Hypothesis / aims of study
According to the recent terminology adopted by ICS, overactive bladder syndrome (OAB) is urgency, with or without urge urinary incontinence, usually with frequency and nocturia, in the absence of infection or other obvious bladder pathology. Urgency, the complaint of a sudden, compelling desire to pass urine that is difficult to defer is now considered as the driving symptom that may lead to frequency, nocturia and urge urinary incontinence. Although extremely difficult to define by someone that never experienced it, it is clearly an abnormal sensation associated with the bladder behaviour during the filling phase.

In spite of the fact that urgency is an abnormal sensation, specific treatments directed to modulate the sensory arm of the bladder innervation are surprisingly nonexistent. In fact, antimuscarinic drugs are expected to act predominantly on the efferent arm in spite of the recent demonstration of muscarinic receptors on bladder sensory fibers.

Resiniferatoxin (RTX) is a neurotoxin that specifically reduces sensory input conveyed in type C afferent fibers expressing the vanilloid (capsaicin) receptor. Recent open label studies have suggested that intravesical administration of this neurotoxin decreased urgency and urge urinary incontinence (1,2). Unfortunately none of these studies used specific tools to measure urgency or were placebo controlled. Thus, to fill this gap, we decide to compare the effect of intravesical RTX with a placebo solution in urgency using an adapted urgency severity scale (4).

Study design, materials and methods
Eight patients (4 with neurogenic diseases and 4 without neurogenic pathology) with moderate to severe urgency and urge urinary incontinence gave written informed consent to this study. None were taking anticholinergic medication. All patients were screened by haematological and biochemical blood tests, microbiological urinary investigation and ultrasonographic evaluation of the urinary system. Patients were asked to fill a seven day bladder diary where they registered the intensity of urgency at each micturition episode. In short the scale had 0 to 4 levels in which 0 indicated the absence of urgency, 1 mild urgency, 2 moderate urgency, 3 severe urgency and 4 urgency incontinence. Then patients were instilled with 100 ml of the placebo solution (RTX vehicle, 10% ethanol in saline) and 30 days later a second seven day bladder diary was collected. At this point patients were instilled with 100 ml of a 50 nM RTX solution in 10% alcohol in saline, left inside the bladder during 30 minutes. Thirty days later a third seven day bladder diary was collected.

Results
At baseline the mean total urgency score per week (sum of the all the scores registered in the seven day bladder diary), the mean urgency score per micturition and the mean number of severe urgency and urge urinary incontinence episodes (grades 3 and 4) per week were 224±92, 2.9±0.6 and 61.7±32.5, respectively.

After placebo instillation, the mean total urgency score per week was 228±100, mean urgency score per micturition was 2.8±0.6 and mean number of severe urgency and urge urinary incontinence episodes per week was 64.3±38. These numbers were not significantly different from baseline.
Treatment with RTX did not cause pain or any significant discomfort. Mean total urgency score per week decreased to 151±93 (p<0.05), mean urgency score per micturition decreased to 2.1±0.8 (p<0.001) and mean number of severe urgency and urge urinary incontinence episodes per week decreased to 35.7±37.6 (p<0.05).

**Interpretation of results**

Although preliminary and involving a small number of patients, this study strongly suggests that intravesical RTX decreases the sensation of urgency to urinate and diminishes the number of urge urinary incontinence episodes in patients with overactive bladder syndrome.

**Concluding message**

In the future it might be worth exploring the use of intravesical RTX instillation as an alternative treatment option to offer to patients with refractory overactive bladder syndrome.

(1) The effect of intravesical resiniferatoxin in patients with idiopathic detrusor instability suggests that involuntary detrusor contractions are triggered by C-fiber input. J Urol 2002; 168: 575-579

(2) Intravesical resiniferatoxin improves lower urinary tract symptoms and urodynamic parameters in patients with urgency and frequency due to increased bladder sensation. Eur Urol 2005; 3 (suppl 4): 142, abstract