



**TITLE:** *Effectiveness of GLP1-RAs in type 2 diabetes: a gender analysis*

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**ABSTRACT**

In type 2 diabetes (T2D), several differences have been described between men and women, concerning risk factors, clinical manifestations and chronic complications. The impact of gender on the efficacy and safety of hypoglycaemic drugs is still to be clarified. Some data suggest that GLP1-RAs may have greater efficacy on body weight in women, but comparable efficacy on glycaemic control and cardiovascular risk (CVD) in both sexes. The aim of our study was to evaluate in real-life clinical practice the possible influence of gender on the effectiveness and safety of GLP1-RAs long-acting therapy in T2D outpatients. In this single-centre observational study, we evaluated laboratory parameters, chronic complications, hypoglycaemic episodes, and any adverse events of subjects with T2D who started treatment with GLP1-RAs long-acting between 1.06.2018 and 31.05.2019, in add on to metformin or other hypoglycaemic drugs, and who practised this therapy for at least two years. In the present analysis, 391 subjects with T2D were included (men 59.3%, women 40.7%), with a mean age of 64.1 years and mean duration of diabetes of 18.4 years. At baseline, patients were on average obese (BMI 32.8 kg/m<sup>2</sup>) with an inadequate glycaemic control (HbA1c 7.8%). Women had higher BMI values than men; glycaemic

control was similar in both genders. After two years of follow-up, therapy with GLP1-RAs long-acting determined a significant reduction of BMI and blood pressure values, HbA1c, fasting glucose and GPT levels and an improvement in lipid profile. The reduction observed in BMI values was significantly greater in T2D women than in men. At stepwise regression analysis, female gender was among the independent predictors of the effectiveness of GLP1-RAs in terms of BMI reduction, together with fasting blood glucose, but not in terms of reduction of HbA1c levels, which was significantly associated with baseline blood glucose levels and metformin use, irrespective of gender. Overall, the treatment with GLP1-RAs was well tolerated, and only mild gastrointestinal adverse events were observed (n=22; 5.6%, 14 men and 12 women P>0.05), in both genders. In conclusion, in real-life clinical practice, the therapy with GLP1-RAs long-acting is safe and effective in both men and women, and it seems to be associated with a more beneficial effect on body weight in women than in men.