

EFFECTIVITY OF MOXIFLOXACIN THERAPY IN CAP

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AGENDA

- 2019 ATS / IDSA CAP Guideline : the role of moxifloxacin
- Why do we recommend moxifloxacin for CAP treatment ?

2019 ATS / IDSA CAP GUIDELINE

- This guideline addresses the clinical entity of pneumonia that is acquired outside of the hospital setting, with the following focus :
 - Focuses on studies that used radiographic criteria for defining CAP, given the known inaccuracy of clinical signs and symptoms alone for CAP diagnosis
 - Focuses on patients in the US who have not recently completed foreign travel, especially to region with emerging respiratory pathogens
 - Focuses on adults who do not have an immunocompromising condition, such as inherited or acquired immune deficiency or drug-induced neutropenia; including patients actively receiving cancer chemotherapy, patients infected with HIV with suppressed CD4 counts, and solid organ or bone marrow transplant recipients
- Antibiotic recommendation for the empiric treatment of CAP are based on selecting agents effective against the major treatable bacterial causes of CAP.

CRITERIA FOR DEFINING SEVERE CAP

Minor criteria

Respiratory rate ≥ 30 breaths/min

$P_{aO_2}/F_{I_{O_2}}$ ratio ≤ 250

Multilobar infiltrates

Confusion/disorientation

Uremia (blood urea nitrogen level ≥ 20 mg/dl)

Leukopenia* (white blood cell count $< 4,000$ cells/ μ l)

Thrombocytopenia (platelet count $< 100,000$ / μ l)

Hypothermia (core temperature $< 36^\circ\text{C}$)

Hypotension requiring aggressive fluid resuscitation

Major criteria

Septic shock with need for vasopressors

Respiratory failure requiring mechanical ventilation

*Due to infection alone (i.e., not chemotherapy induced).

Validated definition includes either one major criteria or three or more minor criteria

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DIFFERENCES BETWEEN THE 2019 AND 2007 ATS / IDSA CAP GUIDELINE

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Sputum culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or <i>Pseudomonas aeruginosa</i>
Blood culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or <i>P. aeruginosa</i>
Macrolide monotherapy	Strong recommendation for outpatients	Conditional recommendation for outpatients based on resistance levels
Use of procalcitonin	Not covered	Not recommended to determine need for initial antibacterial therapy
Use of corticosteroids	Not covered	Recommended not to use. May be considered in patients with refractory septic shock
Use of healthcare-associated pneumonia category	Accepted as introduced in the 2005 ATS/IDSA hospital-acquired and ventilator-associated pneumonia guidelines	Recommend abandoning this categorization. Emphasis on local epidemiology and validated risk factors to determine need for MRSA or <i>P. aeruginosa</i> coverage. Increased emphasis on deescalation of treatment if cultures are negative
Standard empiric therapy for severe CAP	β -Lactam/macrolide and β -lactam/fluoroquinolone combinations given equal weighting	Both accepted but stronger evidence in favor of β -lactam/macrolide combination
Routine use of follow-up chest imaging	Not addressed	Recommended not to obtain. Patients may be eligible for lung cancer screening, which should be performed as clinically indicated

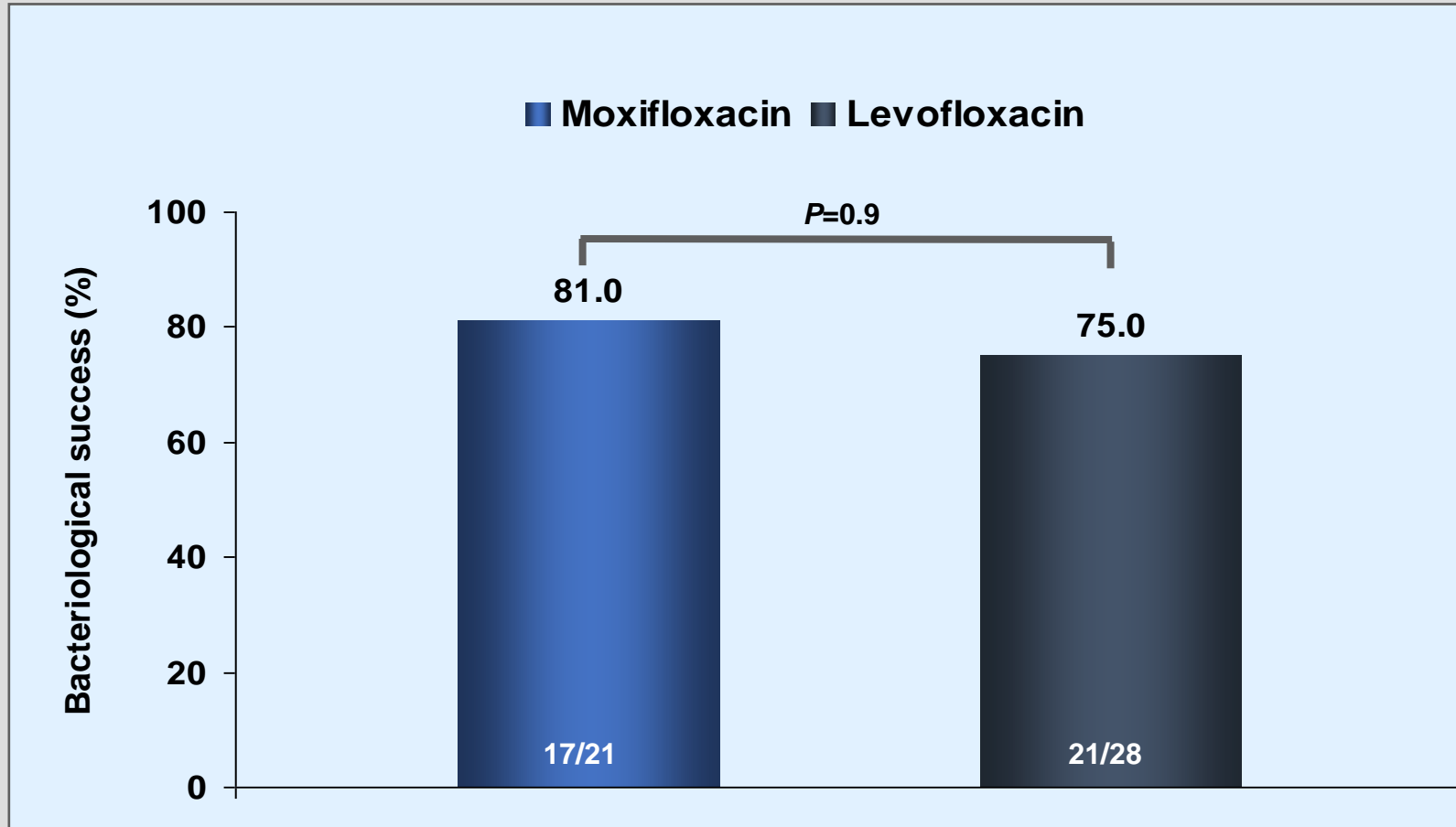
Definition of abbreviations: ATS = American Thoracic Society; CAP = community-acquired pneumonia; IDSA = Infectious Diseases Society of America; MRSA = methicillin-resistant *Staphylococcus aureus*.

ROLE OF MOXIFLOXACIN, ACCORDING TO GUIDELINE

- As **monotherapy**, for initial treatment strategies for *outpatients with CAP, with comorbidities*
 - comorbidities include chronic heart, lung, liver, or renal disease, diabetes mellitus, alcoholism, malignancy, or asplenia
- As **monotherapy**, in the *inpatients settings for empiric treatment of CAP in adults without risk factors for MRSA and P. aeruginosa*

**WHY DO WE RECOMMEND
MOXIFLOXACIN FOR CAP
TREATMENT ?**

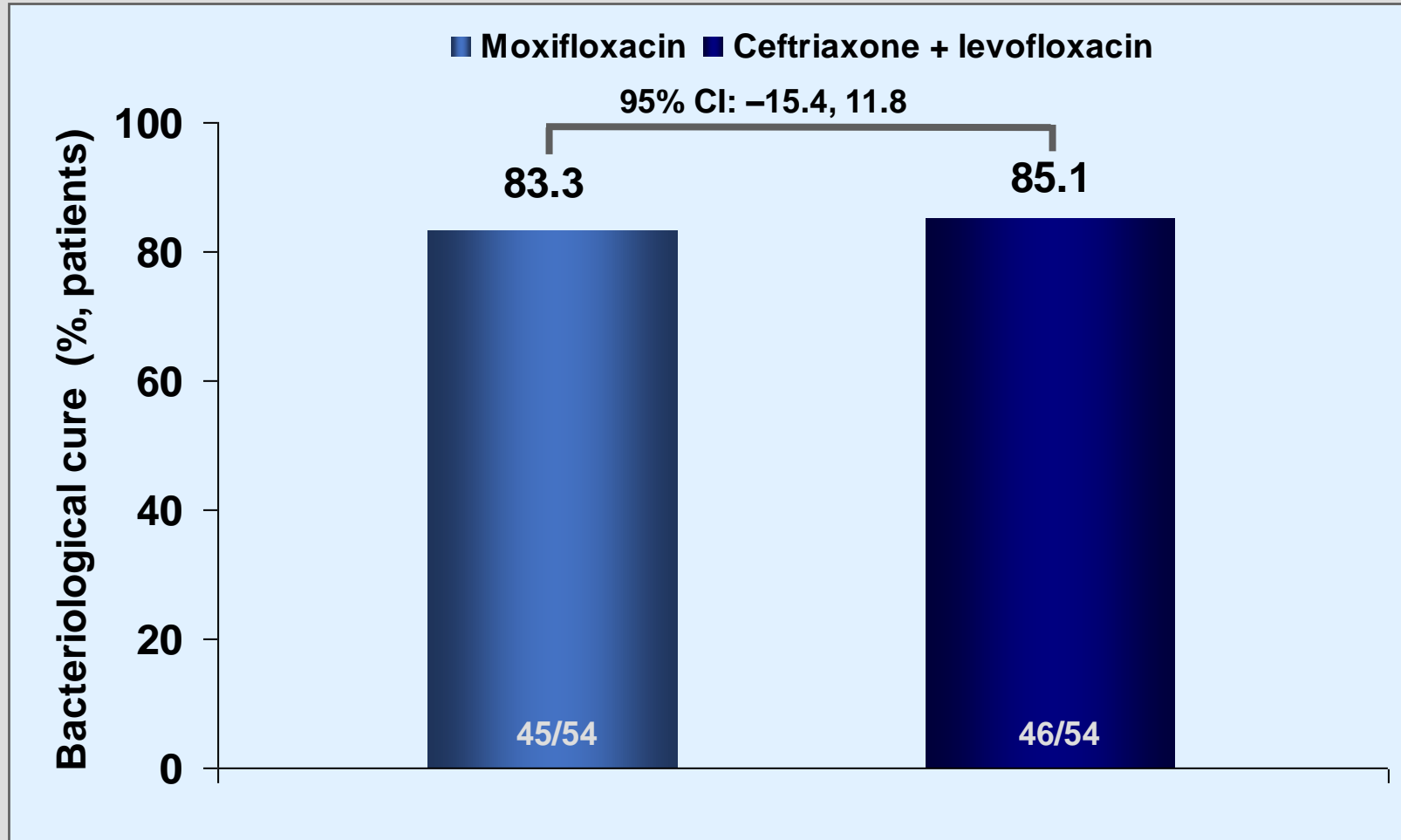
NUMERICALLY HIGHER BACTERIOLOGICAL SUCCESS[‡] RATES FOR MOXIFLOXACIN VS LEVOFLOXACIN IN CAP (CAPRIE)



[‡]Eradication or presumed eradication

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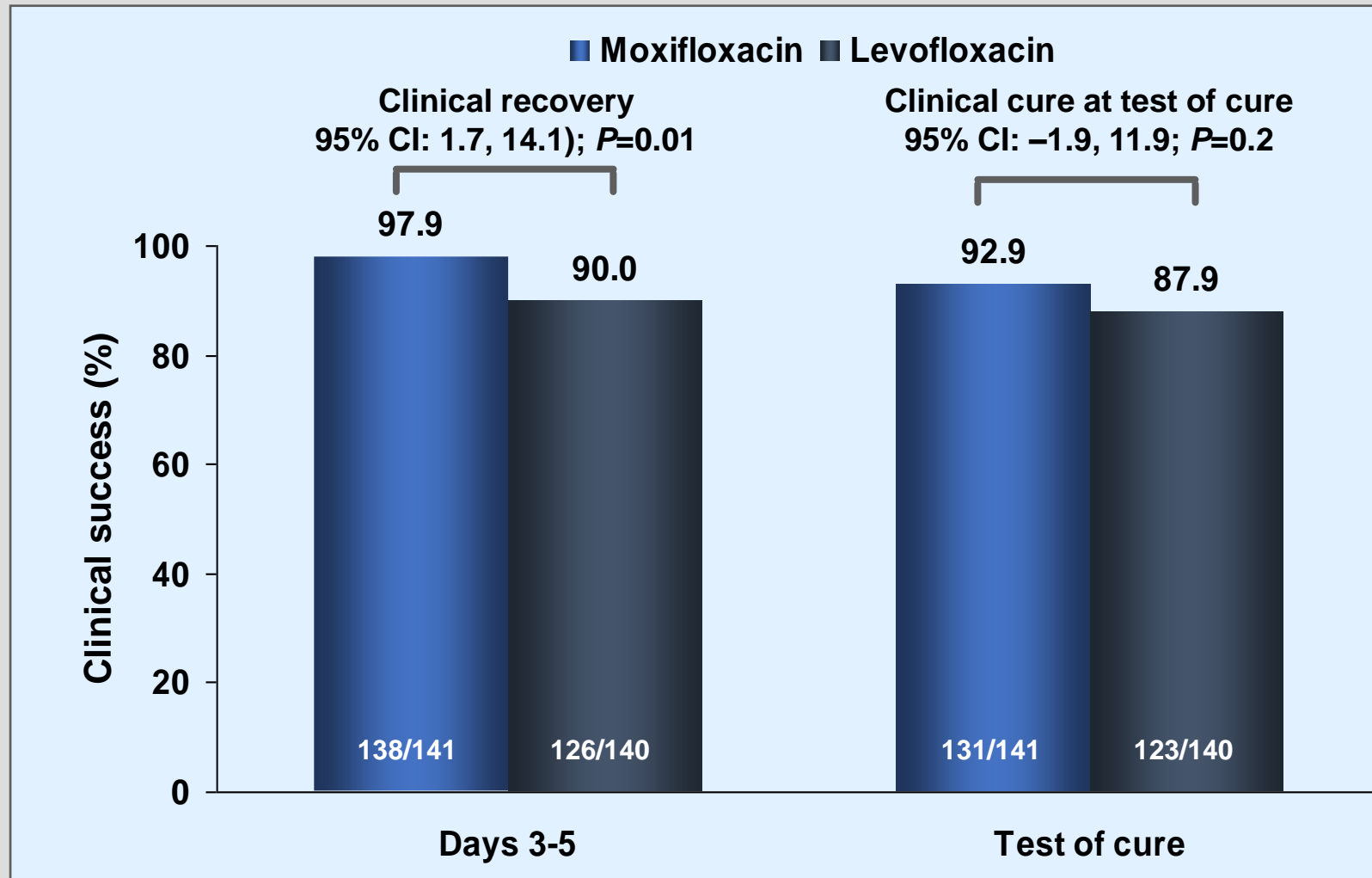
EQUIVALENT BACTERIOLOGICAL SUCCESS[‡] RATES IN CAP FOR MOXIFLOXACIN VS HIGH DOSE COMBINATION CEFTRIAXONE PLUS LEVOFLOXACIN (MOTIV)



[‡]Eradication or presumed eradication; both respiratory and blood sites combined in the microbiologically valid population

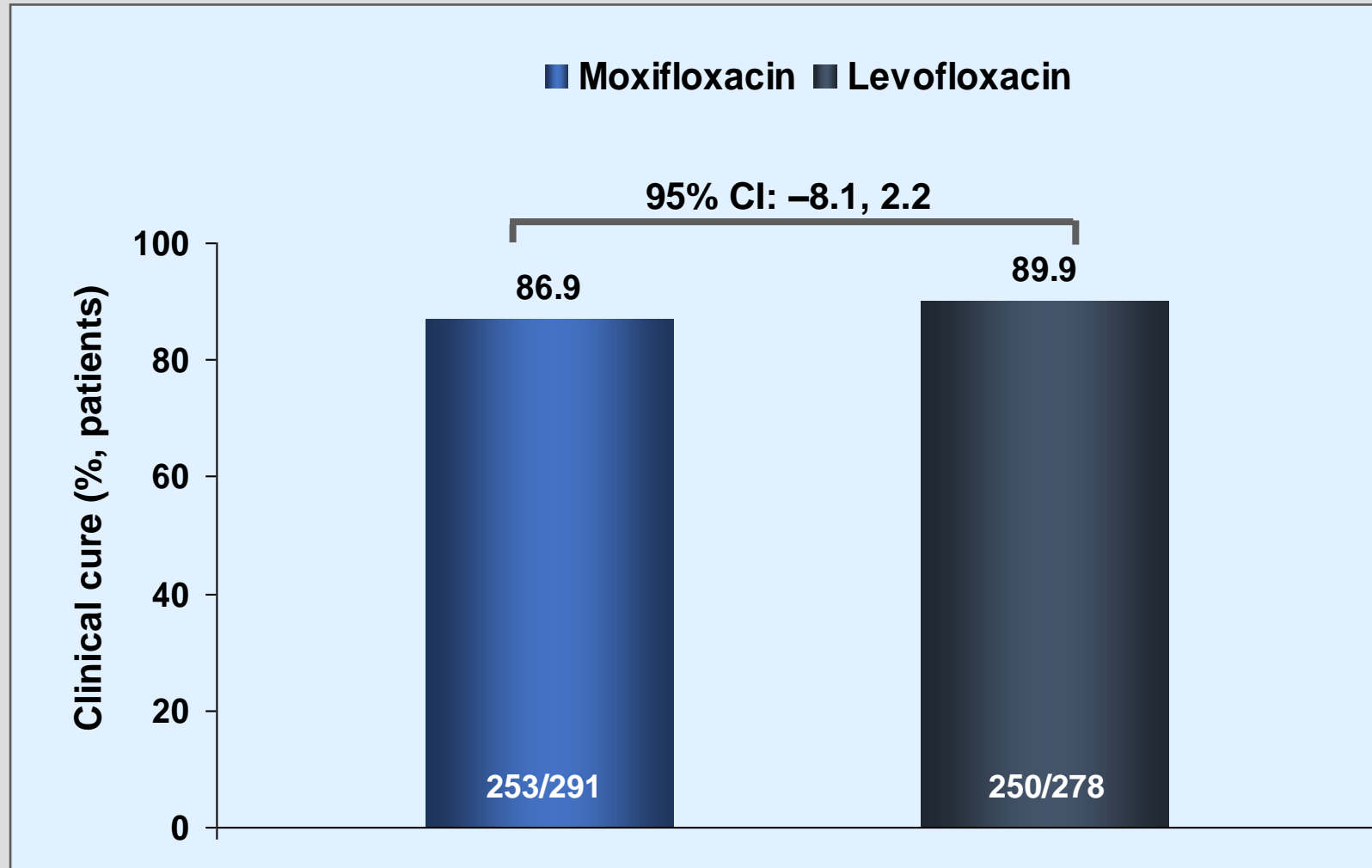
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MOXIFLOXACIN PROVIDES FASTER CLINICAL RECOVERY RATES THAN LEVOFLOXACIN IN CAP (CAPRIE)



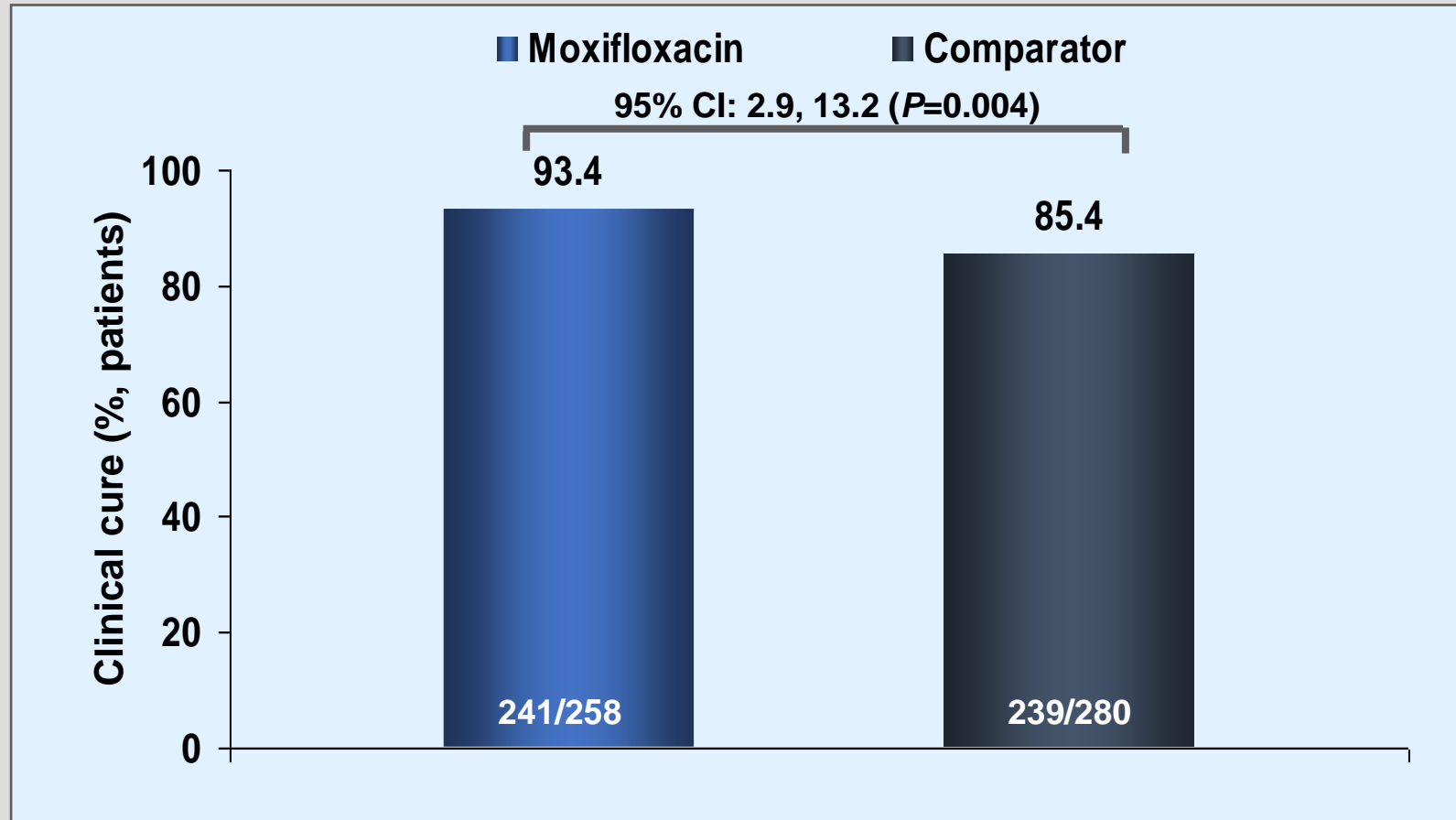
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MOXIFLOXACIN MONOTHERAPY IS AS CLINICALLY EFFECTIVE AS 'STRONG' COMBINATION THERAPY WITH CEFTRIAXONE PLUS LEVOFLOXACIN (MOTIV)



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MOXIFLOXACIN MONOTHERAPY IS AS CLINICALLY EFFECTIVE AS COMBINATION THERAPY WITH CO-AMOXICLAV ± CLARITHROMYCIN (TARGET)



- Monotherapy with IV/PO moxifloxacin also provides faster resolution of fever vs comparator (median 2 days vs 3 days; $P=0.008$)

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MOXIFLOXACIN IS AN EFFECTIVE ORAL TREATMENT FOR CAP

Patient group	Comparators	Outcome
Mild-to-moderate CAP ¹	Amoxicillin 1 g tds PO Clarithromycin 500 mg bd PO Amoxicillin 1 g tds PO + clarithromycin 500 mg bd PO	Moxifloxacin PO as monotherapy is as effective as, and better tolerated than, PO monotherapy or combination therapy with a β -lactam and/or a macrolide
All CAP patients ²	Clarithromycin 500 mg bd PO	Once daily treatment with moxifloxacin PO is as clinically and bacteriologically effective as twice daily PO therapy with a standard macrolide for the treatment of CAP
CAP due to <i>S. pneumoniae</i> and <i>H. influenzae</i> ³	Clarithromycin 500 mg bd PO	Moxifloxacin PO once daily is significantly more effective than treatment twice daily with a standard macrolide in patients with CAP due to <i>S. pneumoniae</i> and/or <i>H. influenzae</i>

1) Torres *et al. Eur Resp J* 2003; **21**: 135–43

2) Hoeffken *et al. Respir Med* 2001; **95**: 553–64

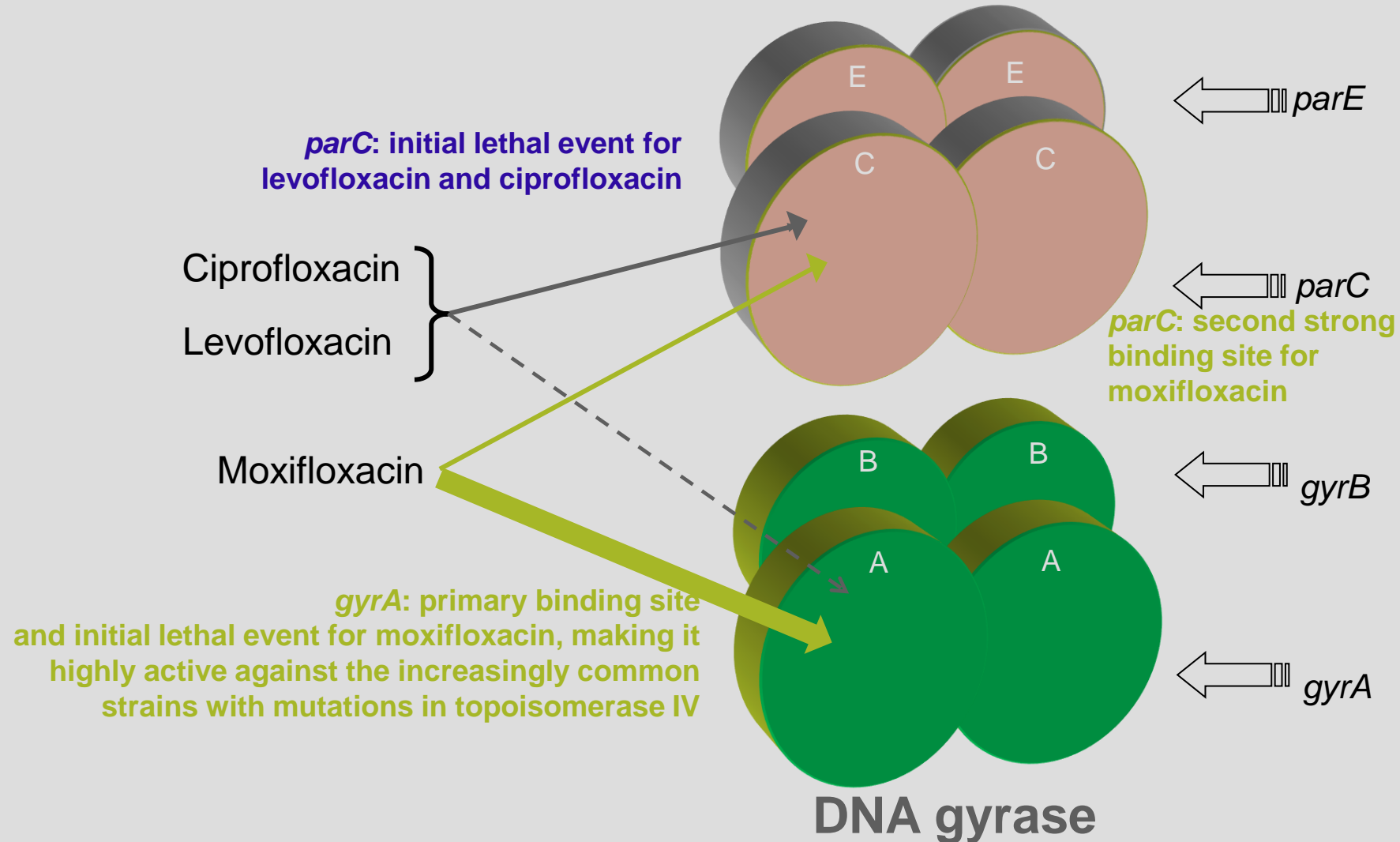
3) Data on file, Bayer

RESISTANCE TO MOXIFLOXACIN REMAINS LOW AND STABLE IN THE CLINICAL ENVIRONMENT

- The susceptibility patterns and the MIC₉₀ values of moxifloxacin for the three major RTI pathogens have remained virtually unchanged in some countries since its launch in 1999¹
 - The serum C_{max} of moxifloxacin 400 mg exceeds the MPC for *S. pneumoniae*, while that of levofloxacin 500 mg does not²
 - The AUC/MIC ratio for moxifloxacin 400 mg is higher than 100, unlike the AUC/MIC ratio for levofloxacin 500 mg or 750 mg^{3,4}
 - Moxifloxacin kills *S. pneumoniae* and other RTI pathogens more rapidly than levofloxacin⁵
 - The dual mechanism of action of moxifloxacin and its high intrinsic affinity for DNA gyrase makes it difficult for resistant mutations to develop⁶

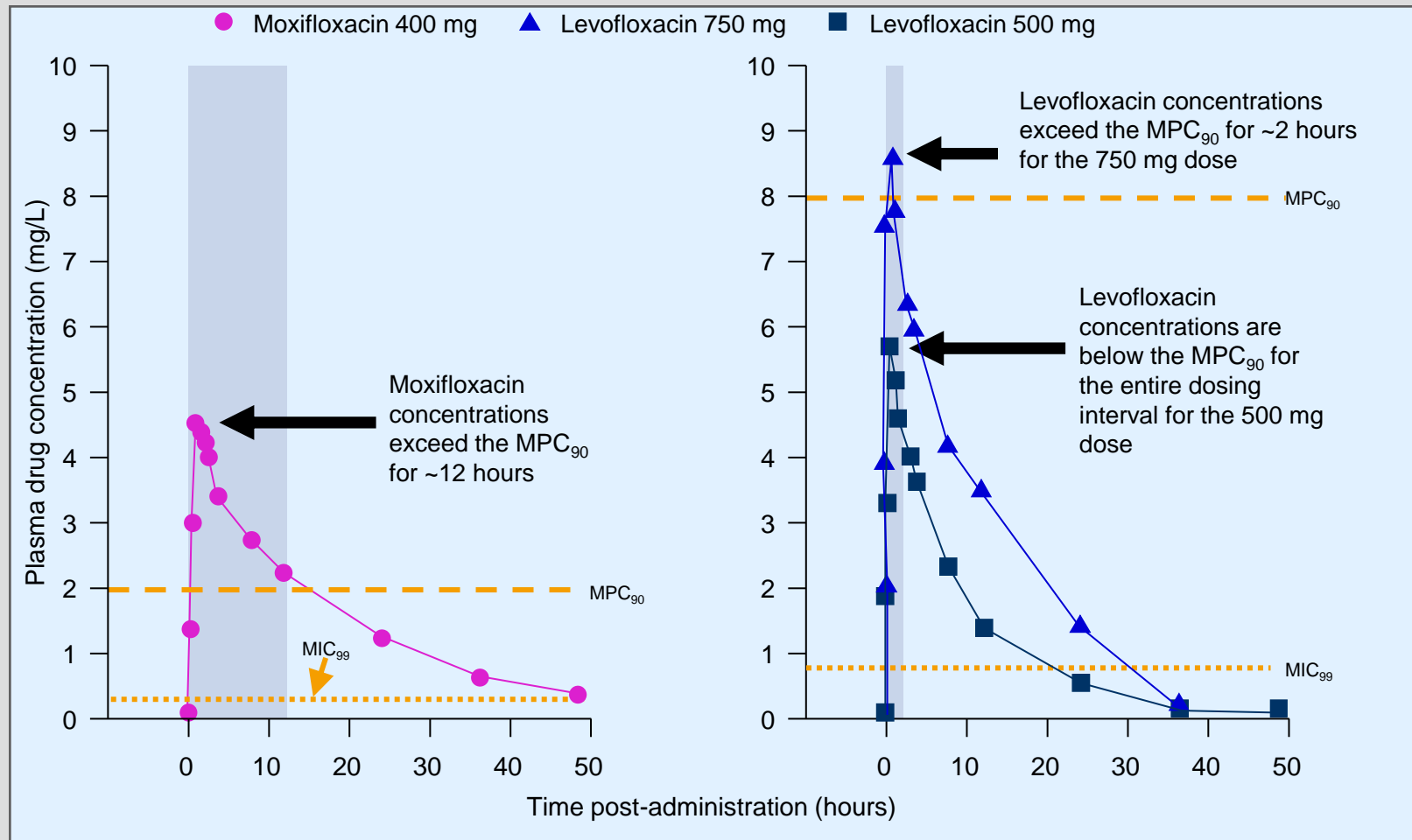
DUAL MODE OF ACTION OF MOXIFLOXACIN REDUCES THE LIKELIHOOD OF RESISTANCE DEVELOPING¹⁻⁴

Topoisomerase IV



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MOXIFLOXACIN IS LESS LIKELY THAN LEVOFLOXACIN TO SELECT FOR RESISTANCE IN *S. PNEUMONIAE*



MPC, mutant prevention concentration for *S. pneumoniae*

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SUMMARY

- 2019 ATS / IDSA CAP Guideline is providing updates on how's treatment management for CAP
- Moxifloxacin is recommended by 2019 ATS / IDSA CAP Guideline for treatment of CAP, both as monotherapy or in combination with other antibiotics
- Avelox® is the original moxifloxacin, providing option for CAP management; with proven efficacy and safety profile.

THANK YOU