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# Antimicrobial activity of ceftaroline against a collection of methicillin-resistant Staphylococcus aureus (MRSA) isolates collected in 2013-2014 at the Geneva University Hospitals (HUG)

Diego Andrey*[1], Patrice François[2], Caroline Manzano[3], Eve-Julie Bonetti[4], Stephan Harbarth[5], Jacques Schrenzel[6], William Kelley[7], Adriana Renzoni[8]

[1]*Geneva University Hospitals and Faculty of Medicine , Service of Infectious Diseases , Department of Medical Specialties, Geneve, Switzerland*

[2]*University of Geneva Hospitals, Genomic Research Laboratory, Service of Infectious Diseases, Department of Medical Specialties, Geneva, Switzerland*

[3]*Geneva University Hospitals and Faculty of Medicine , Service of Infectious Diseases , Department of Medical Specialties, Geneva, Switzerland*

[4]*Geneva University Hospitals and Faculty of Medicine , Genomic Research Laboratory, Service of Infectious Diseases, , Department of Medical Specialties, Geneva, Switzerland*

[5]*Geneva University Hospitals and Medical School, Infection Control Program, Geneva, Switzerland*

[6]*University Hospitals of Geneva, Genomic Research Laboratory, Service of Infectious Diseases, Geneva, Switzerland*

[7]*Geneva University Hospitals and Faculty of Medicine , Department of Microbiology and Molecular Medicine, Geneva, Switzerland*

[8]*Hug, Service of Infectious Diseases , Department of Medical Specialties, Geneva, Switzerland*

**Background:** Ceftaroline is a broad-spectrum antibiotic with activity against MRSA. Preliminary testing of ceftaroline susceptibility using an archived set of 60 MRSA isolates (1994-2003), detected an unprecedented high percentage (66%) of ceftaroline-resistant in clonotypes ST228 and ST247, correlating with mutations in PBP2a (Kelley et al. 2015). Importantly, ceftaroline resistance was observed in archived strains before its commercial introduction. Ceftaroline therapy is based on inhibition of PBP2a, thus the identification of PBP2a mutations of recently circulating clonotypes in our institution is an important observation. This study aims at assessing ceftaroline-resistance in recent HUG-MRSA and establishing a correlation with PBP2a mutations and specific clonotypes.

**Material/methods:** 96 MRSA isolates were analyzed, from independent patients in 2013 and 2014, from blood cultures (22%), deep infections (39%), and superficial (skin or wound) infections (39%). Ceftaroline was supplied by the manufacturer (AstraZeneca). Ceftaroline activity was measured by broth microdilution and disc diffusion assays following standard procedures (EUCAST breakpoints recommendations). MRSA ceftaroline susceptible strain ATCC29213, MIC 0.25 µg/ml, was used as the EUCAST quality control strain. ST type determination was done using MLVA and MLST techniques following standard procedures. PBP2a determination was done by PCR and sequencing.

**Results:** Our 2013-2014 strain collection showed a ceftaroline MIC range between 0.25-2 µg/ml or 0.25-4 µg/ml at 24h or 48h of incubation, respectively. Using ceftaroline 5 µg discs, our strain collection showed diameters ranging from 10 to 30 mm with a majority of strains showing diameters ≥20 mm. Based on EUCAST breakpoints, 76% (73/96) of isolates showed susceptibility to ceftaroline (EUCAST microdilution breakpoints S≤1 and R>1 µg/ml; disc diameters breakpoints S≥20 and R<20 mm). Nevertheless we still observed 24% (23/96) of resistant isolates showing an MIC = 2µg/ml. All resistant isolates (MIC ≥ 2 µg/ml) were assigned to the South German clonotype ST228 and carried N146K mutation in the non penicillin binding domain of PBP2a. Only two ST228 strains showed ceftaroline susceptibility.

**Conclusions:** With this study we show that the majority of recent circulating MRSA isolates from Geneva University Hospitals (2013-2014) show ceftaroline susceptibility. However, ceftaroline resistant isolates are still present. Ceftaroline reduced susceptibility in this isolates collection is linked to the existing clonotype South German ST228 carrying PBP2a allosteric N146K mutation.