



Worst postbaseline TSH levels were not associated with dose modification of lenvatinib, study drug withdrawal, treatment exposure, or lenvatinib-related adverse events. However, lenvatinib-related thyrotoxicosis and exacerbation of hypothyroidism occurred primarily in patients who had worst postbaseline TSH levels >5.0 mIU/L. In addition, QTc prolongation occurred more frequently in patients who had worst postbaseline TSH levels of >5.0 mIU/L (12.5%) compared with patients who had worst postbaseline TSH levels of >0.5 to 5.0 mIU/L (6.4%) or ≤ 0.5 mIU/L (4%). PFS, overall survival, and overall response rate were not significantly different among the worst postbaseline TSH level categories.

Dr Sherman indicated that the data from this exploratory analysis of the SELECT trial suggest that there is no association between worst postbaseline TSH levels on overall lenvatinib safety or efficacy, as well as lenvatinib exposure. In addition, although increased TSH levels occurred frequently, it was not known if the rise was a result of lenvatinib or modification of TSH-suppression therapy because of patient intolerance to TSH suppression. Dr Sherman stated that a longitudinal analysis of TSH levels may be warranted and could provide further information than this single-time point analysis.

Liraglutide, Roflumilast Improve Body Weight in Obese Women With PCOS

Written by Emma Hitt Nichols, PhD

Treatment of obese women with polycystic ovarian syndrome (PCOS) with liraglutide or roflumilast, but not metformin, resulted in a significant decrease in body weight and improvement in metabolic and endocrine parameters. Mojca Jensterle, MD, University Medical Center Ljubljana, Ljubljana, Slovenia, presented data from the PDE-4 Inhibitor Roflumilast and GLP-1 Agonist Liraglutide in Polycystic Ovary Syndrome trial [NCT02187250].

Women with PCOS struggle with weight loss, and weight reduction through lifestyle changes and pharmacotherapy such as metformin may improve cutaneous manifestations and menstrual cycle regularity and fertility and reduce cardiovascular disease factors. Potential alternatives to metformin include glucagon-like peptide-1 (GLP-1) receptor agonists [Kahal H et al. *Clin Endocrinol (Oxf)*. 2014; Elkind-Hirsch K et al. *J Clin Endocrinol Metab*. 2008] or PDE4 inhibitors, which increase GLP-1 plasma levels through completely different pathways involved in PDE4 regulation of signaling cascades linked to GLP-1 release [Vollert S et al. *Diabetologia*. 2012; Wouters EF et al. *J Clin Endocrinol Metab*. 2012; Calverley PMA et al. *Lancet*. 2009].

The purpose of this study was to determine if treatment of obese women with PCOS with liraglutide or roflumilast improved body weight compared with metformin. In this prospective, open-label, phase 4 trial, 45 obese women with PCOS were randomly assigned to receive metformin, liraglutide, or roflumilast for 12 weeks. At baseline, mean body mass index was 38.6 ± 6.0 kg/m², and mean age was 30.7 ± 7.9 years. Women were eligible if they had no significant cardiovascular, kidney, or hepatic disease; had no history of neuropsychiatric events; and did not use a medication known to affect reproductive or metabolic functions. The primary outcome of the study was changes in anthropometric measures of obesity.

Compared with baseline, patients who received liraglutide and roflumilast experienced a significant decrease in body weight of 3.1 kg (± 3.5 kg; $P = .006$) and 2.1 kg (± 2.0 kg; $P = .002$), respectively, whereas patients who received metformin did not experience a significant body weight loss (-0.1 ± 1.9 kg). In the liraglutide arm, but not the metformin or roflumilast arms, there was a significant decrease in visceral adipose tissue area from baseline (160.3 ± 67.9 cm² to 140.7 ± 60.8 cm²; $P = .015$).

Significant improvement was detected in some metabolic and endocrine parameters among patients who received liraglutide and roflumilast. There was a significant decrease in mean serum glucose levels before and after a 120-minute oral glucose tolerance test in the liraglutide arm ($P \leq .05$ for both), but not the metformin or roflumilast arms. In the roflumilast arm, total testosterone levels and free androgen index significantly decreased from baseline ($P = .05$ and $P = .016$, respectively).

In conclusion, Dr Jensterle stated that the results from this study suggest that treatment of obese women with PCOS with liraglutide was superior to metformin and roflumilast in the reduction of body weight and improvement in body composition, with roflumilast superior to metformin. However, treatment with roflumilast, but not metformin or liraglutide, reduced testosterone levels.

LH and Testosterone Significantly Reduced With NKB Receptor Antagonist in PCOS

Written by Toni Rizzo

Polycystic ovary syndrome (PCOS) affects 5% to 10% of women of reproductive age. PCOS is characterized by accelerated luteinizing hormone (LH) pulse frequency and elevated serum testosterone concentrations, menstrual irregularity, and polycystic ovaries. Currently, there is no approved treatment for PCOS. Recently, hypothalamic neurokinin B (NKB) has been characterized