

TIMES2 study shows that Tostran^{®*} (2% testosterone gel) in hypogonadal[†] men with Type 2 diabetes and/or metabolic syndrome improves insulin resistance and other cardiovascular risk factors

Results from the first, large, randomised placebo controlled study of transdermal testosterone in hypogonadal men with Type 2 diabetes and/or metabolic syndrome

30th March, 2011 Results of the TIMES2 (Testosterone replacement In hypogonadal men with either **ME**tabolic **S**yndrome or type **2** diabetes) study published this month in *Diabetes Care* show that Tostran[®] significantly improves insulin resistance, lipid profile, and measures of sexual dysfunction in hypogonadal men with Type 2 diabetes (T2D) and/or metabolic syndrome (MetS).

Professor Hugh Jones from the Centre for Diabetes and Endocrinology at Barnsley Hospital NHS Foundation Trust and the University of Sheffield commented “The results of the TIMES2 study strongly support a role for TRT in the treatment of hypogonadal patients with T2D and/or MetS. Not only does this study add to the body of literature demonstrating a link between these three pathologies, but it also strongly supports a more holistic approach to treatment of these patient groups”.

Previous small, or non-placebo controlled studies have showed positive effects of testosterone therapy on glucose control, insulin resistance, lipid profile, measures of obesity in men with T2D and MetS [Muraleedharan and Jones, 2010], but TIMES2 is the first large, randomised, placebo-controlled, multi-centre clinical trial to show the benefits of testosterone therapy on metabolic parameters in patients men with hypogonadism and either T2D or MetS over 12 months.

The TIMES2 trial demonstrated that after 6 months of treatment with testosterone gel (60mg), insulin resistance (measured by homeostasis model assessment of insulin resistance; HOMA-IR) was reduced by 15.2%, compared with placebo (P=0.018). An effect that was maintained for up to 12 months (16.4% reduction compared with placebo, P=0.006).

*Tostran[®] is also called Tostrex[®], Fortigel[®] and Ilnogen

†Hypogonadism was defined as early morning [08:00–10:00] total testosterone ≤ 11 nmol/L or free testosterone ≤ 255 pmol/L on two occasions ≥ 1 week apart), with at least two symptoms of hypogonadism

At 6 months, testosterone gel, compared with placebo, also significantly reduced Lipoprotein a (Lpa) in the T2D and/or MetS group (P=0.019) and Lpa (P=0.008), total cholesterol (P=0.003) and LDL-cholesterol (P=0.012) in the .MetS group.

In addition to these metabolic effects, hypogonadal men, with either T2D or MetS, treated with testosterone gel had significantly greater increases from baseline in total International Index of Erectile Function (IIEF) score (P=0.024) and in the sexual desire domain (P= >0.05) at 6 months. At 12 months significant improvements in IIEF total score and sexual desire and intercourse satisfaction domain scores were also observed.

Importantly, there were no significant differences in the frequencies of adverse events or serious adverse events between men treated with testosterone gel and placebo; most adverse events (>95%) were mild or moderate.

The *Endocrine Society Clinical Practice Guideline* recommends testosterone therapy for symptomatic men with classical androgen deficiency syndromes (including hypogonadism) [Bhasin et al]. The ISA, ISSAM, and EAU recommendations published in 2006 recommended that, until positive effects of testosterone on blood glucose control were definitively demonstrated, diabetes should be evaluated and treated before or simultaneously with testosterone substitution [Nieschlag et al, 2006]. The TIMES2 study contributes to the understanding of the field by showing the positive effects of testosterone gel therapy on insulin resistance and other symptoms of MetS and T2D in hypogonadal men.

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About TIMES2

The TIMES2 study is the first large, double-blind, placebo-controlled study to investigate the effects of restoring testosterone levels on insulin resistance, lipids, body composition and sexual dysfunction in men with hypogonadism and T2D and/or MetS over 12 months. The study was carried out in two phases: Phase I, in which adjustments to diabetes, lipid-lowering and antihypertensive medications were not allowed, and Phase II, in which adjustments were allowed. In total, 220 patients were randomised and received at least one dose of the study drug; of these 118 patients completed the study: the number and characteristics of patients that withdrew was similar across study groups.

The objective of the study was to evaluate the effects of a metered-dose, topical 2% testosterone gel, Tostran[®], on insulin resistance and associated cardiovascular risk factors in hypogonadal men with T2D and/or MetS, compared with placebo. The study was carried out in eight European countries between February 2006 and March 2007. Men aged ≥ 40 years were eligible for inclusion in the study if they had: confirmed hypogonadism (a total serum testosterone concentration of ≤ 11 nmol/L or free serum testosterone ≤ 255 pmol/L); at least two symptoms of hypogonadism; fulfilled criteria for MetS and/or T2D.

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About hypogonadism

Hypogonadism in men is a clinical syndrome that results from failure of the testis to produce physiological levels of testosterone (androgen deficiency) and the normal number of spermatozoa because of disruption of one or more levels of the hypothalamic-pituitary-gonadal (HPG) axis. [Bhasin et al 2006] Late-onset hypogonadism is a clinical *and* biochemical syndrome associated with advancing age and characterized by typical symptoms and a deficiency in serum testosterone levels. It may result in significant detriment in the quality of life and adversely affect the function of multiple organ systems [Nieschlag et al 2006].

References

- Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori, VM. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical
- Practice Guideline *J Clin Endocrinol Metab* 2006 **91**: 1995–2010
- Muraleedharan V, Jones TH. Testosterone and the metabolic syndrome *Ther Adv Endocrinol Metab* 2010 **1**: 207–223
- Nieschlag E, Swerdloff R, Behre, HM, Gooren LJ, Kaufman JM, Legros JJ *et al* Investigation, treatment, and monitoring of late-onset hypogonadism in males: ISA, ISSAM, and EAU Recommendations *Int J Androl* 2005 **28**: 125–127

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