radcliffe cardiology

Title: ECO 24: Semaglutide in Body Weight & Reversion of Normoglycaemia: STEP 10
Participants: Dr Barbara McGowan
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Dr Barbara McGowan

"Hello, my name is Professor Barbara McGowan. I am a consultant endocrinologist and obesity physician at Guy's and St Thomas' Hospital, where I also serve as a professor of endocrinology and diabetes.

Overview of the STEP-10 Trial

The STEP-10 trial was designed to investigate the effects of semaglutide 2.4 mg in individuals living with obesity and pre-diabetes. While previous trials have explored semaglutide 2.4 mg for weight loss, this study focused specifically on a population with pre-diabetes.

Study Design

This trial was a randomised, double-blind, controlled, multicentre study. Key inclusion criteria were adults aged 18 and above with a BMI of 30 and above, all of whom had pre-diabetes as defined by NICE (HbA1c between 6% and 6.4%, and/or fasting plasma glucose between 5.5 mmol/L and 6.9 mmol/L). A total of 207 patients were randomised in a 2:1 ratio to receive either semaglutide 2.4 mg once a week or placebo. There was a dose escalation period followed by a maintenance period of up to 52 weeks. All participants received lifestyle intervention with dietary and physical activity advice. After 52 weeks, there was an off-treatment period up to 80 weeks where patients received healthy lifestyle counselling.

Primary and Secondary Endpoints

The primary endpoint was weight loss at week 52 and the proportion of participants reverting to normal glycemia. Secondary endpoints at week 52 included changes in

HbA1c, fasting plasma glucose, waist circumference, systolic blood pressure, other cardiovascular markers, categorical weight loss, reversion to normal glycemia at week 80, and the progression of type 2 diabetes at both week 52 and week 80.

Baseline Characteristics

The trial population was mostly female (31%), with an average age of 53 years. The majority were white (88%), with the rest being Asian, black, and other ethnicities. The mean body weight was over 111 kg, with a mean BMI of just over 40 and a waist circumference of 120.1 cm. Baseline mean HbA1c was 5.9%, fasting plasma glucose was 5.9 mmol/L, and mean blood pressure was 131 mm Hg.

Results

At 52 weeks, the semaglutide 2.4 mg group saw a 13.9% decrease in body weight, compared to 2.7% in the placebo group. Categorical weight losses (5%, 10%, 15%, and 20%) were significantly greater in the semaglutide group, with just under 50% achieving at least 15% weight loss compared to 1.5% in the placebo group, and 24.8% achieving 20% weight loss compared to the placebo.

Regarding reversion to normal glycemia, 81% in the semaglutide group achieved this at 52 weeks, compared to 14.1% in the placebo group. At 80 weeks, after stopping medication, reversion to normal glycemia reduced to 44.2% in the semaglutide group compared to 18.3% in the placebo group.

Additional Findings

There was a greater reduction in waist circumference and blood pressure in the semaglutide group at 52 weeks. However, stopping the medication led to increases back towards baseline in these parameters. HbA1c and fasting plasma glucose reductions were also seen in the semaglutide group at 52 weeks but regressed towards baseline after stopping the medication.

Conclusions

The STEP-10 trial demonstrated that semaglutide 2.4 mg provides superior reductions in body weight and reversion to normal glycemia compared to placebo, alongside improvements in cardiometabolic risk factors. The safety profile was consistent with the GLP-1 agonist class, with no new adverse events.

Implications and Next Steps

These results reinforce the benefits of obesity management and the potential to slow the progression to type 2 diabetes. Early intervention with semaglutide 2.4 mg in pre-diabetes could be beneficial. However, challenges such as medication cost and global supply issues need addressing. It is crucial to advocate for early treatment of obesity and its complications to achieve long-term health benefits and cost savings."