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"Evaluation of Tolterodine Tartrate versus Placebo in the Treatment of Overactive Bladder"

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۞قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ
مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ
الْحَكِيمُ۞

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(البقرة – 32)

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LIST OF ABBREVIATIONS

ATFP	Arcus Tendineus Fasciae Pelvis
ATLA	Arcus Tendineus Levator Ani
β-NGF	B-Nerve Growth Factor
bid	Two Times A Day
BMI	Body Mass Index
CMG	Cystometrogram
DDAVP	Desmopressin (1-Deamino-8-D-Arginine-Vasopressin)
DHIC	Detrusor Hyperactivity With Impaired Contractility
FDA	Food And Drug Administration
FLUTS	Bristol Female Lower Urinary Tract Symptoms Questionnaires
HSV	Human Simplex Virus
ICS	International Continence Society
IIQ	Incontinence Impact Questionnaire
IQOL	Incontinence QOL
IR	Immediate Release
KHQ	King's Health Questionnaire
KUB	Kidney, Ureter, Bladder
LA	Extended Release
M3	Muscarin-3
MDA	Maximum Detrusor Activity
MP	Maximum Pressure
NK	Neurokinin
NMP22	Nuclear Matrix Protein 22
OAB	Overactive Bladder
P_{det}	Detrusor Pressure
PVRV	Postvoid Residual Urine Volume
qd	Once A Day
qid	Four Times A Day
Q_{infus}	Infusion Flow Rate
QOL	Quality Of Life
tid	Three Times A Day
TTX	Tetrodotoxin
UDI	Urogenital Distress Inventory
UI	Urge Incontinence
UTI	Urinary Tract Infection
V_{infus}	Infused Volume
VR1	Vanilloid Receptor Subtype 1
VS	Versus

XL	Extended Release
YIPS	York Incontinence Perception Scale

INTRODUCTION

Overactive bladder (OAB), which is characterized by symptoms of frequency, urgency and urge incontinence (UI) (either alone or in combination), is a common and distressing condition that has a profound effect on daily living of affected individuals ***(Jackson, 1997; Johannesson et al., 1997; Kobelt et al., 1999).*** In the USA, OAB affects at least 17 million individuals, while in Europe 17% of the population aged over 40 years experience this debilitating condition ***(Wein and Rovner, 1999).***

According to the International Continence Society (ICS), OAB disorder is characterized by involuntary detrusor contractions that may occur spontaneously or may be provoked (by rapid filling, alterations of posture, coughing, walking and jumping ***(Hampel et al., 1997).*** An OAB of neurogenic origin usually has been referred to as a hyperflexic disorder, whereas one that is nonneurogenic is referred to as an unstable disorder ***(Hampel et al., 1997).***

This disorder is treated predominantly with antimuscarinic drugs ***(Andersson, 1988; Andersson, 1997).*** Prior to the introduction of tolterodine, the most commonly used antimuscarinic agent was oxybutynin. This drug, while effective in many instances, has limited clinical utility due to tolerability problems, particularly bothersome dry mouth ***(Yarker et al., 1995; Drutz et al., 1999).*** Furthermore, unwanted cognitive effects are of concern. These tolerability concerns have negative implications for the treatment of OAB, especially since this condition normally requires prolonged therapy to maintain symptomatic relief ***(Katz, 1998).***

Tolterodine is an antimuscarinic agent developed specifically for the treatment of the OAB. Unlike oxybutynin, tolterodine shows selectivity for the bladder over the salivary glands both *in vitro* and *in vivo*, a profile that seems to translate into a more pronounced and longer-lasting effect on the bladder than on salivation ***(Nilvebrant et al., 1997; Nilvebrant et al., 1997; Stahl et al., 1995).*** In clinical

studies, significantly fewer patients on tolterodine 2 mg twice daily experienced dry mouth at therapeutically equivalent dosages when compared with oxybutynin 5 mg three times daily ***(Drutz et al., 1999; Appell, 1997; Abrams et al., 1998).*** Tolterodine therefore overcomes many of the limitations of present pharmacological options for the treatment of OAB. Indeed, follow-up studies confirmed that the therapeutic effect of tolterodine is maintained during long-term treatment, with high rates of patient compliance ***(Atan et al., 1999; Wein et al., 1999).***

OAB is manifested by a complex of interrelated symptoms, all of which significantly impact on patients' lives. Therefore, any therapy for this condition needs to address this complex of symptoms and not merely decrease one symptom with increases in other associated symptoms. Ultimately, however, the way in which patients perceive treatment is central to determining the impact of therapy ***(Chancellor et al., 2000).***