
## 30 SETTEMBRE 2022

**I SESSIONE** — Moderatori: Paolo Lanzafame - Elisa Vian

| | |
|---|---|
| 08.30-09.00 | Registrazione partecipanti |
| 09.00-09.30 | Presentazione del congresso e saluti |
| 09.30-12.30 | **TAVOLA ROTONDA:**<br>**LA LEZIONE DEL SARS-CoV-2:**<br>**QUALE ESPERIENZA UTILE PER IL FUTURO?**<br>Partecipano:<br>**Lucia Collini**: Dirigente Biologo Unità Operativa di Microbiologia e Virologia, Trento - Presidio Ospedaliero S.Chiara<br>**Roberta Corazza**: Ufficio stampa Azienda APSS Trento<br>**Antonio Ferro:** Direttore generale azienda APSS Trento<br>**Isabella Monne**: ISZVe - Ruolo dei centri di sequenziamento<br>**Elisabetta Pagani:** Direttore microbiologia Bolzano<br>**Serena Pancheri:** APSS Trento<br>**Laura Regattin**: Direttore Sanitario ASUFC<br>**Roberto Rigoli**: Direttore del Sociale AULSS2<br>**Francesca Russo**: Direzione Prevenzione servizio di igiene pubblica Regione Veneto<br>**Assunta Sartor**: Dirigente medico UOC Microbiologia ASUFC Presidio ospedaliero "Santa Maria della Misericordia" Udine<br>**Claudio Scarparo**: Direttore UOC Microbiologia Ospedale dell'Angelo, Mestre (VE) - AULSS3 Serenissima<br>**Marco Sterzi**: Azienda Zero - Regione Veneto<br>**Sandra Zuzzi**: Responsabile approvvigionamento Azienda Zero Regione Veneto |
| 12.30-14.00 | Lunch |

**II SESSIONE** — Moderatori: Roberto Rigoli - Claudio Scarparo

| | |
|---|---|
| 14.00-14.45 | Metodi per la ricerca di patogeni nelle emocolture e le modalità di refertazione<br>Patrizia Cambieri, Mara Felicetti |
| 14.45-15.30 | La sorveglianza dei microorganismi sentinella e la loro refertazione<br>Marco Coppi, Massimo Crapis |
| 15.30-15.45 | Discussione |
| 15.45-16.15 | Coffee break |
| 16.15-16.35 | Ruolo e utilità dei software nella gestione del dato microbiologico<br>Lucia Collini |
| 16.35-17.05 | Ruolo dei software negli alert di sorveglianza<br>Roberto Cocconi |
| 17.05-17.25 | Sviluppo software dedicati alla microbiologia<br>Daniele Garibaldi |
| 17.25-18.00 | Discussione e chiusura della giornata |
| 18.00-18.30 | Assemblea dei soci.<br>Presentazione dei candidati per l'Elezione del nuovo Consiglio Direttivo NewMicro 2022-2024<br>Votazioni |

## 01 OTTOBRE 2022

**III SESSIONE** — Moderatori: Lucia Collini - Elisa Vian

| | |
|---|---|
| 08.30-09.15 | La ricerca dei patogeni e refertazione nei materiali respiratori<br>Assunta Sartor, Bruno Viaggi |
| 09.15-9. 40 | Infezioni e colonizzazione: il punto di vista del pediatra<br>Marta Miorin |
| 09.40-10.00 | POCT: utilità e limiti nella gestione della pandemia<br>Serena Pancheri |
| 10.00-10.30 | Coffee break |
| 10.30-10.50 | POCT: quale ruolo strategico ed "intelligente" per le microbiologie: il modello hub/spoke dopo il Covid<br>Vittorio Sambri |
| 10.50-11.10 | Le novità europee dei Laboratori<br>Giovanni Casiraghi |
| 11.10-11.30 | Discussione |
| 11.30-12.15 | SIMPOSIO (Sessione non accreditata ECM) |
| 12.15-13.00 | SIMPOSIO (Sessione non accreditata ECM) |
| 13.00 | Lunch e chiusura dei lavori |

# La ricerca dei patogeni e refertazione nei **materiali respiratori**

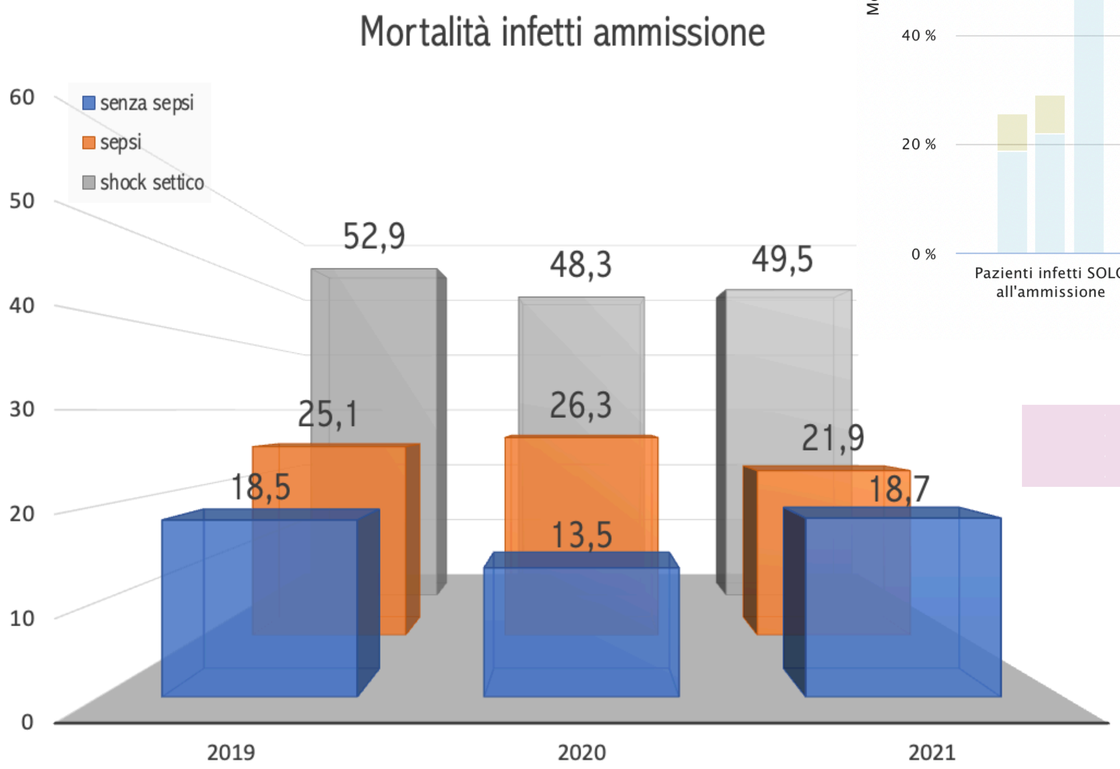
**Dr Bruno Viaggi**
Dipartimento di Anestesia
NeuroAnestesia e
Rianimazione AOU Careggi

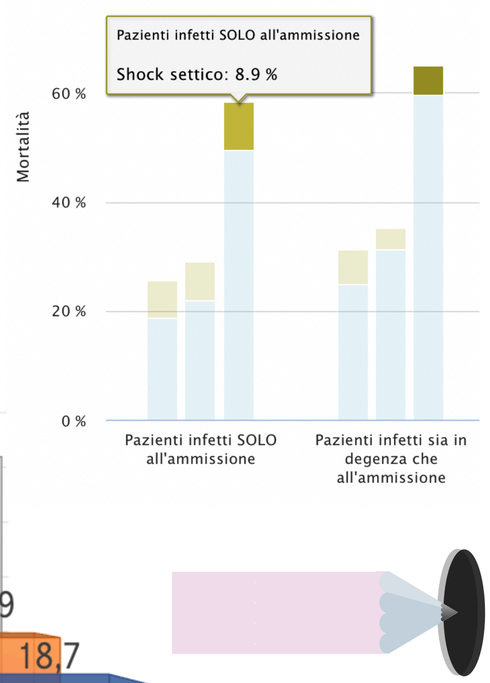
Gruppo Tecnico Programma Lotta alla Sepsi
Coordinamento e Gruppo Tecnico AID
REGIONE TOSCANA

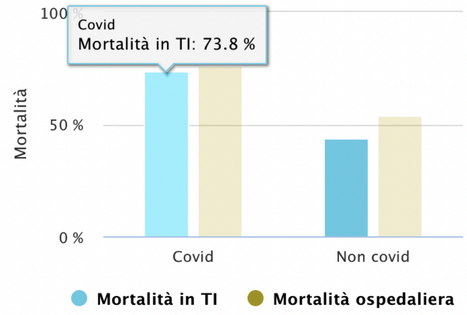
**Dichiarazione su potenziali conflitti di interesse**
Consulenze, partecipazione advisory boards, speaker's bureau, contratti/contributi di ricerca e di eventi studio:
**Abbott, Accelerate Diagnostics, Ada, Advanz Pharma, Alifax, Angelini, Becton Dickinson, Bellco, Biomerieux, Biotest, Cepheid, Correvio, Emmegi Diagnostica, Gilead, Menarini, MSD Italia, Nordic Pharma, Pfizer, Shionogi, Thermo Fischer Scientific, Viatris**

# REPORT INFECTION - Prosafe GiViTi 2021 Nr = 34021

Infections in **ICU**:
the new challenges

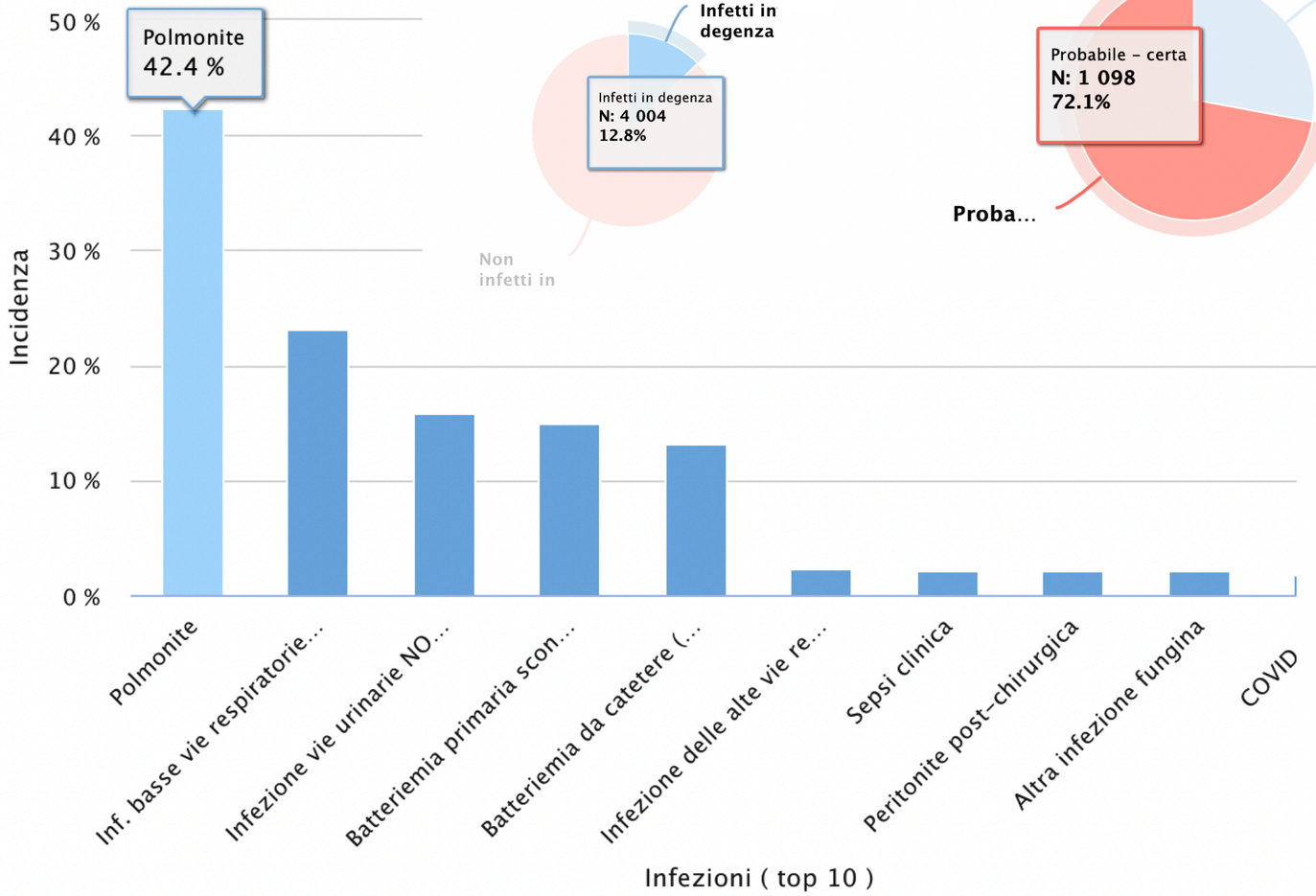



| | Mortalità | | | | | |
|---|---|---|---|---|---|---|
| **Pazienti** | **N pazienti** | **N morti TI** | **TI** | **N pazienti (escluso riamm.)** | **N morti H** | **H** |
| Covid | 1199 | 883 | 73.8 | 1180 | 892 | 75.9 |
| Non covid | 2988 | 1308 | 43.8 | 2836 | 1519 | 53.9 |

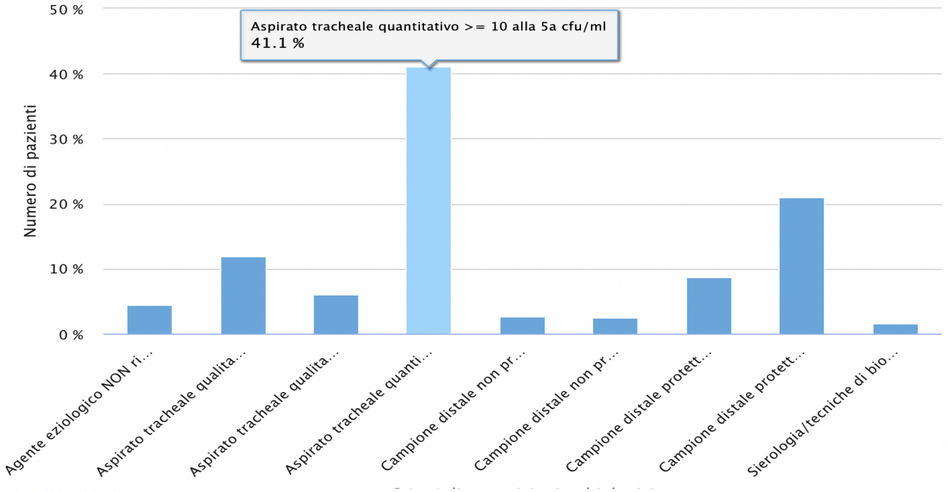
# 8.15 Infezioni in degenza ( top 10 )

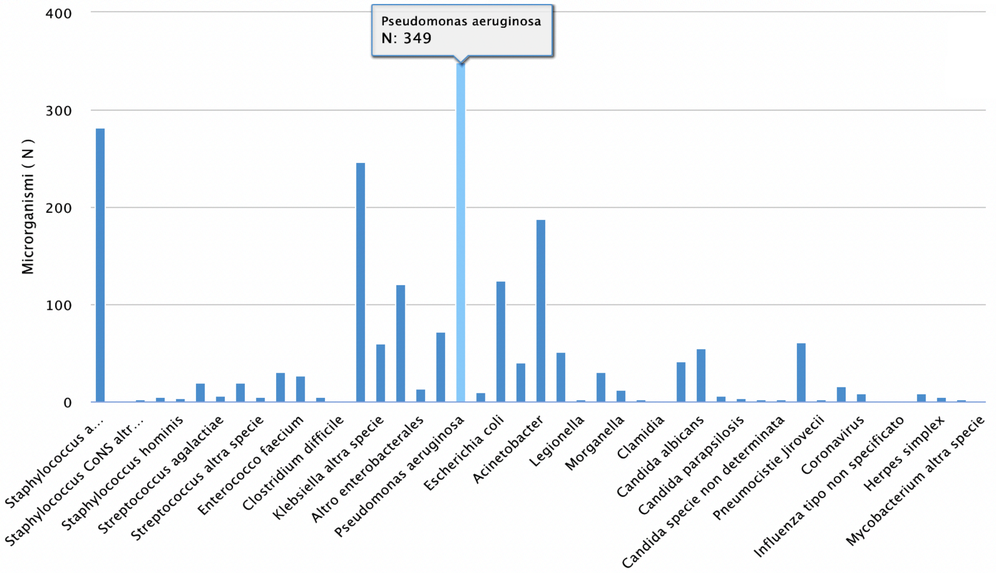



## Diagnosi

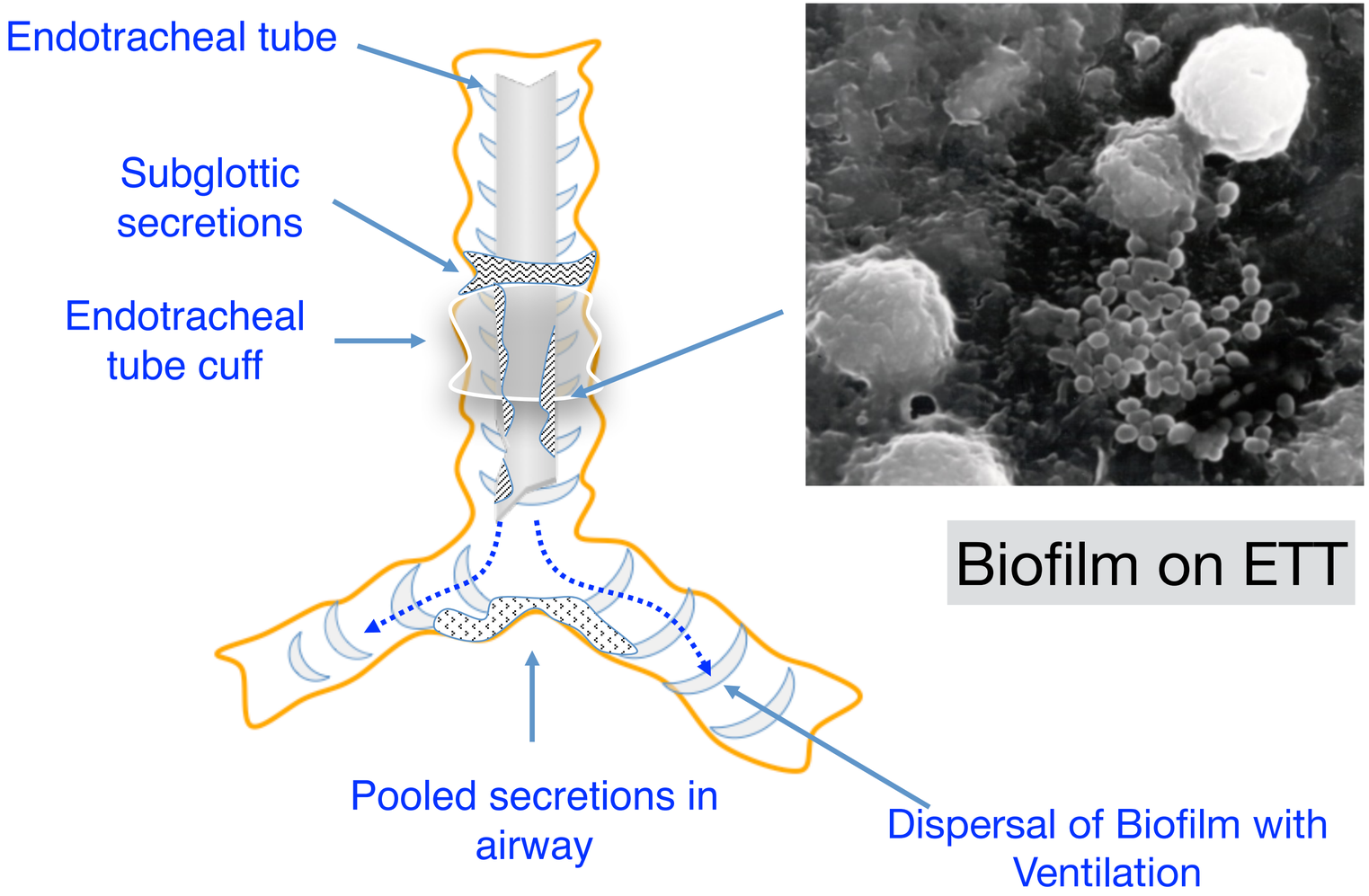



## Criteri diagnostici microbiologici



# *IVAC* pathogenesis

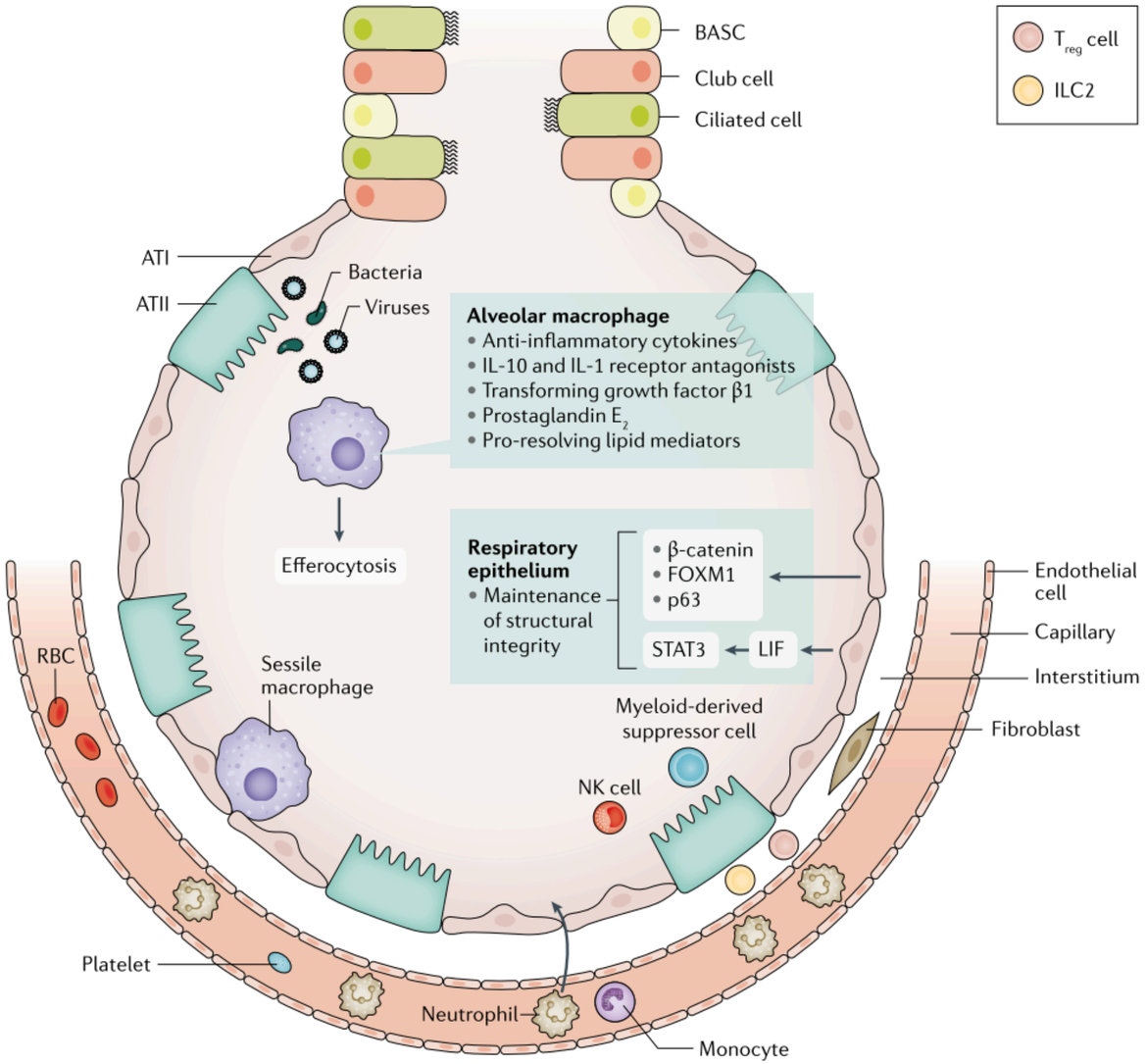





Biofilm on ETT

# Pneumonia

**Antoni Torres** et al. *Nature Rewiews DISEASE PRIMERS* 2021




***New antibiotic and non-antibiotic therapies***, in addition to ***rapid and accurate diagnostic tests*** that can detect pathogens and antibiotic resistance will improve the management of pneumonia

***Monoclonal or polyclonal antibodies*** to specific MDR pathogens, including *S. aureus* and *P. aeruginosa*, are the ultimate narrow-spectrum agents, being both extremely safe and having the great advantage of not disturbing the commensal microbiota

Tissue resilience ***is essential in controlling excessive inflammation whilst sustaining effective protection*** against microbes

*Tissue Resilience*


# Difficult-to-Treat **Resistance** in Gram-negative

**Table 1. Phenotypic Definitions of Difficult-to-Treat Resistance and Centers for Disease Control and Prevention-defined Individual Resistance Phenotype Among 5 Taxa of Gram-negative Bloodstream Infections**

| Definitions | Agents Included | Defining Criteria |
|---|---|---|
| 2015 CDC definitions | | |
| Carbapenem resistant[a] | Imipenem, meropenem doripenem ertapenem[b] | Resistance to ≥1 carbapenem (*Escherichia coli, Klebsiella* spp, *Enterobacter* spp); intermediate or resistant to ≥1 carbapenem (*Pseudomonas aeruginosa, Acinetobacter baumannii)* |
| Extended-spectrum cephalosporin-resistant[c] | Ceftazidime, cefotaxime | |
| Fluoroquinolone resistant[a] | Ciprofloxacin, | |
| Proposed definition | | |
| Difficult-to-treat resistance | Intermediate ing addition | |

| Antibiotico | MIC mg/l |
|---|---|
| Piperacillina/tazobactam | ≥128 R |
| Ceftazidime | 64 R |
| Cefepime | 64 R |
| Aztreonam | ≥64 R |
| Imipenem | 32 R |
| Meropenem | 16 R |
| Amikacina | ≥64 R |
| Gentamicina | >32 R |
| Ciprofloxacina | >32 R |
| Ceftolozane/tazobactam | ≥8 R |
| Fosfomicina | 128 IE |
| Colistina | 1 S |
| Cefiderocol | 1 S |

*Pseudomonas aeruginosa* **VIM-1**

| Antibiotico | MIC mg/l |
|---|---|
| Imipenem | >32 R |
| Meropenem | 64 R |
| Amikacina | 32 R |
| Gentamicina | >16 R |
| Ciprofloxacina | >32 R |
| TMP/SMT | >320 R |
| Colistina | 1 S |
| Cefiderocol | 2 S IE |

*Acinetobacter baumannii* **OXA-23**

| Antibiotico | MIC mg/l |
|---|---|
| Piperacillina/tazobactam | ≥128 R |
| Ceftriaxone | ≥4 R |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Imipenem | 16 R |
| Meropenem | >64 R |
| Fosfomicina | 32 S |
| Amikacina | ≥16 R |
| Gentamicina | 2 S |
| Ciprofloxacina | >4 R |
| Tigeciclina | 0.5 IE |
| Colistina | 8 R |
| CAZ/AVI | 2 S |
| MEM/VAB | 0.5 S |
| Cefiderocol | 2 S |

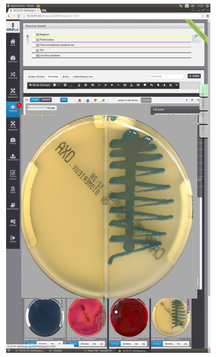
*Klebsiella pneumoniae* **KPC-3**

| Antibiotico | MIC mg/l |
|---|---|
| Piperacillina/tazobactam | ≥128 R |
| Ceftriaxone | ≥4 R |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Imipenem | >16 R |
| Meropenem | >64 R |
| Fosfomicina | 32 S |
| Amikacina | >16 R |
| Gentamicina | >8 R |
| Ciprofloxacina | >4 R |
| Tigeciclina | 1 IE |
| Colistina | 0.5 S |
| CAZ/AVI | >16 R |
| MEM/VAB | >16 R |
| Cefiderocol | 1 S |

*Klebsiella pneumoniae* **NDM-1**

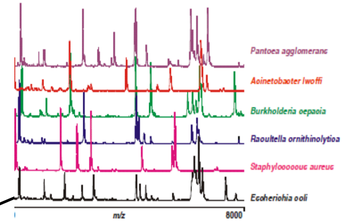
# Conventional and syndromic molecular diagnostics: **where are we going?**

## Lab automation



## Maldi-TOF Mas spectrometry

Rapid ID
Rapid typing
R mechanisms




## SC time-lapse microscopy

Rapid ID
& pieno AST

## Fast ID System

## Molecular biology

HM-NAATs/microarrays

Rapid ID
R mechanisms

## T2Candida

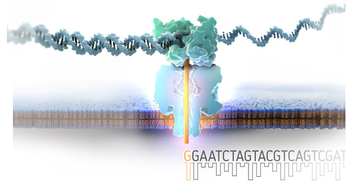
## ATB con light-scattering

Rapid ID
& pieno AST

## LFIA

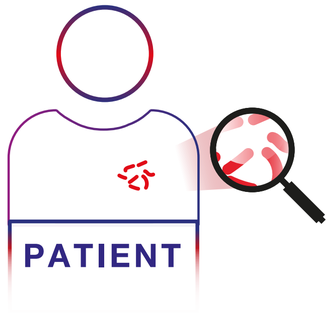
Rapid ID
R mechanisms

## Nanopore sequencing



B Biomarkers <1h
Mono/dual approach
Pro-ADM
Link to SOFA
PCT
PPV
Think about value
NPV
Advanced imaging
TC total body MdC TTE

A Microbiological Parameters
Colonization
Local epidemiology




C Scores
In terms of assistance in microbiological diagnostics
CRE
ESBL

C Scores
Critical patient severity
SOFA
PITT
CPISm

*"The role of stratification of the risk of infection"*

"Who goes into rapid diagnostics? Or rather, who is the right patient who can best benefit by rapid diagnostics?"

LRTI
RAPID Syndromic Panel for Low Respiratory Tract Infections
*BIOFIRE® FILMARRAY® Pneumonia Plus Panel*
1,30 h

BSI-CR-BSI
Lateral Flow assay for quick detection of the "big 5" carbapenemase enzymes
*NG-Test® CARBA 5*
15 min

RAPID Syndromic Panel for Bloodstream Infections
*BIOFIRE® BCID2 Panel*
1 h

RAPID antibiotic susceptibility testing
*ASTar® system*
within 6h

BAS
BAL
Daily monitoring of DYNAMIC change of PCT
LRTI
BSI

HIGH RISK
EMPIRICAL ANTIMICROBIAL THERAPY
POSITIVE BLOOD CULTURE (posBC) + Maldi ToF Identification
SEMI-TARGETED ANTIMICROBIAL THERAPY
PERSONALIZED ANTIMICROB IAL THERAPY
2-6H
24H
RAPID DIAGNOSTIC TEST Phenotypic & Molecular methods
SINERGY TEST + TDM + Precise MIC definition
SELECTED NEW ANTIBIOTICS (Companion Diagnostics) CDX

Determinants of the empirical choice of atb
Anatomical site of infection
Immunocompetent vs not
Colonisation with MDR
Susceptibility patterns
Antimicrobial dosing (PK/PD)
Impact of CRRT
Broad spectrum vs narrow
Combo vs mono therapy
Algorithms in decision making

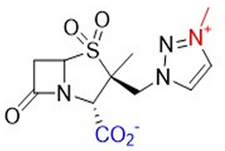
LOW RISK
EMPIRICAL ANTIMICROBIAL THERAPY
POSITIVE BLOOD CULTURE (posBC) + Maldi ToF Identification
TARGETED ANTIMICROBIAL THERAPY

# Coverage of CPE by new β-lactamase inhibitor combinations (**BLICs**) and new β-lactams

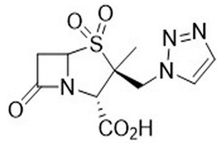
In this new era of renewed activity of BL and BL/BLI combinations against CR-GNB, ***the determinants of carbapenem resistance have assumed a crucial importance in guiding*** both empirical and targeted therapies

**Anti-CPE agents exhibit different activity profiles *vs*. strains producing different enzymes: importance to detect the resistance mechanism**

| Mechanism | CAZ/AVI | MER/VAB | TOL/TAZ | IMI/REL | ATM/AVI | FEP/TANI | FEP/ZIDE | FEP/ENM | MER/NACU | CFL |
|---|---|---|---|---|---|---|---|---|---|---|
| KPC | + | + | - | + | + | + | + | +/- | + | + |
| OXA-48 | + | - | - | + | + | + | + | + | + | + |
| VIM | - | - | - | - | + | + | + | - | + | + |
| NDM | - | - | - | - | + | + | + | - | +/- | + |
| IMP | - | - | - | - | + | - | ? | - | + | |



Enmetazobactam



Tazobactam

The non-ESBL-producing *K. pneumoniae* isolates mostly belong to sequence type 512 (**ST512**), whereas the KPC- and ESBL-producing isolates mostly belong to **ST307**

**Bush & Bradford** *Cold Spring Harb Perspect Med*. 2016; 6(8). pii: a025247
**Pogue** et al. *Clin Infect Dis* 2019
**Choi & McCarthy** *Exp Op Invest Drugs* 27:2, 193-197
**Thomson** et al. *Antibiotics* 2019; 8:32
**Mushtaq** et al. *JAC* 2019; 74:953
www.venatorx.com

**Shapiro S** *Antimicrob Agents Chemother* may 2022

the **copresence** of an ESBL gene <u>downregulated</u> the expression of the KPC gene to a level where the isolates were essentially just ESBL producers

**Vázquez-Ucha JC** *Antimicrob Agents Chemother* may 2022

New MICs of cefepime and cefepime/enmetazobactam for KPC-carrying isolates are determined by the clonality of the isolates

latest news

a multicentre, retrospective study enrolling patients with monomicrobial BSI caused by CRE from January 2013 to December 2016

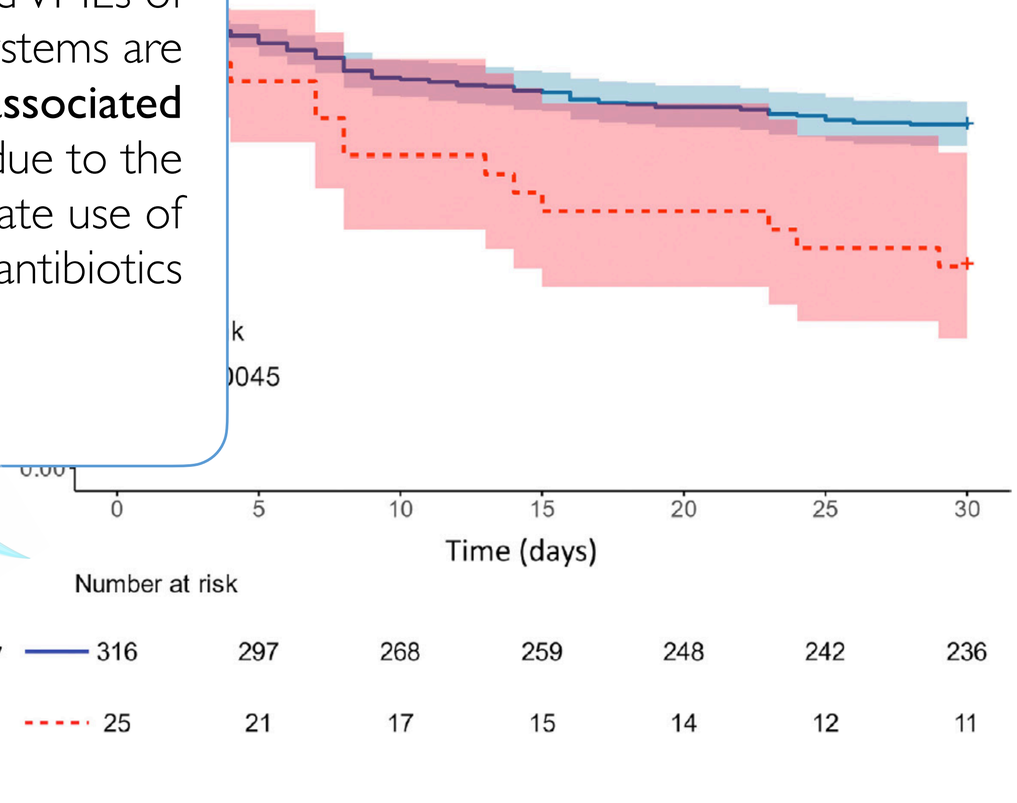
## **Clinical consequences** of very major errors with semi-automated testing systems for antimicrobial susceptibility of carbapenem resistant *Enterobacterales*

**Bartoletti M** et al. *Clin Microbiol Infect* apr 2022 - article in press

**Results**: We enrolled **366** patients with CRE-BSI. W
compared with the results of the reference metho
those of the semi-automated systems exhibited va
rates of very major errors (**VMEs**; i.e. ***false suscepti***
and major errors (**MEs;** i.e. ***false resistances***). The h
rates of VMEs were observed with **fosfomycin**
(**14%**) and **colistin** (**13.9%**), and the highest rates of MEs
were observed with **gentamicin** (**21%**),
**fosfomycin** (**7.7%**), and **tigecycline** (**34%**)

Overall, VMEs and MEs led clinicians to prescribe or confirm ineffective therapy in 25 of 341 patients (**7%**)

In conclusion, our results showed that MEs and VMEs of semiautomated AST systems are common and **might be associated with poor outcome** due to the more frequent inappropriate use of antibiotics





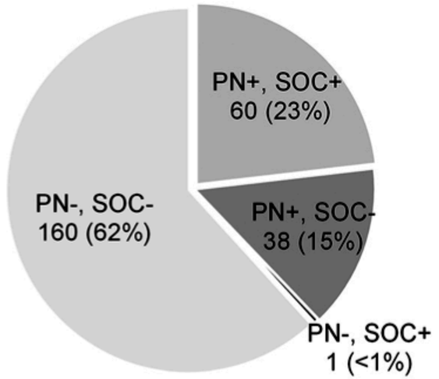

NewMicro Network di Microbiologia e Virologia del Nord Est

# Practical Comparison of the ***BioFire*** FilmArray Pneumonia Panel to Routine Diagnostic Methods and Potential Impact on Antimicrobial Stewardship in Adult Hospitalized Patients with Lower Respiratory Tract Infections: ***IVAC***

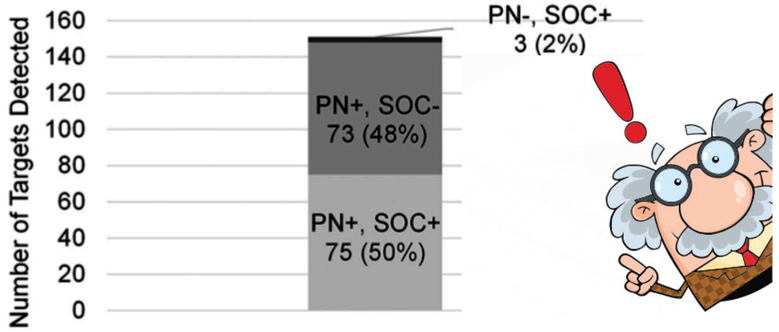
**Buchan BW** et al. *J Clin Microbiol* 2020

- We examined the impact of the multiplexed, semiquantitative BioFire FilmArray Pneumonia panel (PN panel) test on laboratory reporting for ***259*** adult inpatients submitting BAL specimens for laboratory analysis

**A** Total number of BAL Specimens (n=259) with Bacterial Target(s) Detected

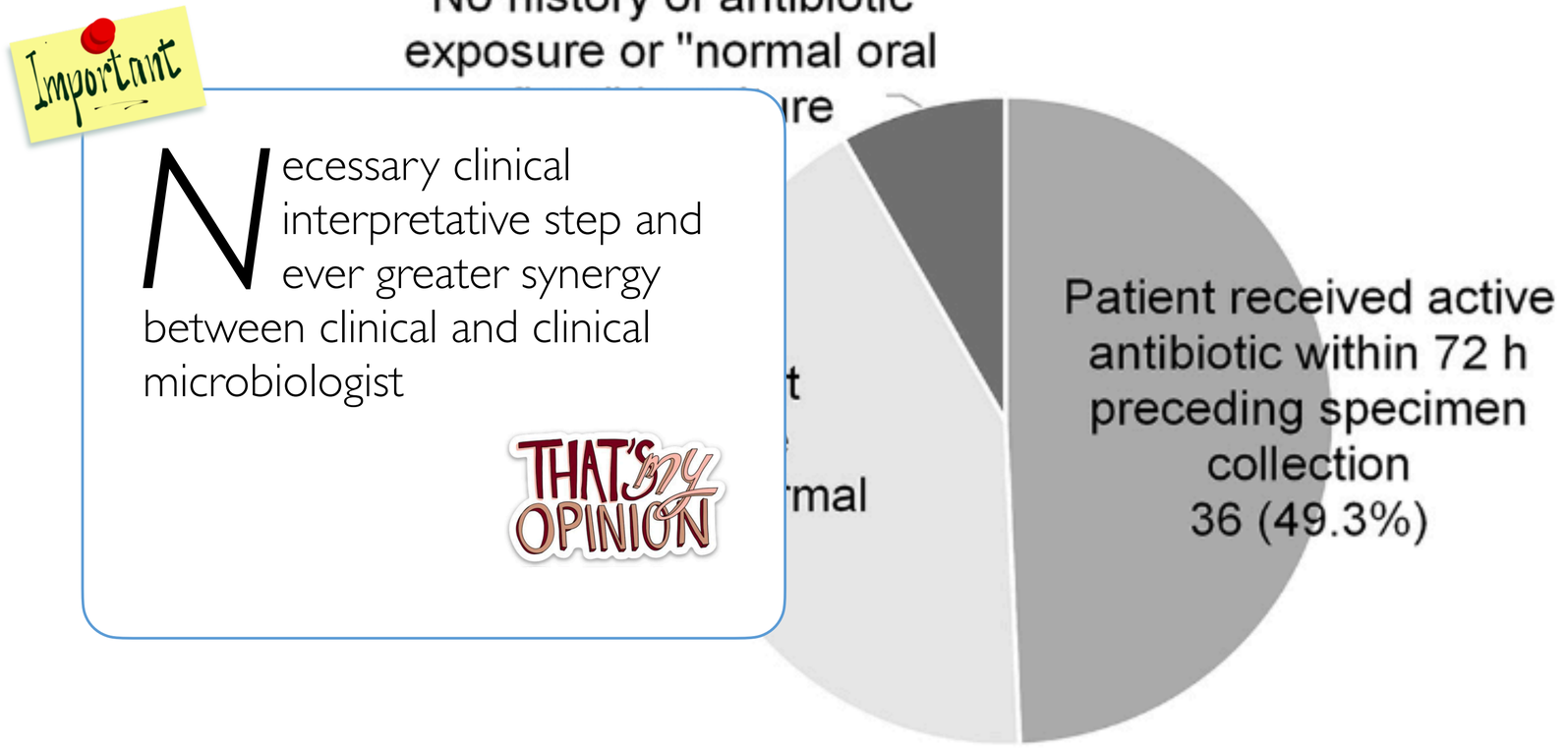



**B** Number of Bacterial Targets (n=151) Detected in all BAL Specimens






Culture-Negative Detections (n=73)







Necessary clinical interpretative step and ever greater synergy between clinical and clinical microbiologist

## **Potential Impact** of the PN panel result on Atb utilization

**Buchan BW** et al. *J Clin Microbiol* 2020

**TABLE 7** Potential impact of the BioFire PN panel result on antibiotic utilization

| Potential modification | No. of antimicrobials | No. (%) of patients | No. of hrs |
|---|---|---|---|
| Appropriate de-escalation/discontinuation | 206 | 122 (48.2) | 18,284.07 |
| Appropriate escalation/initiation | 11 | 11 (4.3) | 184.66 |
| Inappropriate de-escalation/discontinuation | 4 | 4 (1.6) | |
| Inappropriate escalation/continuation | 42 | 42 (16.6) | |
| No change | | 74 (29.2) | |
| Unable to assess[a] | | 16 | |

[a]No stop date was listed for antimicrobials, concomitant infection was present, or antimicrobials were used for longer durations than would be used for a lower respiratory tract infection (>30 days).


The PN panel ***will not be used as a replacement*** for routine culture. However, ***as an adjunctive test*** for patients with symptoms of lower respiratory tract infection, the PN panel ***has the potential to provide*** rapid identification of bacterial and viral pathogens that can be used to aid in definitive etiologic diagnosis and positively impact efforts to meet infection prevention and antibiotic stewardship objectives

## Molecular Diagnosis of Pneumonia (Including Multiplex Panels)

**Buchan BW** et al. *Clin Chemistry* 2022
Mini-Review

- Several benefits are expected from the use of rapid molecular testing, including antibiotic stewardship, hospital or intensive care unit (ICU) length of stay, infection control measures, cost of care, and importantly mortality and patient outcomes

- The ability to report semiquantitative results creates ***another opportunity for result contextualization***. Laboratories may choose to avoid reporting of organisms below a specific semiquantitative threshold based on organism and specimen, similar to culture-based results. When reported, results may be communicated in different ways, including: (a) reporting "***as is***" (i.e. $10^4$, (b) reporting qualitatively, or (c) reporting relatively (i.e., $10^4$ is "***rare***" or "1+")

| | |
|---|---|
| CTX | Non rilevato |
| KPC | **Rilevato** |
| VIM | Non rilevato |
| IMP | Non rilevato |
| NDM | Non rilevato |
| OXA-48 | Non rilevato |

- Probabile resistenza a tutti i beta-lattamici, compresi i carbapenemi
- Probabile sensibilità ai nuovi BLIC: CAZ-AVI, MEM/VAB, IMI/REL, FDC
- Nessuna informazioni, invece, riguardo sensibilità o resistenza di altre molecole
- Non ho valori di MIC

| ANTIBIOTICO | MIC mg/l |
|---|---|
| Amoxicillina/A. Clav. | R |
| Piperacillina/tazobactam | R |
| Ceftriaxone | R |
| Ceftazidime | R |
| Cefepime | R |
| Ertapenem | R |
| Imipenem | R |
| Meropenem | R |
| Fosfomicina | ? |
| Amikacina | ? |
| Gentamicina | ? |
| Ciprofloxacina | ? |
| Tigeciclina | ? |
| Colistina | ? |
| CZA/AVI | S |
| MEM/VAB | S |
| IMI/REL | S |
| FDC | S |

| ANTIBIOTICO | MIC mg/l |
|---|---|
| Amoxicillina/A. Clav. | >64 R |
| Piperacillina/tazobactam | >128 R |
| Ceftriaxone | >4 R |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Ertapenem | >1 R |
| Imipenem | >16 R |
| Meropenem | >64 R |
| Fosfomicina | >128 R |
| Amikacina | >16 R |
| Gentamicina | 1 S |
| Ciprofloxacina | >4 R |
| Tigeciclina | 0,5 S |
| Colistina | >8 R |
| CZA/AVI | 4 S |

# Antibiogramma molecolare vs convenzionale di *K. pneumoniae* **KPC+**

| | |
|---|---|
| CTX | Non rilevato |
| KPC | **Rilevato** |
| VIM | Non rilevato |
| IMP | Non rilevato |
| NDM | Non rilevato |
| OXA-48 | Non rilevato |

| Antibiotico | MIC mg/l |
|---|---|
| Amoxicillina/clavulanato | >64 R |
| Piperacillina/tazobactam | >128 R |
| Ceftiaxone | >4 R |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Meropenem | >64 R |
| Fosfomicina | 32 S |
| Amikacina | >16 R |
| Gentamicina | 1 S |
| Ciprofloxacina | >4 R |
| Colistina | 1 S |
| CZA | 4 S |
| MVB | 1 S |
| CFD | 1 S |

*K. pneumoniae* KPC-3

| Antibiotico | MIC mg/l |
|---|---|
| Amoxicillina/clavulanato | >64 R |
| Piperacillina/tazobactam | 32 R |
| Ceftiaxone | >4 R |
| Ceftazidime | >128 R |
| Cefepime | 16 R |
| Meropenem | 2 S |
| Fosfomicina | >128 R |
| Amikacina | >16 R |
| Gentamicina | 1 S |
| Ciprofloxacina | >4 R |
| Colistina | 0,5 S |
| CZA | 32 R |
| MVB | 0,5 S |
| CFD | 2 S |

*K. pneumoniae* KPC-31

| Antibiotico | MIC mg/l |
|---|---|
| Amoxicillina/clavulanato | >64 R |
| Piperacillina/tazobactam | >128 R |
| Ceftiaxone | >4 R |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Meropenem | >64 R |
| Fosfomicina | 32 S |
| Amikacina | 8 S |
| Gentamicina | >8 R |
| Ciprofloxacina | >4 R |
| Colistina | >8 R |
| CZA | 16 R |
| MVB | 32 R |
| CFD | 2 S |

*K. pneumoniae* KPC-3 IPERESPRESSA

Courtesy Prof Rossolini


Antibiogramma
**convenzionale** vs **molecolare**

## *Klebsiella pneumoniae*

| Antibiotico | MIC mg/l |
|---|---|
| Piperacillina/tazobactam | 8 S |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Ertapenem | >1 R |
| Meropenem | 1 S |
| Amikacina | >16 R |
| Gentamicina | >8 R |
| Ciprofloxacina | >4 R |
| Colistina | 0.5 S |
| CAZ/AVI | >32 R |
| MEM/VAB | 1 S |

PCR
Real-time

KPC


Test LFIA

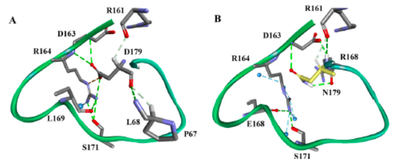
NEGATIVO

Pannello
sindromico

KPC

CZA meccanismi di R acquisita in Kbs-pn KPC

Mutanti enzima KPC (**KPC-31**)




Spesso selezionati
sotto tp con CZA

I mutanti possono mostrare
ridotta attività su:
Piperacillina/tazobactam
Aztreonam
Carbapenemi

**Haidar** *et al. AAC* 2017
**Compain** & **Arthur**. *AAC* 2017
**Shields** *et al. AAC* 2017
**Humphries** & **Hamarajata** *AAC* 2017
**Shields** *et al. Open Forum Infect Dis* 2017
**Barnes** *et al mBio* 2018
**Wand** *et al. JGAR* 2019

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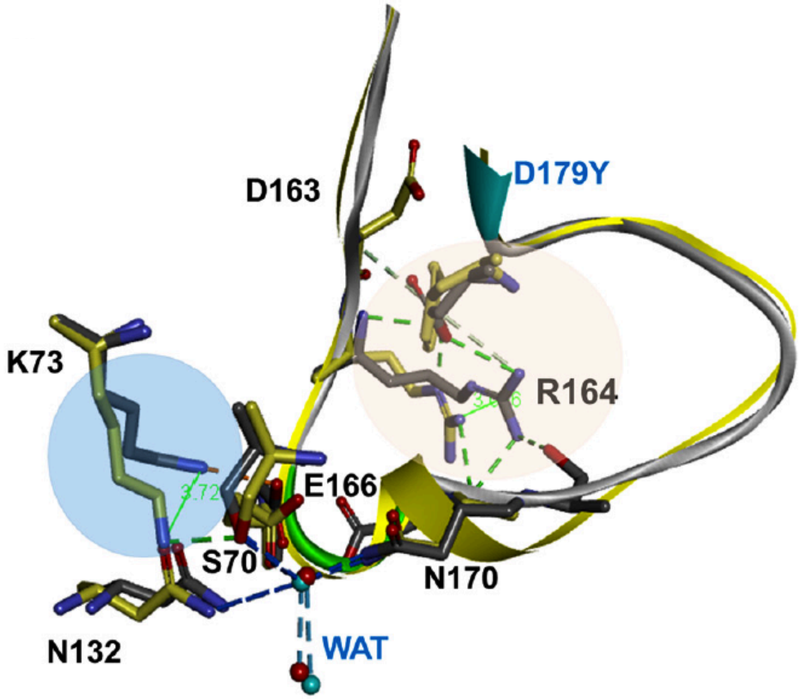
# Different Conformations Revealed by NMR Underlie Resistance to Ceftazidime/Avibactam and Susceptibility to Meropenem and Imipenem among **D179Y Variants** of KPC β-Lactamase

**Taracila MA** et al. *Antimicrob Agents Chemother* apr 2022

This coupled with the observation that the D179Y variant proteins are less stable, potentially accumulating less in steady state, suggests that a functional carbapenemase is not present to hydrolyze IMI or MEM. The IMI or MEM that is still free can inactivate the PBPs, hence bringing about a susceptible phenotype in the D179Y variants

**Results**: Using timed mass spectrometry, the D179Y variant formed prolonged acyl-enzyme complexes with imipenem (IMI) and meropenem (MEM) in KPC-2 and KPC-3, which could be detected up to 24 h, ***suggesting that*** IMI and MEM act as covalent β-lactamase inhibitors more than as substrates for D179Y KPC-2 and -3




In the WT KPC-2 and KPC-3, IMI is hydrolyzed rapidly, making it inactive and thereby conferring a resistant phenotype for IMI. In the case of the D179Y variants, IMI is **"trapped"** in the active site for a very long period of time, acting primarily as an inhibitor rather than as a substrate

Important

| | |
|---|---|
| CTX | Non rilevato |
| KPC | Non rilevato |
| VIM | Non rilevato |
| IMP | Non rilevato |
| NDM | **Rilevato** |
| OXA-48 | Non rilevato |

***Klebsiella pneumoniae***


- Probabile resistenza a tutti i β-lattamici, inclusi i carbapenemi e i nuovi BLIC (CZA, IMI/REL, MEM/VAB)
- Probabile sensibilità ad aztreonam in associazione con avibactam e a cefiderocol

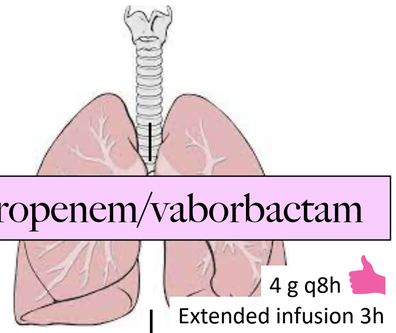
| ANTIBIOTICO | MIC mg/l |
|---|---|
| Amoxicillina/A. Clav. | R |
| Piperacillina/tazobactam | R |
| Ceftriaxone | R |
| Ceftazidime | R |
| Cefepime | R |
| Ertapenem | R |
| Imipenem | R |
| Meropenem | R |
| Fosfomicina | ? |
| Amikacina | ? |
| Gentamicina | ? |
| Ciprofloxacina | ? |
| Tigeciclina | ? |
| Colistina | ? |
| CZA/AVI | R |
| MEM/VAB | R |
| IMI/REL | R |

| ANTIBIOTICO | MIC mg/l |
|---|---|
| Amoxicillina/A. Clav. | >64 R |
| Piperacillina/tazobactam | >128 R |
| Ceftriaxone | >4 R |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Ertapenem | >1 R |
| Imipenem | >16 R |
| Meropenem | >64 R |
| Fosfomicina | >128 R |
| Amikacina | >16 R |
| Gentamicina | >8 R |
| Ciprofloxacina | >4 R |
| Tigeciclina | 0,5 S |
| Colistina | 1 S |
| CZA/AVI | >8 R |

# Antibiogramma convenzionale di *K. pneumoniae* **KPC+**

| Antibiotico | MIC mg/l |
|---|---|
| Amoxicillina/clavulanato | >64 R |
| Piperacillina/tazobactam | >128 R |
| Ceftiaxone | >4 R |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Meropenem | >64 R |
| Fosfomicina | 32 S |
| Amikacina | >16 R |
| Gentamicina | 1 S |
| Ciprofloxacina | >4 R |
| Colistina | 1 S |
| CZA | 4 S |
| MVB | 1 S |
| CFD | 1 S |

*K. pneumoniae* KPC-3



Meropenem/vaborbactam

4 g q8h
Extended infusion 3h

***Imipenem/relebactam***

1.25 g q6h
In 30 min

Ceftazidime/avibactam*

2.5 g q8h
continous infusion

Cefiderocol

FDC 2 g q8h
continous infusion

*+/- partners**
***FOSFOMYCIN***
*Meropenem*

*TMP/SMX if ST101*
*(Adjusted in targeted therapy)*

fosfo 6 g q6h
continous infusion

meropenem 2 g q8h
extended infusion

Ceftazidime/avibactam

2.5 g q8h
continous infusion

Meropenem/vaborbactam

4 g q8h
Extended infusion 3h

Imipenem/relebactam

1.25 g q6h
In 30 min

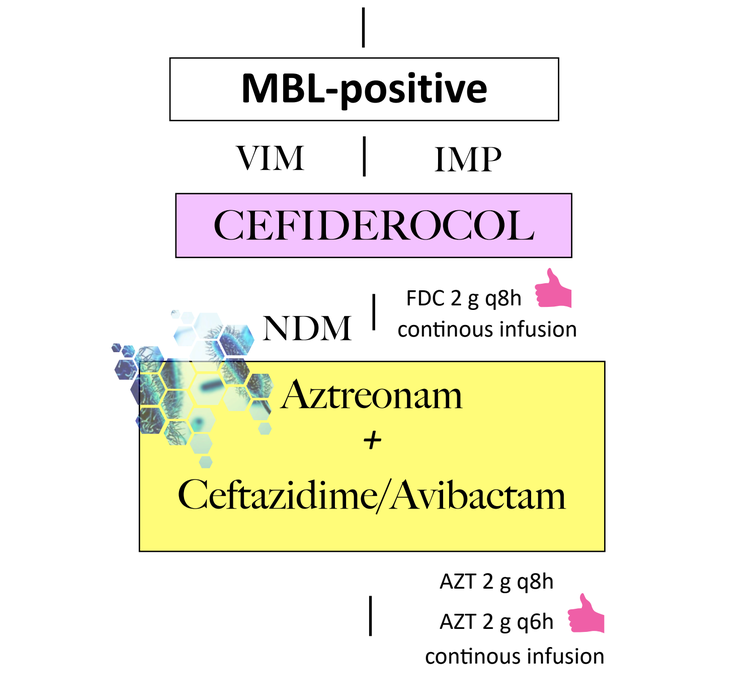
Cefiderocol

FDC 2 g q8h
continous infusion

**Gatti M, Viaggi B, Rossolini GM, Pea F, Viale P**
*Exp Rev Anti Infect Ther* Sep 2021
*Infect Drug Resist* Jun 2021

# Antibiogramma convenzionale di *Enterobacterales* **MBL+**

| Antibiotico | MIC mg/l |
|---|---|
| Amoxicillina/clavulanato | >64 R |
| Piperacillina/tazobactam | >128 R |
| Ceftiaxone | >8 R |
| Ceftazidime | >128 R |
| Cefepime | >32 R |
| Meropenem | >64 R |
| Fosfomicina | 32 S |
| Amikacina | >16 R |
| Gentamicina | >8 R |
| Ciprofloxacina | >4 R |
| Colistina | 1 S |
| CZA | >32 R |
| MVB | >32 R |




Conventional anti-CPE
(Fosfomycin + genta? + meropenem HD? + colistin?)

**Gatti M, Viaggi B, Rossolini GM, Pea F, Viale P**
*Exp Rev Anti Infect Ther* Sep 2021
*Infect Drug Resist* Jun 2021

# **Penetration of Antibacterial Agents** into Pulmonary Epithelial Lining Fluid: An Update

**Drwiega EN** et al. *Clin Pharmacokinet* 2021

| Antibacterial agent | Dosage regimen | ELF to plasma ratio based on AUC |
|---|---|---|
| Ceftaroline | 600 mg IV q12h x 7 doses | 0.23 |
| Cefiderocol | 2000 mg IV x 1 dose | 0.24 |
| Piperacillin/tazobactam | Piperacillin 4 g IV q6h x 3 doses<br>Tazobactam 0.5 g IV q6h x 3 doses | 0.26<br>0.54 |
| Ceftolozane/tazobactam | Ceftolozane 1 g IV q8h x 3 doses<br>Tazobactam 0.5 g IV q8h 3 doses | 0.48<br>0.44 |
| Ceftazidime/avibactam | Ceftazidime 2000 mg IV q8h x 9 doses<br>Avibactam 500 mg IV q8h x 9 doses | 0.31<br>0.35 |
| Cefepime/zidebactam | Cefepime 2 g IV q8h x 7 doses<br>Zidebactam 1 g IV q8h x 7 doses | 0.39<br>0.38 |
| Cefepime/enmetazobactam | Cefepime 2 g IV over 2h q8h x 9 doses<br>Enmetazobactam 1 g IV over 2h q8h x 9 doses | 0.61<br>0.53 |
| Meropenem/vaborbactam | Meropenem 2 g IV q8h x 3 doses<br>Vaborbactam 2 g IV q8h x 3 doses | 0.63/0.65<br>0.53/0.79 |
| Imipenem/relebactam | Imipenem 500 mg IV q6h x 5 doses<br>Relebactam 250 mg IV q6h x 5 doses | 0.44/0.55<br>0.43/0.54 |

Based on the ratio of AUC 12 in ELF to AUC 12 in unbound plasma, assuming 20% protein binding in plasma

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| | | |
|---|---|---|
| Durlobactam/ sulbactam | Durlobactam 1 g IV q6h x 3 doses<br>Sulbactam 1 g IV q6h x 3 doses | 0.50/0.81<br>0.37/0.41 |


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