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Brief report

Vildagliptin more effectively achieves a composite endpoint of $HbA_{1c} < 7.0\%$ without hypoglycaemia and weight gain compared with glimepiride after 2 years of treatment

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ABSTRACT

This post hoc analysis reports that overall proportion of patients achieving a composite endpoint of HbA1c < 7.0% (<53.0 mmol/mol) without hypoglycaemia and weight gain was higher with vildagliptin than glimepiride after 2 years in type 2 diabetes patients inadequately controlled on metformin monotherapy, regardless of age and duration of diabetes.

1. Introduction

Although individualisation of treatment targets has become an important consideration in patients with type 2 diabetes (T2D) [1], achieving the glycaemic target of $HbA_{1c} < 7.0\%$ (<53.0 mmol/mol) is recommended for most patients by current treatment guidelines to reduce the risk of long-term complications [2]. Hypoglycaemia [3] and weight gain [4], however, represent major limiting factors in getting patients to target.

Sulphonylureas (SUs) are often used in patients with T2D who do not achieve or cannot maintain glycaemic targets on metformin monotherapy. Although SUs have a well-established efficacy and overall safety profile, they can be associated with undesirable side effects including hypoglycaemia and weight gain [1,2].

Vildagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor that improves both α- and β-cell responsiveness to glucose [5]. Consequently, vildagliptin improves glycaemic control in patients with T2D, both as monotherapy or combination therapy, is associated with a low risk of hypoglycaemia, and is weight-neutral [6]. Vildagliptin and glimepiride were previously shown to provide comparable HbA_{1c}-lowering efficacy as add-on therapy to metformin [7,8].

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Table 1 – Patient demographics and baseline characteristics in the ITT population.

Patient characteristics	Vildagliptin 50 mg b.i.d. + metformin (N = 1051)	Glimepiride up to 6 mg daily + metformin (N = 1011)	Total (N = 2062)
Age (years)	57.50 ± 9.14	57.40 ± 9.15	57.50 ± 9.14
Sex, n (%)			
Male	566 (53.9%)	529 (52.3%)	1095 (53.1%)
Female	485 (46.1%)	482 (47.7%)	967 (46.9%)
Body weight (kg)	90.00 ± 18.49	88.90 ± 18.39	89.40 ± 18.45
BMI (kg/m^2)	32.10 ± 5.40	31.80 ± 5.36	31.90 ± 5.38
HbA_{1c}, % (mmol/mol)[a]	7.60 ± 0.53 (59.56 ± 5.81)	7.60 ± 0.55 (59.56 ± 6.01)	7.60 ± 0.54 (59.56 ± 5.87)
T2D duration (years)	5.90 ± 5.20	6.20 ± 5.20	6.10 ± 5.20

Data shown are mean ± SD, unless otherwise stated.
[a] Per IFCC units.
BMI, body mass index; HbA_{1c}, hemoglobin A_{1c}; IFCC, International Federation of Clinical Chemistry; ITT, intent-to-treat; T2D, type 2 diabetes.

In order to provide a more integrated assessment of the therapeutic benefit of vildagliptin, the present analysis evaluated a composite endpoint (CEP) defined as glycaemic control ($HbA_{1c} < 7.0\%$ [<53.0 mmol/mol]), no hypoglycaemia and no weight gain, with the aim of comparing vildagliptin versus glimepiride as add-on therapy to metformin for the number of patients reaching this CEP. The present work also investigated whether there were differences in reaching the CEP in relationship to the age of patients and duration of diabetes.

2. Methods

This was a post hoc analysis of data from a 2-year, randomised, double-blind, active-controlled study comparing the addition of vildagliptin 50 mg b.i.d. and glimepiride (up-titrated to a maximum of 6 mg/day) in patients with T2D inadequately controlled (HbA_{1c} 6.5–8.5% [48–69 mmol/mol]) on metformin monotherapy (≥1500 mg). Further details of the study design were reported by Matthews et al. [8].

A CEP of reaching $HbA_{1c} < 7.0\%$ (<53.0 mmol/mol) with no hypoglycaemic events (HEs) (defined as symptoms with plasma glucose < 3.1 mmol/L) and no weight gain (< 3.0%), using last observation carried forward, was evaluated. The proportion of patients (%) in vildagliptin and glimepiride groups who achieved the CEP and relative success rate (SR) of achieving the CEP were assessed in the overall population as well as in the subgroups in relationship to the age of patients and duration of diabetes. The relative SR was calculated by taking the ratio of the number of patients achieving the CEP in the vildagliptin and glimepiride groups, and 95% confidence interval (CI) was reported.

3. Results

Of the 3118 randomised patients, 2062 patients with a baseline $HbA_{1c} \geq 7.0\%$ (≥53.0 mmol/mol) were included in this post hoc analysis (vildagliptin, n = 1051; glimepiride, n = 1011). Patient demographics and baseline characteristics were generally comparable between the two treatment groups (Table 1).

The overall proportion of patients achieving the CEP of $HbA_{1c} < 7.0\%$ (<53.0 mmol/mol), with no hypoglycaemia and no weight gain, was higher in patients treated with vildagliptin (29.8%) than glimepiride (19.4%) after 2 years of treatment (Fig. 1). In addition, relative SR of achieving the CEP was significantly greater with vildagliptin than glimepiride (SR = 1.54; 95% CI: 1.31–1.80) (Table 2).

The proportion of patients and relative SR of achieving the CEP were also found to be significantly higher in patients treated with vildagliptin than glimepiride across subgroups of age (<50, 50 to <60, 60 to <70 and 70 to <80 years) and diabetes duration (<2, 2 to <5 and ≥5 years) (Table 2).

4. Discussion

It is increasingly recognised that, in addition to HbA_{1c} reduction, controlling weight and avoiding hypoglycaemia are important treatment goals in the management of T2D [1].

To assess the overall clinical benefit, the present post hoc analysis measured the proportion of patients achieving the CEP of $HbA_{1c} < 7.0\%$ (<53.0 mmol/mol) without hypoglycaemia and weight gain for vildagliptin and glimepiride in patients with T2D inadequately controlled on metformin monotherapy. The relative SR of achieving the CEP in the overall population was more than 50% higher in the vildagliptin group than the glimepiride group.

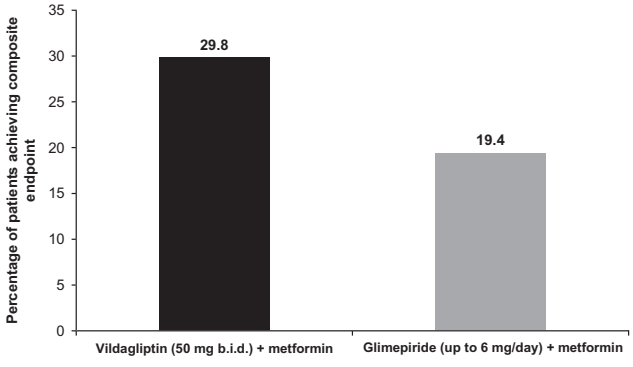

Fig. 1 – Overall proportion of patients (%) achieving composite endpoint of HbA1c < 7.0%, with no hypoglycaemia and no weight gain, after 2 years of the treatment.