JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes
LETTER TO THE EDITOR

Disease duration as an indicator of the efficacy of liraglutide in patients with type 2 diabetes mellitus

We would like to comment on the recent article of Usui *et al*[1] and highlight findings of our study. Usui *et al.* showed that the glucose-lowering effect of liraglutide as add on therapy to insulin relies on the remaining β-cell function in type 2 diabetes.[1] Counterintuitively, this effect was not dependent on disease duration. We retrospectively analyzed data from our cohort of type 2 diabetes patients (n = 69) at Slingeland Hospital, Doetinchem, the Netherlands, who instantaneously switched from insulin to liraglutide between 2010 and 2016. Inclusion criteria for switch were body mass index ≥35 kg/m^2 and glycated hemoglobin (HbA1c) >53 mmol/mol (>7.0%). Response was defined as a decrease in HbA1c; non-responding necessitates discontinuing liraglutide due to insufficient glycemic control or side-effects. Effects on weight and HbA1c were analyzed with a mixed model, and response by a multivariate Cox survival analysis.

The mean age of the patients was 62 years (standard deviation 7.9 years), and 54% were men. The median disease duration was 13 years (interquartile range 25–75, range 6–17.7 years), and the mean HbA1c was 68.8 mmol/mol (8.4%) during insulin therapy at a median daily dose of 96 units (range 54–129 units). At 3, 6, 12 and 24 months, the response rates were 65, 63, 51 and 23% for the total cohort, and 84, 84, 76 and 41% for patients with disease duration <10 years (n = 25). Responders' median weight reduction at 3, 6 and 12 months was 1 kg (range 0–4.5 kg), 3 kg (range 0–6.3 kg) and 5 kg (range 1–11 kg), respectively. Responders' median HbA1c reduction at 3, 6 and 12 months was 4 mmol/mol (range 0–12.2 mmol/mol), 8.5 mmol/mol (range 2–26.5 mmol/mol) and 7 mmol/mol (range 1–18 mmol/mol), respectively, 2.5% (range 0–3%), 2.9% (range 2.3–4.6%) and 2.8% (range 2.2–3.8%). Insufficient glycemic control was the main reason for non-responding (89%).

Longitudinal analysis adjusted for age and sex showed a significant positive association of disease duration with HbA1c (0.33, 95% confidence interval 0.07–0.58). Survival analysis, adjusted for age, sex and body mass index, showed a significant association between disease duration and non-responding to liraglutide, with a hazard ratio of 2.39 (95% confidence interval 1.20–4.76) when disease duration was dichotomized in <10 years or ≥10 years (Figure 1).

Intriguingly, the present results seem to conflict with the finding of Usui *et al.* not establishing a relationship between disease duration and successful therapy of liraglutide in combination with insulin. On the contrary, our results fit with their finding that liraglutide is most effective in patients with the highest remaining β-cell function, as it is well known that β-cell function declines with disease duration. We conclude that instantaneously switching from insulin to liraglutide is an option for severely obese patients with type 2 diabetes with a short disease duration.

ACKNOWLEDGMENT

We thank Marleen Duizer MD for her assistance during the data acquisition.

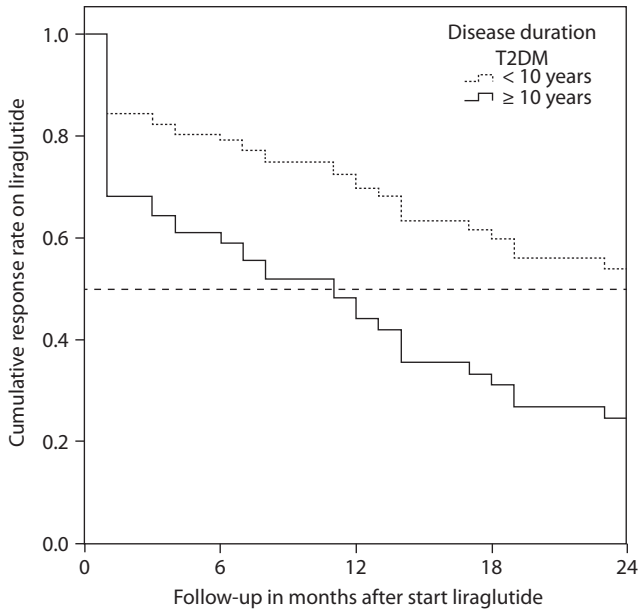

Figure 1 | Kaplan–Meyer curve response of liraglutide regarding disease duration of type 2 diabetes mellitus <10 years *vs* ≥10 years.

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Received 6 April 2018; revised 13 April 2018; accepted 19 April 2018

DISCLOSURE

The authors declare no conflict of interest.

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Doi: 10.1111/jdi.12857