solothurner spitäler ag

kantonsspital olten

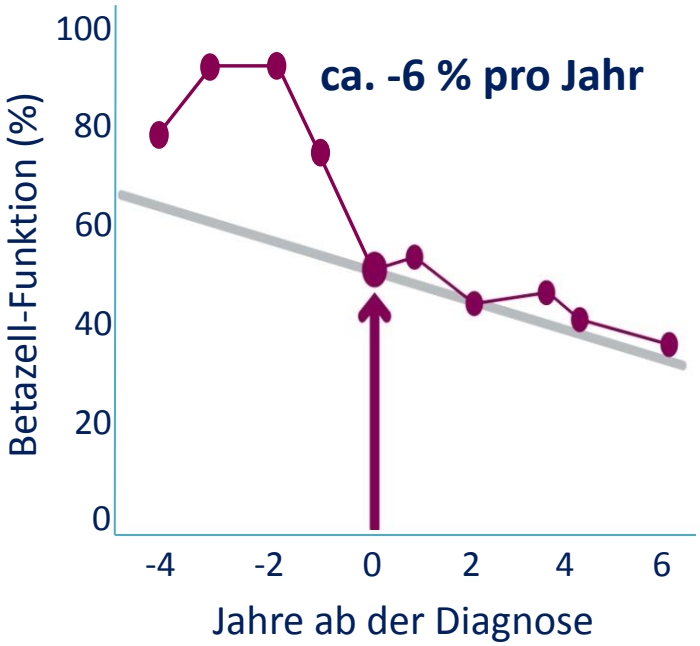
Update:
Typ 2 Diabetes - Insulintherapie

Gottfried Rudofsky
Kantonsspital Olten
Endokrinologie, Diabetologie & Klinische Ernährung

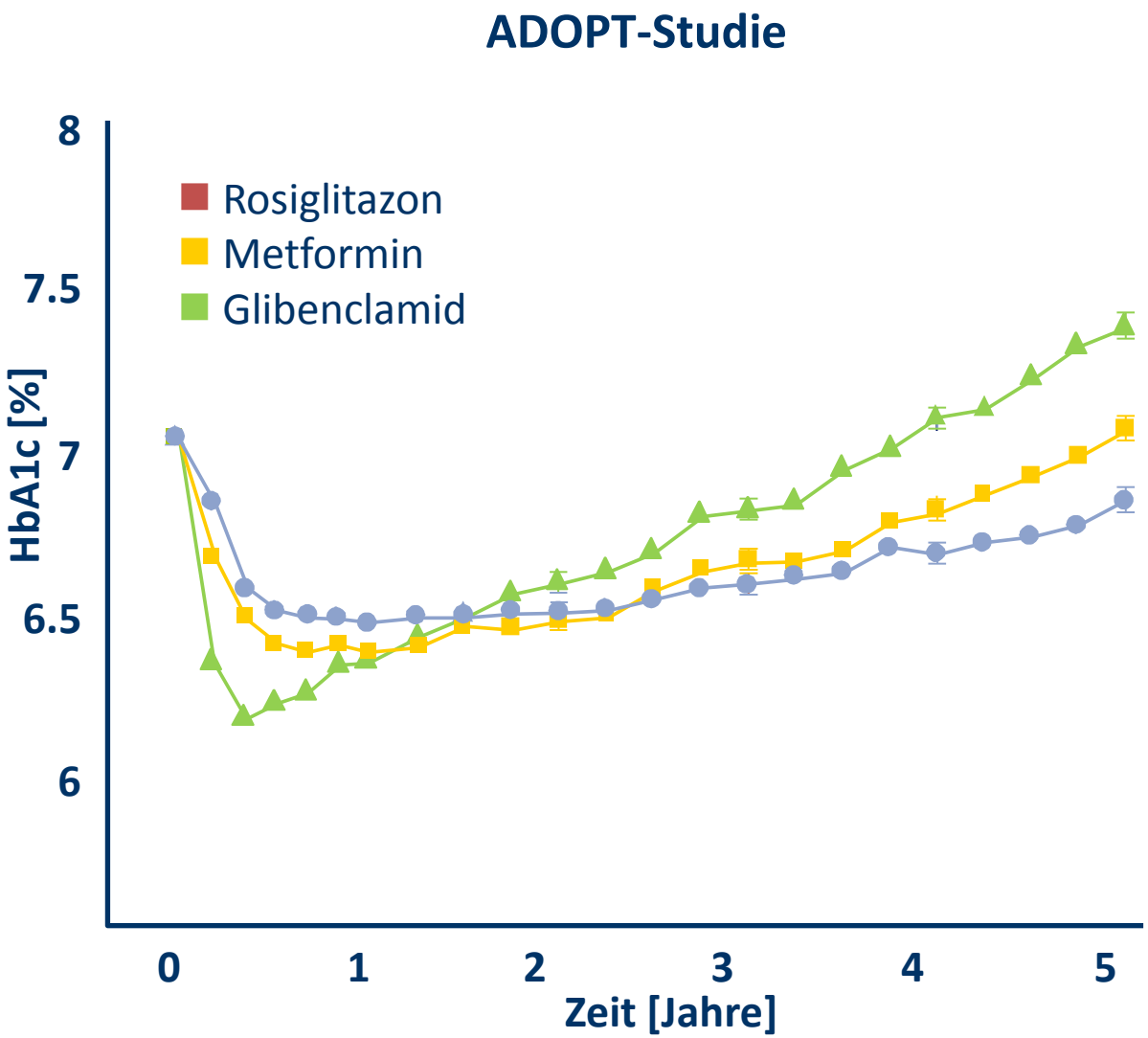
Nicht-Insulin-Diabetes-Therapeutika

Qtern
Vokanamet
Eperzan
Bydureon
Xelevia
Janumet
Gliclazid
Januvia
Metformin
Vipdomet
KombiglyzeXR
Xultophy
Galvus
Xigduo
Vipidia
Trulicity
Competact
Byetta
Jardiance
Glimepirid
Onglyza
Repaglinide
Trajenta
Jentaduetto
Victoza
Actos
Velmetia
Galvumet
Invokana
Forxiga
Acarbose

Abnahme der Insulinsekretion



Tabák AG et al. Lancet 2009;373(9682):2215-2221



Kahn et al., N Engl J Med 355:2427–2443, 2006

Individualisierte Therapie

Diabetologia (2012) 55:1577–1596
DOI 10.1007/s00125-012-2534-0

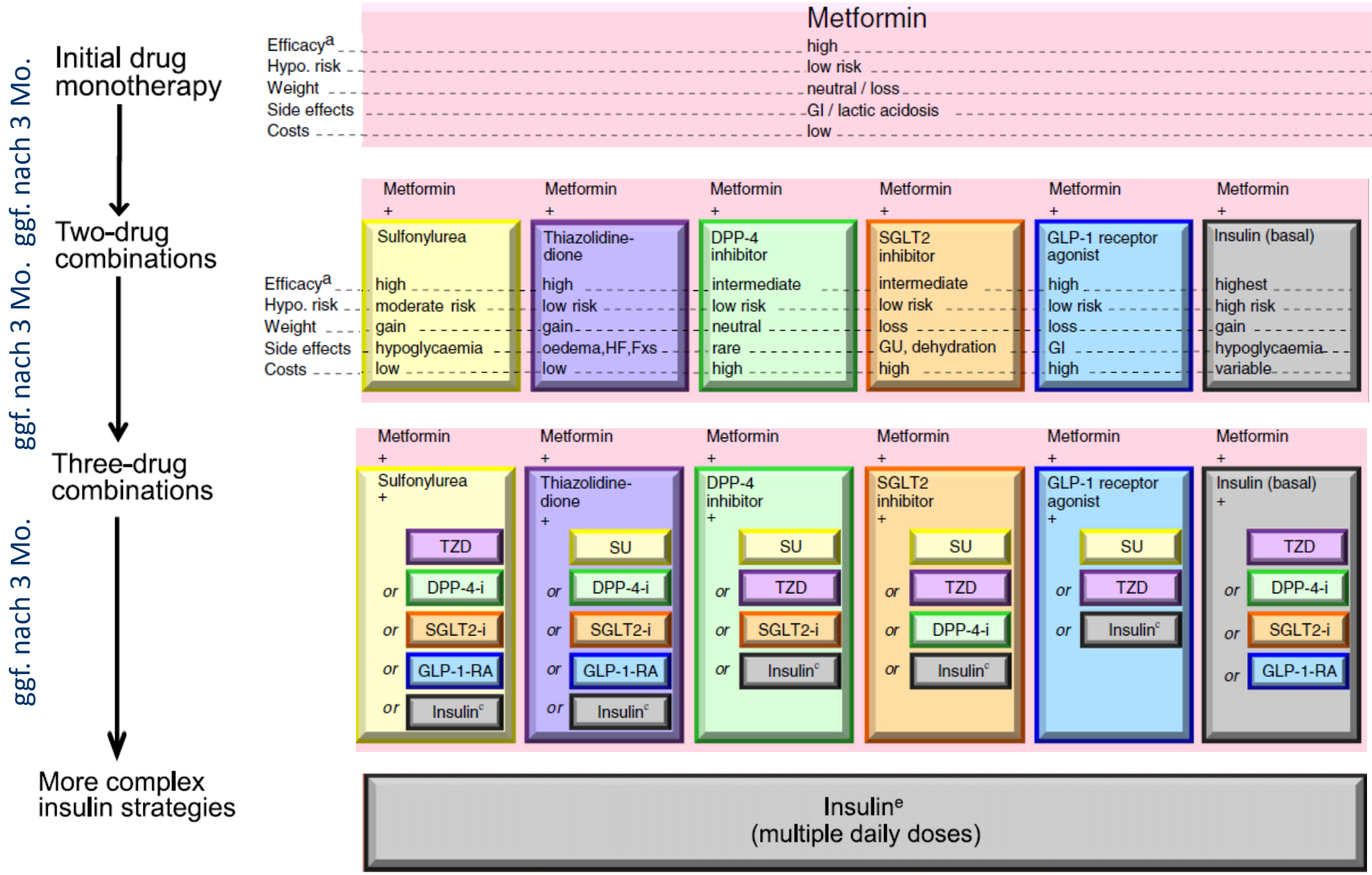
POSITION STATEMENT

Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

S. E. Inzucchi · R. M. Bergenstal · J. B. Buse · M. Diamant · E. Ferrannini · M. Nauck · A. L. Peters · A. Tsapas · R. Wender · D. R. Matthews

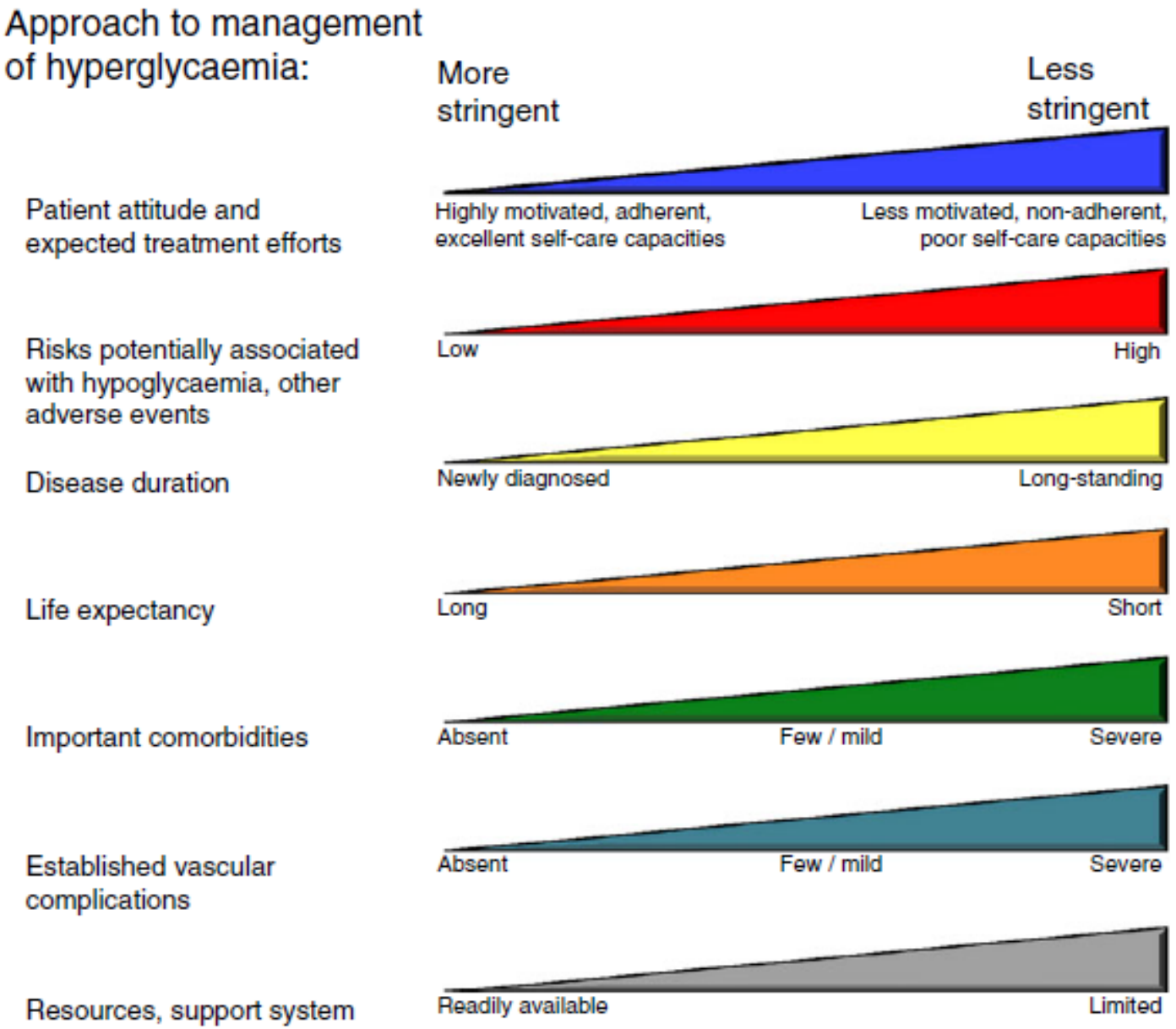
Inzucchi SE et al. Diabetologia 55:1577–1596, 2012

Therapieschema



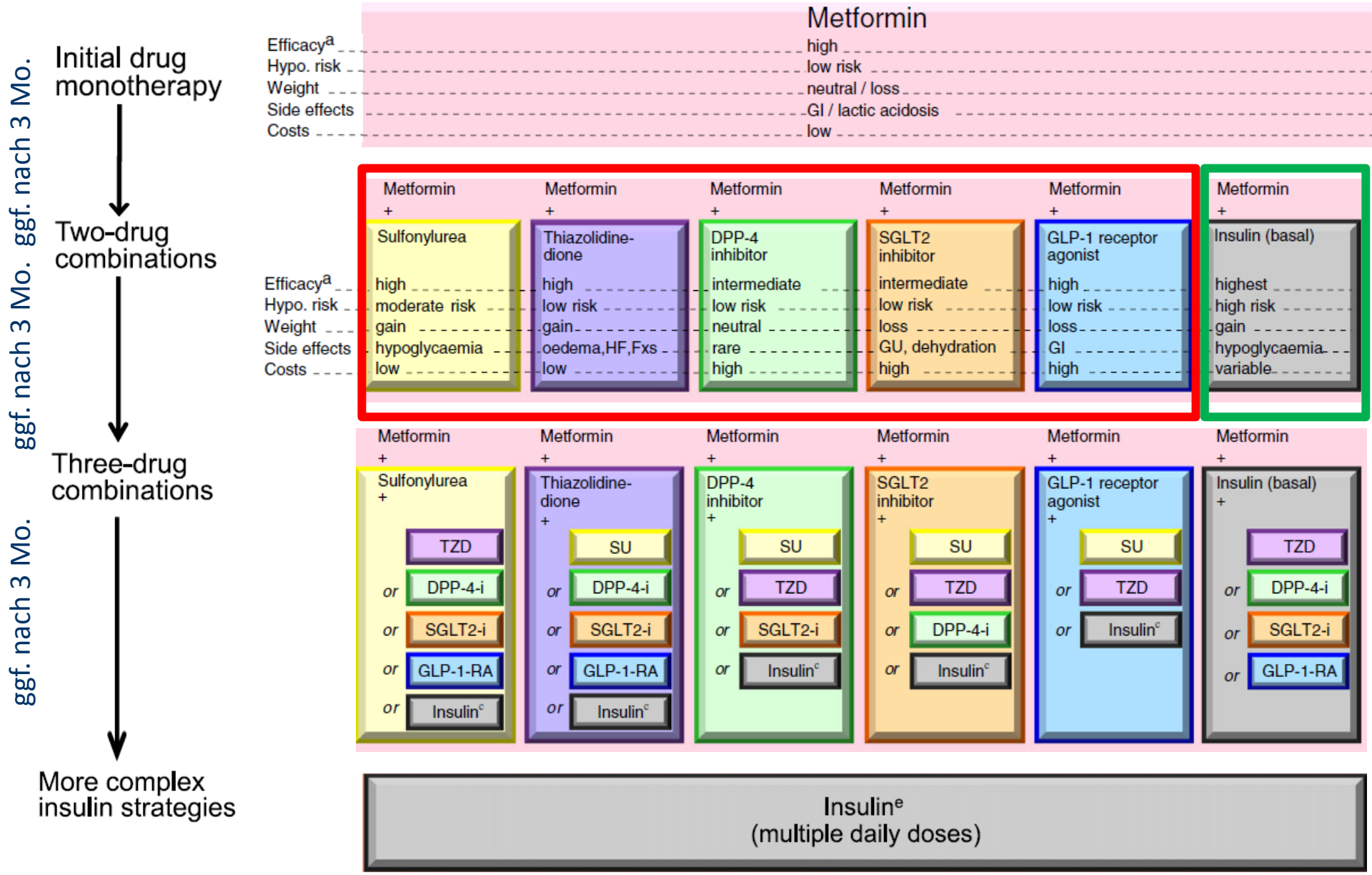
Inzucchi SE et al. Diabetologia 58:429–442, 2015

Individualisierte Therapie



Inzucchi SE et al. Diabetologia 55:1577–1596, 2012

Therapieschema



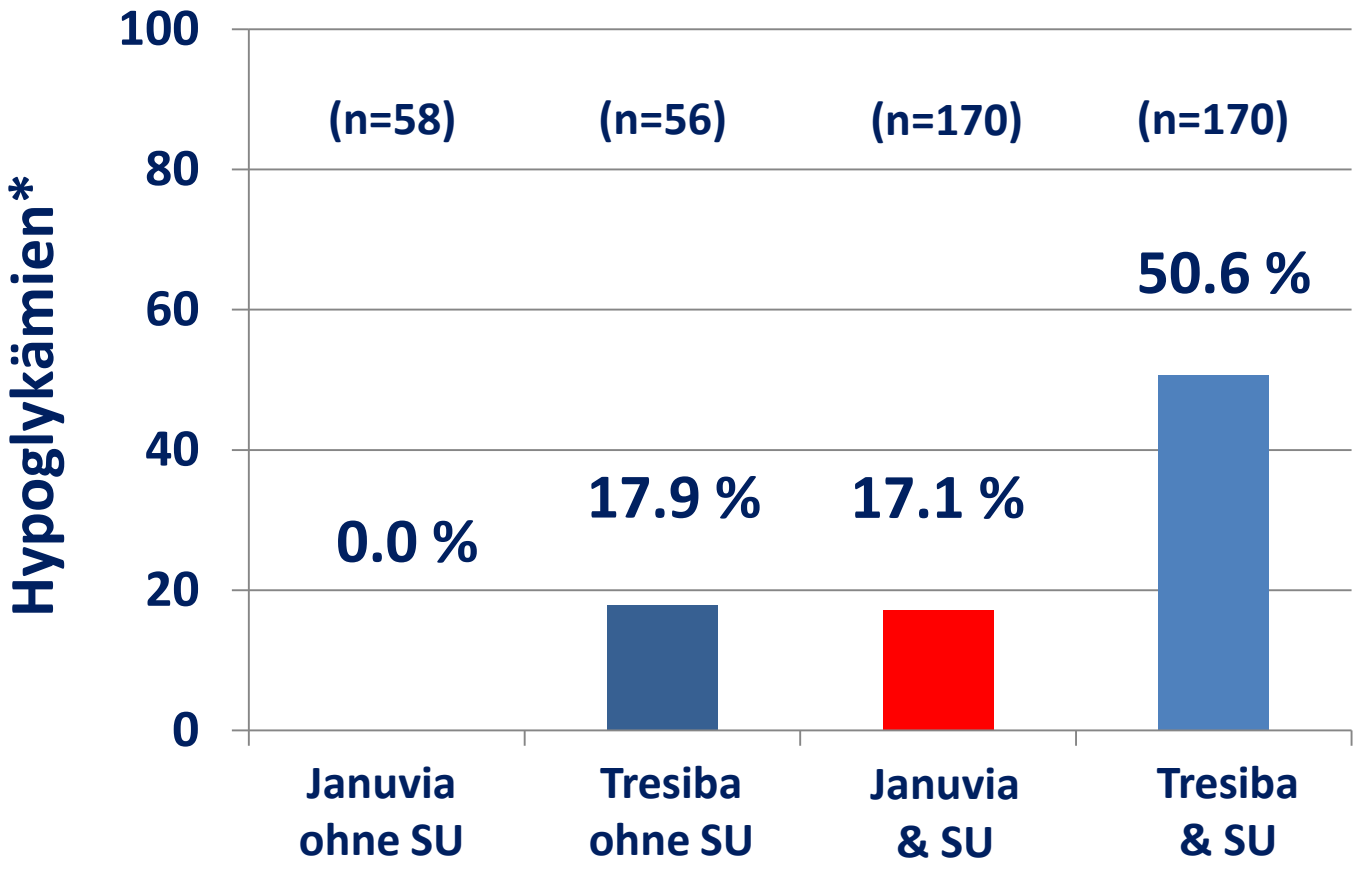
Inzucchi SE et al. Diabetologia 58:429–442, 2015

Wann Insulin bei Typ 2 Diabetes?

- Wenn mit 2-3 OADs nicht im Zielbereich
- Dekompensierte Stoffwechsellage
- Kontraindikationen für OADs (z. B. NI)
- Komorbidität
- Hochdosierter Glukokortikoidtherapie
- Schwangerschaftsdiabetes

Für Insulin gibt es keine Kontraindikationen

Insulintherapie und Hypoglykämie

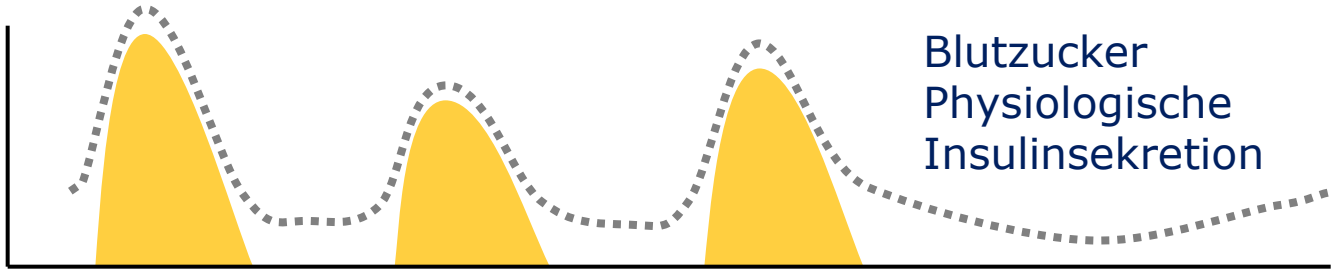


*Hypoglykämie: BZ < 3.9 mmol/L

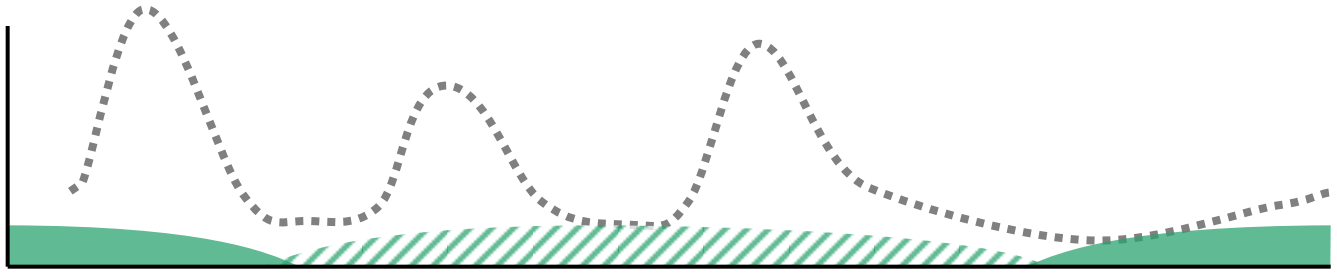
Philis-Tsimikas A et al. „Effect of insulin degludec versus sitagliptin in patients with type 2 diabetes uncontrolled on oral antidiabetic agents“ Diabetes Obes Metab 15:760-766, 2013

Therapiestrategien

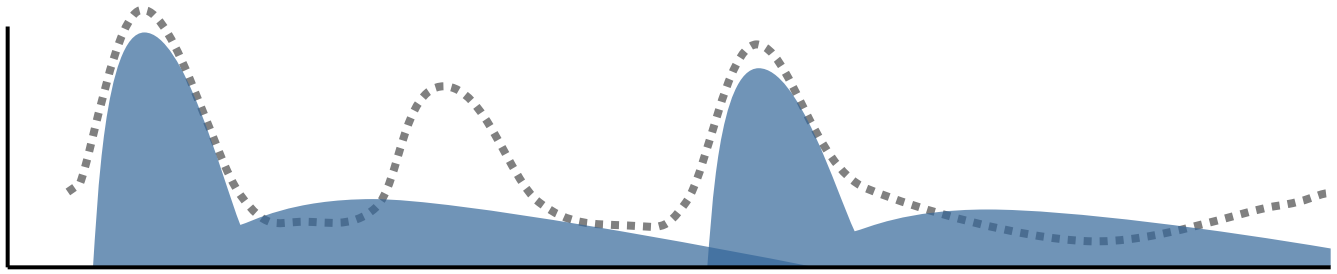
Prandial



Basal + OAD
(BOT)



CT



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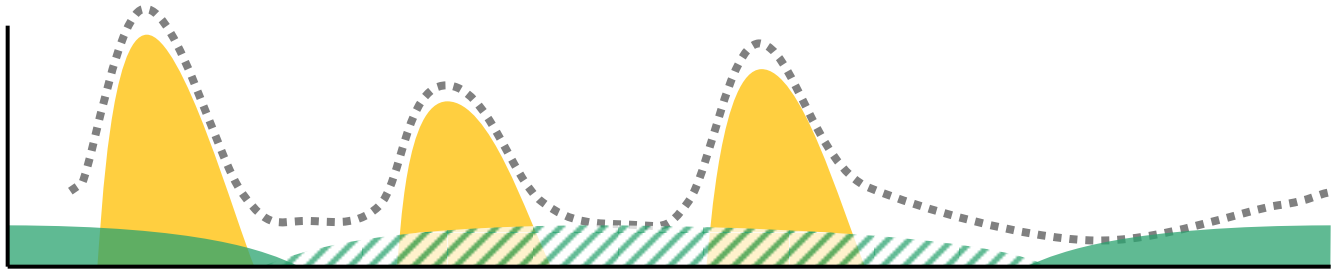
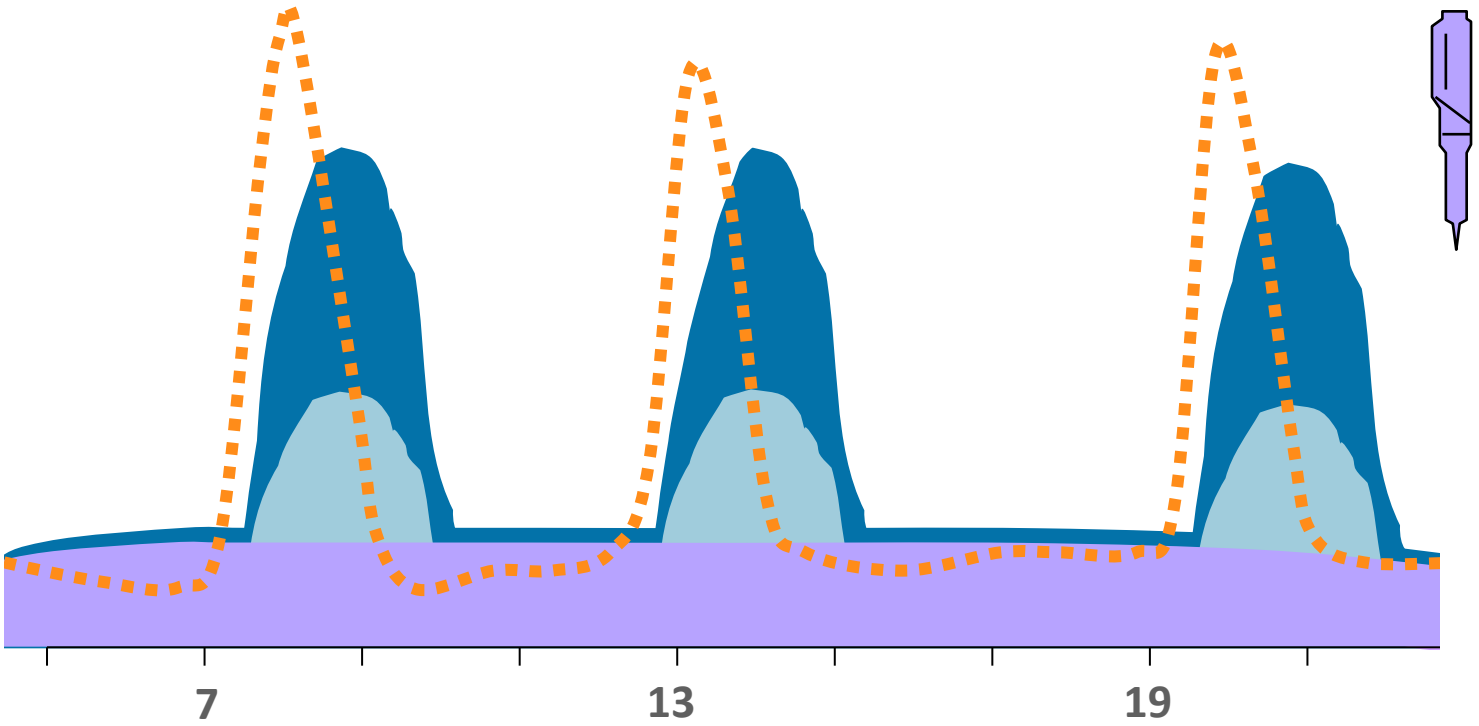


Idee der BOT

BOT: Basalinsulin **ersetzt** zum Teil endogenes Insulin für die Basalrate → Entlastung der Betazellen



Exogenes Insulin

- Insulinausschüttung bei Stoffwechselgesunden
- Basalinsulin

Endogenes Insulin

- Geringer Anteil für Basalrate benötigt, Rest steht z.B. für Mahlzeitensekretion zur Verfügung
- „Vormals alleine“ Anteil für Mahlzeitensekretion

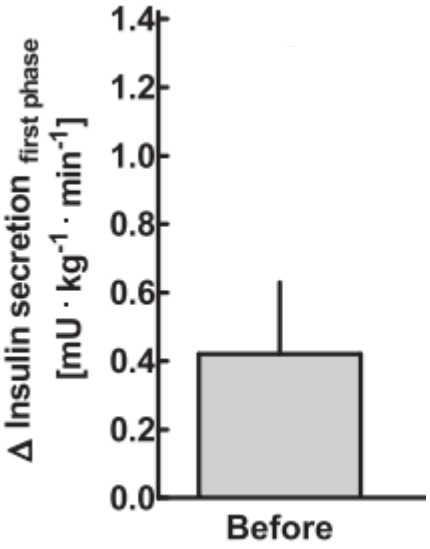
Wiederhergestellte Sekretion

14 Patienten mit DMT2

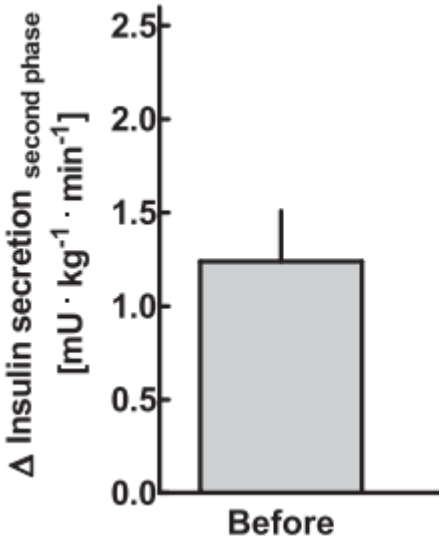
Absenkung der Nü-Glukose mit Insulin glargin
von **179.6** ± 7.5 mg/dl auf **117.6** ± 6.5 mg/dL

Insulinsekretion nach IVGTT

Erste Phase 0-10. Min.



Zweite Phase 10-180. Min.



IVGTT = intravenöser Glukosetoleranztest

Pennartz C et al. Diabetes Care 34:2048–2053, 2011

Und wie die Insulintherapie beginnen?

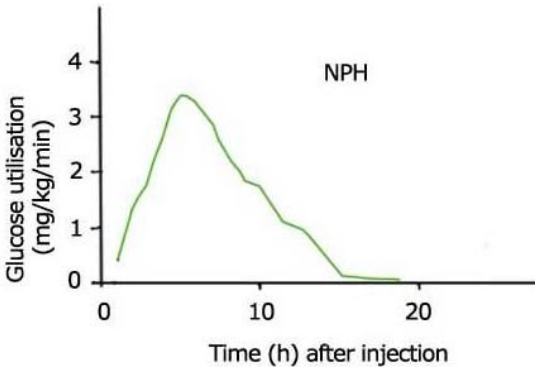
Praktische Durchführung

- Beginn mit 10 E Basalinsulin (NPH, Glargin, Glargin U300, Degludec)
- Dosisvariation in Abhängigkeit vom erreichten Nüchtern-BZ
- Ziel Nüchtern-BZ: < 7 mmol/l

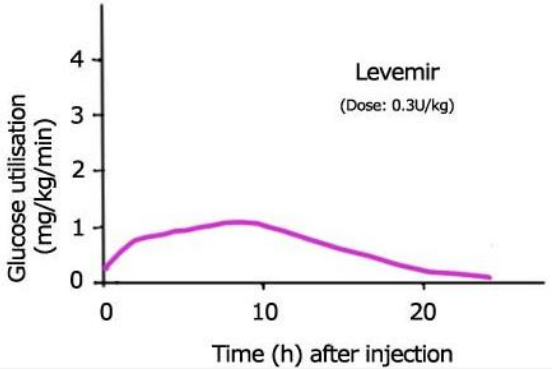
**Nüchtern-Blutzucker	Dosisanpassung
> 7 mmol/l	+ 2 E
> 8 mmol/l	+ 4 E
> 9 mmol/l	+ 6 E
> 10,0 mmol/l	+ 8 E
< 3,9 mmol/l	- 2 E

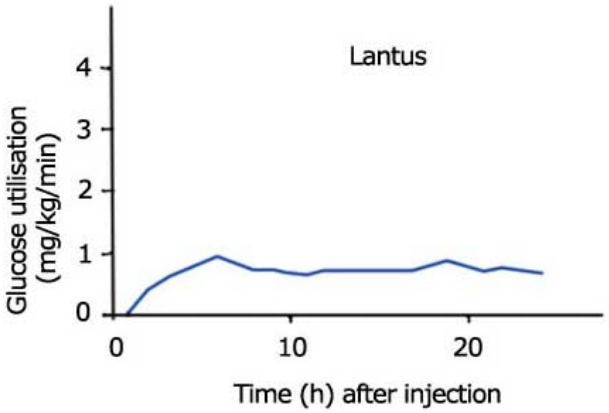
Riddle MC et al. Diabetes Care 26: 3080-3086, 2003

Wirkprofile der Basalinsuline



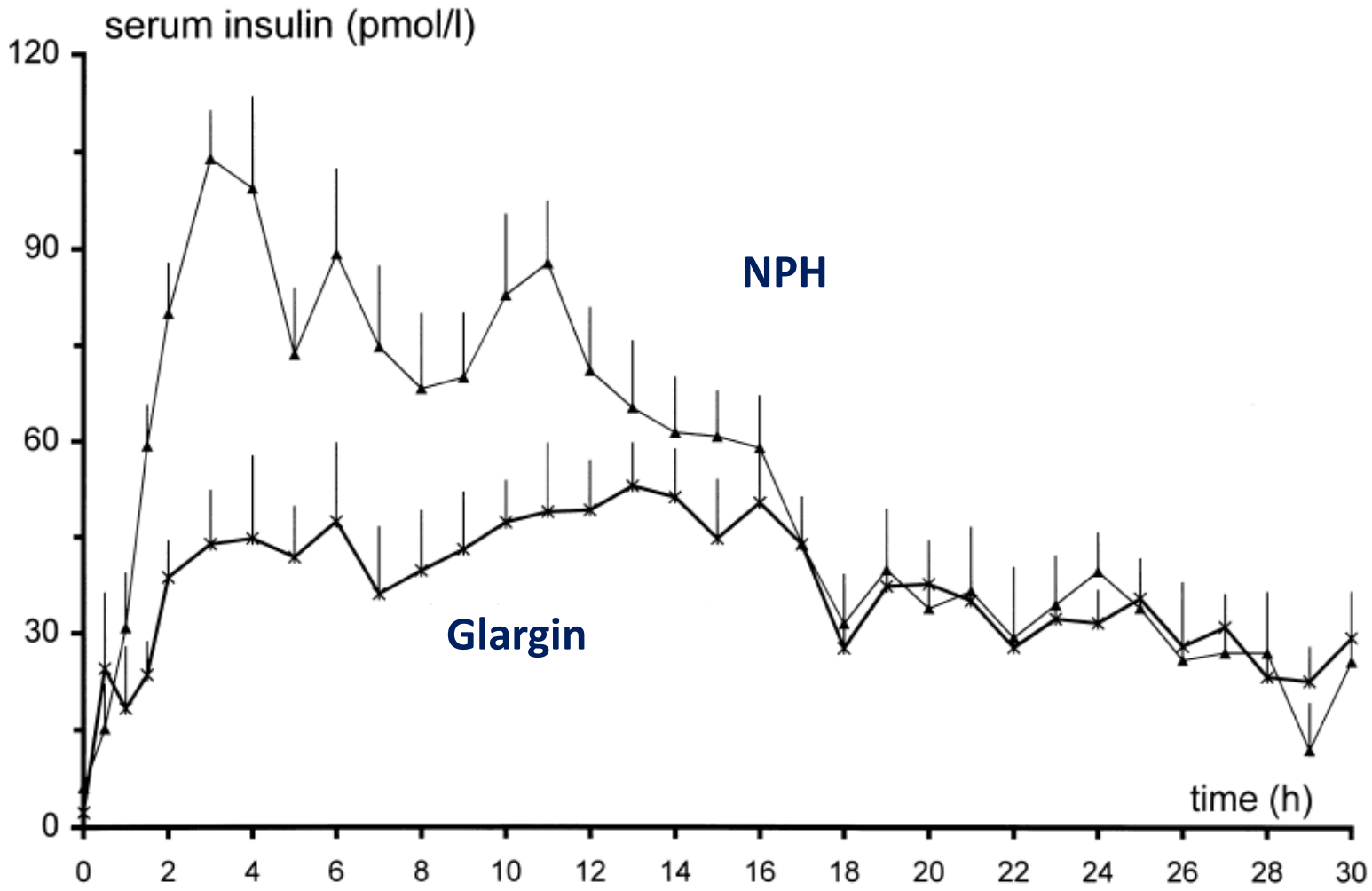
Levemir®
insulin detemir (rDNA origin) injection





Bolli GB, Owens DR. Lancet 356(9228):443-445, 2000
Hordern SV et al. Diabetologia 48(3):420-426, 2005

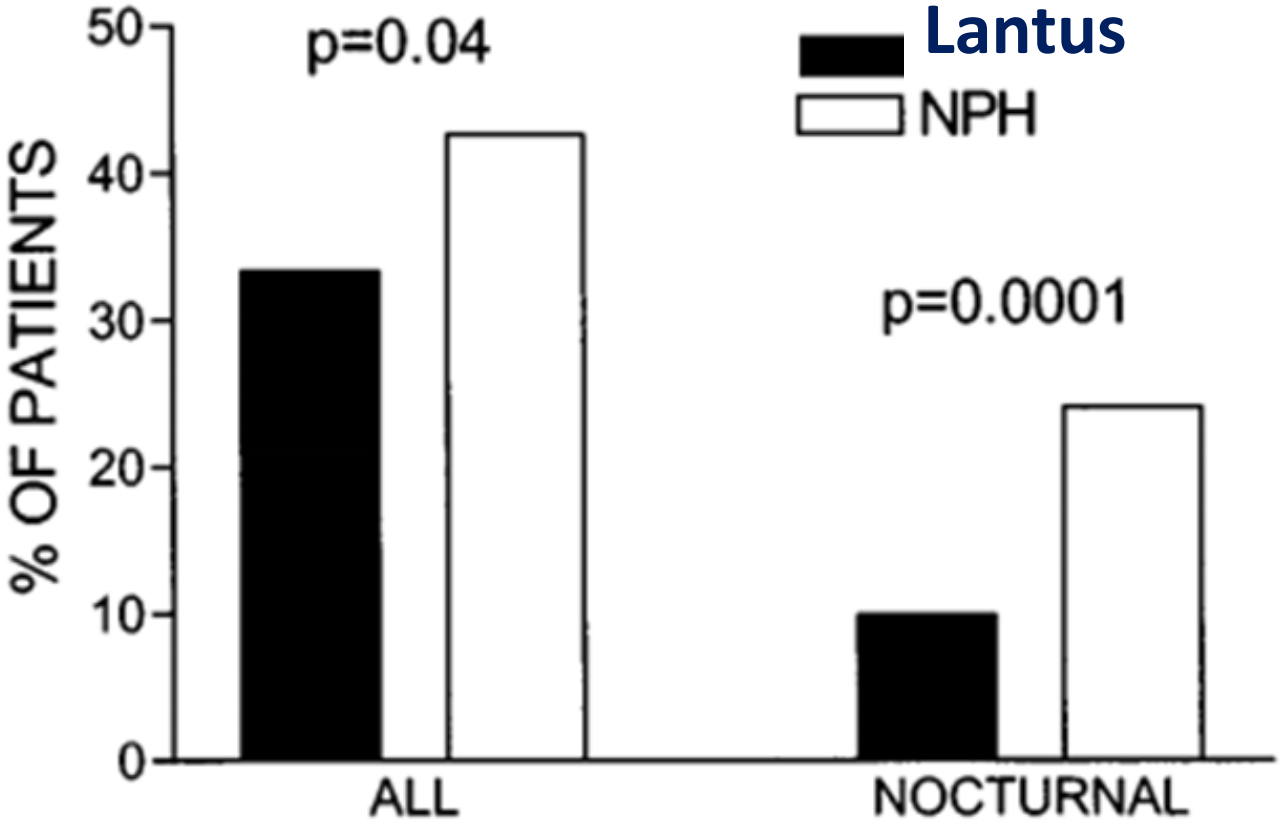
Wirkprofile Lantus vs. NPH



Heinemann L et al. Diabetes Care 23:644–649, 2000

Lantus vs. NPH*

Symptomatische Hypoglykämien



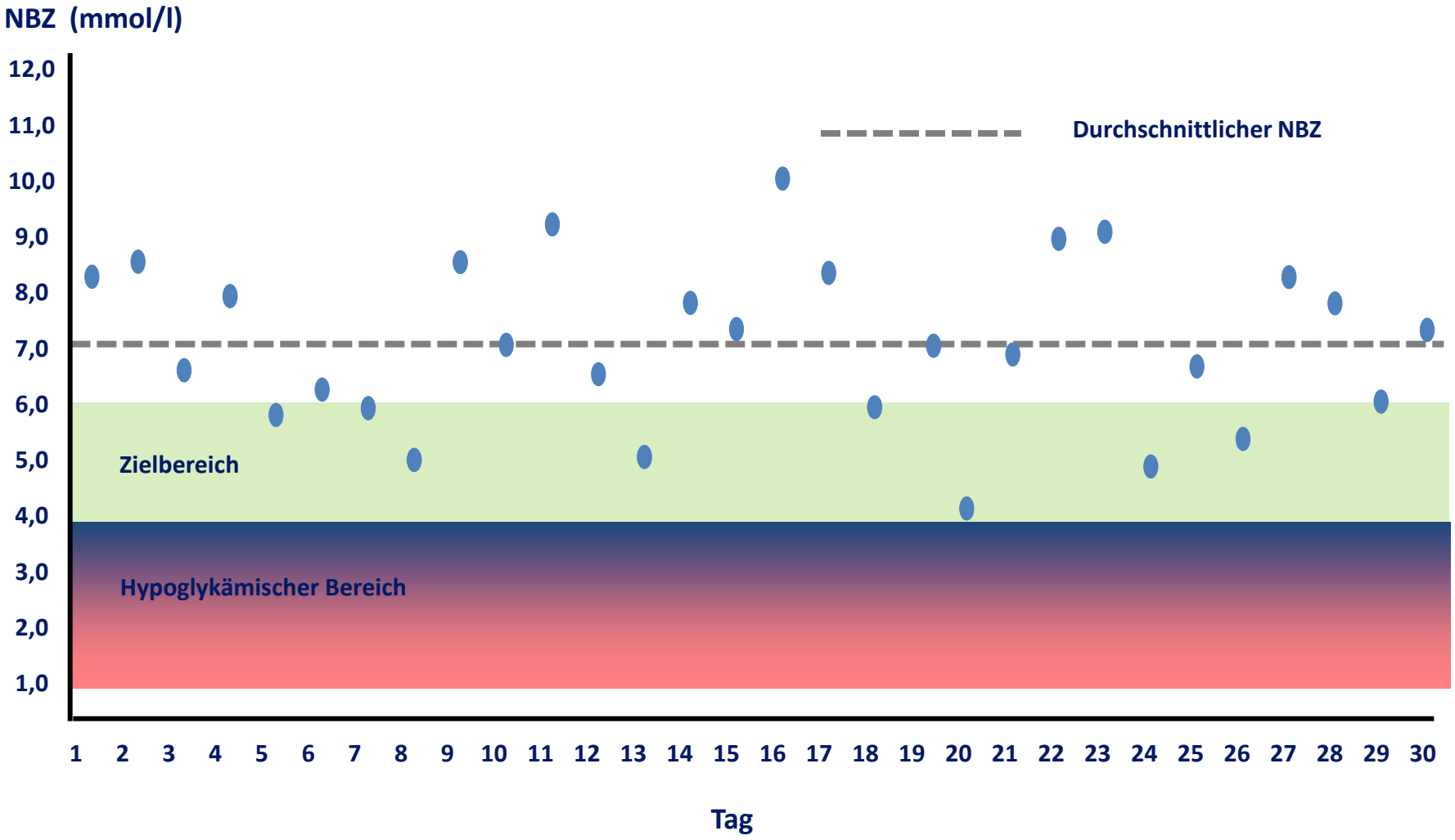
Hypoglykämie:
BZ < 2.8 mmol/l (50 mg/dl)

Ziel:
FBG-Ziel < 6.7 mmol/l (120 mg/dl)

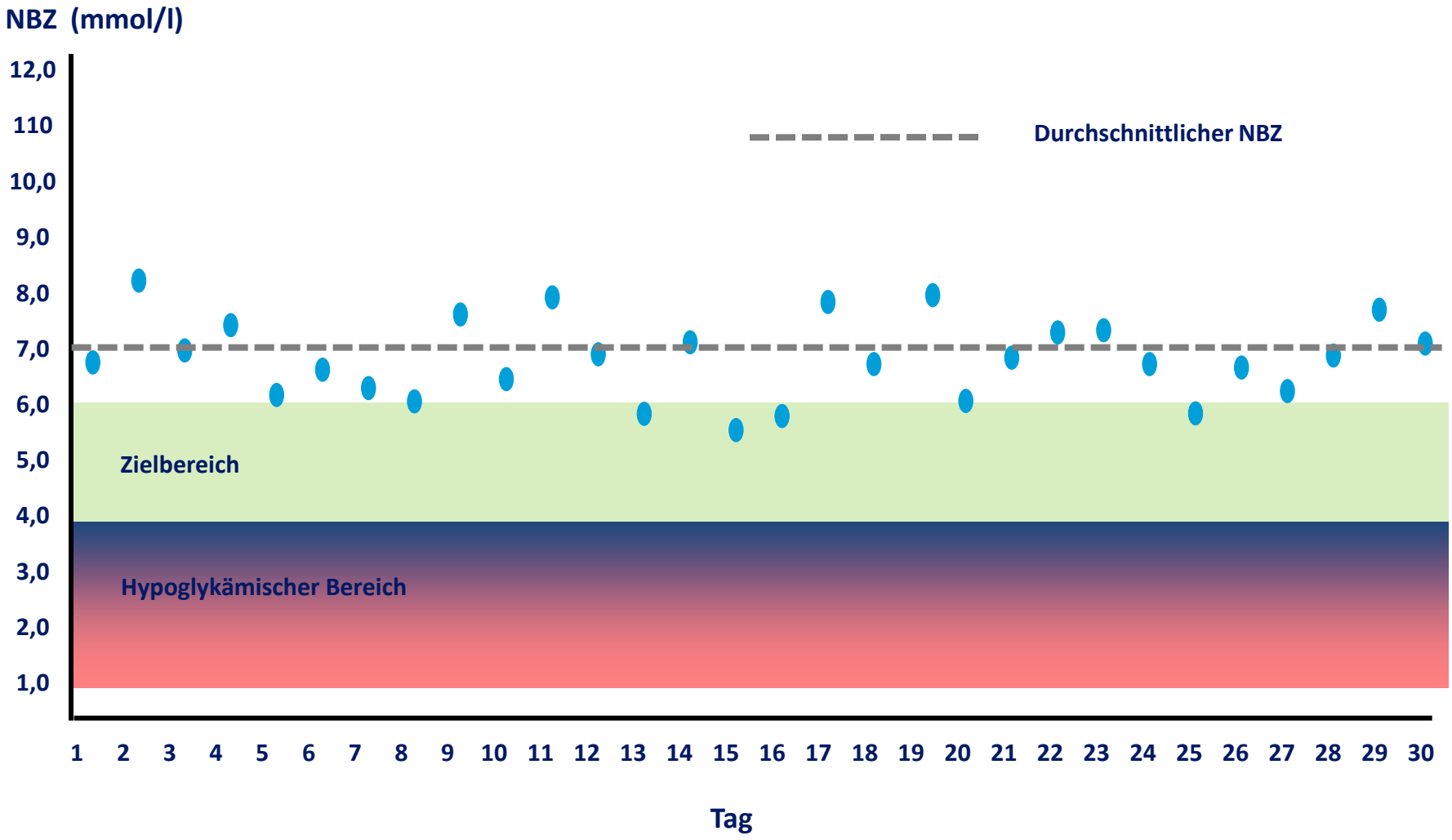
*NPH = Insulatard, Huminsulin basal etc.

Yki-Järvinen H et al. Diabetes Care 23:1130-1136, 2000

Alte Insuline



ideales Insuline



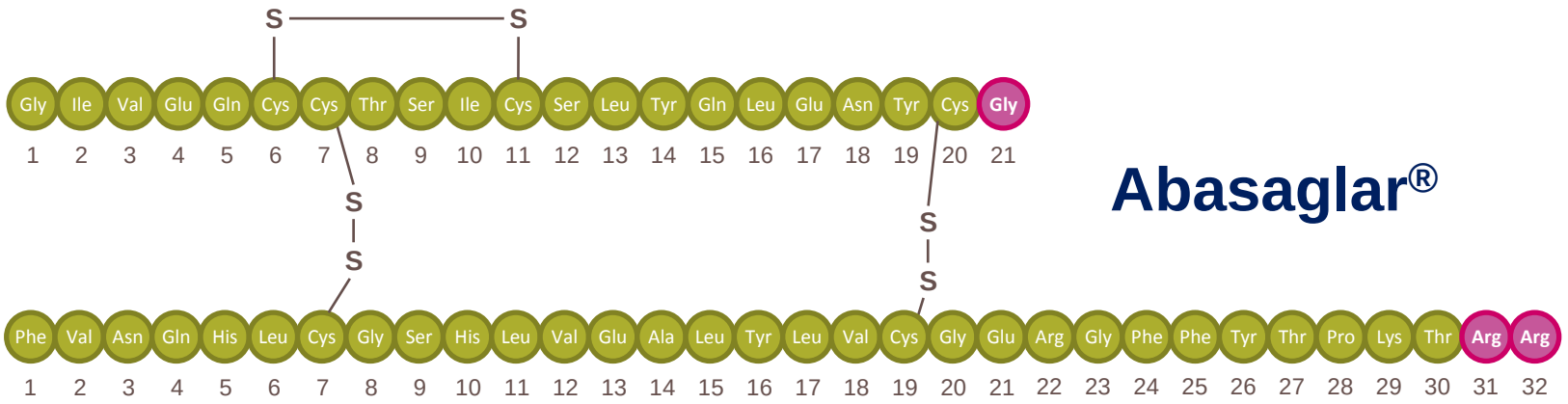
Neuere Basalinsuline

Insulin degludec

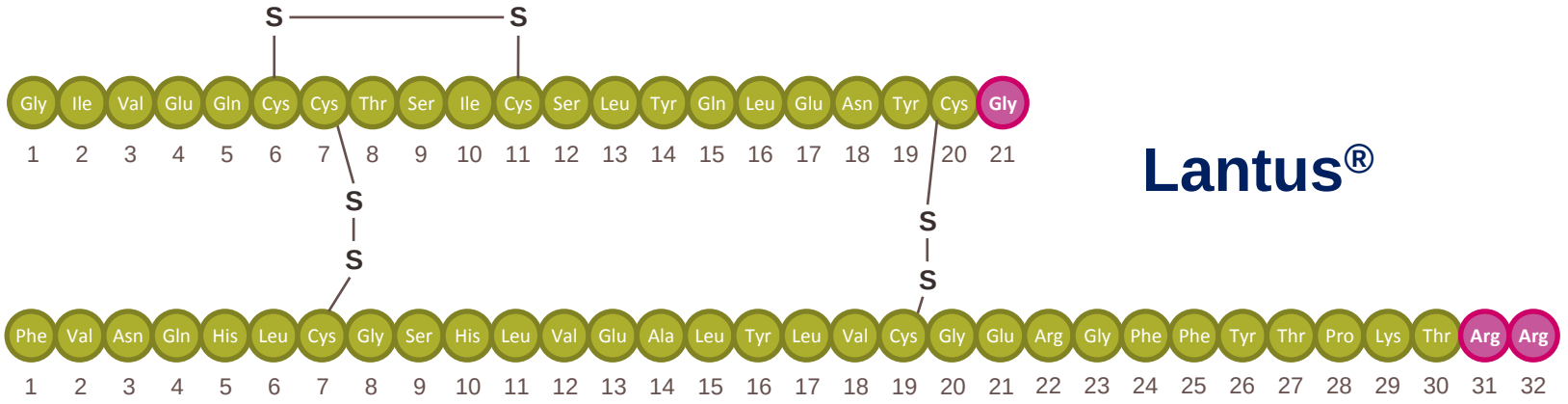
Insulin glargine U 300

Insulin glargine U 100

„Neuere“ Basalinsuline



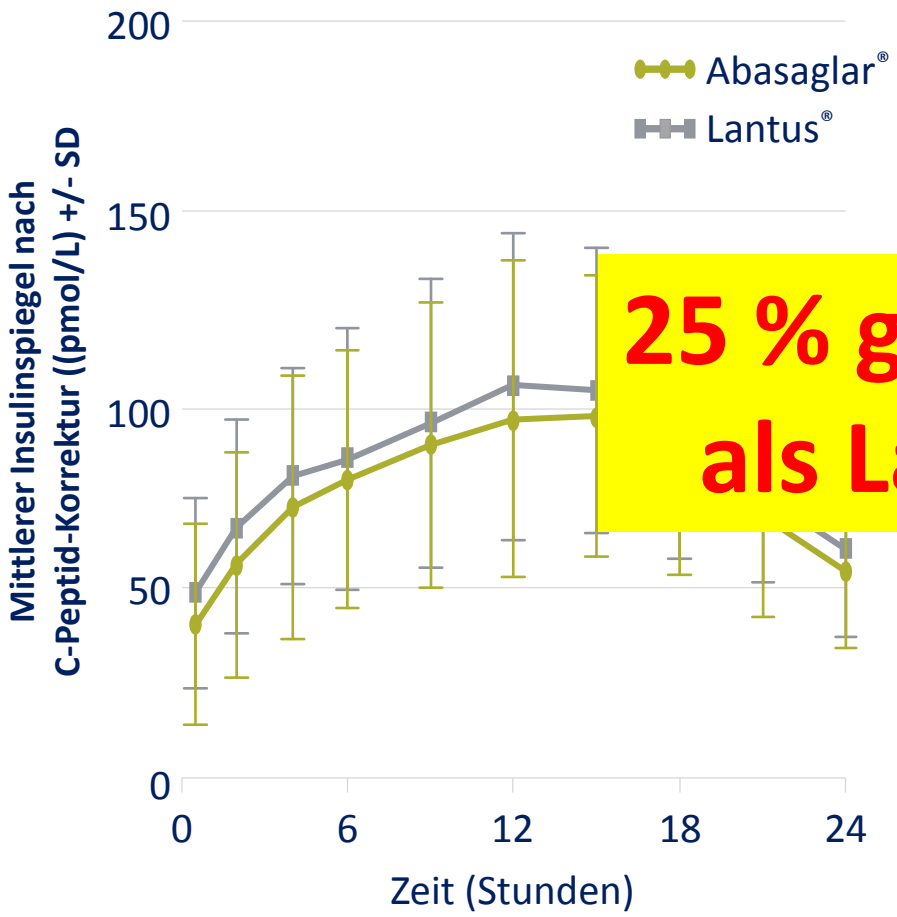
Abasaglar®



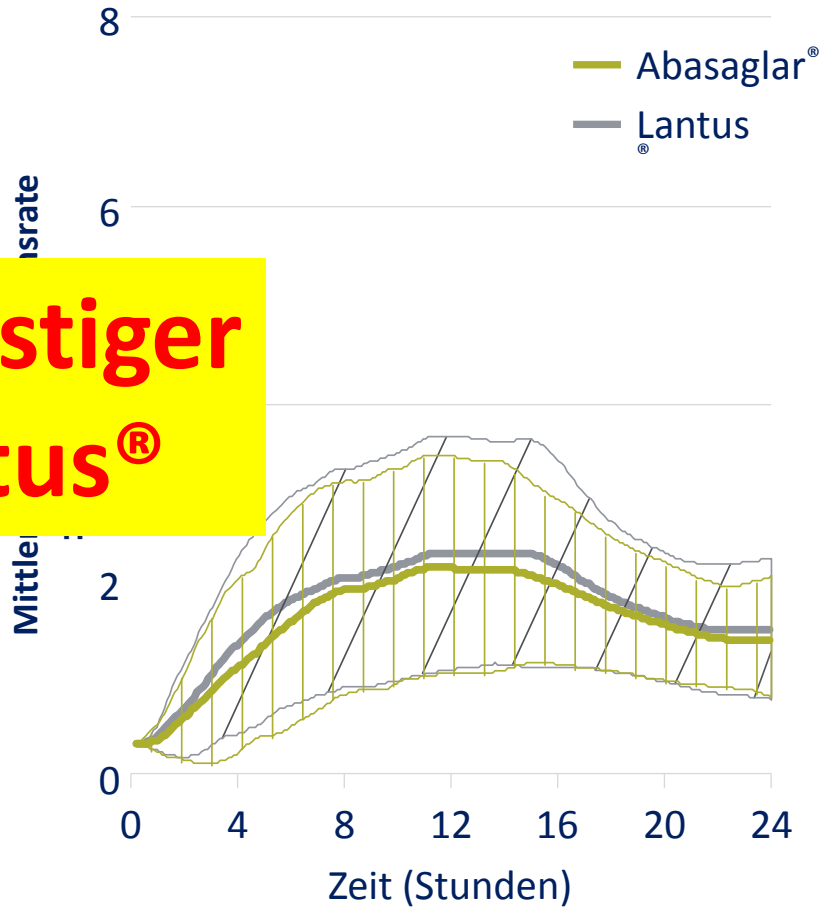
Lantus®

Lantus® Fachinformation, Stand: 04/2015. Abasaglar ® Fachinformation, Stand 12/2014; EMA-Assessment Report 24.3.2015

Abasaglar vs. Lantus



25 % günstiger als Lantus®



Linnebjerg H et al. Diabetes Care. 2015 Aug 25. pii: dc142623. [Epub ahead of print]

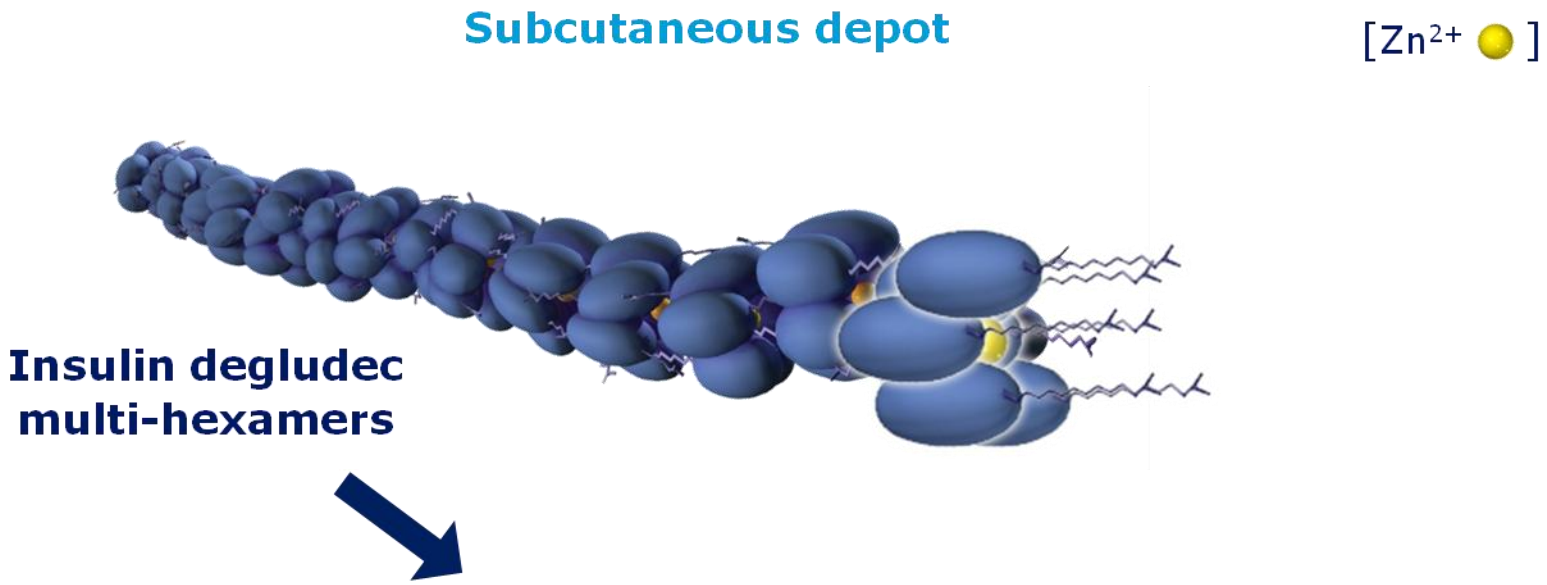
Neuere Basalinsuline

Insulin degludec

Insulin glargine U 300

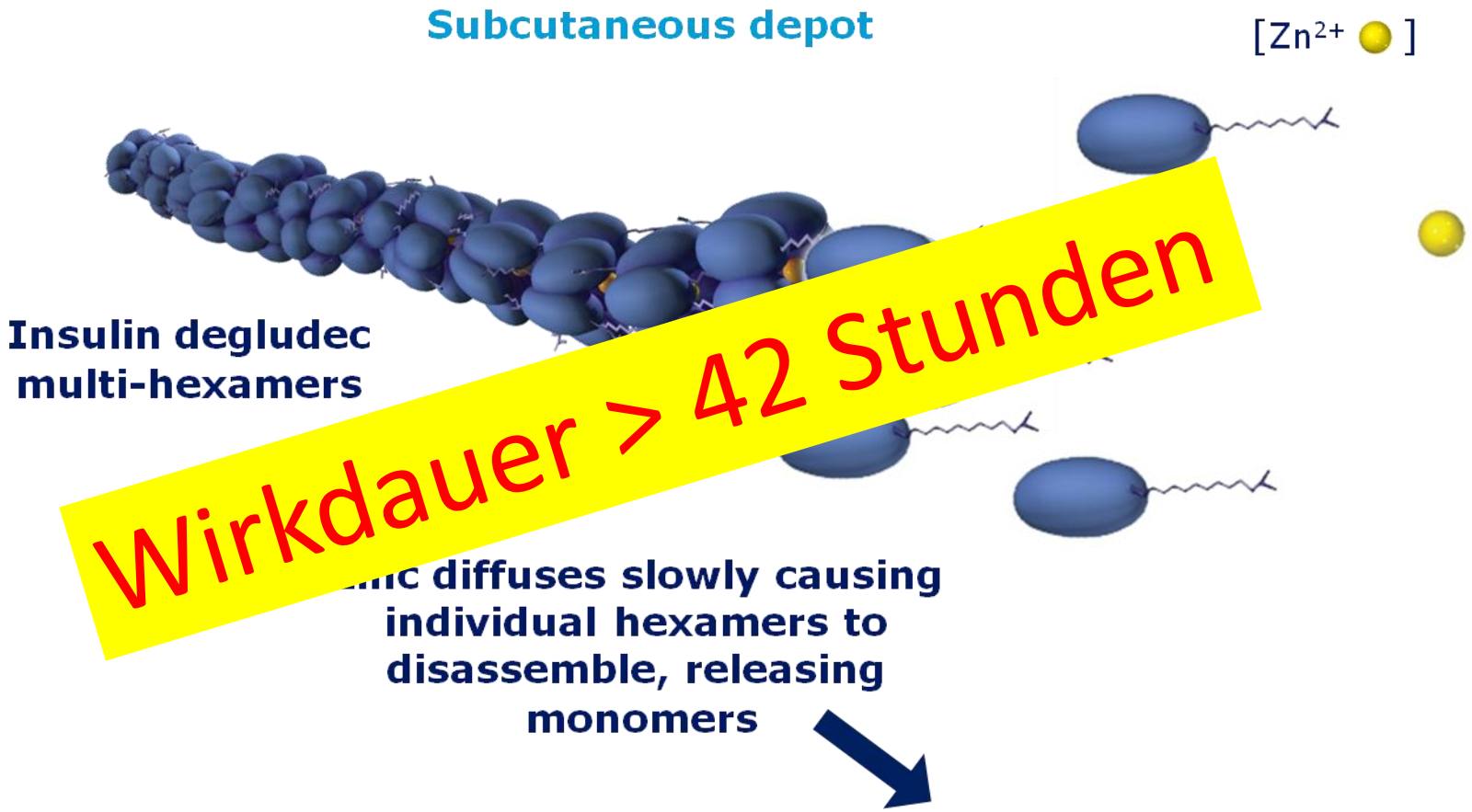
Insulin glargine U 100

Degludec: Freisetzung



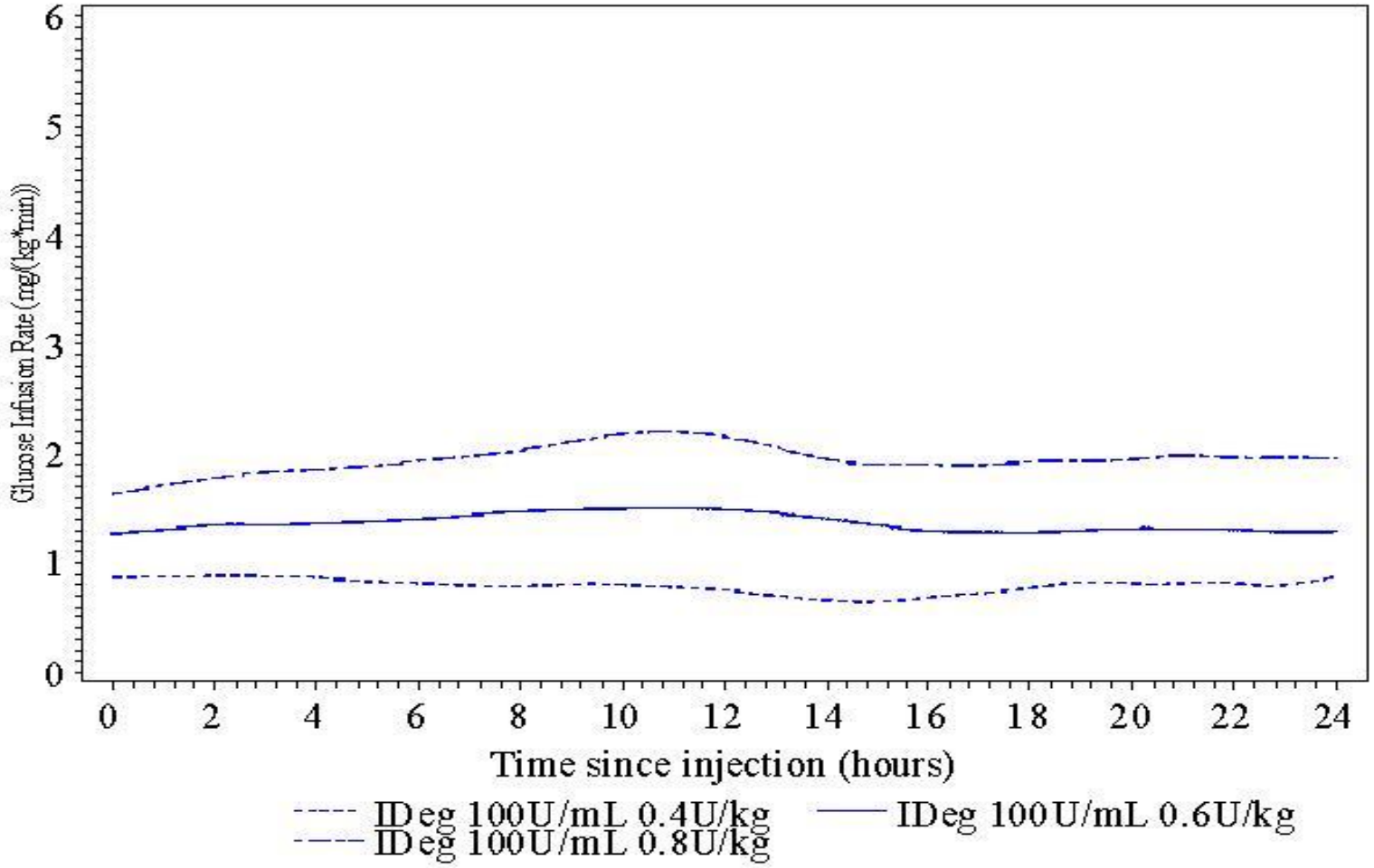
Jonassen et al. Pharmaceutical Research. 29:2104-2114, 2012

Degludec: Freisetzung



Jonassen et al. Pharmaceutical Research. 29:2104-2114, 2012

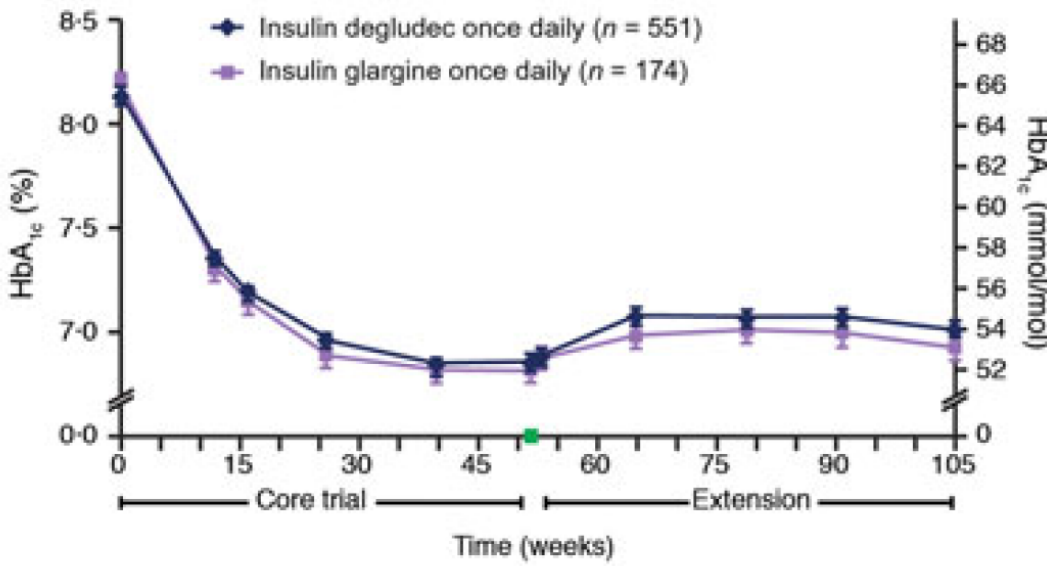
Degludec: Wirkprofil



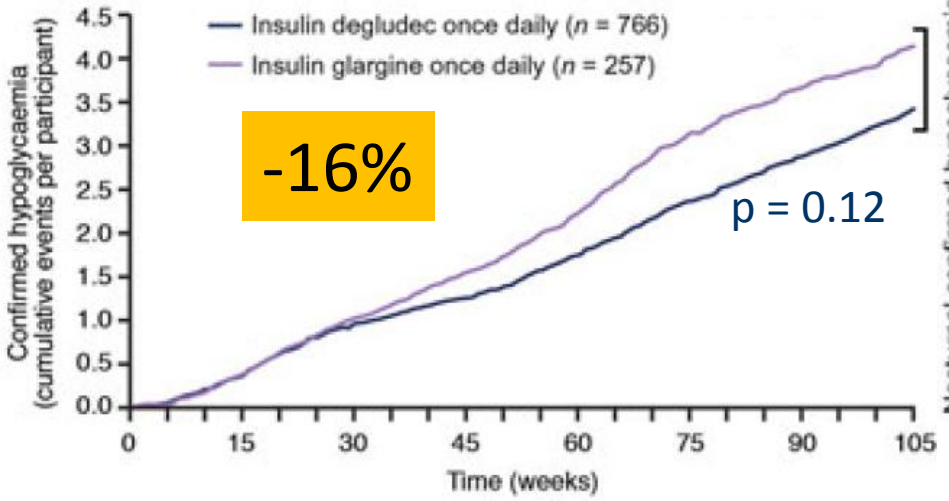
Heise T et al. Diab Obes Metab 2012;14: 859–964

Degludec: 2-Jahresdaten BOT

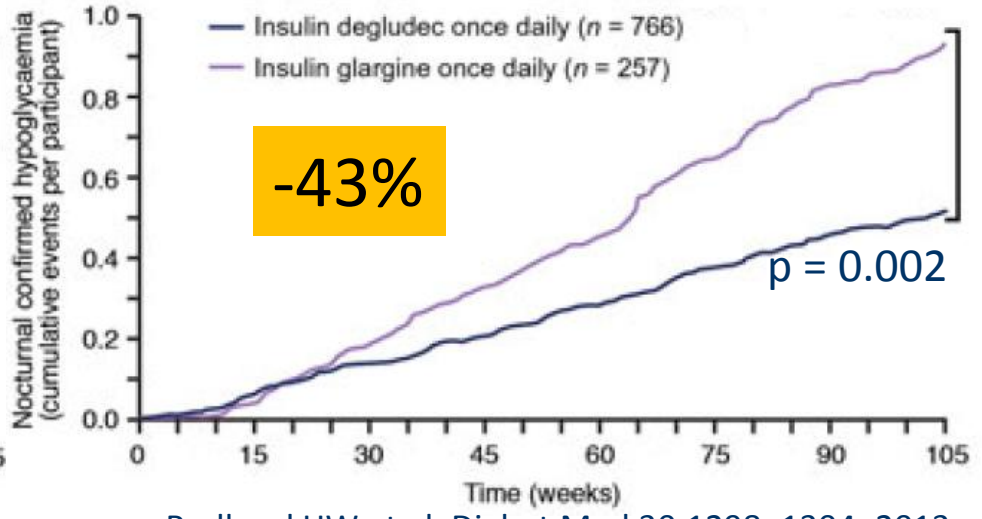
"Basal insulin was titrated
to target pre-breakfast
plasma glucose of 3.9–4.9 mmol/l "



Hypoglykämien



Nächtliche Hypoglykämien



Rodbard HW et al. Diabet Med 30:1298–1304, 2013

Neuere Basalinsuline

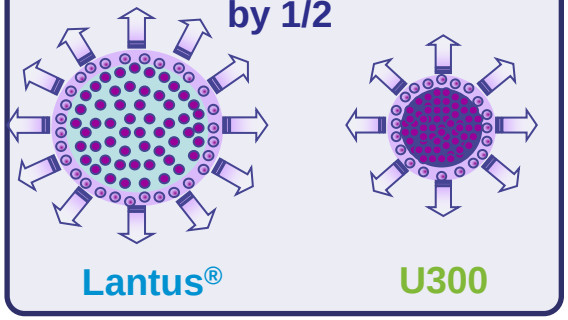
Insulin degludec

Insulin glargine U 300

Insulin glargine U 100

Toujeo: Wirkprofil

Reduction of depot surface by 1/2



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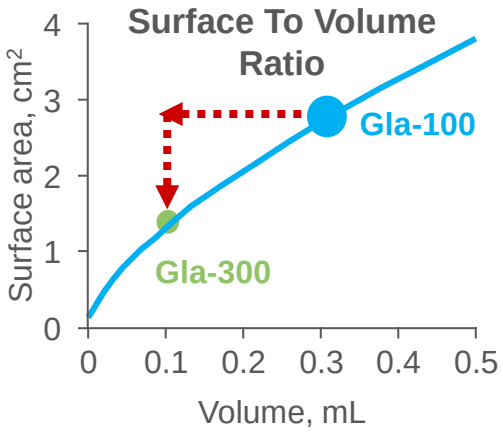
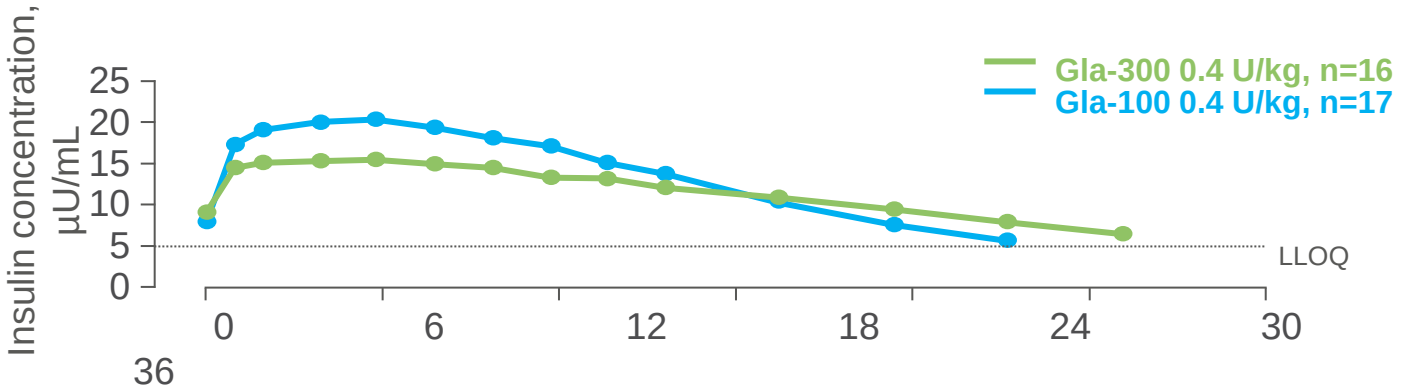
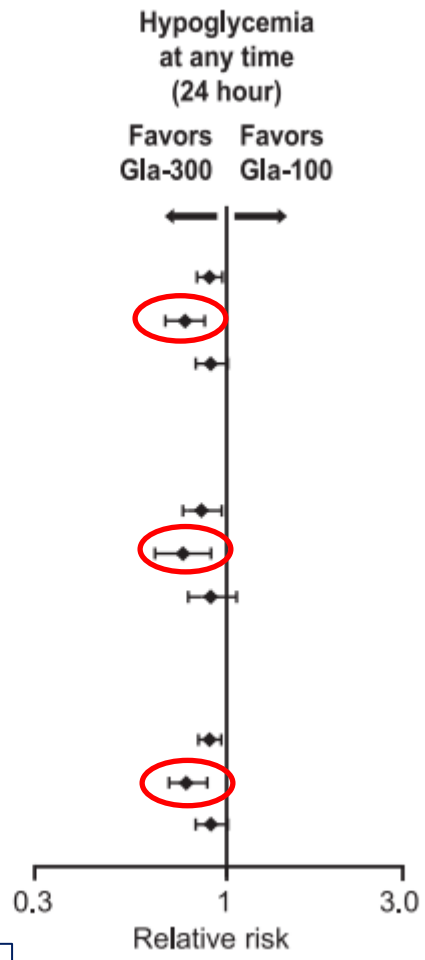




Becker RH et al. Diabetes Care 38:637-43, 2015

Toujeo: Hypoglykämien

	Hypoglycemia at any time (24 hour)		Nocturnal hypoglycemia (00:00–05:59 hour)	
	RR	95% CI	RR	95% CI
Any hypoglycemia				
Baseline to month 6	0.90	0.83–0.98	0.73	0.61–0.88
Baseline to week 8	0.77	0.68–0.88	0.54	0.40–0.71
Week 9 to month 6	0.91	0.82–1.01	0.80	0.63–1.00
Documented symptomatic hypoglycemia (≤3.9 mmol/L [≤70 mg/dL])				
Baseline to month 6	0.86	0.76–0.98	0.73	0.58–0.92
Baseline to week 8	0.76	0.63–0.92	0.43	0.30–0.63
Week 9 to month 6	0.91	0.78–1.07	0.86	0.66–1.13
Confirmed (≤3.9 mmol/L [≤70 mg/dL]) or severe hypoglycemia				
Baseline to month 6	0.90	0.83–0.98	0.71	0.58–0.86
Baseline to week 8	0.78	0.69–0.89	0.53	0.39–0.72
Week 9 to month 6	0.91	0.82–1.02	0.77	0.60–0.97



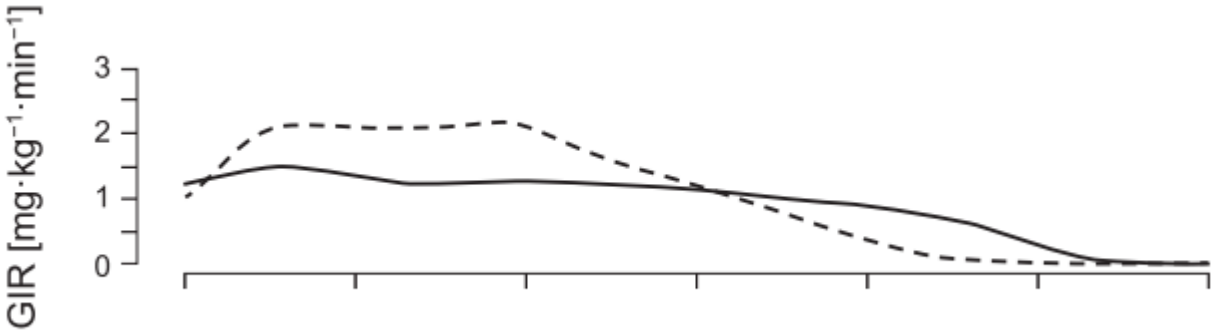
Bestätigte Hypoglykämie:
Plasma-Glukose < 3.9 mmol/L
< 3.0 mmol/L

FBG-Zielwert:
4.4-5.6 mmol/L (80-100 mg/dL)

Yki-Jarvinen H et al. Diabetes Care 37:3235–3243, 2014

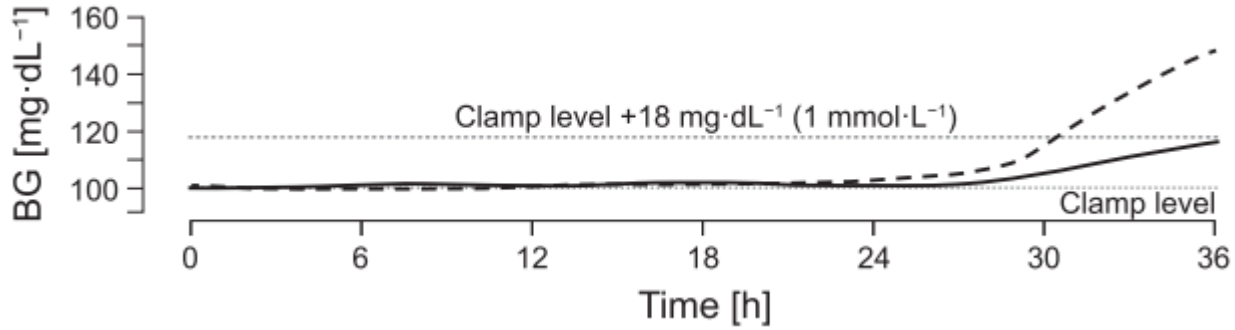
Toujeo: Vorteile

Glukoseinfusionsrate:



Blu

1. Flexible Gabe +/- 3 Stunden möglich



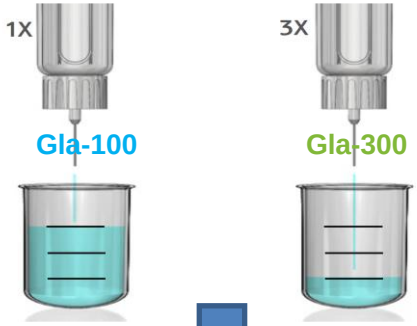
– – – Lantus®

——— Toujeo®

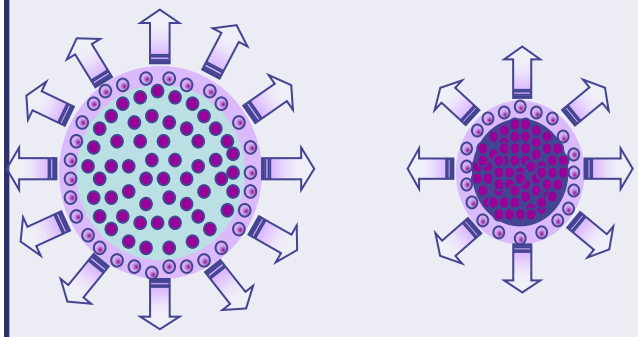
Becker Rh et al. Diabetes Care 38:637-643, 2015

Jeandidier N et al. P-961 EASD 2014

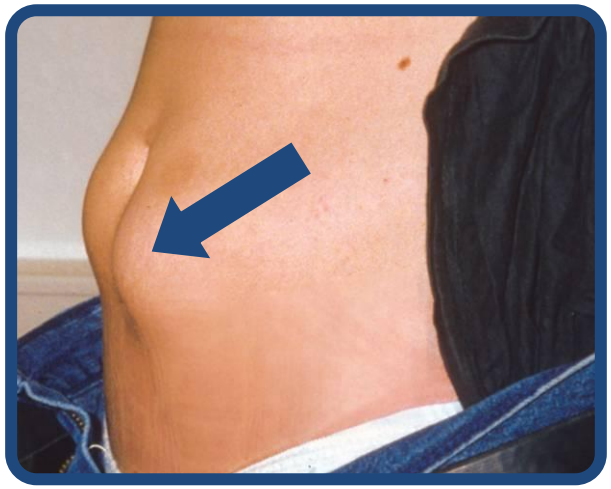
Toujeo: Vorteile



Reduction of depot surface by 1/2



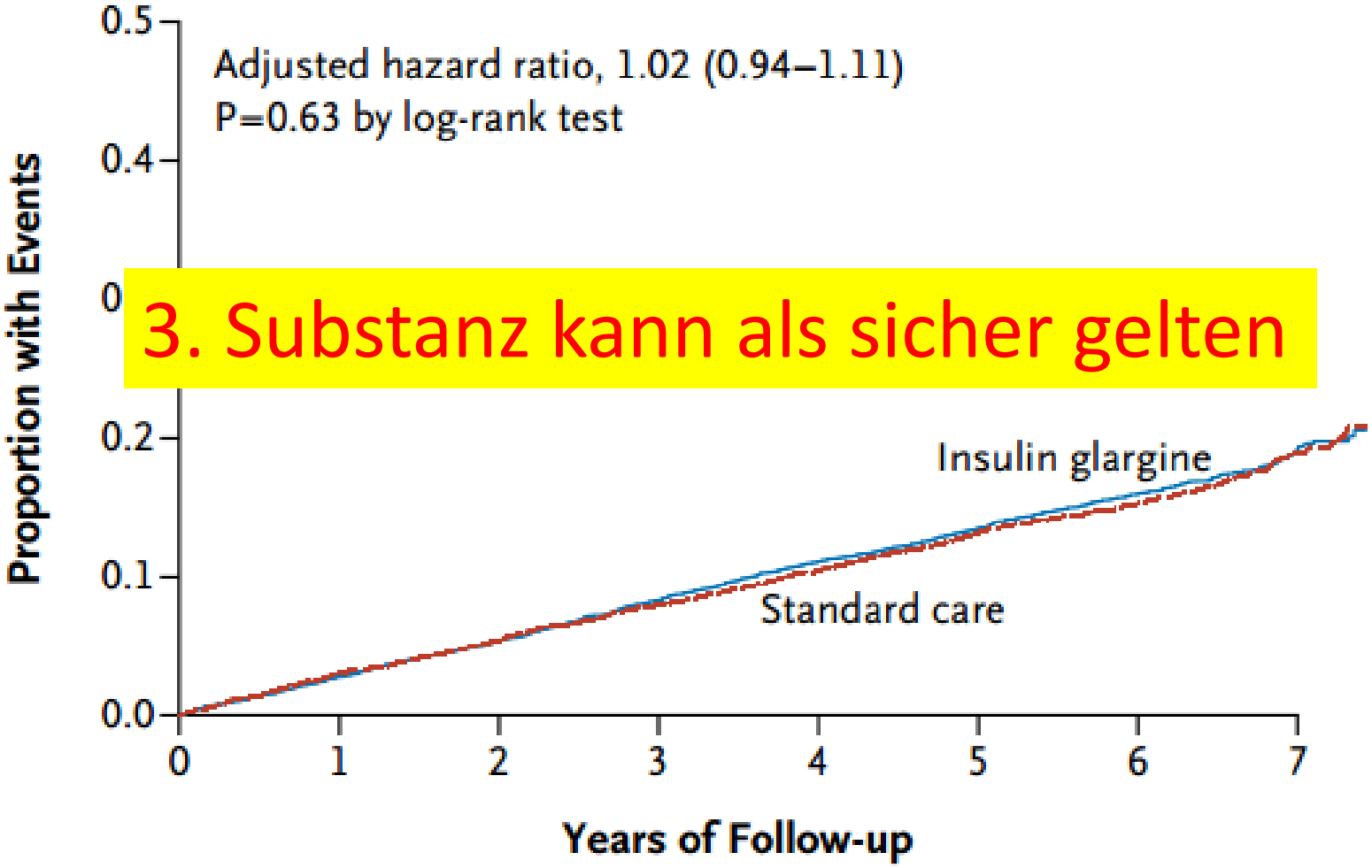
2. Kleineres Volumen



Becker RH et al. Diabetes Care 38:637-43, 2015

Toujeo: Sicherheit

Myocardial Infarction, Stroke, or Death from Cardiovascular Causes (Coprimary Outcome)



3. Substanz kann als sicher gelten

ORIGIN Trial Investigators N Engl J Med 367:319-328, 2012

Gewichtsentwicklung unter BOT

Degludec:	+ 2.7 kg
Glargine :	+ 2.4 kg
	p = 0.31

Rodbard HW et al. Diabet Med 30:1298–1304, 2013

Individuelle Therapieziele

Diabetologia (2012) 55:1577–1596
DOI 10.1007/s00125-012-2534-0

POSITION STATEMENT

Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

S. E. Inzucchi · R. M. Bergenstal · J. B. Buse · M. Diamant · E. Ferrannini · M. Nauck · A. L. Peters · A. Tsapas · R. Wender · D. R. Matthews

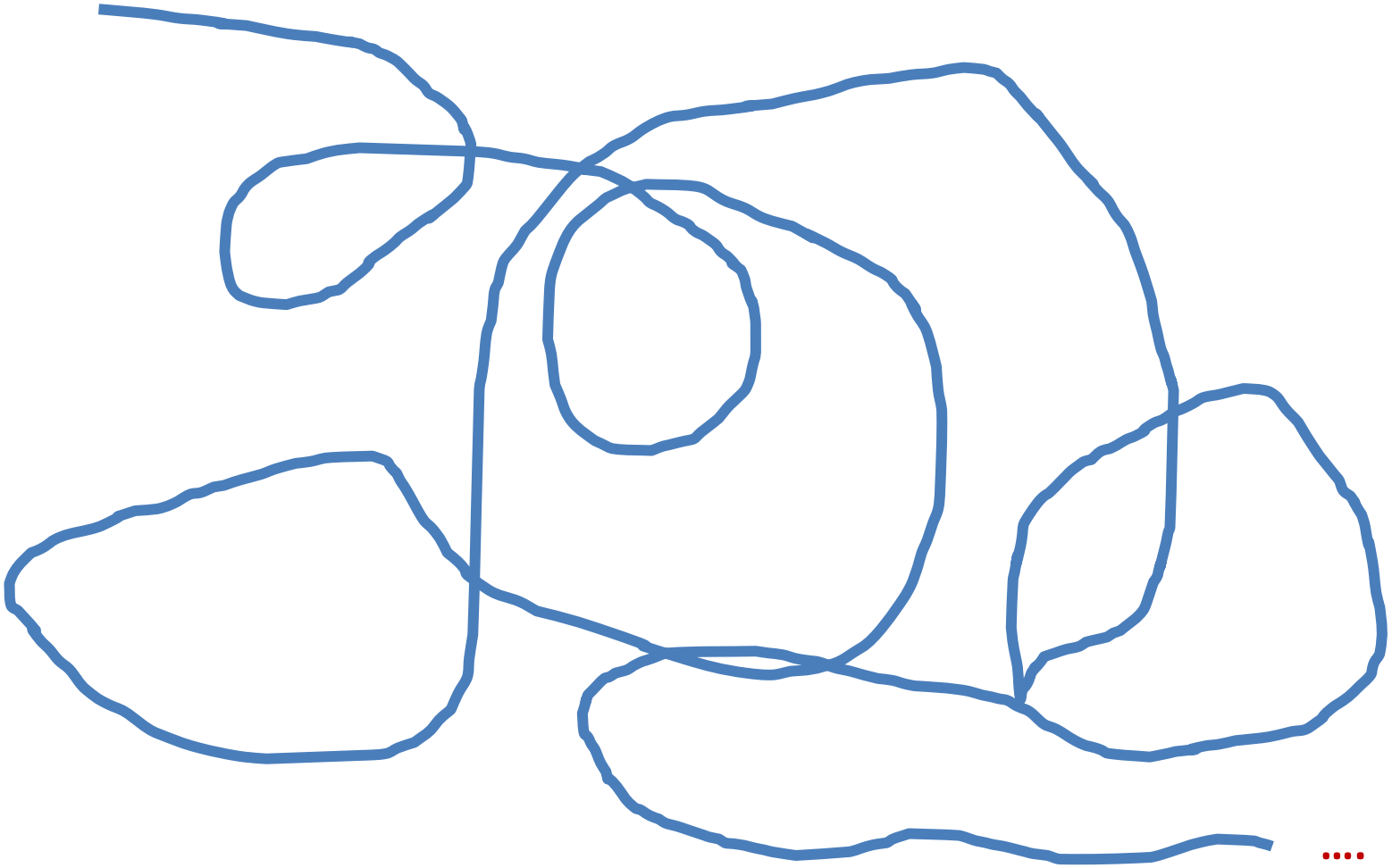
"…ideally, fasting and pre-meal glucose should be maintained at ***< 7.2 mmol/L*** *(130 mg/dl)…"*

FBG-Zielwert:
3.9-4.9 mmol/L (70-90 mg/dL)

Inzucchi SE et al. Diabetologia 55:1577–1596, 2012

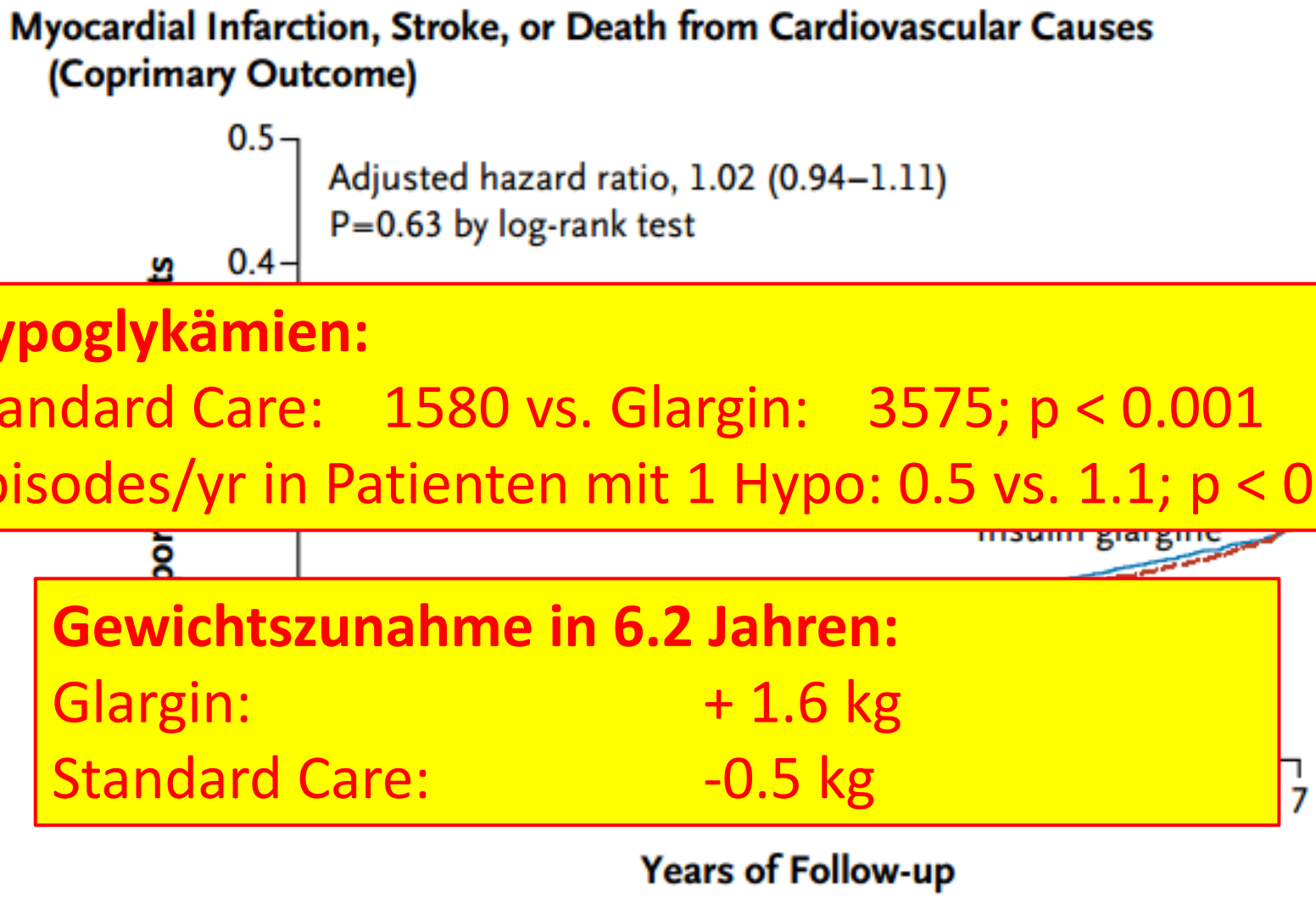
Endpunkte

Anfang



Zinman B et al. NEJM DOI: 10.1056/NEJMoa1504720

Frühe Insulintherapie



Hypoglykämien:

Standard Care: 1580 vs. Glargin: 3575; $p < 0.001$

Episodes/yr in Patienten mit 1 Hypo: 0.5 vs. 1.1; $p < 0.001$

Gewichtszunahme in 6.2 Jahren:

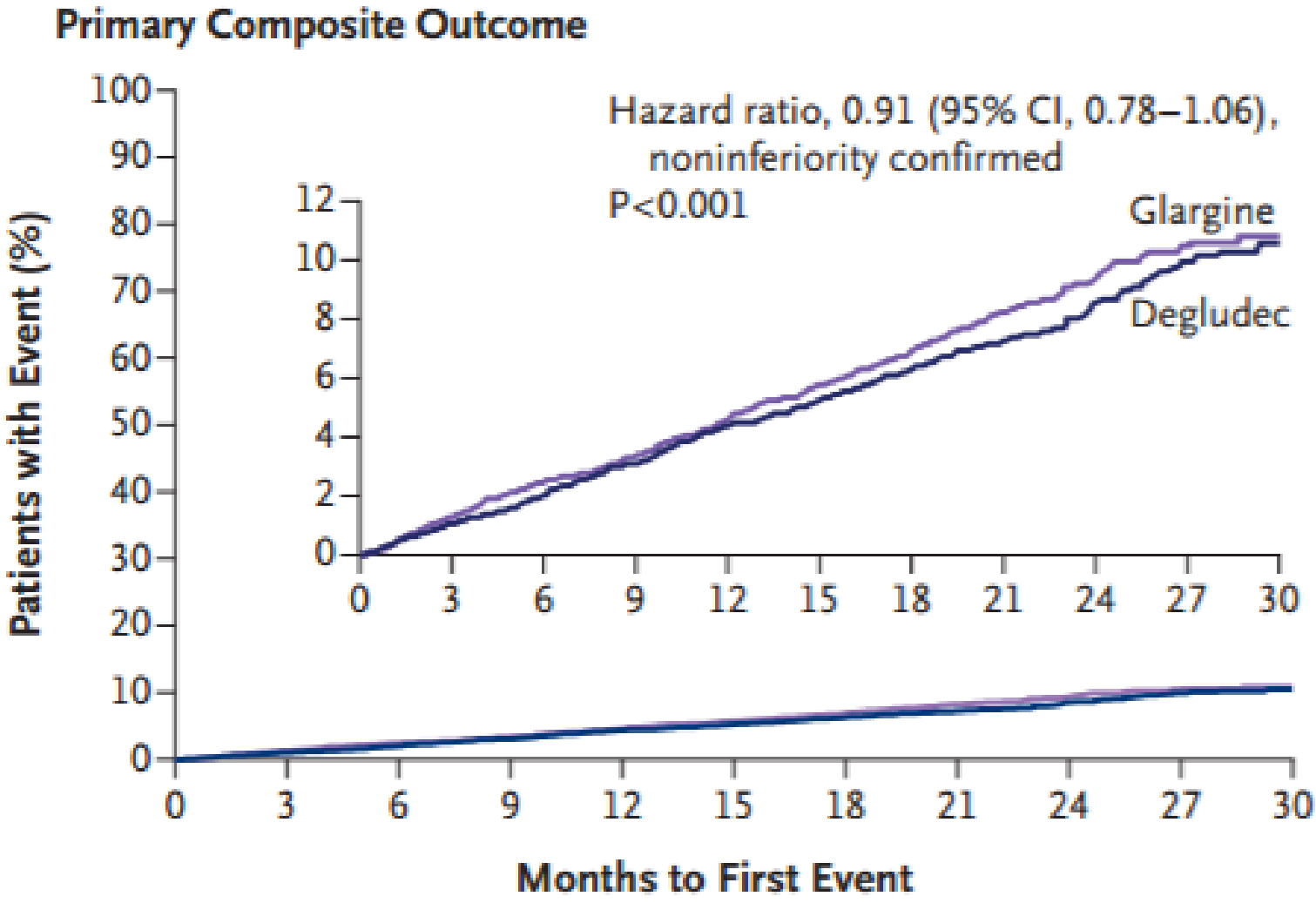
Glargin: + 1.6 kg

Standard Care: -0.5 kg

ORIGIN Trial Investigators N Engl J Med 367:319-328, 2012

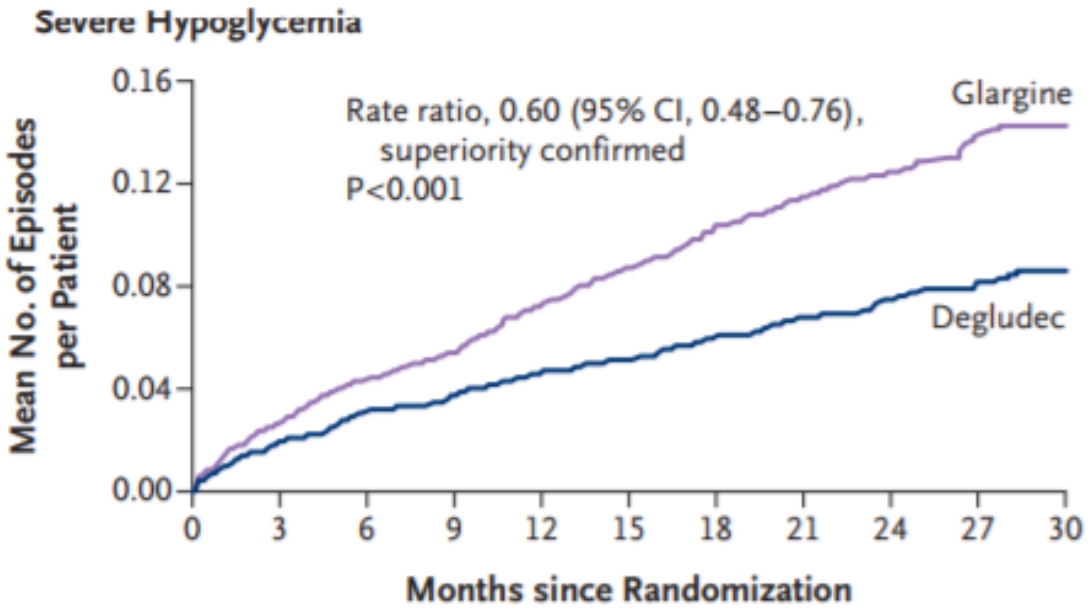
Tresiba vs. Lantus in Typ 2 DM

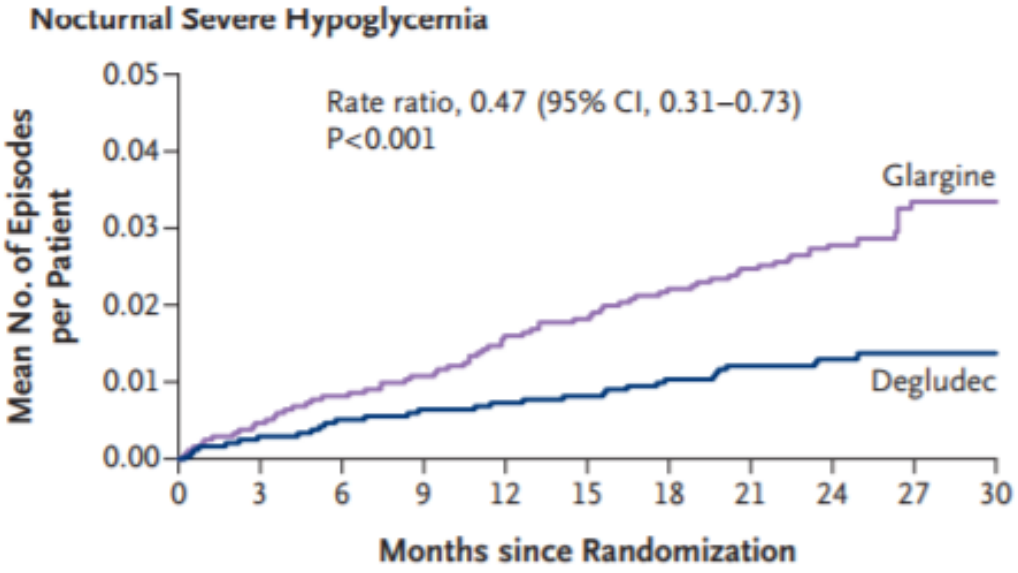
DEVOTE-Trial



Marso SP et al. N Engl J Med. 2017 Jun 12. doi: 10.1056/NEJMoa1615692

Tresiba vs. Lantus in Typ 2 DM





Marso SP et al. N Engl J Med. 2017 Jun 12. doi: 10.1056/NEJMoa1615692

Insulintherapie – Fazit für die Praxis

- bei Typ 2-Diabetes abendliche Basalinsulingabe bevorzugen
- Analoginsuline (Abasaglar, Lantus, Toujeo, Tresiba) 1. Wahl
- Abasaglar ist preislich die günstigste Alternative
- Nüchtern-BZ-Zielbereich: 5.X-7 mmol/L (im Alter 6-8 mmol/L)
- Startdosis: 10 Einheiten
- bei hohem HbA1c und/oder Adipositas höhere Startdosis wählen

Herzlichen Dank für Ihre Aufmerksamkeit