

# Successful Treatment of Complicated Gram Negative Sinopulmonary Infections Treated in Infectious Disease (ID) Physician Office Infusion Centers (POICs)

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## Abstract

**Background:** Complicated sinopulmonary infections may involve gram negative pathogens, especially in patients (pts) who are antibiotic experienced or those with significant underlying pulmonary disease. These pts often require intravenous antibiotics (IVAB), most frequently initiated in a hospital setting. The purpose of this study was to examine the safety and outcomes of therapy for complicated sinopulmonary infections treated in ID POICs.

**Methods:** Pts ≥ 18 years old receiving IVAB for sinopulmonary infections in ID POICs in 2009 were identified from a computer database. Pts were limited to those treated with an IVAB possessing gram negative activity. The pool was limited to those with cultures demonstrating at least one gram negative pathogen from patient practice records. These were then reviewed for pertinent demographic and clinical data, setting for initiation of therapy, adverse events, and outcomes.

**Results:** Total enrollment was 104 pts from 8 ID POIC sites across the country. Mean age was 63 years. Therapy was initiated in the ID POIC in 69 pts (67%) overall. The most common infections were sinusitis, pneumonia and bronchiectasis. Polymicrobial infections occurred in 30%. All pts except one had co-morbidities. Infectious etiologies included *Pseudomonas* (57%), *Serratia* (6%) and *E. coli* (5%). Cefepime was used most frequently (n=54, 42%), followed by piperacillin/tazobactam (n=19, 15%) and ceftriaxone (n=18, 14%). Pts received IVAB for a mean duration of therapy of 25 days (range = 5-99). Treatment success, defined by achieving cure or improvement, was achieved in 93% of patients. Overall incidence of adverse events (AEs) was 24%, but no antibiotic changes were made in 52% of these patients. Two AEs were serious, both involving hematologic parameters. The most common mild and moderate AEs were gastrointestinal (40%). Catheter-related blood stream infections occurred in 2 pts (0.67 infections per 1000 catheter days).

**Conclusions:** Successful treatment of complicated sinopulmonary infections was achieved in POICs, avoiding hospitalization in two-thirds of pts. Adverse event incidence was low and catheter-related infections were infrequent in this patient population.

## Introduction

Respiratory infections account for significant morbidity and mortality among patients. Lower respiratory tract infections were the third leading cause of death worldwide in 2004.<sup>1</sup> Increases have been seen over the last decade in gram negative pulmonary infections overall and in multidrug resistant (MDR) gram negative pathogens, often in patients (pts) who are antibiotic experienced or those with significant underlying pulmonary disease. These pts often require intravenous antibiotics (IVAB), traditionally initiated in a hospital setting. The purpose of this study was to examine the treatment, safety and outcomes of therapy for complicated gram negative sinopulmonary infections treated in ID POICs.

## Methods

A retrospective database and chart review was conducted to identify all patients ≥ 18 years old with culture-confirmed gram negative infections who received therapy with one or more intravenous antibiotics possessing gram negative activity in 8 POICs nationally.

### Inclusion Criteria:

- Treatment with one or more IVAB possessing gram negative activity.
- Culture-confirmed complicated sinopulmonary gram-negative infections.
- Age ≥ 18 years old.

### Exclusion Criteria:

- None.

### Patient Selection:

- All patients were identified who were treated with IVAB for culture-confirmed gram negative pulmonary infections.
- Each patient identified that met criteria was evaluated for demographics, infectious agent, sensitivities for each organism, 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.

### Data Analysis:

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

## Results

### Patient Demographics and Therapy Characteristics:

- A total of 104 patients were treated across 8 sites.
- Patient demographic data was similar across all sites.
- All patients except for one had co-morbidities, most commonly underlying pulmonary disease.
- Two-thirds of patients had treatment initiated in the POIC, including line placement, first dosing and subsequent therapy.
- Patients previously hospitalized received inpatient therapy an average of 5.4 days prior to POIC treatment (median 5 days, range 1-18 days). The longest inpatient treatments were for *Pseudomonas* pneumonia (18 days) and empyema (16 days).
- Primary reasons for IVAB therapy were MDR organisms, failed oral therapy and drug allergies to oral agents.

Table 1: Demographics

Characteristics (n=104)	No. (%)	Range
<b>Gender</b>		
Female	63 (61%)	
Male	41 (39%)	
<b>Weight (mean, kg)</b>	77	(39-145)
<b>Age (overall mean)</b>	63	(19-88)
19-35	10 (10%)	
35-50	12 (12%)	
51-65	28 (27%)	
≥ 66	54 (52%)	
<b>Underlying Diseases</b>		
COPD/Asthma/Emphysema	64 (62%)	
Diabetes	26 (25%)	
Cancer/Chemo/Radiation	17 (16%)	
Immune deficiency disorder	13 (13%)	
None	1 (1%)	
Catheter placement/self-cath	1 (1%)	
<b>Location Prior to Treatment</b>		
Community	69 (67%)	
Hospital	35 (33%)	

Table 2: Infection Types

Diagnosis (n=104)	No. (%)
Sinusitis	43 (41%)
Pneumonia	37 (36%)
Bronchiectasis	11 (11%)
Bronchitis	9 (9%)
Tracheobronchitis	2 (2%)
Lung Abscess	1 (1%)
Empyema	1 (1%)

Figure 1. Location Prior to POIC Treatment

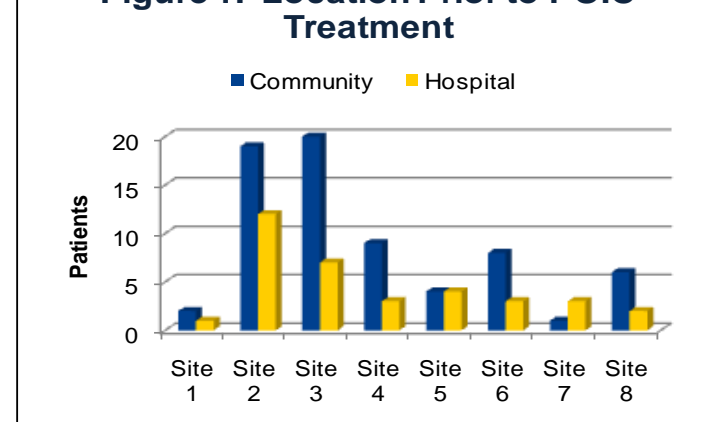
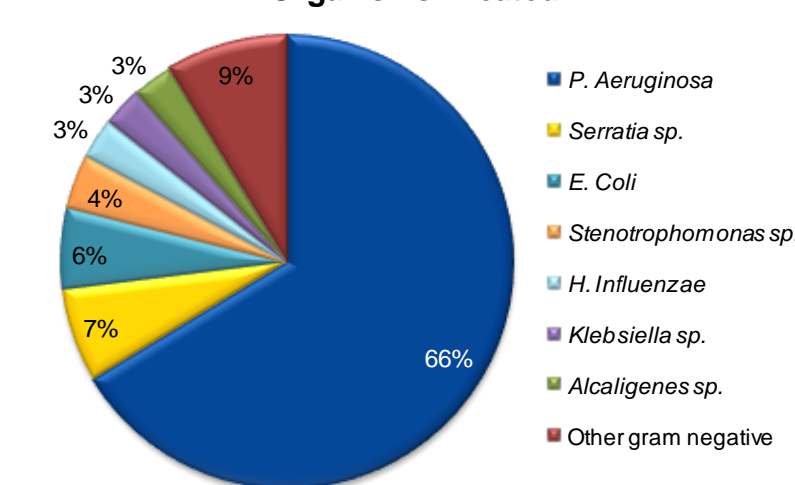


Figure 2. Primary Gram Negative Organisms Treated



### Microbiologic Data:

- 30% of patients had polymicrobial infections, which included 6 gram positive pathogens and 3 with mold or fungus.

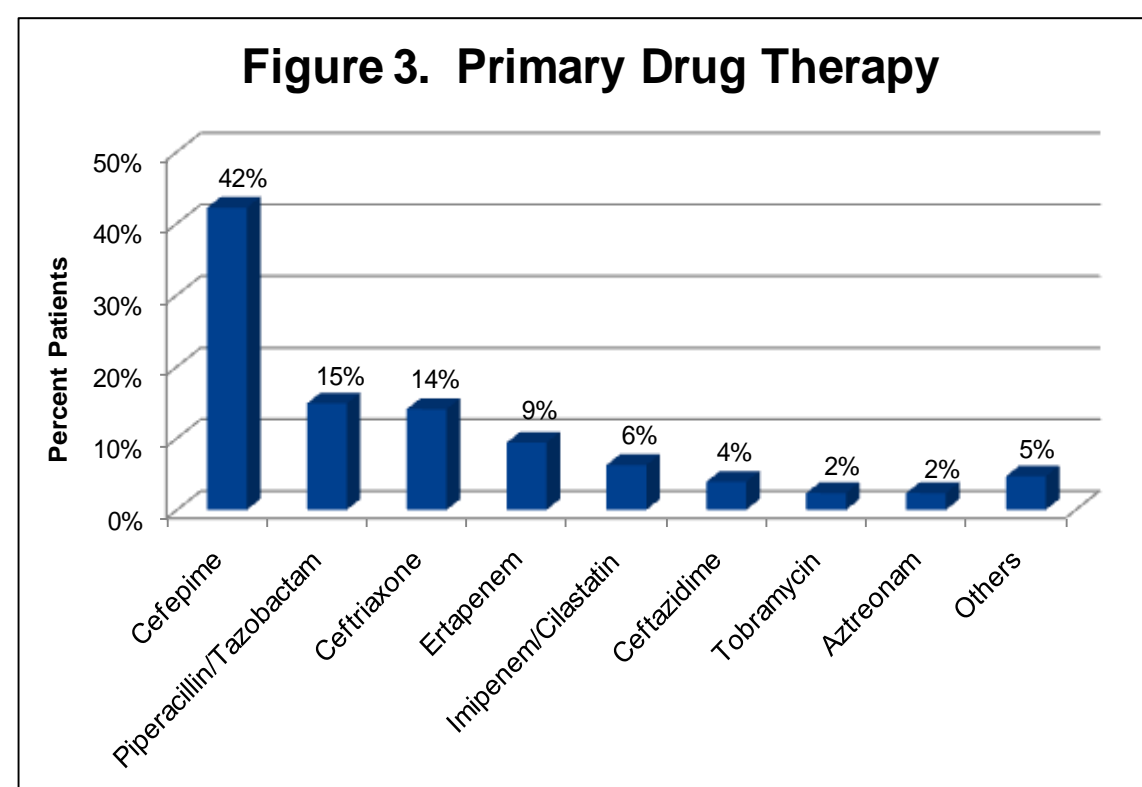
- Most common resistance patterns were *Pseudomonas* and *E. coli* resistance to ceftriaxone, ciprofloxacin and levofloxacin.

Table 3. Culture and Sensitivity Data

Total Organisms Treated (n=160)	No. (%) Total	MDR Organisms*		ESBL Producing No. (%)
		No. Tested	No. (%)	
<i>Pseudomonas aeruginosa</i>	81 (51%)	69	26 (38%)	2 (3%)
<i>Serratia sp.</i>	9 (6%)	7	7 (100%)	
<i>Escherichia coli</i>	7 (4%)	7	5 (71%)	2 (29%)
<i>Stenotrophomonas sp.</i>	7 (4%)	7	6	
<i>Klebsiella sp.</i>	4 (3%)	4		
<i>Enterobacter sp.</i>	3 (2%)	3	2 (67%)	
<i>H. Influenzae</i>	3 (2%)	1	1 (100%)	1 (100%)
<i>Moraxella morgani</i>	3 (2%)	3	3 (100%)	3 (100%)
<i>Alcaligenes sp.</i>	3 (2%)	2	2 (100%)	
<i>Acinetobacter sp.</i>	2 (1%)	2	1 (50%)	
<i>Pasteurella sp.</i>	2 (1%)	2	1 (50%)	
<i>Proteus mirabilis</i>	2 (1%)	2	2 (100%)	
<i>Achromobacter xylosoxidans</i>	1 (1%)	1	1 (100%)	
<i>Neisseria sp.</i>	1 (1%)	not available		
Mixed Organisms	32 (20%)			

\*Total tested = 109

### Drug Therapy:



- The most commonly used antimicrobial agent was cefepime, followed by piperacillin/tazobactam.
- Concomitant drugs were used in 8 patients.
- Therapy was changed in 19 patients.
- Overall mean duration of therapy in the POIC was 25 days (range 1-99 days). Two long-term patients were treated for resistant *pseudomonas* and *acinetobacter + enterobacter* sinusitis, respectively.
- Doses were standard for evaluated patients.

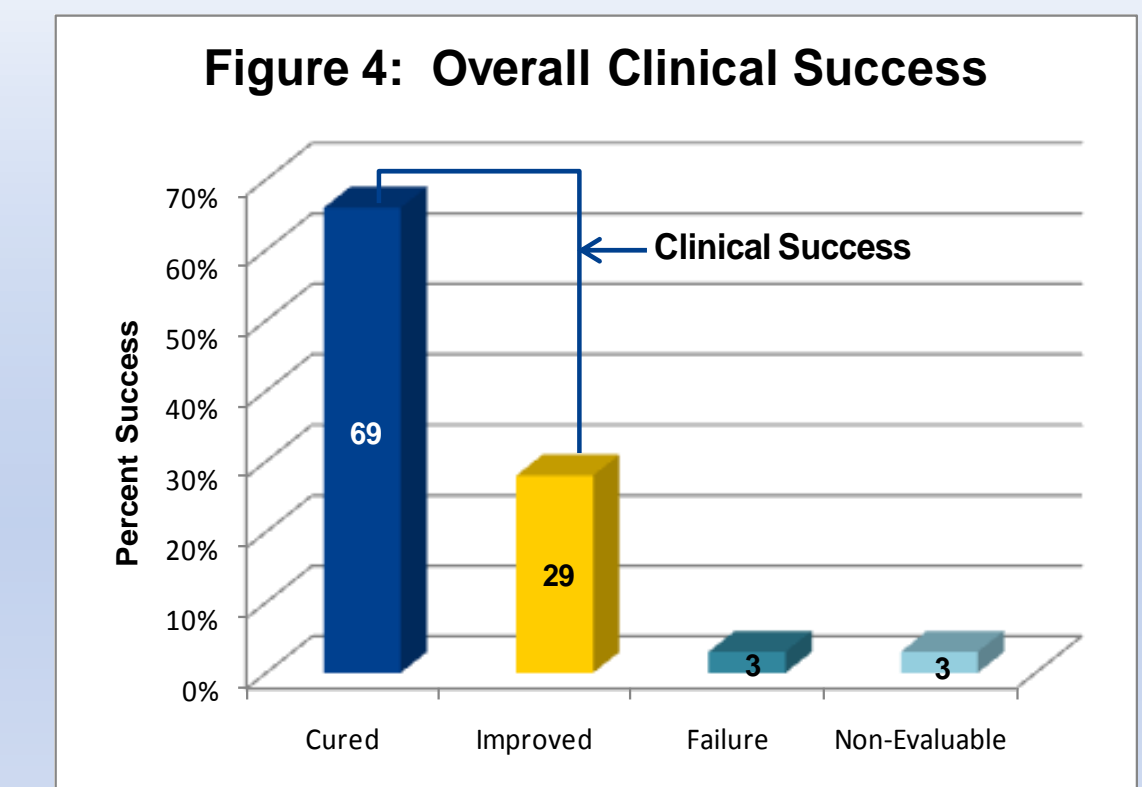
### Safety:

- 25 patients (24%) experienced drug-related adverse events, 2 serious.
- The most common AE was gastrointestinal disturbance (n=10, 40%).
- ADRs occurred most with piperacillin/tazobactam (n=10, 40%) followed by cefepime (n=7, 28%).
- All resolved except 2, one unknown and the other ongoing during the study.
- 3 patients were hospitalized, but only 1 related to drug therapy.
- 1 patient initiated in the POIC was hospitalized with neutropenia secondary to piperacillin/tazobactam.
- 2 previously hospitalized patients were readmitted, 1 with increasing SOB and 1 for reasons unrelated to drug therapy.
- Intravenous catheter infections occurred in 2 patients (0.67 infections per 1000 catheter days).

Table 4: Drug-Related Adverse Events

Adverse Events (n=25)	No.	Drug	Severity	Discontinued Treatment	Outcome
Abdominal cramps/pain	1	Cefepime	Moderate	No	Ongoing
	1	Ceftriaxone	Moderate	No	Unknown
<i>C. difficile</i>	1	Piperacillin/tazobactam	Moderate	No	Resolved
Decreased appetite, weakness, tingling	2	Ertapenem	Moderate	Yes	Resolved
Diarrhea	1	Ertapenem	Mild	No	Resolved
	3	Piperacillin/tazobactam	Moderate		
Eosinophilia	1	Piperacillin/tazobactam	Mild	No	
Leukopenia, neutropenia	1	Piperacillin/tazobactam	Mild	Yes	Resolved
Neutropenia	1	Piperacillin/tazobactam	Serious	Yes	
Thrombocytopenia	1	Cefepime	Serious	Yes	
	1	Cefepime	Mild	Yes	
Nausea	1	Ceftriaxone	Moderate	Yes	Resolved
	1	Piperacillin/tazobactam	Moderate	Yes	
	2	Cefepime		No/Temporarily	
	1	Ceftazidime		No	
Thrush	1	Impenem/cilastatin	Mild	No	Resolved
	1	Piperacillin/tazobactam		No	
Rash	1	Cefepime		Yes	Resolved
	1	Piperacillin/tazobactam	Moderate	Yes	
Vaginal yeast	1	Cefepime	Mild	No	Resolved
Unknown reaction/poor tolerance	1	Cefepime	Mild	Yes	Resolved

### Outcome Analysis:



- 93% of patients achieved a successful outcome as defined by those who were cured or improving at completion of IVAB.
- 69 patients (66%) were completely cured at completion of IVAB.
- 29 patients (28%) improved at the end of IVAB, 20 of which were switched to oral antibiotics and 9 continued with wound care.
- 3 patients failed therapy (1-*pasteurella* sinusitis, 1-sinusitis with multiple strains of *pseudomonas*, 1-*pseudomonas* bronchitis complicated with MRSA).
- Tracheobronchitis had the highest cure rate (n=2) and pneumonia had the second highest cure rate (28/35 patients).
- *Pseudomonas* infections were the most predominant with a 78% cure rate.

Figure 5: Outcome by Diagnosis

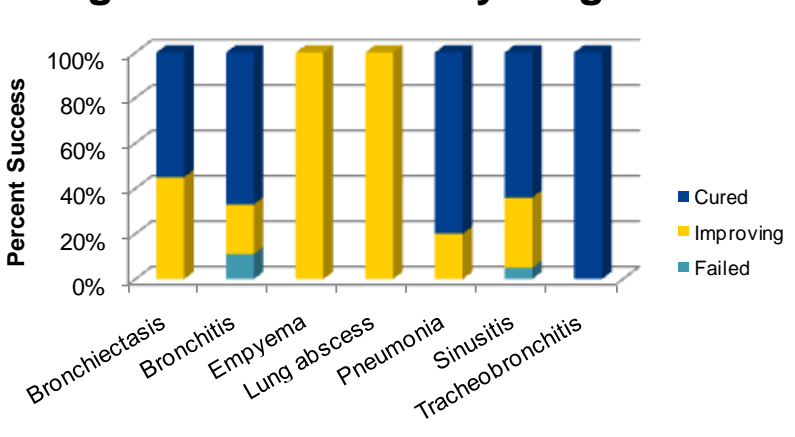
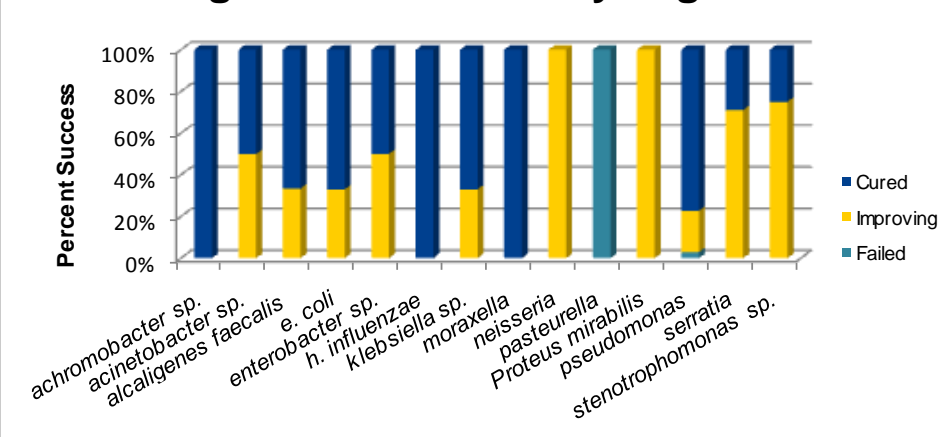


Figure 6: Outcome by Organism



## Discussion

- Trends indicate increasing prevalence of gram negative respiratory patients being treated in the outpatient setting.
- Therapy was initiated in the ID POIC in 69 patients (67%), which included IV line placement, first dosing of medication and subsequent management of patients.
- Primary infectious etiologies included *pseudomonas* (57%), *serratia* (6%) and *E. coli* (5%). Of reported cultures and sensitivities, 47% were multi-drug resistant.
- Cefepime was used most frequently (n=54, 42%), followed by piperacillin/tazobactam (n=19, 15%) and ceftriaxone (n=18, 14%).
- Overall incidence of adverse events (AEs) was 24%, but no antibiotic changes were made in 52% of these patients. Two AEs were serious, both involving hematologic parameters, resolving upon discontinuation of the drug. The most common mild and moderate AEs were gastrointestinal (40%).
- Catheter-related blood stream infections occurred in 2 patients (0.67 infections per 1000 catheter days).
- Overall treatment success, defined by achieving cure or improvement, was achieved in 93% of patients.

## Conclusions

- Successful treatment of complicated sinopulmonary infections was achieved in POICs.
- Initiation and subsequent treatment occurred entirely in the outpatient setting in two-thirds of patients, avoiding hospitalization. Additional study quantifying those infections that were hospital acquired versus community-acquired would be warranted.
- Adverse event incidence overall was low and resulted in no long term sequelae. Catheter-related infections were very infrequent in this treatment setting.
- This data supports prompt discharge of hospitalized patients and avoidance of hospitalization when possible for treatment and management in a POIC.

## References

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