DIABETES WORKSHOP EMEA

Improved treatments :
medication for children/adolescents with diabetes mellitus

Aim: to identify the best possible research approaches for new medication in the field of diabetes in childhood and adolescence

17 april 2009

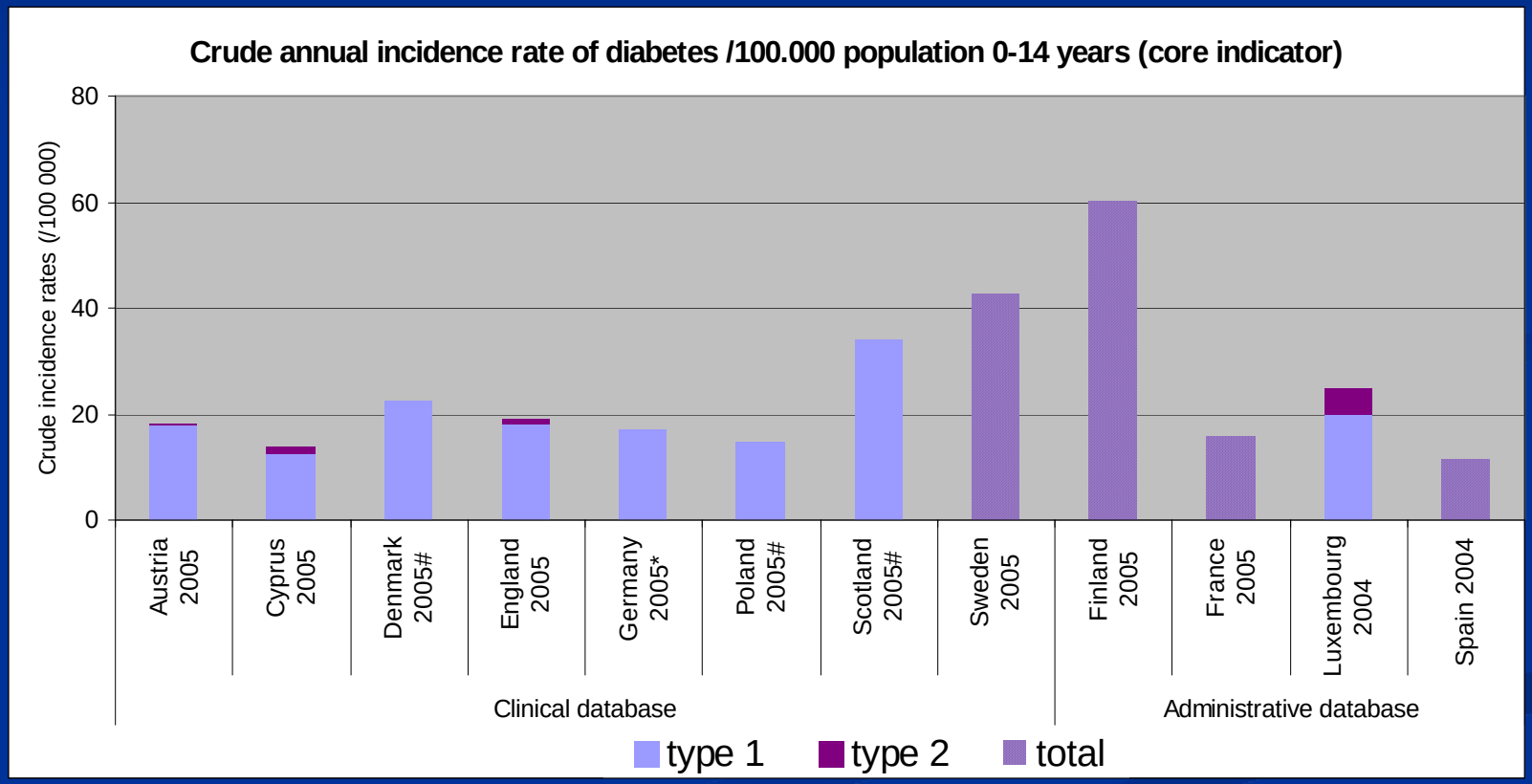
Type 1 and 2 diabetes in children and adolescents

Actual known numbers in the EU

Short introduction on actual situation : new products → non insulin and insulin

Results of the premail questions

EUCID EU study 2006



PRE meeting questions

Type 2 dm

1) For non inferiority studies in paediatric diabetes
   vs insulin/metformin : what delta HbA1c should be considered significant
   Delta HbA1c : 0.3-0.5 %
   Not different from adults (CHMP 0.3-0.4%)

2) For new insulin analogues :are data in t2dm adolescents needed?
   Or – extrapolation t1dm children
   - extrapolation t2dm adults
   Pathophysiology between t1dm and t2dm varies ,
   Age/developmental phase may/will influence
   PK/PD/clinical safety studies are necessary
(Good studies in adults are lacking as well…)
   ----Extrapolation is considered is well

PRE meeting questions

3)Are additional long acting analogues in t1dm needed?

No (no unmet need)→

Yes actually available are still far from perfect..

4) Should hypoglycaemia be primary – co primary , or secondary outcome?

Co primary secondary

PRE meeting questions

5) Best way to identify nocturnal hypoglycaemia?

For the 3 age groups

CGMS, independent of age

6) If CGMS is used : how frequent and duration in order to establish differences between products?

CGMS : 3x 6 x24 hrs (=3 sensors)

case by case

PRE meeting questions

7) Enough t1dm patients between 1-6 yrs to perform studies?

Evaluating recent incidence studies : yes

Premeeting questions

TYPE 2DM in ADOLESCENTS

8) Are long acting insulin analogues needed?

YES (so far)

9) When studying the efficacy of a new drug vs placebo
Can one include in one study metformin treated and naive patients (only diet/lifestyle)

May be : depends on product

Separate

10 Can postprandial glucose levels be considered as primary endpoint ?

YES

NO only as co primary , No only as secondary

Can we extrapolate Safety/Efficacy from adults? →If so, what could be extrapolated ?

Studies to evaluate new products for use in T2DM adolescents

Run in period : - how long with diet/lifestyle only?

Subject inclusion criteria - naïve ? never treated/only treated for a limited time with glucose lowering medication;
- if previously treated patients are included :
how long should they be without medication prior to inclusion?
- Can add-on to metformin be acceptable to evaluate the effect of NEW treatments?

Questions Type 2 diabetes mellitus in children/adolescents

Study duration — How long should these studies be,
placebo controlled: 12 --16 --- other wks?

Outcome Parameters — Primary vs Secondary –

HbA1c — What delta HbA1c could be considered significant
-Non inferiority compared to metformin,
to insulin,
-Superiority to placebo

Glucose — Fasting and/or post prandial to be included or not?

Glycaemic variability — Role for CGMS?

Vascular pathology: Primary or secondary endpoint
what to include/how to evaluate,
time frame to evaluate
Renal, Retinal, Liver, Flow mediated dilation

Evaluation of beta cell preservation:
What tests can be accepted

Insulin analogs in T2DM short and basal analogs: are they indicated?

Type I diabetes Questions

Can we extrapolate safety / efficacy from adults? If so, what?

<u>Prevention of type 1 diabetes</u>

- Study duration
- Primary endpoints →
- Secondary endpoints →

Remission // criteria: complete,
partial,
HbA1c , ? <
insulin rescue medication,
HbA1c + 4 Ins Dose in U/kg

Beta cell preservation testing

Auto immune modification humoral
cellular

Treatment

Primary outcome:

HbA1c : What delta should be considered significant in superiority / non inferiority studies to existing insulins with the rapid-intermediate-long acting profile

All age groups to be included ! 1-<6, 6- <12, 12- <18 yrs

Co primary outcome: hypoglycaemia ? only in the <6 yrs? definitions (ISPAD) in all ages ?

How to evaluate HPGM : 8 controls /24 hrs, CGMS, If CGMS : how long and how frequent should it be used

Glycaemic variability Primary /secondary ? How to evaluate (see CGMS)

Quality of Life outcome To be included or not?

Duration of the studies

Secondary outcome/long term outcome – micro- macrovascular to be included ?

Safety monitoring