Dietary habits

Low levels of physical activity

Prevalence of concurrent medications, including alternative medicines

Conclusion

Clear differences between Asian and non-Asian studies highlight the need for studies specifically designed to elucidate differences in treatment outcomes in T2D clinical trials, using liraglutide as an example.

References

Impact of Ethnicity on the Efficacy and Safety Outcomes of Anti-diabetes Drugs – Case Study of Liraglutide in Asian and Non-Asian Populations


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Objective/Introduction

Fuelled by dietary changes, increased sedentary lifestyles, and greater urbanisation in the Asia-Pacific region, there has been an increase in the number of people suffering from T2D types 2 and 3.

Understanding the impact of ethnicity on the efficacy and safety of anti-diabetes drugs is necessary to optimise drug development strategies and shorten the time lag between drug approval in the West and in Asia. The purpose of this study was to examine the differences in treatment outcomes in T2D clinical trials, using liraglutide as an example.

Methods

Targeted searches were performed in PubMed and clinical trials.gov to identify relevant studies. To be included in our analysis the study had to have been a completed, double-blind phase II clinical trial of liraglutide, include patients with T2D and report BMI and/or HbA1c, as an outcome.

The included studies were divided by country of study, followed by subsequent extraction of relevant baseline characteristics and safety data. Study design and eligibility criteria applied were also compared between the clinical trials conducted in Asian and non-Asian countries.

Results

Three Asian and five non-Asian studies satisfied all inclu- sion criteria. A detailed study profile is provided in Table 1 and baseline characteristics are provided in Table 2. Both the Japanese study and the North American study were double-blind.

In the Japanese study, HbA1c levels decreased by 1.93 percentage points compared to the North American study (1.2 mg/dl), and weight gain in the Japanese study was substantially lower (0.9 kg) compared to the North American study (2.0 kg).

Discussion

The pathophysiology of T2D includes lack of insulin secretion from beta-cells, weight gain and loss of insulin sensitivity in target tissues over time. The main cause for hyperglycaemia in Japanese patients is thought to be a lack of insulin secretion from beta-cells rather than insulin resistance; the opposite is true for Caucasian patients. Liraglutide is a glucagon-like peptide-1 receptor (GLP-1) agonist that stimulates insulin secretion from beta-cells and also addresses the lack of insulin secretion rather than insulin resistance.

The role of the ethnic factor is complicated by the ambiguous definition of ethnicity. In this case, we used the term 'ethnicity' to refer to the genetic differences between people of different ethnic origins, which can be understood by genetic testing.

Conclusion

Clear differences between Asian and non-Asian studies highlight the need for studies specifically designed to elucidate differences in treatment outcomes in T2D clinical trials, using liraglutide as an example.

Baseline characteristics

Upon comparing the studies of Saini et al. and Garber et al., it was noted that the duration of disease was longer in Japan, which is consistent with the higher mean age of study subjects. This suggests that T2D started around the same age in both study populations, and the Japanese subjects had a later stage of disease progression.

Safety

The most common treatment-emergent adverse events (TEAEs) by system organ class were the same in both studies (Table 4). Treatment discontinuation due to AEs was very infrequent in both studies. The use of sequential AEs by system organ class was also similar.

Treatment efficacy

Due to the open-label extension period in the last 28 weeks of the Japanese study, we decided to compare BMI, HbA1c levels at week 24, when both the Japanese study and the North American study were double-blind.

In the Japanese study, HbA1c levels decreased by 1.93 percentage points (0.9 mg/dl) in Japanese group after 24 weeks. In the North American study, HbA1c levels decreased by 1.0 percentage point with liraglutide 1.2 mg/dl and 1.20 percentage points with liraglutide 1.8 mg/dl. This non-direct comparison suggests that liraglutide is more effective in lowering HbA1c levels in Asian patients than in non-Asian patients (Figure 3).