Volume 155 May 1996 Number 5

# The Journal of UROLOGY®



## AUA Ninety-First Annual Meeting
## May 4-9, 1996

Important: The number preceding the title of a presentation is the abstract number.

ISSN 0022-5347
AUA Program

(issued by Library of Congress)
Price $25 per copy

## 736

CLINICAL OUTCOME OF T1 BLADDER CANCER. Miguel Antelo, Colin P. Dinney and H. Barton Grossman, Houston, TX (Presentation by Dr. Antelo)

INTRODUCTION AND OBJECTIVES: Patients with T1 bladder cancer harbor neoplasms with documented invasive potential. We evaluated the therapeutic interventions and clinical outcome in 89 patients with T1 disease.

METHODS: Eligible patients had T1 bladder cancer diagnosed at the University of Texas MD Anderson Cancer Center from August, 1975 through April, 1994 who had follow-up data. 89 patients met these criteria and had a mean and median follow-up of 4.1 and 3.4 years respectively (range 0.9 to 19.9 years). Treatment included transurethral resection, intravesical chemotherapy, BCG, and/or cystectomy.

RESULTS: The mean survival for all 89 patients was 12.6 years. The 5 and 10 year survival rates were 69% and 54% respectively. The rates of recurrence and progression were 40% and 26% respectively. The recurrence and progression rates for 36 patients receiving BCG were 42% and 22% respectively. 35 patients were treated with cystectomy (21 early and 14 delayed). Progression (P) and death from bladder cancer (D) occurred in patients treated with both early (5P, 3D) and delayed cystectomy (7P, 3D).

| | # Pts. | Median Survival | Confidence Interval | Bladder Ca Deaths |
|---|---|---|---|---|
| No Cystectomy | 54 | 8.7 years | 7.1 - 10.3 | 17% |
| Cystectomy | 35 | 9.8 years | 8.9 - 10.7 | 17% |

CONCLUSIONS: Most patients with T1 bladder cancer have a long survival. Cystectomy does not afford protection from progression and death from bladder cancer and does not improve survival. Patients presenting with T1 bladder cancer need careful monitoring with aggressive therapy (cystectomy) reserved for recurrent invasive bladder cancer or disease refractory to local therapy.

Supported in part by grant U01-CA56973 from NCI, NIH.

## 737

**UK-92,480, A NEW ORAL THERAPY FOR ERECTILE DYSFUNCTION, A DOUBLE-BLIND, PLACEBO CONTROLLED TRIAL WITH TREATMENT TAKEN AS REQUIRED**

Ian Eardley (Leeds, UK), Robert J Morgan (London, UK), Wallace W Dinsmore (Belfast, UK), Josephine Pearson, Maria B Wulff, Mitradev Boolell (Sandwich, UK). (Presentation by Mr I Eardley).

INTRODUCTION AND OBJECTIVES

Nitric oxide, via cGMP, is critical for the relaxation of the corpus cavernosum, a key factor in penile erection. UK-92,480 is an orally active potent inhibitor of type V cGMP-specific PDE, the predominant isoenzyme in the human corpus cavernosum and as such has the potential to enhance penile erectile activity. The efficacy and safety of UK-92,480 in improving erectile activity was evaluated in patients with MED without an established organic cause.

METHODS

42 patients with a mean age of 53 years (range 34 - 70) a mean duration of MED of 3 years (range 0.5 - 10) took placebo or UK-92,480 (25, 50 or 75mg) as required for 28 days in a double blind, randomised, two-way, crossover study.

RESULTS

Of the patients with complete efficacy data, 34/37 (92%) reported an improvement in the quality of erections on UK-92,480 compared to 10/37 (27%) on placebo ($p < 0.0001$). This was confirmed by the patients partner: 33/36 (91%) felt that there was an improvement in their partners erection on UK-92,480 compared to 7/36 (19%) on placebo ($p < 0.0001$). The mean number of erections which were sufficiently rigid for penetrative sexual intercourse over 28 days was 18.4 (14 - 24.3, 95% confidence interval) on UK-92,480 compared to 5.6 (4.1 - 7.4) on placebo ($p < 0.0001$). The frequency of use of UK-92,480 was 12.5 doses over 28 days compared to 8.6 for placebo. In general UK-92,480 was well tolerated, the most commonly reported adverse events were headache, dyspepsia and muscle aches

## 738

UK-92,480, A NEW ORAL TREATMENT FOR ERECTILE DYSFUNCTION: A DOUBLE-BLIND, PLACEBO-CONTROLLED, ONCE DAILY DOSE RESPONSE STUDY. Clive J C Gingell, Bristol, UK; Alain Jardin, Paris, France; Arne M Olsson, Lund, Sweden; Wallace W Dinsmore, Belfast, UK; Ian H Osterloh, John Kirkpatrick, Michelle Cuddigan, Sandwich, UK; and the Multicentre Study Group. (Presentation by Dr Gingell).

INTRODUCTION: It is now recognised that penile erection is mediated by the action of nitric oxide/cGMP (cyclic guanosine monophosphate). UK-92,480 is a selective inhibitor of Type 5 phosphodiesterase, the predominant isoenzyme causing breakdown of cGMP in the human corpus cavernosum.

METHODS: This trial (protocol 148-353) recruited 351 male patients (mean age 53, range 24-70 years) with erectile dysfunction (ED) of no known organic cause. After a 2-week run-in on no treatment, patients were randomly allocated to receive oral capsules of 10mg, 25mg or 50mg of UK-92,480 or double-blind placebo administered once daily for 28 consecutive days. Efficacy instruments included patient assessment of whether treatment improved erections, a 15-item self-administered sexual function questionnaire (SFQ), and diary records of erections.

RESULTS: The proportions of patients reporting that treatment had improved their erections were 38% (placebo), 65% (10mg), 79% (25mg) and 89% (50mg) ($p$ for treatment effect $<0.001$). SFQ analyses showed similar dose-response relationships for frequency, hardness and duration of erections ($p < 0.001$) and other parameters of sexual function including number of satisfactory intercourses and quality of sex life.

UK-92,480 treatment was generally well-tolerated. Headache, flushing, dyspepsia and muscle aches were reported more times than other adverse events. The overall proportion of patients discontinuing treatment because of adverse events was less than 5% and the proportions were similar for all treatment groups.

CONCLUSIONS: The results indicate that UK-92,480 is an effective, well-tolerated, oral treatment of ED in patients with no known organic cause.

## 739

**UK-92,480, A NEW ORAL TREATMENT FOR ERECTILE DYSFUNCTION. A DOUBLE-BLIND, PLACEBO CONTROLLED CROSSOVER STUDY DEMONSTRATING DOSE RESPONSE WITH RIGISCAN AND EFFICACY WITH OUTPATIENT DIARY.** **Mitradev Boolell (Sandwich UK), Sam Gepi-Attee & Clive Gingell (Bristol UK) and Michael Allen (Sandwich UK) (Presented by Clive Gingell).**

**INTRODUCTION AND OBJECTIVES**: Male erectile dysfunction (MED) is a common condition for which there is no satisfactory oral therapy. Recent studies suggest that erection is dependent on nitric oxide and its second messenger, cyclic guanosine monophosphate (cGMP). UK-92,480 is a potent selective inhibitor of type 5 (cGMP-specific) phosphodiesterase, the predominant isoenzyme in the human corpus cavernosum. UK-92,480 was evaluated in patients with MED without an established organic cause.

**METHODS:** 12 patients entered a double blind randomised placebo controlled crossover study. In the first phase (4-way crossover) efficacy was evaluated by the duration of penile rigidity (RigiScan) during 2 hours of visual sexual stimulation following single doses of UK-92,480 (10mg, 25mg, 50mg and placebo). In the second phase (2-way crossover) efficacy was assessed by a diary record of erectile activity following daily doses of UK-92,480 (25mg) and placebo for 7 days.

**RESULTS:** Mean duration of rigidity >80% (in minutes) at the base of the penis was 1.3 (95% confidence interval, 0.4-3.1) on placebo, 3.5 (1.6-7.3) on 10mg ($p=0.095$), 8.0 (3.7-16.7) on 25mg ($p=0.003$), and 11.2 (5.6-22.3) on 50mg ($p=0.0004$). Corresponding values at the tip of the penis were 1.2 (0.4-2.7) on placebo, 4.6 (2.4-8.5) on 10mg ($p=0.014$), 6.9 (3.5-13.1) on 25mg ($p=0.002$), and 7.4 (3.9-13.4) on 50mg ($p=0.001$). From the diary, the mean number of erections of sufficient rigidity for penetrative sexual intercourse was 6.1 (3.2-11.4) on UK-92,480 and 1.3