

The Impact of Antibiotics and Proton Pump Inhibitors in Neoadjuvant Treatment of HER2+ Breast Cancer

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Background

Anti-HER2 monoclonal antibodies improved the pathologic complete response (pCR) rates and prognostic of human epidermal growth factor receptor 2 positive (HER2+) breast cancer (BC). Antibiotics (ATB) and proton pump inhibitors (PPI) may affect the efficacy of cancer therapies by modulating gut microbiota, and consequently disturb the immune response. Here we aimed to evaluate the impact of ATB and PPI in HER2+ BC neoadjuvant treatment response.

Methods

- Retrospective observational study.
- HER2+ BC patients, treated in our centre, with neoadjuvant chemotherapy plus trastuzumab and pertuzumab, between July 2016 and March 2022.
- Achieving a pCR was compared regarding the use of ATB during the first 30 days, as well as the baseline use or initiation of PPI, in the first 30 days of the neoadjuvant scheme.
- Excluded: cancers of unknown primary site treated as BC; uncompleted neoadjuvant scheme; absence of pathologic assessment after treatment; additional treatments performed.
- Normality was evaluated by the Shapiro-Wilk test. χ^2 or Fisher exact tests were used to assess differences between categorical variables, when applicable. T test was used to evaluate differences between continuous variables. All tests were 2-tailed, and $p < 0.05$ was considered significant.

Results

Characteristics	Overall n=54 (100.0 %)	Non-pCR n=25 (46.3%)	pCR n=29 (53.7%)	p
Age, mean (SD)	52.9 (1.5)	54.9 (2.4)	51.3 (1.9)	0.236
> 65 years, n (%)	7 (13.0)	4 (16.0)	3 (10.3)	0.692
TNM Staging, n (%)				
T1	6 (11.1)	4 (16.0)	2 (6.9)	0.736
T2	29 (53.7)	13 (52.0)	16 (55.2)	
T3	13 (24.1)	6 (24.0)	7 (24.1)	
T4	6 (11.1)	2 (8.0)	4 (13.8)	
Positive regional lymph nodes	30 (55.6)	15 (60.0)	15 (51.7)	0.542
Pathological factors, n (%)				
Ki-67 score $\geq 30\%^*$	39 (75.0)	19 (79.2)	20 (71.4)	0.521
Positive HR	39 (72.2)	21 (84.0)	18 (62.1)	0.073

Table 1. Demographics, clinical and pathological characteristics of the study population. *2 missing values. SD – Standard deviation; HR – Hormone receptor

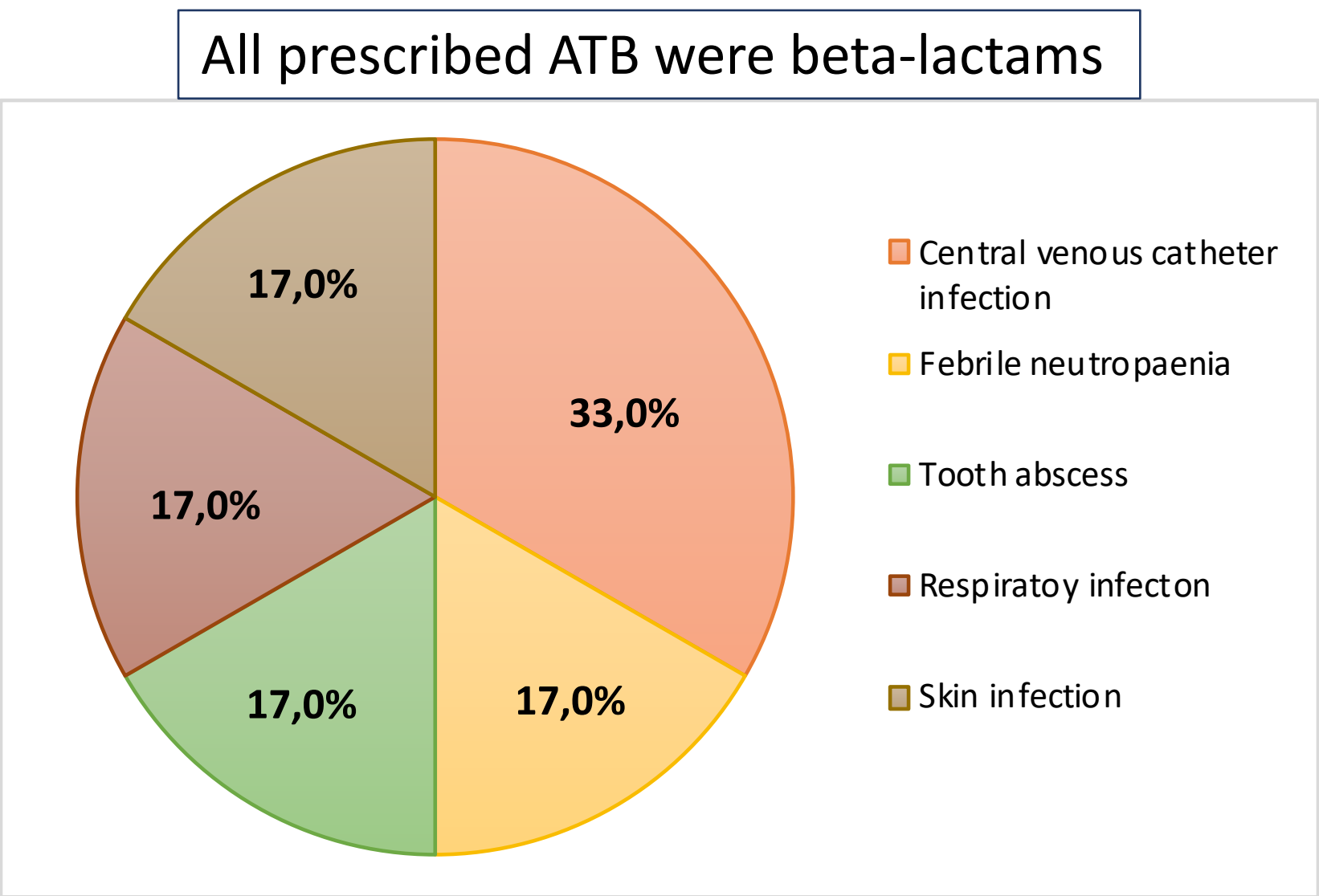


Figure 1. Distribution of diagnoses for which ATB were prescribed.

Characteristics	Overall n=54 (100.0%)	Non-pCR n=25 (46.3%)	pCR n=29 (53.7%)	p
ATB within 30 days, n (%)	6 (11.1)	2 (8.0)	4 (13.8)	0.675
PPI at baseline or within 30 days, n (%)	27 (50.0)	14 (56.0)	13 (44.8)	0.413
ATB and PPI at baseline or within 30 days, n (%)	4 (7.4)	1 (4.0)	3 (10.3)	0.615

Table 2. Analysis of the impact of ATB and PPI in the response to BC neoadjuvant treatment. pCR – Pathologic complete response; ATB – Antibiotics; PPI – Proton pump inhibitors

Conclusions: In our sample ATB and/or PPI intake was not associated with lower rates of pCR, obtained after neoadjuvant HER2+ BC treatment. Future studies with long-term prognostic assessment are still needed.

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