# Daptomycine
# Cubicin®

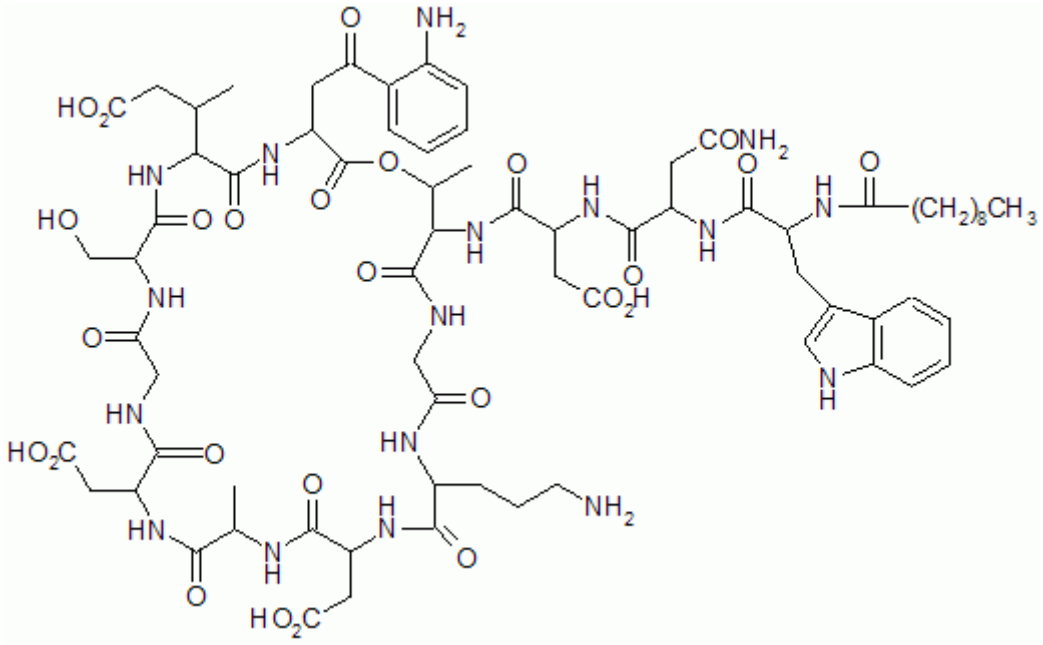
Novartis Europharm Limited

Journée des Référents

JNI, Dijon, Juin 2007

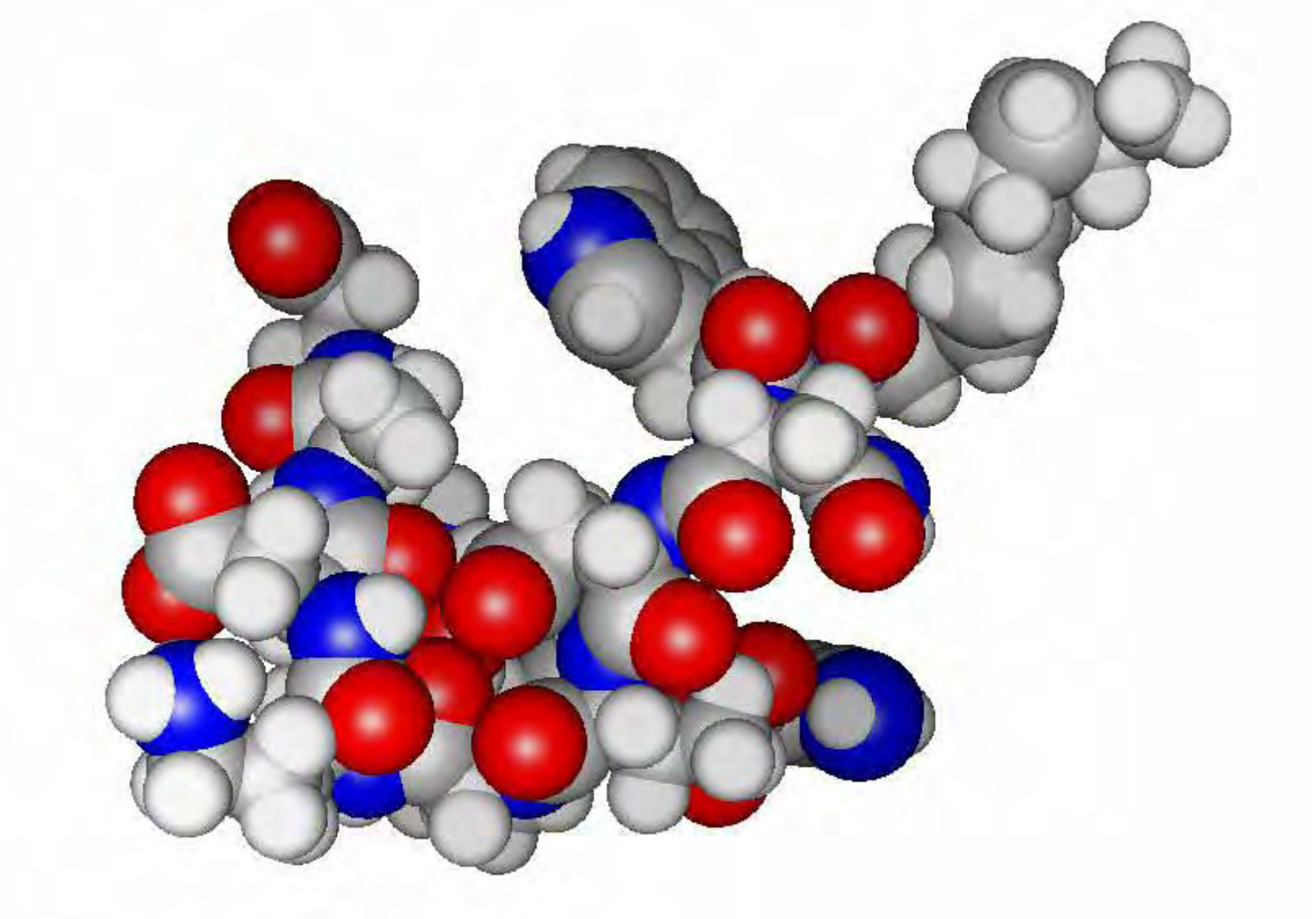
P Chavanet

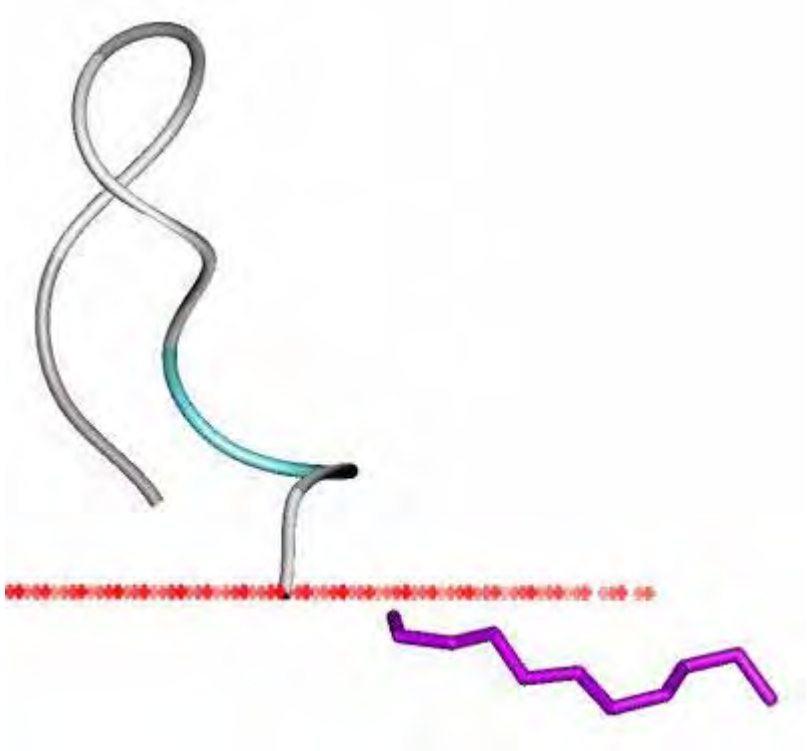
# daptomycin

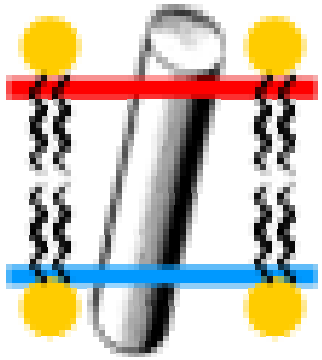



Lipopetide

Streptococcus roseosporus

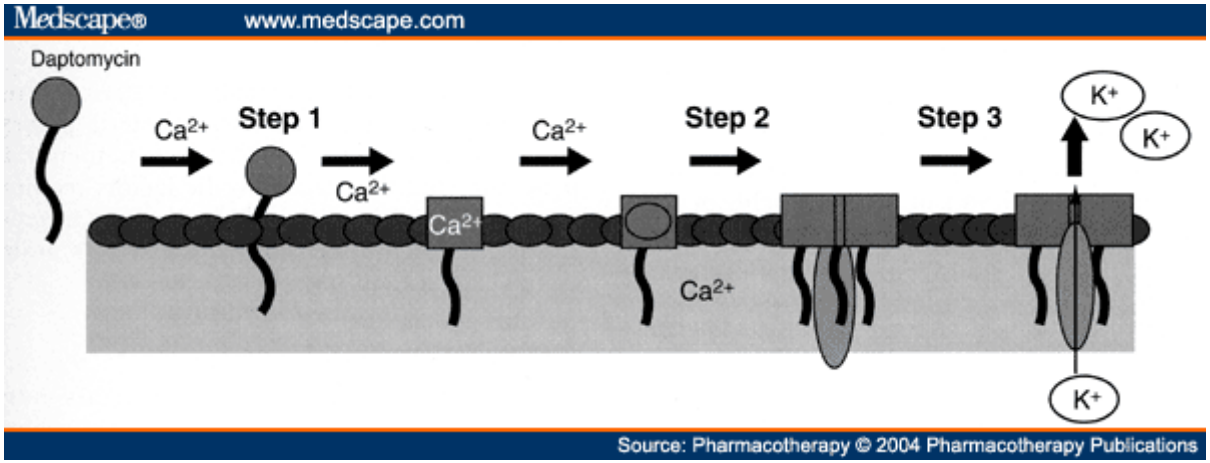






out side

in side




« collapsus » électro-chimique de la membrane

- Arrêt de :
  - la synthèse des protéines,
  - ARN
  - ADN
  - Peptoglycan
  - Acide lipoteichoique
- => bactéricide sans bactériolyse

# Dapto – in vitro 1

| | CMI90 (mg/l) |
|---|---|
| • **Gram +** | |
| – **SA** | |
| • **MS** | **0.5-1** |
| • **MR** | **0.25-1** |
| • **GI ou R** | **4** |
| • **heamolyticus** | **0.25-0.5** |
| – **S coag neg** | |
| • **MS** | **0.25-2** |
| • **MR** | **0.5-1** |
| – **E faecalis** | |
| • **Vanco S** | **1-2** |
| • **Vanco R** | **0.5-4** |
| – **E faecium** | |
| • **Vanco S** | **1-4** |
| • **Vanco R** | **0.5-4** |

**CA-SFM 2007**
**Dapto S ≤ 1**
**R > 1**

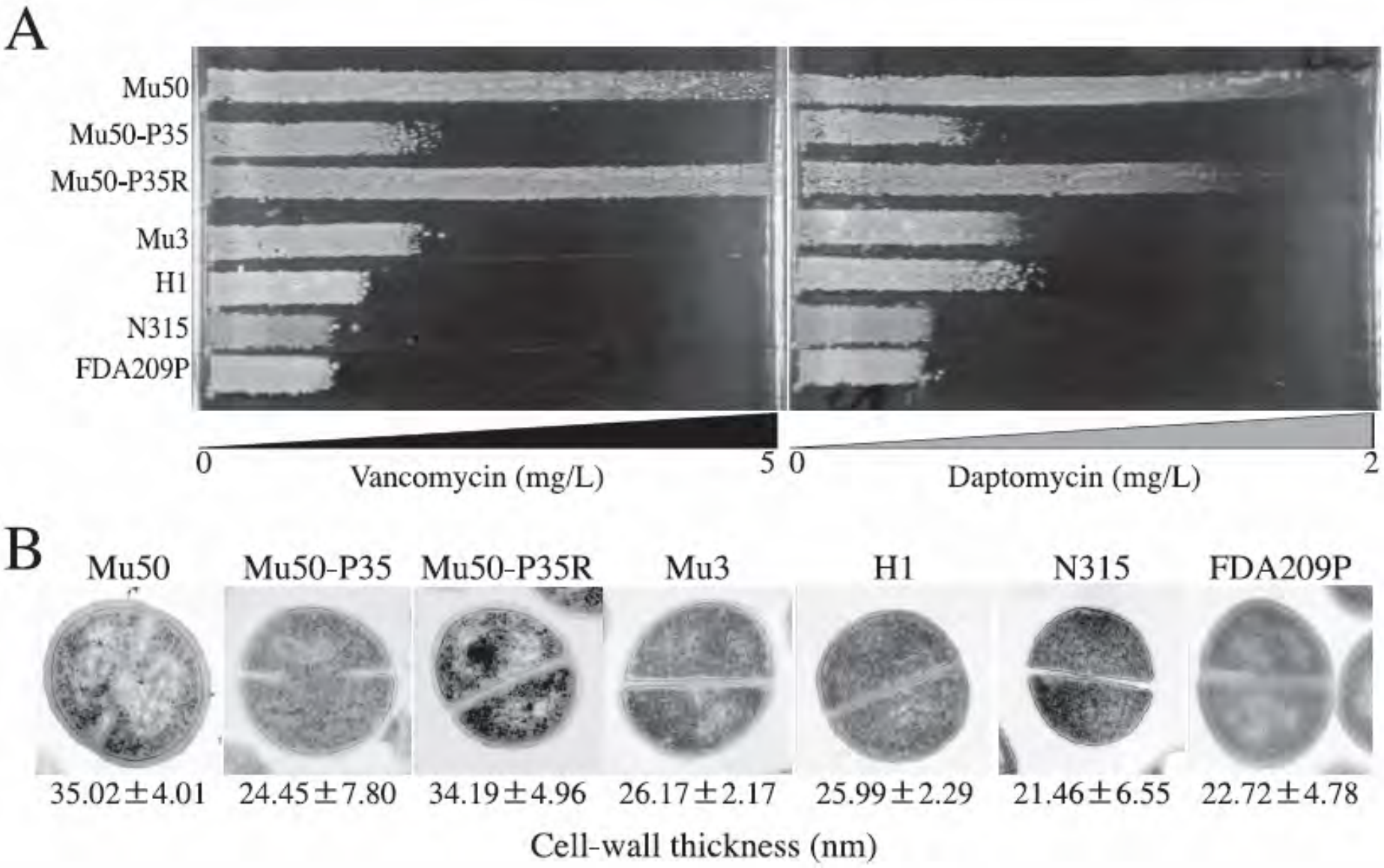
**CA-SFM 2007**
**……**

# Dapto – in vitro 2

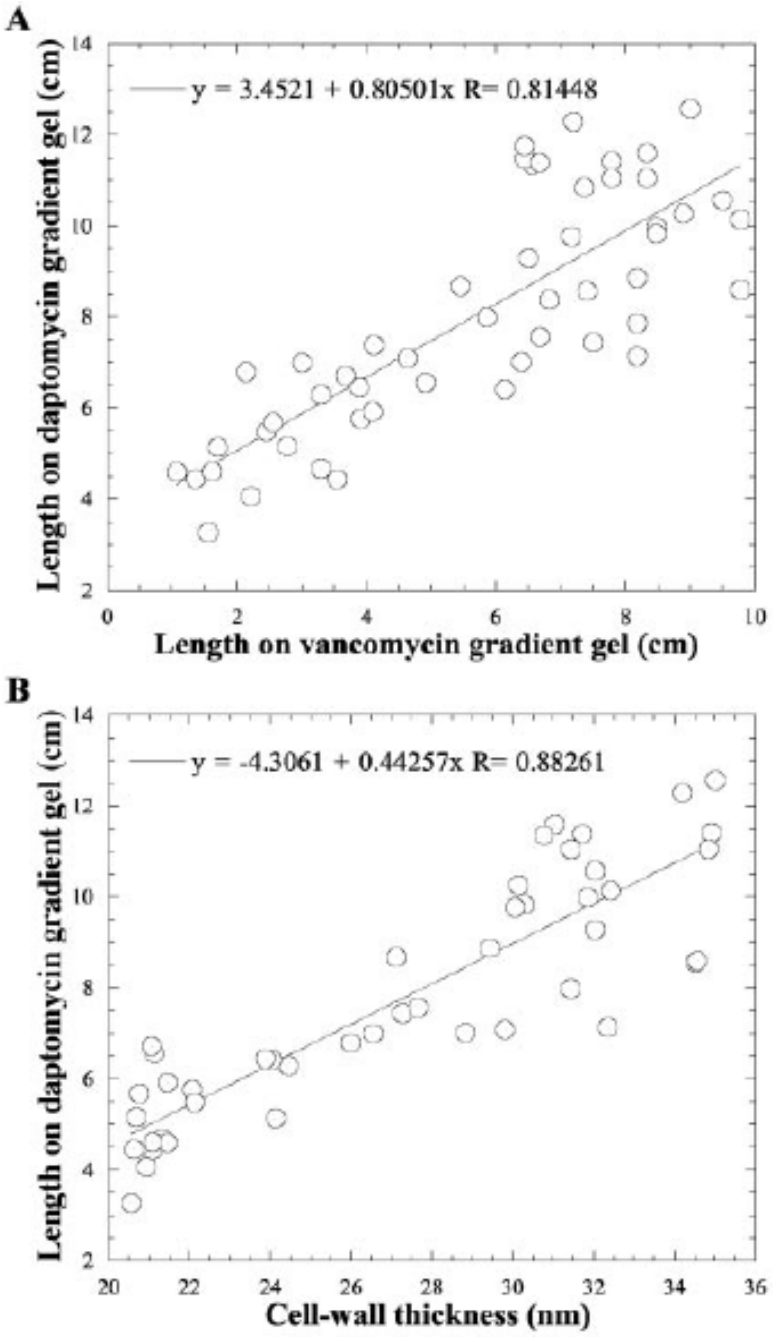
| | CMI90 (mg/l) |
|---|---|
| • Anaerobie | |
| – Actinomyces | 4 |
| – C difficile | 1 |
| – C perfringens | 0.5 |
| – Lactobacillus | 16 |
| – Peptostretococcus | 0.06-1 |
| – Propionibacterium | 2 |
| – C jeikeium | 0.25 |
| • BGN | |
| – = pénétration ? | |

# Dapto - résistance

- SAMR – foyer osseux
  - Marty FM, JCM 2006
  - Skiest DJ, JCM 2006
- SA
  - VISA : souches de référence




Cui L, AAC 2006;50:1079

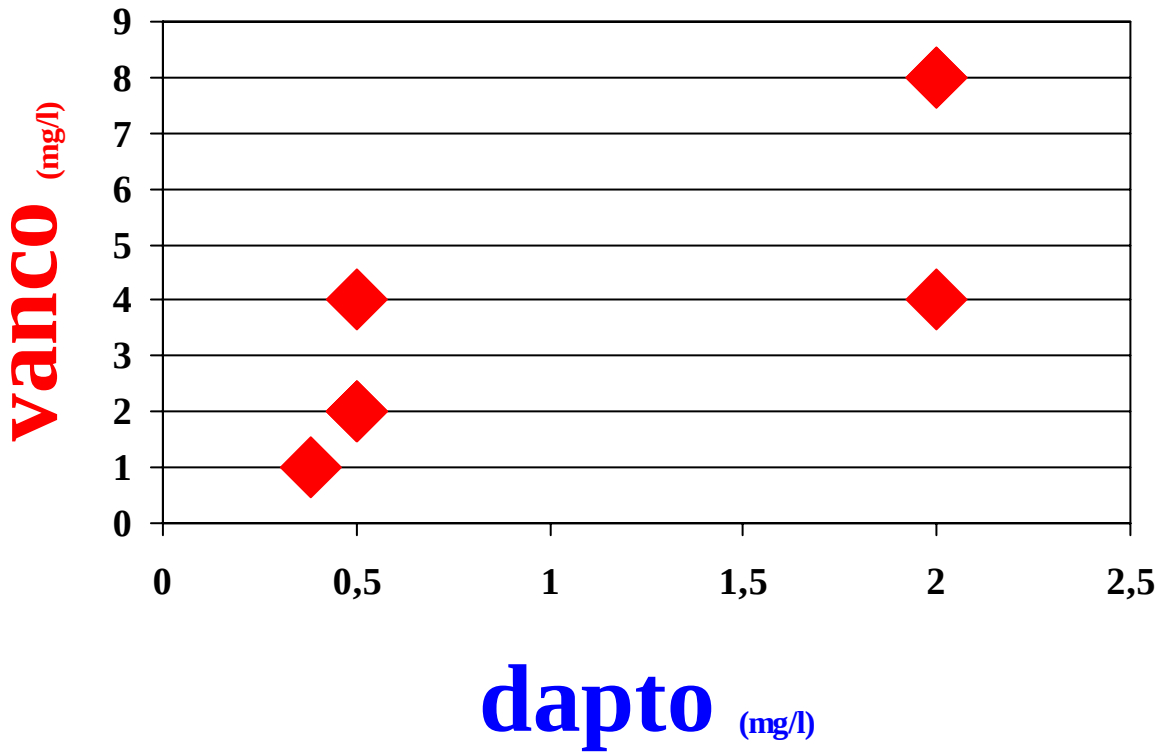



Cui L, AAC 2006;50:1079

# Dapto - résistance

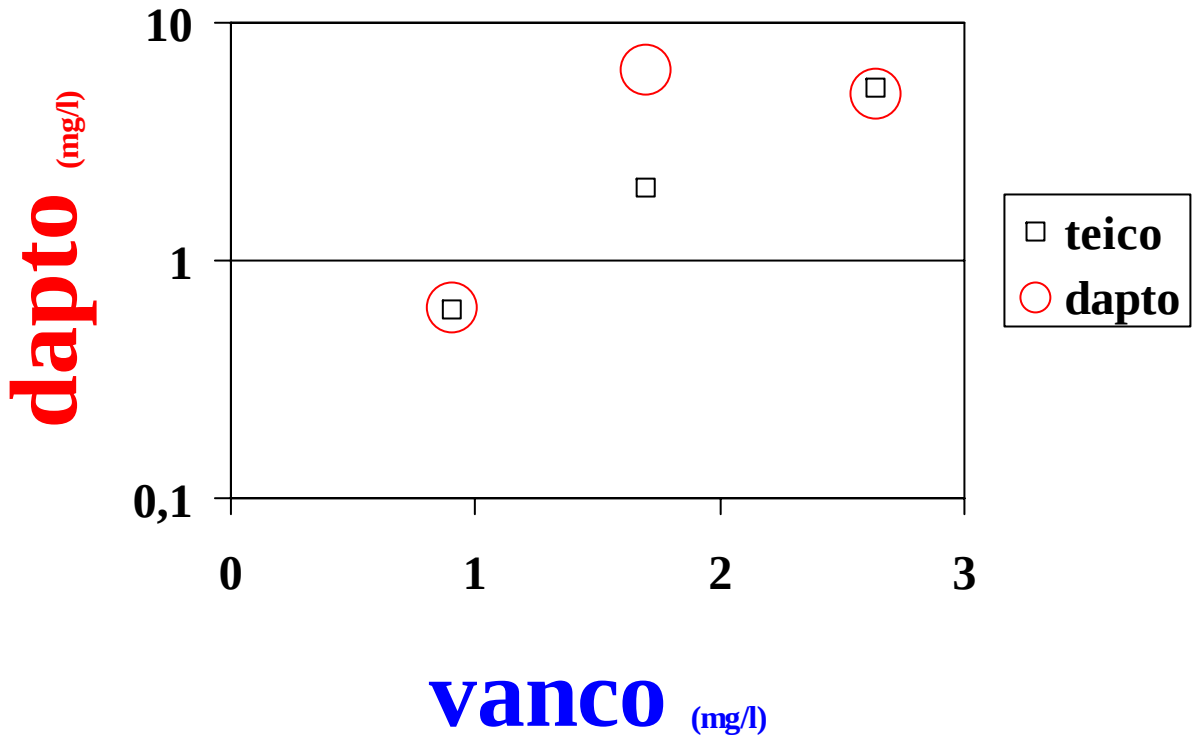
- SAMR – foyer osseux
  - Marty FM, JCM 2006
  - Skiest DJ, JCM 2006
- SA
  - VISA : souches de référence
    - » Cui L, AAC 2006;50:1079
  - Souches cliniques pré-exposées à la vanco
    - » Sakoulas G, AAC 2006;50:1581
- Enterocoque résistant à la vanco

# Pré-exposition vanco > dapto



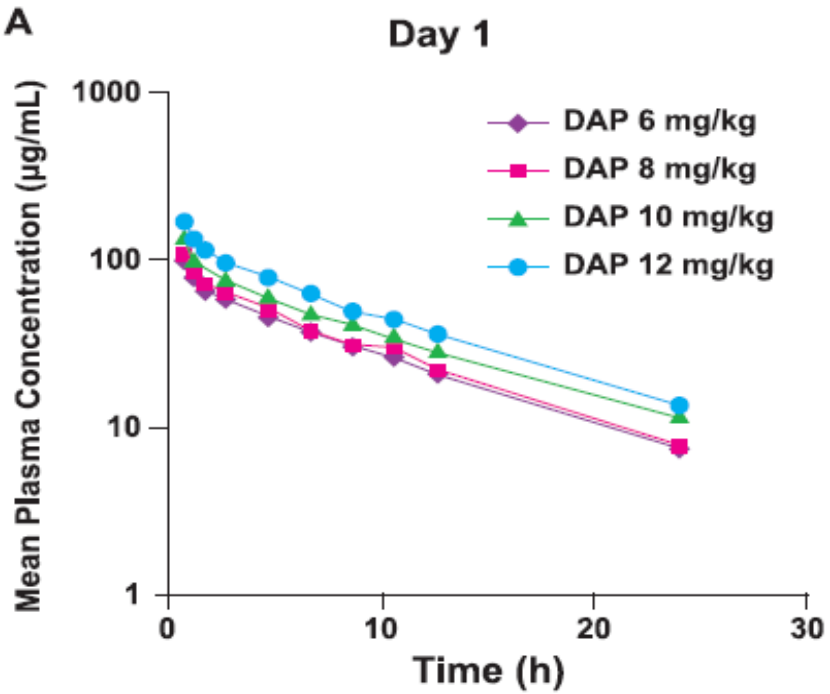

D'après Sakoulas G, AAC 2006;50:1581

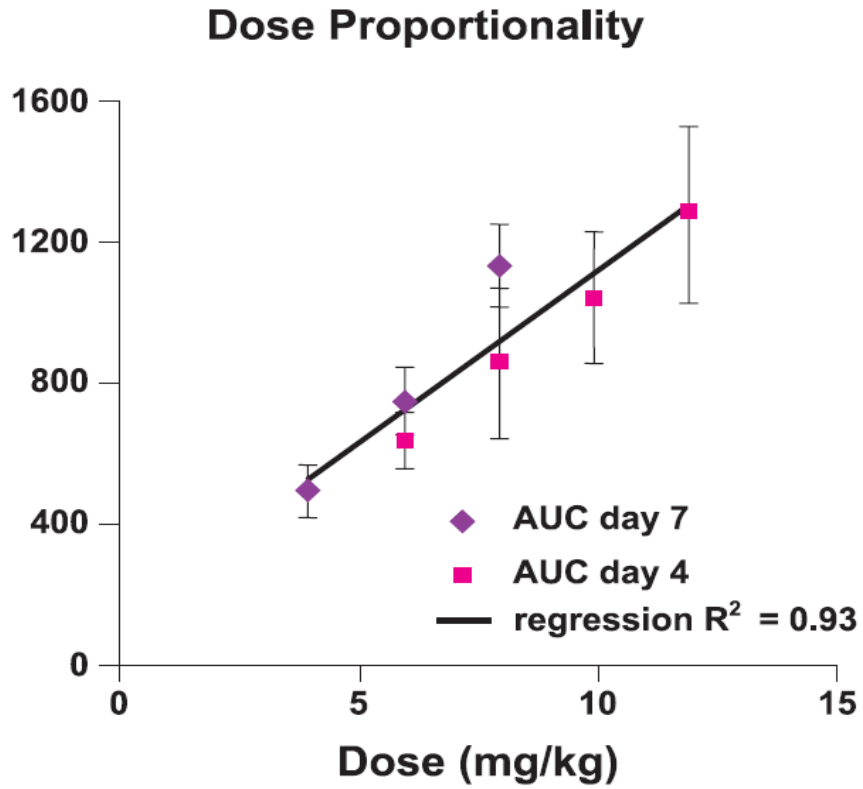
# Pré exposition dapto > glycopeptide




Kaatz GW, International Journal of Antimicrobial Agents 28 (2006) 280–287

# Dapto pk




| Clairance ml/mn | T1/2 (h) |
|---|---|
| ➢>80 | 8-11 |
| ➢ 40-80 | 9 |
| ➢ <40 | 19 |
| ➢Dialyse | 29 |

Dvorchik B, AAC 2004;48:2799

Benvenuto M AAC 2006;50:3245

# Dapto: clinique - efficacité

| | dapto | comparateur |
|---|---|---|
| **Peau – tissus mous** | **4 mg/kg/j od** | **PeniM, vanco..** |
| | **74%** | **73%** |
| **SA, Strepto** | **82%** | **71%** |
| **Endocardite SA** | **6 mg/kg/j od** | **PeniM, vanco..** |
| | **44.2%** | **41.7%** |
| • **Rechute (n)** | **19** | **11** |
| | **augmentation de CMI dapto** | **si vanco augmentation CMI** |
| **Pneumonie comm.** | **4 mg/kg/j od** | **ceftriaxone 1g** |
| **usa** | **85.7%** | **84.8%** |
| **europe** | **74.3%** | **85.3%** |

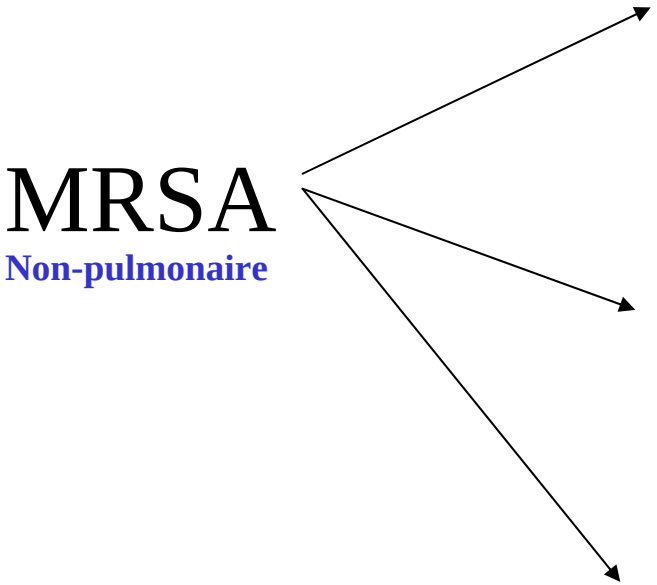
Surfactant, Silverman JA, JID 2005; 191:2149–52

# Dapto: clinique - toxicité

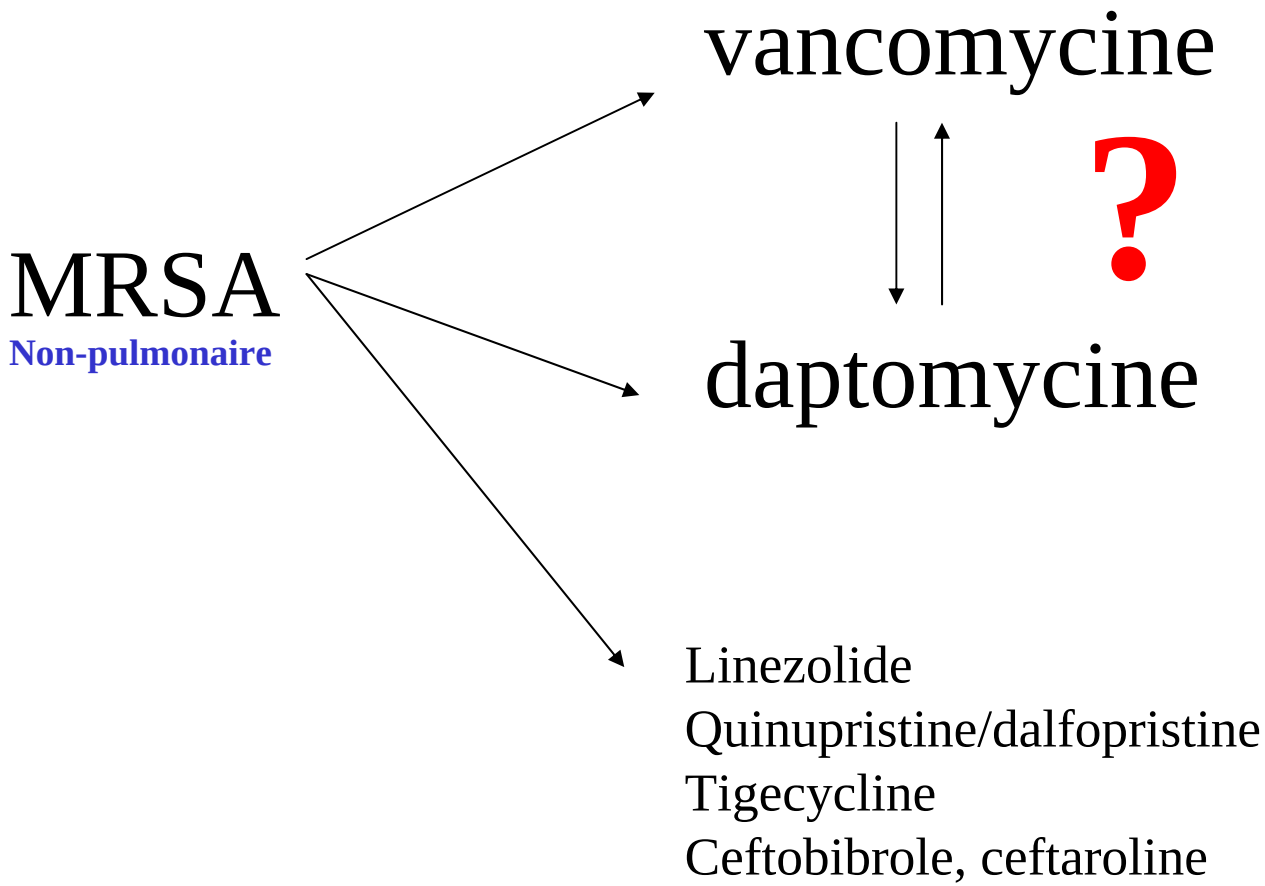
- **Troubles digestifs**
- **Douleur – inflammation au site de perfusion**
- **Céphalées**
- **Arrêt pour toxicité: 2.8%**

- **CPK augmentées 5-10%**

**Succession ineluctable et dangereuse, rompre le cercle**
**Gram +, nécessité d'une diversité anti-staphylococcique**



**Succession ineluctable et dangereuse, rompre le cercle**
**Gram +**



# Dapto - espoir

- Daptomycine
  - Rapidement bactéricide
  - Sans bactériolyse

  - => traitement des méningites bactériennes
    - » Grandgirard D, AAC 2007;51:2173
    - » Stucky A, AAC 2007;51:2249
    - » Gerber P JAC 2006;57:720

Merci de votre attention

# Posaconazole
# Noxafil®

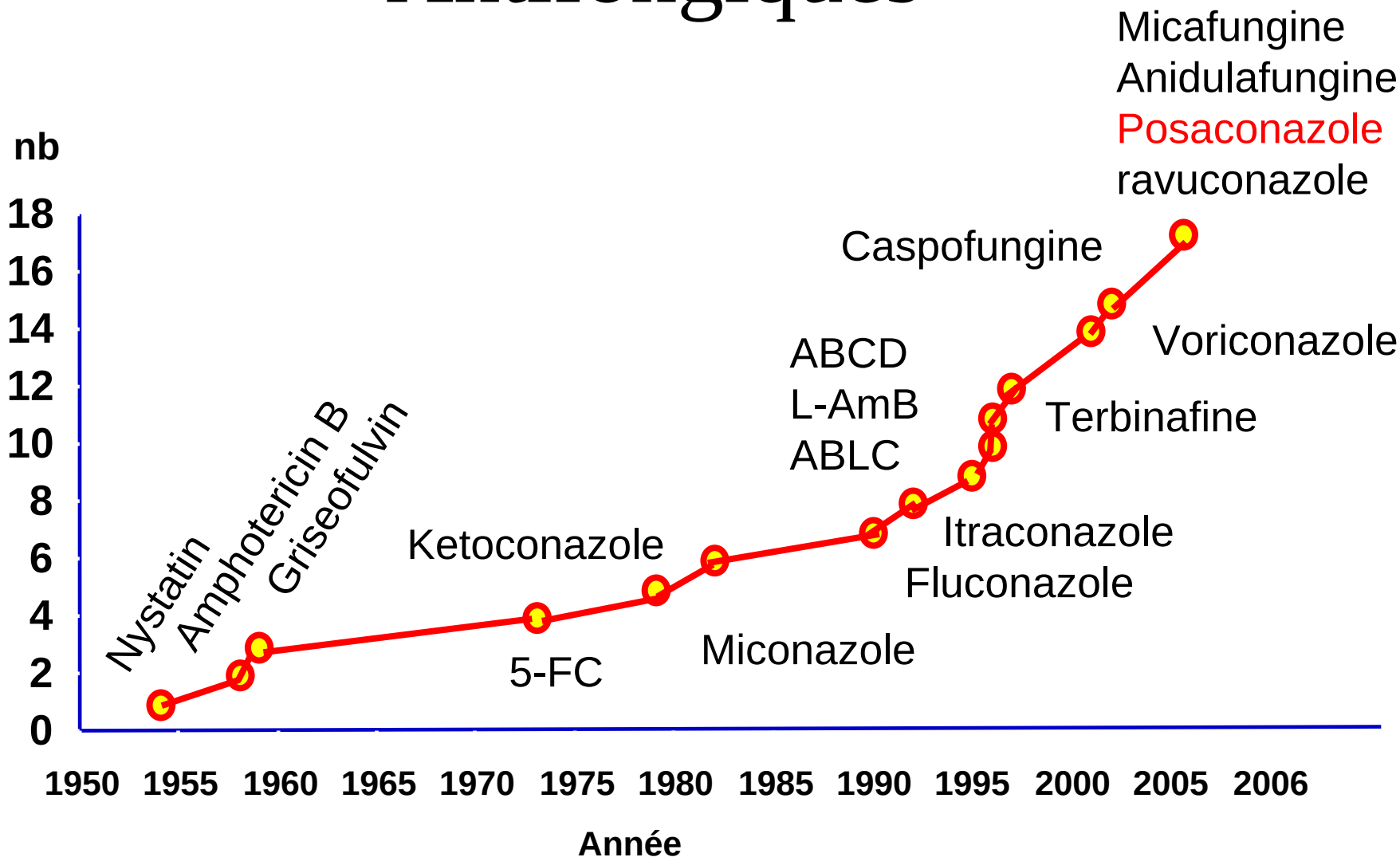
Schering Plough

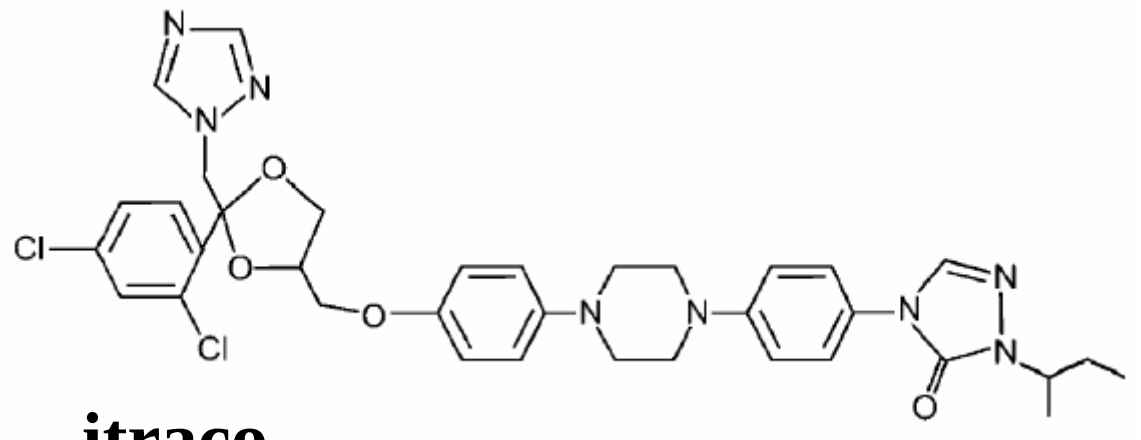
Journée des Référents

JNI 2007

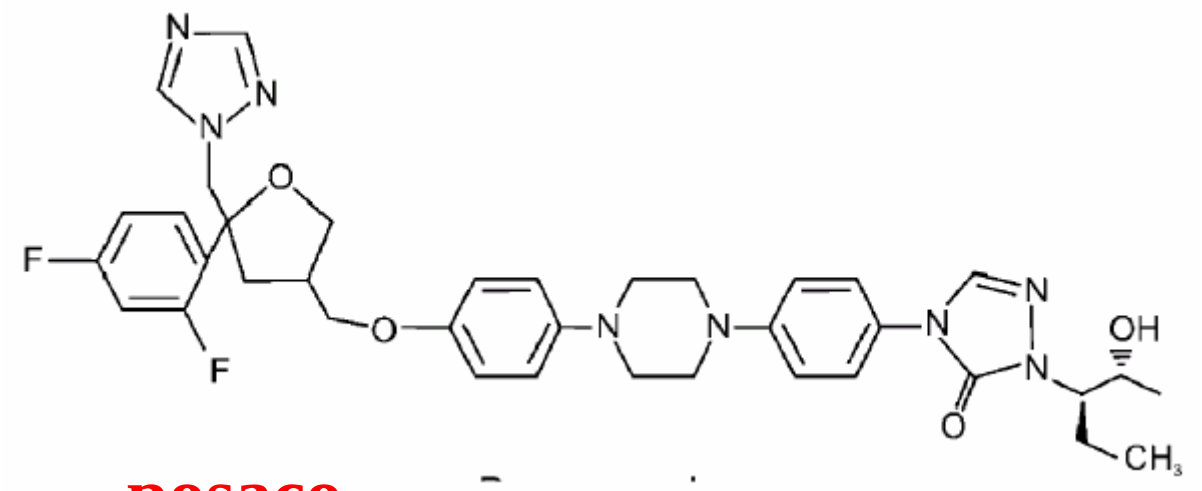
P Chavanet

# Antifongiques

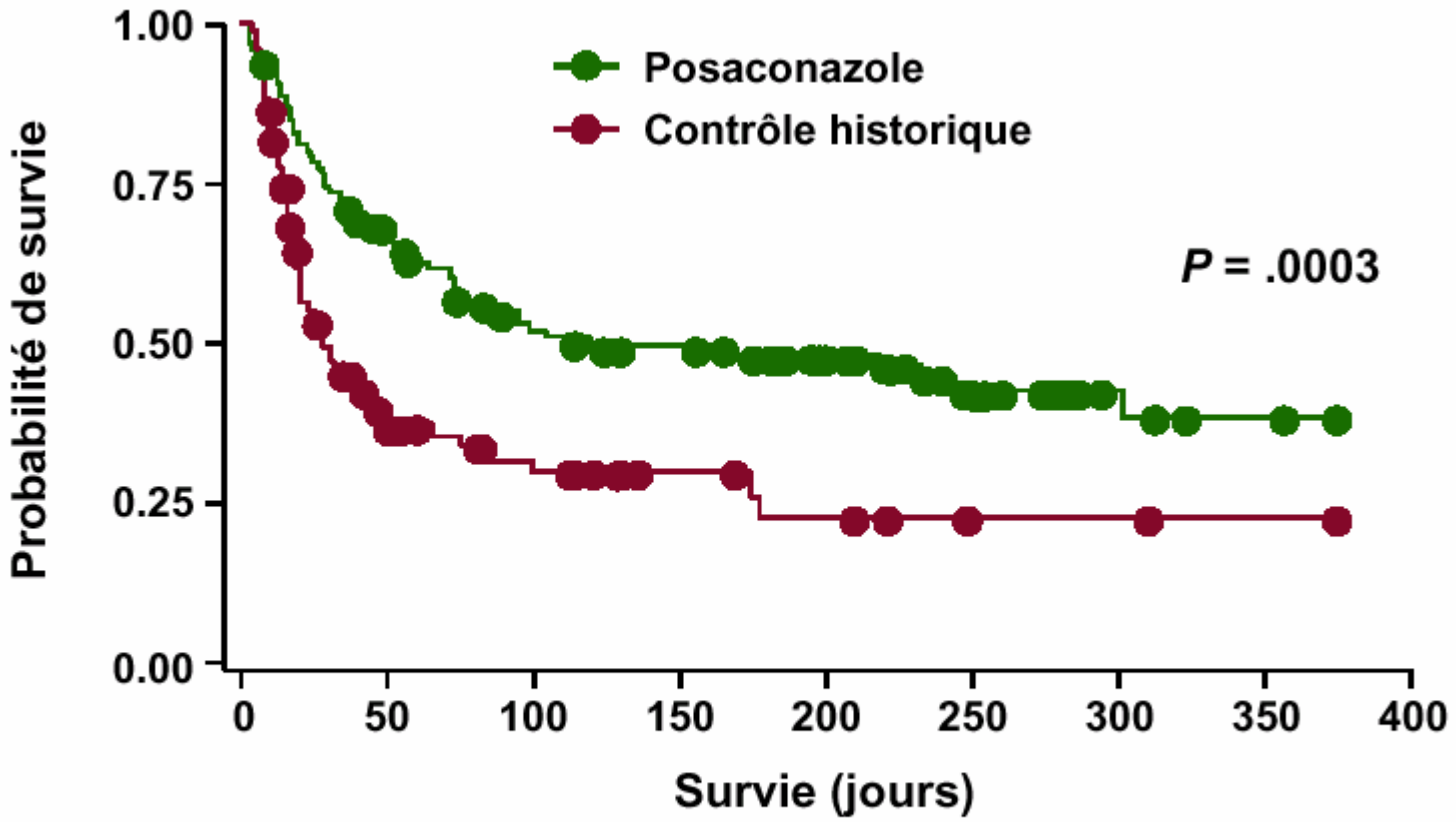




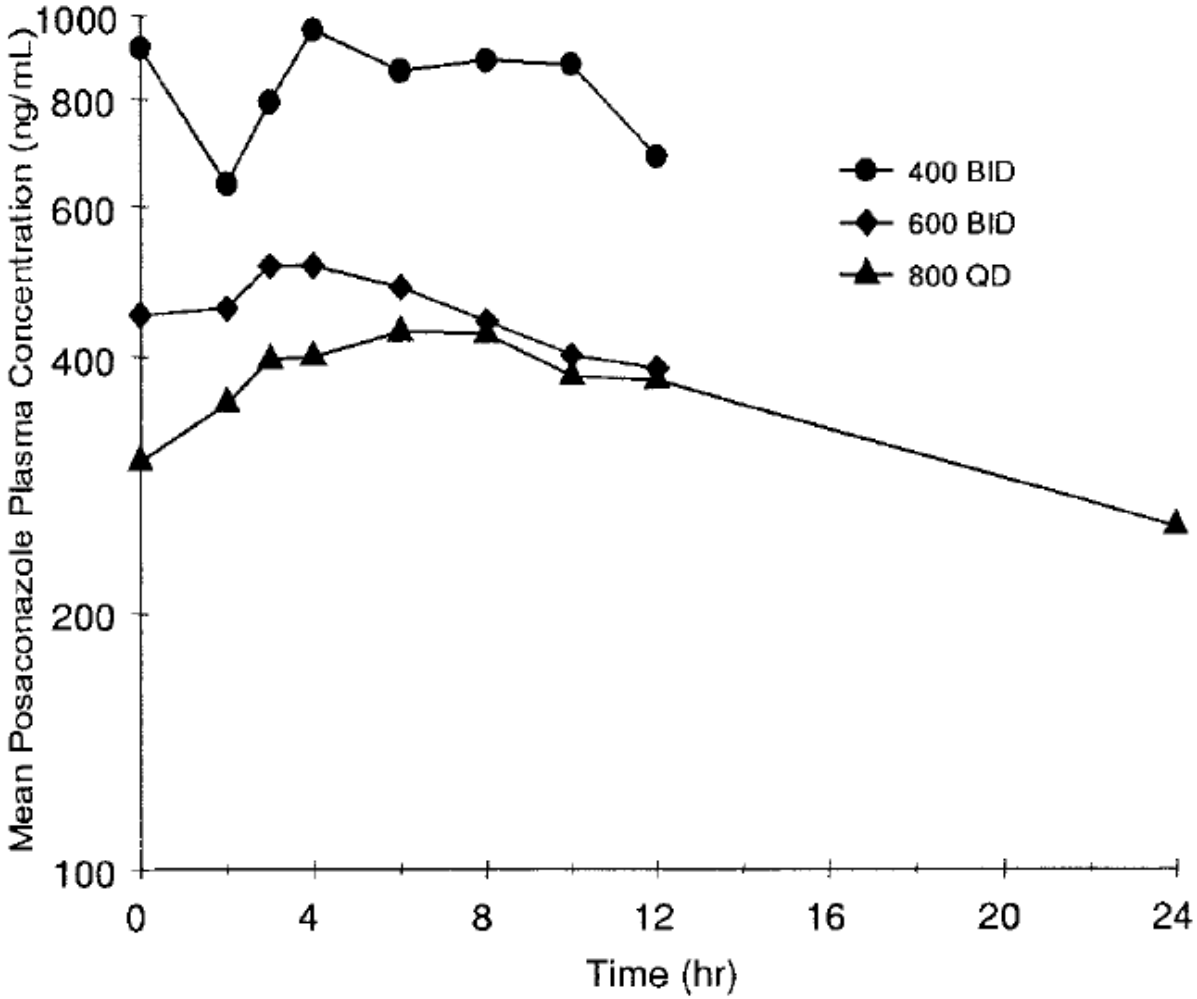

**itraco**



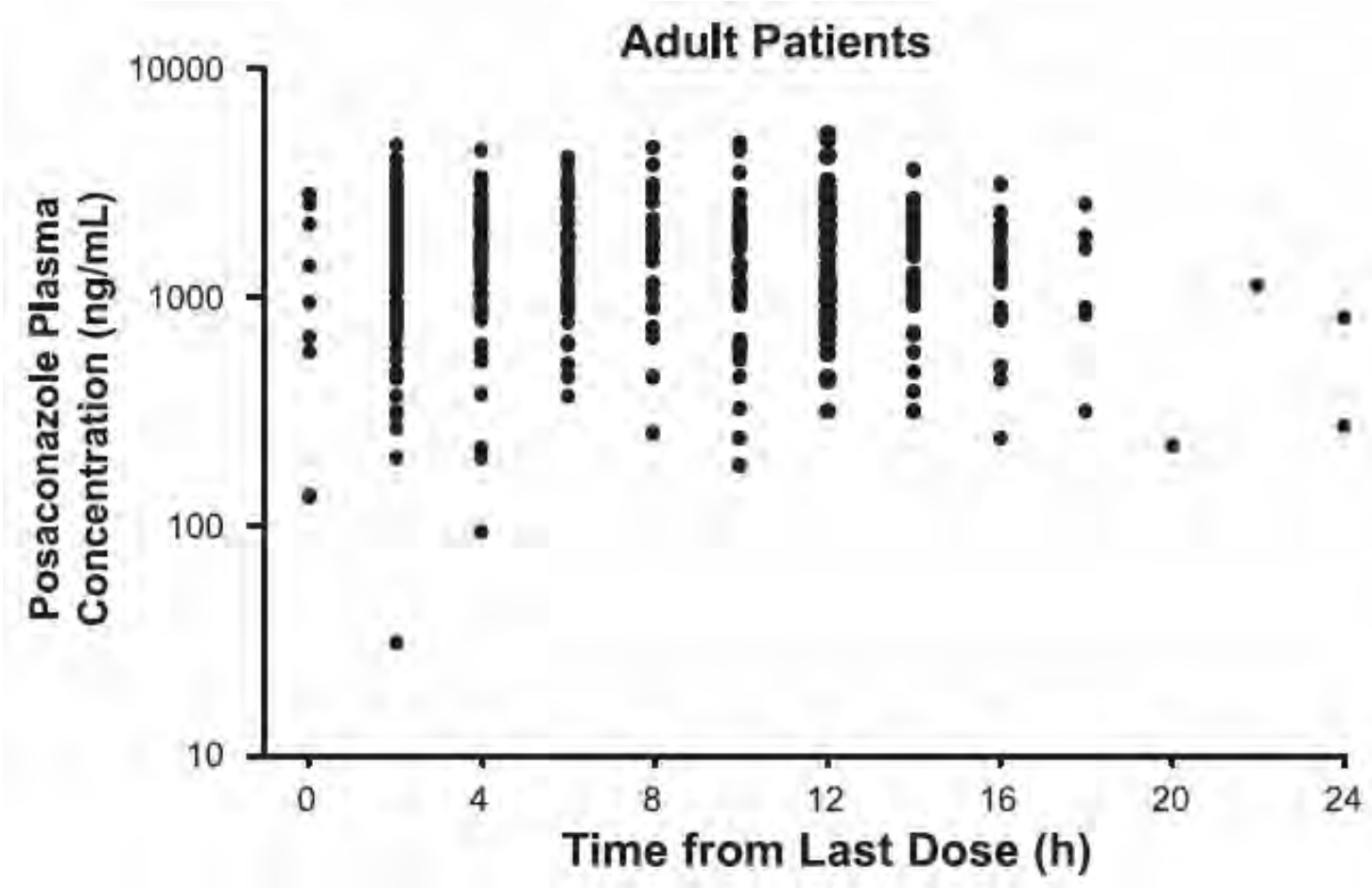

**posaco**



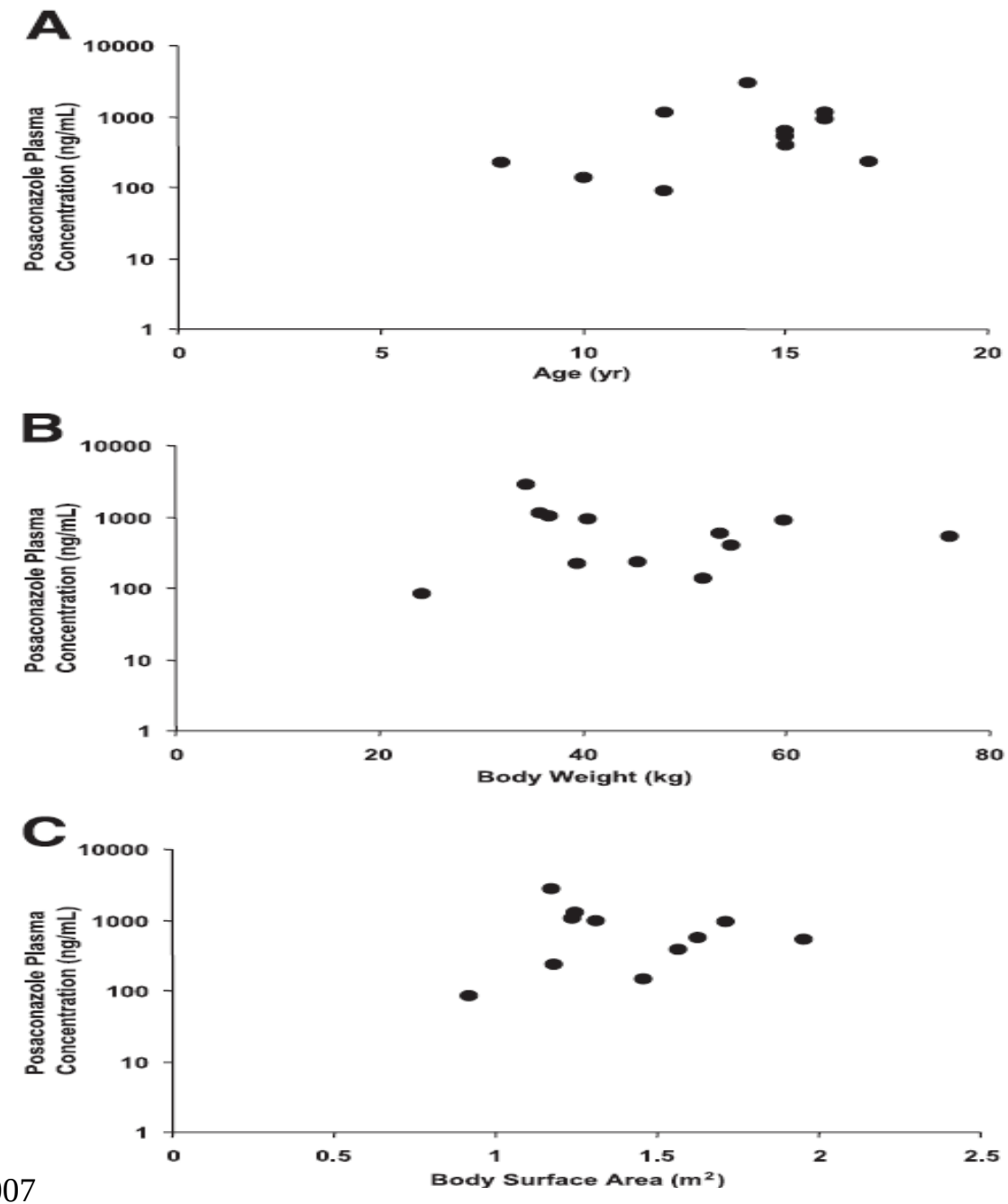

Raad I et al. ICAAC 2004. Abstract M-669.


Mean Posaconazole Plasma Concentration (ng/mL)
1000
800
600
400
200
100
0
4
8
12
16
20
24
Time (hr)
400 BID
600 BID
800 QD

# Posaco pk




Krishna et al AAC 2007




Krishna et al AAC 2007

# Posaco PK

- 800 x 1 < **400 x 2** << 200 x 4

# Posaco PK

- 800 x 1 < **400 x 2** << 200 x 4

- Interactions ++
- Suivi des concentrations ?
  - 0.25 mg/l au creux ?

# Comparaisons in vitro des antifongiques azolés

## -Candida

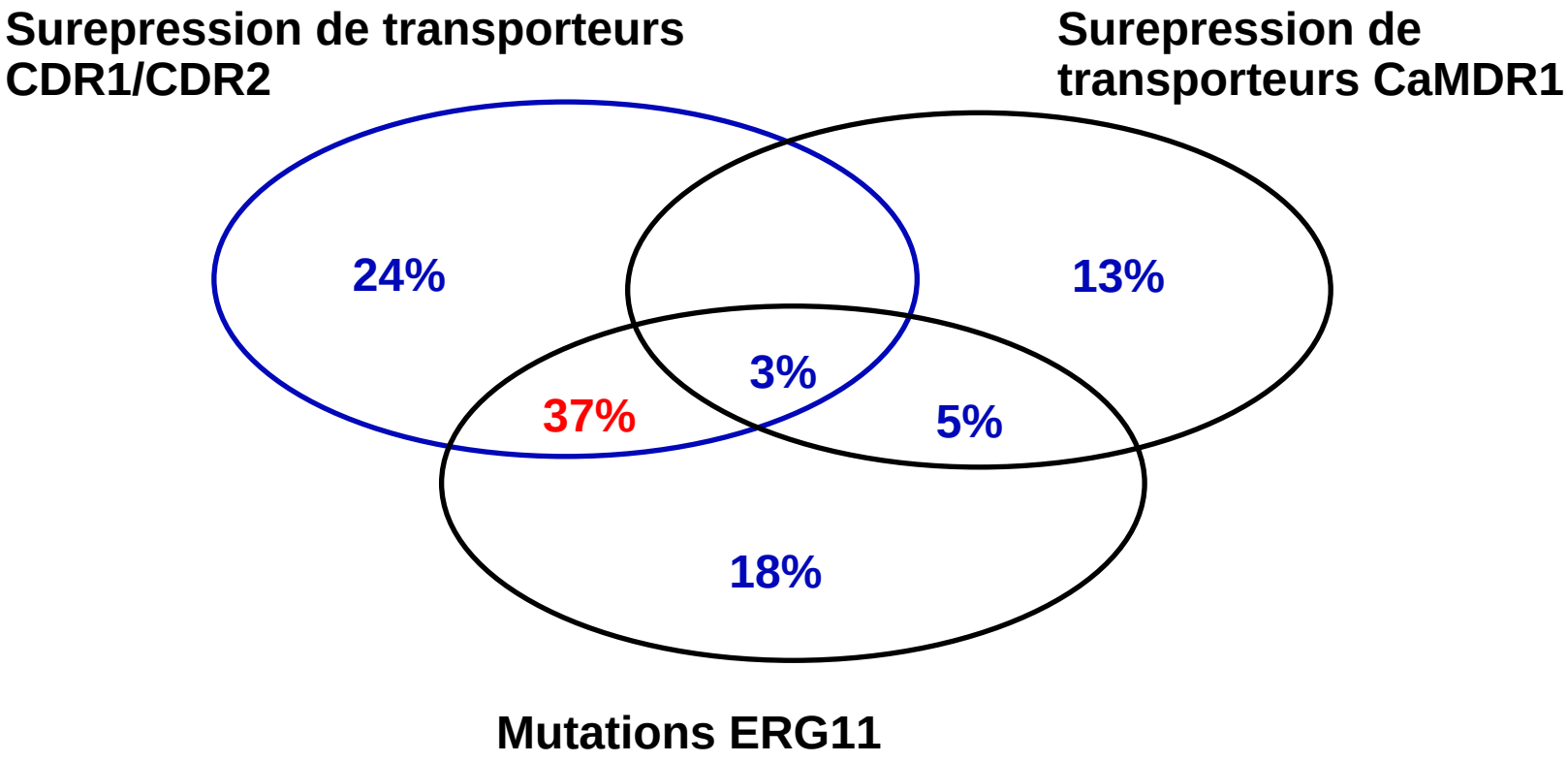
| | CMI 90 | | | |
|---|---|---|---|---|
| | **Fluco** | **Itra** | **Vori** | **Posa** |
| **C.albicans** | **16** | **1** | **0,5** | **0.063** |
| **C.glabrata** | **64** | **4** | **2** | **2** |
| **C.paraps** | **4** | **0.5** | **0.125** | **0.25** |
| **C.tropical** | **4** | **0.5** | **0.5** | **0.25** |
| **C.krusei** | **>64** | **1** | **0.5** | **1** |

Sabatelli R, AA 2006;50:2009-15

# Posaco vs candidose oeosphagienne « vih »

- **Candidose oesophagienne**
  - **Fluco = posaco** (Vasquez CID 2006)

# Résistance aux azolés chez C.albicans




**Fluco <<< vorico < posaco**

# Comparaisons in vitro des antifongiques azolés

## -Candida

| | CMI 90 | | | |
|---|---|---|---|---|
| | **Fluco** | **Itra** | **Vori** | **Posa** |
| **C.albicans** | **16** | **1** | **0,5** | **0,063** |
| C.glabrata | 64 | 4 | 2 | 2 |
| C.paraps | 4 | 0.5 | 0.125 | 0,25 |
| C.tropical | 4 | 0.5 | 0.5 | 0.25 |
| C.krusei | >64 | 1 | 0.5 | 1 |
| **Sur souche fluco-R** | | | | |
| **C. albicans** | **-** | **32** | **32** | **16** |
| **C. glabrata** | **-** | **16** | **8** | **16** |

*> x 250*

Sabatelli R, AA 2006;50:2009-15

# Posaco vs candidoses orales VIH résistantes au fluco

- Posaco
- Succès: 73-75%
  - en rattrapage des candidoses orales VIH résistantes au fluco:
    - Skiest Dj, CID 2007

# Comparaisons in vitro des antifongiques azolés

## -Aspergillus

| | CMI 90 | | |
|---|---|---|---|
| | **Itra** | **Vori** | **Posa** |
| **A flavus** | **1** | **1** | **0.25** |
| **A fumigatus** | **1** | **0.5** | **0.5** |
| **A niger** | **2** | **2** | **0.5** |
| **A terreus** | **0.5** | **0.5** | **0.25** |

Sabatelli R, AA 2006;50:2009-15

# Posaco vs aspergillose

- Rattrapage de candin et/ou vorico
  - Succès = 42%
    - Walsh TJ, CID 2007 Jan 1;44(1):2-12

# Posaco vs zygomycetes in vitro

= trou du vorico

**In vitro**

| | posaco | | vorico | |
|---|---|---|---|---|
| | **CMI 90** | **<0.5 (%)** | **CMI 90** | **<2 (%)** |
| **Rhizopus** | **1** | **80** | **>8** | **5** |
| **Mucor** | **2** | **70** | **>8** | **0** |
| **Absidia c** | **0.03-0.25** | **-** | **>8** | **-** |
| **Cunninghamella** | **0.01-1** | **75** | **>8** | **10** |

Almyroudis NG, AAC 2007

# Posaco vs zygomycose des succès cliniques

- Van Burik CID 2006
  - 91 pts en sauvetage
  - Succès: 60%

- Greeberg AAC 2006
  24 pts en sauvetage
  - Succès: 79% (+ chir.)

- Mullane K, Transpl Infect Dis. 2007 Jun;9(2):89-96

- Page RL, Pharmacotherapy. 2007 Feb;27(2):290-8

- ……..

# Posaconazole en 2007

- Zygomycose
- Protocoles
  - Curatif
  - prophylaxie

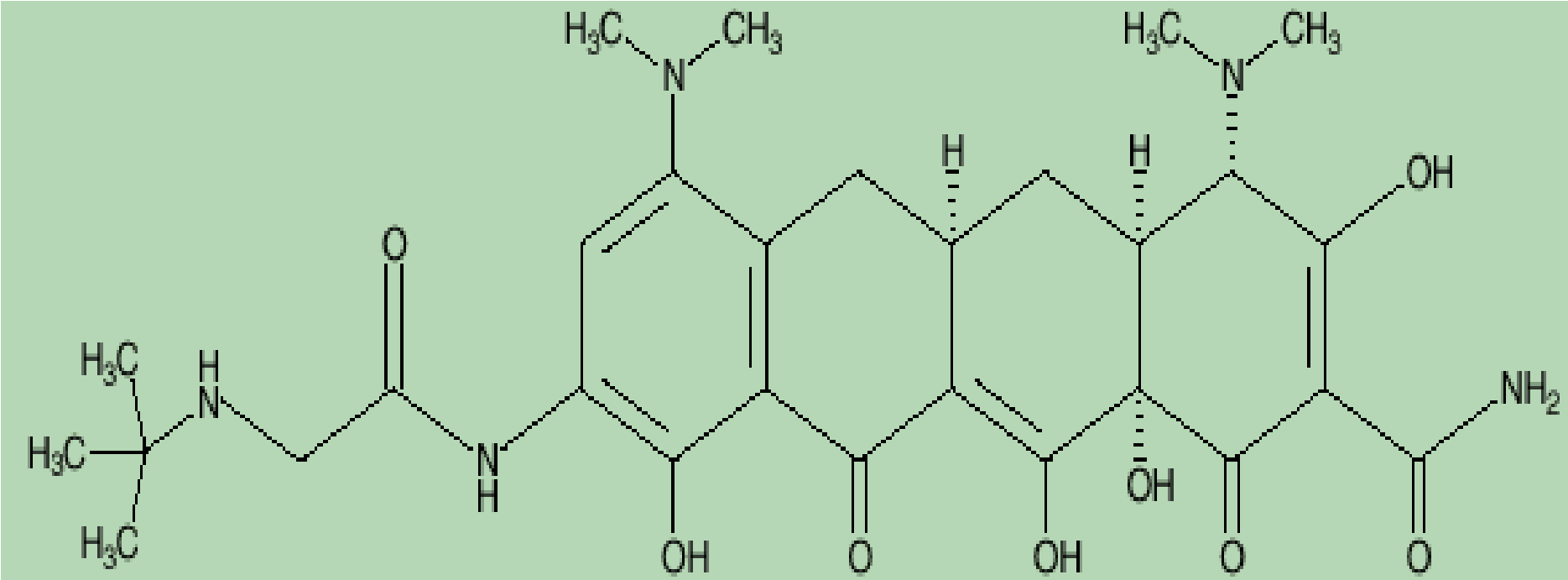
# Tigecycline

# Tigacyl®, Wyeth

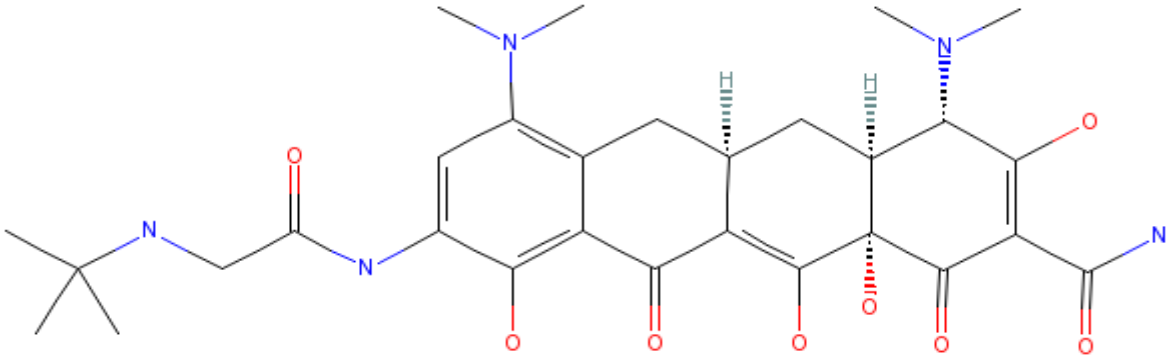
Journée des Référents

JNI 2007, Dijon

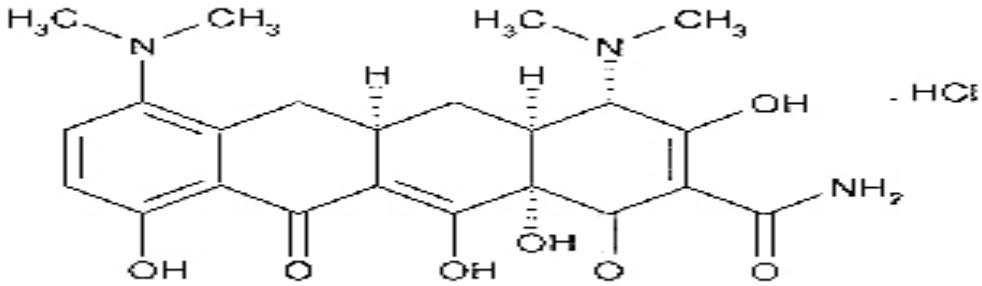
P Chavanet


H3C
CH3
N
H3C
CH3
N
H
H
OH
O
H3C
H
N
NH2
H3C
N
H
OH
OH
O
OH
O
O
H3C

tigecycline



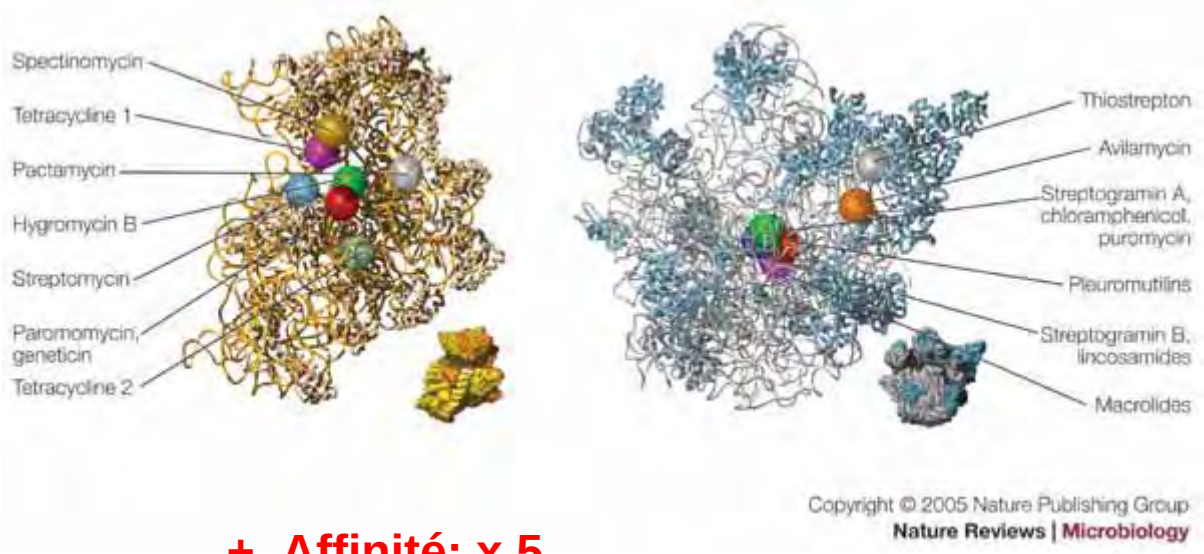
minocycline



# tigecycline

Mb bacterienne

**+ Tet +, +, ……**
**+ acrA/B, AdeABC**




**+ Affinité: x 5**
**+ ↓ synth. Prot: x 10**

# Sensibilité « aerobie »

## BGN Soussy CJ, icaac 06

| BACTERIAL SPECIES ( Number of strains ) | MIC 50 ( µg / mL ) | | MIC 90 ( µg / mL ) | |
|---|---|---|---|---|
| | A | B | A | B |
| *Enterobacteriaceae* (400) except *Proteus spp* | 0.5 | 0.5 | 2 | 2 |
| *Proteus spp* (100) | 2 | 1 | 8 | 4 |
| *P. aeruginosa* (100) | 16 | 8 | 32 | 32 |
| *A. baumannii* (100) | 0.5 | 0.25 | 2 | 2 |
| *S. maltophilia* (50) | 0.5 | 0.25 | 2 | 2 |

# Sensibilité « aerobie »

## Gram + Soussy CJ, icaac 06

| BACTERIAL SPECIES ( Number of strains ) | MIC 50 ( µg / mL ) | | MIC 90 ( µg / mL ) | |
|---|---|---|---|---|
| | A | B | A | B |
| MSSA (100) | 0.12 | 0.06 | 0.5 | 0.5 |
| MRSA (150) | 0.12 | 0.06 | 0.5 | 0.5 |
| GISA (30) | 0.25 | 0.12 | 0.5 | 0.5 |
| MSCNS (50) | 0.12 | 0.06 | 0.5 | 0.5 |
| MRCNS (50) | 0.25 | 0.12 | 0.5 | 0.5 |
| *E. faecalis* (100) | 0.12 | 0.06 | 0.5 | 0.5 |
| *E. faecium* (50) | 0.12 | 0.06 | 0.25 | 0.25 |
| Streptococci A, C & G (100) | 0.06 | 0.03 | 0.25 | 0.25 |
| PSSP (50) | 0.03 | 0.03 | 0.12 | 0.12 |
| PRSP (48) | 0.03 | 0.03 | 0.12 | 0.12 |

# Sensibilité « aerobie »

Soussy CJ, icaac 06

| BACTERIAL SPECIES ( Number of strains ) | MIC 50 ( µg / mL ) | | MIC 90 ( µg / mL ) | | C. critique |
|---|---|---|---|---|---|
| | A | B | A | B | |
| *Enterobacteriaceae* (400) except *Proteus spp* | 0.5 | 0.5 | 2 | 2 | ≤2 |
| *Proteus spp* (100) | 2 | 1 | 8 | 4 | |
| *P. aeruginosa* (100) | 16 | 8 | 32 | 32 | |
| *A. baumannii* (100) | 0.5 | 0.25 | 2 | 2 | |
| *S. maltophilia* (50) | 0.5 | 0.25 | 2 | 2 | |
| MSSA (100) | 0.12 | 0.06 | 0.5 | 0.5 | ≤0.5 |
| MRSA (150) | 0.12 | 0.06 | 0.5 | 0.5 | |
| GISA (30) | 0.25 | 0.12 | 0.5 | 0.5 | |
| MSCNS (50) | 0.12 | 0.06 | 0.5 | 0.5 | |
| MRCNS (50) | 0.25 | 0.12 | 0.5 | 0.5 | |
| *E. faecalis* (100) | 0.12 | 0.06 | 0.5 | 0.5 | ≤0.25 |
| *E. faecium* (50) | 0.12 | 0.06 | 0.25 | 0.25 | |
| Streptococci A, C & G (100) | 0.06 | 0.03 | 0.25 | 0.25 | |
| PSSP (50) | 0.03 | 0.03 | 0.12 | 0.12 | |
| PRSP (48) | 0.03 | 0.03 | 0.12 | 0.12 | |

# Sensibilité « anaerobie »

Dubreuil L, icaac 06

**TABLE 1. ACTIVITY OF TIGECYCLINE AGAINST 230 ANAEROBIC BACTERIA**

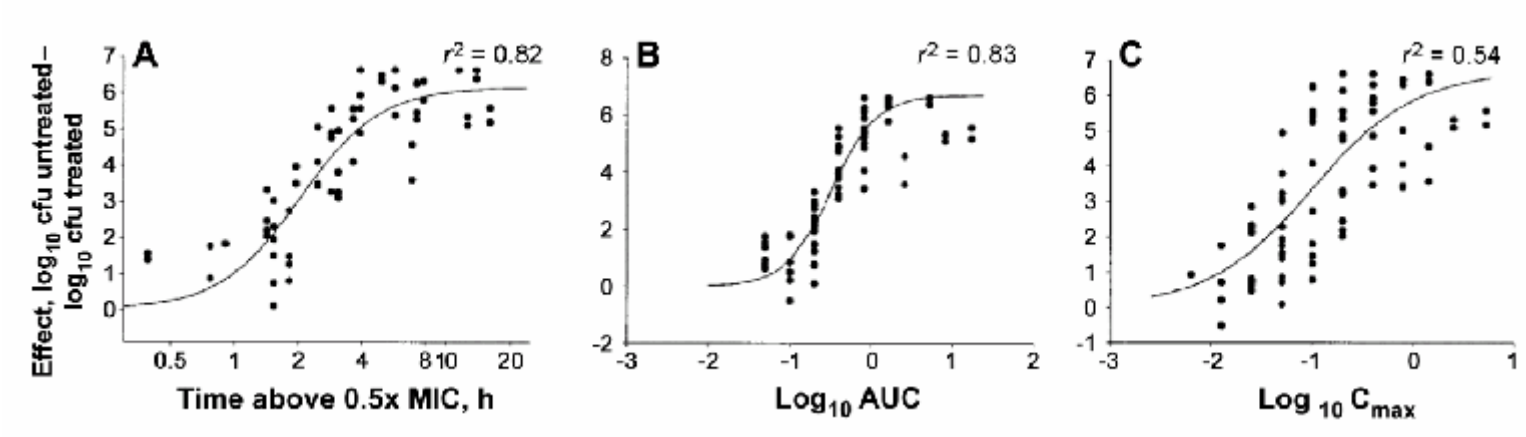
| BACTERIAL SPECIES | MIC RANGE (mg / L) | MIC (mg / L) | |
|---|---|---|---|
| | | $MIC_{50}$ | $MIC_{90}$ |
| *Bacteroides fragilis* (84) | [ 0.06 - 16 ] | 0.5 | 2 |
| *Bacteroides thetaiotaomicron* (14) | [ 0.06 - 16 ] | 2 | 16 |
| Other *Bacteroides* (19) [1] | [ 0.06 - 2 ] | 0.25 | 1 |
| **All *Bacteroides* of the fragilis group** (117) | [ 0.06 - 16 ] | 0.5 | 2 |
| *Prevotella spp* (4) [2] | [ 0.06 - 0.125 ] | N D | N D |
| **All gram-negative anaerobes** (121) | [ 0.06 - 16 ] | 0.5 | 2 |
| *C. perfringens* (48) | [ 0.06 - 2 ] | 0.5 | 1 |
| *C. difficile* (18) | [ 0.06 - 0.25 ] | 0.125 | 0.25 |
| Other clostridia (6) [3] | [ 0.06 - 0.5 ] | N D | N D |
| *Finegoldia magna* (13) | [ 0.06 - 0.5 ] | 0.125 | 0.25 |
| *Parvimonas (Micromonas) micros* (10) | [ 0.06 - 0.5 ] | 0.125 | 0.25 |
| Other GPAC: gram-positive cocci (14) [4] | [ 0.06 - 0.5 ] | 0.125 | 0.25 |
| **All gram-positive anaerobes** (109) | [ 0.06 - 2 ] | 0.125 | 1 |
| **All anaerobes** (230) | [ 0.06 - 16 ] | 0.25 | 2 |

***C critique***

***≤ 4***

# Tigecylcine
# relation dose response

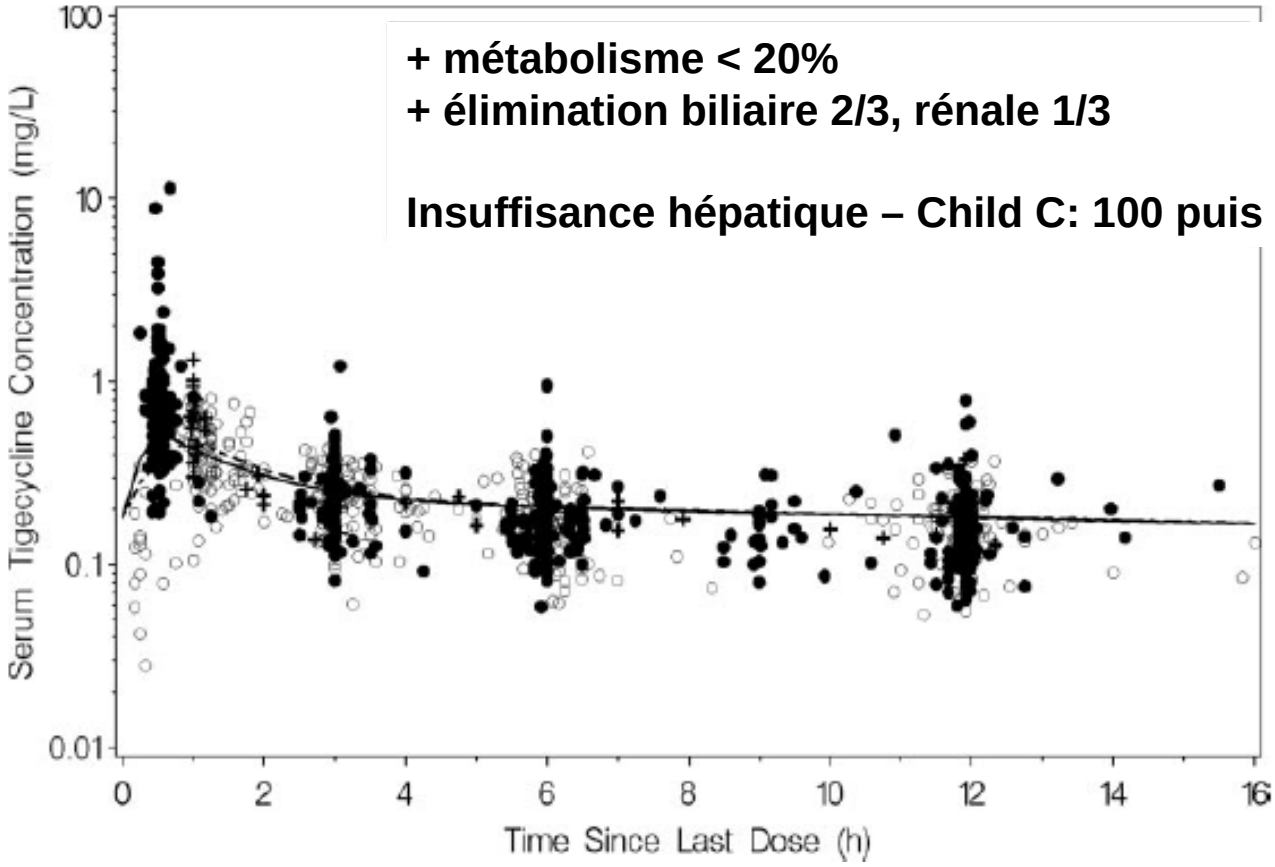
**Infection cuisse -** Souris neutropéniques




**Chez l'homme**
AUC/MIC ???

mais antibiotique intra-cellulaire

# Tigecycline: PK




**+ métabolisme < 20%**
**+ élimination biliaire 2/3, rénale 1/3**

**Insuffisance hépatique – Child C: 100 puis 25 x 2**

# Tigecycline
# elf, cellules

| | Cmax | Tmax | Cmin | AUC 0-12 | T1/2 |
|---|---|---|---|---|---|
| **Serum** | **0.72** | **0.52** | **0.1** | **1.73** | **15** |

Conte JE, International J Antimicrob Agents 2005;25:523-9

# Tigecycline elf, cellules

| | Cmax | Tmax | Cmin | AUC 0-12 | T1/2 |
|---|---|---|---|---|---|
| **Serum** | **0.72** | **0.52** | **0.1** | **1.73** | **15** |
| **Film alvéolaire** | **0.37** | **6** | **0** | **2.28** | **39** |

Conte JE, International J Antimicrob Agents 2005;25:523-9

# Tigecycline elf, cellules

| | Cmax | Tmax | Cmin | AUC 0-12 | T1/2 |
|---|---|---|---|---|---|
| **Serum** | **0.72** | **0.52** | **0.1** | **1.73** | **15** |
| **Film alvéolaire** | **0.37** | **6** | **0** | **2.28** | **39** |
| **Cellules alvéolaires** | **15.2** | **2** | **6.4** | **134** | **23.7** |

Conte JE, International J Antimicrob Agents 2005;25:523-9

# Efficacité 1

***Infections « tissus mous »***

| | tige (%) | vanco+aztreo (%) |
|---|---|---|
| **succès** | **75.5-84.3** | **76.9-86.9** |

# Efficacité 2

*Infections « tissus mous »*

| | tige (%) | vanco+aztreo (%) |
|---|---|---|
| succès | 75.5-84.3 | 76.9-86.9 |

***Infection « abdominales »***

| | **tige (%)** | **imipenem(%)** |
|---|---|---|
| **succès** | **80.6-91.3** | **82.4-89.9** |

# Efficacité pneumonie

Dukart G, ICAAC 2006

| | **tige (%)** | **levo (%)** |
|---|---|---|
| *Fine II-IV* | *80.7* | *74.4* |
| **succès** | **89.7** | **86.3** |

# Efficacité pneumonie

Dukart G, ICAAC 2006

| | **tige (%)** | **levo (%)** |
|---|---|---|
| *Fine II-IV* | *80.7* | *74.4* |
| **succès** | **89.7** | **86.3** |
| Pneumo | 92.3 | 88.9 |
| **Bactériémie pneumo** | **90** | **72** |

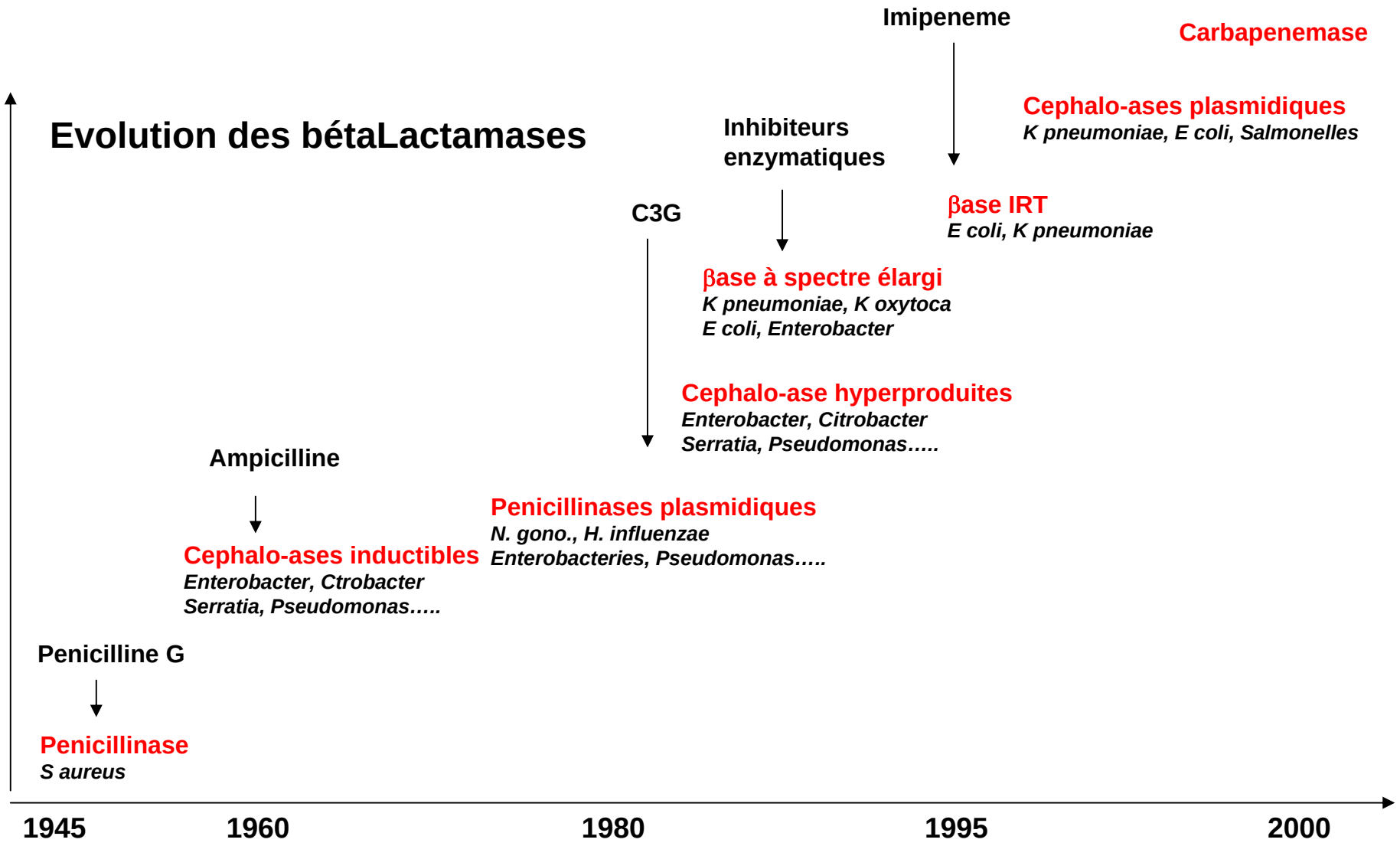
# Tigecycline

- Bacteriostatique
  - => prudence (a priori)
    - Immunodéprimés:
      - Neutropéniques
    - Septicémie
    - Mais bonne efficacité sur pneumococcémies
- « intracellulaire »
  - Pkpd intracellulaire

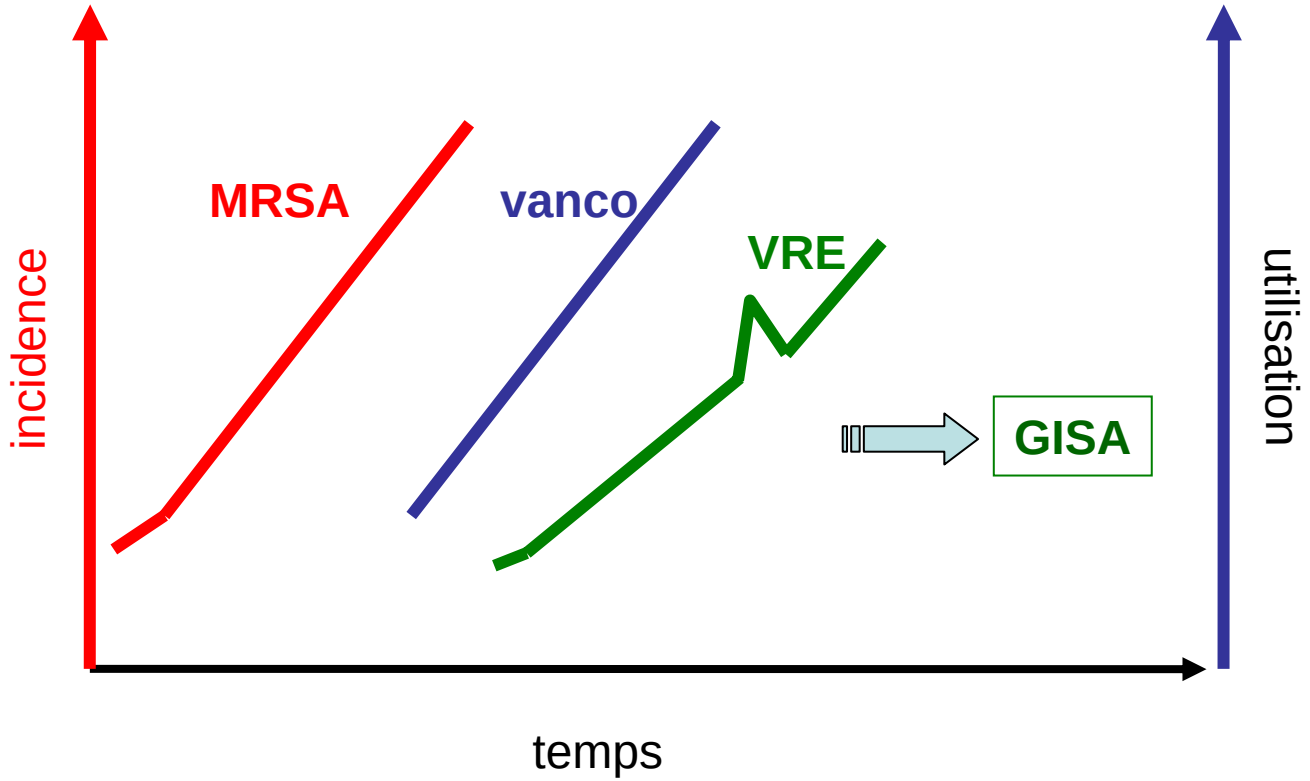
# Tigecycline

- Large spectre
  - Aero + anaerobie
- => infection mixte:
  - Pied du diabètique
  - Pneumopathie du « vieillard »
  - Infections « muqueuses »
    - gynecologiques
    - abdominales
    - stomato – ORL
  - ……

# Succession ineluctable et dangereuse rompre le cercle Gram -



# Succession ineluctable et dangereuse rompre le cercle Gram +



# Tigecycline: in vitro

## **pan-R** (souches cliniques)

TABLE 1. In vitro activity of tigecycline against 392 multiple-drug-resistant strains

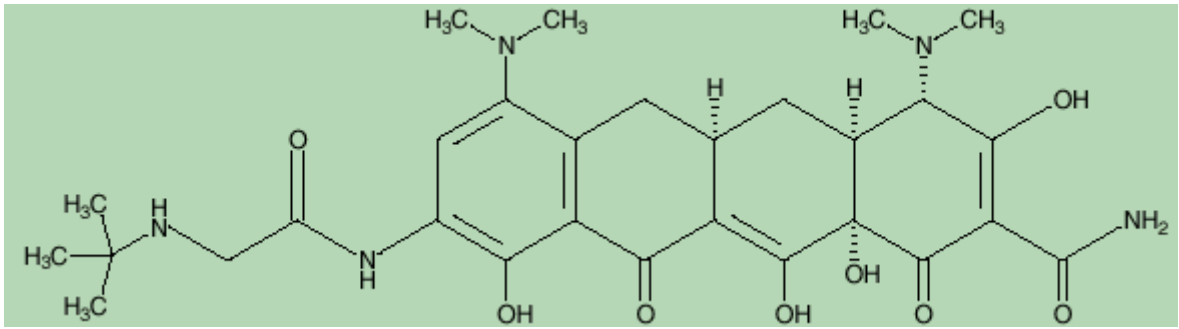
| Organism (no. of isolates) | $MIC_{50}$ (μg/ml) | $MIC_{90}$ (μg/ml) | % Susceptible[a] | No. of isolates with MIC (μg/ml) of: | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | ≤0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | ≥8 |
| *K. pneumoniae* (98) | 0.5 | 2 | 96.9 | 0 | 1 | 4 | 26 | 37 | 11 | 16 | 3 | 0 |
| *K. pneumoniae*, ESBL positive (27) | 1 | 2 | 92.6 | 0 | 0 | 0 | 5 | 8 | 4 | 8 | 2 | 0 |
| *K. pneumoniae*, MBL positive (26) | 0.5 | 2 | 100 | 0 | 0 | 3 | 9 | 9 | 2 | 3 | 0 | 0 |
| *K. pneumoniae*, ESBL and MBL positive (28) | 0.5 | 2 | 100 | 0 | 0 | 1 | 7 | 13 | 2 | 5 | 0 | 0 |
| *K. pneumoniae*, colistin resistant (15) | 0.5 | 0.5 | 100 | 0 | 1 | 1 | 3 | 9 | 0 | 1 | 0 | 0 |
| *K. pneumoniae*, minocycline resistant (28) | 2 | 4 | 89.3 | 0 | 0 | 0 | 0 | 2 | 8 | 15 | 3 | 0 |
| *E. coli* (43) | 0.12 | 0.5 | 100 | 0 | 8 | 18 | 11 | 5 | 1 | 0 | 0 | 0 |
| *E. coli*, ESBL positive (33) | 0.12 | 0.5 | 100 | 0 | 8 | 13 | 8 | 3 | 1 | 0 | 0 | 0 |
| *E. coli*, MBL positive (6) | NA[c] | NA | 100 | 0 | 0 | 3 | 2 | 1 | 0 | 0 | 0 | 0 |
| *E. coli*, minocycline resistant (10) | 0.12 | 0.5 | 100 | 0 | 1 | 4 | 3 | 1 | 1 | 0 | 0 | 0 |
| *A. baumannii* (100) | 0.5 | 1 | 99 | 0 | 0 | 1 | 5 | 46 | 44 | 3 | 1 | 0 |
| *A. baumannii*, colistin resistant (3) | NA | NA | 100 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 |
| MRSA (91) | 0.25 | 0.25 | 98.9 | 0 | 0 | 27 | 58 | 5 | 0 | 1 | 0 | 0 |
| *E. faecium*, VR[b] (60) | 0.03 | 0.06 | 100 | 46 | 12 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| *E. faecium*, VR, linezolid resistant (5) | NA | NA | 100 | 2 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

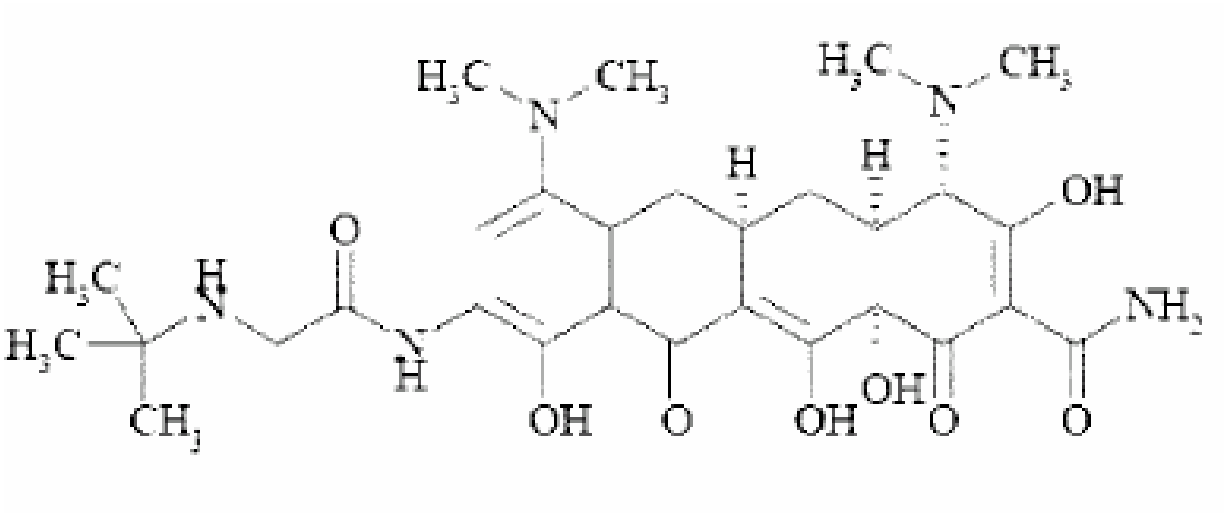
Souli M et al., AAC 2006;50:3166-9

# Tigecycline

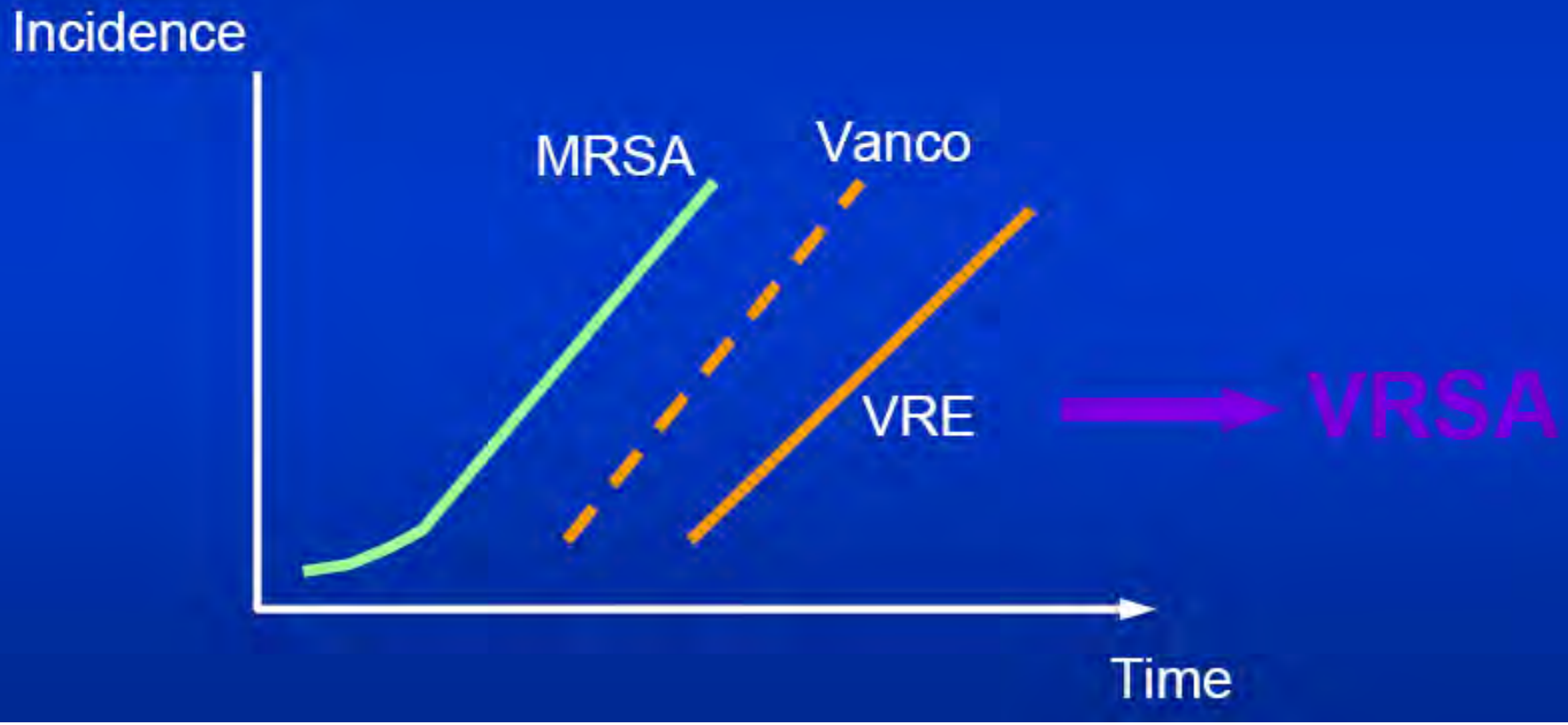
- Large spectre
- => alternative (ou stratégie)
- BGN-R:
  - Beta-lactamines
  - Fluoroquinolone
  - Colimycin
- Gram + (MRSA)
  - Glycopeptide
  - Lipopeptide
  - Linezolide
  - Ceftobibrole, ceftaroline

# Merci de votre attention

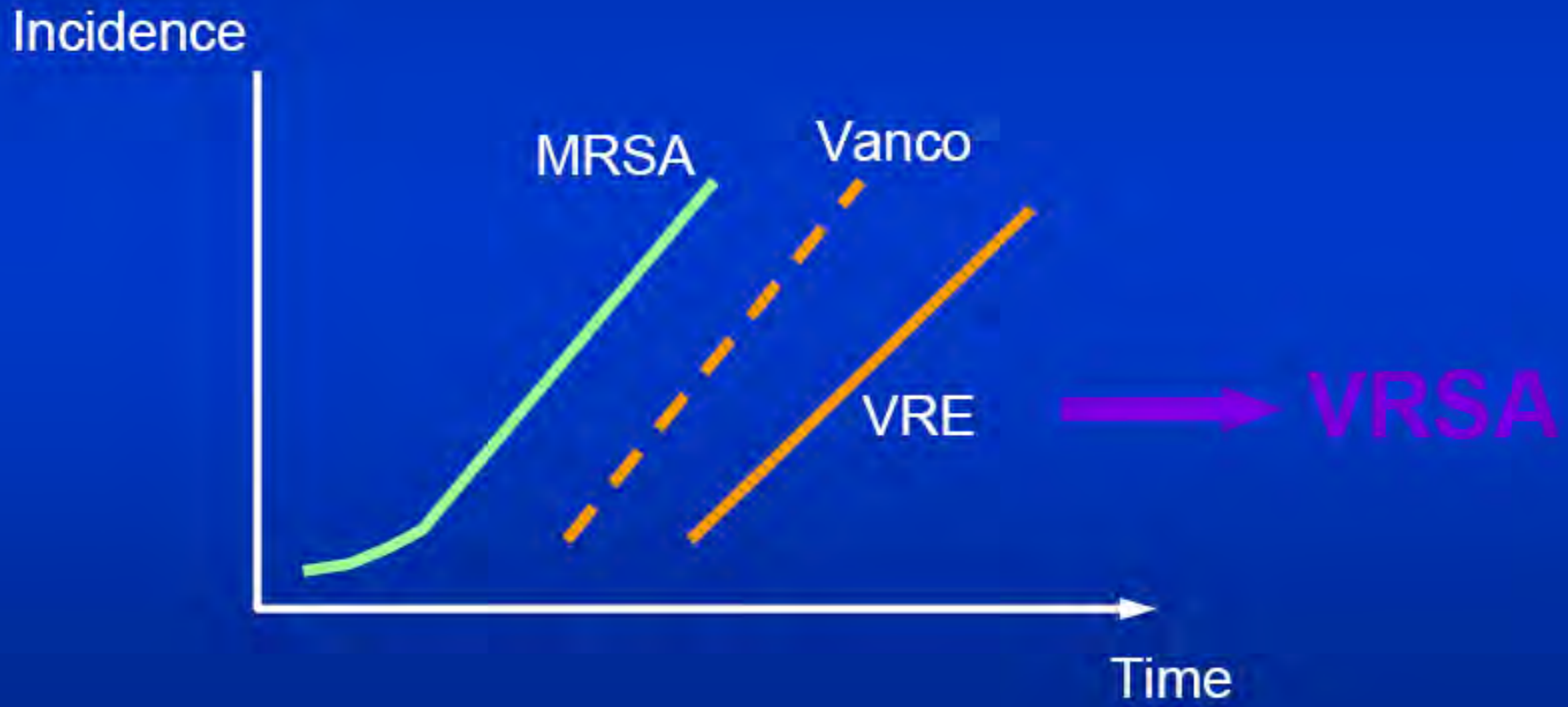

H3C
N
CH3
H3C
N
CH3
OH
H
H
O
H3C
H
N
N
H
H3C
H3C
OH
O
OH
OH
O
O
NH2
O


H3C
CH3
N
H3C
CH3
N
H
H
OH
O
H3C
H
N
H3C
CH3
H
NH2
OH
O
OH
OH
O
O

# A Bad Mixture… *A Terrible Fear*



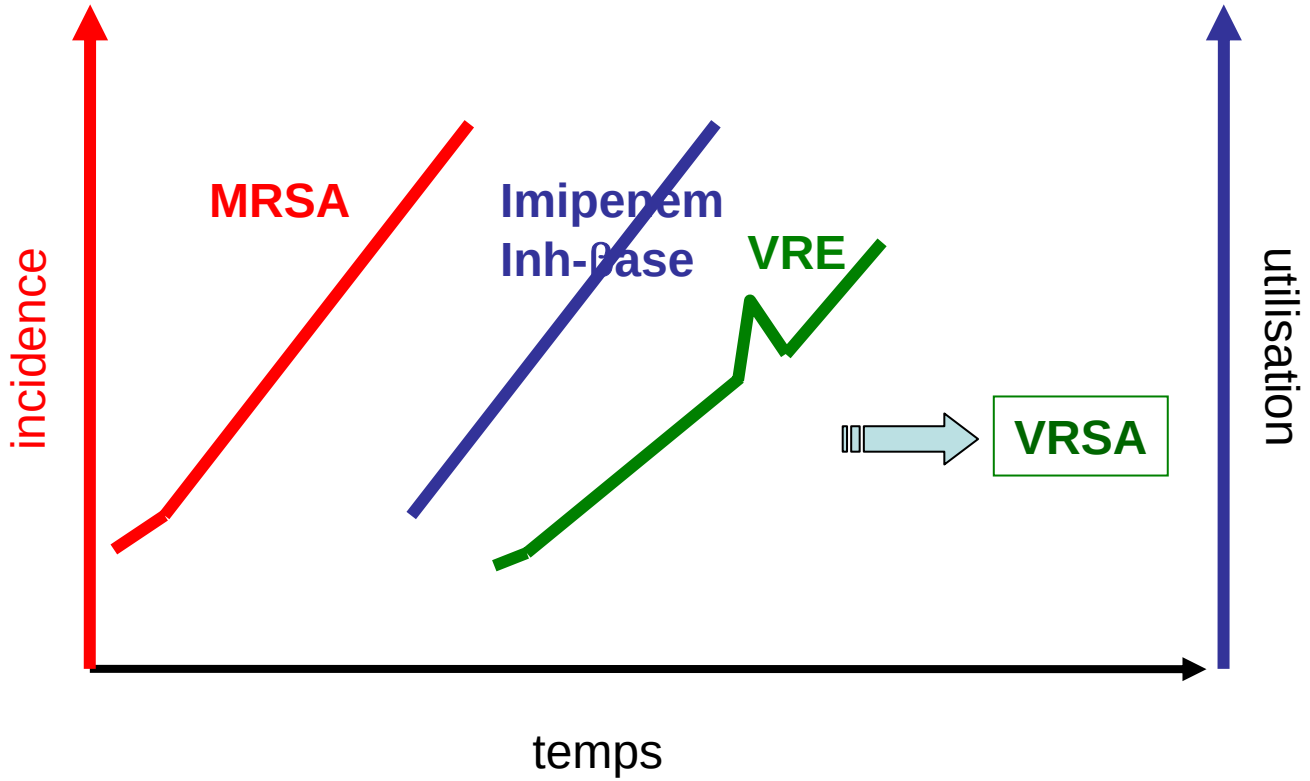
# A Bad Mixture… *A Terrible Fear*

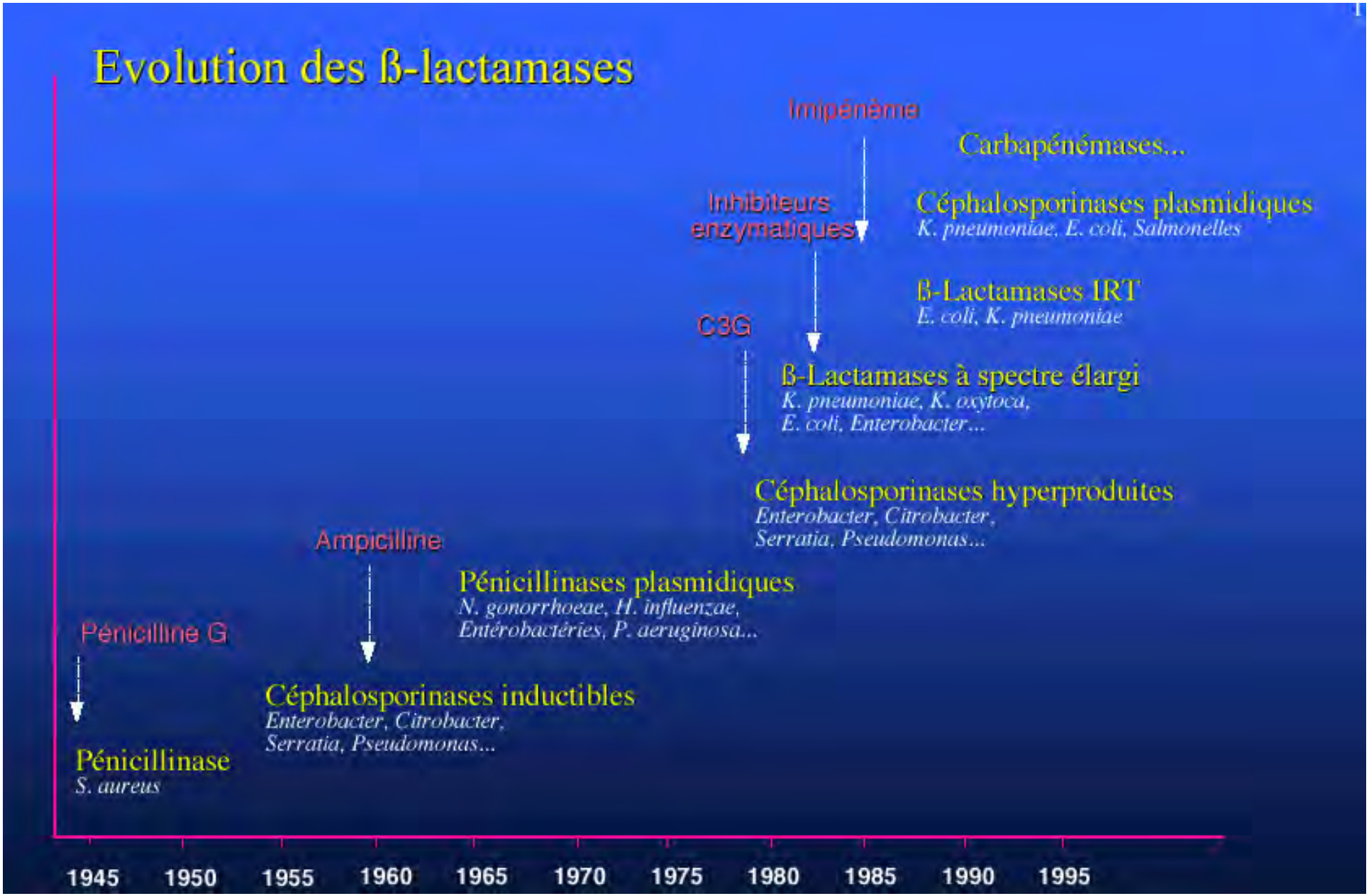


# MRSA: New therapeutic Options

- Daptomycin
- Other Novel lipopeptides
- Linezolid
- Quinu/dalfo
- Novel anti-MRSA cephalosporin

# Succession ineluctable et dangereuse rompre le cercle Gram -




Evolution des ß-lactamases
Imipénème
Carbapénémases...
Inhibiteurs enzymatiques
Céphalosporinases plasmidiques
K. pneumoniae, E. coli, Salmonelles
ß-Lactamases IRT
E. coli, K. pneumoniae
C3G
ß-Lactamases à spectre élargi
K. pneumoniae, K. oxytoca, E. coli, Enterobacter...
Céphalosporinases hyperproduites
Enterobacter, Citrobacter, Serratia, Pseudomonas...
Ampicilline
Pénicillinases plasmidiques
N. gonorrhoeae, H. influenzae, Entérobactéries, P. aeruginosa...
Pénicilline G
Céphalosporinases inductibles
Enterobacter, Citrobacter, Serratia, Pseudomonas...
Pénicillinase
S. aureus
1945
1950
1955
1960
1965
1970
1975
1980
1985
1990
1995

# MRSA: New therapeutic Options

- Daptomycin
- Other Novel lipopeptides
- Linezolid
- Quinu/dalfo
- Novel anti-MRSA cephalosporin

# In vitro break point

P. Hawkey, R. Finch
Clin Microbiol Infect 2007; 13: 354–362

| Organism | FDA breakpoint (mg/L) | % Susceptible | EUCAST breakpoint (mg/L) | % Susceptible |
|---|---|---|---|---|
| *Escherichia coli* ($n$ = 721) | ≤2 | 100 | ≤1 | 100 |
| *Serratia* spp. ($n$ = 168) | ≤2 | 94 | ≤1 | 80 |
| *Enterobacter* spp. ($n$ = 405) | ≤2 | 96 | ≤1 | 90 |
| *Klebsiella* spp. ($n$ = 582) | ≤2 | 98 | ≤1 | 92 |

Modified from [36]. EUCAST breakpoints for tigecycline were published during 2006 [56].

# EFFETS INDESIRABLES

- Troubles gastro-intestinaux, vomissements+++
- Allongement TCA et TP
- Vertiges, céphalées
- Prurit, rash
- Affections vasculaires: phlébites
- Photosensibilité
- Hyperpigmentation, hyperplasie dentaire
- Effet anti-métabolite: augmentation de l’urée sanguine, hypophosphatémie

# CI / IM

## ***1) CI:***

- Déconseillé chez adolescents de -18 ans
- Absolue chez enfant de -8 ans
- Grossesse, allaitement (passage dans le lait maternel?)

## ***2) IM:***

- Warfarine → [ ]° augmente
- Utilisation concomitante d'ATB et de contraceptifs oraux peut diminuer leur efficacité
- Sels de fer ,pansements gastriques

# PRECAUTIONS D'EMPLOI

- ***Surveillance*** des tests de coagulation des patients sous anticoagulants: *TCA, TP*

- ***Modalité d'administration:***

  - Rincer la tubulure de perfusion (NaCl 0,9% oudextrose)si elle est utilisée pour l'administration de plusieurs substances actives

  - Ampho B, chlorpromazine,méthylprednisolone et voriconazole ne peuvent être administrées en même temps

# tet

P. Hawkey, R. Finch

Clin Microbiol Infect 2007; 13: 354–362

**Table 1.** Distribution of *tet* resistance genes among selected Gram-negative bacteria

| Efflux | Ribosomal protection and/or efflux |
|---|---|
| Single genes | |
| *Chlamydia*: *tet*(C) | *Eikenella*: *tet*(M) |
| *Stenotrophomonas*: *tet*(35) | *Campylobacter*: *tet*(O) |
| Two or more genes | |
| *Providencia*: *tet*(B), (E), (G) | *Haemophilus*: *tet*(B), (K), (M), (A) |
| *Enterobacter*: *tet*(B), (C), (D), (M) | *Bacteroides*: *tet*(M), (Q), (X), (36) |
| *Citrobacter*: *tet*(A), (B), (C), (D) | *Acinetobacter*: *tet*(A), (B), (H), (M), (39) |
| *Proteus*: *tet*(A), (B), (C), (J) | *Neisseria*: *tet*(M), (O), (Q), (W), (B) |
| *Klebsiella*: *tet*(A), (B), (C), (D), (M) | |
| *Escherichia*: *tet* (A), (B), (C), (D), (E), (G), (M), (Y) | |
| *Pseudomonas*: *tet* (A), (B), (C), (E), (G), (M), (34) | |