Merck receives Complete Response Letter for inclusion of TECOS data on Januvia label - April 7, 2017

Merck announced this morning that the FDA has issued a Complete Response Letter (CRL) for the inclusion of TECOS data on the Januvia (sitagliptin), Janumet (sitagliptin/metformin), and Janumet XR (sitagliptin/metformin extended-release) labels - this is very surprising. Results from the CVOT, presented first at ADA 2015, were resoundingly neutral: The DPP-4 inhibitor demonstrated non-inferiority for the primary endpoint of three-point MACE (non-fatal MI, non-fatal stroke, or CV death) plus hospitalization for unstable angina with a hazard ratio of 0.98 (95% CI=0.89-1.08), and also showed non-inferiority for the secondary endpoint of three-point MACE with a hazard ratio of 0.99 (95% CI=0.89-1.10). Still, inclusion of TECOS data on the labels for the Januvia franchise could distinguish Merck's DPP-4 inhibitor from others in its class and put to bed concerns about the DPP-4 inhibitor being associated with heart failure. Notably, the SAVOR-TIMI trial of AZ's Onglyza (saxagliptin) found a worrisome 27% increased risk for heart failure hospitalization (p=0.007), and the EXAMINE trial for Takeda's Nesina (alogliptin) found a similar heightened risk for heart failure, whereas TECOS reported a neutral hazard ratio for this endpoint of 1.00 (95% CI=0.8-1.20). The CARMELINA and CAROLINA CVOTs for Lilly/BI's Tradjenta (linagliptin) are expected to complete in January 2018 and March 2019, respectively. We are looking particularly forward to these data because one SFU was included here and we will see (one hopes) more about the long-term impact of this class. Of course, SFUs will likely "show" better in an RCT than in the real world. Currently, they are widely used in patients who cannot afford any other drug; new drug classes like DPP-4 inhibitors will become available at generic prices to a much broader group of patients in the next decade. SFUs are perfectly fine to use for some patients, of course, who cannot afford other drugs; those at risk of hypoglycemia and those for whom weight gain isn't healthy, however, have much less positive experiences taking these. The threat of beta cell burnout continues to be a question with some SFUs, as well. Merck is reviewing the CRL and plans to discuss next steps with the FDA. We look forward to an update on this during the company's 1Q17 earnings call on May 2.

-- by Payal Marathe, Helen Gao, and Kelly Close