**498**

Kubota Y[1], Sasaki S[1], Kojima Y[1], Kohri K[1], Biers S[2], Brading A[2]
1. Department of Nephro-urology, Nagoya City University Graduate School of Medical Sciences, 2. Department of Pharmacology, Oxford University

# THE EFFECTS OF IMATINIB MESYLATE (GLIVEC() AS A C-KIT TYROSINE KINASE INHIBITOR IN THE GUINEA-PIG URINARY BLADDER –POSSIBLE NEW DRUG THERAPY FOR OVERACTIVE BLADDER-

**Hypothesis / aims of study**
In the gastrointestinal tract (GIT), slow wave activity in smooth muscle is generated by the interstitial cells of Cajal (ICC). Detrusor smooth muscle strips of most species show spontaneous contractions which are triggered by action potential bursts, however, the pacemaker mechanisms for the detrusor are still unknown. Recently, ICC-like cells have been found in guinea-pig bladder, using antibodies to the c-kit receptor. We have investigated the effects of Glivec (STI571), a c-kit tyrosine kinase inhibitor, on spontaneous action potentials in guinea-pig detrusor and intravesical pressure of isolated guinea-pig bladders.

**Study design, materials and methods**
Changes in the membrane potential were measured in detrusor smooth muscles of the guinea-pig, using conventional microelectrode techniques. Pressure changes in the bladder were recorded using whole organ bath techniques.

**Results**
Detrusor smooth muscle cells exhibited spontaneous action potentials, and spontaneous pressure rises occurred in isolated bladders. Glivec (10 microM) converted action potential bursts into continuous firing with no effects on individual action potentials. Glivec (50microM) abolished spontaneous action potentials and reduced the amplitude of spontaneous pressure rises in the whole bladder in a dose dependent manner.

**Interpretation of results**
The results suggest that ICC-like cells may be responsible for generating bursts of action potentials and contractions in detrusor smooth muscle.

**Concluding message**
Drugs inhibiting the c-kit receptor may prove useful for treating the overactive bladder.