

# Clinical trials of insulin therapy for diabetes type 2 in all type of patients

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## 1 a

| Trial                                                                    | Treatments                                                                                                                                      | Patients | Trials design and methods |
|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|----------|---------------------------|
| <b>lispro twice daily + NPH insulin vs regular insulin + NPH insulin</b> |                                                                                                                                                 |          |                           |
| Vignati<br>n=NA<br>follow-up:                                            | twice-daily insulin lispro in combination with<br>NPH human insulin<br>versus<br>regular human insulin in combination with<br>NPH human insulin | -        |                           |

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## 2 AAA

| Trial                                              | Treatments                                                                                              | Patients                                                | Trials design and methods |
|----------------------------------------------------|---------------------------------------------------------------------------------------------------------|---------------------------------------------------------|---------------------------|
| <b>lispro mixture vs glargine once daily</b>       |                                                                                                         |                                                         |                           |
| Chan META-ANALYSIS ,<br>2009<br>n=NA<br>follow-up: | insulin lispro mixtures, given twice or thrice<br>daily<br>versus<br>insulin glargine, given once daily | patients with type 2 diabetes treated with<br>metformin |                           |

### References

#### Chan META-ANALYSIS, 2009:

Chan JY, Leyk M, Frier BM, Tan MH, Relationship between HbA1c and hypoglycaemia in patients with type 2 diabetes treated with different insulin regimens in combination with metformin. Diabetes Metab Res Rev 2009;25:224-31. [[19156705](#)] [10.1002/dmrr.929](#)

## 3 basal + bolus

| Trial                                                          | Treatments                                                                                                             | Patients                                                                                                                                      | Trials design and methods                       |
|----------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| <b>insulin glulisine + glargine vs glargine once daily</b>     |                                                                                                                        |                                                                                                                                               |                                                 |
| <a href="#">Owens , 2011</a><br>n=49/57<br>follow-up: 3 months | basal+bolus (single dose of insulin glulisine immediately prior to the main meal)<br>versus<br>basal insulin (glargin) | patients withT2DM using any basal insulin and HbA1c >7.0% after 3-month of insulin glargine titrated to optimize fasting bloodglucose control | Parallel groups<br>open-label<br>US, UK, Russia |
| <b>lispro + NPH vs NPH twice daily</b>                         |                                                                                                                        |                                                                                                                                               |                                                 |
| <a href="#">Ceriello , 2007</a><br>n=NA<br>follow-up: 12 weeks | premeal insulin lispro+bedtime neutral protamine Hagedorn (NPH)<br>versus<br>twice-daily NPH                           | patients with type 2 diabetes treated by a 2-month lead-in with twice-daily NPH treatment                                                     | Cross over<br>open-label                        |

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### Owens, 2011:

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### Ceriello, 2007:

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## 4 basal insulin

| Trial                                                               | Treatments | Patients | Trials design and methods |
|---------------------------------------------------------------------|------------|----------|---------------------------|
| <b>glargine vs</b>                                                  |            |          |                           |
| <a href="#">Eliashewitz</a><br>n=231/250<br>follow-up: 24 weeks     | -          | -        |                           |
| <a href="#">Fonseca</a><br>n=52/48<br>follow-up: 28 weeks           | -          | -        |                           |
| <a href="#">Massi</a><br>n=293/285<br>follow-up: 52 weeks           | -          | -        |                           |
| <a href="#">Pan</a><br>n=220/223<br>follow-up: 24 weeks             | -          | -        |                           |
| <a href="#">Philis-Tsimikas</a><br>n=334/164<br>follow-up: 20 weeks | -          | -        |                           |
| <a href="#">Rosenstock</a><br>n=259/259<br>follow-up: 28 weeks      | -          | -        |                           |

continued...

| Trial                                                       | Treatments                                                                                                           | Patients                                                                                                   | Trials design and methods     |
|-------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|-------------------------------|
| Wang<br>n=16/8<br>follow-up: 12 weeks                       | -                                                                                                                    | -                                                                                                          |                               |
| Yki-Yarvinen<br>n=214/208<br>follow-up: 52 weeks            | -                                                                                                                    | -                                                                                                          |                               |
| Yki-Yarvinen<br>n=61/49<br>follow-up: 36 weeks              | -                                                                                                                    | -                                                                                                          |                               |
| Yokoyama<br>n=31/31<br>follow-up: 26 weeks                  | -                                                                                                                    | -                                                                                                          |                               |
| <b>morning insulin glargine vs bedtime insulin glargine</b> |                                                                                                                      |                                                                                                            |                               |
| Fritche<br>n=463/232<br>follow-up: 24 weeks                 | morning insulin glargine<br>versus<br>bedtime insulin glargine                                                       | patients with type 2 diabetes previously<br>treated with oral antidiabetic agents                          | open                          |
| <b>glargine vs NPH</b>                                      |                                                                                                                      |                                                                                                            |                               |
| Riddle POC 4002 Glargine ,<br>2003<br>n=NA<br>follow-up:    | bedtime glargine<br>versus<br>NPH once daily                                                                         | overweight men and women with inadequate<br>glycemic control (HbA(1c) >7.5% ) on one or<br>two oral agents | Parallel groups<br>open-label |
| HOE 901/3002 , 2000<br>n=NA<br>follow-up:                   | bedtime insulin glargine<br>versus<br>bedtime NPH insulin                                                            | insulin-naive type 2 diabetic patients with<br>poor glycemic control on oral antidiabetic<br>agents        |                               |
| <b>glargine vs NPH + SU</b>                                 |                                                                                                                      |                                                                                                            |                               |
| Riddle<br>n=367/389<br>follow-up: 24 weeks                  | bedtime glargine<br>versus<br>NPH                                                                                    | overweight men and women with inadequate<br>glycemic control (HbA(1c) >7.5% ) on one or<br>two oral agents | open                          |
| <b>insulin detemir vs NPH insulin</b>                       |                                                                                                                      |                                                                                                            |                               |
| Hermansen<br>n=236/237<br>follow-up: 26 weeks               | insulin detemir twice-daily<br>versus<br>NPH insulin                                                                 | insulin-naive people with type 2 diabetes                                                                  |                               |
| <b>detemir vs NPH insulin (add on aspart)</b>               |                                                                                                                      |                                                                                                            |                               |
| 65279;Haak<br>n=341/164<br>follow-up: 65279;26 weeks        | insulin detemir either once or twice daily<br>according to their pretrial insulin treatment<br>versus<br>NPH insulin | patients with type 2 diabetes                                                                              | open                          |

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## 5 insulin therapy

| Trial                               | Treatments | Patients | Trials design and methods |
|-------------------------------------|------------|----------|---------------------------|
| <b>insulin vs control</b>           |            |          |                           |
| UGDP<br>n=414/205<br>follow-up:     | -          | -        |                           |
| UKPDS 33<br>n=911/896<br>follow-up: | -          | -        |                           |

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## 6 lixisenatide

| Trial                                                                             | Treatments                                                                                                                | Patients                                                                                        | Trials design and methods              |
|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|----------------------------------------|
| <b>lixisenatide vs glargine once daily</b>                                        |                                                                                                                           |                                                                                                 |                                        |
| GETGOAL-L <i>unpublished</i><br>[NCT00715624]<br>n=328/167<br>follow-up: 24 weeks | AVE0010 (10,15 and 20 g) in association with basal insulin, with or without metformin versus placebo on top basal insulin | Type 2 diabetes mellitus insufficiently controlled with basal insulin with or without metformin | Parallel groups<br>double-blind<br>USA |

## References

GETGOAL-L, 0:

## 7 once daily premixed insulin analogue

| Trial                                                               | Treatments                                                                                                | Patients                                                                                                              | Trials design and methods             |
|---------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|---------------------------------------|
| <b>BIAsp 70/30 twice daily vs glargine once daily</b>               |                                                                                                           |                                                                                                                       |                                       |
| <b>Kalra , 2010</b><br>n=76/79<br>follow-up: 26 weeks               | BIAsp 30 once-daily biphasic insulin aspart 70/30 (NovoMix 30 FlexPen) versus insulin glargine once daily | Asian subjects with type 2 diabetes inadequately controlled with oral anti-diabetic drugs                             | Parallel groups<br>open-label<br>Asia |
| <b>INITIATE (Raskin) , 2005</b><br>n=117/116<br>follow-up: 28 weeks | BIAsp 70/30, prebreakfast and presupper versus once-daily insulin glargine                                | insulin-naive patients with HbA(1c) values >/=8.0% on >1,000 mg/day metformin alone or in combination with other OADs | Parallel groups<br>open-label         |
| <b>Strojek , 2009</b><br>n=239/241<br>follow-up: 26 weeks           | biphasic insulin aspart 30 (BIAsp 30) once daily versus insulin glargine once daily                       | patients with type 2 diabetes inadequately controlled with oral drugs                                                 | Parallel groups<br>open-label         |

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## 8 thrice daily premixed insulin analogue

| Trial                                                                      | Treatments                                                                                                                              | Patients                                                                                                                                                                                | Trials design and methods                                                                                              |
|----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|
| <b>premix lispro 50/50 thrice time vs glargine once daily</b>              |                                                                                                                                         |                                                                                                                                                                                         |                                                                                                                        |
| <b>Robbins , 2007</b><br>[NCT00191464]<br>n=158/159<br>follow-up: 24 weeks | lispro mix 50/50 (50% insulin lispro protamine suspension [ILPS] and 50% lispro) TID for 24 weeks versus insulin glargine QD at bedtime | patients with type 2 diabetes mellitus and an HbA(1c) level of 6.5% to 11.0% , who were receiving metformin and/or a sulfonylurea with a stable dose of 0 to 2 daily insulin injections | Parallel groups<br>open-label<br>Australia, Greece, India, The Netherlands, Poland, Puerto Rico, and the United States |

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| Trial                                                            | Treatments                                                                                                        | Patients                                                                       | Trials design and methods                |
|------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------------------------|
| <a href="#">Kazda , 2006</a><br>n=54/53<br>follow-up: 24 week    | 3x daily lispro mid mixture (MidMix; 50% lispro, 50% protaminated lispro),<br>versus<br>1x daily insulin glargine | patients with type 2 diabetes starting insulin treatment                       | Parallel groups<br>open-label<br>Germany |
| <b>premix lispro thrice daily vs glargine once daily</b>         |                                                                                                                   |                                                                                |                                          |
| <a href="#">Jacober , 2006</a><br>n=60/60<br>follow-up: 4 months | intensive insulin lispro mixture therapy for 4 months<br>versus<br>once-daily insulin glargine                    | insulin-naive patients with type 2 diabetes receiving oral antidiabetes agents | Cross over                               |

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## 9 twice-daily premixed insulin analogue

| Trial                                                                                    | Treatments                                                                                                         | Patients                                                                                                                                        | Trials design and methods             |
|------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|
| <b>BIAsp 70/30 twice daily vs detemir once daily</b>                                     |                                                                                                                    |                                                                                                                                                 |                                       |
| <a href="#">4T (Holman) , 2007</a><br>[ISRCTN51125379]<br>n=235/234<br>follow-up: 1 year | biphasic insulin aspart (NovoMix 30) twice daily<br>versus<br>basal insulin detemir once daily (twice if required) | patients with a suboptimal glycated hemoglobin level (7.0 to 10.0% ) who were receiving maximally tolerated doses of metformin and sulfonylurea | Parallel groups                       |
| <b>BIAsp 70/30 twice daily vs glargine once daily</b>                                    |                                                                                                                    |                                                                                                                                                 |                                       |
| <a href="#">Kalra , 2010</a><br>n=76/79<br>follow-up: 26 weeks                           | BIAsp 30 once-daily biphasic insulin aspart 70/30 (NovoMix 30 FlexPen)<br>versus<br>insulin glargine once daily    | Asian subjects with type 2 diabetes inadequately controlled with oral anti-diabetic drugs                                                       | Parallel groups<br>open-label<br>Asia |

continued...

| <b>Trial</b>                                                                 | <b>Treatments</b>                                                                                                               | <b>Patients</b>                                                                                                                                       | <b>Trials design and methods</b> |
|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| INITIATE (Raskin) , 2005<br>n=117/116<br>follow-up: 28 weeks                 | BIAsp 70/30, prebreakfast and presupper<br>versus<br>once-daily insulin glargine                                                | insulin-naive patients with HbA(1c) values<br>>/=8.0% on >1,000 mg/day metformin alone<br>or in combination with other OADs                           | Parallel groups<br>open-label    |
| Strojek , 2009<br>n=239/241<br>follow-up: 26 weeks                           | biphasic insulin aspart 30 (BIAsp 30) once<br>daily<br>versus<br>insulin glargine once daily                                    | patients with type 2 diabetes inadequately<br>controlled with oral drugs                                                                              | Parallel groups<br>open-label    |
| <b>premix lispro 75/25 twice daily vs glargine once daily</b>                |                                                                                                                                 |                                                                                                                                                       |                                  |
| DURABLE (Buse)<br>DOUBLONS , 2011<br>n=NA<br>follow-up:                      | lispro mix 75/25 twice daily<br>versus<br>once-daily insulin glargine                                                           | type 2 diabetes patients                                                                                                                              |                                  |
| DURABLE (Buse) , 2009<br>[NCT00279201]<br>n=1045/1046<br>follow-up: 24 weeks | twice-daily lispro mix 75/25<br>versus<br>daily glargine                                                                        | patients with type 2 diabetes mellitus failing<br>to achieve control with starter insulin<br>treatment and continuing oral<br>antihyperglycemic drugs | Parallel groups                  |
| Malone , 2004<br>n=105/105<br>follow-up: 16 week                             | mixture of 75% insulin lispro protamine<br>suspensionand 25% insulin lispro (Mix 75/25)<br>BID<br>versus<br>insulin glargine QD | patients with type 2 diabetes beginning<br>insulin therapy                                                                                            | Cross over<br>open-label<br>USA  |
| Malone , 2005<br>n=97/97<br>follow-up: 32 weeks                              | insulin lispro mixture (25% insulin lispro and<br>75% NPL) twice daily<br>versus<br>once-daily insulin glargine                 | patients with Type 2 diabetes inadequately<br>controlled with intermediate insulin, or<br>insulin plus oral agent(s) combination therapy              | Cross over                       |
| <b>BIAsp 70/30 twice daily vs NPH twice daily</b>                            |                                                                                                                                 |                                                                                                                                                       |                                  |
| Christiansen , 2003<br>n=NA<br>follow-up: 18 weeks                           | Twice daily biphasic insulin aspart (BIAsp30)<br>versus<br>NPH insulin twice daily                                              | patients with type 2 diabetes not optimally<br>controlled by oral hypoglycaemic agents,<br>NPH insulin or a combination of both                       | Parallel groups<br>double-blind  |
| <b>premix aspart70/30 twice daily vs once daily insulin glargine</b>         |                                                                                                                                 |                                                                                                                                                       |                                  |
| INITIATE (Raskin)<br>DOUBLON , 2008<br>n=NA<br>follow-up:                    | biphasic insulin aspart 70/30 (BIAsp 70/30,<br>prebreakfast and presupper)<br>versus<br>once-daily insulin glargine             | insulin-naive patients with HbA1c values<br>8.0% on 1,000 mg/day metformin alone or in<br>combination with other OADs                                 | Parallel groups                  |

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## 10 About TrialResults-center.org

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The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

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