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Impact on the gut microbiota of intensive and prolonged antimicrobial therapy in patients with bone and joint infection

Nicolas Benech,[2,3] Benoît Levast, [1] Cyrielle Gasc,[1] Cécile Batailler,[2,3] Eric Senneville,[4] Sébastien Lustig,[2,3] Cécile Pouderoux,[2,3] David Boutoille,[5] Lilia Boucihna,[1]Frederic-Antoine Dauchy,[6] Valérie Zeller,[7] Marianne Maynard,[2] Charles Cazanave,[6,8] Thanh-Thuy Le Thi,[2] Jérôme Josse,[2,3] Joël Doré,[10] Frederic Laurent,[2,3,9] Tristan Ferry[2,3,9],* on behalf of the OSIRIS study Group

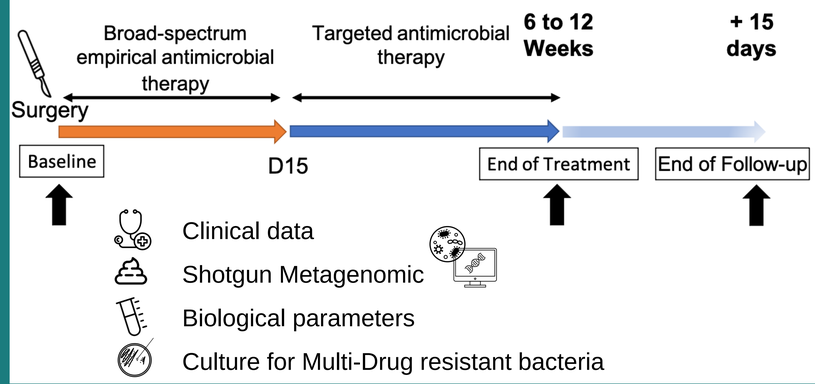
[1]MaaT Pharma, Lyon, France ; [2] Hospices Civils de Lyon, Lyon, France ; [3] Université Claude Bernard Lyon 1, Lyon, France ; [4] Université de Lille; France ; [5] CHU de Nantes; [6] CHU de Bordeaux, France; [7] GH Diaconesses-Croix Saint-Simon, Paris, France; [8] Université de Bordeaux, France; [9] CIRI – Centre International de Recherche en Infectiologie, Inserm, Lyon, France; [10] INRA, Institut National de la Recherche Agronomique, US1367 MetaGenoPolis, Jouy en Josas, France

BACKGROUND

Bone and joint infections (BJI) need frequently prolonged antibiotic treatment at high dosage for a total of 6 or 12 weeks depending the type of infection. Impact of such prolonged antibiotic exposure on the gut microbiota has never been assessed.

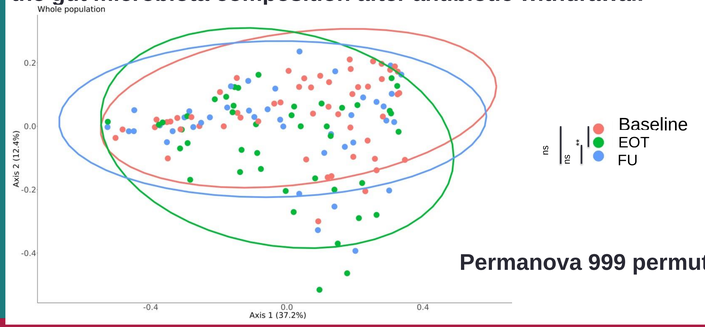
METHODS

We performed a national multicentric prospective study of patients with BJI to monitor the gut microbiota dynamic all along antimicrobial treatment involving 5 referent center for BJI managment.



RESULTS

Figure 1. Beta-diversity analysis (Bray-Curtis) shows rapid recovery of the gut microbiota composition after antibiotic withdrawal.



Permanova 999 permutations

Table 1. Patients characteristics.

BJI population	Native BJI (n=27)	Osteosynthesis-related BJI (n=14)	PJI (n=21)	Total (n=62)
Male (n, %)	17 (63)	10 (71.5)	13 (62)	40 (64.5)
Age (years)*	56.1 (13.2)	51.8 (17.6)	65.3 (9.1)	58.6 (14.1)
Antibiotics duration (days)*	58.8 (26.7)	69.8 (28.4)	68.3 (29.3)	64.5 (27.8)
BMI (mean)*	25.6 (6.5)	28.1 (5.8)	29.5 (7.0)	27.5 (6.6)
MDR carriage at baseline (n, %)	3 (11.1)	1 (7.1)	5 (23.8)	9 (14.5)
- MRSA	0	0	0	0
- ESBL producing enterobacteriae	3 (11.1)	1 (7.1)	5 (23.8)	9 (14.5)
- HREB	0	0	0	0
C. difficile carriage at baseline (n, %)	1 (3.7)	0	0	1 (1.6)

*Data are expressed in mean (standard deviation)

BJI: Bone Joint Infection; PJI: Prothesis Joint Infection; BMI: Body Mass Index; MDR: Multidrug Resistant; MRSA: Methicillin-resistant staphylococcus aureus; ESBL: extended-spectrum beta-lactamases; HREB: highly resistant emergent bacteria.

Figure 2. Alpha-diversity of the gut microbiota is decreased at the end of treatment and shows partial recovery after 15 days (A). Recovery differs according to the type of BJI (B)

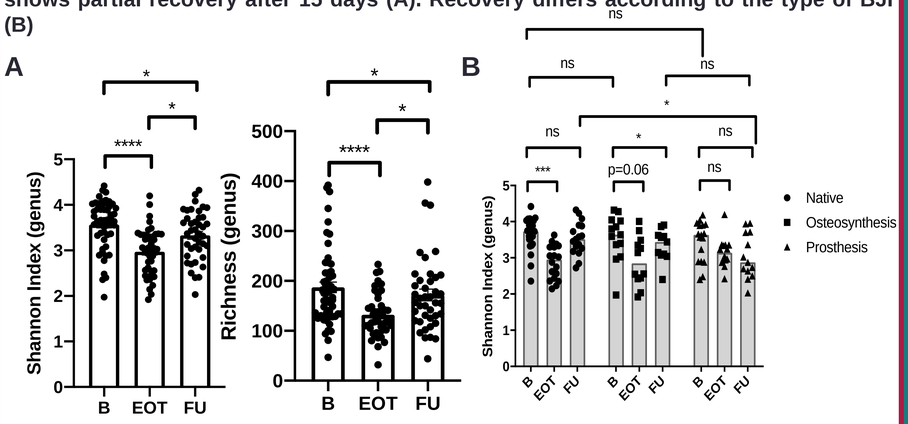


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Figure 3. No difference in term of gut microbiota recovery according to beta-(A) and alpha diversity (B) analysis between 6 and 12 weeks of treatment.

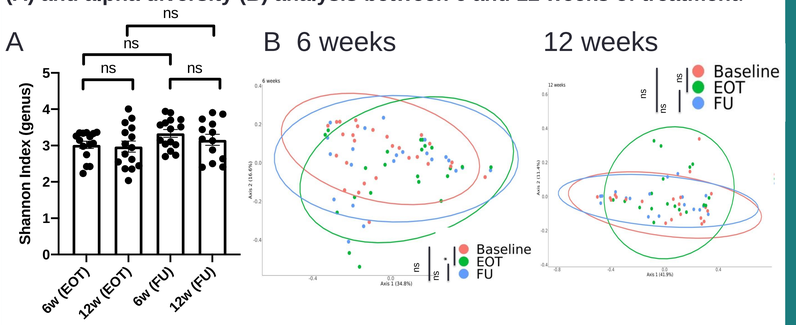
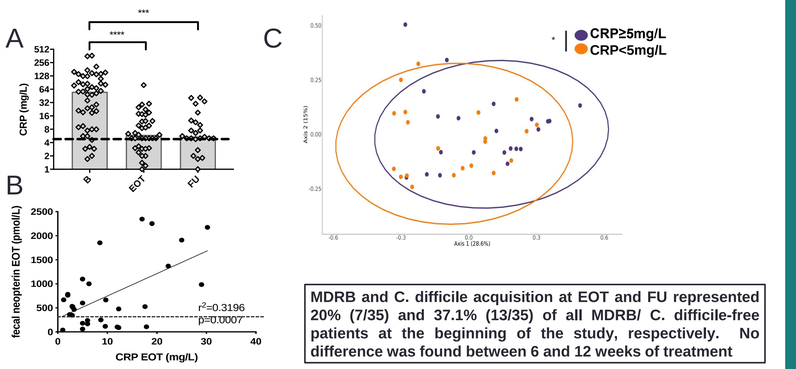


Figure 4. Patients with increased CRP at the end of treatment have increased marker of intestinal inflammation and a distinct microbiota. (A) Evolution of the plasmatic level of C-reactive protein (CRP) at the different time points. (B) Correlation between fecal neopterin and plasmatic CRP, simple linear regression. (C) Beta diversity. Principal coordinate analysis of Bray–Curtis distance at EOT according to the level of CRP.



MDRB and C. difficile acquisition at EOT and FU represented 20% (7/35) and 37.1% (13/35) of all MDRB/ C. difficile-free patients at the beginning of the study, respectively. No difference was found between 6 and 12 weeks of treatment

SUMMARY CONCLUSION

In patients with BJI, antibiotics altered the gut microbiota diversity and composition with only partial recovery 2 weeks after antibiotic withdrawal, independently on the duration of the therapy and on the type of the antibiotic used. Elevated CRP at EOT might reflect persistent alteration of the gut microbiota. Assessment of long-term impact after the end of treatment is on-going.