# An International, Multicenter, Retrospective Study of Nosocomial Pneumonia due to *Pseudomonas aeruginosa*

Scott T. Micek, PharmD[1], Richard Wunderink, MD[2], Marin H. Kollef, MD[3],Catherine Chen, MD[3], Jordi Rello,MD[4], Jean Chastre, MD[5], Massimo Antonelli, MD[6], Tobias Welte, MD, PhD[7], Bernard Clair MD[8], Helmut Ostermann, MD, PhD[9], Esther Calbo, MD[10], Antoni Torres, MD[11], Francesco Menichetti, MD, PhD[12], Vandana Menon, MD[13]

[1]St. Louis College of Pharmacy, USA; [2]Northwestern University Feinberg School of Medicine, USA; [3]Washington University School of Medicine, USA; [4]Hospital Vall D'Hebron, Spain; [5]Groupe Hospitalier Pitie-Salpetriere, France; [6]Policlinico Universitario A Gemelli, Italy; [7]Medizinische Hochschule Hannover, Germany; [8]Hôpital Raymond Poincaré, France; [9]University Hospital of Munich, Germany; [10]Hospital Universitari Mutua de Terrassa, Spain; [11]Hospital Clínic de Barcelona, Spain;[12]Azienda Ospedaliera Universitaria Pisana, Italy; [13]Cubist Pharmaceuticals, USA

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## BACKGROUND

Recent trends show an increase in the prevalence of nosocomial pneumonia (NP) caused by multidrug resistant (MDR) bacteria, most commonly *Pseudomonas aeruginosa* with documented resistance to β-lactams, carbapenems, aminoglycosides, and fluoroquinolones. The therapeutic effectiveness of current therapies for nosocomial pneumonia are limited by the increasing prevalence of pathogens that express extended spectrum β-lactamases (ESBLs), AmpC β-lactamases, or methicillin resistance, emphasizing the need for development of new and effective antimicrobials.

Initial empiric antibiotic treatment for NP may include the use of cephalosporins, aminoglycosides, fluoroquinolones, penicillins or carbapenems alone or in combination. Antibiotic selection is typically individualized based on a given patient's risk factors for MDR pathogens and local susceptibility patterns. Prompt and adequate antimicrobial therapy has been shown to reduce mortality and improve morbidity associated with NP.

## STUDY PURPOSE

The purpose of this preliminary analysis is to describe the clinical characteristics, antibiotic resistance patterns and outcomes of patients with *Pseudomonas aeruginosa* nosocomial pneumonia.

## STUDY DESIGN AND PARTICIPATING SITES

**Study Design**

This retrospective multicenter, hospital-based, medical record abstraction study collected data on hospitalized patients with a clinical diagnosis of NP comprising hospital associated pneumonia (HAP), ventilator associated pneumonia (VAP) and health care associated pneumonia (HCAP), due to *P. aeruginosa*.

**Participating Sites**

- France: Groupe Hospitalier Pitie-Saltpetriere, Hôpital Raymond Poincaré
- Germany: University Hospital of Munich, Medizinishe Hochschule Hannover
- Italy: Policlinico Universitario A. Gemelli, Azienda Ospedaliera Universitaria Pisana
- Spain: Hospital Universitari Mutua de Terrassa, Hospital Vall D'Hebron, Hospital Clínic de Barcelona
- United States : Barnes-Jewish Hospital, Mayo Clinic, Northwestern Memorial Hospital

## ELIGIBILITY CRITERIA

1. Aged 18 years or older
2. Admitted for index hospitalization 36 months prior to study initiation at each site
3. Clinical diagnosis of NP defined as findings consistent with pneumonia on chest x-ray or CT-scan and either temperature > 38.3°C or leukocytosis >10,000 cells/mm$^3$ or both.
4. Microbiologic cultures (qualitative or quantitative) obtained within the 24-h period surrounding initiation of antibiotics.
5. *P. aeruginosa* organism cultured from a respiratory specimen including sputum, pleural puncture, flexible bronchoscopy with protected specimen brush, bronchoalveolar fluid, "mini-BAL" or transbronchial biopsy, and tracheobronchial aspirate in intubated patients.

## BASELINE CHARACTERISTICS

| Variable | N = 396* |
|---|---|
| Age, yrs: | 60 ± 16 |
| Male, n (%): | 278 (70) |
| Location Prior to Hospitalization, n (%) | |
| Home | 199 (50) |
| Skilled Nursing Facility | 40 (10) |
| Long-Term Care Facility | 18 (5) |
| Assisted Living | 5 (1) |
| Inpatient Rehabilitation | 30 (8) |
| Other | 100 (25) |
| Coexisting conditions, n (%): | |
| Sepsis | 71 (18) |
| Acute Coronary Syndrome | 43 (11) |
| Valvular Heart Disease | 42 (11) |
| Hypertension | 192 (49) |
| Venous Thromboembolism | 23 (6) |
| COPD/Asthma | 106 (27) |
| Other Respiratory Disease | 99 (25) |
| Diabetes | 119 (30) |
| Chronic Kidney Disease | 98 (25) |
| Chronic Liver Disease | 39 (10) |
| Hospitalized in the previous 6 months, n (%): | 198 (50) |
| Antibiotics in the past 30 days, n (%) | 150 (38) |
| Presenting Symptoms, n (%): | |
| Temperature ≥38$^O$ C or <36$^O$C | 267 (67) |
| WBC count > 12,000 or < 4,000 mm$^3$ | 293 (74) |
| Pulse Rate > 100 bpm | 230 (58) |
| Respiratory Rate > 20 breaths/min | 213 (54) |
| SBP < 90 mmHg | 145 (37) |

* Denominator varies for each variable based on data availability

## ANTIBIOGRAM

| | Aminoglycoside | AP-PCN + β-lactamase Inhibitor | Carbapenem | AP Cephalosporin | Fosfomycin | Aztreonam | Ciprofloxacin | Colistin |
|---|---|---|---|---|---|---|---|---|
| No. Isolates Tested (Susceptible %) | 347 (73) | 345 (71) | 346 (64) | 344 (74) | 99 (73) | 231 (60) | 344 (66) | 193 (94) |

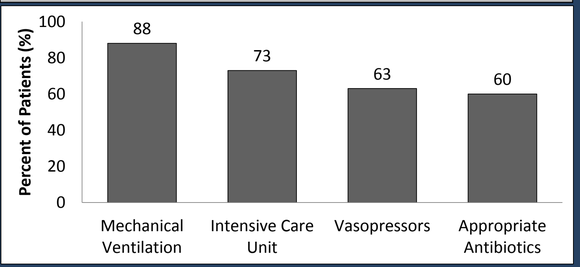
Aminoglycoside: Amikacin, Gentamicin, Tobramycin
Antipseudomonal Penicillin (AP-PCN) + β-Lactamase Inhibitor: Piperacillin-Tazobactam, Ticarcillin-Clavulanate
Carbapenem: Doripenem, Imipenem-Cilastatin, Meropenem
Antipseudomonal Cephalosporin: Cefepime, Ceftazidime

**MDR (defined as intermediate or resistant to ≥3 antipseudomonal drug classes) present in 31% of pneumonia cases**

## MULTIDRUG-RESISTANT ANTIBIOGRAM

| Antibiotic | No. MDR Isolates Tested (Susceptible %) |
|---|---|
| Aminoglycoside | 108 (32) |
| AP-PCN + β-Lactamase Inhibit | 107 (21) |
| Carbapenem | 108 (14) |
| AP Cephalosporin | 108 (31) |
| Fosfomycin | 33 (55) |
| Aztreonam | 84 (17) |
| Ciprofloxacin | 107 (19) |
| Colistin | 79 (97) |

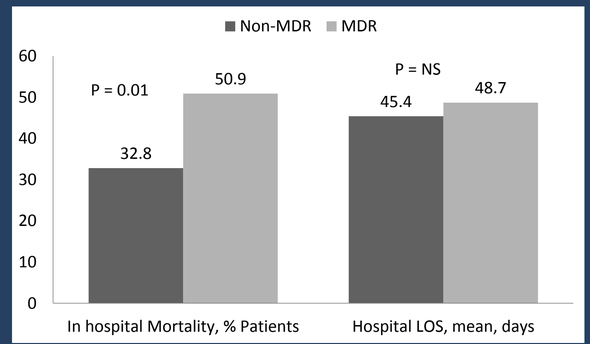
## PROCESS OF CARE VARIABLES




## CLINICAL & ECONOMIC OUTCOMES

| Outcome | Value |
|---|---|
| In-Hospital Mortality, No. (%) | 165/396 (42) |
| 30-Day Mortality, No. (%) | 138/314 (44) |
| Hospital Length of Stay, Days | median 30 (IQR 17, 56) |
| Ventilator Duration, Days | median 18 (IQR 9, 30) |
| ICU Length of Stay, Days | median 21 (IQR 12, 35) |

## OUTCOMES BY MDR STATUS




## CONCLUSIONS AND FUTURE DIRECTION

This retrospective analysis of patients hospitalized with a diagnosis of nosocomial pneumonia due to *P. aeruginosa* reveals high rates of antibiotic resistance, inappropriate antibiotic therapy, in-hospital mortality and resource utilization.

A final database of 742 patients will compare the clinical and economic outcomes between patients who received initial inappropriate therapy versus appropriate therapy and between patients with resistant versus susceptible *P. aeruginosa*. *In addition,* practice patterns and treatment pathways as well as the epidemiology and resistance patterns of NP at each participating site will be evaluated.