

# Antibiotics & treatment of Acute Bacterial Sinusitis



*Walid Reda*  
*Product Manager*



Do your antimicrobial options meet your needs?



# Antimicrobial Effects: *What's involved?*

## Effect in Humans:

- Serum concentration profile
- Penetration to site of infection

Pharmacokinetics

## Effect in Bacteria:

- Potency (MICs)
- Mechanism of killing

Pharmacodynamics

**Clinical Effectiveness**



# Evaluating antibiotic options in the treatment of Bacterial sinusitis

- Spectrum of bacterial coverage
- High penetration at the site of infection  
(Higher concentration than the MIC's)
- Low potential for Bacterial resistance development
- Resolution of signs and symptoms
- Fast relief
- Tolerable
- An antibiotic that can help both acute and chronic sinusitis patients




# Acute Bacterial Sinusitis

- One of the most common conditions treated in outpatient setting
- The 5<sup>th</sup> most common diagnosis for which an antibiotic was prescribed
- Etiology rarely established therefore initial management is empiric

Sinus and Allergy Health Partnership. *Otolaryngol Head Neck Surg.* 2004;130:1-44.



# Goals of Therapy

- Eradicate bacterial infection 
- Re-establish patency of osteomeatal complex
- Reduce inflammation
- Restore drainage of affected sinuses
- Minimize risk of complications

Sinus and Allergy Health Partnership. *Otolaryngol Head Neck Surg.* 2004;130:1-44.



## Current challenges

- Recent national and international surveillance studies have shown
  - ◆ Increase in isolation frequency of B-lactamase producing strains



**30%** of *H. influenzae*



**90%** of *M. Catarrhalis*

## Current challenges

- ◆ Decreased susceptibility of pneumococcal strains to penicillin's

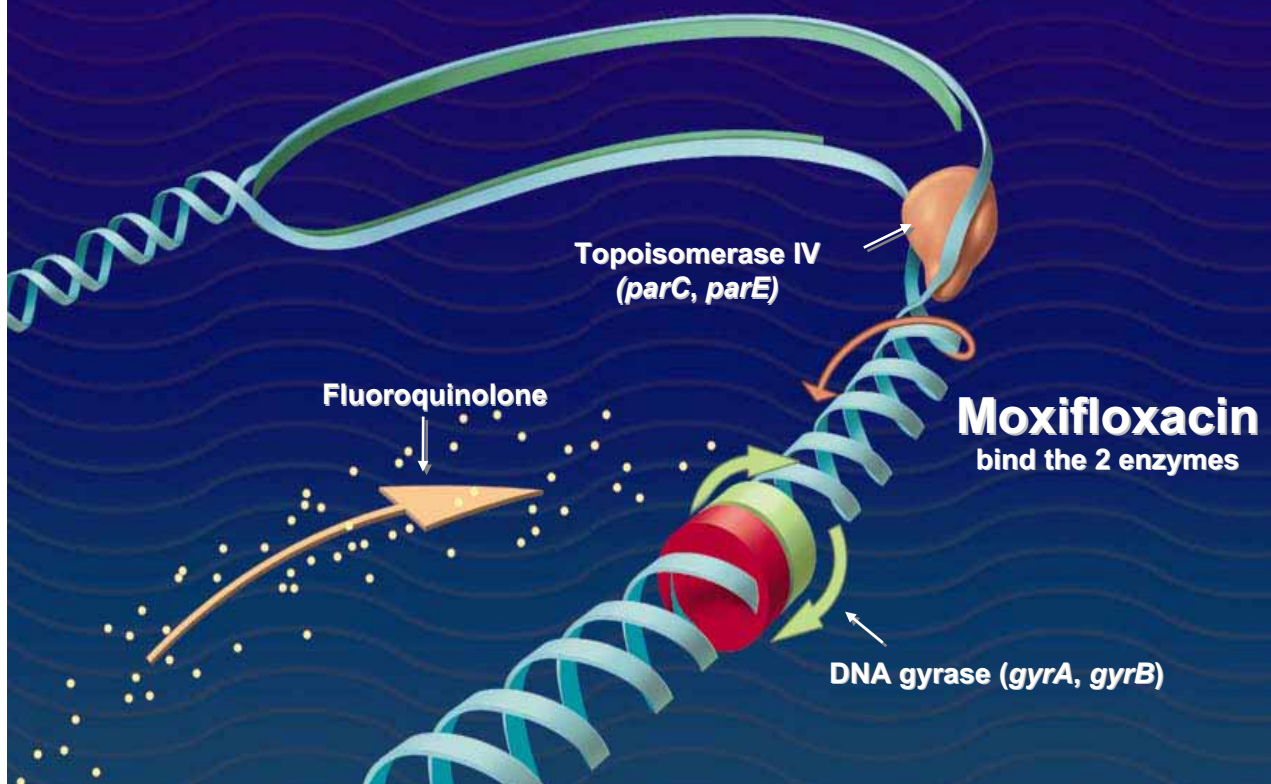


**40%** ( Intermediate susceptibility or resistant strains)

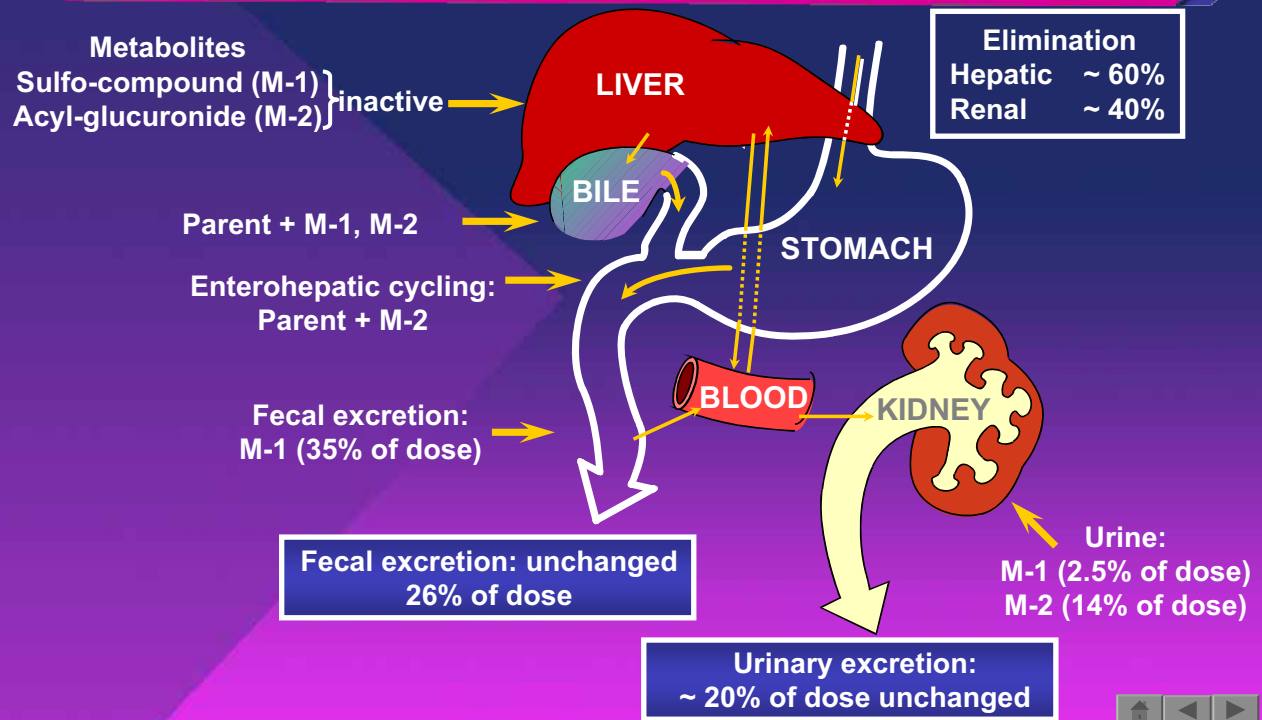
# Avalox<sup>®</sup>



## Mechanism of Action of Moxifloxacin



# Moxifloxacin: Metabolism and Elimination



Effective against most causative  
organisms

## Avalox MIC<sub>90</sub>s Against Common Respiratory Pathogens

Organism	Moxifloxacin
<i>S. pneumoniae</i> (PenS)	0.06-0.25
<i>S. pneumoniae</i> (PenR)	0.12-0.25
<i>H. influenzae</i> BL (-)	0.03-0.06
<i>H. influenzae</i> BL (+)	0.03-0.06
<i>M. catarrhalis</i> BL (-)	0.012-0.06
<i>M. catarrhalis</i> BL (+)	0.012-0.06

BL =  $\beta$ -lactamase; MIC = minimum inhibitory concentration (mg/L).

Blondeau JM. *J Antimicrob Chemother.* 1999;43(suppl B):1-11.



## Moxifloxacin: Excellent Activity Against Atypicals

Pathogen	MIC <sub>90</sub> (µg/ml)
<b><i>Atypical micro-organisms</i></b>	
<b><i>C.pneumoniae</i></b>	<b>0.2</b>
<b><i>M.pneumoniae</i></b>	<b>0.12</b>
<b><i>L.pneumophila</i></b>	<b>.015</b>

Blondeau JM. *J Antimicrob Chemother.* 1999;43 (suppl B):1-11.

Wise R. *Clin Drug Invest* 1999;17:365-387.

Ackermann A. *Eur J Clin Microbiol Infect Dis.* 2000;19:228-232.



## Moxifloxacin: Excellent Activity Against Respiratory Pathogens, Including Less Common Pathogens

Pathogen	MIC <sub>90</sub> (µg/ml)
<i>S aureus</i>	0.12
<b>Anaerobes</b>	
<i>Bacteroides fragilis</i>	2
<i>Peptostreptococcus spp</i>	<0.25
<i>Prevotella spp</i>	2

Blondeau JM. *J Antimicrob Chemother.* 1999;43 (suppl B):1-11.  
 Wise R. *Clin Drug Invest* 1999;17:365-387.  
 Ackermann A. *Eur J Clin Microbiol Infect Dis.* 2000;19:228-232.



## Avalox<sup>®</sup> - Superior Antimicrobials activity

MIC<sub>90</sub> (mg/l) range

	<i>Avalox</i>	Amoxicillin-clavulanate	Clarithromycin	Levofloxacin
<i>S. pneumoniae</i>	0.12	0.015	0.06	1.0
<i>H. influenzae</i>	0.06	0.5	16	0.03
<i>M. catarrhalis</i>	0.06	0.015	0.12	0.06
<i>M. pneumoniae</i>	0.12	>32	0.031	0.5
<i>C. pneumoniae</i>	0.12	>32	0.007	0.5
<i>L. pneumophila</i>	0.015	>32	0.5	0.015

Bayer, data on file



# Fluoroquinolone MIC<sub>90</sub>s Against Common Respiratory Pathogens

Organism	Moxifloxacin	Gatifloxacin	Levofloxacin
<i>S. pneumoniae</i> (PenS)	0.06-0.25	0.5	1-2
<i>S. pneumoniae</i> (PenR)	0.12-0.25	0.5	1-2
<i>H. influenzae</i> BL (-)	0.03-0.06	<0.03	0.03-0.32
<i>H. influenzae</i> BL (+)	0.03-0.06	<0.03	0.03-0.47
<i>M. catarrhalis</i> BL (-)	0.012-0.06	<0.03	0.06
<i>M. catarrhalis</i> BL (+)	0.012-0.06	<0.03	0.06-0.094

BL =  $\beta$ -lactamase; MIC = minimum inhibitory concentration (mg/L).

Blondeau JM. *J Antimicrob Chemother.* 1999;43(suppl B):1-11.



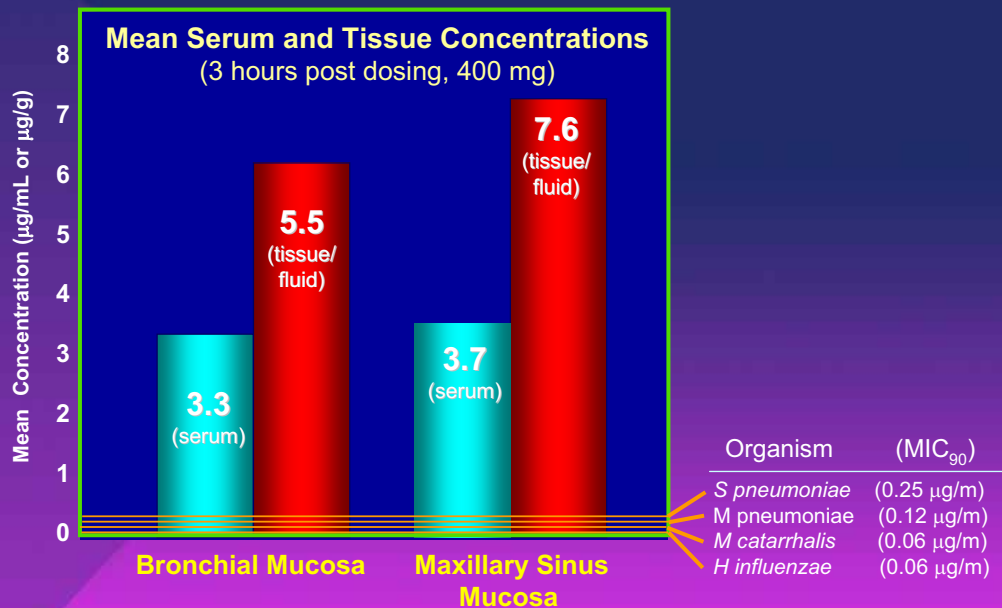
# Avalox<sup>®</sup> - Antimicrobials vs. Resistant Pathogens

	MIC <sub>90</sub> (mg/l) range			
	Avalox	Amoxicillin-clavulanate	Cefuroxime axetil	Clarithromycin
<i>S. pneumoniae</i> Pen-S	0.12	0.015	0.03	0.06
<i>S. pneumoniae</i> Pen-R	0.12	1	4	>64
<i>S. pneumoniae</i> Erythrom-R	0.12	1	4	>64
<i>H. influenzae</i> Beta lactam - ve	0.06	0.5	1	16
<i>H. influenzae</i> Beta lactam +ve	0.06	2	2	16

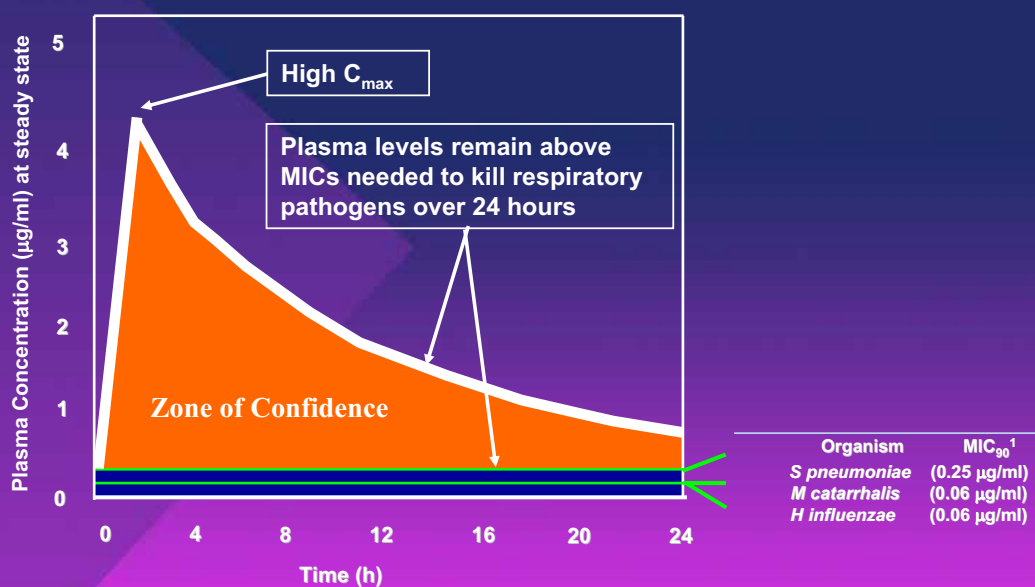
Bayer, data on file



# Avalox<sup>®</sup> ... Rapidly Penetrates Hard-to-Reach Respiratory Tract Tissues and Fluids



# Moxifloxacin provides Adequate plasma concentration that fights against dislodged micro-organisms

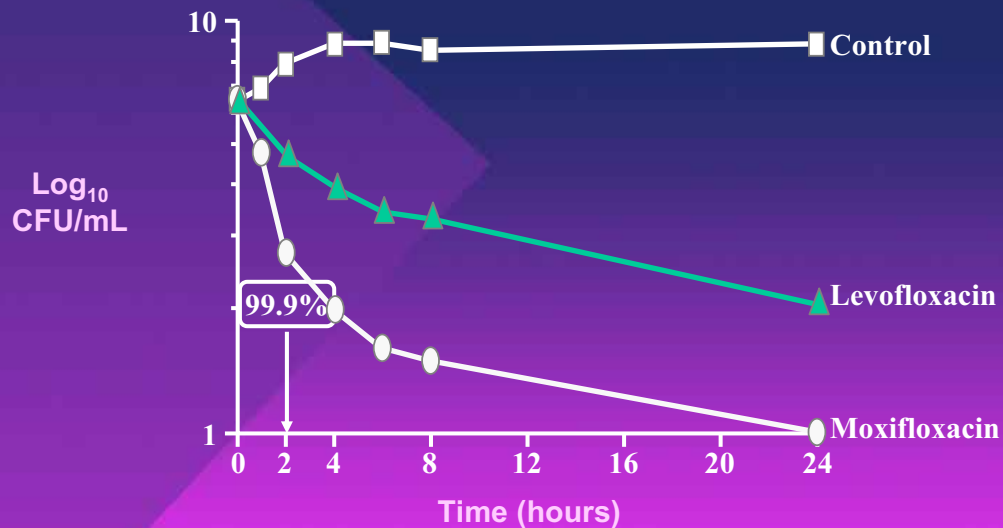


## Fast Resolution Of Symptoms



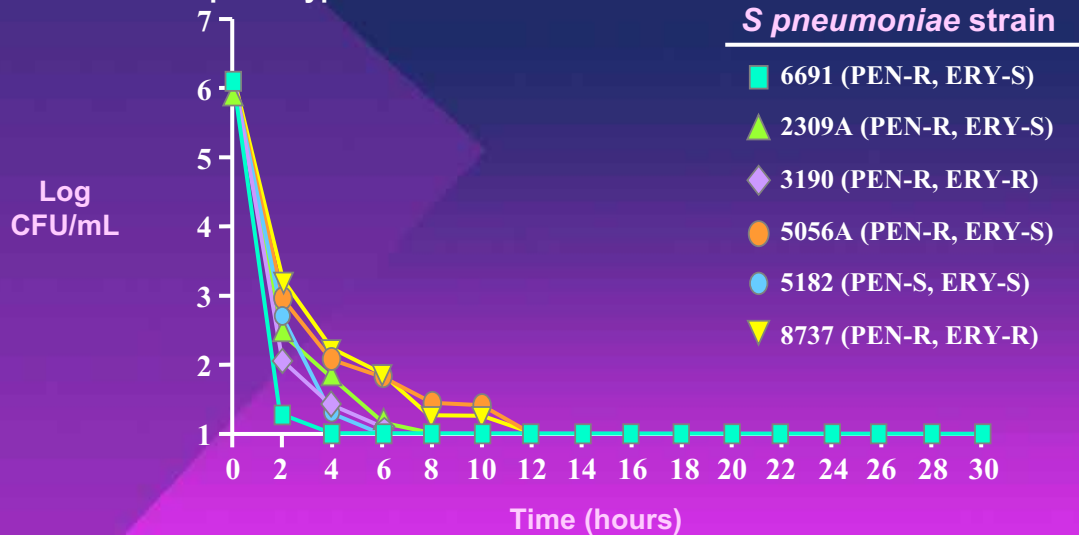
## Moxifloxacin Achieves Rapid Killing of *S pneumoniae* in Vitro

- Rapidly bactericidal: 99.9% kill within 2 h
- Increased potency and more favorable PK vs levofloxacin ⇒ enhanced PD activity



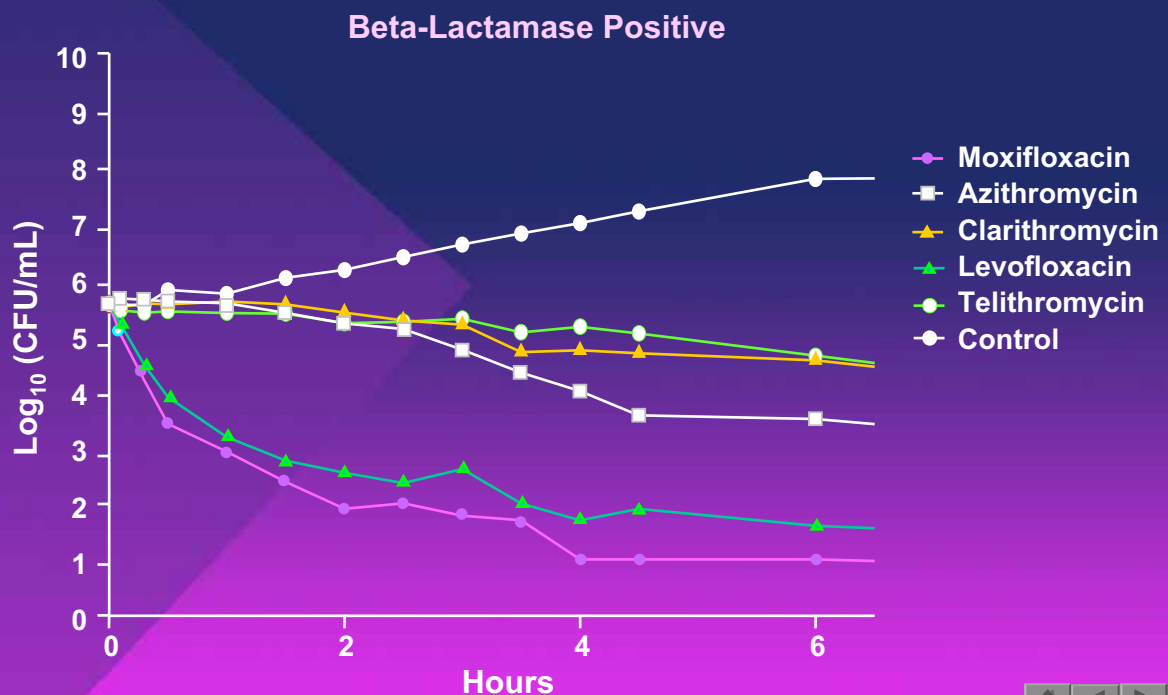
## Moxifloxacin: Rapid Killing of Drug-Resistant *S pneumoniae* in an *in Vitro* Pharmacodynamic Model

- Two-compartment PD model; simulated po 400-mg od moxifloxacin
- Rapidly bactericidal: 99.99% kill of all strains within 6 h regardless of resistance phenotype



Zinner S et al. ICAAC 1998. Poster A-26.

## Antimicrobial activity against *H. influenzae* in vitro at 4× MIC



Herrington et al. Submitted to ECCMID 2004.

# Moxifloxacin in the treatment of acute maxillary sinusitis after first-line treatment failure and acute sinusitis with high risk of complications

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Published in The Journal of International Medical Research: September 26, 2003, volume 31



## Introduction

- **Multicentre, Prospective and non-comparative clinical study**
- **The study was conducted in France by community-based ear, nose and throat specialists: 52 investigators**
- **258 patients with radiologically confirmed acute sinusitis were enrolled**
- **216 patients (83.7%) Qualified for per protocol efficacy analysis (Group 1, no. 175 ; Group 2, no. 41), and 92 for bacteriological analysis**
- **Samples were collected from the middle meatus**



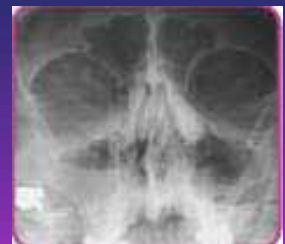
# Study population

- Patients with maxillary sinusitis after first-line treatment therapy failure ( n = 175).
- Patients with high risk of complications defined as frontal or sphenoidal and pansinusitis (n = 41).



# Patients

- 255 eligible patients.
- Above 18 years of age.
- Purulent rhinorrhoea confirmed by nasal endoscopy.
- Symptoms included nasal congestion and at least one of the following:
  - Spontaneous/induced infra-orbital pain.
  - Frontal cephalgia.
  - Cough or frequent throat-clearing.
  - Temperature > 38.0°C
- Radiological and/or tomodensitometric tests were conducted within 48 h prior to treatment initiation and were evaluated by the study co-ordinator (centralized review).
- First-line therapy failure was defined as persistence of symptoms after administration of a systemic antimicrobial (not a fluoroquinolone) course of therapy for at least 3 days.



# Treatment

All patients were treated with 400 mg/day of moxifloxacin orally for 7 days.



Profile of the antibiotics administered to patients in the per protocol population to treat the current episode of sinusitis before entry into this study:

**1st Generation Cephalosporins**  
2.1%

Cefatrizine  
Cefadroxil  
Cefaclor

**2nd Generation Cephalosporins**  
7.5%

Cefuroxime axetil

**Macrolides**  
14.4%

Pristinamycin

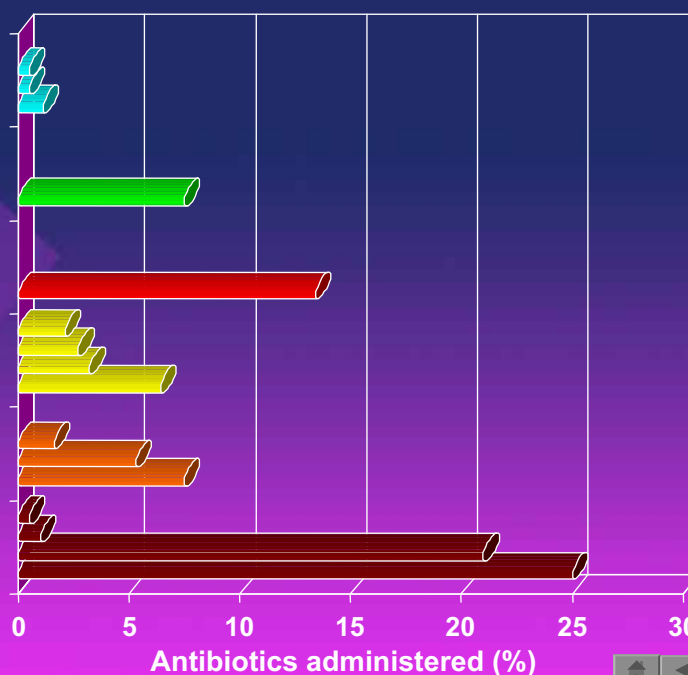
Spiramycin  
Josamycin  
Roxithromycin  
Clarithromycin

**3rd Generation Cephalosporins**  
14.4%

Cefixime  
Cefpodoxime proxetil  
Cefotiam hexetil

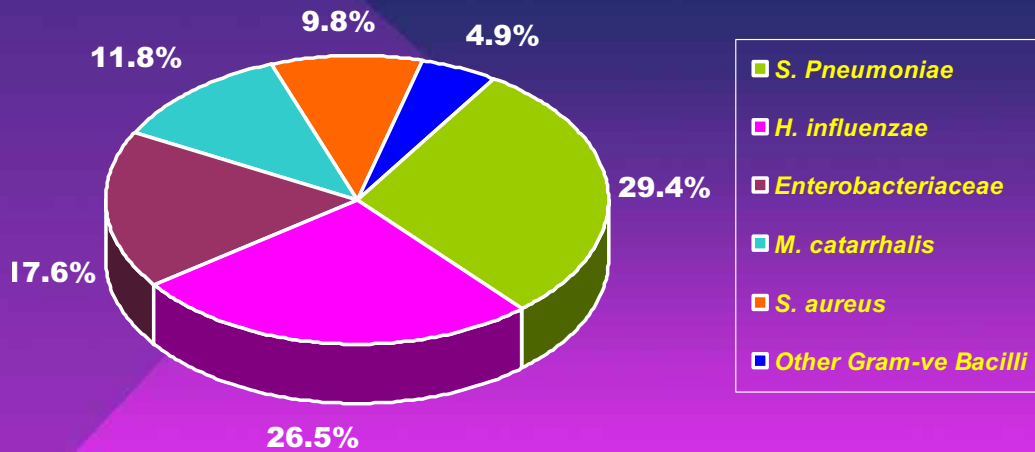
**Penicillins**  
48.1%

Oxacillin  
Bacampicillin  
Amoxicillin  
Amoxicillin Clavulanate



# Bacteriological Isolates

- Main bacterial species isolated from sinus secretions from 92 of the 216 patients in the per protocol population at inclusion.



# Efficacy Evaluation

V2: Day 3 or 4



V3: Day 7 or 10



Phone contact:  
4-5 weeks

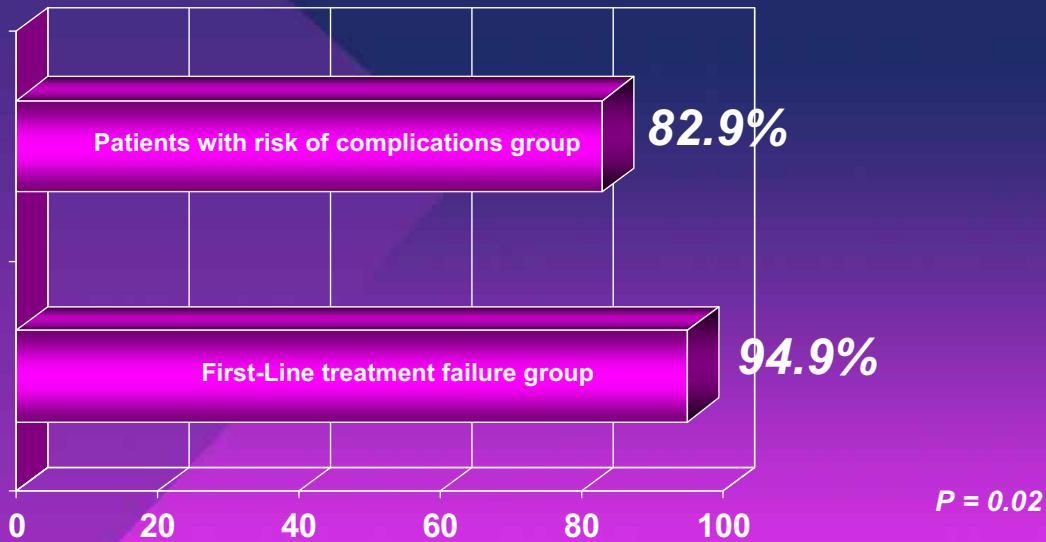
- Clinical response
- Bacteriological response
- Clinical Success
- Complete resolution of all clinical signs and symptoms
- Bacteriological eradication
- Follow-Up



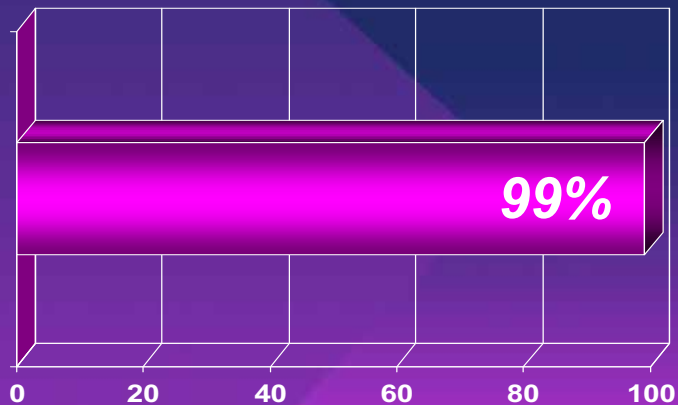


## Clinical Efficacy At Day 7-10

- Avalox offers the high clinical response rate



## Clinical Efficacy At 4-5 weeks Post-treatment

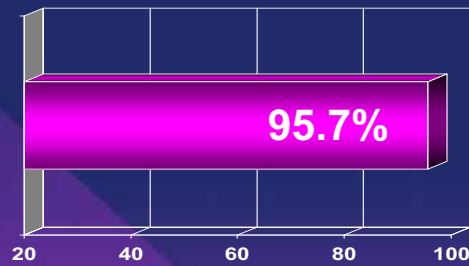


Avalox insures  
Maintained clinical  
efficacy & Continued  
resolution at 4-5  
weeks Post-  
treatment

$P = 0.01$

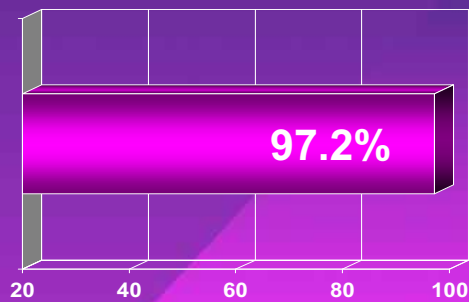
# Bacteriological Analysis

- At Day 3

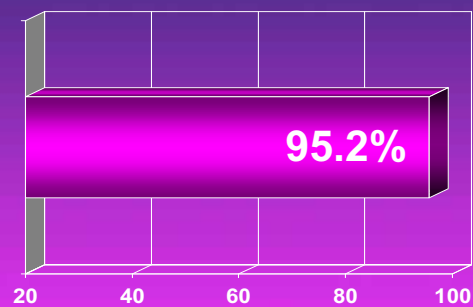


- At Day 7-10

First-Line treatment failure group



Patients with risk of complications group



# Tolerability

- Drug related adverse events , including

Adverse event	%
● Abdominal pain	2.4%
● Nausea	2.4%
● Diarrhoea	1.2%
● Dizziness	0.8%
● Arthralgia	0.8%

## Conclusion

- Overall, Moxifloxacin therapy resulted in rapid bacteriological eradication, with a high rate of clinical success.
  - Avalox demonstrated superiority to other commonly used antimicrobial, Although this was not a comparative study
  - Among the group of patients with first-line treatment failure, approximately
    - 25% had failed Amoxicillin-Clavulanate therapy
    - 24% had failed Cephalosporin therapy
    - 14% had failed Macrolide therapy
- The mean duration of prior antimicrobial therapy was 7.2 days



## Conclusion

To conclude,

The results of this study demonstrate that oral administration of 400 mg/day moxifloxacin for 7 days is an effective & well tolerated treatment for acute maxillary sinusitis after first-line treatment failure, and acute sinusitis with high risk of complications.





*The Potent & **Fast** Choice  
for*

*Acute Bacterial Sinusitis*



## **Avalox: The Potent & Fast Choice for ABS**

- **Potent Therapy in ABS**
- **Fast Recovery in Record Time**
- **Excellent Safety Profile**
- **Avalox 400 mg Once Daily for 7 days**



# Guidelines for Treatment – US Sinus Allergy Health Partnership 2004

- patients with:

**mild**

+

**no antibiotics for past 4 to 6 weeks**

- Patient with

**mild**

+

**antibiotics for past 4 to 6 weeks**

- Moderate infection:

Sinus and Allergy Health Partnership. *Otolaryngol Head Neck Surg.* 2004;130:1–44.



# Guidelines for Treatment – US Sinus Allergy Health Partnership 2004

- For patients with **mild** symptoms, with **no antibiotics for past 4 to 6 weeks:**

- ◆ Amoxicillin/clavulanate
- ◆ Amoxicillin
- ◆ Cefuroxime axetil
- ◆ Cefpodoxime proxetil
- ◆ Cefdinir

- If mild symptoms and **antibiotics in past 4 to 6 weeks** or **moderate** disease:

- ◆ **Moxifloxacin**, gatifloxacin, levofloxacin
- ◆ Amoxicillin (high dose) /clavulanate
- ◆ Ceftriaxone
- ◆ Combination therapy: high dose amoxicillin or clindamycin, plus cefixime or rifampin

Macrolides for *H.influenzae*:

“Most of the available eradication and efficacy studies suggest an activity that is similar to or marginally higher than that of placebo”

Sinus and Allergy Health Partnership. *Otolaryngol Head Neck Surg.* 2004;130:1–44.





*Thank you*