

# Data from an ongoing clinical trial: Five cases of acute cystitis caused by ESBL-producing *Escherichia coli* were successfully treated with pivmecillinam 400 mg *t.i.d* for 3-5 days

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**Background:** Acute cystitis (AC) is common and one of the most frequent infections in women. We are currently conducting a randomized, double-blinded, placebo-controlled clinical phase IV study (EudraCTno.: 2014-001321-32), to compare the efficacy of pivmecillinam 400 mg *t.i.d* in a 3-day respectively 5-day regimen, against community acquired AC. We have earlier demonstrated effective outcomes of pivmecillinam 400 mg *t.i.d* against ESBL producing *Escherichia coli*, and here we wish to confirm those findings with more detailed prospective data on seven cases with community-acquired AC caused by ESBL producing *E. coli*.

**Material/methods:** We have to date included >275 patients (March 2017). Seven of the cases were caused by ESBL-producing *E. coli*, similar to the prevalence in the primary sector of Denmark. Patients with clinical features of AC without exclusion criteria were included according to GCP. Dysuria, pollakiuria and urgency were scored from 0-3 on day 0, and a symptom load  $\geq 2$  was considered significant for AC. The patients received a double-blinded antibiotic therapy (*i.e.* 3 or 5 day regimen of pivmecillinam), questionnaires for day 0-7 and day 28. The patients answered questions on their symptom load and supplied a urine sample on day 9 and day 28. Patients were followed for 6 months for bacteraemia or any relapsing bacteriuria.

## Results:

### Baseline data:

- Six patients followed up on all the questionnaires and urine samples. One patient dropped out just after inclusion.
- Four patients had experienced recurrent UTIs the last year prior to enrolment.
- Five patients informed that they had travelled out-side of Scandinavia within the last 6 months.
- All patients scored  $\geq 5$  in symptom load of AC on day 0.

### Bacteriological efficacy:

- Four of six patients with follow-up data were bacteriologically cured at the first control urine sample and without recurrence. One patient had early relapse AC and one patient still had asymptomatic bacteriuria, which vanished without antibiotic therapy.
- One patients had new bacteriuria in the second control urine (*E. faecalis*).
- None had bacteraemia or relapse of bacteriuria with ESBL-producing *E. coli* in the long-term follow-up.

### Clinical efficacy:

- All patients with follow-up data experienced high clinical efficacy during day 2 - day 7.

### Relapse:

- One patient had early clinical and bacteriological relapse on day-7, with the same isolate that caused the infection.
- She was successfully treated with a 5-day regimen of pivmecillinam 400 mg *t.i.d*, with no clinical or bacteriological relapse.

Case	Age	Bacteriological data (CFU/ml)			Clinical data (AC symptom load)				
		First urine sample	Control urine 1	Control urine 2	Day-0	Day-2	Day-4	Day-7	Day-28
1	29	10 <sup>4</sup>	10 <sup>4</sup>	0	5	0	0	0	0
2	37	10 <sup>3</sup>	0	210 <sup>4</sup>	8	3	5	2	0
3	21	10 <sup>4</sup>	0	0	6	0	0	0	0
4	62	10 <sup>5</sup>	0	0	5	0	0	0	0
5	52	10 <sup>5</sup>	No data		8	No data			
6	79	10 <sup>4</sup>	0	0	9	1	0	0	Clinical Relapse
7	25	10 <sup>4</sup>	10 <sup>5</sup>	0	7	3	0	<sup>3</sup> Clinical Relapse	0

<sup>1</sup>Asymptomatic and no new therapy was given; <sup>2</sup>*E. faecalis*; <sup>3</sup>New therapy: Pivmecillinam 400 mg *t.i.d* during five days

**Conclusions:** Pivmecillinam 400 mg *t.i.d* for 3-5 days was effective in patients with AC caused by ESBL-producing *E. coli*. One patient experienced relapse on day 7, but was cured with a new pivmecillinam regime. We therefore confirm that pivmecillinam, given as 400 mg *t.i.d* is effective and a relevant option against ESBL-producing *E. coli*.

\*Detailed results will be published after de-blinding of the trial.

**Key words:** UTI, pivmecillinam, ESBL