Associations between the gut microbiome and aromatase inhibitor (AI)-associated musculoskeletal symptoms (AIMSS)

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Introduction

- AIMSS commonly affect AI-treated patients, and may lead to early treatment discontinuation[1]
- Etiology of AIMSS is poorly understood, though inflammation is a recognized contributor[1,2]
- The gut microbiome is associated with inflammation, and is both influenced by estrogen and influences estrogen levels[3,4]
- *Bifidobacteria*, members of the phylum Actinomycetota, in the stool have been associated with decreased systemic inflammation[5]

Objectives

1. Examine whether AI therapy alters the composition of the gut microbiome
2. Examine whether there are associations between the microbial composition and development of AIMSS

Methods

- Enrolled 53 females with breast cancer starting AI therapy (clinicaltrials.gov NCT05700006)
- Collected 151 stool samples, before initiation of treatment (n=53) and after 4 and/or 12 weeks (n=98)
- Also collected stool samples from 10 patients with breast cancer not initiating endocrine therapy
- Extracted DNA and performed 16S rRNA sequencing to characterize and compare microbial communities
- Participants were followed prospectively to assess persistence with AI therapy and reasons for discontinuation
- Wilcoxon signed rank tests were used to compare microbial communities from patients who did and did not develop AIMSS

References

1. Henry et al, JCO 2012
2. Henry et al, Br J Cancer 2010
3. Baker et al, Maturitas 2017
4. Org et al, Gut Microbes 2016
5. Riviere et al, Front Microbiol 2016

Characteristic	Value (N=53)
Age, mean (SD)	63.4 (9)
Endocrine Therapy	Anastrozole = 52 Exemestane = 1
Body mass index, mean (SD)	29.2 kg/m2 (6.1)
Chemotherapy	12 (22.6%)

Table 1. Characteristics of participants starting AI therapy

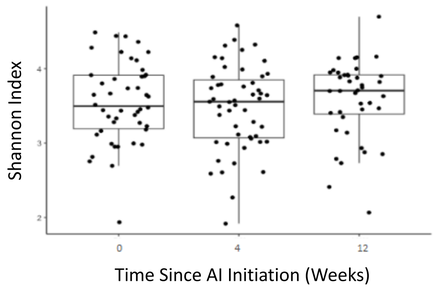


Figure 1. No change in alpha diversity (Shannon Index) after AI initiation.

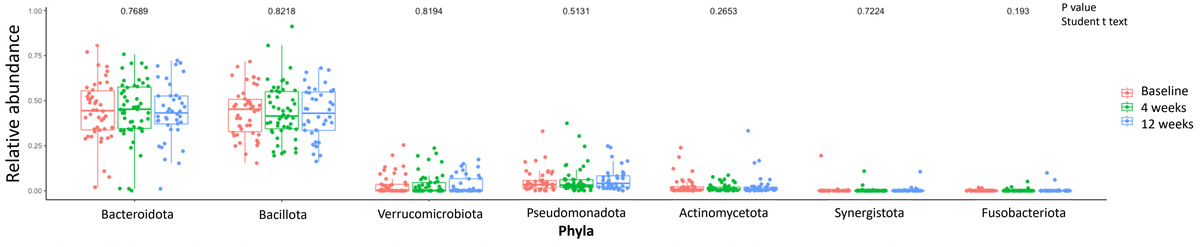


Figure 2. Comparison of phyla at baseline (before initiation of AI therapy) by timepoint in AI-treated patients

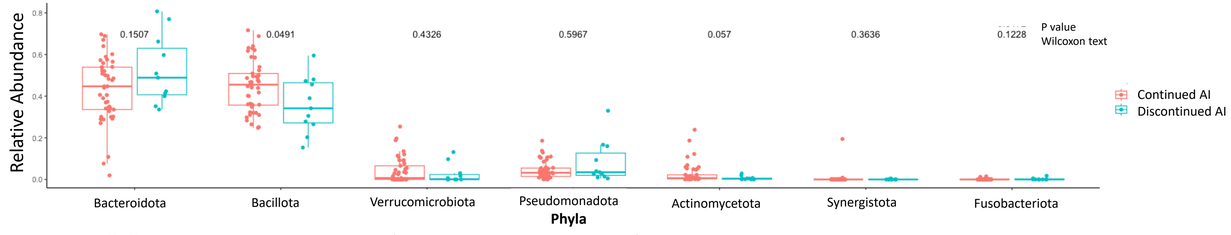


Figure 3. Comparison of phyla at baseline (before initiation of AI therapy) in AI-treated patients who did and did not discontinue AI therapy because of musculoskeletal toxicity

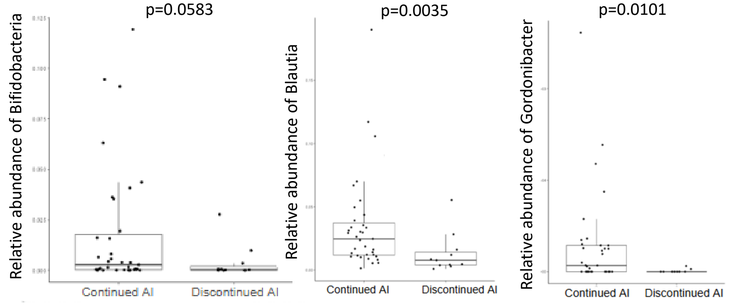


Figure 4. Comparison of Actinomycetota species at baseline in AI-treated patients who did and did not discontinue AI therapy because of musculoskeletal toxicity

Results

- No differences in gut microbiome diversity (alpha or beta) or phyla were identified after AI therapy initiation in the entire population
- By 6 months, 12 (22.6%) enrolled participants had discontinued the initially-prescribed AI therapy because of AIMSS
- We identified a potential association between higher relative abundance of healthy bacteria (such as *Bifidobacteria*) and decreased likelihood of discontinuing AI therapy because of AIMSS (p=0.058)

Conclusions

- We identified a potential association between increased relative levels of healthy bacteria (i.e., *Bifidobacteria*) before AI therapy initiation and decreased likelihood of developing AIMSS
- Future studies can investigate whether gut microbiome alteration can decrease the incidence of AIMSS, thereby enabling increased persistence with AI therapy and improved quality of life

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