



Centre
International
de Recherche
en Infectiologie



Efficacy of antibiotic combinations in PMMA cement

Results from a novel *in vitro* biofilm model

Jérôme JOSSE



Heraeus

CRIODac Lyon: reference center for complex PJs



Prof. Tristan FERRY
ID specialist
Coordinator



Prof. Sébastien LUSTIG
Orthopaedic Surgeon



Prof. Frédéric LAURENT
Clinical Microbiologist

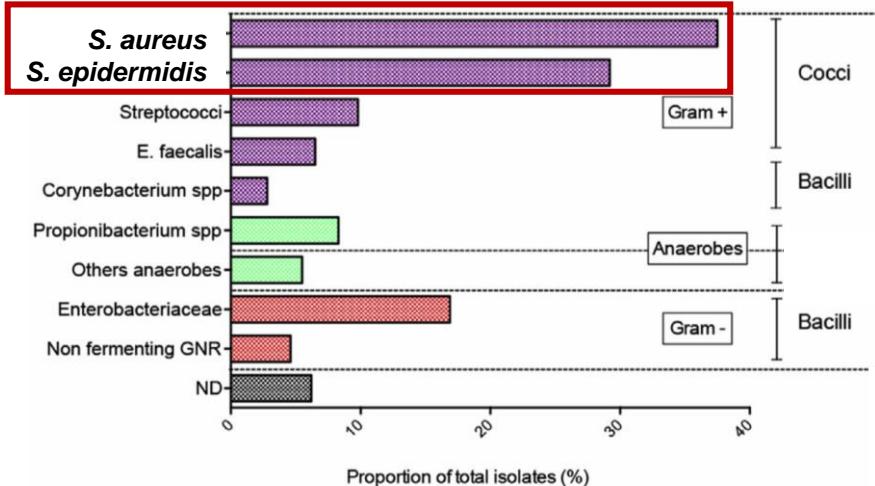


Applied Research lab (CIRI)
In vitro pre-clinical BJI/PJI models

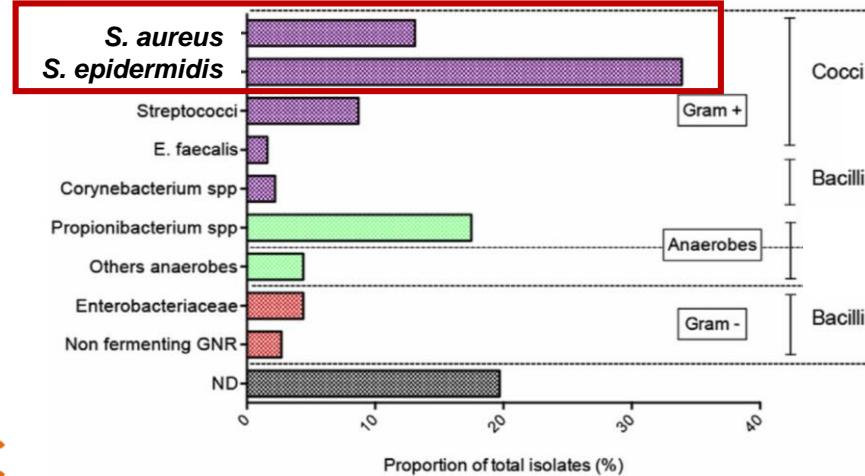


Staphylococci in Prosthetic Joint Infection

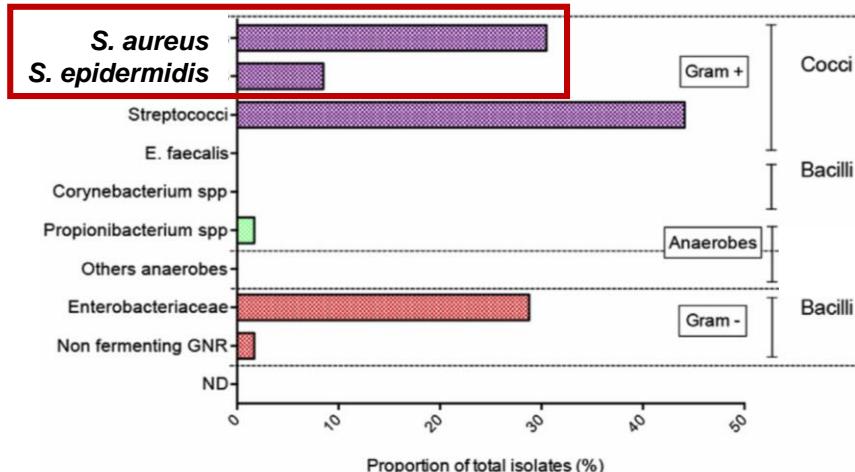
Early/Delayed PJI



Late chronic PJI

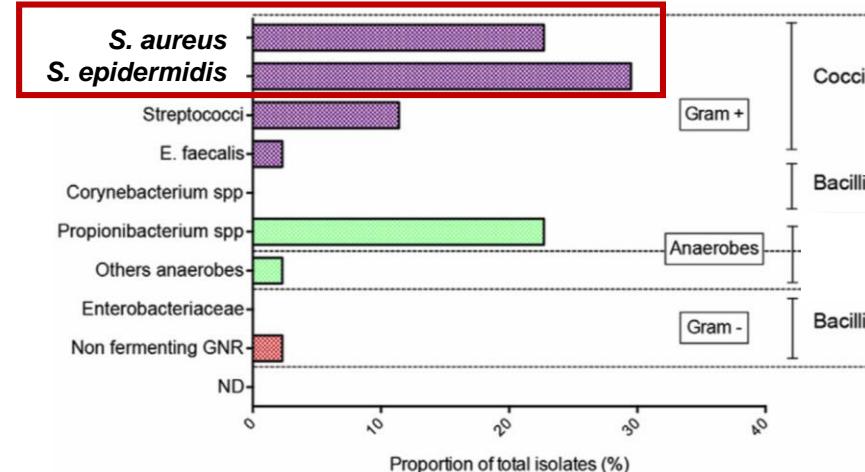


Late acute PJI



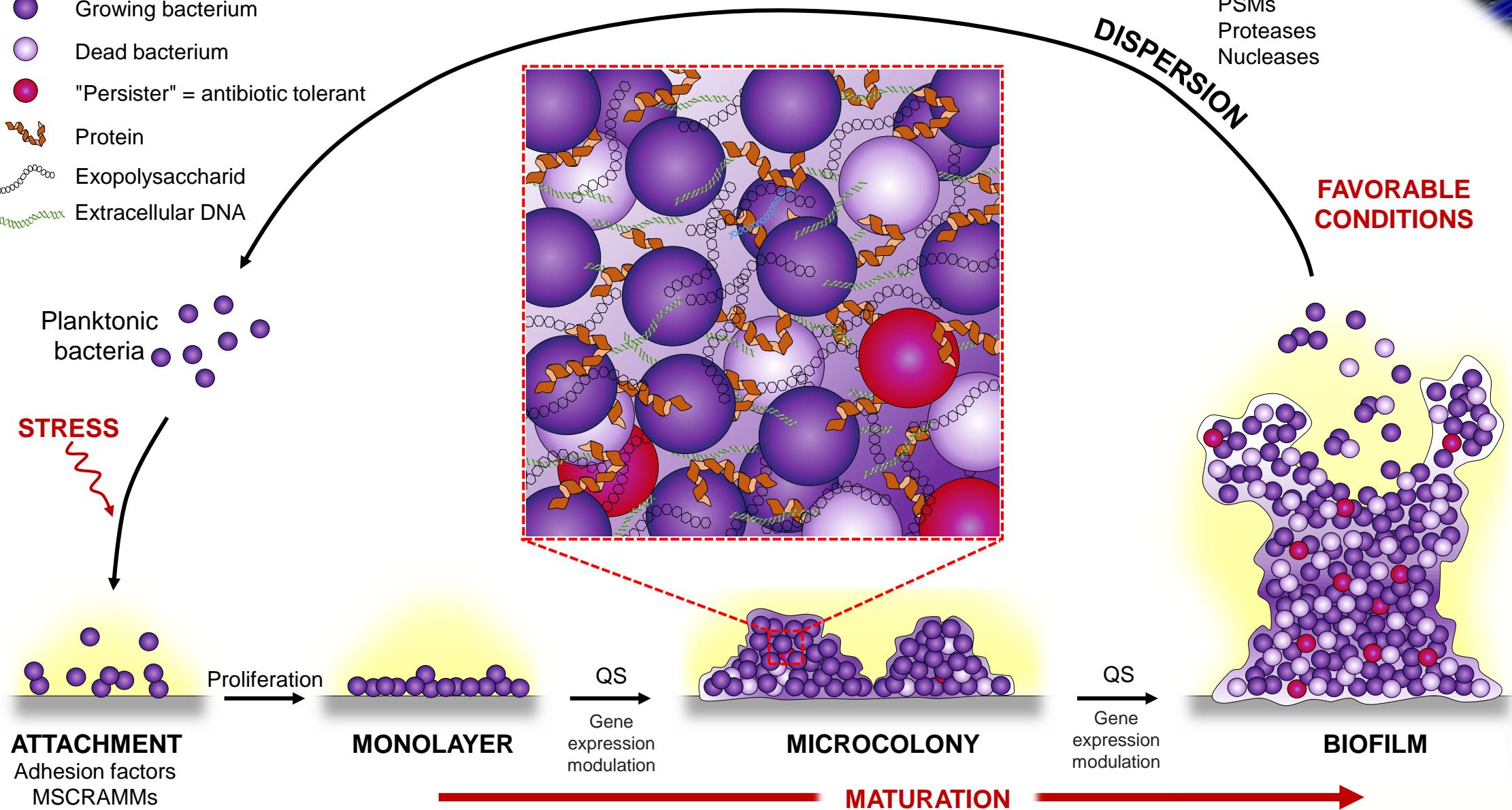
511 cases

Late exacerbated PJI



Biofilm-associated PJI

- Growing bacterium
- Dead bacterium
- "Persister" = antibiotic tolerant
- Protein
- Exopolysaccharid
- Extracellular DNA



Antibiotic-Loaded Bone Cements (ALBCs)

Complications of 1-stage / 2-stage procedures for PJI management:

- Biofilm neoformation by the initial pathogen(s)
- Superinfection

→ Use of Antibiotics-Loaded Bone Cements

- **Indication = prophylactic effect**
- Most used ALBC = loaded with gentamicin
 - Development of ALBCs with **antibiotic combinaisons**
 - **Gentamicin + Vancomycin**
 - **Gentamicin + Clindamycin**
- Manufactured bi-antibiotic ALBCs
 - Mechanical properties
 - Elution kinetic properties

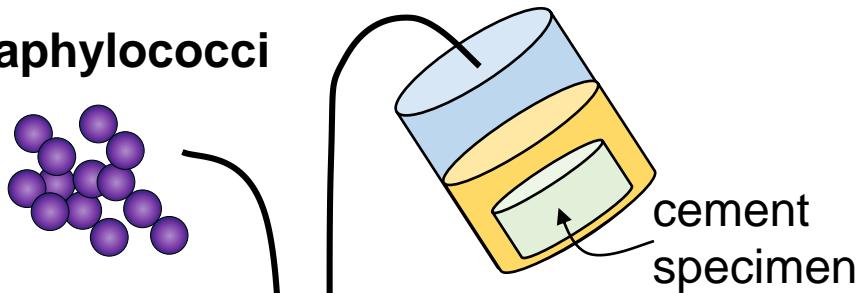


In vitro biofilm formation model

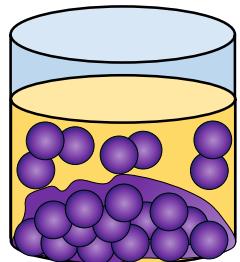


Elution solution
(TSB + 1% glucose)
medium change every day

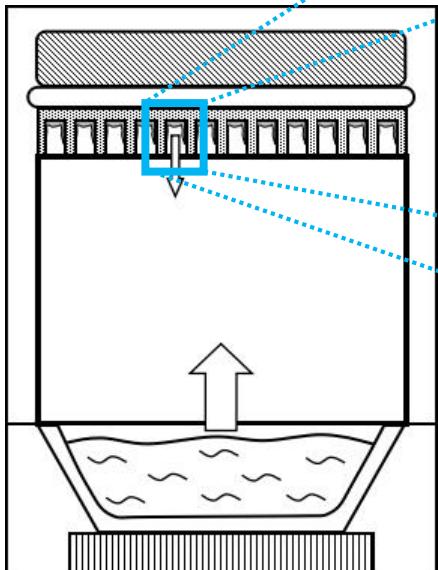
Staphylococci



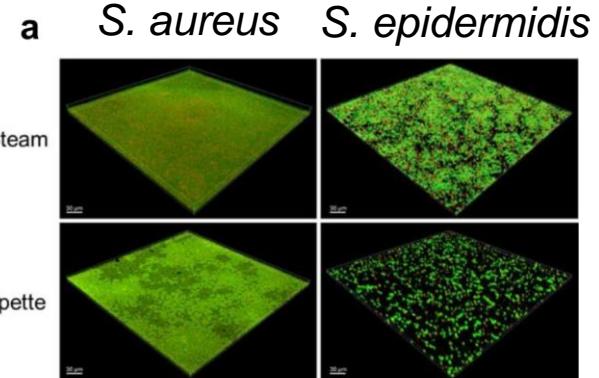
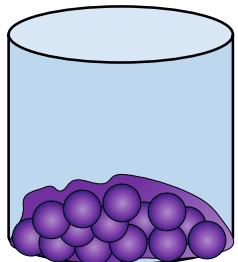
24h
37°C



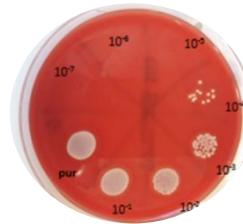
**Wash of inadherent
bacteria with
Steam method
BiofilmCare**



**Resuspension,
sonication
& plating**



**Number of viable
bacteria inside biofilm**

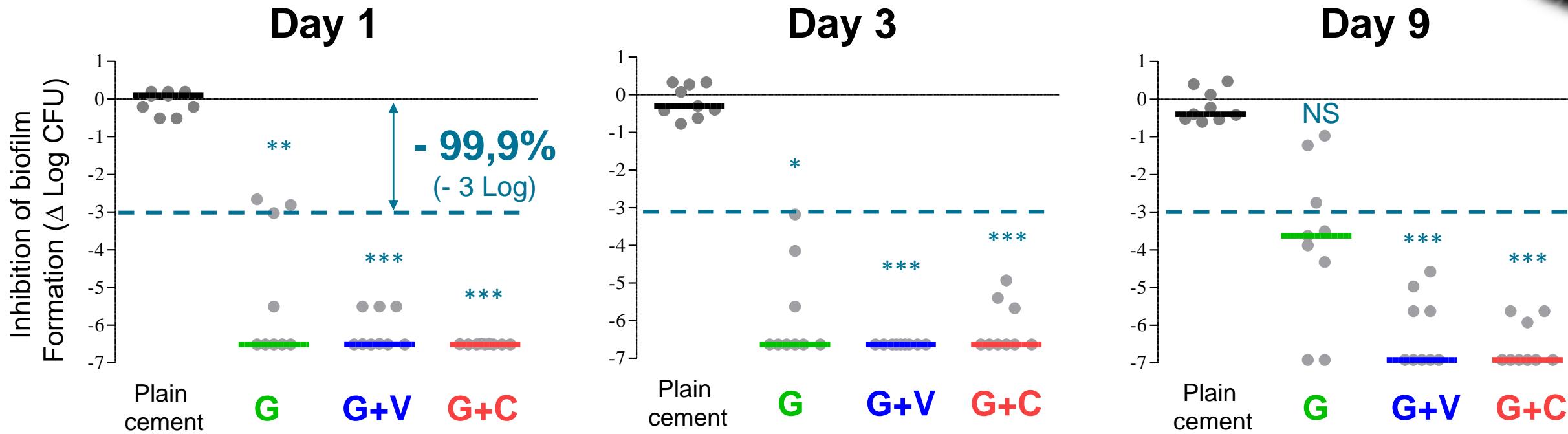


Effect of ALBCs on *S. aureus* strains

- ALBCs elution solutions from Day 1, Day 3 and Day 9
- Tested ALBCs:
 - Plain cement (no antibiotic)
 - ALBC with gentamicin only = G (0,5g)
 - ALBC with gentamicin + vancomycin = G (0,5g) + V (2g)
 - ALBC with gentamicin + clindamycin = G (1g) + C (1g)
- Tested clinical strains:
 - Meticillin-sensible *S. aureus* = MSSA
 - Meticillin-resistant *S. aureus* = MRSA
 - Gentamicin-resistant MRSA = GentaR MRSA
 - Vancomycin-resistant MSSA = VancoR MSSA
 - Clindamycin-resistant MRSA = ClindaR MRSA (Gentamicin tolerant)
 - Clindamycin-resistant MSSA = ClindaR MSSA

All strains merged

Effect of ALBCs on MSSA biofilm formation

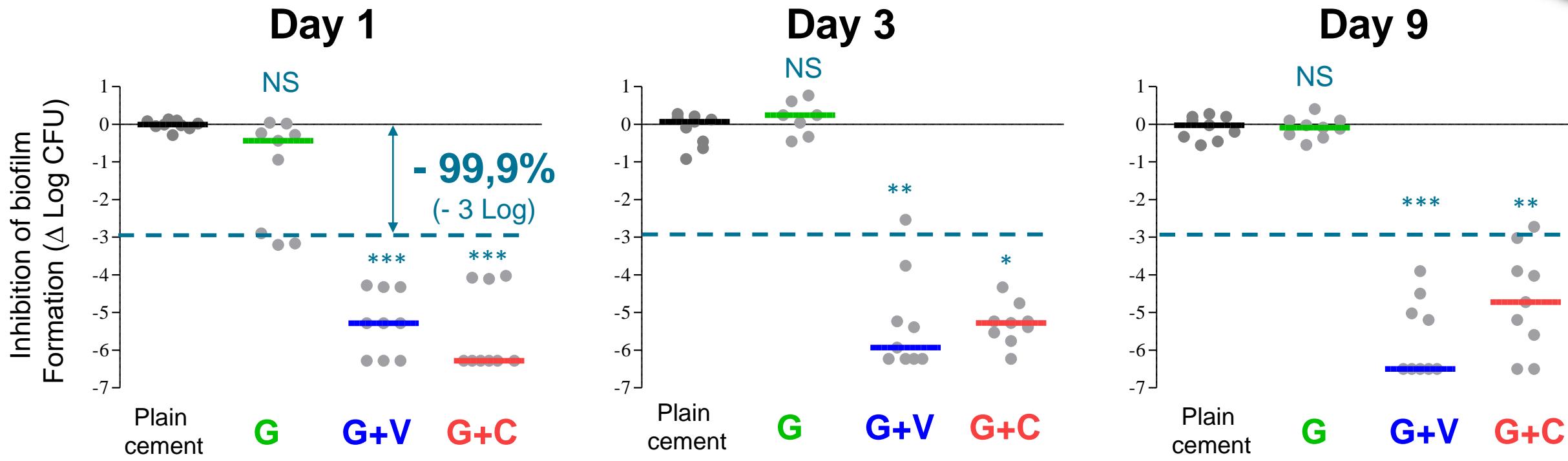


G+V and G+C are more effective than G

to prevent biofilm formation in septic revision with **MSSA**

→ Still efficient at Day 9

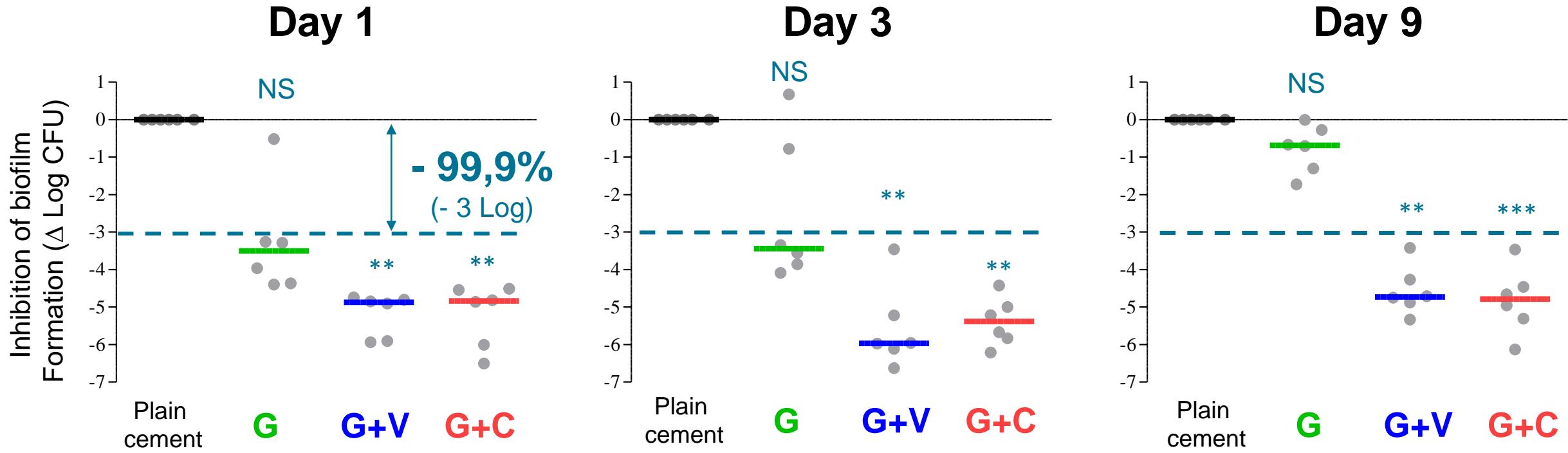
Effect of ALBCs on GentaR MRSA biofilm formation



G+V and G+C are more effective than G

to prevent biofilm formation in septic revision with GentaR MRSA

Effect of ALBCs on *S. aureus* biofilm formation (all strains merged)



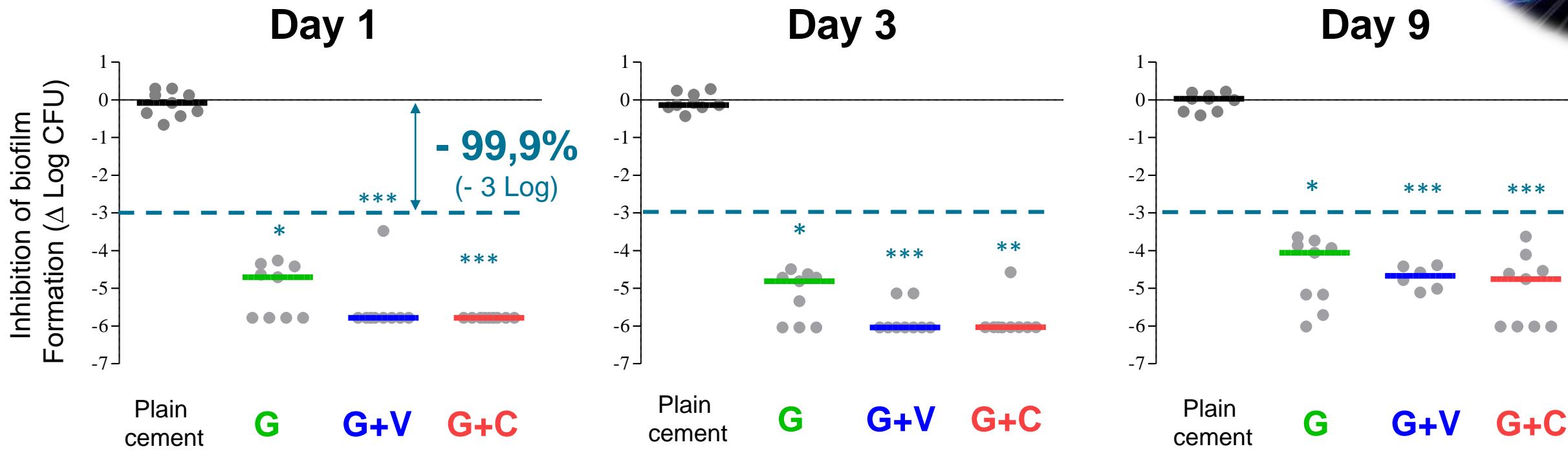
**G+V and G+C are more effective than G to prevent biofilm formation
in septic revision with GentaR, VancoR, ClindaR MSSA/MRSA**

Effect of ALBCs on *S. epidermidis* strains

- ALBCs elution solutions from Day 1, Day 3 and Day 9
- Tested ALBCs:
 - Plain cement (no antibiotic)
 - ALBC with gentamicin only = G (0,5g)
 - ALBC with gentamicin + vancomycin = G (0,5g) + V (2g)
 - ALBC with gentamicin + clindamycin = G (1g) + C (1g)
- Tested clinical strains:
 - Meticillin-sensible *S. epidermidis* = MSSE
 - Meticillin - resistant *S. epidermidis* = MRSE
 - Gentamicin - resistant MSSE = GentaR MSSE
 - Vancomycin - resistant MSSA = VancoR MRSE
 - Clindamycin - resistant MRSA = ClindaR MRSE

All strains merged

Effect of ALBCs on MRSE biofilm formation

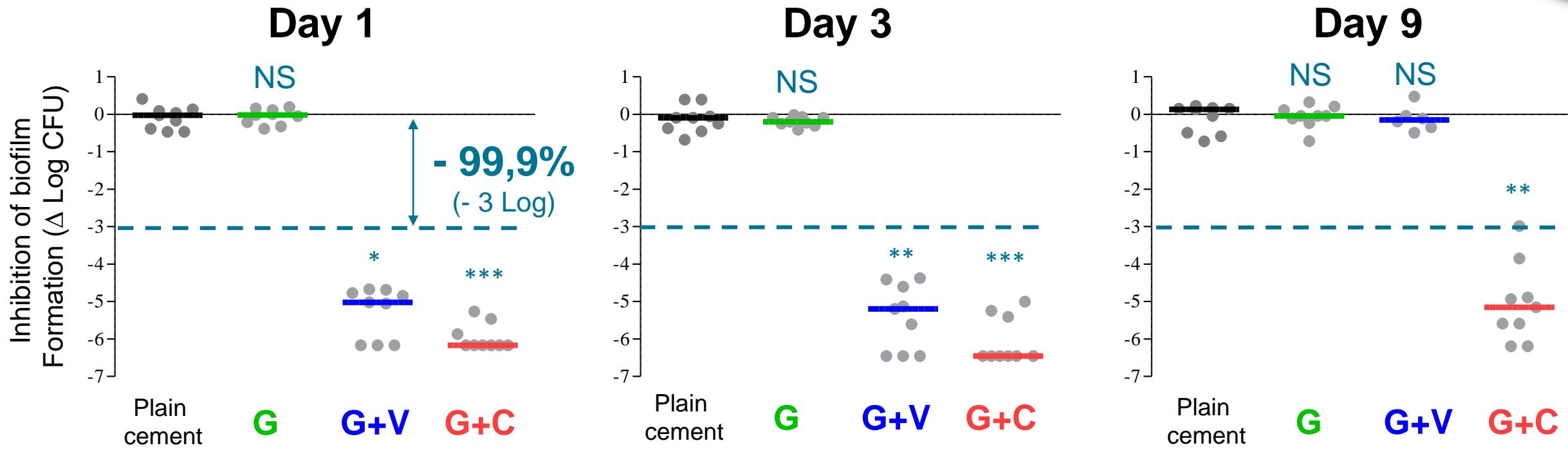


G+V and G+C are more effective than G

to prevent biofilm formation in septic revision with MRSE

→ more efficient at Day 9

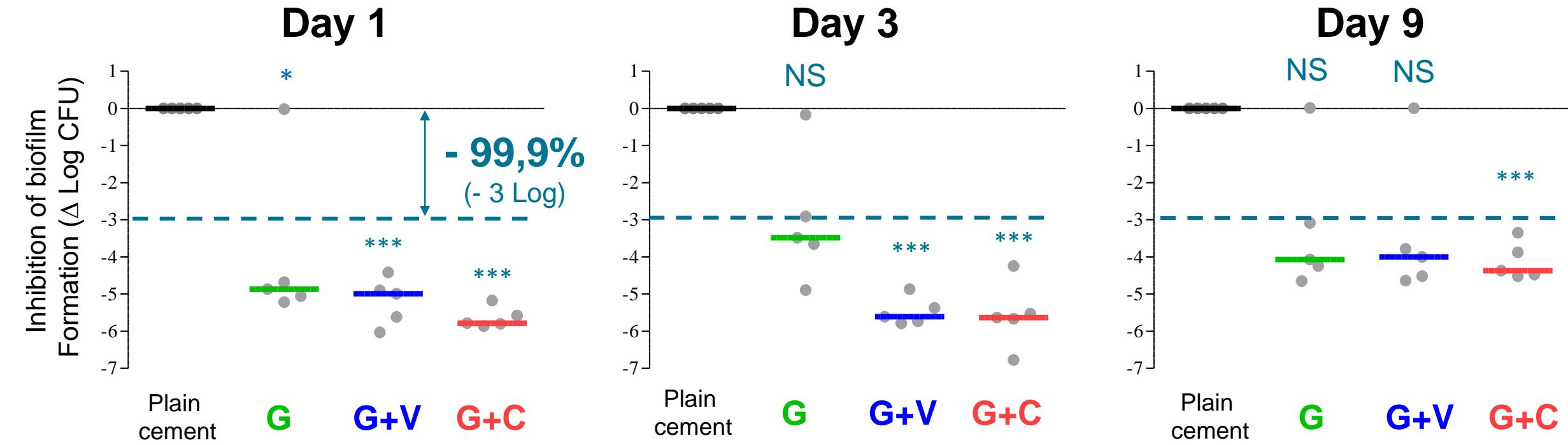
Effect of ALBCs on GentaR MSSE biofilm formation



G+C (and G+V) are more effective than G

to prevent biofilm formation in septic revision with GentaR MSSE

Effect of ALBCs on *S. epidermidis* biofilm formation (all strains merged)



G+C (and G+V) are more effective than G to prevent biofilm formation in septic revision with GentaR, VancoR, ClindaR MSSE/MRSE

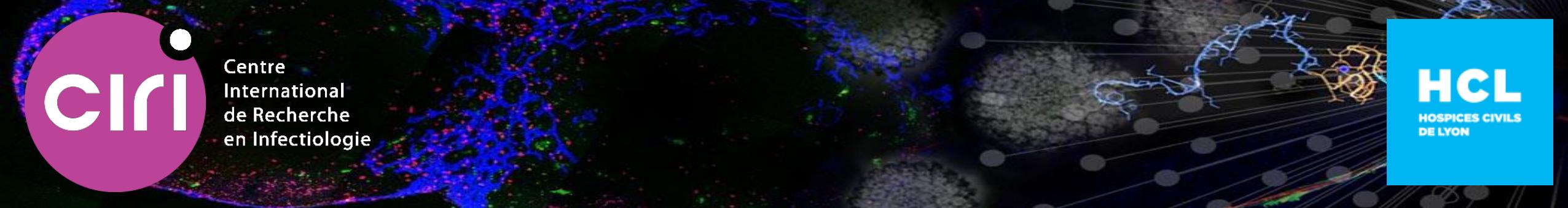
Conclusion & Outlook

G+V and **G+C** are more effective than **G** alone to prevent biofilm formation by **S. aureus** and **S. epidermidis** in our *in vitro* model



Combinations of antibiotics in ALBCs may help to prevent more efficiently biofilm neoformation and superinfection in septic revision

→ *What about enterobacteria ? work in progress*



**Thank you
for your attention**

