon



Glucosefreisetzung ↑



Sättigung ↑



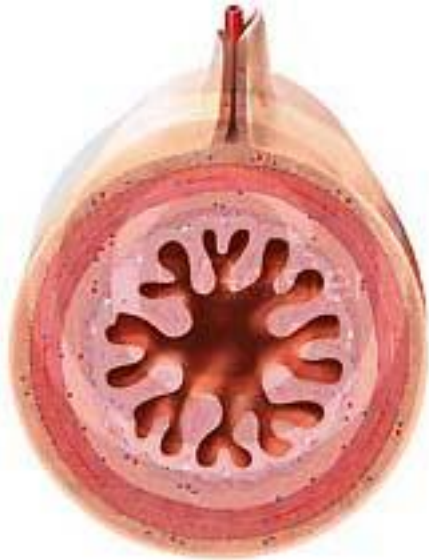
Lipolyse ↑



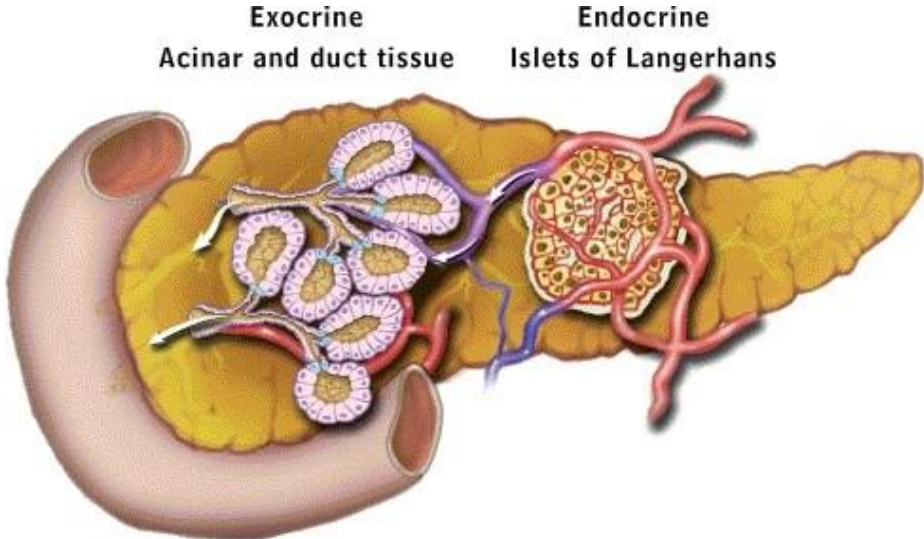
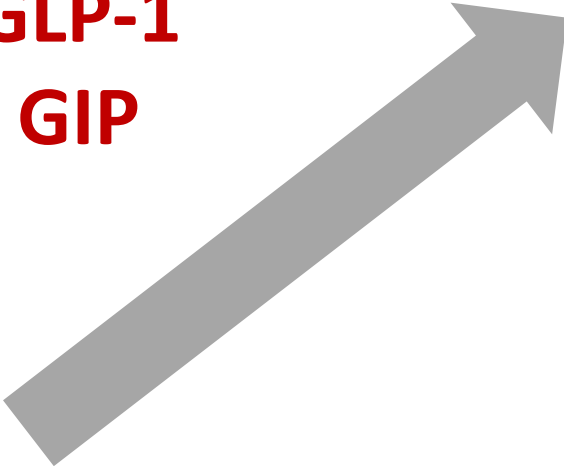
Energieumsatz ↑

Glucagon

+



GLP-1
GIP



Unimolekulare Monoagonisten

Glucagon

-RA

GLP-1-RA

GIP-RA



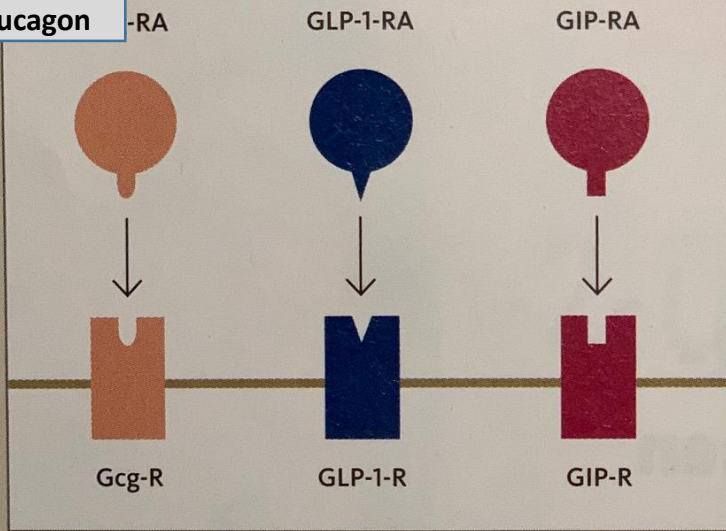
Gcg-R

GLP-1-R

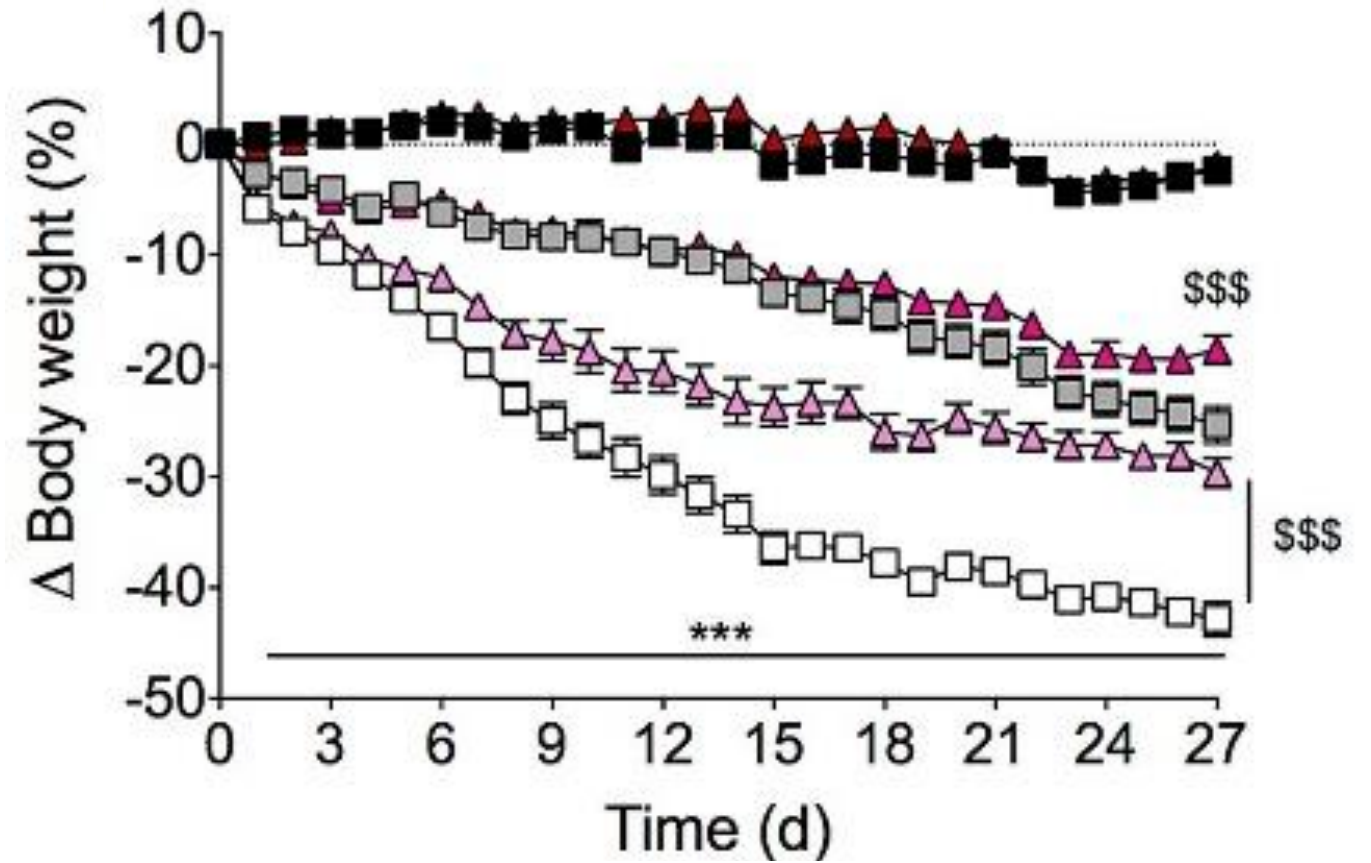
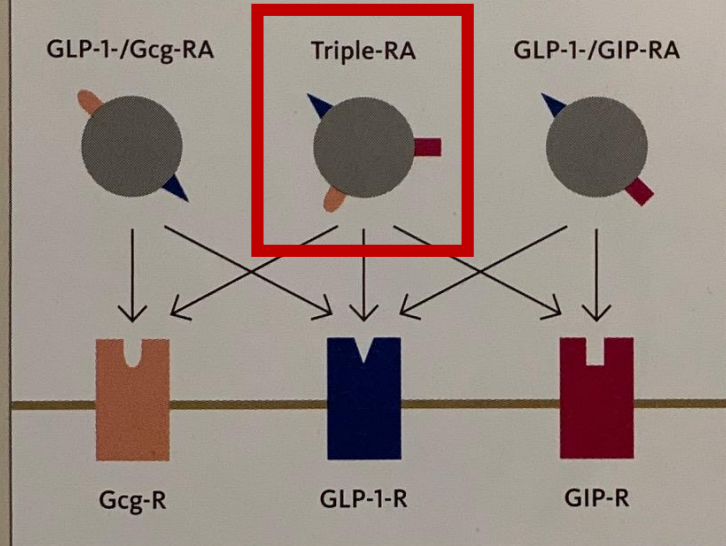
GIP-R

Glucagon

Unimolekulare Monoagonisten

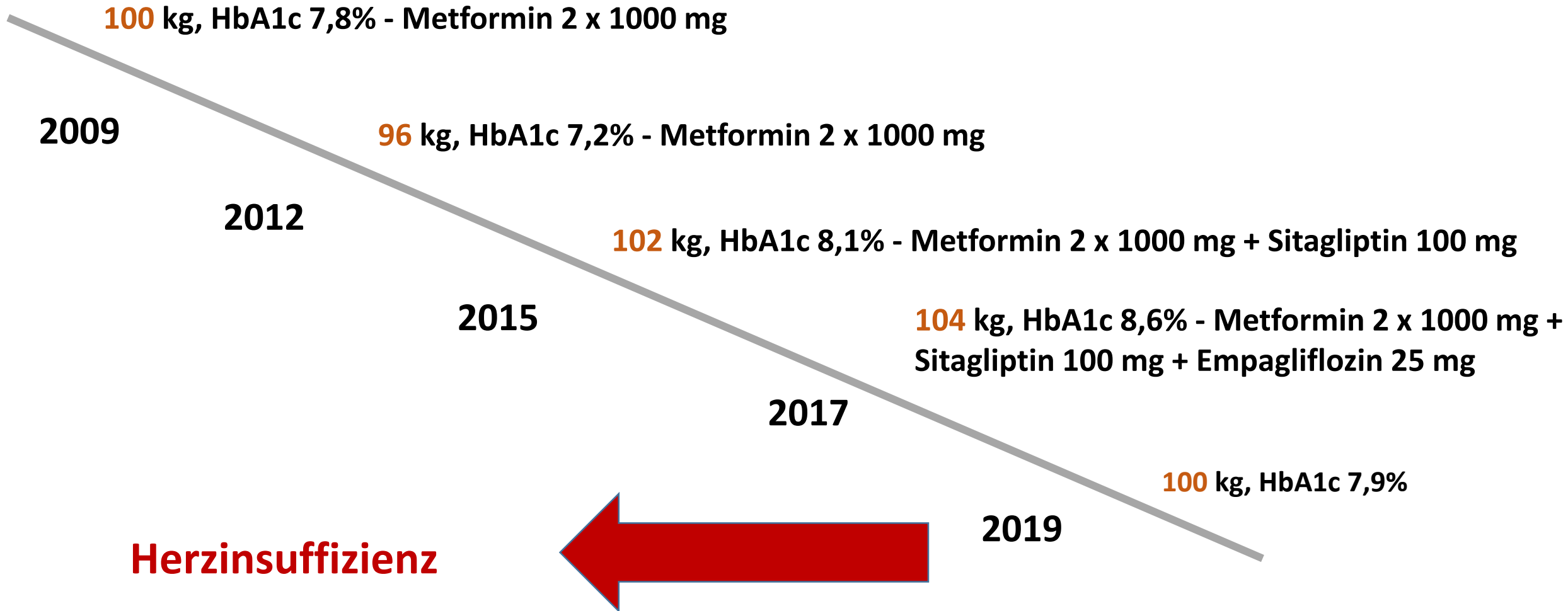


Unimolekulare Dual- und Triple-Agonisten

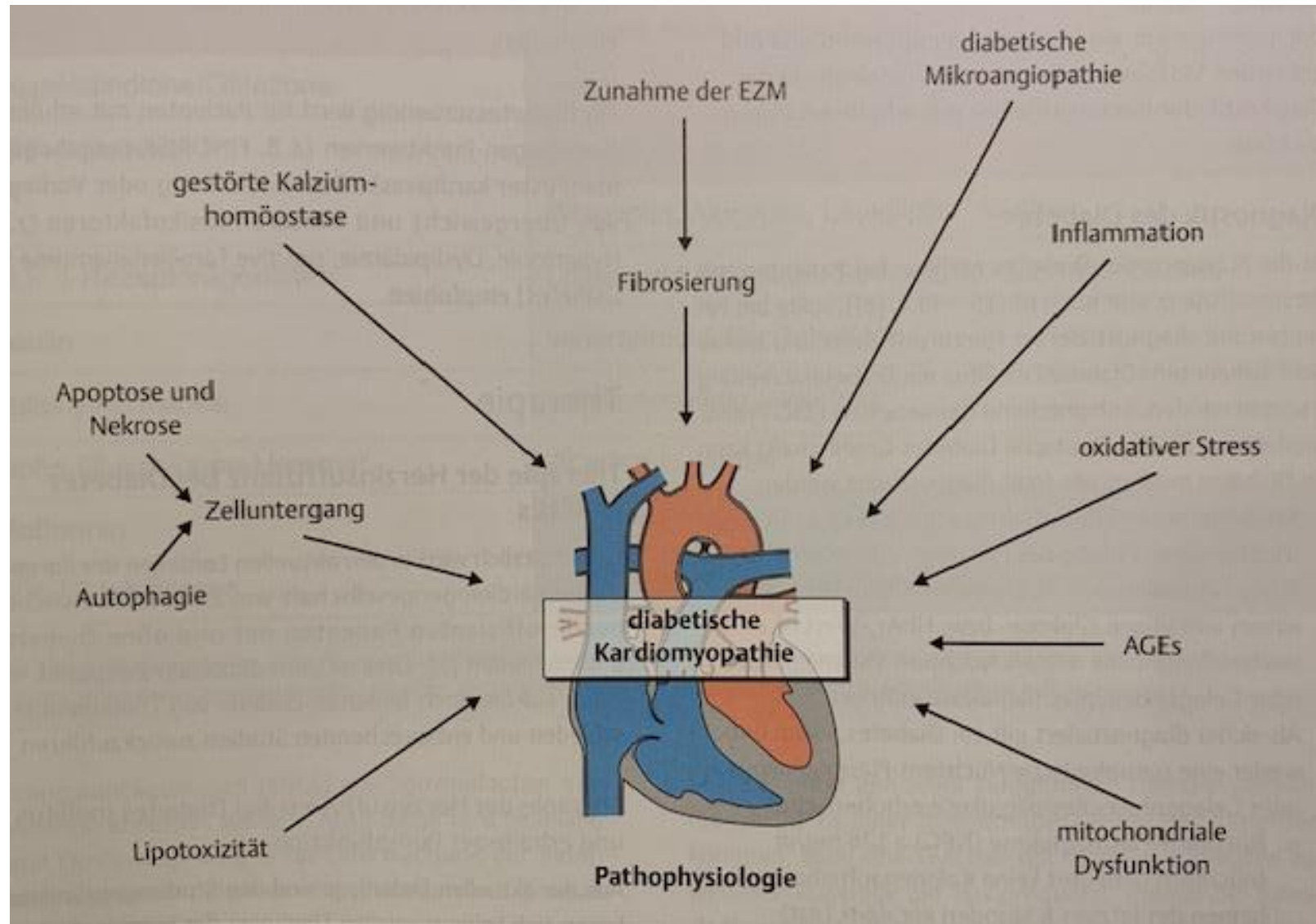


- / ■ Female Vehicle
- / ■ Female Triagonist 5 nmol/kg
- / ■ Female Triagonist 10 nmol/kg
- / ■ DIO Male Vehicle
- / ■ DIO Male Triagonist 5 nmol/kg
- / ■ DIO Male Triagonist 10 nmol/kg

Diabetespatient, m, 183cm, geb. 13.6.1959

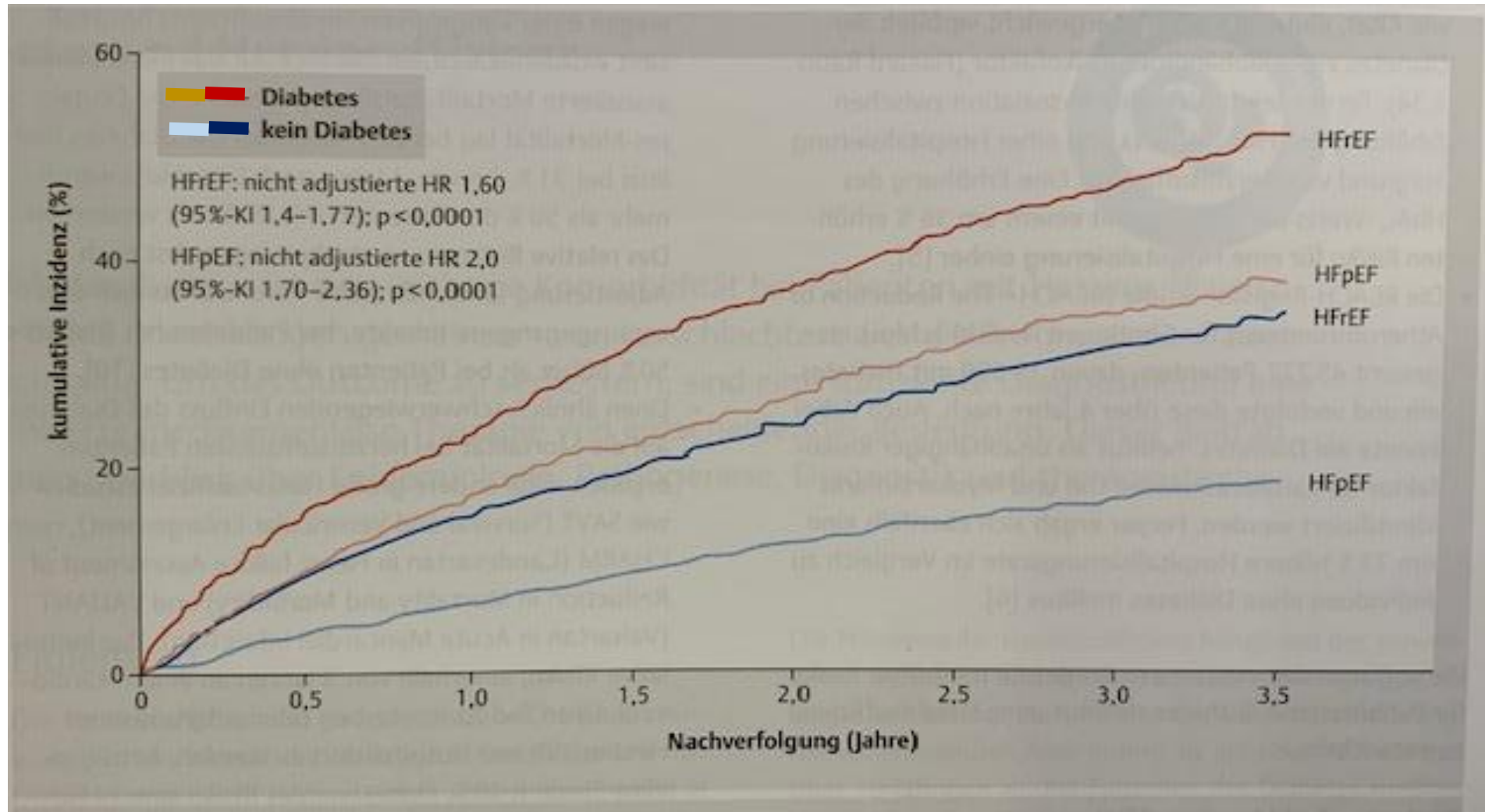


Pathophysiologie der diabetischen Kardiomyopathie



Kardiovaskulärer Tod / Hospitalisierung bei Patienten mit und ohne Diabetes mellitus

Kristensen et al., *Circ Hear Fail* 9; 1-12, 2016



HF_rEF (Heart Failure with **reduced** Ejection Fraction)

HF_pEF (Heart Failure with **preserved** Ejection Fraction)

Substanz	Einfluss auf die Herzinsuffizienz
Thiazolidindione / Glitazone	ungünstig
DPP-4-Inhibitoren	Saxagliptin ungünstig
	Sitagliptin, Alogliptin, Linagliptin: neutral
GLP-1-Rezeptoragonisten	Lixisenatid, Liraglutid, Semaglutid, Exenatid: neutral
Insulin	widersprüchliche Datenlage
Sulfonylharnstoffe	möglicherweise ungünstig
Alpha-Glukosidase-Inhibitoren	Acarbose: neutral
Metformin	möglicherweise günstig
SGLT-2-Inhibitoren	Empagliflozin, Canagliflozin, Dapagiflozin: günstig

Diabetespatient, m, 183cm, geb. 13.6.1959

100 kg, HbA1c 7,8% - Metformin 2 x 1000 mg

2009

96 kg, HbA1c 7,2% - Metformin 2 x 1000 mg

2012

102 kg, HbA1c 8,1% - Metformin 2 x 1000 mg + Sitagliptin 100 mg

2015

104 kg, HbA1c 8,6% - Metformin 2 x 1000 mg +
Sitagliptin 100 mg + Empagliflozin 25 mg

2017

100 kg, HbA1c 7,9%

2019

GLP-1-Analoga
anstatt Sitagliptin



Herzinsuffizienz



Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

B Death from Cardiovascular Causes



Aus den Daten errechnet sich, **dass 39 Patienten** über den Studienzeitraum behandelt werden mussten, **um einen Todesfall zu verhindern.**

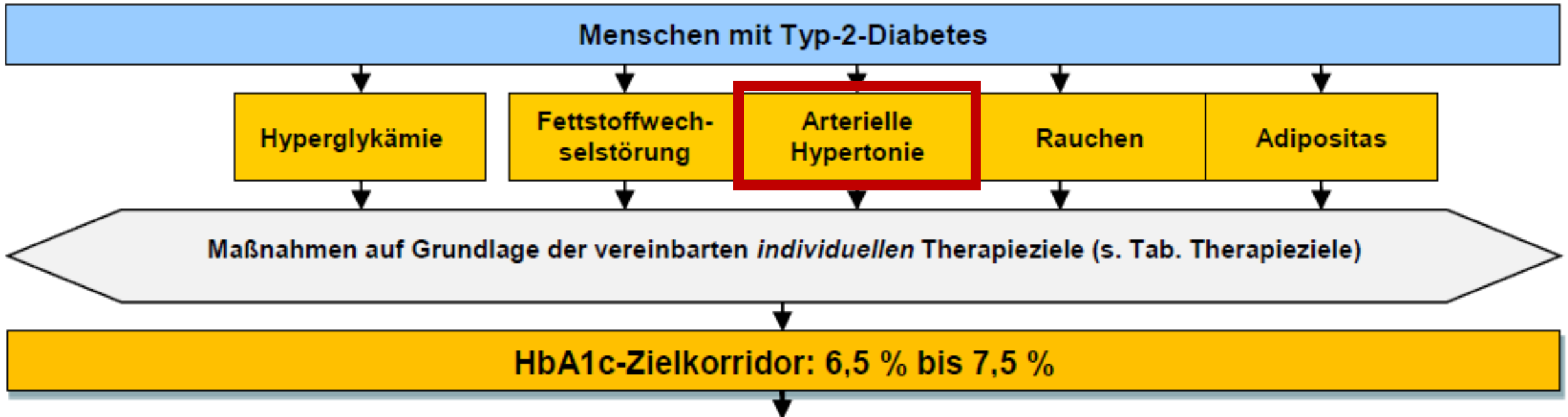
(CV-Mortalität -38% - Gesamt-Mortalität -32%)

CONCLUSIONS

Patients with type 2 diabetes at high risk for cardiovascular events who received empagliflozin, as compared with placebo, had a lower rate of the primary composite cardiovascular outcome and of death from any cause when the study drug was added to standard care.

N Engl J Med 373:2117-2128, Nov. 2015

Nationale Versorgungsleitlinie 2014: Therapie des Typ-2-Diabetes mellitus



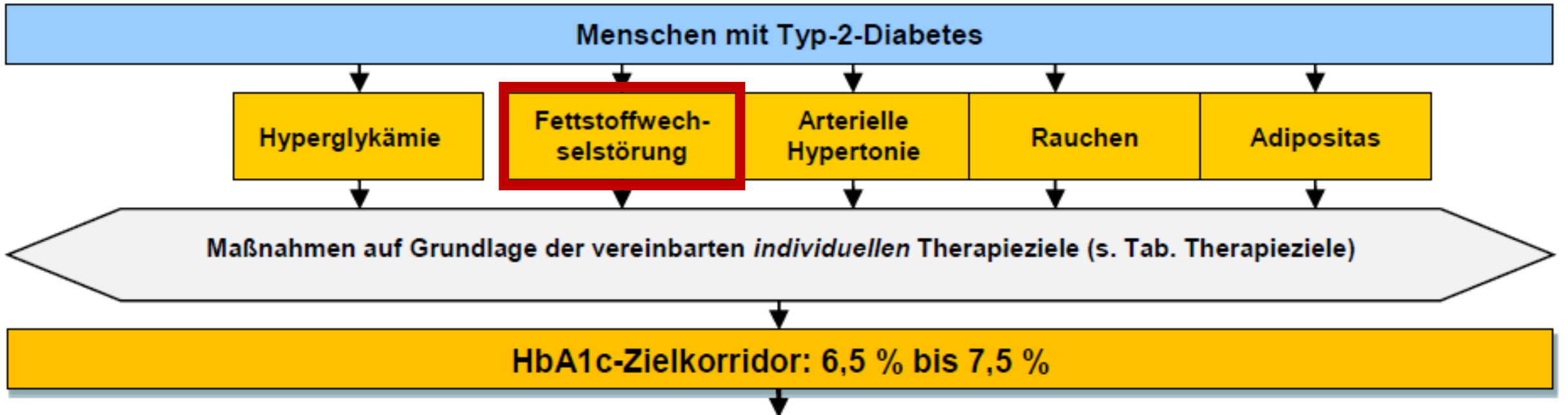
Zielblutdruck: Typ-2-Diabetes mellitus



Generell	kardiovaskulären Risiko
< 140/90 mmHg	130-140/80-85 mmHg (eher in dem unteren Bereich)

ACE-Inhibitoren und AT1-Antagonisten sind die Mittel der ersten Wahl.

Nationale Versorgungsleitlinie 2014: Therapie des Typ-2-Diabetes mellitus



Empfehlungen zur Diagnostik und Therapie von Fettstoffwechselstörungen

bei Vorhandensein einer Gefäßerkrankung (z. B. Herzinfarkt), Diabetes oder ein 10-Jahres-Risiko für eine Gefäßerkrankung, das über 20% liegt

- **LDL-Cholesterin < 100** mg/dl (2,58 mmol/l)
- Triglyzeridwerte < 150 mg/dl (1,70 mmol/l)

bei Vorhandensein einer Gefäßerkrankung (z. B. Herzinfarkt) und Diabetes, bei Zustand **nach akutem Koronarsyndrom**

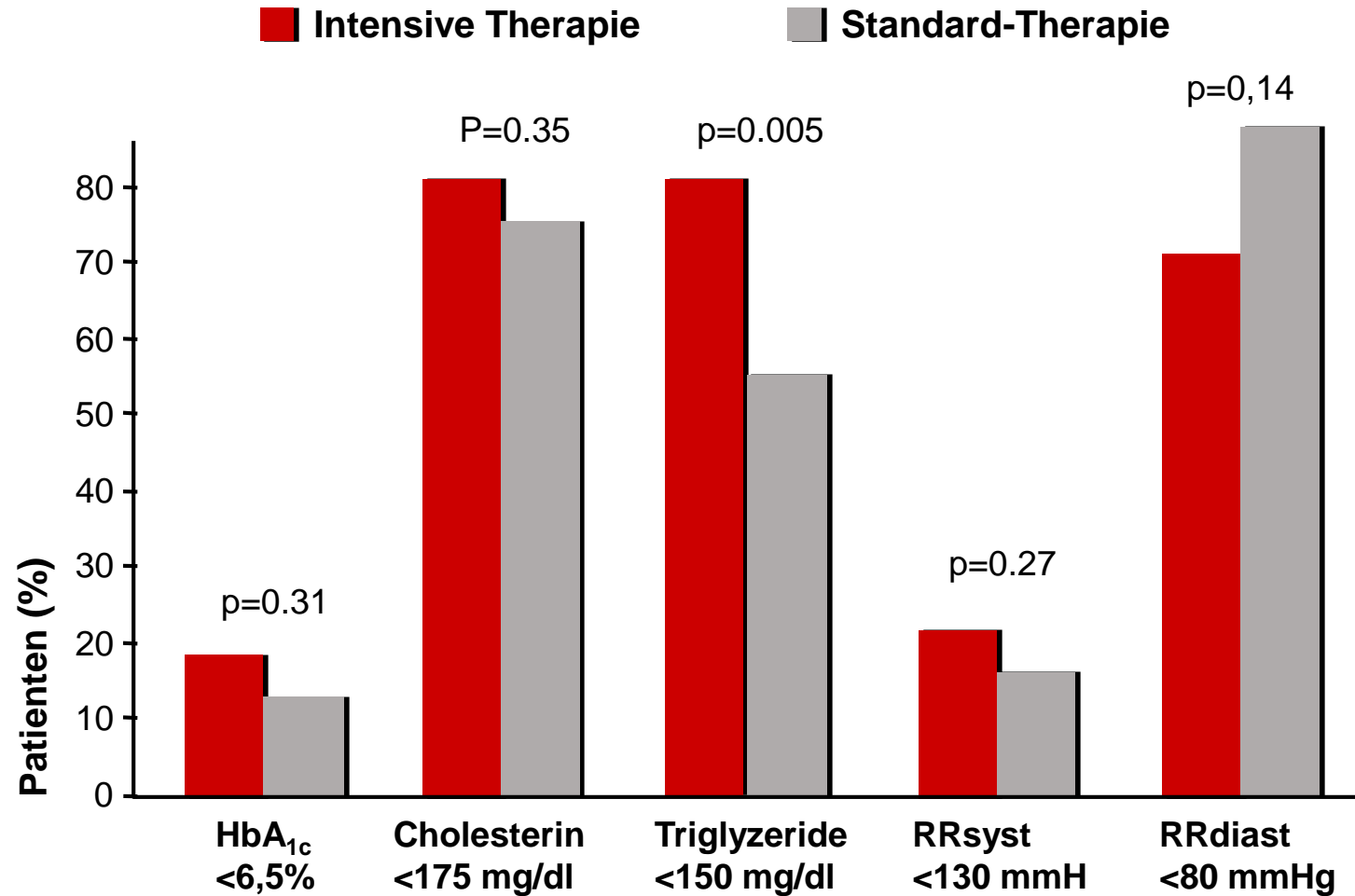
- **LDL-Cholesterin < 70 mg/dl** (1,80 mmol/l)
- Triglyzeridwerte < 150 mg/dl (1,70 mmol/l)



Deutsche Gesellschaft zur Bekämpfung von
Fettstoffwechselstörungen und ihren Folgeerkrankungen DGFF
(Lipid-Liga) e. V. – Stand 2019

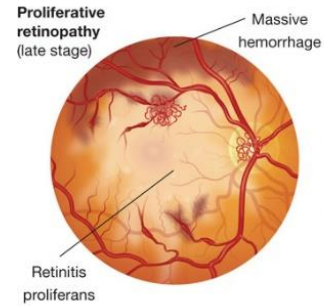
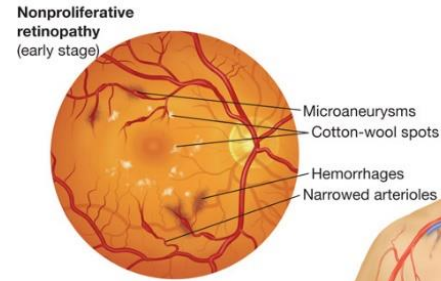
STENO-2

Erreichen der Ziele für die intensive Therapie nach 7,8 Jahren – 160 Typ-2-Diabetiker mit Mikroalbuminurie



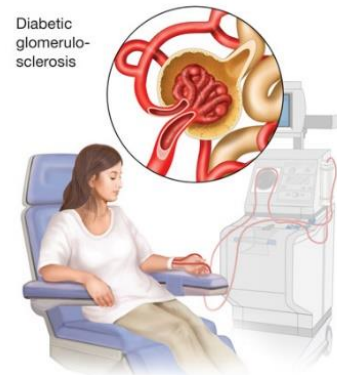
Diabetische Retinopathie

1 x Jahr
Konsil/Augenarzt



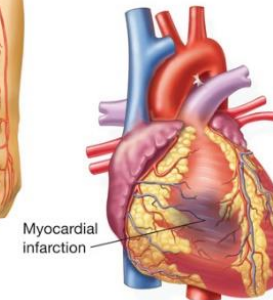
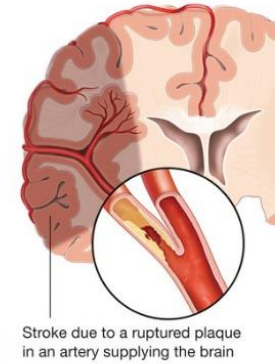
Diabetische Nephropathie

Serum-Kreatinin
Harnstoff
Harnsäure
Albumin im Urin

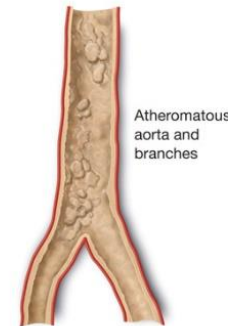


Diabetes mellitus is the leading cause of end-stage renal disease in the Western world

Kardio-Vaskuläre Erkrankungen



Heart disease including heart attack, which accounts for 70% of the mortality in people with diabetes



B-EKG
NT-Pro-BNP
(Echo)
Blutdruck
LDL
HDL
Lp(a)
Apo-B

Neuigkeiten aus der Diabetologie anhand eines Fallberichtes



Prof. Dr. Burkhard L. Herrmann

Endokrinologie /// Diabetologie /// Innere Medizin

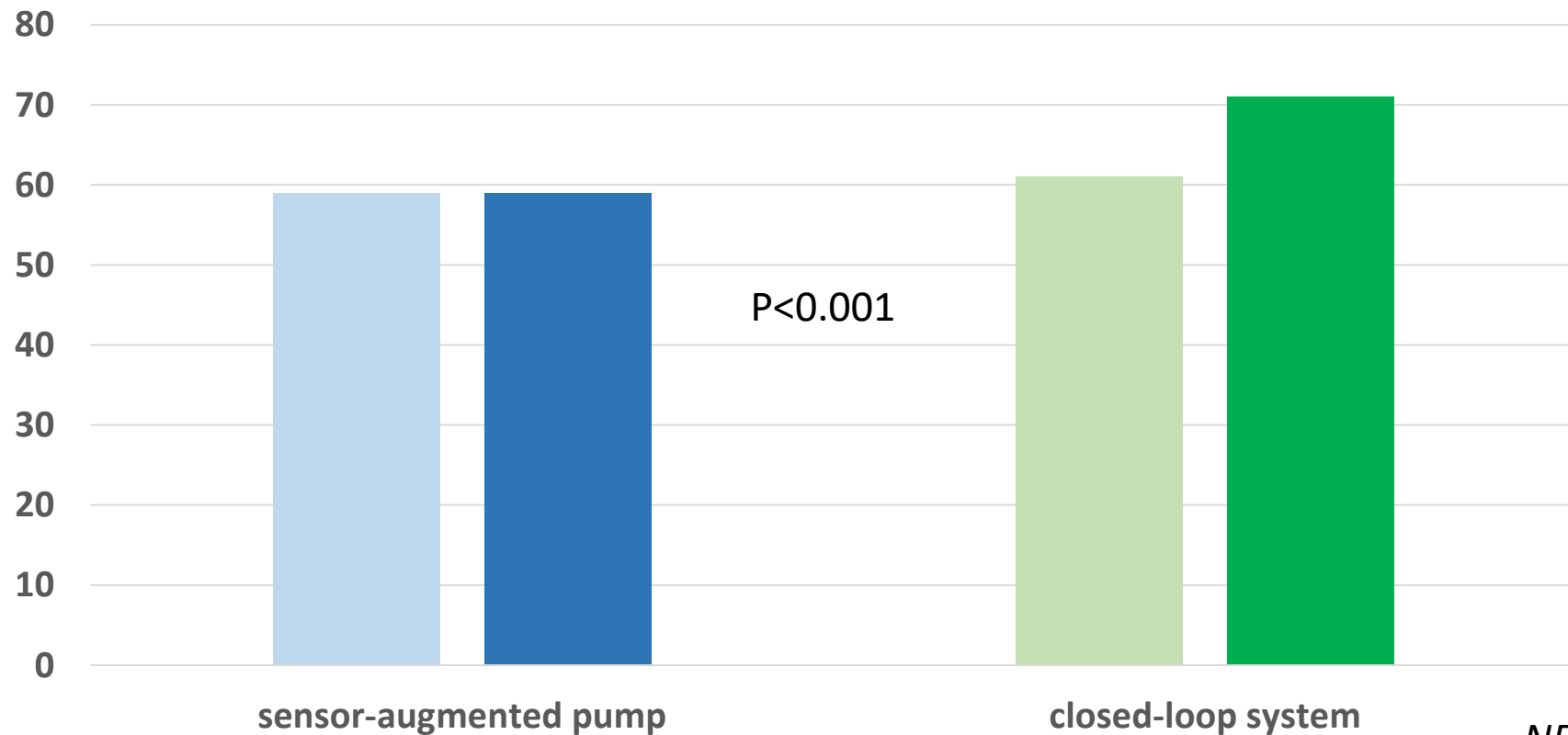
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Springorumallee 2 - 44795 Bochum*

www.endo-bochum.de

6-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes

168 patients: 56 control group, 112 closed-loop group
age range 14 to 71 yrs, HbA1c: 5.4 to 10.6%.

The mean (\pm SD) percentage of time that the glucose level was within the target range



Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes

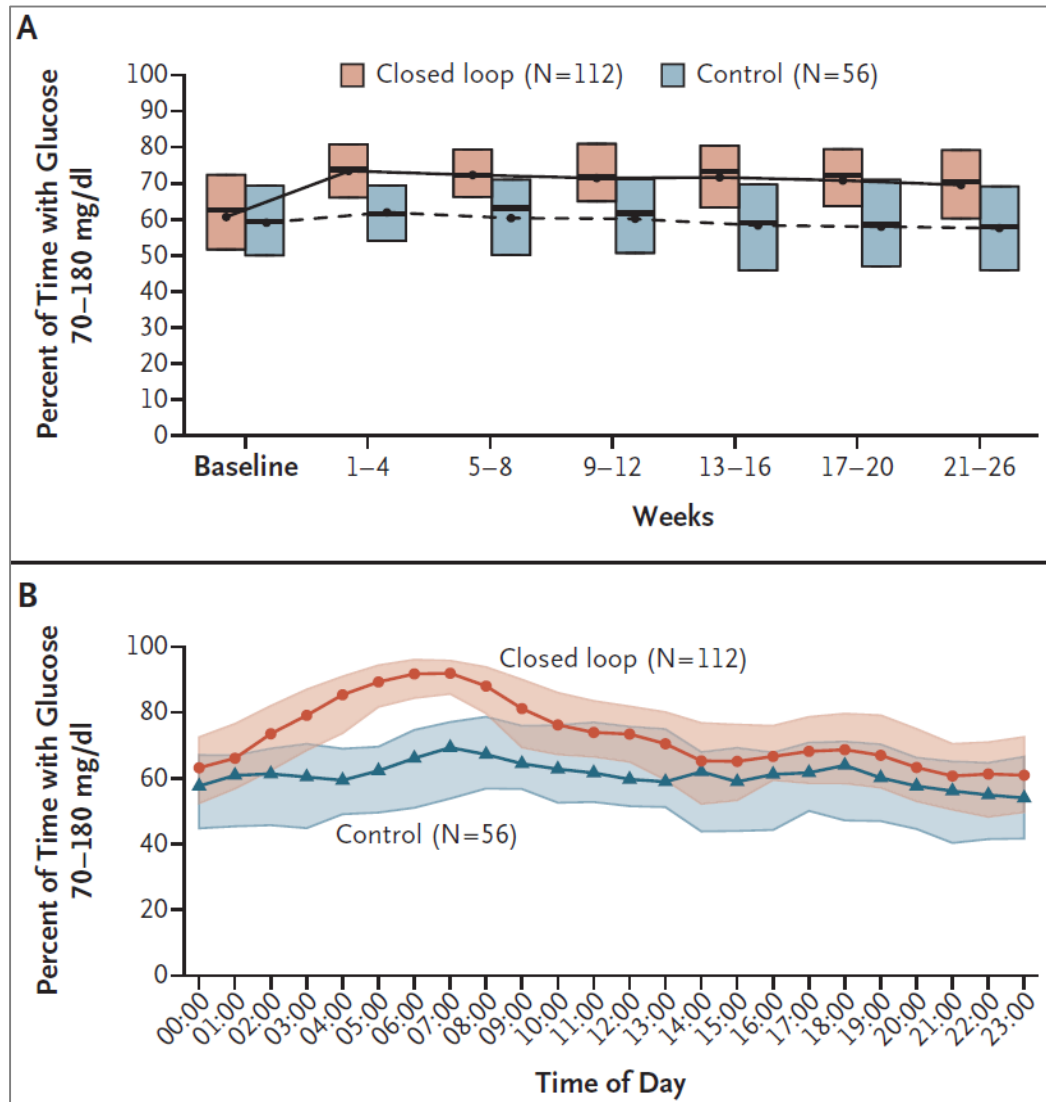


Figure 1. Percentage of Time with Glucose Level in Target Range.

Panel A shows a box plot of the percentage of time that the glucose level was within the range of 70 to 180 mg per deciliter (3.9 to 10.0 mmol per liter), as measured by continuous glucose monitoring, during 4-week periods over 6 months among patients who were assigned to receive treatment with either a closed-loop system (closed loop) or a sensor-augmented pump (control). Black dots indicate the mean values, horizontal bars in the boxes indicate the medians, and the bottom and top of each box represent the 25th and 75th percentiles, respectively. Panel B shows an envelope plot of the same outcome according to the time of day. Symbols denote the hourly median values, and the shaded regions are defined by the 25th and 75th percentiles.

Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes

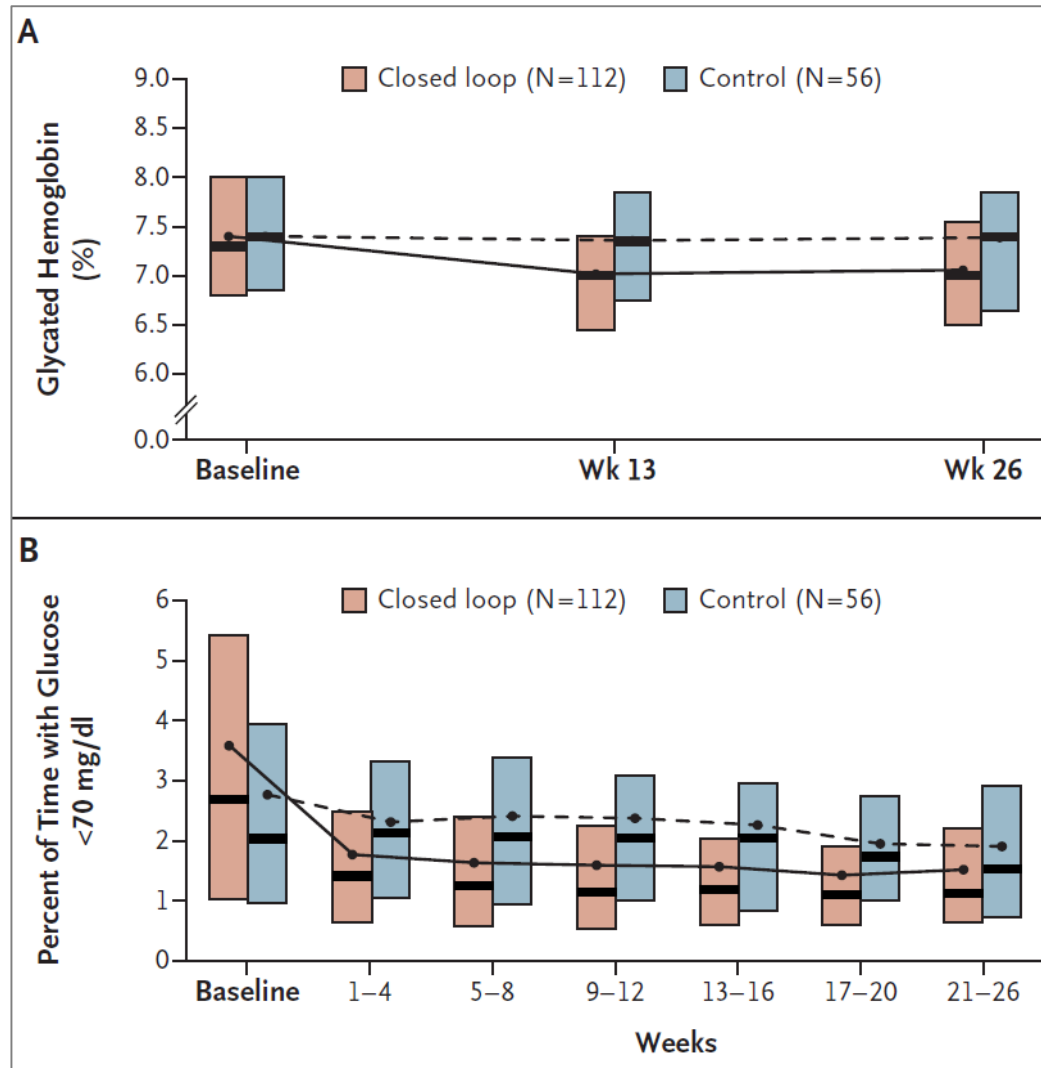


Figure 2. Glycated Hemoglobin Level and Percentage of Time with Glucose Level Less Than 70 mg per Deciliter.

Panel A shows a box plot of the glycated hemoglobin level at baseline, week 13, and week 26 among patients who were assigned to receive treatment with either a closed-loop system (closed loop) or a sensor-augmented pump (control). One patient in the control group and one patient in the closed-loop group completed the 26-week follow-up visit outside the pre-specified window, and the corresponding values were excluded. Panel B shows a box plot of the percentage of time that the glucose level was less than 70 mg per deciliter, as measured by continuous glucose monitoring, during 4-week periods over 6 months in each treatment group. In both panels, black dots indicate the mean values, horizontal bars in the boxes indicate the medians, and the bottom and top of each box represent the 25th and 75th percentiles.