pioglitazone HCl

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The COMPACT-Study®: Pioglitazone vs. Insulin for the Treatment of Patients with Type 2 Diabetes Mellitus – A Medical and Pharmacoeconomic Analysis

[1]Lübben G[1], Fennenkötter U[1]; Weidenhammer J[2], Golbach U[2], Kusterer K[3], Lundershausen R[4], Münscher C[5], Potthoff F[5]

[1]TAKEDA PHARMA GMBH, Aachen, Germany; [2]Institut für Gesundheits- und Systemforschung GmbH, Kiel, Germany; [3]Diabetic Centre, Mannheim, Germany; [4]Clinic Bergfried Saalfeld, Saalfeld, Germany; [5]MNC - Medical Netcare GmbH, Münster, Germany

Background: Pioglitazone, a thiazolidinedione, is a member of a class of oral antidiabetic agents targeted to treat insulin resistance, the major underlying cause of type 2 diabetes mellitus. Insulin is believed to be the "gold standard" for achieving optimal glycaemic control. The COMPACT-Study aimed to compare both treatment options with regard to metabolic control and cost effectiveness in a real-life setting.

Method: COMPACT is a prospective, multi-center, controlled, non-randomized observational study where patient selection, allocation to treatment, and dose were left to the physicians' discretion. Quality standards included plausibility checks, regular monitoring, and a central laboratory. The primary variable was change in HbA1C compared to baseline (Δ HbA1C), where a difference of < 0.5 % points between both arms was set for defining non-inferiority. Analyses were performed under the perspective of the German Statutory Health Care System.

Results: The effectiveness analysis was conducted according to a modified intention-to-treat method (pioglitazone, 437 and insulin, 290 eligible patients). An adjustment to baseline was made for every analysis. The mean Δ in HbA1C was –0.65 in the pioglitazone group and –0.44 %points in the insulin group. The Δ in fasting plasma glucose was –24.5 in the pioglitazone and –16.4 mg/dL in the insulin group. Responder rates (Δ HbA1C ≥ 0.6 %points) were 50.4 % (pioglitazone) and 38.1 % (insulin). The cost-effectiveness analysis was conducted for the per-protocol-population (pioglitazone, 299 and insulin, 218 eligible patients). Mean total treatment costs were 1,207 € (pioglitazone) and 1,510 € (insulin). Mean costs for antidiabetic medication and glucose self monitoring were assessed as 646 € (pioglitazone) and 774€ (insulin). Compared to insulin, pioglitazone was revealed to be the most cost-effective (Δ HbA1C/1,000 € and costs/0,5 %points Δ HbA1C) in the insulin resistant individuals, the more obese individuals, and individuals with a shorter diabetes duration (< 5 years).

Conclusions: Pioglitazone proved to be non-inferior to insulin treatment in terms of metabolic control as well as cost-effectiveness.

BACKGROUND

Type 2 diabetes mellitus is a chronic disease with increasing prevalence and creating an enormous socioeconomic burden. Assuming a 4–5 % prevalence of type 2 diabetes in Germany, 3.5 to 4 million people are currently suffering from the disease. However, this number is most likely higher due to high rates of unknown or undiagnosed cases. With regards to the total economic impact, little is known and costs are often based on estimations.

Insulin resistance and decreased beta cell function are the leading pathophysiological characteristics of type 2 diabetes. Pioglitazone (PIO) is an insulin-sensitizing oral antidiabetic agent. Activating the Peroxisome Proliferator Activating Receptors (PPAR-g) pioglitazone amplifies the effect of insulin (INS) on peripheral tissue. Thiazolidinediones allow, for the first time, the specific treatment of insulin resistance. Treatment with PIO results clinically in a considerable and permanent decrease of blood glucose as well as in an improvement of diabetic dyslipidemia.

Aims

•To generate data comparing the effectiveness of PIO treatment and INS treatment in a real-life setting

•To evaluate the therapeutic effectiveness with regard to cost effectiveness

Study objectives

•Primary: change in HbA1c after 24 weeks of treatment compared to baseline

•Secondary: demographic factors, diabetes duration, risk factors, concomitant diseases, antidiabetic and concomitant medication, direct and indirect costs, safety

METHODS

Study design

• Prospective, multicenter, controlled, non-randomised observational comparison of parallel groups, real-life setting

• Study Period: April 2001 through October 2002

• Centers: 51 physicians (specialised diabetologists)

• Patients: Patients with type 2 diabetes and HbA1c within the range 6.5 and 10 %, who were insufficiently treated with their current therapy and in whom a new antidiabetic agent had been introduced during the period of observation

• Therapy either PIO (437 patients), other oral or INS (290 patients); treatment was left to physicians' discretion

• Observation period: 26 weeks

• Visits: before therapy (baseline), after 12 weeks, and after 26 weeks of treatment

Economic perspective

• Cost-effectiveness analysis
  Change of HbA1c per 1 000 €
  Costs per reduction in HbA1c ≥ 0.5 %points
• Payer's perspective

RESULTS

Effectiveness analysis (ITT)

PIO treatment proved to be non-inferior to INS treatment regarding the following objectives:

• Change in HbA1C compared to baseline: PIO, -0.65 %points [95% CI: -0.55; -0.75] vs. INS, -0.44 %points [95% CI: -0.31; -0.56]

• Responder rates (Δ HbA1C ≥ 0.6 %points): PIO, 50.4% vs. INS, 38.1%

• Δ fasting plasma glucose: PIO, 24.5 mg/dL [95% CI: -20.0; -29.0] vs. INS, 16.4 mg/dL [95% CI: -10.7; -22.1]

Cost effectiveness analysis (PP)

PIO treatment proved to be non-inferior to INS treatment regarding the following objectives:

• Mean total treatment costs were 1,207 € (PIO) and 1,510 € (INS) (Fig.1)

• Reduction in HbA1C per 1,000 € (Fig. 3)

• Cost per 0.5 %points reduction in HbA1C (Fig. 3)

• Costs are predominantly associated with macrovascular diabetes complications (Fig. 4a/4b).

Patients treated with INS and those treated with PIO differed with regard to the frequency of macrovascular complications (17.4% vs. 8.0%, respectively). When focusing on those patients without macrovascular complications, no differences in terms of cost proportion compared to the total study population were revealed.

Self monitoring of blood glucose (PIO: 89€, INS: 326 €) as well as total treatment cost (antidiabetic medication + glucose self-monitoring) for diabetes (INS: 774 €, PIO 646 €) differed between both treatment arms (Fig. 2).

• Patient Profile: PIO dominated the INS alternative especially in insulin resistant, obese patients (BMI ≥ 26 kg/m2) diabetes duration < 5 years (Fig. 5-8).

CONCLUSION / DISCUSSION

• PIO proved to be non-inferior to INS treatment in terms of metabolic control as well as cost effectiveness. In addition, significantly more patients in the PIO arm showed an HbA1C decrease of > 0.6% compared to INS using the ADA criteria for treatment response.

• The results of the COMPACT Study underline the crucial importance to target therapies to specific patient profiles in order to achieve the best clinical outcomes with the lowest amount of resources spent.

• The greatest proportion of treatment costs was allocated to the management of vascular complications. Therefore, it is key to focus therapeutic interventions on primary and secondary prevention of those complications. The UKPDS as well as several other studies have consistently shown that strict glycaemic control reduces the prevalence of microvascular complications. In addition to ACE-inhibitors ARBs and statins, further therapeutic options targeting macrovascular complications in these high-risk patients are urgently needed.

• Outcome studies with thiazolidinediones are currently underway. The European Outcome Study with Pioglitazone (PROactive) is designed to study the effects of PIO on cardiovascular morbidity and mortality in the secondary prevention setting in more than 5,200 patients and is expected to complete in 2005.

Figure 1: Mean Costs per patient (observation period 26 weeks)

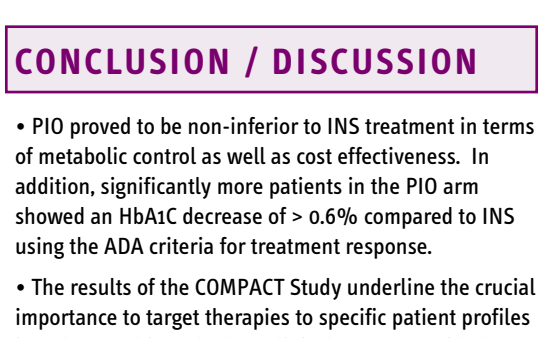

Figure 2: Costs-antidiabetic medication plus blood glucose self monitoring per patient (observation period 26 weeks)

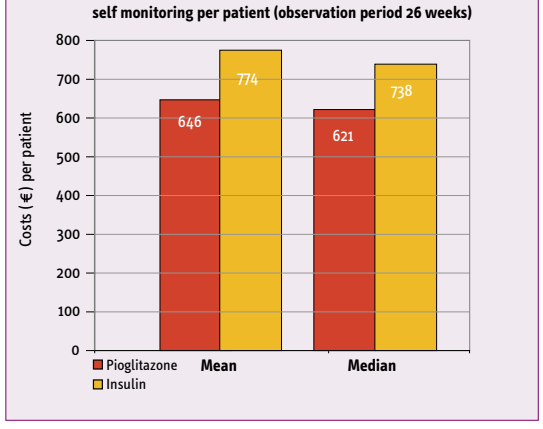

Figure 3: Costs and effectiveness

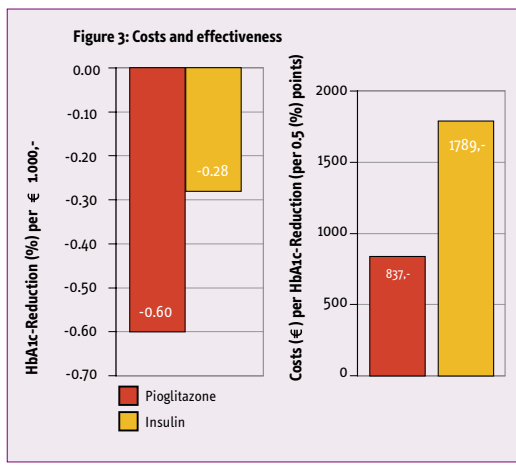

Figure 4a: Mean costs with or without complications

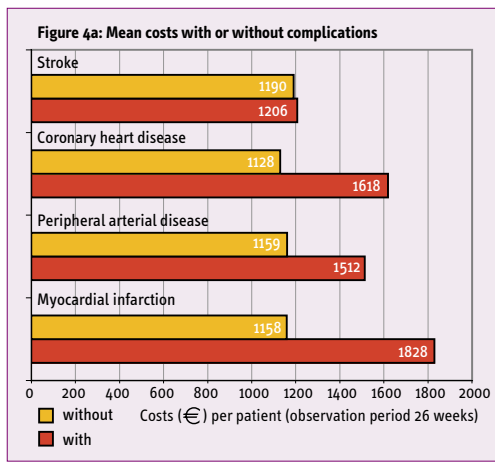

Figure 4b: Mean Costs with or without vascular complications

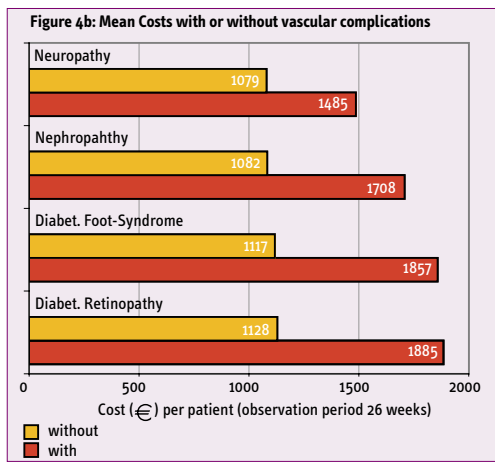

Figure 5: Costs/effectiveness clustered for insulin resistance (ATP-III-Score)

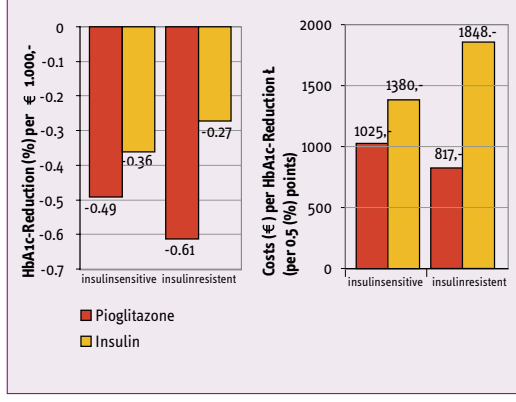

Figure 6: Cost/effectiveness clustered for age groups

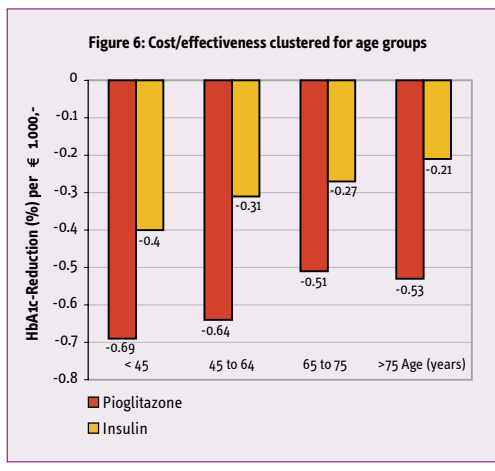

Figure 7: Cost/effectiveness clustered for diabetes duration

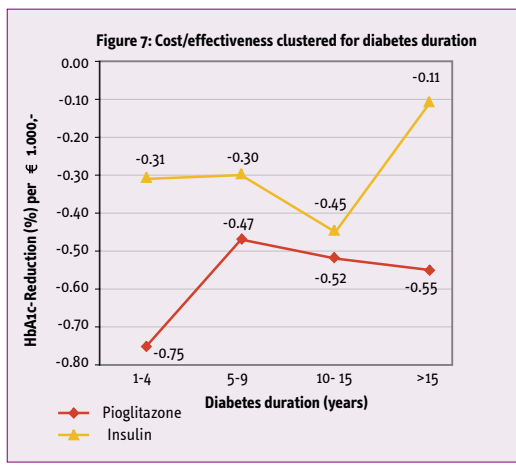

Figure 8: Costs and effectiveness clustered for Body Mass Index (BMI)