Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes Clinical Trial Summary

(SELECT (CVOT)-Lincoff AM et al. N England Journal of Medicine, 2023)

North Carolina State Health Plan
FOR TEACHERS AND STATE EMPLOYEES
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Per the request of the Board of Trustees at the October board meeting, we have summarized the following study.

On November 11, 2023, the New England Journal of Medicine published the study of a clinical trial investigating if semaglutide, a glucagon-like peptide-1 receptor agonist, reduces the risk of adverse cardiovascular events in patients with overweight or obesity without diabetes. Below is a summary of the clinical trial and its findings.

Clinical Trial Demographics

- 17,604 adults
- Mean age of 61.6 (+/- 8.9 years)
- 72.3% male
- Pre-existing cardiovascular disease
    - > ¾ previous myocardial infarction
    - ¼ chronic heart failure
- Medical Therapies
    - 90.1% were receiving lipid-lowering medications
    - 86.2% were receiving platelet-aggregation inhibitors
    - 70.2% taking beta-blockers
    - 45% taking ACE-Inhibitors and 29.5% taking ARBs
- Mean BMI was 33.3 +/- 5.0
    - 71.5% obese (≥30)
- No history of diabetes
    - 66.4% met A1C criteria for pre-diabetes (5.7-6.4%)

Clinical Trial Results

- Absolute vs. relative risk reductions when evaluating the primary end point of MACE (major adverse cardiovascular event: death from a cardiovascular event, nonfatal myocardial infarction, or nonfatal stroke).
    - 20% relative reduction in risk of MACE with semaglutide vs. placebo on top of standard care.
        - This 20% relative reduction is actually a **1.5% absolute reduction**, from 8.0% in placebo-treated patients to 6.5% in those taking semaglutide (hazard ratio: 1.0-0.8=0.2 (20% relative risk reduction).
        - Meaning that **67 very high**-risk patients must be treated to prevent **1 MACE.**
        - Contrastingly, only **39 high-**risk patients must be treated to prevent **1 MACE** when using a statin (which cost 98% less).

- Risk reductions were similar in men and women and across different ethnicities, patient ages and baseline levels of body weight.
    - "Relative risks have the appealing feature of summarizing two numbers (the risk in one group and the risk in the other) into one. However, this feature also represents their major weakness, that the underlying absolute risks are concealed, and **readers tend to overestimate the effect when it is presented in relative terms**."
    - "In many situations, the absolute risk gives a better representation of the actual situation and also from the patient's point of view absolute risks often give more relevant information."

If Novo Nordisk gets FDA approval for decreasing cardiovascular disease in **patients without diabetes who are overweight and had a previous cardiovascular event**, then they can expand the indication to include these patients **IN ADDITION** to patients seeking weight loss.

Having an additional indication would help Novo Nordisk achieve more market penetration and fare better competitively with new drugs in the pipeline only indicated for obesity (Zepbound and other future products).

References

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