

10ª EDIZIONE Giornate Diabetologiche Salernitane

È stata inoltrata richiesta di Patrocinio a:

- Regione Campania
- Ministero della Salute
- Università degli Studi di Salerno
- A.M.D. Associazione Medici Diabetologi
- S.I.D. Società Italiana di Diabetologia
- Scuola Medica Diabetologica Salernitana
- O.S.D.I. Regione Campania
- Ordine dei Medici ed Odontoiatri della Provincia di Salerno
- Associazione Diabetici Arcobaleno A.D.A. ONLUS
- Provincia di Salerno
- Comune di Salerno
- Comune di Vietri sul Mare
- Comune di Mercato S. Severino



COMITATO SCIENTIFICO

M. Agrusta, U. Ametia, R. Basile,
P. Calatola, G. Ghirlanda, C. Lambiase

L'evento si inserisce nel programma
di Educazione Continua in Medicina (ECM).

www.giornatediabetologichesalernitane.com

10ª EDIZIONE Giornate Diabetologiche Salernitane 8_9_10 Marzo 2012

PRESIDENTE DEL CONVEGNO
Prof. Giovanni Ghirlanda

DIRETTORE DEL CONVEGNO
Dott. Claudio Lambiase



In collaborazione con:



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Dott. V. Prisco



PRESIDENTE
Dott. L. Gentile



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Dott. A. Aiello

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Teorema Consulting srl
Via C. Napolitani, 4 - 84083 Castel San Giorgio (SA)
Tel. 081 951642/081 3220196 - Fax 081 9535912
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Corso di aggiornamento
teorico-pratico per infermieri
Convegno per medici chirurghi

Lloyd's Baia Hotel
Vietri sul Mare (SA)

SABATO 10 MARZO

II SESSIONE

Innovazioni terapeutiche

Moderatori: S. Gentile; V. Armentano

h 8.30 - 8.50

La terapia insulinica: il presente.....il futuro

P. Marchetti

h. 8.50 - 9.10

Le incretine: un passo avanti

F. Dotta

h 9.10 - 10.30

Discussione interattiva

h 10.30 - 10.45

Coffee Break



Il presente

- Insuline umane
- Analoghi rapidi
- Analoghi lenti
- Miscele precostituite



Insuline umane

•Lilly

- | | |
|----------------|------------|
| •Humulin R | flaconcino |
| •Humulin I | flaconcino |
| •Humulin 30/70 | flaconcino |

•Novo

- | | |
|----------------|------------|
| •Actrapid | flaconcino |
| •Protaphane | flaconcino |
| •Actraphane 30 | flaconcino |

•Sanofi

- | | |
|----------------|---|
| •Insuman Rapid | flaconcino/penna preriempita (Solostar) |
| •Insuman Basal | registrata, non commercializzata |
| •Insuman Combo | registrata, non commercializzata |



Analoghi rapidi

- Lilly

- Humalog

lispro

- Novo

- Novorapid

aspart

- Sanofi

- Apidra

glulisina



Analoghi lenti

- Lilly

- Humalog basal

lispro protamina

- Novo

- Levemir

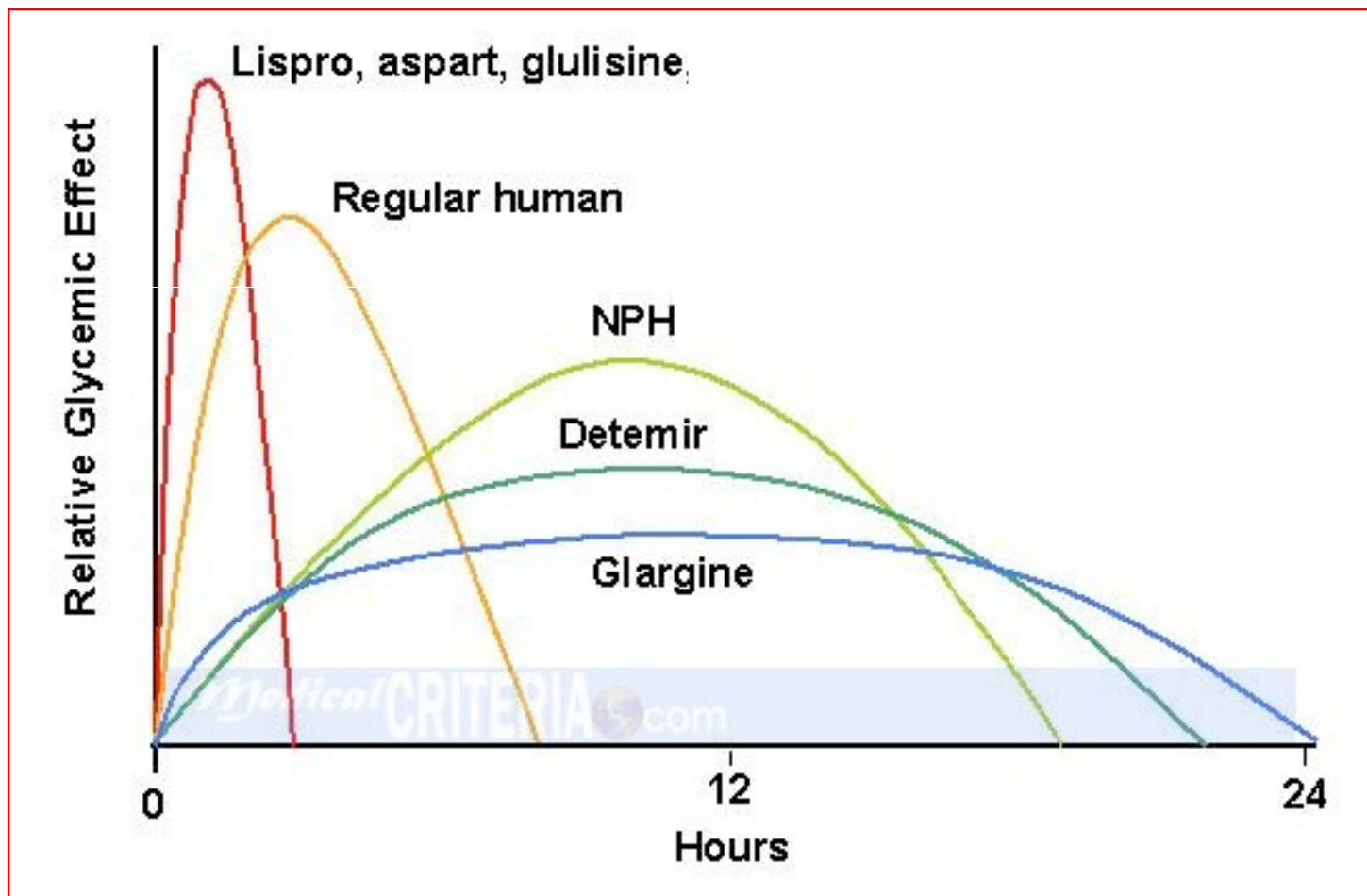
detemir

- Sanofi

- Lantus

glargina

Gli analoghi dell'insulina



Miscele di analoghi precostituite

- Lilly

- Humalog mix 25
- Humalog mix 50

- Novo

- NovoMix 30
- NovoMix 50
- NovoMix 70



Confronto di efficacia

Short acting insulin analogues vs regular human insulin in patients with diabetes mellitus (Cochrane Database Syst Rev 2006): ***only a minor benefit of short acting insulin analogues in the majority of T1DM/T2DM patients***

Long-acting insulin analogues (glargine, detemir) vs human NPH insulin in T2DM (Cochrane Database Syst Rev 2007): ***metabolic control did not differ in a clinical relevant way between treatment groups***

Systematic review: Comparative effectiveness and safety of premixed insulin analogues in T2DM (Ann Intern Med 2008): ***premixed insulin analogues were similar to premixed human insulin in decreasing fasting glucose levels and HbA1c levels***

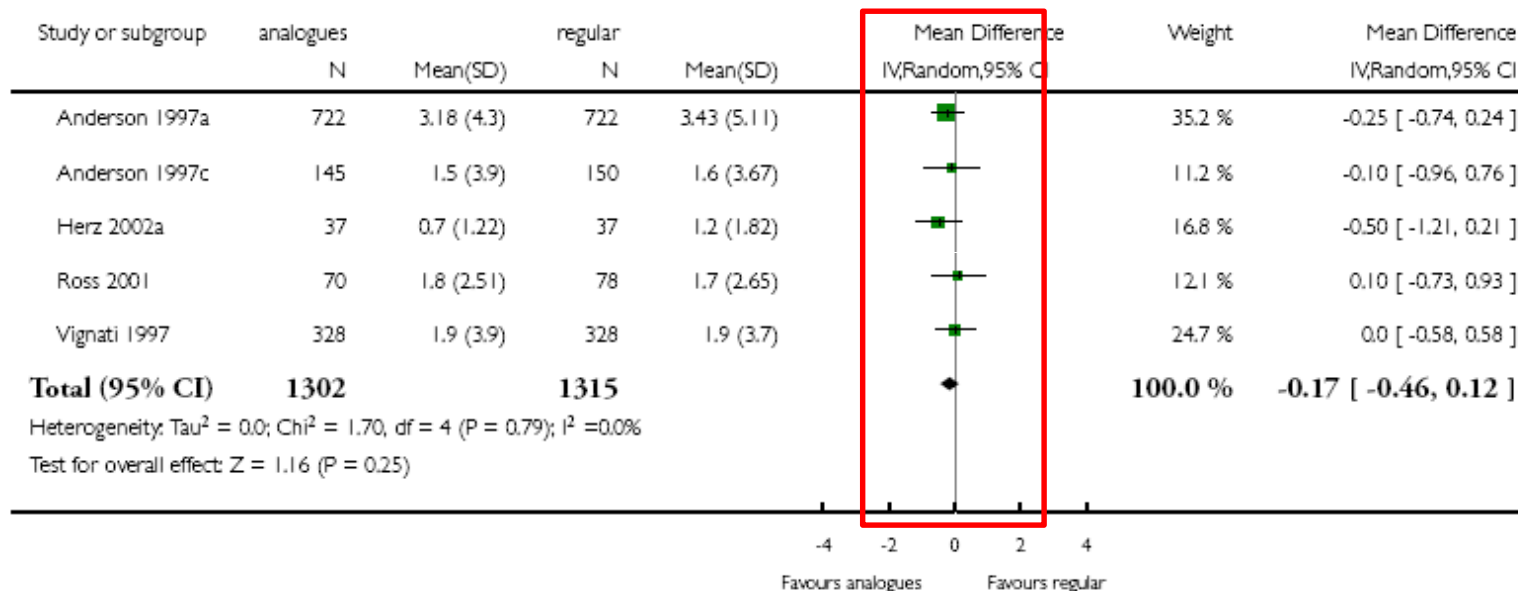
The role of different insulins: hypoglycemia

Analysis 2.2. Comparison 2 Type 2 diabetic patients: short acting insulin analogues versus structurally unchanged insulin, Outcome 2 Hypoglycaemic episodes.

Review: Short acting insulin analogues versus regular human insulin in patients with diabetes mellitus

Comparison: 2 Type 2 diabetic patients: short acting insulin analogues versus structurally unchanged insulin

Outcome: 2 Hypoglycaemic episodes



Short acting insulin analogues versus regular human insulin in patients with diabetes mellitus (Review)
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Severe hypoglycemias (episodes per 100 person-years):
0 to 30.3 (median 0.6) with short acting analogues
0 to 50.4 (median 2.8) with regular insulin

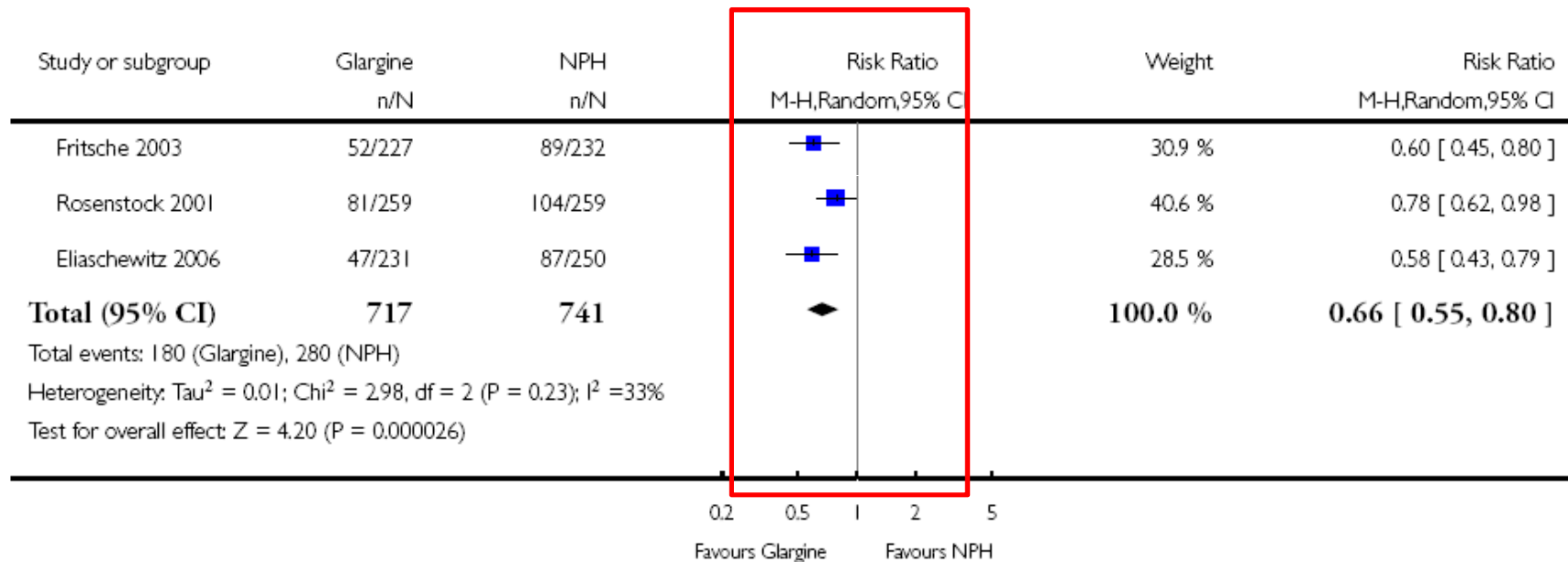
The role of different insulins: hypoglycemia

Analysis 1.5. Comparison 1 Hypoglycaemia, Outcome 5 Nocturnal hypoglycaemia - Glargine vs. NPH.

Review: Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus

Comparison: 1 Hypoglycaemia

Outcome: 5 Nocturnal hypoglycaemia - Glargine vs. NPH



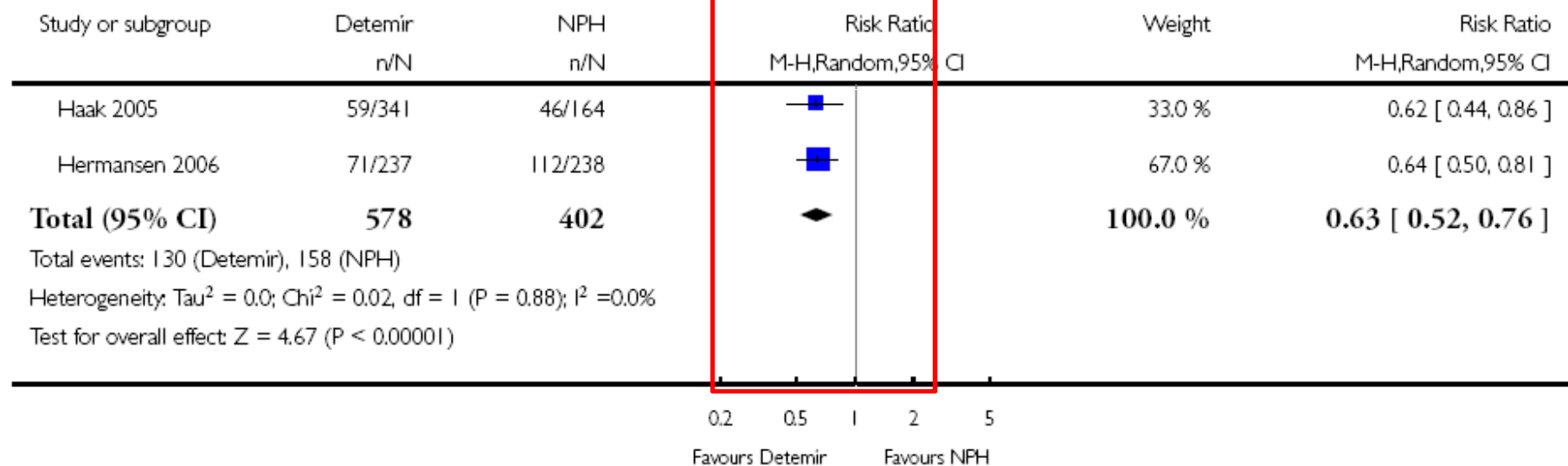
The role of different insulins: hypoglycemia

Analysis 1.6. Comparison 1 Hypoglycaemia, Outcome 6 Nocturnal hypoglycaemia - Detemir vs. NPH.

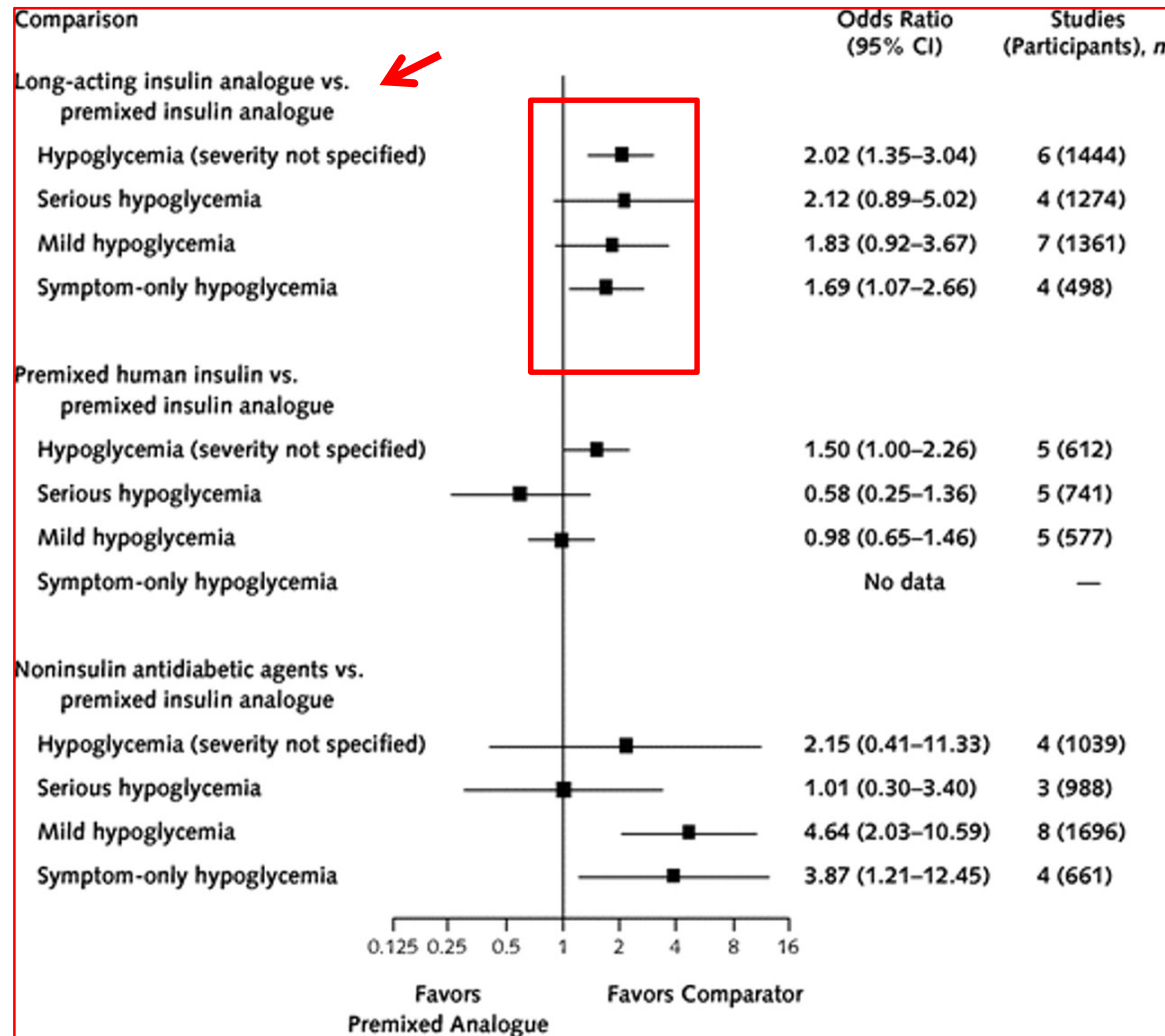
Review: Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus

Comparison: 1 Hypoglycaemia

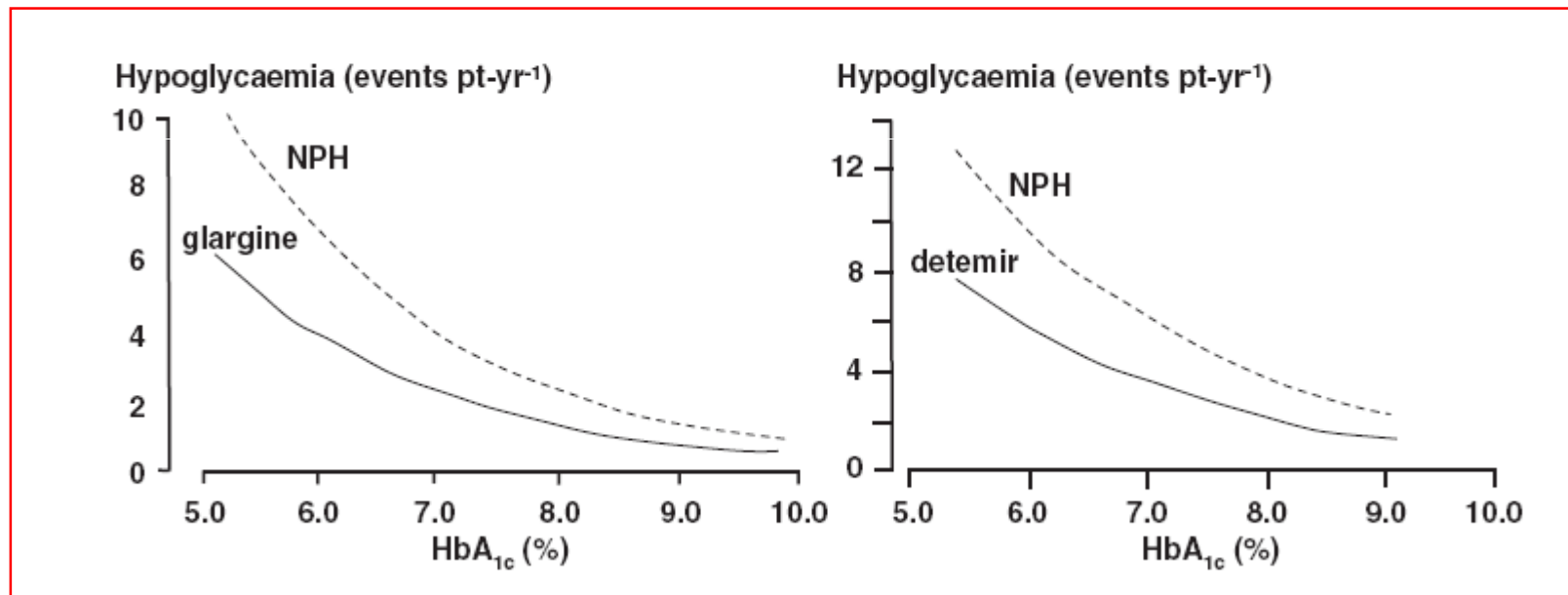
Outcome: 6 Nocturnal hypoglycaemia - Detemir vs. NPH



The role of different insulins: hypoglycemia



Controllo glicemico vs ipoglicemia





Il presente, quindi...

- Propone numerosi tipi di insulina, che, se usati congruamente, consentono di ottenere risultati, in termini efficacia, relativamente poco diversi tra di loro (*anche se gli analoghi presentano, rispetto alle insuline umane, alcuni vantaggi di farmacocinetica*).
- Più importanti sono le differenze per quanto riguarda gli eventi ipoglicemici, relativamente meno frequenti con gli analoghi rapidi rispetto all'insulina pronta umana (?) e meno probabili (soprattutto quelli notturni) con gli analoghi lenti.



Limitazioni della terapia insulinica attuale

- Rischio di ipoglicemie
- Insulinizzazione basale non sempre soddisfacente
- Insulina glargina e detemir non miscibili con insuline ad azione rapida

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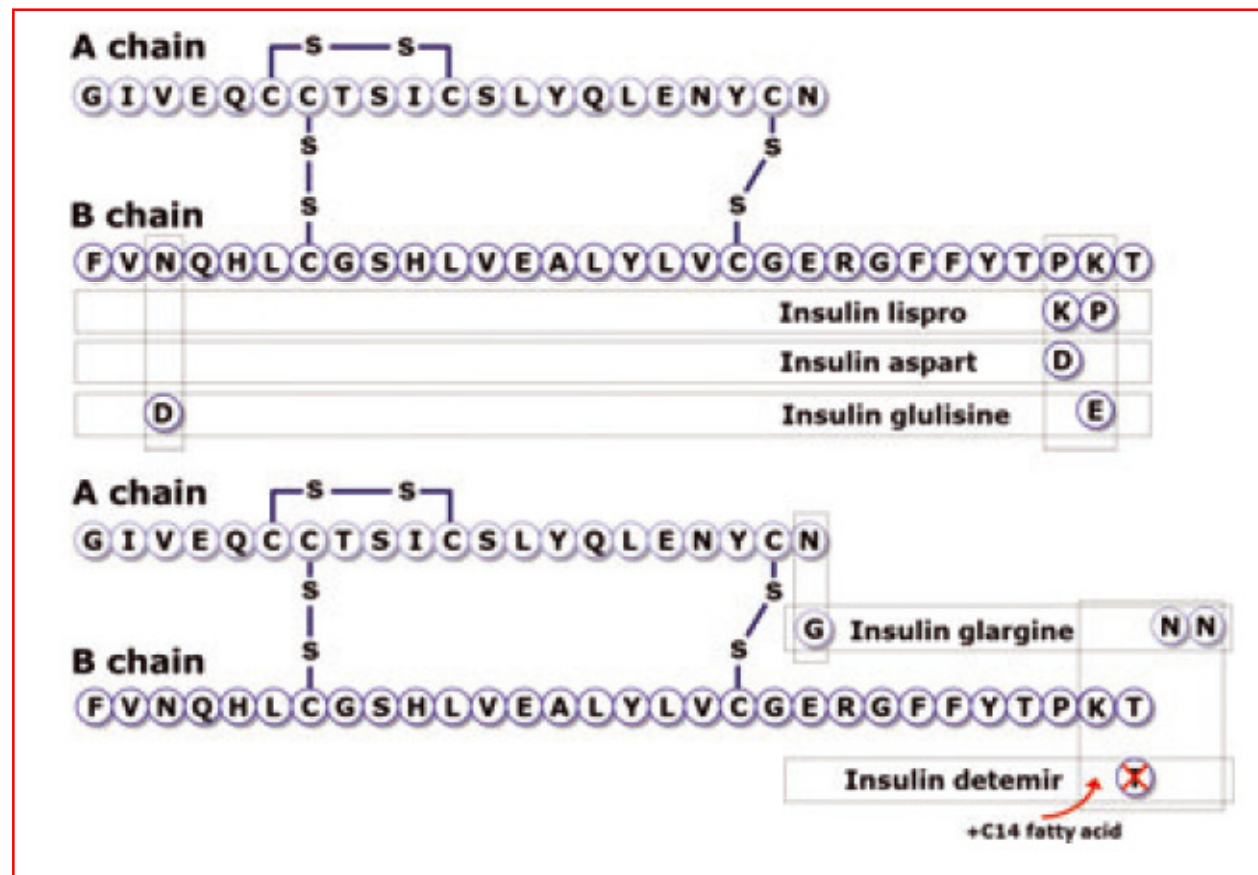
Giornate Diabetologiche Salernitane



Il futuro

- Analoghi rapidi
- Analoghi lenti

Gli analoghi dell'insulina





Lilly's two basal insulin analogue candidates are expected to enter Phase III clinical testing in 2011.

Lilly's two basal insulin analogue candidates are:
LY2605541, a structurally novel basal insulin analogue,
and LY2963016, a new insulin glargine product.

LY2605541

- **1 phase-1 trial:**

pharmacokinetics, pharmacodynamics, safety, and tolerability of LY2605541 in 18 patients with type 2 diabetes mellitus after multiple, daily subcutaneous doses.

This study has been completed, but results have not yet been published or presented.

- **2 phase-2 trials:**

clinical efficacy and safety of LY2605541OD compared with IGlargin OD.

One is a 16-week crossover trial in type 1 diabetes patients. The other, a parallel trial with a duration of 12 weeks, is performed in type 2 diabetes patients. In the latter trial two dosing algorithms of LY2605541 will be tested.

Both phase 2 trials have been completed at the beginning of 2011

- **1 phase-3 trial:**

IMAGINE 2: double-blind, randomized study comparing LY2605541 to glargine as basal insulin in combination with OAD in insulin-naive Type 2 diabetic patients

Airin C.R. Simon and J. Hans DeVries. Diabetes Technology & Therapeutics. June 2011, 13(S1): S-103-S-108. doi:10.1089/dia.2010.0251.

<http://www.clinicaltrials.gov/>

LY2963016

- **1 phase-1 trial:**

pharmacokinetics and pharmacodynamics of LY2963016 compared to those of basal insulin. Safety and tolerability of LY2963016 in healthy subjects. The study is approximately 12 weeks.

This study has been completed, but results have not yet been published or presented.

- **2 phase-3 trials:**

- The ELEMENT 2 Study: prospective, randomized, double-blind trial comparing LY2963016 to glargine in adult patients with type 2 diabetes

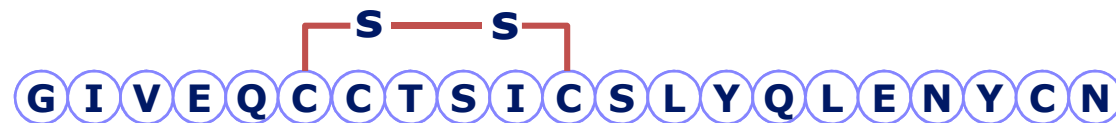
- prospective, randomized, open-label trial comparing LY2963016 to glargine in combination with Lispro in adult patients with Type 1 diabetes

Both trials are ongoing

<http://www.clinicaltrials.gov/>

Insulin degludec structure

LysB29(Nε-hexadecandioyl-γ-Glu) des(B30) human insulin

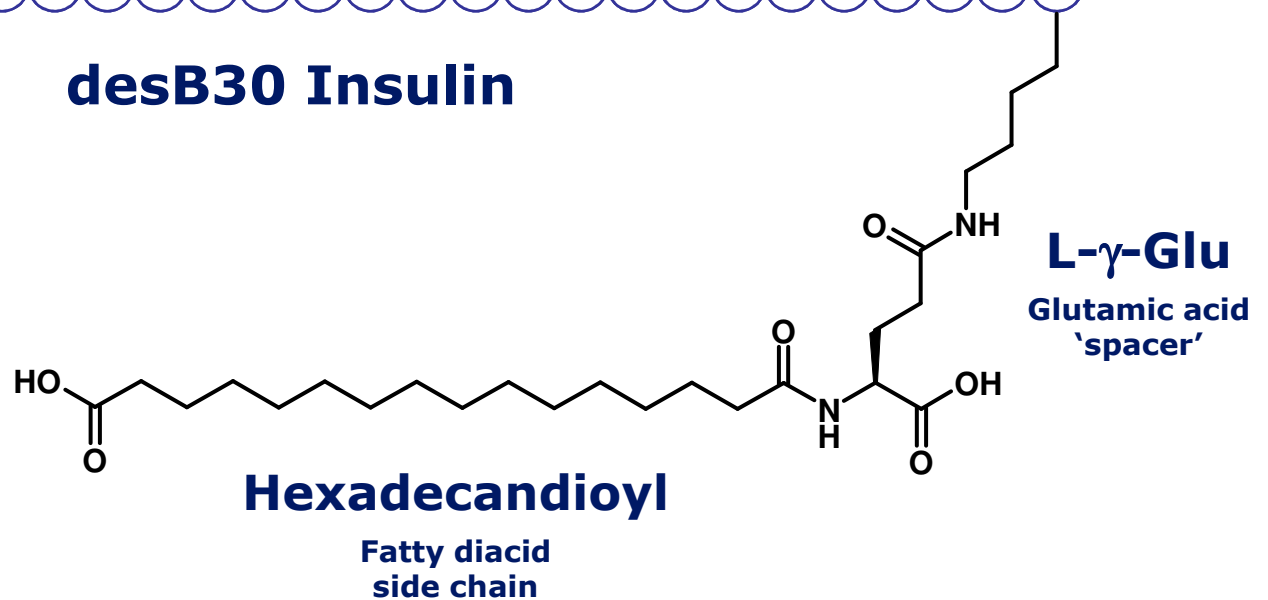


A chain



B chain

desB30 Insulin



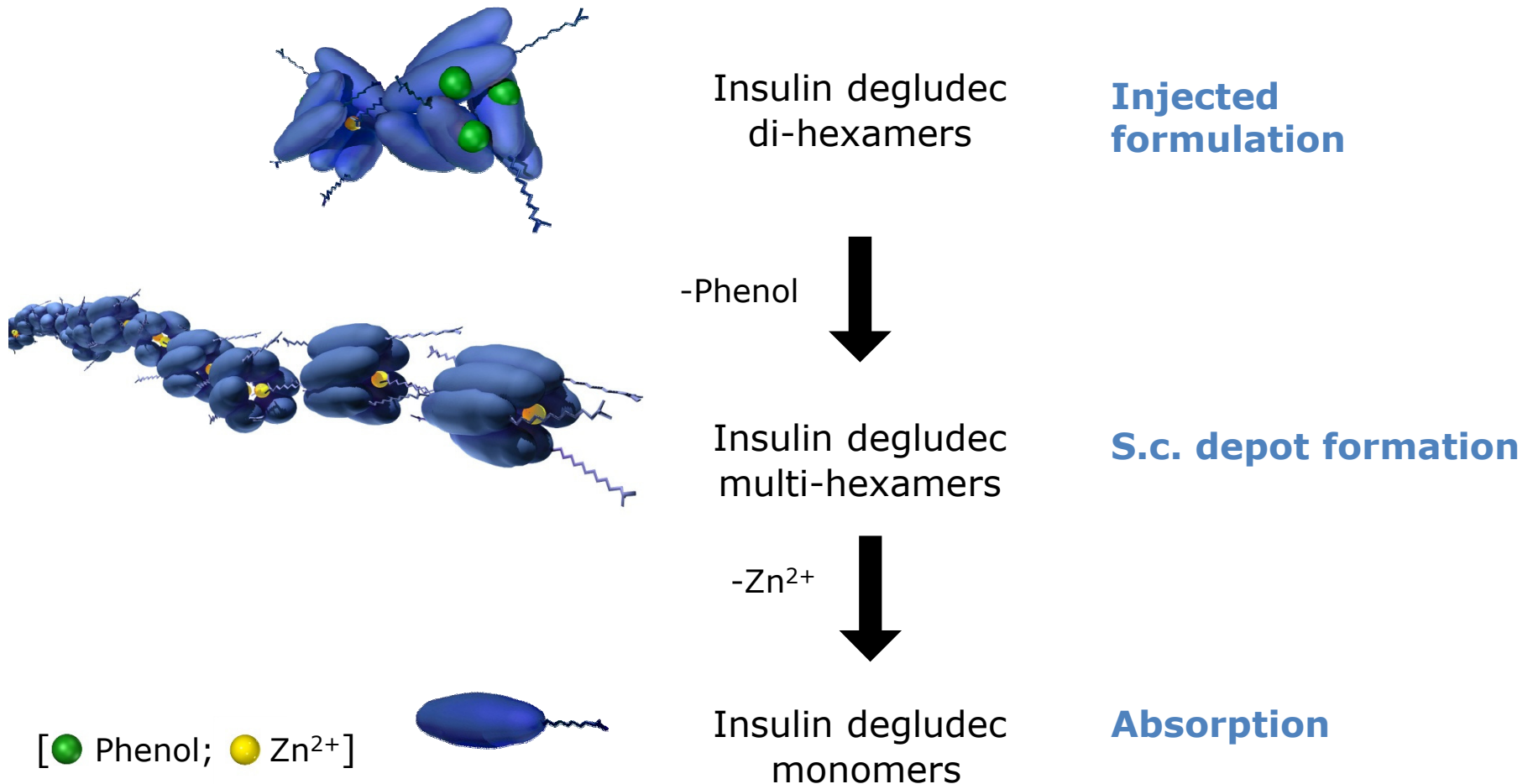
I Jonassen et al. Diabetes 59 (Suppl. 1): A11, 2010

I Jonassen et al. Diabetologia 2010;53(Suppl.1):S388 972-P

Insulin degludec association

From injection to absorption

Multi-hexamer formation key to protraction mechanism

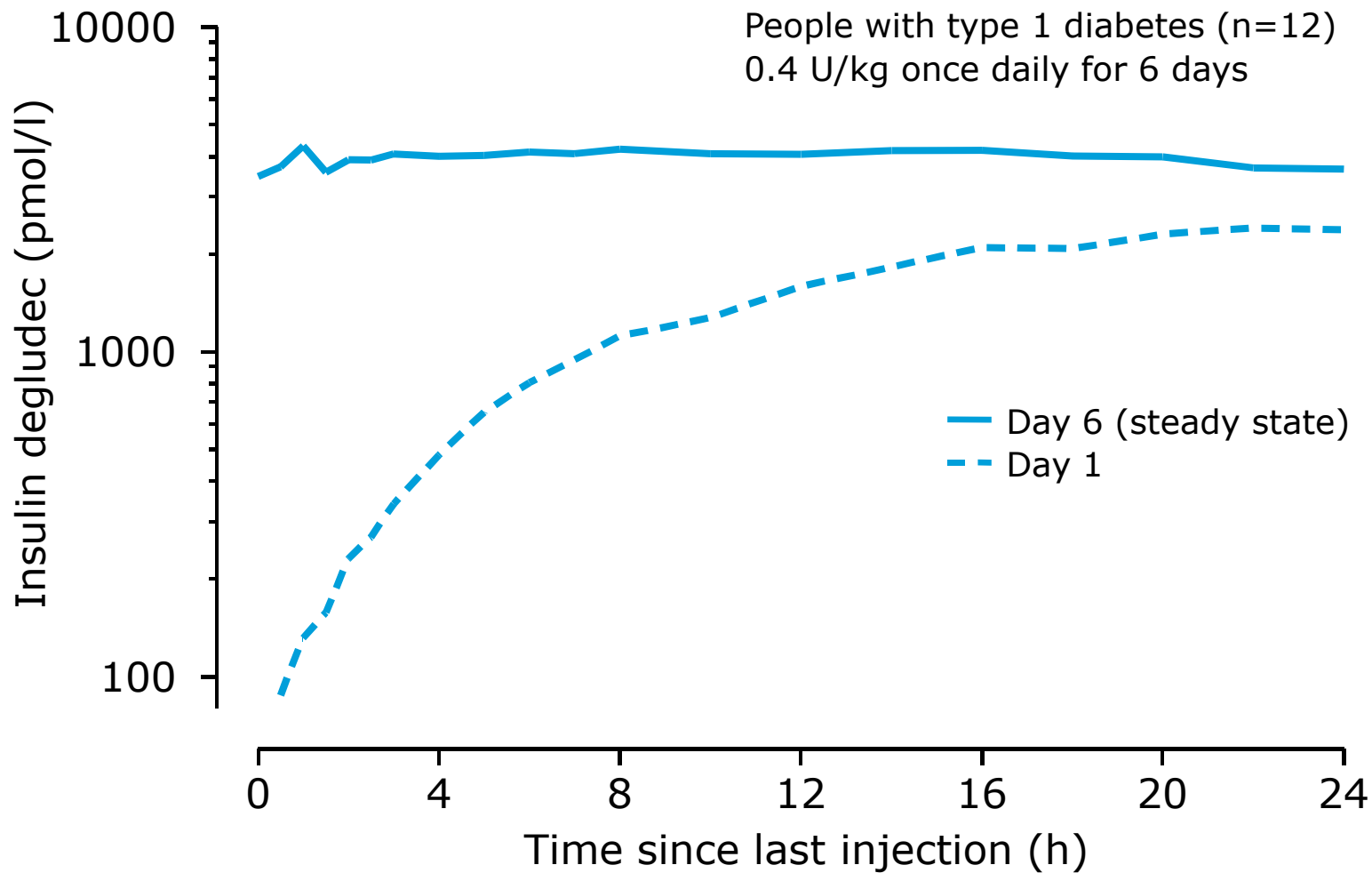


I Jonassen et al. Diabetes 59 (Suppl. 1): A11, 2010

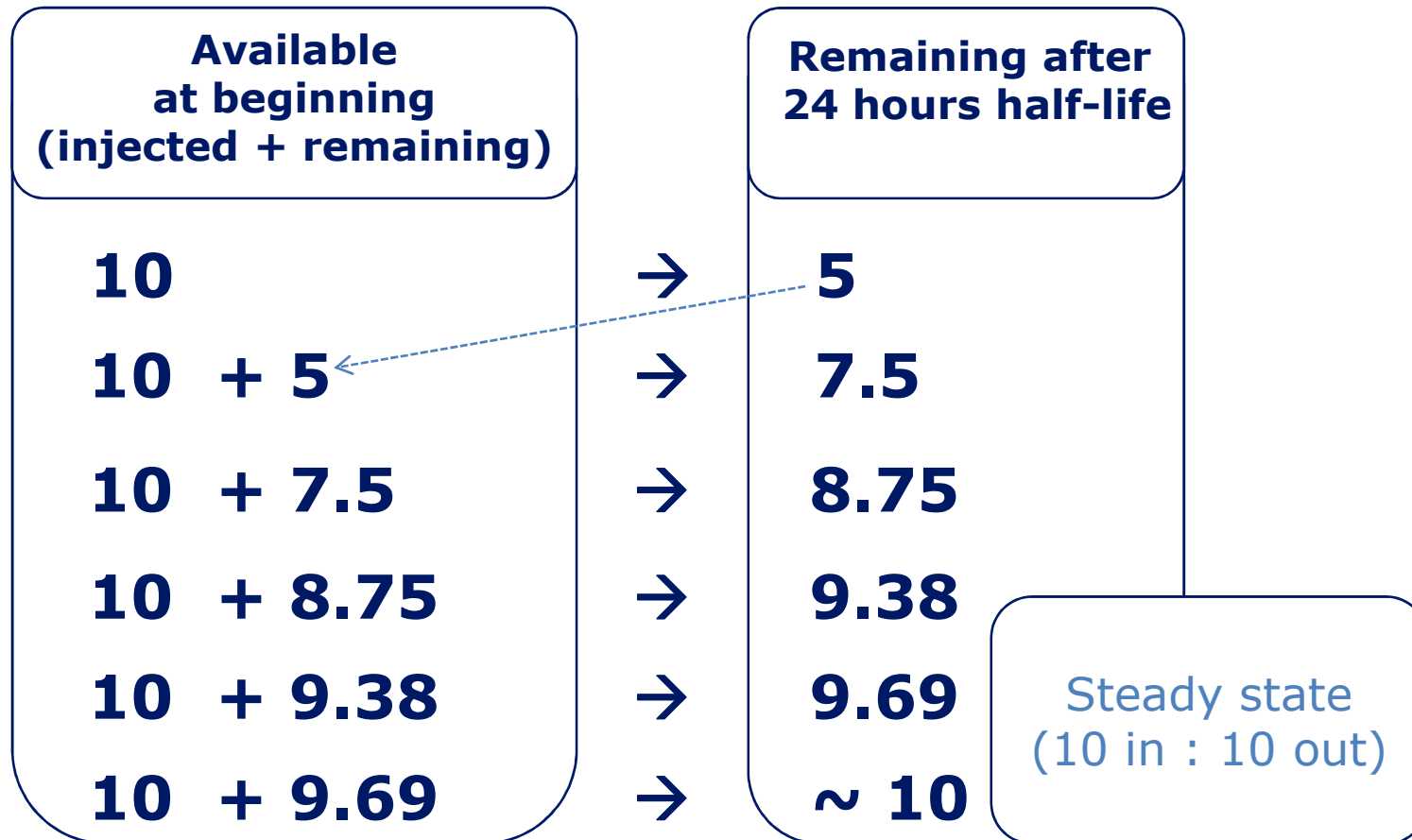
I Jonassen et al. Diabetologia 2010;53(Suppl.1):S388-972-P

Insulin degludec pharmacokinetic profile

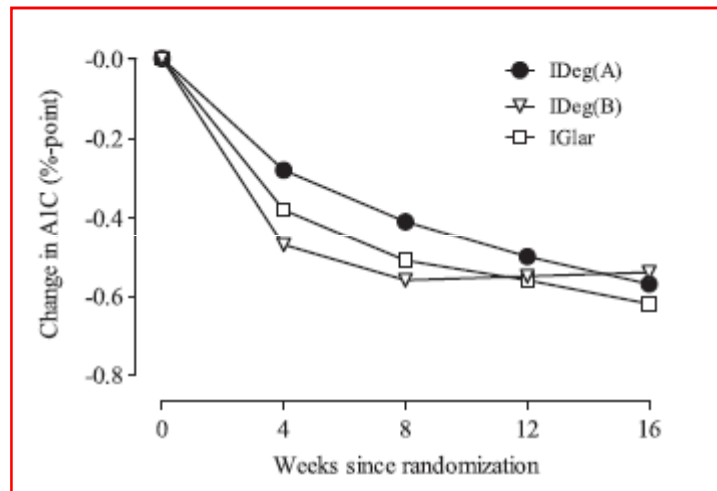
Single dose and steady state



Linear kinetics



Degludec in T1D



Birkeland KI et al, Diabetes Care 2011

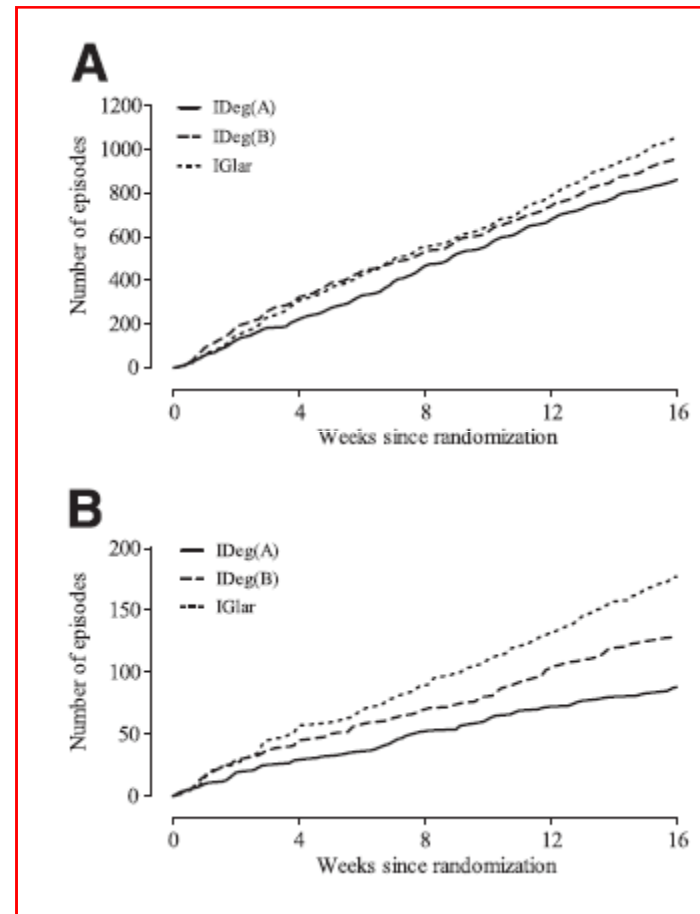
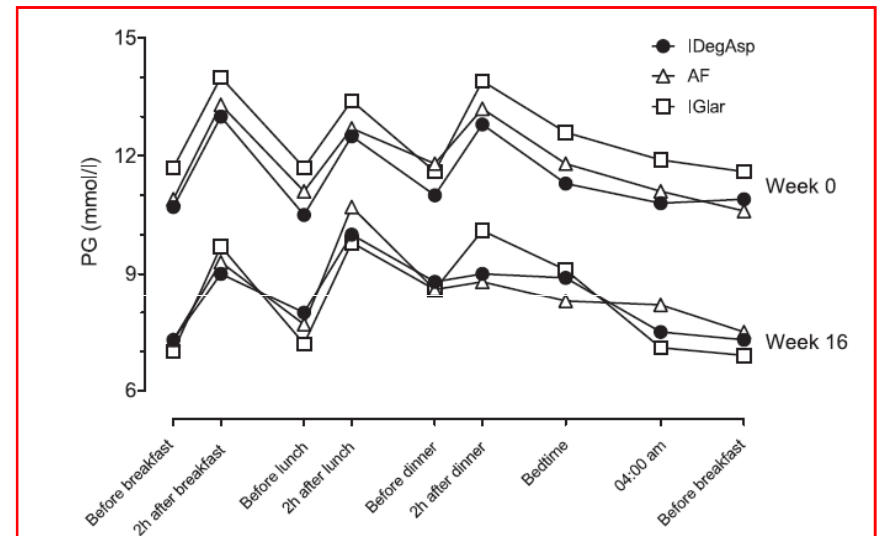
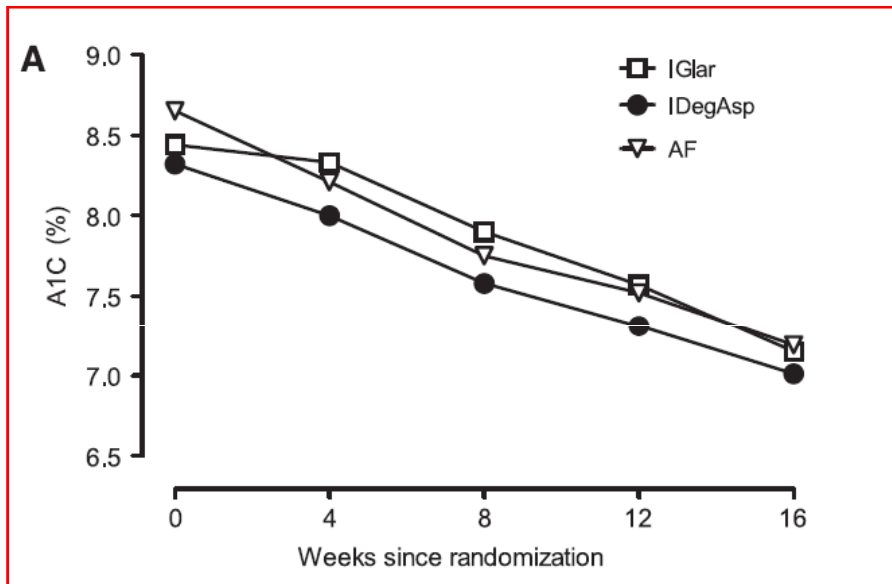


Figure 2—Cumulative number of hypoglycemic episodes. A: confirmed episodes (PG < 3.1 mmol/L or requiring assistance). B: Nocturnal episodes (all confirmed episodes between 2300 and 0559 h, inclusive).

Degludec in T2D



Heise T et al, Diabetes Care 2011

Sanofi Diabetes

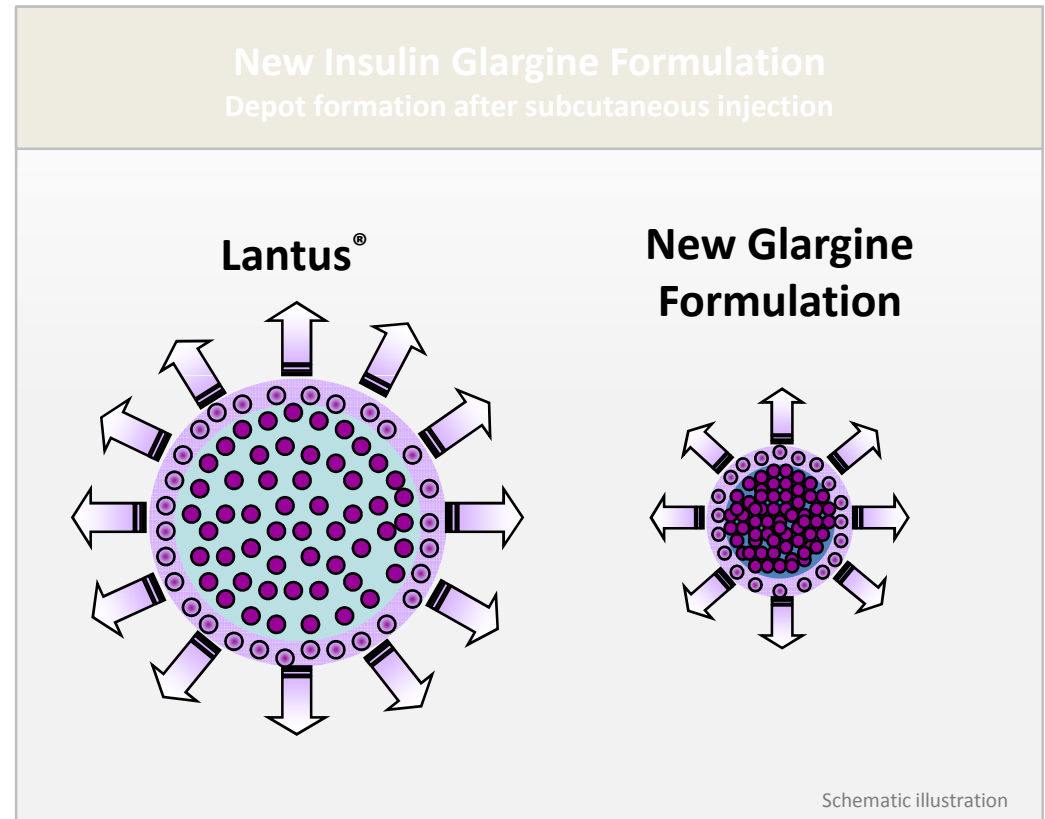
HOE901:

New basal insulin

(new formulation of glargine)

New glargine formulation with unique pharmacokinetics

- **New glargine formulation provides**
 - **Unique flat PK/PD profile**
 - **Lower injection volume**
- **Phase III trials recently initiated**



PK/PD: Pharmacokinetic/pharmacodynamic
T2D: Type 2 Diabetes



Il futuro, quindi, proporrà...

- 1) Soprattutto nuove insuline basali, delle quali sapremo ovviamente di più nei prossimi mesi
- 2) Ma anche eventi in grado di modificare i livelli glicemici a prescindere dal tipo e dalla dose di insulina, di cui sapremo ovviamente di più tra pochi giorni....

CHAMPIONS LEAGUE 2011/2012

OTTAVI DI FINALE

