Bactéries émergentes dans la mucoviscidose et les dilatations des bronches : le point de vue du clinicien

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Pas de lien d’intérêt en rapport avec cette présentation

“Bactéries émergentes”

Amélioration de la détection de certaines bactéries

Cultures plus systématiques

Milieux spéciaux

Techniques moléculaires (séquençage 16s, microbiome)

Spectrométrie de masse

Changements de taxonomie

Changement de population

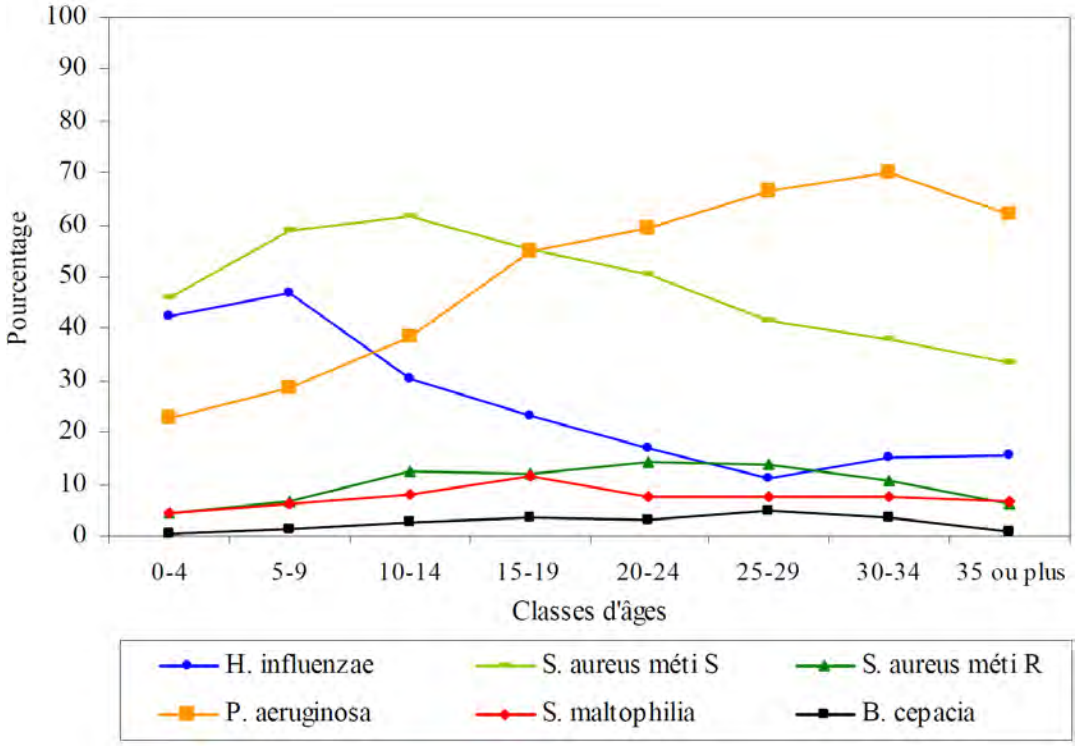
Vieillissement de la population de Mucoviscidose

Impact des antibiotiques (oraux/IV/inhales):

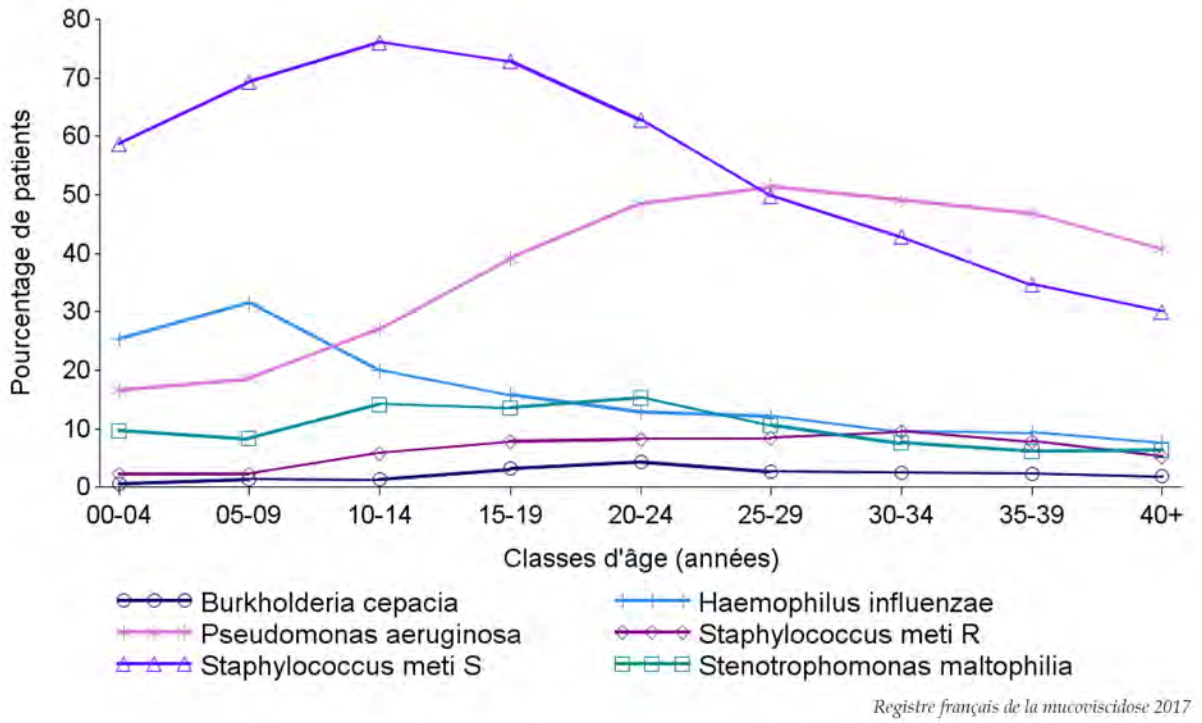
- Souches résistantes (“Pan R”)
- Espèces résistantes

Registre Français de la Mucoviscidose

2007

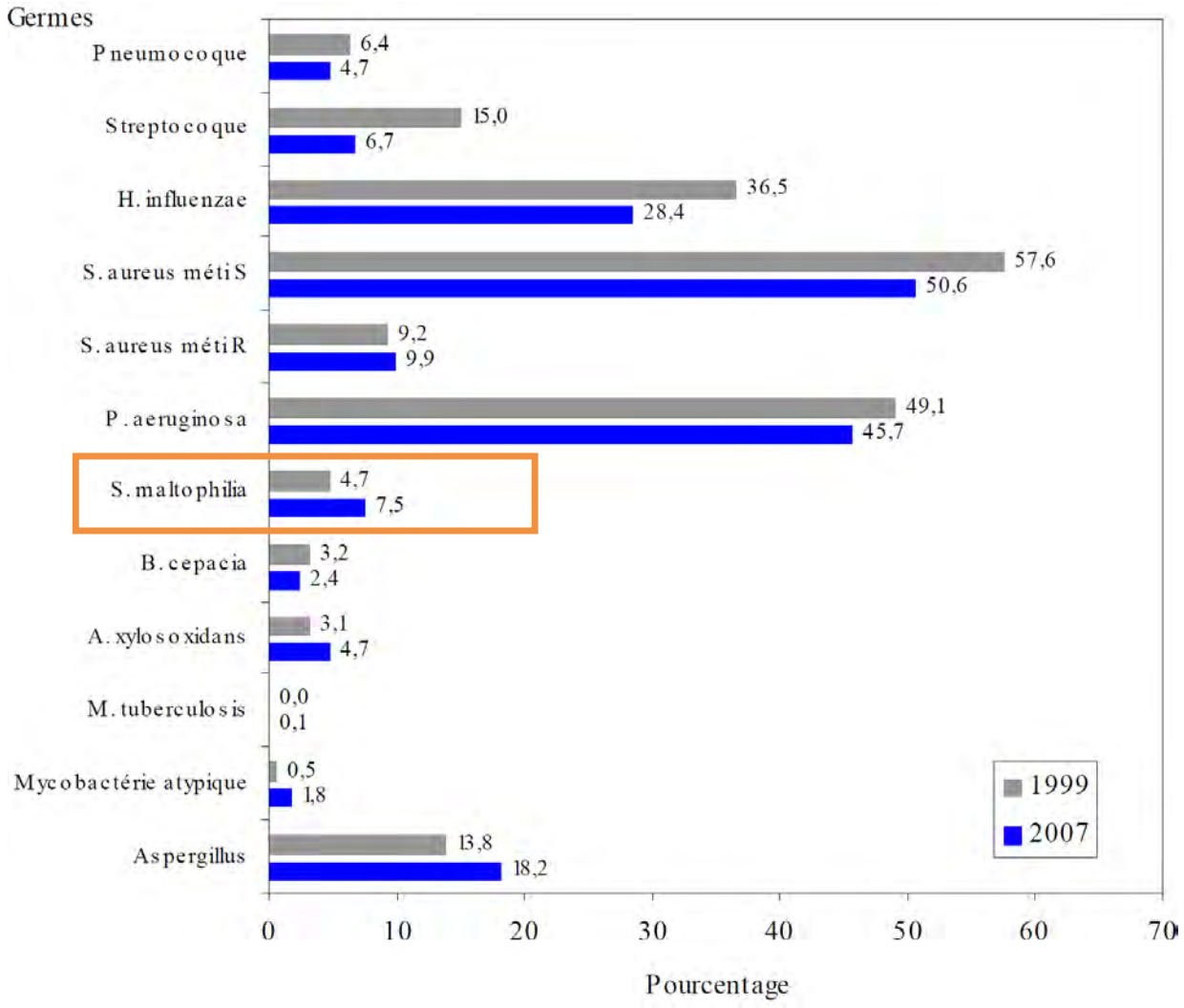


2017

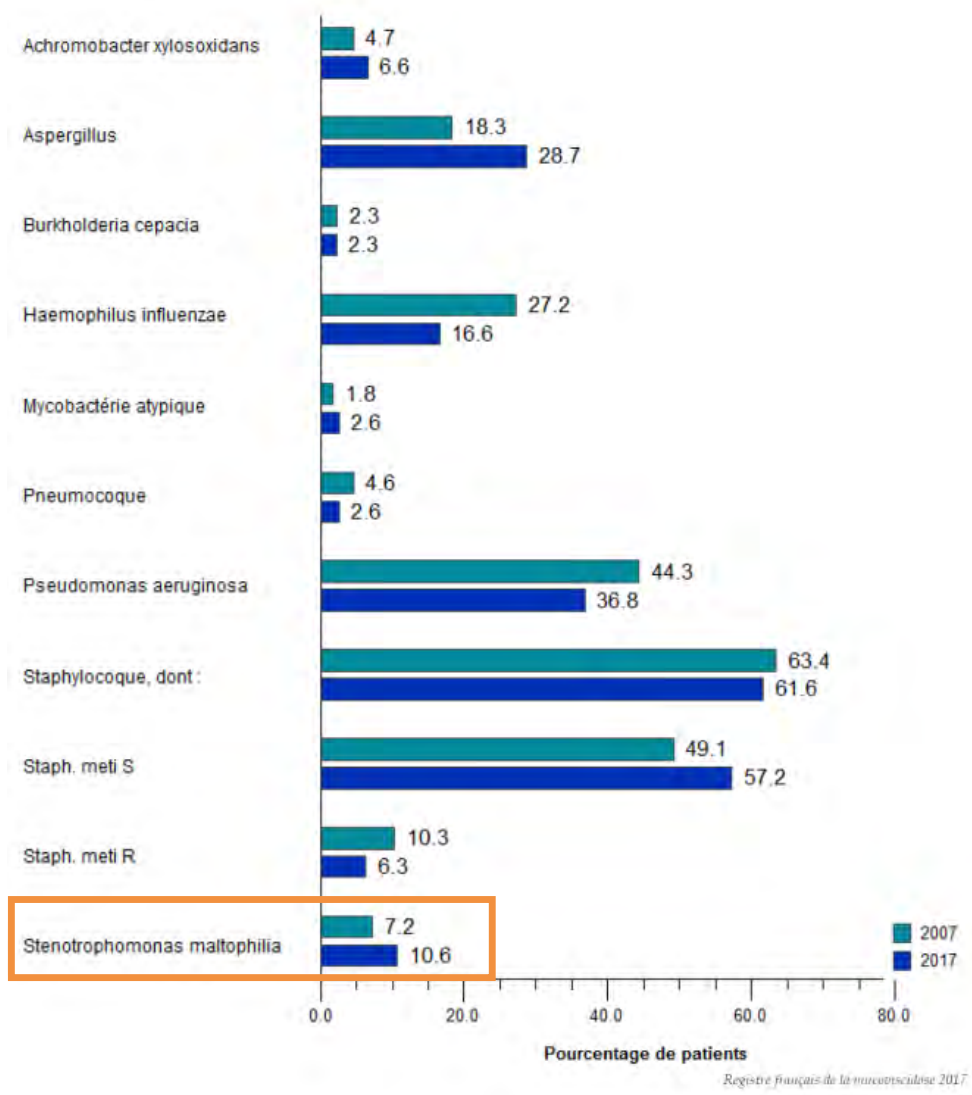


Registre Français de la Mucoviscidose

1999-2007



2007-2017



CURRENT OPINION

Emerging Gram-negative bacteria: pathogenic or innocent bystanders

Purpose of review

The current review examines the current literature around 'emerging' Gram-negative bacteria other than *Pseudomonas aeruginosa* in cystic fibrosis (CF), paying particular focus on the recent literature for those that are more frequently encountered: *Pandoraea*, *Achromobacter*, *Ralstonia* and *Stenotrophomonas* species.

Recent findings

The recent literature is evolving our understanding of the clinical consequences of infection with an 'emerging' Gram-negative bacteria in CF. There is an increase in reported prevalence for many species. They are commonly isolated from patients who already have low baseline lung function. Initial infection can lead to chronic carriage, often with evidence of an associated host immune response and subsequent clinical deterioration. For some species occasional cases of bacteraemia have been reported.

Summary

There are a number of Gram-negative organisms, other than *P. aeruginosa*, that can cause chronic infection in patients with CF. There is data to suggest that some of these so-called emerging Gram-negative bacteria are increasing in prevalence and can be pathogenic in patients with CF. The prevalence and clinical consequences however differ from species to species. There is a pressing need to agree a definition of chronic infection for these organisms to compare data between studies.

Keywords

Achromobacter, cystic fibrosis, emerging pathogens, *Pandoraea*, *Ralstonia*, *Stenotrophomonas*

Table 1. Species of *Achromobacter*

Achromobacter aegrifaciens
Achromobacter agilis
Achromobacter aloeverae
Achromobacter animicus
Achromobacter anxifer
Achromobacter deleyi
Achromobacter denitrificans
Achromobacter dolens
Achromobacter insolitus
Achromobacter insuavis
Achromobacter kerstersii
Achromobacter marplatensis
Achromobacter mucicolens
Achromobacter panacis
Achromobacter pestifer
Achromobacter piechaudii
Achromobacter pulmonis
Achromobacter ruhlandii
Achromobacter spanius
Achromobacter xylosoxidans
Previously described species of *Achromobacter*, now reclassified
Achromobacter sediminum – reclassified to novel genus *Verticia sediminum*
Achromobacter spiritinus – reclassified as *Achromobacter marplatensis*

Curr Opin Pulm Med 2018

Detection of Anaerobic Bacteria in High Numbers in Sputum from Patients with Cystic Fibrosis

Michael M. Tunney[1], Tyler R. Field[1], Thomas F. Moriarty[1], Sheila Patrick[2], Gerd Doering[3], Marianne S. Muhlebach[4], Matthew C. Wolfgang[5,6], Richard Boucher[6,7], Deirdre F. Gilpin[1], Andrew McDowell[2], and J. Stuart Elborn[2]

TABLE 1. BACTERIA ISOLATED BY CULTURE FROM THE SPUTUM OF ADULT PATIENTS WITH CYSTIC FIBROSIS

Anaerobic Isolates			Aerobic Isolates		
Genera*	No. Isolates	No. Patients	Genera	No. Isolates	No. Patients
Prevotella	20	11	*Pseudomonas*	51	28
Actinomyces	9	8	*B. cepacia* complex	4	4
Veillonella	8	7	*Rothia*	30	17
Propionibacterium	7	7	*Streptococcus*	27	19
Peptostreptococcus	2	2	*Staphylococcus*	23	20
Bulleidia	2	2	*Micrococcus*	4	3
Bifidobacterium	2	1	*Nessieria*	4	4
Gemella	2	2	*Bacillus*	3	3
Lactobacillus	2	2	*Escherichia*	3	2
Fusobacterium	1	1	*Stenotrophomonas*	2	1
Clostridium	1	1			
Staphylococcus	2	2			
Streptococcus	19	13			
Rothia	1	1			
Total	78			151	

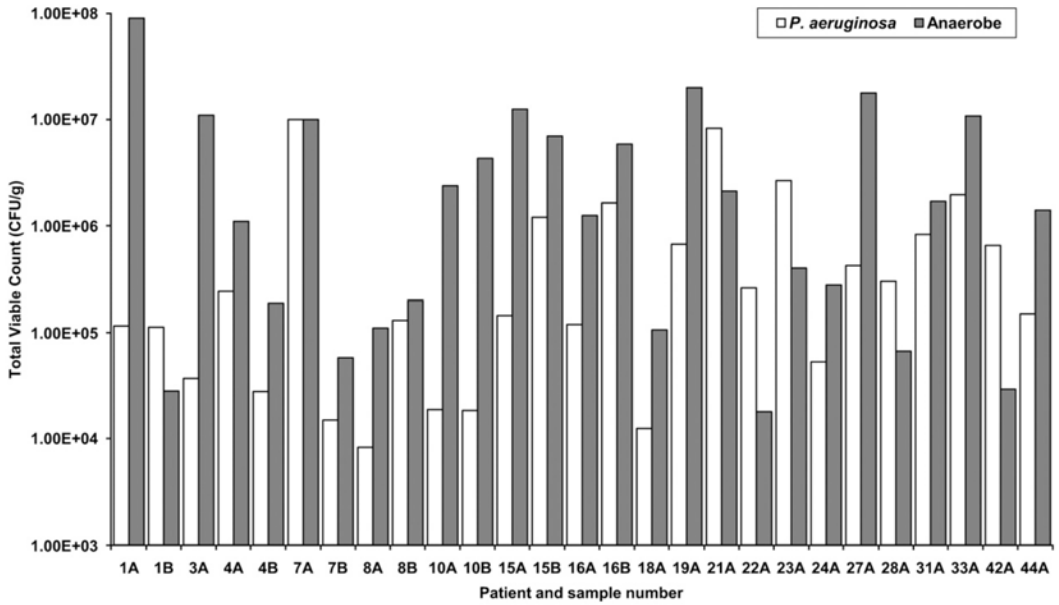
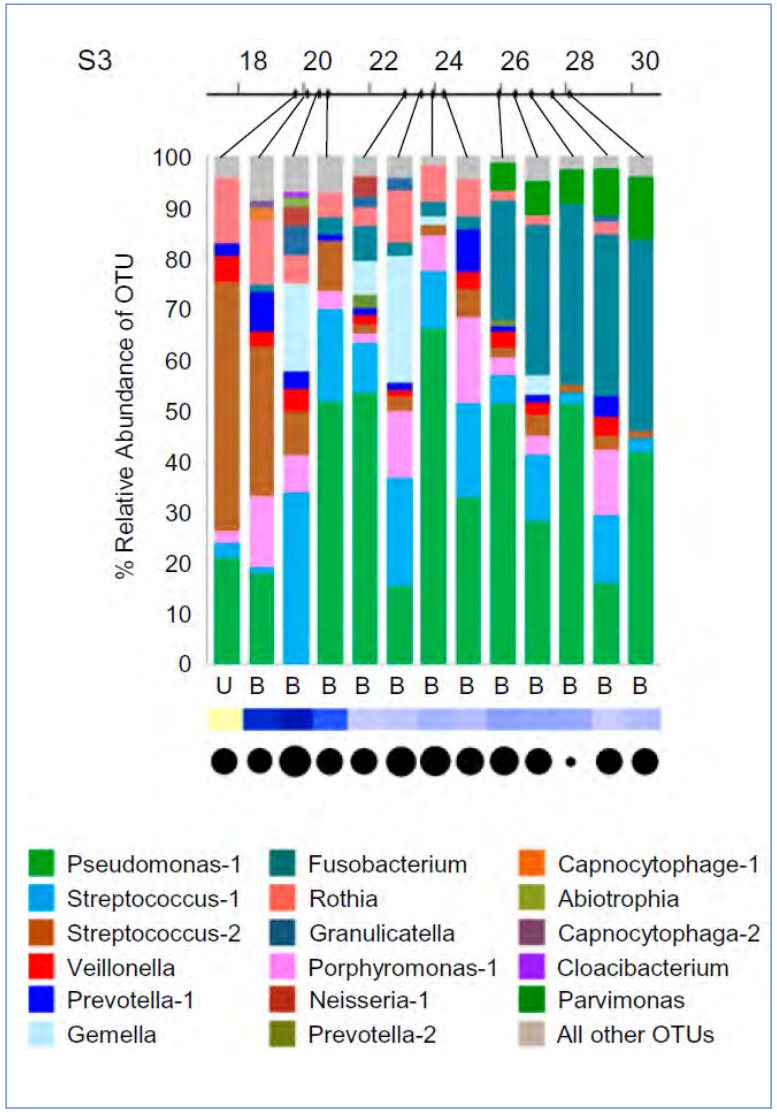


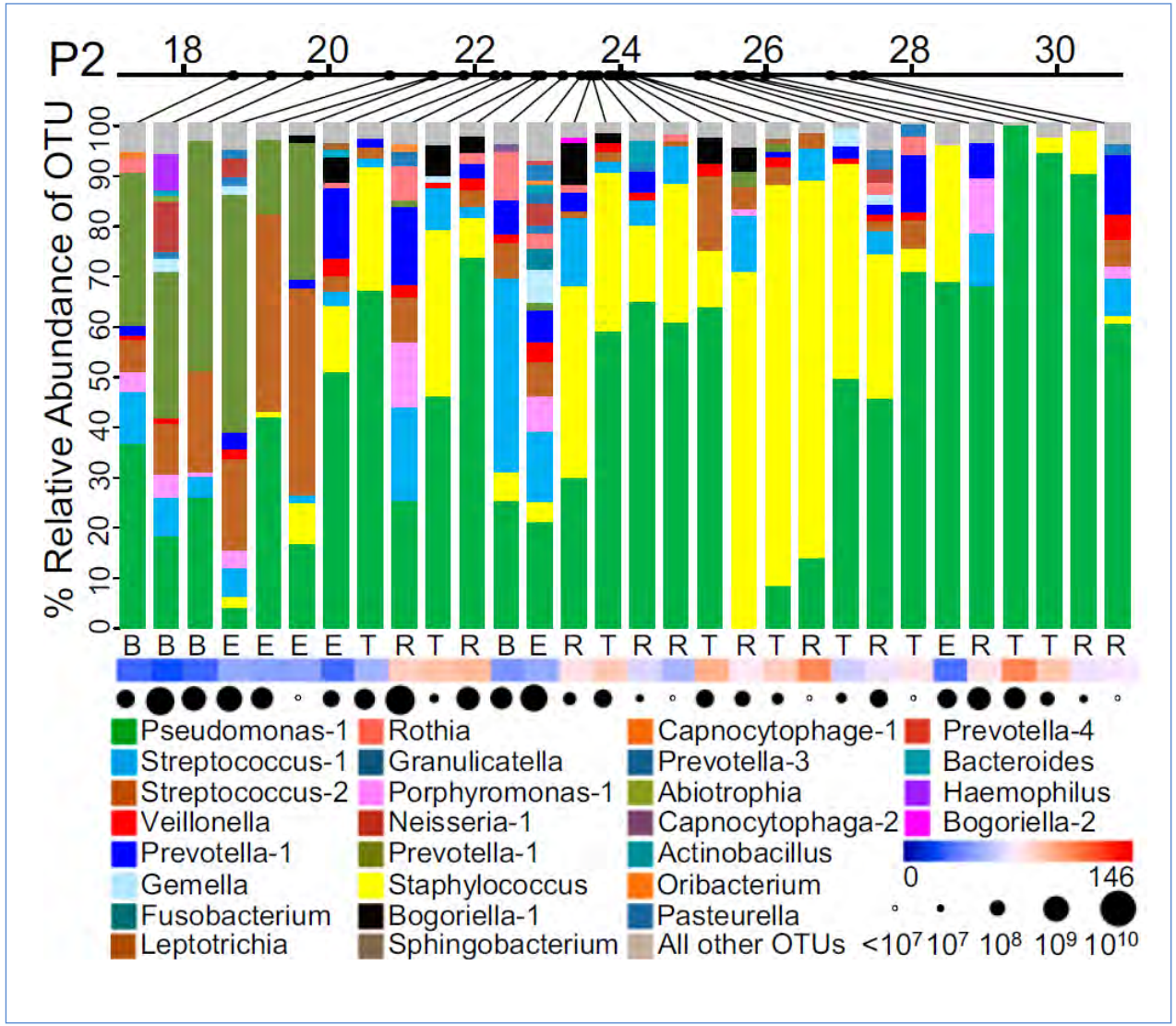
TABLE 2. ANTIMICROBIAL SUSCEPTIBILITY OF ANAEROBIC BACTERIA ISOLATED FROM THE SPUTUM OF ADULT PATIENTS WITH CYSTIC FIBROSIS

	Ampicillin			Clindamycin			Meropenem			Metronidazole			Piperacillin/Tazobactam		
Genera (no. isolates)	MIC_{50}	MIC_{90}	Suscept* (%)	MIC_{50}	MIC_{90}	Suscept (%)	MIC_{50}	MIC_{90}	Suscept (%)	MIC_{50}	MIC_{90}	Suscept (%)	MIC_{50}	MIC_{90}	Suscept (%)
All isolates (39)	0.25	16	67	0.25	> 256	79	0.064	0.5	100	8	> 256	53	0.38	> 256	87
Prevotella (14)	0.094	24	64	0.19	> 256	64	0.047	0.094	100	0.094	> 256	54	0.125	2	93
Veillonella (5)	0.25	1	60	0.125	1	100	0.094	0.19	100	0.75	1	80	> 256	> 256	20
Propionibacterium (5)	0.064	0.125	80	0.032	0.19	100	0.064	0.25	100	> 256	> 256	20	0.094	0.5	100
Actinomyces (8)	0.125	1.5	62.5	0.19	2	87.5	0.032	1	100	8	64	62.5	0.038	6	100
Other (7)	0.125	1.5	71	0.19	> 256	71	0.047	0.125	100	6	> 256	43	0.25	0.5	100

Am J Respir Crit Care Med Vol 177. pp 995–1001, 2008

La mucoviscidose, une maladie infectieuse polymicrobienne





Zhao et al, PNAS 2012;109:5809-14

Antimicrobial resistance in the respiratory microbiota of people with cystic fibrosis

Laura J Sherrard, Michael M Tunney, J Stuart Elborn

- Complex culture and molecular methods have shown that cystic fibrosis pulmonary infection is polymicrobial, and that the types and abundance of bacteria present in cystic fibrosis respiratory samples differ between individuals and over time
- Emergence of antimicrobial resistance and selection of highly antibiotic-resistant recognised cystic fibrosis pathogens is expected as patients are living longer and ultimately exposed to an increasing number and combination of antibiotics
- Antibiotic resistance has been reported in bacteria belonging to the cystic fibrosis airway microbiota, whose clinical significance is unknown

***Lancet* 2014; 384: 703–13**

Overcoming an Extremely Drug Resistant (XDR) Pathogen: Avibactam Restores Susceptibility to Ceftazidime for *Burkholderia cepacia* Complex Isolates from Cystic Fibrosis Patients

Krisztina M. Papp-Wallace[†,‡,Π,*,Γ], **Scott A. Becka**[†], **Elise T. Zeiser**[†], **Nozomi Ohuchi**[§], **Maria F. Mojica**[†,Π], **Julian A. Gatta**[†], **Monica Falleni**[Σ], **Delfina Tosi**[Σ], **Elisa Borghi**[Σ], **Marisa L. Winkler**[†,#], **Brigid M. Wilson**[†], **John J. LiPuma**[⊗], **Michiyoshi Nukaga**[§], and **Robert A. Bonomo**[†,‡,#,⊥,Π,*,Γ]

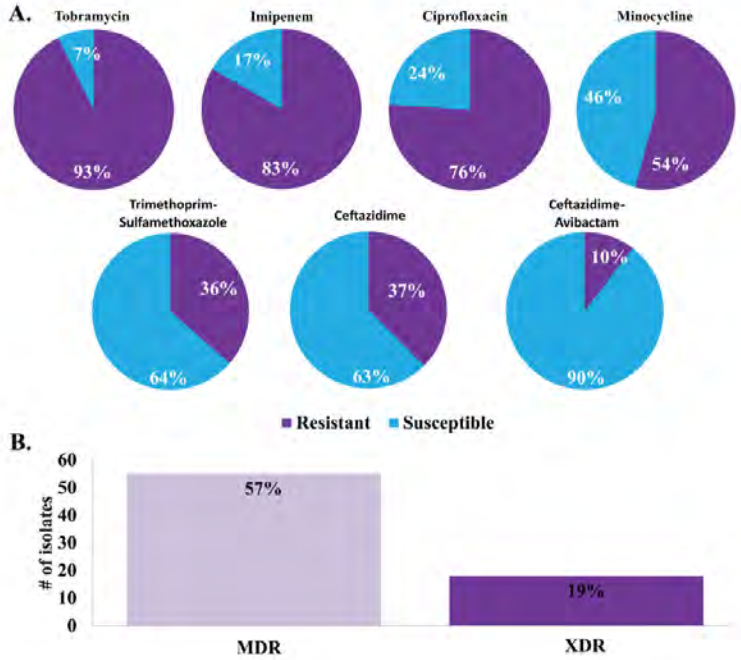


Figure 5.
Susceptibility testing of the 96 clinical non-*B. multivorans Burkholderia* spp. isolates from CF patients. (A) Summary pie charts of the susceptibility testing results (susceptible (blue) and resistant (purple)) conducted with tobramycin, imipenem, ciprofloxacin, minocycline, trimethroprim–sulfamethoxazole, ceftazidime, and ceftazidime–avibactam. (B) Bar graph representing the number of isolates that are MDR and XDR.

ACS Infect Dis. 2017 July 14; 3(7): 502–511. doi:10.1021/acsinfecdis.7b00020

In Vitro Activity of Ceftolozane-Tazobactam against Multidrug-Resistant Nonfermenting Gram-Negative Bacilli Isolated from Patients with Cystic Fibrosis

Patrick Grohs,[a] Gary Taieb,[a] Philippe Morand,[b,c] Iheb Kaibi,[a] Isabelle Podglajen,[a,c] Marie Lavollay,[a,c,d] Jean-Luc Mainardi,[a,c,d] Fabrice Compain[a,c,d]

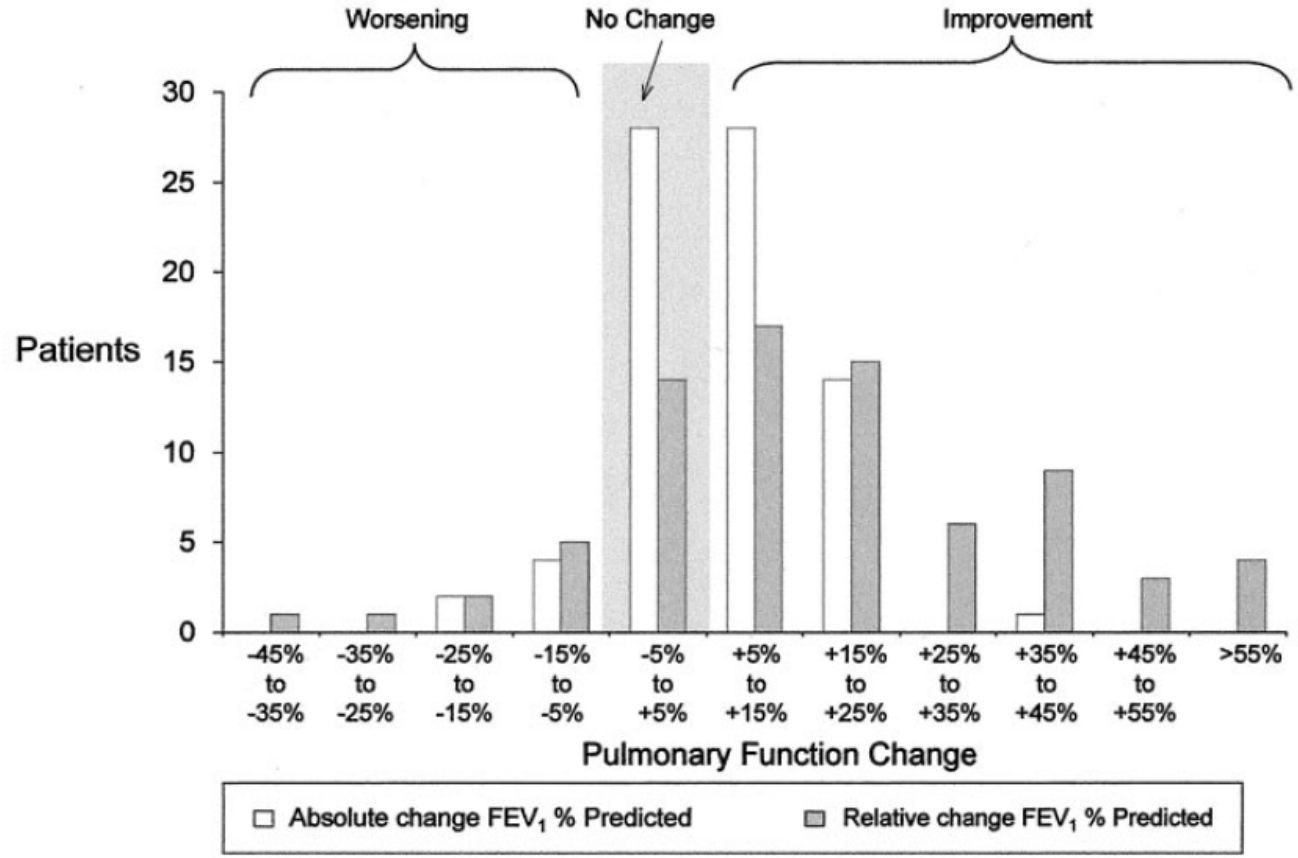
AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

April 2017 Volume 61 Issue 4 e02688-16

Species and antimicrobial agent(s)	MIC (μg/ml)			EUCAST clinical breakpoint (μg/ml)	No. of strains			Proportion of susceptible strains (%)
	MIC range	MIC_{50}	MIC_{90}		Resistant	Intermediate	Susceptible	
All isolates (n = 58)								
Ceftolozane	0.5 to >128	16	>128					
Ceftolozane + tazobactam	0.5 to >128	16	>128					
Ceftazidime	4 to >128	128	>128					
Piperacillin + tazobactam	1 to >128	64	>128					
Meropenem	0.5 to >128	32	>128					
Pseudomonas aeruginosa (n = 35)								
Ceftolozane	0.5 to >128	4	128					
Ceftolozane + tazobactam[a]	0.5 to >128	4	128	≤4 to >4	16		19	54
Ceftazidime	4 to >128	128	>128	≤8 to >8	31		4	11
Piperacillin + tazobactam	2 to >128	128	>128	≤16 to >16	26		9	26
Meropenem	1 to >128	16	128	≤2 to >8	26	6	3	9
Stenotrophomonas maltophilia (n = 12)								
Ceftolozane	16 to >128	64	>128					
Ceftolozane + tazobactam	16 to >128	64	>128	≤4 to >4	12		0	0
Ceftazidime	16 to >128	128	>128	≤8 to >16	11	1	0	0
Piperacillin + tazobactam	8 to >128	128	>128	≤4 to >16	11	0	1	8
Meropenem	4 to >128	>128	>128	≤2 to >8	10	2	0	0
Achromobacter xylosoxydans (n = 11)								
Ceftolozane	>128	>128	>128					
Ceftolozane + tazobactam	>128	>128	>128	≤4 to >4	11		0	0
Ceftazidime	32 to >128	>128	>128	≤4 to >8	11	0	0	0
Piperacillin + tazobactam	1 to 64	16	32	≤4 to >16	3	6	2	18
Meropenem	0.5 to >128	32	128	≤2 to >8	9	1	1	9

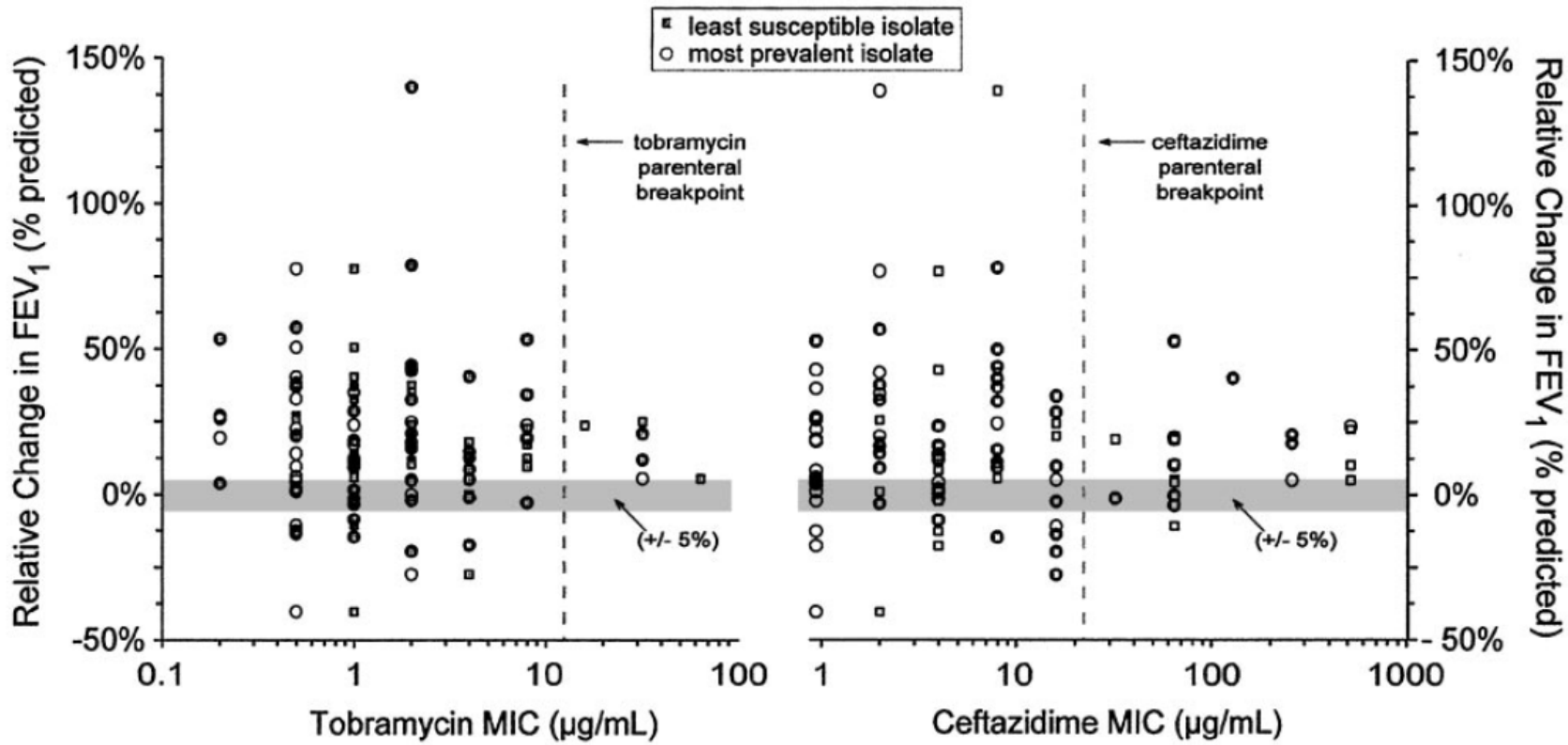
Susceptibility Testing of Pseudomonas aeruginosa Isolates and Clinical Response to Parenteral Antibiotic Administration: Lack of Association in Cystic Fibrosis

VEMS post antibiothérapie IV



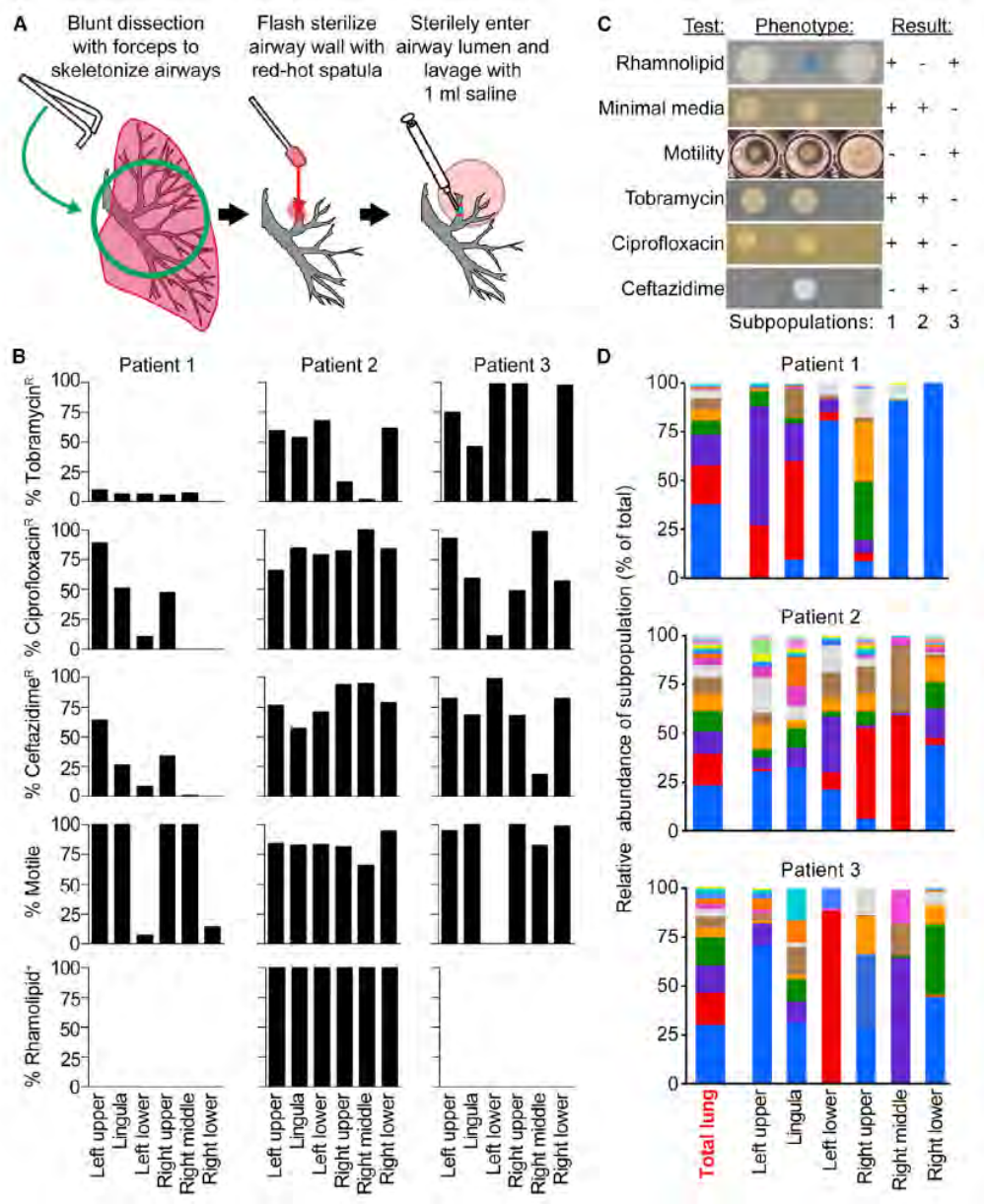
Smith et al. *Chest* 2003;123;1495-1502

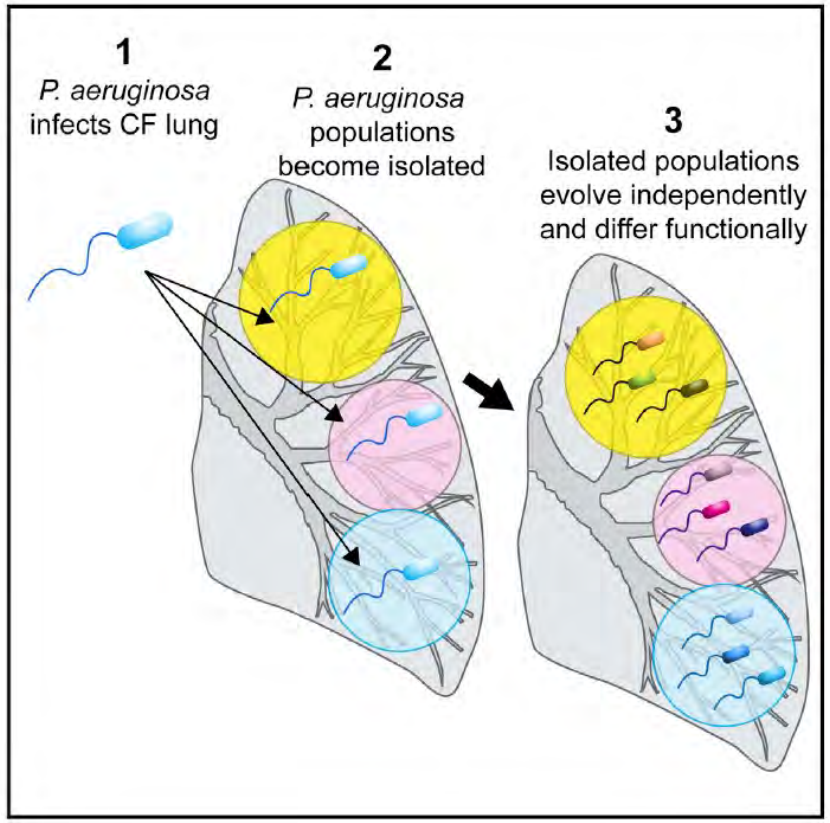
Susceptibility Testing of Pseudomonas aeruginosa Isolates and Clinical Response to Parenteral Antibiotic Administration: Lack of Association in Cystic Fibrosis



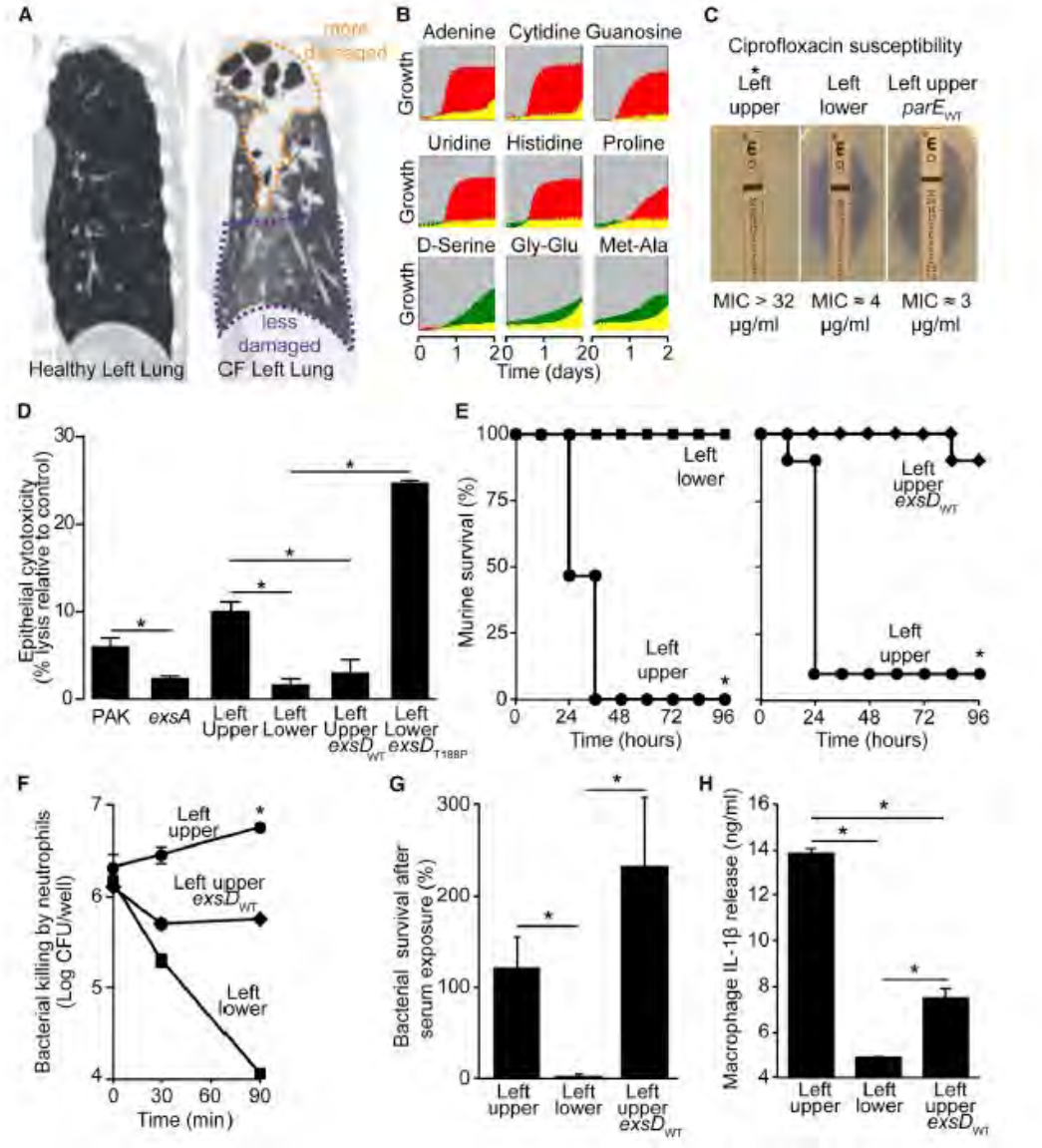
Smith et al. *Chest* 2003;123;1495-1502

Regional Isolation Drives Bacterial Diversification within Cystic Fibrosis Lungs





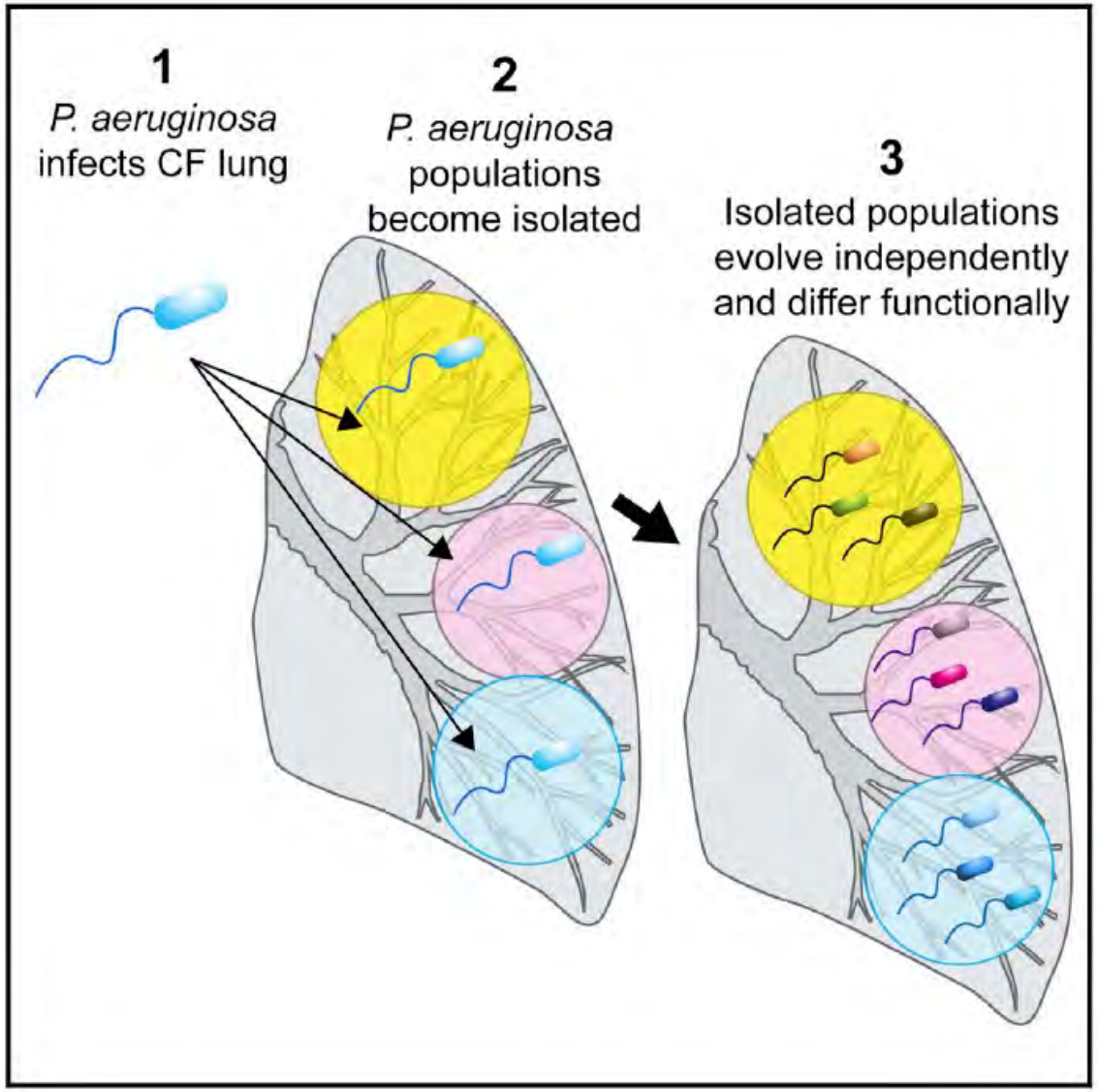
Jorth et al., 2015, Cell Host & Microbe 18, 307–319



Pas d'intérêt clinique de l'antibiogramme sur l'ECBC lors de l'infection bactérienne chronique à P. aeruginosa de la mucoviscidose

Jorth et al., 2015, Cell Host & Microbe 18, 307–319

Diversité de Pseudomonas dans le poumon mucoviscidosique



Jorth et al. Cell Host Microbe 2015

Antimicrobial Resistance in Cystic Fibrosis

Clinical Infectious Diseases
VIEWPOINTS

Reconciling Antimicrobial Susceptibility Testing and Clinical Response in Antimicrobial Treatment of Chronic Cystic Fibrosis Lung Infections

Valerie J. Waters,[1] Timothy J. Kidd,[2] Rafael Canton,[3] Miquel B. Ekkelenkamp,[4] Helle Krogh Johansen,[5] John J. LiPuma,[6] Scott C. Bell,[7] J. Stuart Elborn,[8] Patrick A. Flume,[9] Donald R. VanDevanter,[10] and Peter Gilligan[11]; for the Antimicrobial Resistance International Working Group in Cystic Fibrosis[a]

Journal of Cystic Fibrosis 18 (2019) 236–243
Contents lists available at ScienceDirect
Journal of Cystic Fibrosis
journal homepage: www.elsevier.com/locate/jcf

Original Article

Antimicrobial susceptibility testing (AST) and associated clinical outcomes in individuals with cystic fibrosis: A systematic review

Ranjani Somayaji [a], Michael D. Parkins [b], Anand Shah [c,d], Stacey L. Martiniano [e], Michael M. Tunney [f], Jennifer S. Kahle [g], Valerie J. Waters [h], J. Stuart Elborn [d], Scott C. Bell [i], Patrick A. Flume [j], Donald R. VanDevanter [k,*], on behalf of the Antimicrobial Resistance in Cystic Fibrosis International Working Group

Contents lists available at ScienceDirect
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Original article

Antimicrobial resistance in cystic fibrosis: A Delphi approach to defining best practices

Edith Zemanick [a], Pierre-Régis Burgel [b,l], Giovanni Taccetti [c], Alison Holmes [d], Felix Ratjen [e], Catherine A. Byrnes [f], Valerie J. Waters [g], Scott C. Bell [h], Donald R. VanDevanter [i], J. Stuart Elborn [j], Patrick A. Flume [k,*], on behalf of the Antimicrobial Resistance International Working Group in Cystic Fibrosis

Journal of Cystic Fibrosis 17 (2018) 696–704
www.elsevier.com/locate/jcf

Review

Defining antimicrobial resistance in cystic fibrosis

Timothy J. Kidd [a], Rafael Canton [b], Miquel Ekkelenkamp [c], Helle Krogh Johansen [d], Peter Gilligan [e], John J. LiPuma [f], Scott C. Bell [g], J. Stuart Elborn [h], Patrick A. Flume [i], Donald R. VanDevanter [j], Valerie J. Waters [k,*], on behalf of the Antimicrobial Resistance in Cystic Fibrosis International Working Group

Original article

Antimicrobial resistance in cystic fibrosis: A Delphi approach to defining best practices

Edith Zemanick[a], Pierre–Régis Burgel[b,l], Giovanni Taccetti[c], Alison Holmes[d], Felix Ratjen[e], Catherine A. Byrnes[f], Valerie J. Waters[g], Scott C. Bell[h], Donald R. VanDevanter[i], J. Stuart Elborn[j], Patrick A. Flume[k,*], on behalf of the Antimicrobial Resistance International Working Group in Cystic Fibrosis

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Statements		Median*	IQR	Consensus
Overall	Bacteria identification results should be used to guide antibiotic choices (i.e. genus and species).	10	9–10	Very Good
	Susceptibility results should be used to guide antibiotic choices	6	5–8	Good
New pathogen	Bacteria identification results should be used to guide antibiotic choices (i.e. do not wait for susceptibility test results).	8	7–9.5	Good
	Susceptibility results should be used to guide antibiotic choices (i.e. wait for susceptibility test results).	4	1–7	None
	Susceptibility results should be used to change antibiotic choices (i.e. do not wait for repeat culture data but change antibiotics based on susceptibility test results).	5.5	4–7.5	None
Chronic infection	Bacteria identification results should be used to guide antibiotic choices (i.e. genus and species).	9	8–10	Very Good
	Susceptibility results should be used to guide antibiotic choices.	2	1–5.5	Some
	Antibiotics for chronic suppressive therapy should be changed (i.e. either stopped or switched to another antibiotic) based on results from recent susceptibility testing.	2	1–5.5	Some
Exacerbation	Previous treatment should be used to guide antibiotic choices.	8	7.5–9	Good
	Bacterial identification results (i.e. genus and species) should be used to guide antibiotic choices.	9	8–10	Very Good
	Susceptibility results should be used to guide antibiotic choices.	6	3–8	None

* Scored on a scale of 0 to 10, where 0 represents complete disagreement and 10 represents complete agreement. IQR = interquartile range.

“A key finding is that clinical response to treatment is used to guide treatment decisions rather than AST results “

Doxycycline improves clinical outcomes during cystic fibrosis exacerbations

Xin Xu[1,2,3,4,5], Tarek Abdalla[1,2], Preston E. Bratcher[1,2], Patricia L. Jackson[1,2,3,4,5], Gina Sabbatini[6], J. Michael Wells[1,2,3,4,5], Xiang-Yang Lou[1,7], Rebecca Quinn[8], J. Edwin Blalock[1,2,3,4,9], J. P. Clancy[10] and Amit Gaggar[1,2,3,4,5,9]

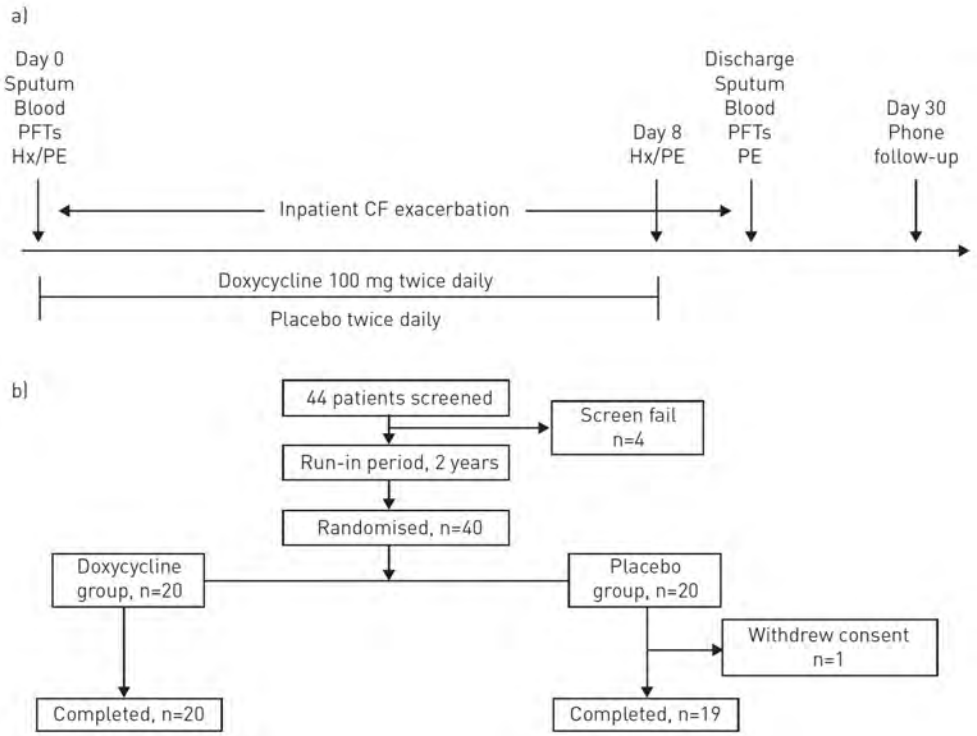


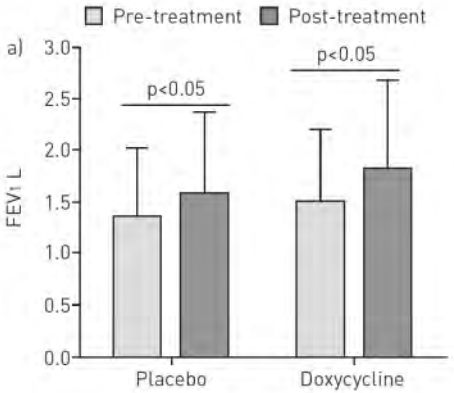
TABLE 1 Baseline patient demographics and disease characteristics

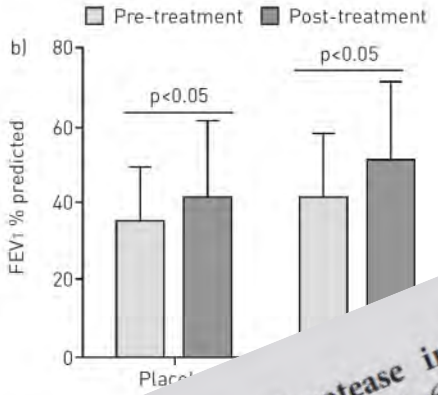
Baseline variable	Doxycycline	Placebo	p-value
Subjects n	20	19	
Age years	29.1±8.9	27.3±9.4	0.55
Ethnicity			
White	18 (90%)	17 (89%)	0.98
Black	2 (10%)	2 (11%)	
Sex			
Male	12 (60%)	13 (68.4%)	0.60
Female	8 (40%)	6 (31.6%)	
Mutation			
Delta F508 homozygous	8 (40%)	9 (47%)	0.66
Delta F508 heterozygous	8 (40%)	8 (42%)	0.91
Other	4 (20%)	2 (11%)	0.43
Lung function			
Admission FEV_1 L	1.50±0.71	1.36±0.67	0.53
Admission FEV_1 % pred	47.4%±19.6	42.4%±11.6	0.24
Admission FVC L	2.55±0.97	2.34±1.00	0.51
Admission FVC % pred	56.8%±13.1	49.0%±15.8	0.16
Admission $FEF_{25-75\%}$ %	33.4%±28.6	16.4%±6.2	0.24
CF-related conditions			
Pancreatic insufficiency	19 (95%)	19 (100%)	0.36
CFRD	6 (30%)	8 (42%)	0.45
Chronic care medications			
Azithromycin	18 (90.0%)	15 (79%)	0.36
Hypertonic saline	7 (35%)	9 (47%)	0.45
Inhaled tobramycin	11 (55%)	9 (47%)	0.65
Dornase-α	18 (90%)	18 (95%)	0.61
Inhaled colistin	7 (35%)	9 (47%)	0.45
Inhaled aztreonam	6 (30%)	3 (16%)	0.31
Sputum bacteriology			
Pseudomonas aeruginosa	20 (100%)	19 (100%)	1.0
Mucoid strain only	8 (40%)	4 (21%)	0.21
Nonmucoid strain only	3 (15%)	7 (37%)	0.13
Mucoid+nonmucoid strain	9 (45%)	8 (42%)	0.87
Staphylococcus aureus	9 (45%)	13 (67%)	0.15
Methicillin-resistant	7 (35%)	11 (57%)	0.16
Methicillin-sensitive	2 (10%)	2 (10.5%)	0.98
Intravenous antibiotics in hospital			
Aminoglycoside+β-lactam	20 (100%)	19 (100%)	1.0
Vancomycin or linezolid	7 (35%)	11 (57%)	0.16
Body mass index	19.9±3.9	20.2±2.7	0.67
Serum CRP	56.1±63	37.8±40.1	0.35

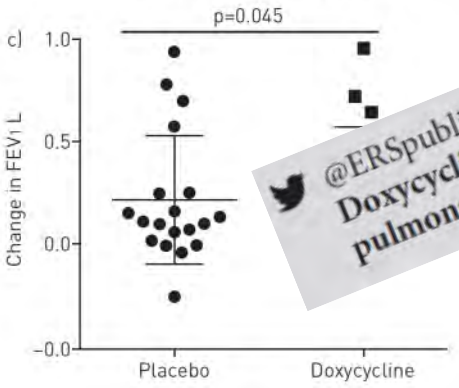
Eur Respir J 2017; 49: 1601102

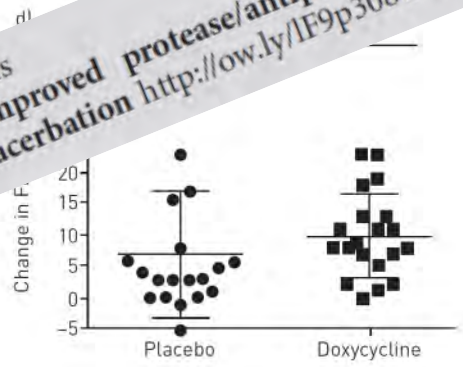
Doxycycline improves clinical outcomes during cystic fibrosis exacerbations

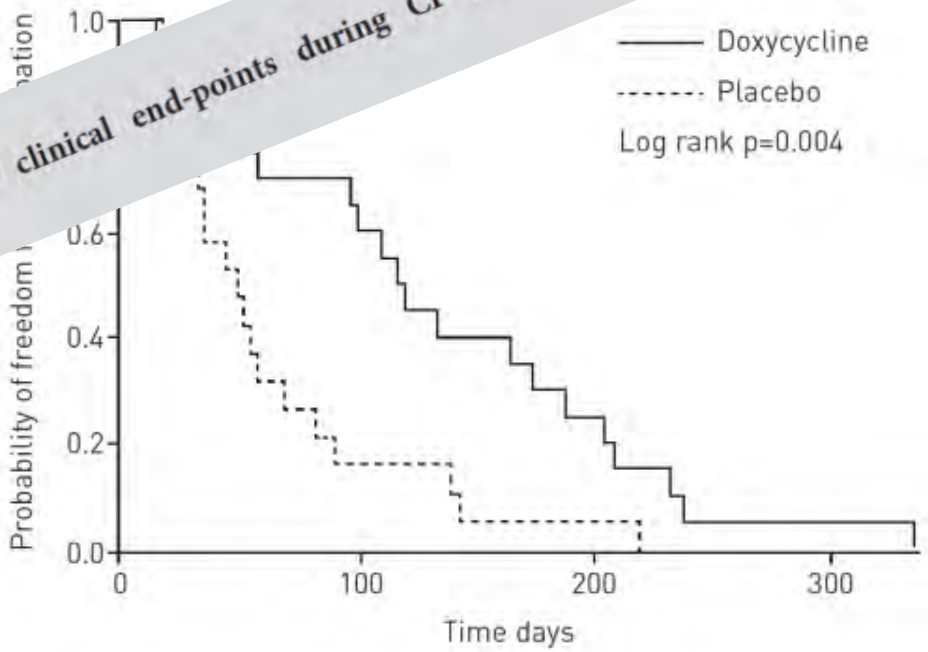
Xin Xu[1,2,3,4,5], Tarek Abdalla[1,2], Preston E. Bratcher[1,2], Patricia L. Jackson[1,2,3,4,5], Gina Sabbatini[6], J. Michael Wells[1,2,3,4,5], Xiang-Yang Lou[1,7], Rebecca Quinn[8], J. Edwin Blalock[1,2,3,4,9], J. P. Clancy[10] and Amit Gaggar[1,2,3,4,5,9]





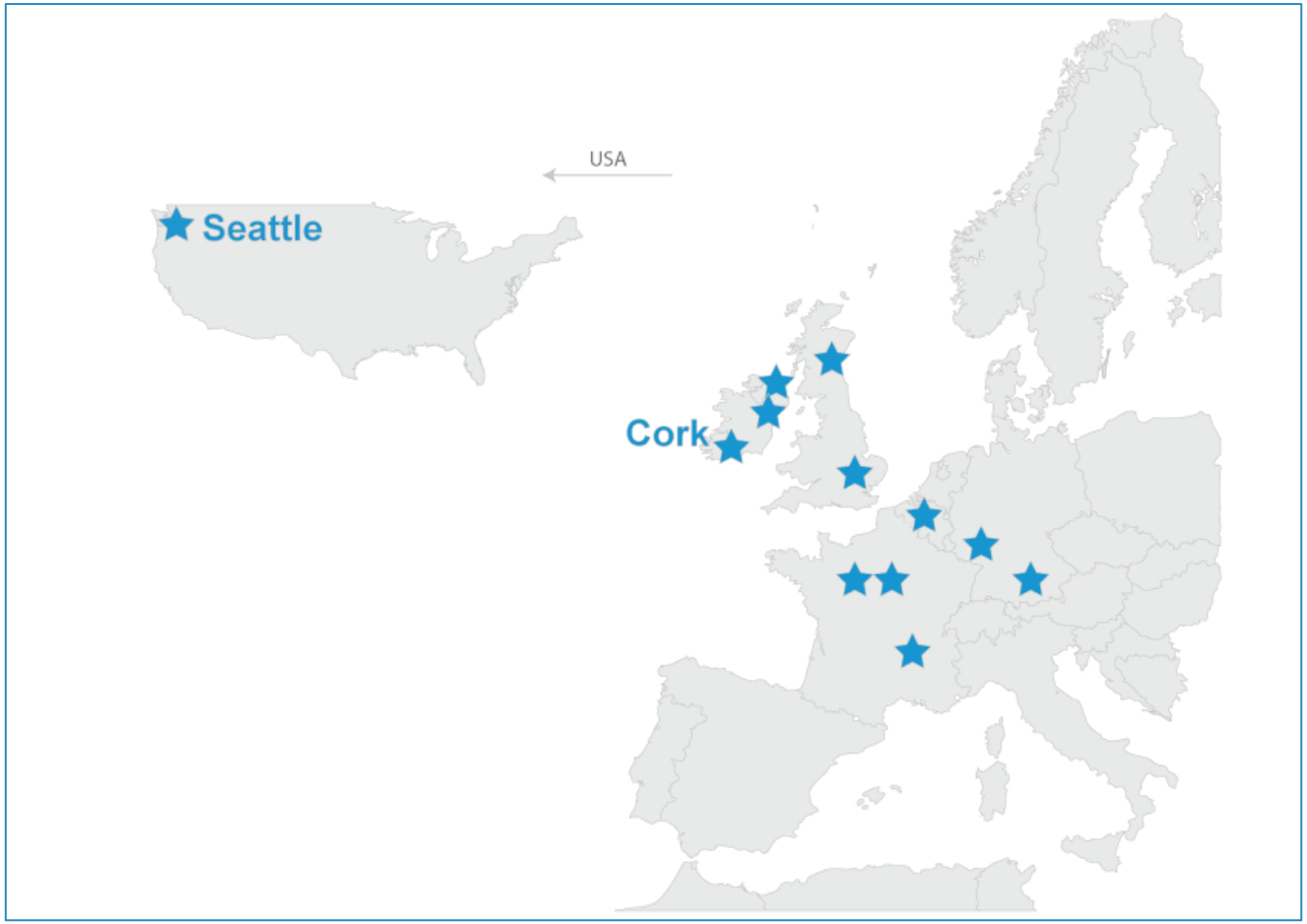






@ERSpublications **Doxycycline improved protease/antiprotease imbalance and clinical end-points during CF acute pulmonary exacerbation** http://ow.ly/IF9p308Ov6i

CFMATTERS: Cystic Fibrosis Microbiome Derived Antimicrobial Therapy Trial in Exacerbations Results Stratified.



http://www.cfmatters.eu/

Coordonnateur: Barry Plant, Dept. of Medicine, University College Cork
FP7-HEALTH-2013-INNOVATION-1: 5.999.748 €, AP-HP: 225.000 €
Durée: 1er Octobre 2013 – 30 Septembre 2016 (3 years)

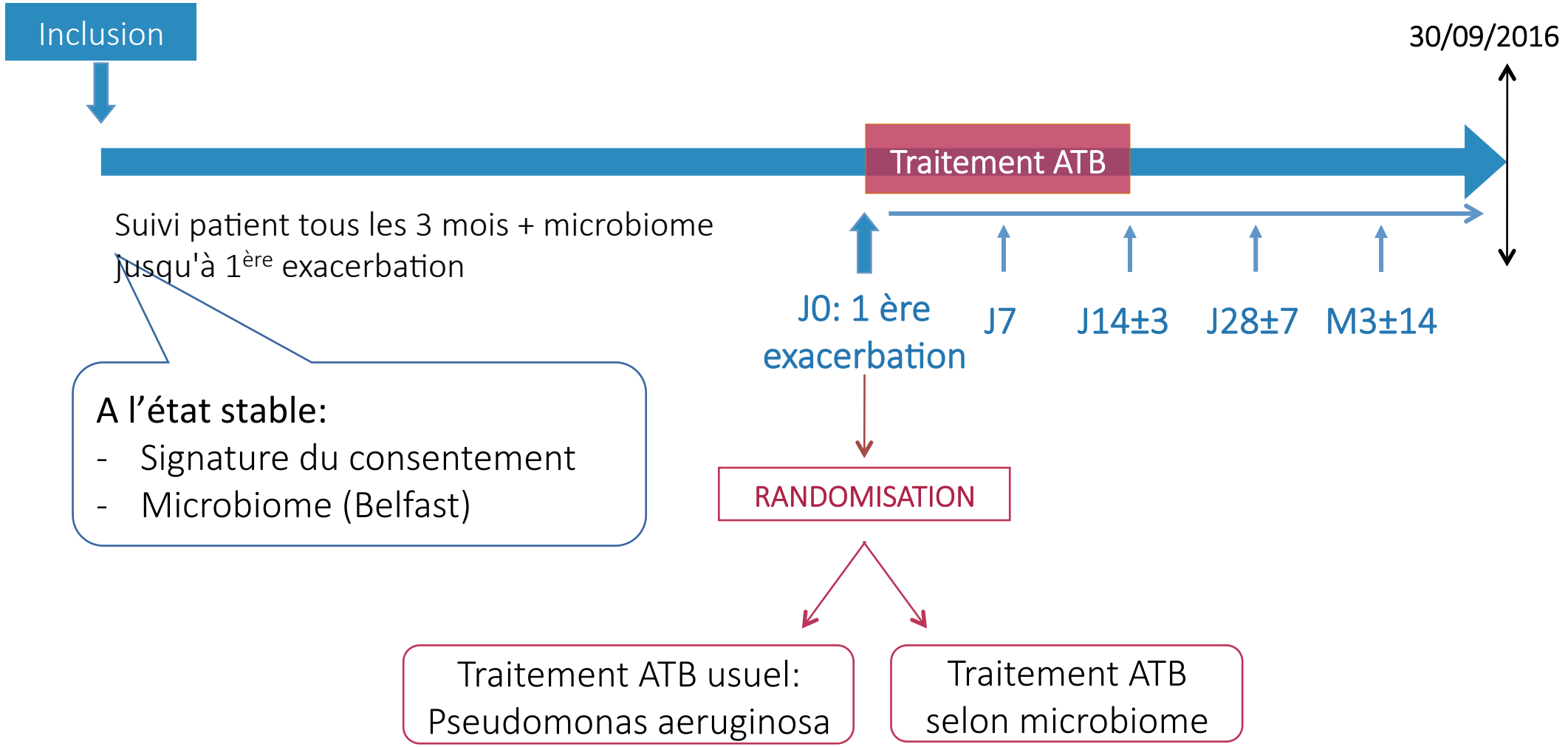
Effet d'un traitement antibiotique déterminé par le microbiome lors d'une exacerbation respiratoire chez le patient atteint de mucoviscidose: Stratification des résultats

Essai clinique international randomisé, ouvert, à 2 bras parallèles, comparant un traitement antibiotique dirigé contre le microbiome analysé par biologie moléculaire au traitement antibiotique habituel dirigé contre le *Pseudomonas aeruginosa* lors d'une exacerbation respiratoire chez le patient atteint de mucoviscidose

- Autres sites participant (1 site/pays): Allemagne, Belgique, Angleterre, Irlande du Nord, USA
- Investigateur coordonnateur en France: I. Fajac
- Autres investigateurs: PR. Burgel, D. Hubert, F. Aubourg, C. Martin

Nombre de patients attendus: 252 et par centre: **40**

Schéma de l'étude



CF matters: résultats de microbiome (ECBC)

Results for the top 5 taxa/organisms detected	
Ranks	**Detected Taxa**
1st Ranked Taxa	Pseudomonas
2nd Ranked Taxa	f_Pseudomonadaceae_Unclassified
3rd Ranked Taxa	Streptococcus
4th Ranked Taxa	Rothia
5th Ranked Taxa	Actinomyces

Results for the top 5 taxa/organisms detected	
Ranks	**Detected Taxa**
1st Ranked Taxa	Pseudomonas
2nd Ranked Taxa	Streptococcus
3rd Ranked Taxa	Neisseria
4th Ranked Taxa	Gemella
5th Ranked Taxa	Porphyromonas

Guiding principles for Microbiome Based Therapy Post Consensus review

	1st line Antibiotic	2nd Line Antibiotic	Rationale
Staphylococcus	Doxycycline	Linezolid	
***Haemophilus influenzae*:**	Moxifloxacin	Doxycycline	Specificity
Pseudomonas aeruginosa	Ceftazadime /Aztreonam and Tobramycin.		This regimen will be initially considered as it has a focused spectrum of activity and will therefore have least impact on other members of the microbiome.
Streptococcus species	Moxifloxacin		
Stenotrophomonas maltophilia	Co-trimoxazole	Doxycycline	
Achromobacter xylosxidans	Tetracycline	Carbapenem. Co-trimoxazole	This organism is often pan-resistant and there is limited data on the best antibiotic for treatment. The most active agents are tetracycline, carbapenems, chloramphenicol and co-trimoxazole.
***Burkholderia cepacia* complex**	Meropenem	Temocillin and Piperacillin/Tazobactam	This organism is also usually pan-resistant.
Prevotella and Veillonella spp.	Metronidazole	Meropenem, Co-Amoxiclav or Piperacillin/Tazobactam.	Primary data from QUB laboratory demonstrates both species in CF are generally sensitive to metronidazole.
Rothia.	Amoxicillin,	Doxycyline, Co-Amoxiclav	There is limited data available regarding the antimicrobial susceptibility of *Rothia* species. In general, they are susceptible to penicillin

Version 1: 09th March 2015

Objectif principal et critères de jugement

Objectif principal:
Evaluer l'effet d'un traitement antibiotique dirigé contre le microbiome lors d'une exacerbation respiratoire chez le patient atteint de mucoviscidose colonisé à *Pseudomonas aeruginosa.*

Critère de jugement principal:
Pourcentage de variation du Volume Expiratoire Maximal en 1 sec (VEMS) entre le 28ème jour (J28) après le début du traitement et le 1er jour (J1) de traitement

Criteres secondaires:
- Période de temps jusqu'à la prochaine exacerbation
- Symptômes à J7 après le début du traitement
- Modification du questionnaire de qualité de vie à J28 et à 3 mois après le début du traitement
- Nombre de jours d'antibiothérapie intraveineuse pendant la durée de l'étude
- Evolution du VEMS pendant la durée de l'étude
- Nombre total d'exacerbations pendant la durée de l'étude

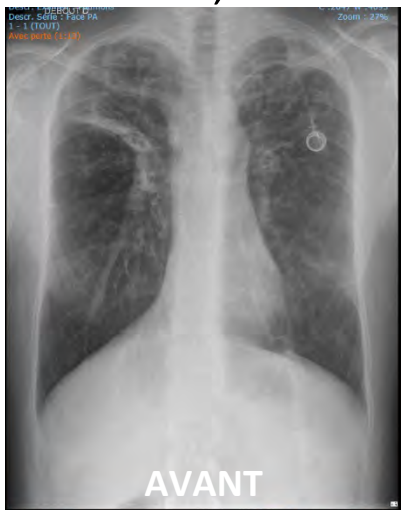
Un exemple clinique

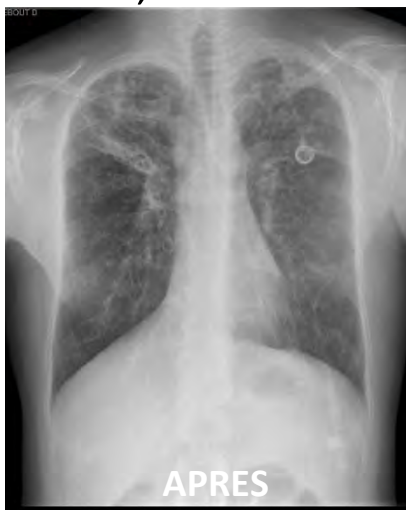
- **Patient de 33 ans**
- **Génotype: phe508del/phe508del**
- **VEMS pré-cure: 29%**
- **3 à 4 cures IV/an**
- **ECBC:**
  - ***P. aeruginosa***
  - ***A. xylosoxydans***
- **Clinique:**
  - **Encombrement bronchique, perte de poids, asthénie**
  - **Atélectasie poumon droit**

Burkholderia cepacia	**Négative**	
Pseudomonas aeruginosa	**Positive** R	
Culture et ou identification		
–	**1.Flore de type oropharyngée .** **2.Alcaligenes xylosoxidans (nv : Achr...** **3.Pseudomonas aeruginosa 1.10e4 U...** 1. 2. 3.	
Identification par	**Spectrom...**	**Spectrom...**
Méthode : Diffusion	**V**	**V**
Oxacilline		
Ceftolozane/Tazobactam		**S 2.0**
Amoxicilline+ac. clavulinique		
Ticarcilline	**S**	**R**
Ticarcilline+ac. clavulanique	**S**	**R**
Pipéracilline	**S**	**R**
Pipéracilline+tazobactam	**S**	**R**
Céfamandole		
Céfotaxime		
Ceftazidime	**R**	**R**
Aztréonam	**R**	**S**
Céfépime	**R**	**S**
Imipénème	**S**	**R**
Méropénème	**S**	**I**
Gentamicine		
Nétilmicine		

Un exemple d'impact incertain d'*A. xylosoxidans*

- Allergies/Intolérances
  - Fortum, Tiénam, Méronem, Tobramycine inhalée, Colistine inhalée, Azactam, Colimycine IV.





- Effet de la cure de Zerbaxa - Ciflox:
  - Pas de réaction allergique
  - VEMS post-cure 30%
  - Diminution de la toux et de l'encombrement

Conclusions: bactéries émergentes

Problème réel

Impact peu clair

Cible mouvante

- Nouveaux antibiotiques
- Modulateurs de CFTR

A suivre!