| *These results are supplied for informational purposes only.*<br>*Prescribing decisions should be made based on the approved package insert in the country of prescription* | |
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| **Sponsor/company:** sanofi-aventis | **ClinialTrials.gov Identifier:** NCT00336921 |
| | **Study Code:** L_9645 |
| **Generic drug name:** Alfuzosin | **Date:** 30 June 2008 |

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| **Title of the study:** | A double-blind, randomized, parallel group study with alfuzosin 10mg OD versus placebo in the return to successful voiding in patients with a first episode of acute urinary retention due to benign prostatic hyperplasia (L_9645) |
| **Investigator(s):** | Prof. Na Yanqun: the first hospital of Beijing university<br>Prof. Ding Qiang: the hospital of Shanghai Fudan university<br>Prof. Huang Yiran: the hospital of Shanghai Renji university<br>Prof. Cai Songliang: the first hospital of Zhejiang university<br>Prof. Zhang Wei: the first hospital of Nanjing university |
| **Study center(s):** | 1. the first hospital of Beijing university Beijing<br>2. the hospital of Shanghai Fudan university Shanghai<br>3. the hospital of Shanghai Renji university Shanghai<br>4. the first hospital of Zhejiang university Hangzhou<br>5. the first hospital of Nanjing university Nanjing |

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| **Publications (reference):** | 1. Berry SJ, Coffey DS, walsh PC, Ewing LL. The development of human benign prostatic hyperplasia with age. J Urol 1984;132:474-479<br>2. Mebust WK, Holtgrewe HL, Cockett ATK, Peters PC,et al. Transurethral prostatectomy: immediate and postoperative complications. A cooperative study of 13 participating institutions evaluating 3885 patients. J Urol 1989;141:243-247<br>3. Jacobsen SJ, Jacobson DJ, Girman CJ, Roberts T0, Rhodes T, Guess HA, et al. Natural history of prostatism : risk factors for acute urinary retention. J Urol 1997;158:481-487<br>4. Pickard R, Emberton M, Neak DE. The managenment of men with acute urinary retention. BrJ Urol 1998:81:712-720<br>5. Ban Kerrebroeck P, Jardin S, Laval KU, Van cangh P, et al. Efficacy and safety of a new prolonged release formulation of alfuzosin 10mg once daily versus alfuzosin 2.5mg thrice daily and placebo in patients with symptomatic benign prostatic hyperplasia. Eur Urol 2000:37:306-313<br>6. Roehrborn CG for the alfus study group. Efficacy and safety of once-daily alfuzosin in the treatment of lower urinary tract symptoms and clinical benign prostatic hyperplasia: a randomized, placebo-controlled trial. Urol 2001:58:953-959<br>7. Hartung R. Do alpha-blocker prevent the occurrence of acute urinary retention? Eur Urol 2001;39:13-18<br>8. McNeil SA, Daruwala PD, Mitchell IDC, Shearer MG,Hargreave TB. Sustained-release alfuzosin and trial without catheter after acute urinary retention: a prospective, placebo-controlled trial. BJU international 1999;84:622-627<br>9. Klarskov P,Andersen JT, Aamussen CF, Brenoe J, Kromann Jensen IL, et al. Symptoms and signs predictive of the voiding pattern after acute urinary retention in men. Scand J Urol Nephrol 1987:21:23-28<br>10. PerrigotM Delauche-Cavallier MC, Amarenco G, Geffriaud C, et al. Effect of intravenous alfuzosin on urethral pressure in patients with neurogenic bladder dysfunction. Neurourol Urodyn 1996;15:119-131<br>11. Cramer P, Neveux E, Regnier F, Depassio J, Berard E. Blader-neck opening test in spinal cord inury patients using a new i.v. alpha-blocking agent, alfuzosin. Paraplegia 1989;27:119-124<br>12. Grasso M, Comi G, Pompa P,Lania C. Castelli M, et al. Effects of intravenous alfuzosin on urethral pressure and residual urine in patients with multiple sclerosis and lower udna urinary tract dysrunction. Abstract 915 of the VIIth congress of the European Association of Urology, Paris, France,1-4 September 1996. Eur Urol 1996;30:245<br>13. MartoranaG, Gibertic, Di Silverio F, Von HelandM, Rigatti P, et al. Effects of short-term treatment with the alph-blocker alfuzosin on urodynamic pressure/flow parameters in patients with benign prostatic hyperplasia. Eur Urol 1997;32:47-53<br>14. McNeill SS, Hargreave TB, Geffriaud C, Santoni JP, Roehrborn CG. Postvoid residual urine in patients with lower urinary tract symptoms suggestive of benign prostatic hyperplasia: pooled analysis of eleven controlled studies with alfuzosin Urol 2001;57:459-465<br>15. Kolmanc, Girman CJ, Jacobsen SJ, Lieber MM. Distribution of post-void residual urine volume in randomized selected men. J Urol 1999;161:122-127<br>16. Taube M, Gajraj H.Thrial without catheter following acute retention of urine. Br J Uro 1989;63:180-182<br>17. Choong S, Emberton M. Acute urinay retention. BJU International 2000:85:186-201 |

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| **Study period:**<br>Date first **patient/subject** enrolled: 08-02-2006<br>Date last **patient/subject** completed: 12-04-2007 | **Phase of development:**<br>Phase II |

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| **Objectives:** | The primary objective of the study is to assess the efficacy of alfuzosin 10mg OD in the return to successful voiding after removal of the catheter following a first episode of acute urinary retention in patients suffering from benign prostatic hyperplasia. Successful voiding is defined as a return to spontaneous voiding as determined by patient's assessment at 24h following catheter removal without re-catheterization.<br>The secondary objective of the study is to evaluate the safety of alfuzosin 10mg OD | | |
| **Methodology:** | multicenters, randomized, double-blind, placebo controlled, parallel group study | | |
| **Number of patients/subjects:** | Planned: 240 | Randomized: 163 | Treated: 81 |

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| **Evaluated:** | Efficacy :<br>Percentage of patients with successful voiding after catheter removal on D3/D4 | Safety:<br>General clinical safety: spontaneous reported adverse events;<br>Cardiovascular safety: changes in vital signs parameters: BP and HR measured in a supine position after 10 minutes rest and after 2 minutes in a standing position;<br>Postural hypotension is defined as a fall in SBP≥20mmHg when standing up compared with that recorded in a supine position;<br>Laboratory safety: standard laboratory tests, but only at baseline. | Pharmacokinetics:<br>NA |
| **Diagnosis and criteria for inclusion:** | Males aged 50-75 years;<br>Presenting with a first episode of painful acute urinary retention related to benign prostatic hyperplasia and with a residual volume between 500ml and 1500ml obtained at the time of catheterization and during the first one hour after catheterization. | | |
| **Investigational product:**<br>Dose:<br>Administration: | Alfuzosin 10mg OD tablet<br>10mg<br>Alfuzosin group: oral route, 1 tablet (10mg) daily at the end of the evening meal | | |
| **Duration of treatment:**<br>3 days (2 days during catheterization, 1 day after catheter removal) | | **Duration of observation:**<br>3 to 4 days | |
| **Reference therapy:**<br>Dose:<br>Administration: | Placebo, matching tablet<br>no<br>Placebo group: oral route, 1 tablet daily at the end of the evening meal | | |
| **Criteria for evaluation:** | | | |
| Efficacy: | Efficacy :<br>Percentage of patients with successful avoiding after catheter removal on D3/D4 | | |
| Safety: | General clinical safety: AEs reported by the patients;<br>Cardiovascular safety: changes in vital signs parameters; blood pressure and heart rate measured in a supine position after 10 minutes rest and after 2 minutes in a standing position. Postural hypotension is defined as a fall in systolic blood pressure ≥20mmHg when standing up compared with that recorded in a supine position.<br>Laboratory safety: standard hematology and blood chemistry, but only at baseline. | | |
| Pharmacokinetics: | NA | | |
| Pharmacokinetic sampling times and bioanalytical methods: | NA | | |

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| **Statistical methods:** | Efficacy: The primary analysis of efficacy is performed on the ITT population. The main analysis of the primary endpoint (successful voiding after catheter removal: yes/no) is the comparison of treatment groups by applying a Chi-square test. The influence on the primary endpoint of 5 potential prognostic factors (age, retention urine volume at D0, active urinary tract infection at D0, constipation and fluid consumption) is tested using logistic regression methods.<br><br>Safety: The analysis of safety data are performed on the exposed population. The number of patients experiencing a treatment emergent adverse event and more particularly a vasodilatory treatment emergent adverse event are summarized by treatment group. Cardiovascular safety focus on the detection of potentially clinically significant abnormalities (PCSA) and of vital signs. In addition, descriptive statistics is provided by treatment group for each parameter. |
| **Summary:** | the sample's expiry date was August 2007, and the weather was summer, less patient was recruited, so we close the study, the total randomized patients number is 163, the treated patient number is 81. |
| Efficacy results: | No significant difference was found between the two groups at enrollment in the efficacy-related indexes.<br><br>In the ITT population the percentage of successful voiding after catheter removal is 71.25% with alfuzosin 10mg OD and 64.63% with placebo [95% CI of the difference between the two groups is _-7.7176 and CI_U_20.9493. In addition, The same result is demonstrated in Per-protocol analysis (PPS) group and the rate of successful voiding after catheter removal is 70.13% with alfuzosin and 62.82%with placebo [95% CI of the difference between the two groups _-7.5074 and CI_U_22.1261].<br><br>The residual urine volume of patients who succeeded in removing urethral catheter was measured. Among FAS (Full Analysis Set) group, mean (SD) of Residual urine volume in the patients successful voiding after catheter removal is 44.07(39.12) ml in the treatment group and 35.02(29.47)ml in the control group, and the value of rank sum test is 1.31(P= 0.2520). In the PPS group, the result is 41.66(37.28) ml in the treatment group and 32.69(26.77)ml in the control group, and the value of rank sum test is 1.35 (P= 0.2451). There is no significant difference between the treatment group and the control group. |
| Safety results: | There are overall 162 subject exposed to study drugs, including 80 cases in the treatment group and 82 cases in the control group.<br>There are respectively 10 AE cases with alfuzosin (12.5%) and 4 AE cases (4.9%) with placebo. There were 3 cases with dizziness, I cases with flush in placebo group and 6 cases with dizziness, 2 cases with drowsiness, 2 cases with discomfort in upper abdomen in Afuzosin group. No serious adverse event occurred in the study and no adverse event resulted in drop-out. No obvious difference was noticed in SBP, DBP and heart rate of the two groups before and after treatment. |
| **Date of report:** | 20 September 2007 |