

# Clinical Success Demonstrated in Treatment of Complicated Genitourinary Gram Negative Infections in a Physician Office Infusion Center (POIC)

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## Abstract

**Background:** Genitourinary (GU) infections commonly involve gram negative (GN) pathogens, and often MDR requiring treatment with intravenous antibiotics (IVAB). These patients typically require multiple hospital admissions and several inpatient treatment days. The purpose of this study was to examine the safety and outcomes of IVAB therapy provided in an ID POIC for complicated GU GN infections due to resistant organisms, recurrent infections and prior treatment failures.

**Methods:** Adult patients were analyzed through a retrospective chart review to quantify pertinent characteristics and assess clinical outcomes. Evaluable patients were limited to those with culture-confirmed GN infections who received therapy with one or more intravenous IVAB. Each patient required a minimum of one culture positive GN pathogen.

**Results:** 210 patients were included in the study from 9 POIC sites nationally. 68% initiated therapy in the POIC. Mean age was 63 years with 62% females. 90% had monomicrobial infections with *E. coli* most predominant (48%), followed by species of *Pseudomonas* (27%), *Klebsiella* (9%), *Serratia* and *Enterobacter* (both <2%). One or more comorbidities were identified in 77%, most common of which were presence of urinary catheter (27%), diabetes (23%) and prior radiation/chemotherapy (16%). The common antimicrobial agents used were ertapenem (24%), ceftriaxone and cefepime (both 16%), with 7% receiving concomitant IVAB. Median treatment duration was 11 days. Treatment success was defined as those who achieved cure or improvement. This was achieved in 76% and 18%, respectively for an overall 94% successful outcome. Adverse events were reported in 29% of patients, with 49 (23%) reporting AEs likely drug related, of which 82% were mild or moderate. The most frequently reported AE was gastrointestinal (57%), with 2 confirmed *C. difficile* infections (1%). Of all patients, no IV catheter infections occurred.

**Conclusions:** Treatment of GN GU infections achieved clinical success and were well tolerated overall, the majority of whom initiated therapy without hospitalization. IV Catheter-related infections did not occur. The POIC is a safe and effective setting for the treatment of complicated GN GU infections with IVAB.

## Introduction

Genitourinary (GU) infections commonly involve gram negative (GN) pathogens, and often multi-drug resistant organisms (MDR) requiring treatment with intravenous antibiotics (IVAB). GU infections are also the most common hospital-acquired infection.<sup>1</sup> Treatment of these complicated GU infections typically require hospital admissions and several inpatient treatment days. Data suggests that therapy initiated appropriately and adjusted based on cultures and clinical response, results in improved outcomes. Treatment exclusively managed by Infectious Disease physicians in an office infusion center can provide diagnosis and appropriate therapy with IV or oral antibiotics in an outpatient setting with optimal results. The purpose of this study was to evaluate the safety and efficacy of treating complicated GU patients with gram negative organisms, often MDR, without inpatient admission whenever medically feasible.

## Methods

A retrospective database and chart review was conducted to identify all patients with culture-confirmed gram negative GU infections who received therapy with one or more intravenous antibiotics in 9 POICs nationally.

### Inclusion Criteria:

- Treatment with one or more IVAB for culture-confirmed GN infections with a GU diagnosis.

### Exclusion Criteria:

- None.

### Patient Selection:

- All patients were identified that were treated with IVAB for culture-confirmed gram negative GU infections. Diagnosis was identified as that recorded in the medical chart.
- Each patient identified that met criteria was evaluated for demographics, infectious agent, drug therapy received and outcome.
- Demographic data collected included age, gender and weight, where available. Data for all drug therapy provided was collected, including drug, dose and duration. Patients receiving multiple agents were identified.
- Culture and sensitivity data was collected for each organism reported and treated. MDR was defined as organisms resistant to one or more antimicrobial agent.

### Data Analysis:

- Descriptive statistics (mean, standard deviation) were used for demographic data.
- Descriptive analyses and percentages were used to report culture data.
- Percentages were used for safety and efficacy data.
- Treatment success was defined as those who achieved cure or improvement.

## Results

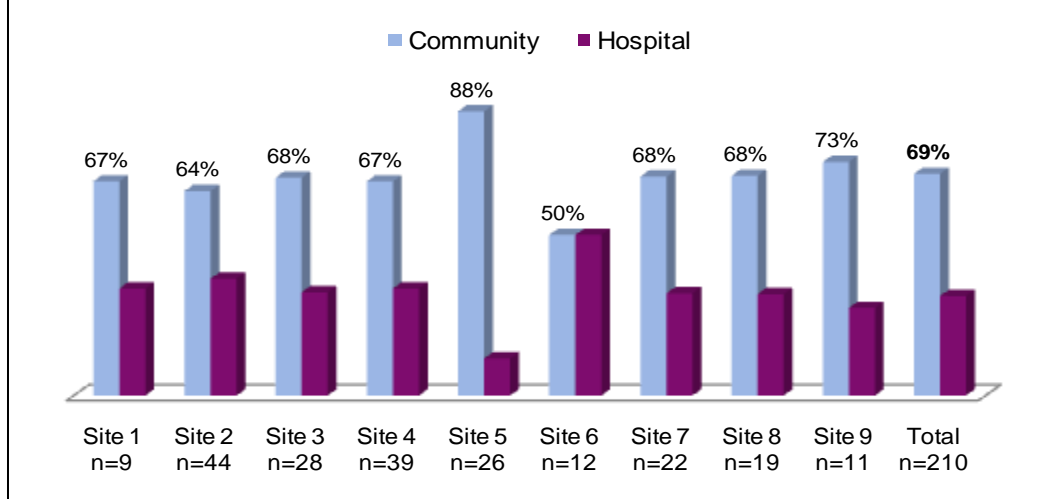
### Demographics:

**Table 1. Patient Demographics**

Characteristic (n=210)	No.	(%)
Gender		
Female	131	(62%)
Male	79	(38%)
Age, mean (yrs)	63	
Weight (kg) mean (range)	81	(36-157)
Underlying Conditions		
Renal Conditions*	55	(26%)
Diabetes	48	(23%)
COPD/Asthma/Emphysema	36	(17%)
Cancer/Chemo/Radiation	33	(16%)
Paralysis	25	(12%)
CRF/ESRD	23	(11%)
Immune deficiency disorder	16	(8%)
HIV/AIDS	2	(1%)
Others	19	(9%)

\*Renal conditions included kidney stones, nephrectomy, nephrolithiasis, neurogenic bladder, etc.

**Figure 1. Patient Location Prior to Admit**



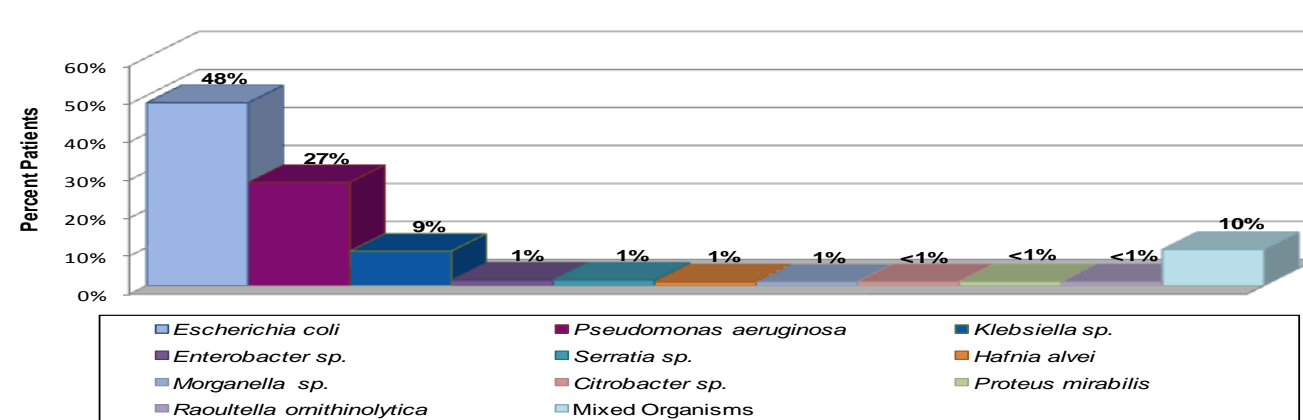
**Table 2. Infection Types**

Infection Types (n=210)	No.	(%)
UTI	138	(66%)
Pyelonephritis	25	(12%)
Prostatitis	19	(9%)
Urosepsis	15	(7%)
Cystitis	7	(3%)
Renal abscess	3	(1%)
Epididymitis & Orchitis	2	(1%)
Endometritis	1	( $<$ 1%)

- 210 patients were treated in 9 POICs nationally.
- 68% were treated without hospitalization.
- 162 (77%) had 327 underlying diseases, most complicated with multiple conditions.
- 57 patients (27%) had urinary catheters or were self-catheterizing.
- 13 patients (6%) had bladder or kidney stents.
- Of 69 reported reasons for use of IVAB, 61% were due to MDR, 19% failed oral therapy, and 14% had significant allergies.

### Microbiology:

**Figure 2. Primary Gram Negative Organism Treated**



**Table 3. Microbiology**

Gram Negative Pathogens	Total Pathogens (n=230)	C & S Data Available (n=204)	ESBL %	ESBL %	MDR %	MDR %
<i>E. coli</i>	116	104	22	21%	78	75%
<i>Pseudomonas sp.</i>	66	58	11	19%	36	62%
<i>Klebsiella sp.</i>	26	23	9	39%	20	87%
<i>Enterobacter sp.</i>	7	7	0%	0%	7	100%
<i>Proteus mirabilis</i>	3	3	0%	0%	2	67%
<i>Haemophilus influenzae</i>	2	2	0%	0%	2	100%
<i>Morganella morganii</i>	2	2	0%	0%	2	100%
<i>Serratia sp.</i>	4	2	1	50%	1	50%
<i>Acinetobacter sp.</i>	1	1	0%	0%	0%	0%
<i>Citrobacter sp.</i>	2	1	0%	0%	1	100%
<i>Raoultella Ornithinolytica</i>	1	1	0%	0%	1	100%

- E. coli* was the most predominant pathogen in each infection, with 21% ESBL-producing strains and an additional 45% with intermediate or no susceptibility to fluoroquinolones. 75% were MDR.
- Pseudomonas* was the second most commonly cultured pathogen with 19% ESBL-producing isolates and 64% additional isolates not susceptible to fluoroquinolones. 62% were MDR.
- 77% of all isolates were resistant to  $\geq$ 3 antibiotics, 14% to 2 antibiotics and 9% resistant to one antibiotic.

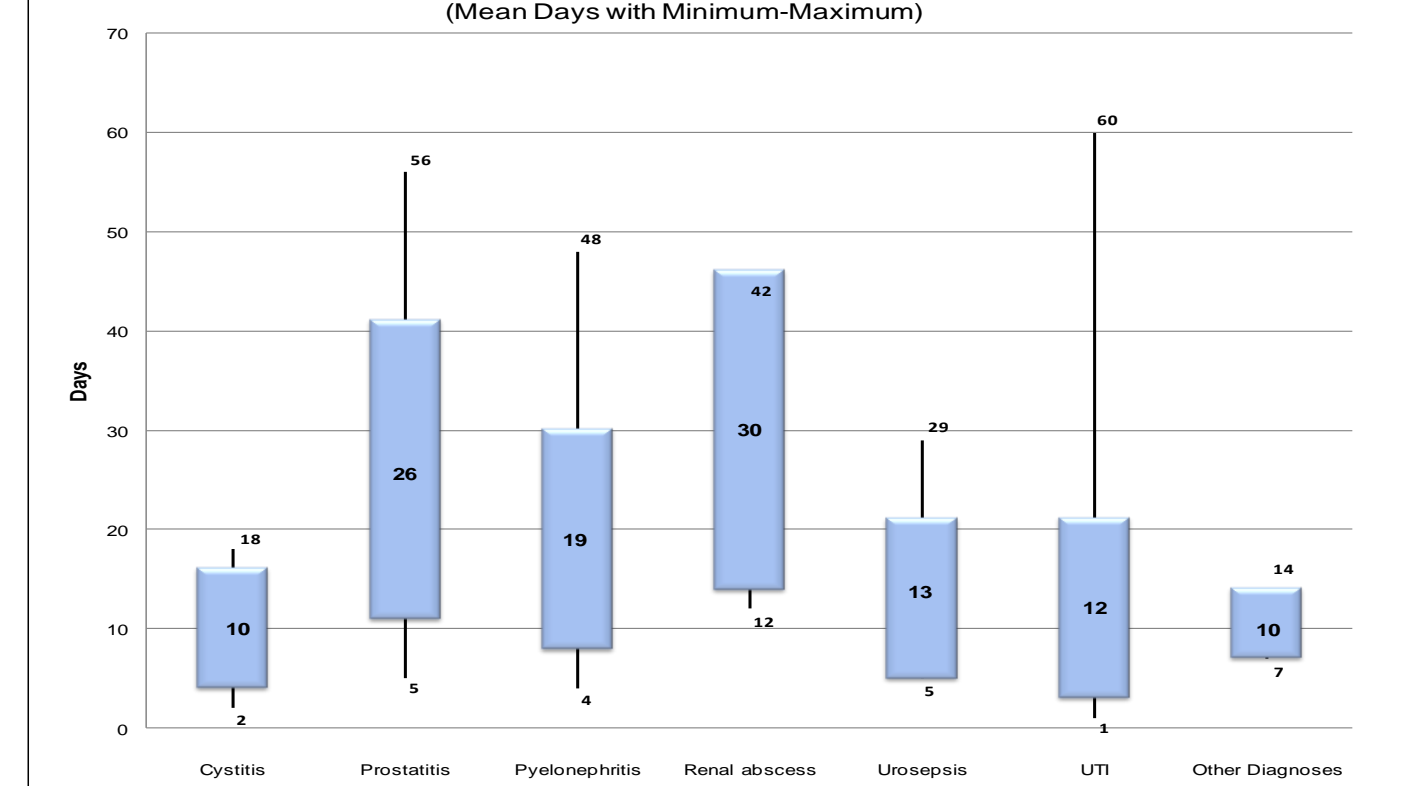
### Therapy Characteristics:

**Table 4. Primary Drug Therapy**

Drug (n=210)	No.	(%)
Ertapenem	47	(22%)
Ceftriaxone	36	(17%)
Cefepime	34	(16%)
Impipenem Cilastatin	20	(10%)
Piperacillin/Tazobactam	18	(9%)
Aztreonam	15	(7%)
Ceftazidime	14	(7%)
Tobramycin	9	(4%)
Tigecycline	6	(3%)
Amikacin	3	(1%)
Meropenem	2	(1%)
Gentamicin	2	(1%)
Others	4	(2%)

- Predominant drug used was ertapenem (22% as primary and 24% in total), followed by ceftriaxone and cefepime.
- The above 3 drugs accounted for over half of all drugs used.
- 15 patients (7%) received concurrent therapy with more than one agent.
- Median duration of therapy over all diagnoses was 11 days; mean duration of therapy was 14 days.
- 39% of patients self-administered medications with elastomeric devices. Pumps were used to administer medications in 34% (ambulatory) and 25% (stationary) of patients.

**Figure 3. Therapy Duration**



### Safety:

- Overall AEs rate was 29% (61 of 210 patients), with 9 (4%) classified as severe.
- Drug-related AE rate was 23% (49 of 210). These are described in Table 4.
- 6 of these AEs (12%) were classified as severe.

Drug (%AE by Drug)	Adverse Event	No.	Severity	Discontinued Treatment	Outcome
Amikacin (53%)	Rash	1	Moderate	Yes	Resolved
	Elevated LFTs	1	Mild	Yes	Unknown
	Nausea/vomiting	3	Mild (1), Moderate (2)	Yes (1)	Resolved (1), Residual effects (1), Ongoing (1)
	Rash	2	Moderate (2)	Yes (1), Temporarily (1)	Resolved
Ceftazidime (14%)	C. difficile infection	1	Moderate	No	Resolved
	Dyspnea	1	Mild	Yes	Resolved
	Fluorid overload	1	Mild	Yes	Resolved
	Neutropenia	1	Mild	Yes	Unknown
Ceftriaxone (17%)	Vaginal yeast	1	Mild	No	Resolved
	C. difficile infection	1	Severe	No	Resolved
	Rash	1	Severe	Yes	Unknown
	Diarrhea	2	Mild (1), Moderate (1)	Yes (1), No (1)	Resolved
Ertapenem (19%)	Abdominal pain/cramping	1	Moderate	No	Resolved
	Nausea/vomiting	1	Mild	Yes	Resolved
	Rash	1	Moderate	Yes	Resolved
	Thrush	1	Mild	No	Resolved
Gentamicin (100%)	Dehydration	1	Severe	Yes	Ongoing
	Nausea/vomiting	1	Severe	Yes	Resolved
	Nausea/diarrhea/itching/swollen lip	1	Mild	Yes	Resolved
	Vaginal yeast	1	Moderate	No	Resolved
Impipenem/Cilastatin (25%)	Diarrhea	2	Mild (1), Moderate (1)	Yes (1), No (1)	Resolved
	Fluoridence	1	Moderate	No	Resolved
	Headache	1	Moderate	No	Resolved
	Rash	1	Mild	Yes	Resolved
Meropenem (50%)	Rash	1	Mild	Yes	Resolved (1), Residual effects (1)
	Diarrhea	2	Moderate (2)	Yes (1), No (1)	Resolved (1), Residual effects (1)
	Ringling in ears	1	Mild	No	Resolved
	Nausea/vomiting	1	Mild	Yes	Resolved
Tigecycline (100%)	Nausea/vomiting	4	Moderate (3), Severe (1)	Yes (1), No (3)	Resolved
	Abdominal pain/cramping	1	Mild	No	Resolved
	Headache	1	Moderate	No	Resolved
	Yeast infection	1	Mild	No	Resolved
Tobramycin (13%)	Weakness, tiredness	1	Mild	No	Resolved
	Double vision, imbalance	1	Severe	No	Unknown

### Safety, cont.:

- Adverse Events occurred with each of the drugs provided.
  - Gentamicin and tigecycline both had 100% occurrence of AEs.
  - Meropenem (50%), amikacin (3%) and cefepime (29%) followed.
- Aminoglycosides were responsible for the highest overall AE rate and most severe, one with possible vestibular toxicity and unknown outcome.
- 2 cases of *C. difficile* occurred, 1 with cefepime (moderate), 1 with ceftazidime (severe), both of which did resolve.
- Overall most common AE was gastrointestinal (13% of all patients).
- There were NO catheter related blood stream infections (CRBSI) in 3,620 total catheter days.
  - 0% rate per 1000 catheter days.

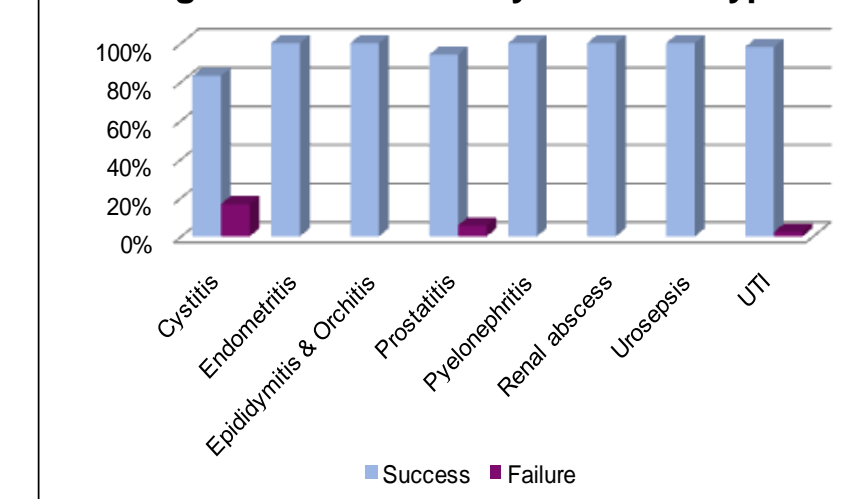
### Efficacy and Outcomes:

**Table 6. Summary of Patient Outcomes**

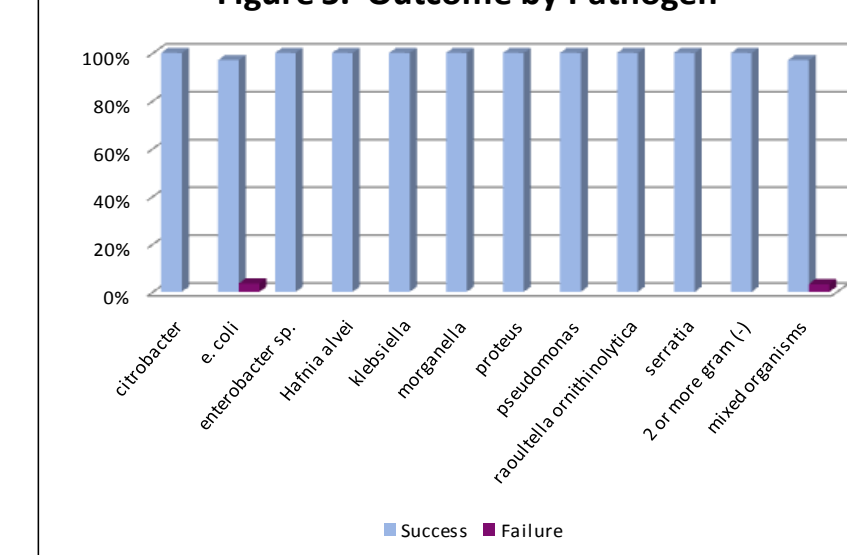
Treatment Outcome (n=210)	Patients	(%)
Cured	159	(76%)
Improving	39	(18%)
With PO abx	31	(15%)
With wound care	8	(4%)
Clinical Success Overall	198	(94%)
Failure	5	(2%)
Non-evaluable	8	(4%)

- Overall clinical success was achieved in 94%, with 76% cured and 18% improving at completion of therapy. Of those improving, 31/39 (79%) completed therapy with oral antibiotics. Eight of 39 (21%) completed IVAB therapy with continuing wound care required.
- The patient failures were in cystitis (1), prostatitis (1) and UTI (3), of which 3 had urinary catheters.
- 6 patients were admitted to the ER (3%) for possible drug or disease-related causes, including confusion, diverticulitis, dehydration secondary to nausea and vomiting, fever, weakness (2). Outcomes were: cured (2), improving (2) and non-evaluable (2).

**Figure 4. Outcome by Infection Type**



**Figure 5. Outcome by Pathogen**



## Discussion

- 210 patients were included in the study from 9 POIC sites nationally, of which 68% had therapy initiated in the POIC.

- Mean age was 63 years with 62% females. One or more comorbidities were identified in 77%, with presence of a urinary catheter in 27%.

- GU treated diagnoses were UTI (66%), followed by pyelonephritis (12%) and prostatitis (9%).

- 90% had monomicrobial infections with *E. coli* most predominant (48%), followed by species of *Pseudomonas* (27%), *Klebsiella* (9%), *Serratia* and *Enterobacter* (both <2%).

- 74% of all organisms were MDR, most predominantly *E. coli*, followed by *pseudomonas*, both with high resistance rates to fluoroquinolones.

- Four pathogens were ESBL-producing, including *Serratia* (50%), *Klebsiella* (39%), *Pseudomonas* (21%) and *E. coli* (19%).

- The antimicrobial agents used most were ertapenem, ceftriaxone and cefepime, accounting for 55% of primary therapy. Only 15 patients (7%) required combination IVAB. Median treatment duration was 11 days.

- Adverse events were reported in 29% of all patients, with 22% likely drug related. Of these, 82% were mild or moderate.

- Aminoglycosides resulted in the highest rate of serious AEs by therapeutic class.

- No IV catheter related infections occurred.

- Treatment success was defined as those who achieved cure or improvement. This was achieved in 76% and 18%, respectively for an overall 94% successful outcome.

## Conclusion

- Therapy was well tolerated overall, the majority of whom initiated treatment in the POIC without hospitalization. This resulted in significant cost-savings by avoiding ER visits and possible hospital admissions.

- Treatment success in this patient population was high, considering a population with many resistant and ESBL-producing pathogens as well as comorbidities.

- Placement and management of IV catheters was successful, resulting in no CRBSI.

- The POIC is a safe and effective setting for the treatment of complicated GN GU infections, allowing for rapid ID intervention with the most efficacious agent and route of therapy.

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