CLOSER LOOK

MEMORANDUM

Saxenda reduces incidence of new-onset diabetes up to 79% - May 9, 2017

Executive Highlights

- A recent Lancet paper finds that people enrolled in the SCALE trial for Novo Nordisk's Saxenda (liraglutide 3.0 mg for obesity) experienced a 79% reduced risk for new-onset type 2 diabetes if they persisted on high-dose liraglutide treatment for three years vs. placebo treatment for three years ($p<0.0001$).
- The GLP-1 agonist extended time to new-onset diabetes by 2.7x vs. placebo ($p<0.0001$).
- This new data points to liraglutide as a potential prediabetes treatment, although no drugs are approved for prediabetes (and likely won't be, until the condition is defined as a disease) and although the cost of population-level intervention with liraglutide in the US alone would be upwards of $1.2 trillion.

A new paper published in the Lancet reports three-year outcomes data from the SCALE program for Novo Nordisk's GLP-1 agonist Saxenda (liraglutide 3.0 mg). Among participants who persisted on liraglutide treatment for three years (n=1,472), 2% were diagnosed with new-onset type 2 diabetes by week 160 vs. 6% of participants who persisted in the placebo arm for three years (n=738). This corresponds to a hazard ratio of 0.21, or an impressive 79% risk reduction for new-onset type 2 diabetes with Saxenda vs. placebo ($p<0.0001$). The primary endpoint of this analysis was time to diagnosis, which liraglutide extended by 2.7x (95% CI=1.9-3.9, $p<0.0001$) - of the 26 individuals on Saxenda who were diagnosed with type 2 diabetes during the course of the trial, the mean time to onset was 99 weeks vs. 87 weeks for the 46 individuals receiving placebo who were diagnosed. Serious adverse events were reported by 15% of liraglutide-treated patients vs. 13% of placebo-treated patients, corresponding to a non-significant difference - a reassuring safety finding for Saxenda.

These results add to the body of evidence showing liraglutide's potential in diabetes prevention. Earlier publications from the SCALE program have found significantly greater weight loss *with Saxenda vs. placebo (6% drop from baseline body weight vs. 2% drop, respectively), a greater proportion of patients in the Saxenda group achieving ≥5% body weight loss (50% vs. 23%), and improvements in metabolic control associated with Saxenda vs. placebo. By quantifying incidence of diabetes for the two groups, this new analysis offers hard data to support Saxenda as a prediabetes intervention (beyond its current indication for obesity management). No drugs are approved for the treatment of prediabetes - because prediabetes has yet to be defined and accepted as a disease in and of itself - but thought leaders have endorsed both metformin and liraglutide for this purpose. Given the size and scope of the diabetes epidemic, reacting to hyperglycemia once it appears will not be enough to curtail this public health problem. We simultaneously need proactive prevention efforts that lower incidence of new-onset type 2 diabetes, and medicines like Saxenda could be one partial solution. Notably, the FDA recently approved the inclusion of three-year SCALE data on the Saxenda label, which will hopefully convince more providers of its safety and long-term efficacy for obesity management. It's also important to acknowledge that all SCALE participants received lifestyle intervention alongside Saxenda or placebo. We have no doubt that lifestyle modification, including healthier diet/exercise, will maintain its central role in diabetes prevention, especially with the proliferation of the Diabetes Prevention Program (DPP) and Medicare's plans to reimburse the DPP starting in January 2018. That said, papers like this one recently-published in the Lancet point to pharmacotherapy as an untapped resource for diabetes prevention, and we'd love to see momentum on this front.*

- **Cost is another important consideration, and Saxenda is not inexpensive.** We learned at WCPD 2016 that it would cost a little over $4 billion to treat the entire US prediabetes population

(86 million Americans) with metformin vs. >$1.2 trillion with liraglutide and ~$1.4 trillion with the DPP (which costs ~$100/person/session). In this context, Saxenda could be scaled to the same level as the DPP, though this would require massive educational efforts to get patients, providers, and payers to see the product as a diabetes prevention solution. We continue to hold out hope that reimbursement prospects for Saxenda will improve - the challenging payer landscape for obesity drugs continues to negatively impact the class. Based on these numbers, metformin is the most appealing option for population-level diabetes prevention. On the flip side, high-dose liraglutide comes with pronounced weight loss benefits (among other positive health effects), and could thus be much more effective in delaying new-onset type 2 diabetes or preventing it altogether. Ultimately, we hope to hear more forward-thinking conversation on pharmacotherapy for diabetes prevention, with due consideration given to both metformin and liraglutide.

-- by Payal Marathe, Jacqueline Anders, and Kelly Close