

## Treatment of Patients with a Late Diagnosis of Klinefelter's Syndrome with Testosterone Undecanoate for a Duration of up to 5 years

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**Introduction:** Males suffering from Klinefelter's Syndrome (KS) experience an increased hospitalization rate from a variety of disorders, some caused by hypogonadism, and some linked to the syndrome *per se*, others not readily explained, maybe socioeconomic. The degree of hypogonadism is variable with the vast majority below the normal range. Mortality in KS is significantly increased, with excess deaths due to diabetes, cardiovascular, respiratory, and gastrointestinal diseases. KS is markedly underdiagnosed with less than 10% of cases identified by puberty and less than 20% ever diagnosed during life. In the present study we describe a cohort of men suffering from KS, diagnosed at advanced age. The majority of the patients had been referred by an orthopedic surgeon after a diagnosis of osteoporosis to be checked for hypogonadism.

**Methods:** Open-label, single-center, cumulative, prospective registry study of 22 middle-aged men with testosterone levels between 2.1 and 3.5 ng/mL (mean:  $3.08 \pm 0.46$ ). 21 men were studied for at least 2 years, 18 for 3 years, 11 for 4 and 8 for at least 5 years. They received parenteral testosterone undecanoate 1000 mg/12 weeks after an initial interval of 6 weeks.

**Results:** After 5 years the following changes were observed: Testosterone (ng/mL) increased from  $3.08 \pm 0.46$  to  $4.86 \pm 0.47$  ng/mL ( $p < 0.0001$ ). Body weight (kg) decreased from  $105.05 \pm 11.18$  (minimum: 70, maximum: 139) to  $90.88 \pm 9.76$  ( $p < 0.0001$  vs baseline). Waist circumference (cm) declined from  $104.32 \pm 6.39$  to  $96.50 \pm 6.63$  ( $p < 0.0001$  vs baseline). The mean T-score increased from  $-2.91 \pm 0.31$  (min -3.90, max -2.60) to  $-1.50 \pm 0.28$  ( $p < 0.0001$  vs baseline). Glucose levels remained unchanged with mean levels below 100 mg/dL at all time-points. Total cholesterol decreased from  $240.95 \pm 18.89$  to  $177.75 \pm 16.69$  ( $p < 0.0001$ ), LDL from  $124.09 \pm 46.4$  to  $64.13 \pm 18.13$  ( $p < 0.0001$ ) and triglycerides from  $235.09 \pm 22.07$  to  $180.75 \pm 7.59$  ( $p < 0.0001$ ). HDL did not change significantly.

**Conclusions:** Raising serum testosterone to normal in patients with a late diagnosis of Klinefelter's syndrome improved body composition including bone mineral density. Other features of the metabolic syndrome were also improved.