Impact of Azithromycin on the Post-Lung Transplant Microbiota

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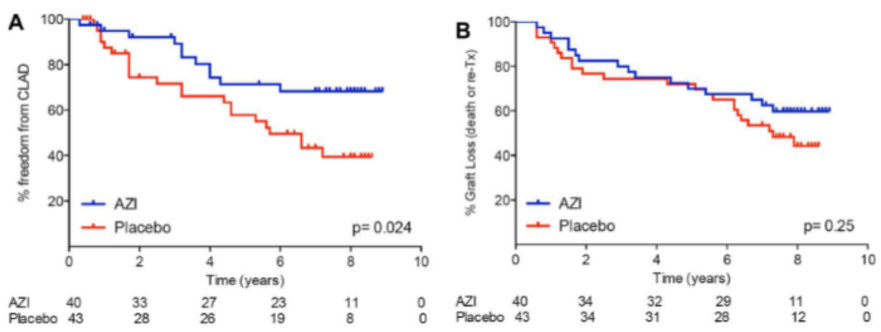
INTRODUCTION

- Azithromycin is a neomacrolide antibiotic used in the treatment of chronic pulmonary diseases
- Azithromycin (250 mg/every two days) increased CLAD-free and overall post-transplant survival [1, 2]
- Mechanism is largely unknown but the anti-inflammatory aspects seem most important

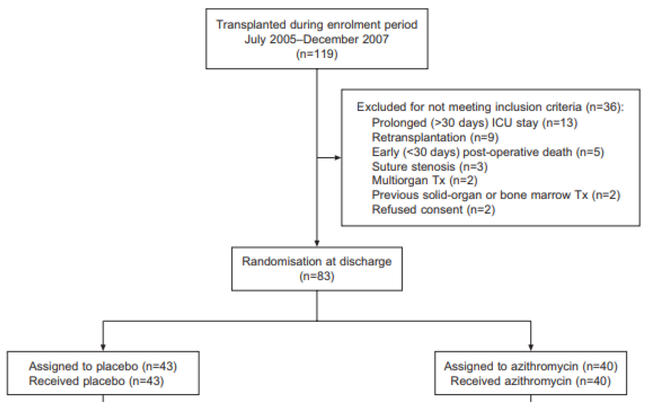


AIM

We wanted to investigate if azithromycin had an effect on the microbial diversity and constitution. Moreover, we wanted to assess if there are significant differences in microbiota during CLAD development, with specific consideration for CLAD phenotypes

METHODS

- Previously performed randomized placebo-controlled trial
- Bronchoalveolar lavage (BAL) samples were collected at discharge, 1, 2 years post-LTx and at suspicion of rejection
- BAL was performed using 2x50 saline, centrifuged and pellet stored in trizol. This pellet is used for DNA extraction
- Bar-coded pyrosequencing of the 16S ribosomal RNA (rRNA) V1–V3 hypervariable region in Queens University Belfast



CONCLUSION

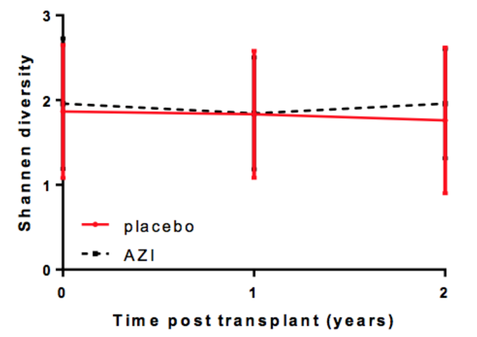
- Except for a slight decrease in the relative abundance of Pseudomonas, there is no difference between AZI and placebo
- There is no difference in microbial diversity at CLAD diagnosis, not between BOS and RAS
- Airway inflammation was associated with microbial presence

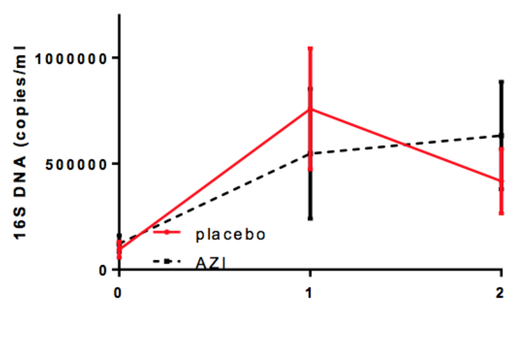
RESULTS

- A total of 221 BAL samples have been analysed
- placebo, n=37, azithromycin, n=32; 3.2 samples per patient

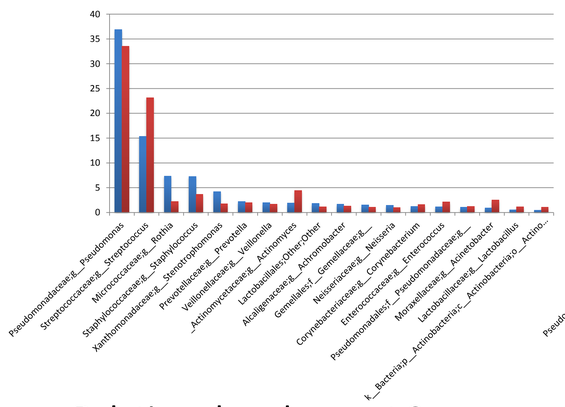
Microbial diversity and Azithromycin

- No difference in Shannon diversity between AZI and placebo
- Tendency to a lower relative abundance of pseudomonas in the AZI group
- Decrease in relative Pseudomonas abundance and increase in Streptococcus abundance in time

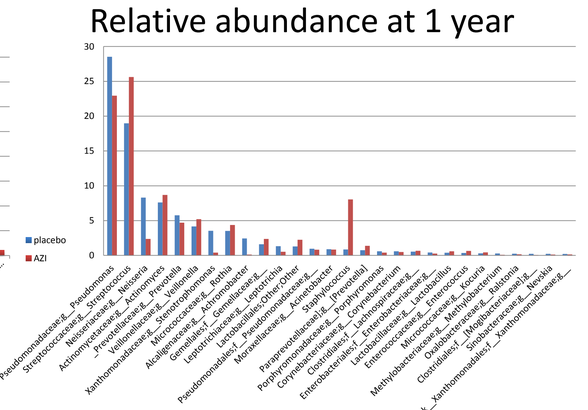




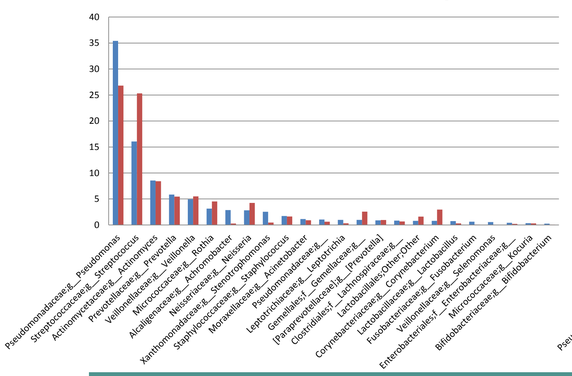
Relative abundance at discharge



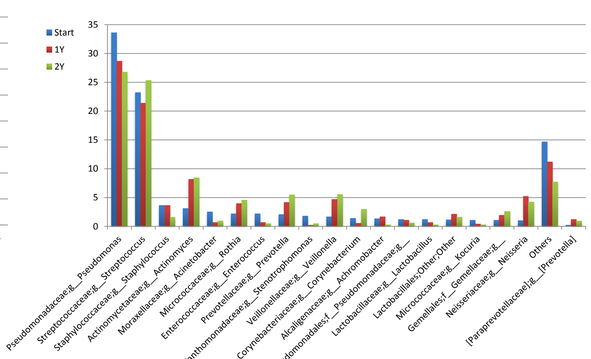
Relative abundance at 1 year



Relative abundance at 2 years

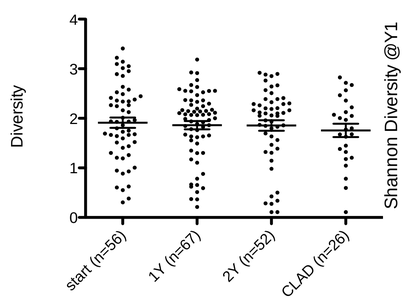


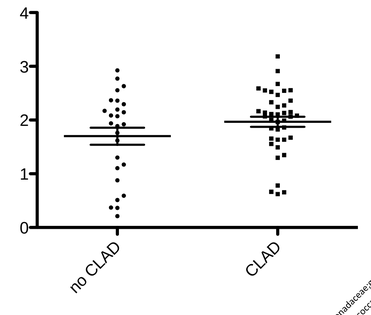
Evolution in time (AZI independent)

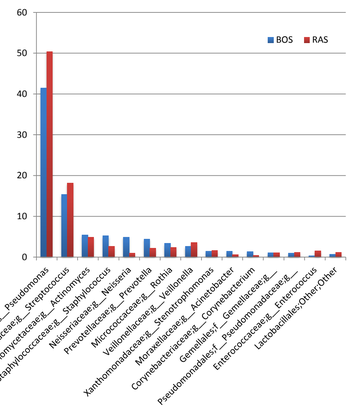


Microbial diversity and CLAD

- No association between microbial diversity and CLAD
- No clear difference between BOS and RAS

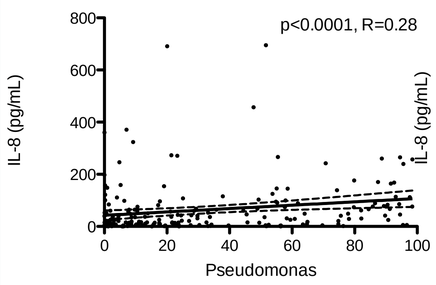


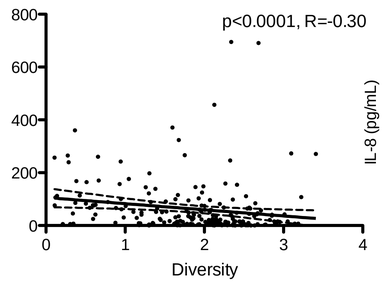


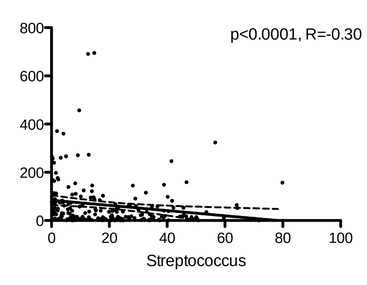


Microbial diversity and BAL inflammation

- Associations between BAL inflammation (IL-8/IL-6) and relative % Pseudomonas
- Negative associations between BAL inflammation (IL-8/IL-6) and 'good bugs'







[1] Ruttens *et al*. AJT. 2016; 16(1): 254-261.
[2] Vos *et al*. ERJ. 2011; 37(1): 164-72

None of the authors have anything to disclose. No off-label and/or investigational use of medical drugs will be discussed.