37th Annual Meeting of the
European Bone and Joint Infection Society

Staphylococcus aureus bone and joint infection: comparison of rifamycin intraosteoblastic activity and impact on intracellular emergence of small colony variants.

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Introduction (1)

Bone and Joint Infection

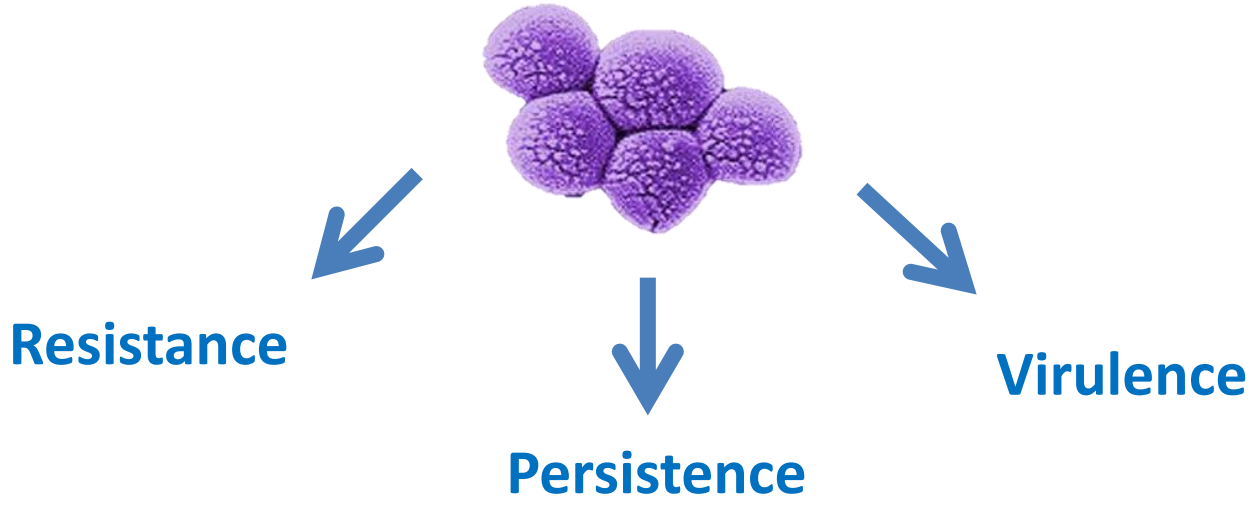
- **5%** mortality & **40%** morbidity
- Long-term and expansive healthcare:

  50 000 – 150 000 € / episode
- Incidence rate: 50 cases / 100 000 / year

Major public health issue

Introduction (2)

Staphylococcus aureus: 30 - 50% of BJI



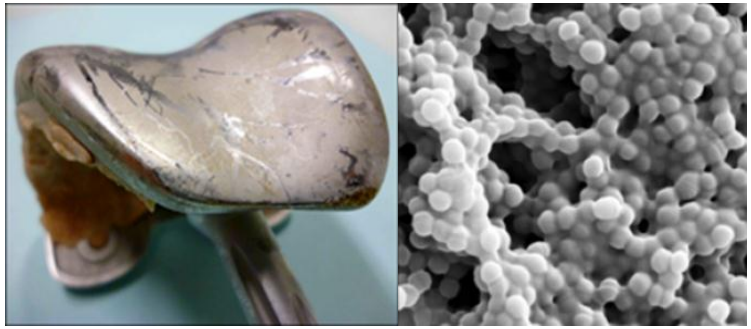
Introduction (2)

Staphylococcus aureus: 30 - 50% of BJI

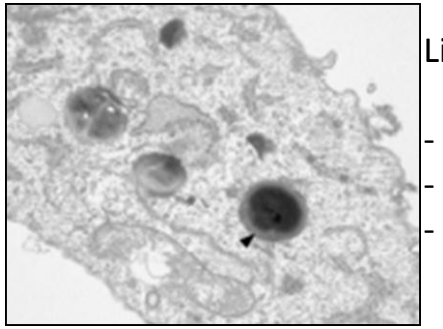
Resistance

Virulence

Persistence



Biofilm formation



Internalization

Limitation of antibiotic activity

- Intracellular diffusion
- Intracellular activity (pH)
- **SCVs emergence**

Introduction (2)

Staphylococcus aureus: 30 - 50% of BJI

Resistance

Virulence

Persistence

Responsible for **20%** treatment failure – relapse after treatment

Chronicity

Introduction (3)

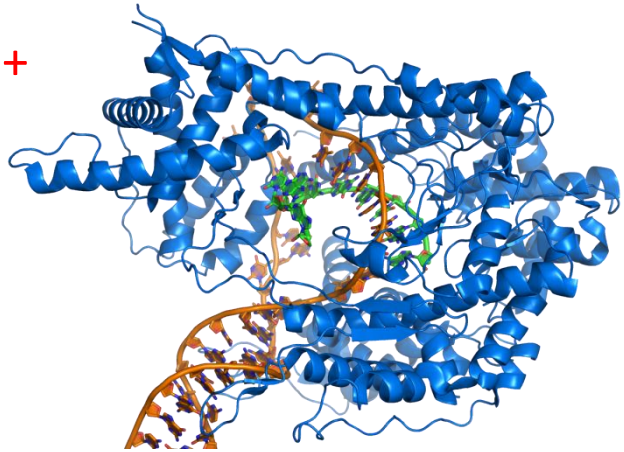
Aim of the study

comparison of rifapentine and rifabutin with rifampin

Mechanism of action : Inhibition of bacterial DNA-dependent RNA polymerase

Advantages: intracellular activity and anti-biofilm +++

Disavantages: side effects and drug interactions +++



Compared to rifampicin, rifapentine and rifabutin :

- anti-staphylococcal activity =
- Resistance rate =
- t1/2 ↑
- Better tissue penetration
- Better intracellular concentration (rifabutin X100, rifapentine)

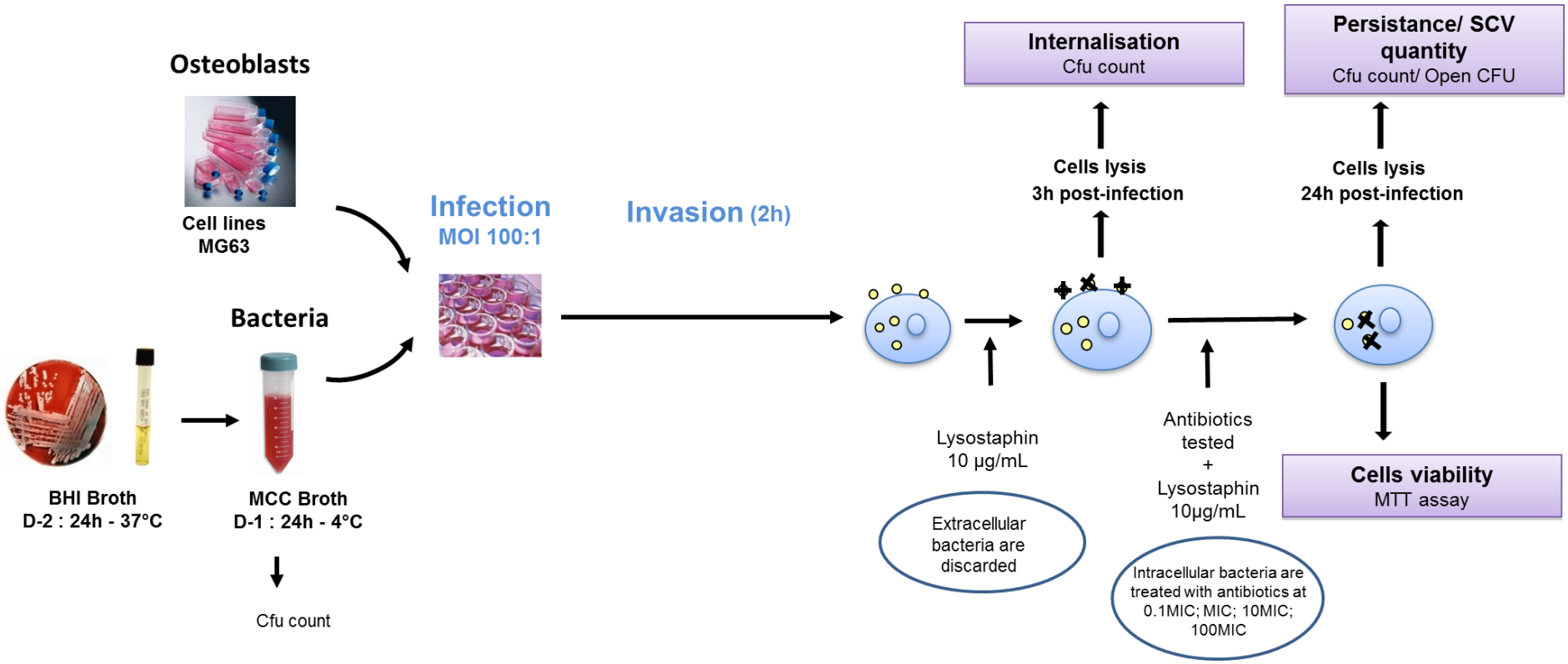
PIETRO EMANUELE VARALDO and al 1985. MICHAEM H. SKINNER and TERRENCE F.BLASCHKE 1995. YOANN CRABOL and al. 2016.

Materials & methods

Acute infection model

Three strains tested :

- reference strain 6850
- two clinical MSSA strains isolated from BJI relapse



All experiences were independant and repeated 3 times in technical triplicates

Materials & methods

Chronic infection model

Three strains tested :

- reference strain 6850
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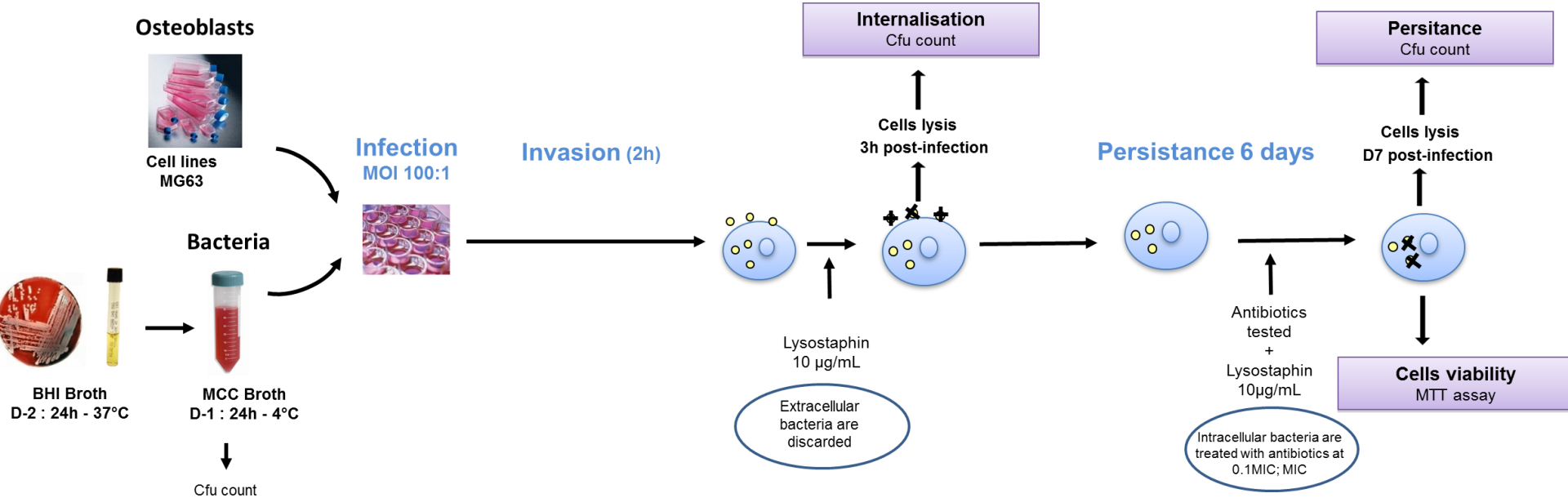
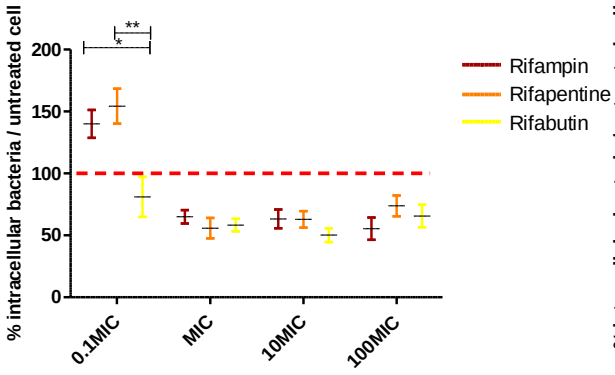


All experiences were independant and repeated 3 times in technical triplicates

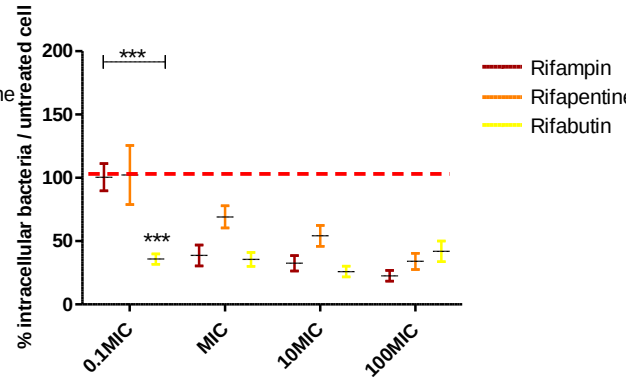
Results (1)

- **Rifamycin intra-osteoblastic activity 24h post-infection (PI)**

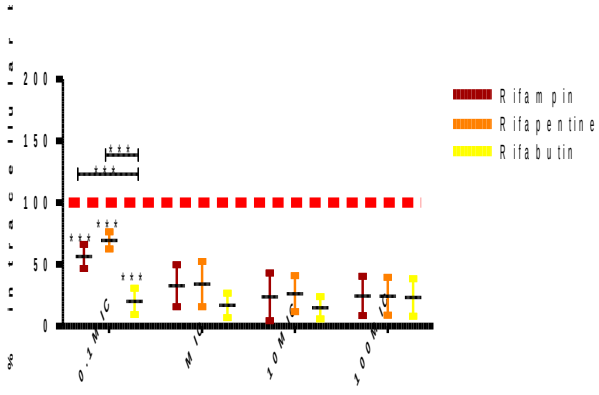
6850



Clinical strain n°1



Clinical strain n°2

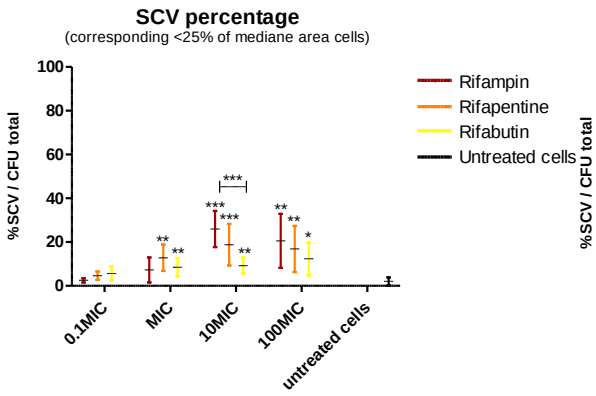


- Rifabutin are efficient from 0.1MIC intracellularly on the three strains
- Rifamycin efficacity is strain-dependant

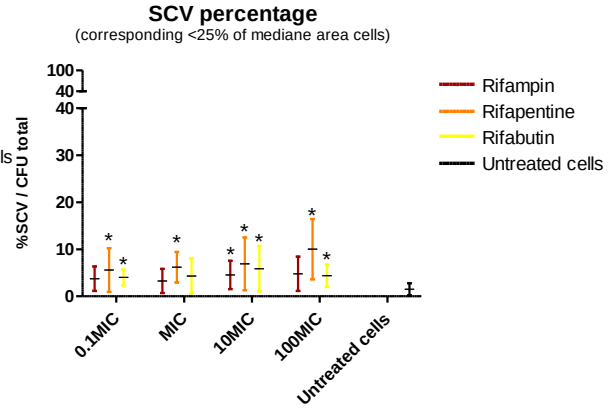
Results (2)

- **SCV emergence after treatment 24h post-infection (PI)**

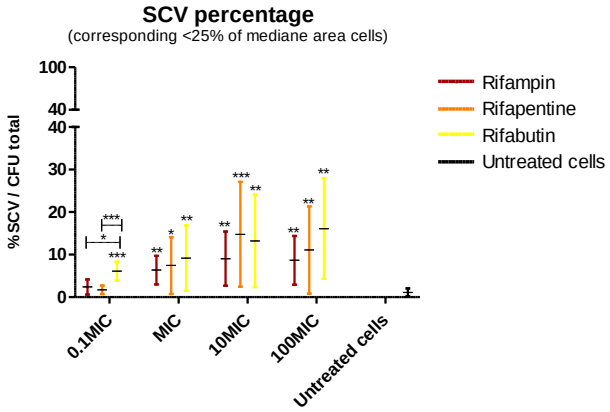
6850



Clinical strain n°1



Clinical strain n°2

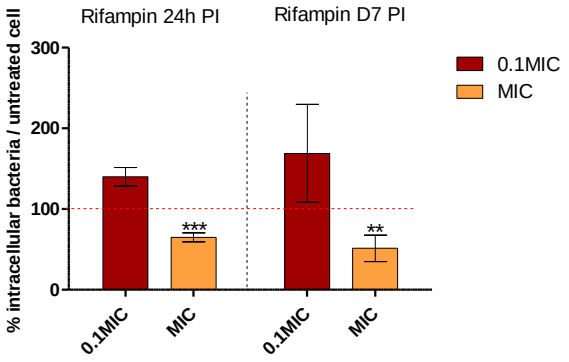


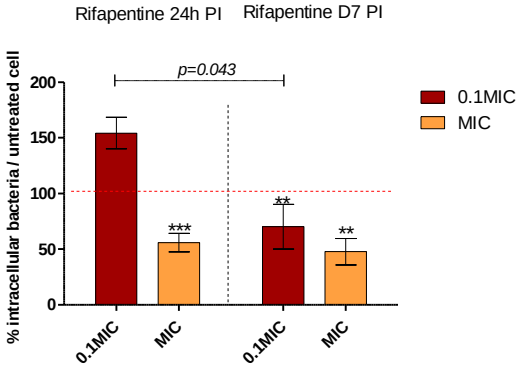
- SCV emergence increased is concentration-dependant
- SCV emergence is strain-dependant

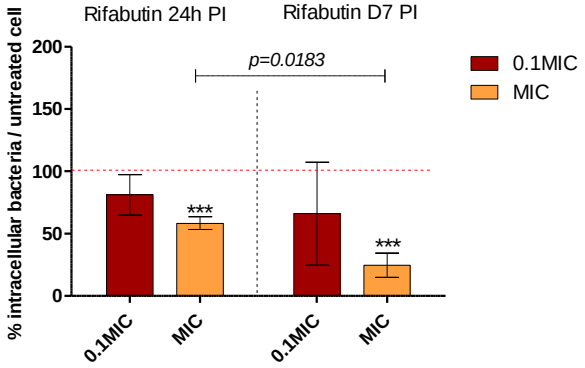
Results (3)

- **Rifamycins intra-osteoblastic activity D7 post-infection (PI)**

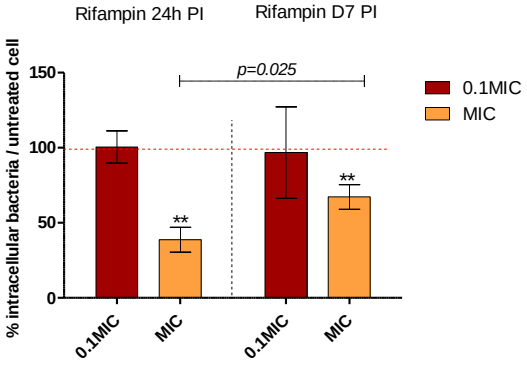
6850

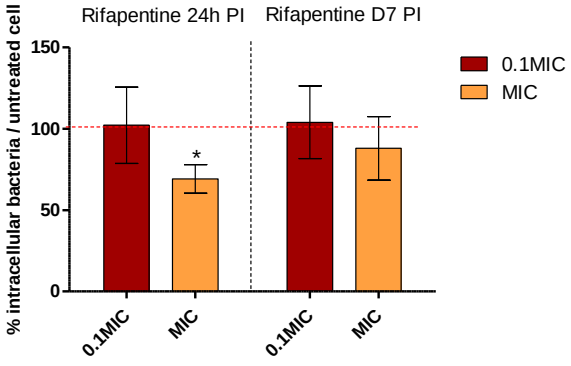


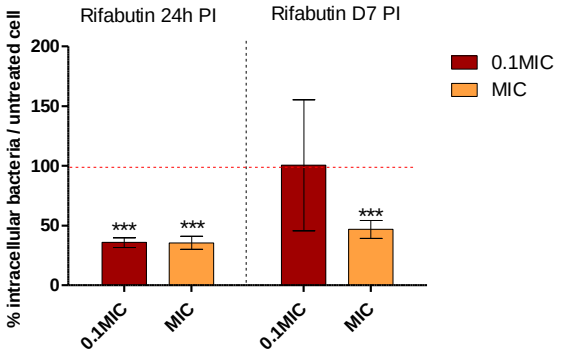




Clinical strain n°1



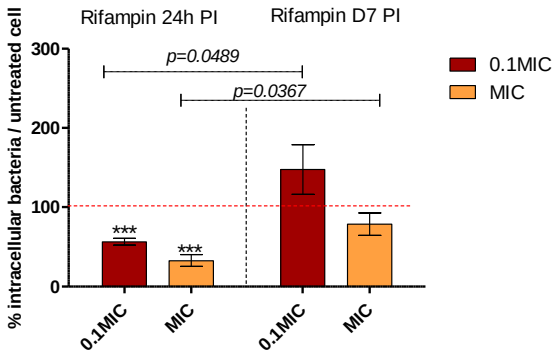


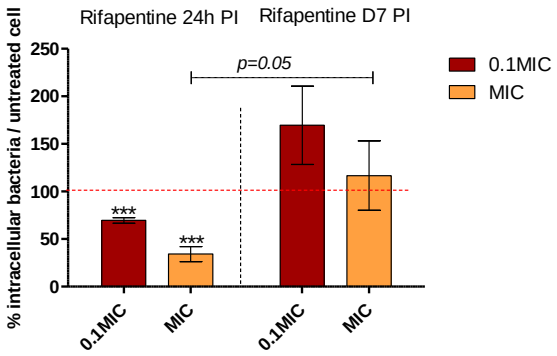


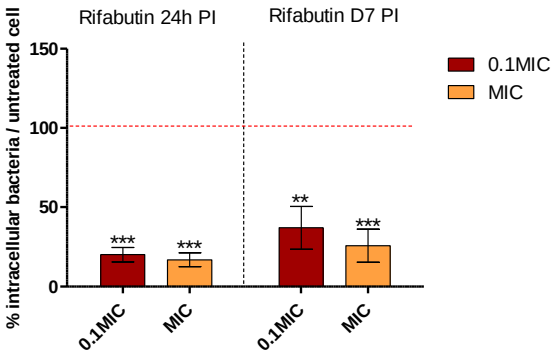
Results (3)

- **Rifamycins intra-osteoblastic activity D7 post-infection (PI)**

Clinical strain n°2







- Rifabutin were still efficient at 0.1MIC intracellularly on the three strains
- Rifapentine and rifampin lost their activity on the two clinical strains

Conclusion & perspectives

- Rifabutin are more **efficient** at lower concentration than rifapentine and rifampicin in acute and chronic intra-osteoblastic infection model.

- Rifabutin at lower concentration could **prevent SCV emergence** and systemic **side effects**.

- Capacity to prevent and eradicate biofilm will be tested.

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