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Effect of Testosterone Enanthate on 24-hour Ambulatory Blood Pressure is Less in Patients with Hypertension at Baseline

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Introduction

- XYOSTED™, the Subcutaneous Testosterone Enanthate Auto-Injector (SCTE-AI) has been designed to improve the convenience of testosterone (T) therapy by allowing patients with testosterone deficiency (TD) to self-administer a premeasured dose of testosterone enanthate (TE) as a single subcutaneous (SC) injection once/week (**Figure 1**)
- XYOSTED was recently approved by the US Food and Drug Administration (FDA) (September 30, 2018) for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone
- The XYOSTED clinical program included a rigorous ambulatory blood pressure monitoring (ABPM) study to fully characterize the potential effects of testosterone replacement on blood pressure (BP). The data demonstrated that BP increases occurred in some patients
- 24-Hour ambulatory blood pressure monitoring (ABPM) is currently accepted as the most informative measurement of blood pressure,[1,2] with a diagnostic threshold of >130/80 mmHg[1]

Figure 1. XYOSTED™ – Subcutaneous Testosterone Enanthate Auto-injector

Objective

- To study the safety of XYOSTED administered subcutaneously once each week to adult males with hypogonadism
- To assess the impact of XYOSTED on BP measurements in adult males with TD
  - Measurements were taken both in the clinic using a standard BP cuff and over a 24-hour period using ABPM
- To assess the impact of XYOSTED on BP elevation in patients with hypertension (HTN) and those taking antihypertensive medications

Methods

- 150 Adult males, 18-75 years of age, with documented symptomatic TD (total testosterone [TT] values <300 ng/dL) initiated treatment with 75 mg TE self-administered weekly with the SCTE-AI (Xyosted™)
- Doses were adjusted beyond week 6 to maintain a trough concentration range of 350-650 ng/dL using a simple titration scheme
- Safety assessments included clinical laboratory measurements, treatment-related adverse events (TRAEs) and injection site reactions (ISRs)
- In-clinic BP was measured at all visits through week 26
- 24-hour ABPM data were collected at Baseline, Week 6, and Week 12
  - During ABPM, BP was assessed every 20 minutes during waking hours and every 60 minutes during sleep
- The impact of XYOSTED on HTN status was analyzed, based on patients' history, ABP consensus thresholds for HTN, and patients' concurrent use of BP-lowering medications

Results

- In total, 133 patients received treatment with XYOSTED across 19 US sites with >99% overall compliance
  - 113 patients completed the study
- At Week 12 in the ABPM study, mean 24-hour systolic BP (SBP) measurements increased from baseline by 3.7 mmHg (**Figure 2**)
  - Diastolic BP (DBP) increased by 1.3 mmHg from baseline
- By Week 26, in-clinic SBP increased by 3.4 mmHg from 125.6 mmHg at baseline to 129.0 mmHg
  - DBP increased by 1.8 mmHg from 78.2 mmHg at baseline to 80.0 mmHg by week 26
- Changes in BP showed a poor correlation with TT concentration (**Table 1**)
- Changes to SBP in the ABPM study were analyzed in patient subgroups determined by baseline HTN status and antihypertensive drug use (**Figure 3**)
  - Patients with HTN at baseline experienced *lower* mean increases in SBP (+0.3 mmHg) at Week 12 than did patients with no HTN (+7.2 mmHg)
  - Week 12 SBP increases were similar whether patients were taking antihypertensive drugs or not
- In total, 34 (25.6%) patients experienced adverse drug reactions (ADRs), most of which were considered mild or moderate (**Table 2**)
  - No ADRs related to HTN or cardiovascular (CV) events were reported throughout the study

Table 1: Mean Changes from Baseline in 24-Hour, Awake, and Asleep Blood Pressure Measurements by Tertiles of Testosterone Assessed at Week 12

	Visit-specific Tertiles of Testosterone Concentration			
	First Tertile	Second Tertile	Third Tertile	*Total*
Systolic Blood Pressure (mmHg)				
24-Hour	4.0	4.1	3.1	3.7
Awake	4.9	4.4	3.1	4.1
Asleep	3.4	0.6	1.1	1.5
Diastolic Blood Pressure (mmHg)				
24-Hour	3.0	0.7	0.6	1.3
Awake	3.9	0.9	0.4	1.7
Asleep	0.4	1.0	-1.4	-0.0

Table 2: Most Frequently Reported Adverse Drug Reactions

Adverse Drug Reaction (ADR)	N (%) of patients experiencing
Increased hematocrit	10 (7.5%)
Injection site hemorrhage	6 (4.5%)
Injection site bruising	4 (3.0%)
Increased prostate-specific antigen	4 (3.0%)

Figure 2: Changes From Baseline in Mean Ambulatory Systolic and Diastolic Blood Pressure Measurements at Weeks 6 and 12

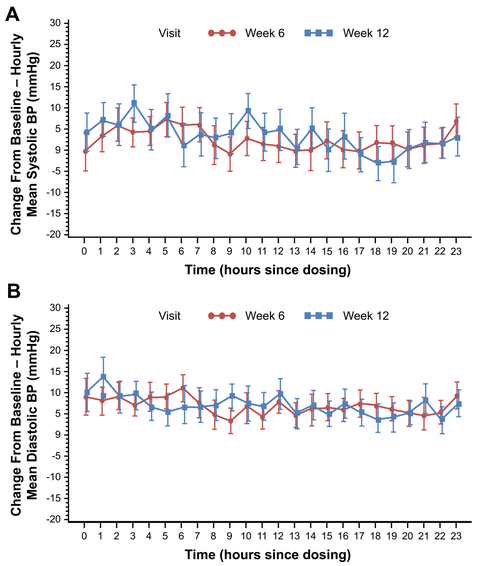
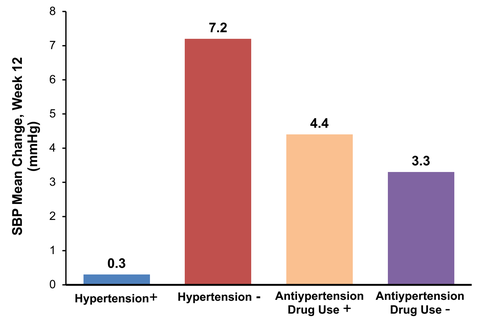


Figure 3: Changes to Systolic Blood Pressure by Baseline Hypertention Status and Antihypertensive Drug Use*, Weeks 12

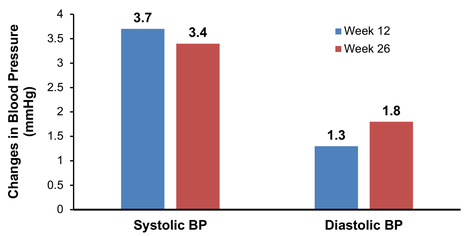


*Hypertension status based on ABP hypertension threshold of 130/80 mmHg[1]

Conclusions

- The XYOSTED clinical studies included a rigorous ABPM study to fully characterize the potential effects of testosterone replacement on blood pressure.
- Mean increases in systolic BP of 3.7 mmHg and 3.4 mmHg from baseline were identified following 12 and 26 weeks of treatment respectively (**Figure 4**).
- Patients with hypertension at baseline BP appeared to experience less impact on BP following treatment.
- Patients using antihypertensive medications experienced comparable BP changes as those not on these medications.
- BP measurements do not demonstrate increased susceptibility to testosterone therapy in patients with HTN at baseline or in those taking concurrent antihypertensive medication
- There was no clear relationship between TT levels and BP (though concentration range in this study was narrow)
- No adverse drug-related CV events were reported
- XYOSTED has a favorable safety profile and is well tolerated.

Figure 4: Mean Increases in Blood Pressure from Baseline to Weeks 12 and 26



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