Clinical Trial Summary

Natesto™, a novel testosterone nasal gel, normalizes androgen levels in hypogonadal men

Rogol AD, et al. Andrology 2016; 4: 46-54

What is the clinical paper about?

- The main focus of this study was to evaluate the efficacy and safety of Natesto™ 4.5% Testosterone Nasal Gel for the treatment of male hypogonadism.
- The primary endpoint was the percentage of patients with serum testosterone C_{avg} within the eugonadal range (300–1050 ng/dL or 10.4-36.4nmol/L) after 90 days.

What is the methodology?

- This was a phase 3, randomized, open-label, dose-ranging, 90-day, two-arm trial in men aged 18 to 80 years with serum testosterone levels <300 ng/dL.
- Patients received study drug either in a fixed-dose arm (three-times daily, 5.5 mg/nostril, 11 mg/dose, 33 mg/day) or in a titration arm (twice-daily, 22 mg/day) with potential dose adjustment to three-times daily (33 mg/day) at Day 45 based on serum testosterone levels.
- Patients were assessed for two additional, sequential safety extension periods of 90 and 180 days, during which they continued to receive Natesto™ at their Day 90 dose level.
- Overall, 228 patients were randomized to the titration arm and 78 to the fixed-dose arm.

What are the key results?

- **Efficacy/pharmacokinetic:** On Day 90, the percentages of patients whose total testosterone C_{avg} were in the normal range was 73% (95% CI: 68, 79) in the total population, 68% (95% CI: 61, 74) in the titration arm, and 90% (95% CI: 83, 97) in the fixed-dose arm.
- Improvement from baseline in mean erectile function ($p<0.0001$ both dose groups) and in mood scores ($p<0.0001$ for mean positive affect, $p<0.01$ for negative affect) achieved statistical significance by Day 90.
- Positive changes from baseline in body composition (increase in lean body mass from baseline, $p=0.0384$ at Day 180) were observed.
- **Safety:** Proportions of patients with ≥1 TEAE and ≥1 possibly drug-related TEAE were, respectively, 63.4% and 30.3% for the two-times daily and 64.6% and 40.9% for the three-times daily dose group.
  - 4.6% had ≥1 severe TEAE.
- Adverse event discontinuation rates were 2.1% (two-times daily) and 3.7% (three-times daily).

What are the key conclusions?

- In this study, treatment with 4.5% testosterone nasal gel restored levels of testosterone in most hypogonadal men and resulted in statistically significant improvements from baseline in erectile function and mood.
- Natesto™ was generally well-tolerated with low incidence of local reaction.
- **However**, this study lacked a placebo or an active comparator control which limited the ability to adequately assess some efficacy measures such as bone mineral density, and the study excluded patients with nasal disorders, limiting its generalisability to this population.