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NOVEL USAGE OF THE UROMUNE© SUBLINGUAL VACCINE TO TREAT RECURRENT URINARY TRACT INFECTIONS IN WOMEN: INITIAL EXPERIENCE IN THE UNITED KINGDOM

Hypothesis / aims of study

Recurrent Urinary Tract Infections (UTIs) in women is a prevalent disease and despite treating the initial infection, recurrence occurs in up to 60% of patients during the first year. Often these women rely on continuous prophylactic antibiotics. However, multi-resistant bacteria are emerging in many regions of the world and therefore it is prudent to investigate prophylaxis that reinforces the natural mechanism of pathogen defence.

We present the first experience in the United Kingdom (UK) of the novel multivalent bacterial vaccine Uromune© in a preliminary cohort of women. Uromune© is currently in the pre-license Phase III development stage and is available under the Named Patient Program.

Study design, materials and methods

Between September 2014 and March 2016, 15 women with a mean age at the beginning of treatment of 62 years (range: 33 - 85) who suffered with recurrent UTIs (as defined by one proven infection every 3 months for the last 2 years) despite lifestyle corrections, antibiotic prophylaxis and several other treatment regimens were identified. Each patient received 3 months of Uromune© vaccines. The vaccine consisted of two vials containing a suspension of 10^9 inactivated whole bacteria per milli-litre. The vaccine was a mixture of equal amounts of selected strains of *Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris* and *Enterococcus Faecalis*. The delivery route was through the sublingual mucosa and the dose was 2 puffs of 100µl each per day (10^8 bacteria per puff).

Follow-up was via a phone consultation by a senior specialist nurse as well as providing the patients with an on-going direct contact number.

Results

13 out of the 15 women completed the course of treatment. Of the 2 who failed to complete treatment, 1 woman who experienced recurrent severe urosepsis prior to treatment with Uromune© discontinued the vaccine after developing another episode of severe urosepsis 9 days into treatment. 1 woman discontinued Uromune© due to lifestyle and personal reasons. 1 woman initially discontinued Uromune© due to a concurrent worsening of her asthma, however restarted and completed the course successfully at a later date.

Of the 13 women who completed the course, 10 reported no urinary tract infections during both the treatment period and subsequent follow-up since. 1 woman experienced cystitis symptoms 1 month into treatment but was given antibiotics by her General Practitioner before sending urine for culture to prove infection. The patient subsequently reported no further UTIs. 1 woman was free of UTIs for 16 months before developing one episode of UTI.

1 woman developed on-going recurrent UTIs despite the vaccine.

In terms of side effects, 1 woman reported post-nasal drip associated with Uromune© which settled spontaneously. 1 woman initially experienced a concurrent worsening of her asthma whilst receiving Uromune©, however the patient restarted and completed the course will no side effects reported. There were no other reported adverse effects.

Interpretation of results

Overall, 87% of patients completed the course of treatment. Of these, 92% experienced dramatic improvements to their symptoms, in particular requiring no further long-term antibiotic prophylaxis.

From the 92% of patients mentioned above, 1 woman had cystitis symptoms that could not be proven to be from a UTI as she was commenced on antibiotics prior to collecting microbiology cultures. To note however, this patient reported no other UTIs or symptoms since starting Uromune© treatment.

Another patient developed no further UTIs for 16 months post Uromune© treatment before having a recurrence. This patient is due to start her second course of Uromune© to assess effectiveness.

The remaining 77% of patients who completed the Uromune© treatment reported no subsequent UTIs during both the treatment period and subsequent follow-ups.

Of the patients who failed to complete treatment, one patient prior to receiving Uromune© used to frequently develop severe urosepsis requiring inotropic support. Her most recent episode occurred a few weeks prior to commencing treatment. This patient developed another episode of urosepsis 9 days into her treatment where inotropic support was again required. Ascertaining a cause and effect from the vaccine to this urosepsis episode is difficult due to the high probability of the underlying cause being the natural disease progression in this patient. The vaccine however was stopped as a precaution.

Another patient experienced an exacerbation of her asthma a few weeks into treatment. Though difficult to associate the cause of the exacerbation directly to the vaccine, the Uromune© treatment was stopped as a precaution. Despite the short incomplete course of treatment, the patient reported substantial therapeutic benefits afterwards. The patient subsequently restarted and successfully completed a new course of Uromune©, expericing no asthmatic exacerbations and remained infection free for over one year.

One patient experienced post-nasal drip during the first month from commencing Uromune©. This spontaneously resolved. The symptoms did not affect the patient's day-to-day activities and the patient was able to complete the treatment course.

Concluding message

The results from this small initial cohort in the UK suggest that Uromune© is both effective and generally safe in UK women with recurrent UTIs who have failed antibiotic prophylaxis. Further studies are required to evaluate the efficacy of this vaccine in a larger group of patients including comparing effectiveness against antibiotic prophylaxis.

Following on from our experience above, a national multi-centre study on the outcomes of Uromune© treatment in the UK is currently being established. In addition, a large international multi-centre Randomised Control Trial is also currently being established with our centre as the UK arm. The results from both of these studies are awaited.

Disclosures

Funding: None **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** This study is registered as an audit Reading Urology Partnership **Helsinki:** Yes **Informed Consent:** Yes