Efficacy of acarbose in different geographical regions of the world: analysis of a real-world data

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Abstract

Introduction

Although alpha-glucosidase inhibitors (αGI), including acarbose, are recommended in several international guidelines, they are not widely used worldwide, mainly due to patient perception that they are less effective in Caucasians than in other ethnicities. No studies have investigated whether differences between ethnicity/regional populations exist.

Methods/Design: We pooled data from 10 non-interventional and post-marketing studies from 21 countries, provinces and country groups from the launch of acarbose through 2001. Data on post-prandial glucose (PPG) and post-prandial plasma glucose (PPG) were analyzed for four major ethnicity/region groups: Caucasians from Europe and Asia from East South East and South Asia.

Results: The efficacy population included 62,320 patients, with 10,000 patients from the four groups of interest. At the 3-month visit, mean HbA1c had decreased by 1.2% (±1.31%) with FPG 46 (±18.02) mg/dL from 172.0 mg/dL (PD at 0.16), and PPG by 70 (±30.50) mg/dL from 283.2 mg/dL (P 0.001) post-treatment in all four. PPG were larger in patients with higher baseline values regardless of ethnicity and region. Data from 30,710 patients from the four groups with non-missing baseline and 3-month HbA1c, data, age and sex were analysed by multivariable ANCOVA. After adjustment for relevant baseline confounding factors, South East and East Asia had slightly better responses to acarbose than South Asians and Europeans. Additionally, however, the differences were numerically small (e.g. relative difference of -0.2% for baseline HbA1c of 8.2% vs. 7.9% for baseline HbA1c of 6.7%). In the safety population (n=77,682), acarbose was well tolerated, with few episodes of hypoglycemia (0.05%) and gastrointestinal adverse events (2.9%).

Conclusion: Acarbose was effective in European Caucasians and Asians; however, after adjustment for confounders, South East and East Asia patients had slightly better responses to acarbose than South Asians and Europeans.

Methods

– Dataset: T2DM and NMS from 21 countries, provinces and country groups across the world from the launch of acarbose to 2001 were pooled in a single database
– Data collection: post-prandial glucose (PPG), fasting plasma glucose (FPG) and body weight data were collected at baseline and post-treatment (3 months and last visit) were used to assess the efficacy of acarbose
– Blinded analysis of covariates (ANCOVA) models were used to assess the relative reduction in HbA1c, versus baseline, with adjustment for body weight, ethnicity/region subgroups and baseline HbA1c
– Multivariable ANCOVA was used to compare HbA1c responses to acarbose in terms of relative change in HbA1c at 3 months versus baseline, with adjustment for baseline HbA1c, ethnicity/region subgroups and additional confounders (gender, ethnicity/region and subgroups, disease duration by subgroup, dose category, body mass index (BMI) (mm/kg²))

Results

Patient population

– 67,852 patients were included in the safety population
– After exclusions, which included duplicate entry data, did not take acarbose, did not have follow-up data, were younger than 18 years or did not have at least two measurements of FPG and PPG, the efficacy population comprised data for 30,710 patients
– The analysis population for four major subgroups included 50,300 patients: 1) - East Asia: Chinese, Hong Kong, Taiwan, Japan, and South Korea (n=7,495, 15%); 2) - East Asia: Thailand, India, Singapore, Malaysia, Indonesia, Philippines, and Vietnam (n=19,074, 38%); 3) - East Asia: South East Asia from 70 countries (n=9,219, 18%); and 4) - East Asia: South East Asia from all countries (n=14,492, 28%)

– After restriction of the original efficacy population to the four major ethnicity/region groups and additional exclusion criteria with missing baseline and/or post-treatment HbA1c data, 30,710 patients were considered for the multivariable ANCOVA analysis
– Mean follow up (SD) for the efficacy population with non-missing post-treatment PPG data was 32.3±8.8 (range 1.0–139.8) weeks

Patient characteristics

– Gender percentages were balanced, except for a higher percentage of men in the South East Asia group (51.5%)
– Elderly patients were more common in the European and East Asian groups (median age of 75.1 and 70 yrs) than South East Asia and South Asian groups (median age of 63.0 and 49 yrs, respectively)
– Patients were heavier in Europe and South Asia (median weight 84 and 74 kg, respectively) than in East Asia and South East Asia (median weight 67 and 65 kg, respectively)
– The proportion of obese patients (using the Western standard definitions for European diabetes and the Asia-Pacific standard for Asians) was higher in South Asia (10.1% and South East Asia (7.4%)); but more patients in the European groups were overweight (10.7%)
– Hypertension and dyslipidemia were more common in European patients (71.6% and 67.0%, respectively) than in South East Asia (53.8% and 46.6%, respectively)
– East Asian (11.7%) and Chinese (12.0%) patients had a significantly higher (t-test) PPG 200– vs. 192– mg/dL and South East Asian (11.1%) patients had a significantly lower PPG 200– mg/dL vs. South East Asian and South Asian (17.4% and 13.8%, respectively) patients
– Micronutrients did not differ greatly between ethnicity/region groups (p>0.17)
– Table 1 summarizes the baseline values for HbA1c, PPG and PPG for the efficacy population overall and the four ethnicity/region groups under evaluation

Table 1: Baseline glycemic values for overall efficacy population and four ethnicity/region groups

Changes in glycemic parameters at follow up: HbA1c

– Mean baseline HbA1c in the total population decreased from 8.4±1.7% at baseline (n=47,786) to 7.4±1.3% at the 3-month visit (n=35,411) and the last visit (n=41,247)
– Absolute reductions in patients with baseline and post-treatment HbA1c data were –1.1±1.5% at 3-month visit (n=26,883) and –1.3±1.5% at the last visit (n=38,084) (p<0.001 for both)
– Relative reductions were baseline dependent and greater at higher baseline HbA1c levels

Fig. 1: Mean change in PPG, after 3 months of treatment with acarbose by baseline category

Fig. 2: Mean change in FPG, after 3 months of treatment with acarbose by baseline category

Safety

– Acarbose was well tolerated with a low adverse event rate (3.10%)
– Patients experienced very few episodes of hypoglycemia (0.03%)

Study limitations

– Our analysis includes individual patient data, and we were able to adjust for confounding factors in individual patients, including baseline HbA1c, which is well known to affect the effect size with acarbose.

– This is the first study to analyze differences in outcome in clinical practice rather than data from clinical trials, and reflects the changes in HbA1c from baseline to discontinuation and patients can respond differently in clinical practice vs. clinical trials.
– Due to the nature of NMS, there was no control placebo group for all patients.
– As a time span existed between the first and the last NMS and as different case forms were used, some data were missing.

Discussion/conclusion

This analysis of a large database of pooled data from real-life practice in different patients from all over the world shows that acarbose is effective across all ethnicities and regions examined, although the effects are more pronounced in some populations, such as South East Asia and East Asia.

The relative reduction in HbA1c with acarbose is more pronounced in patients with higher baseline HbA1c values, this trend is more prominent in East Asia than other regions.

South East Asia and East Asia have slightly but significantly better responses to acarbose than South Asians and Caucasians from Europe after adjustment of relevant baseline confounding factors.

Overall, acarbose has good efficacy regardless of ethnicity and region.

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