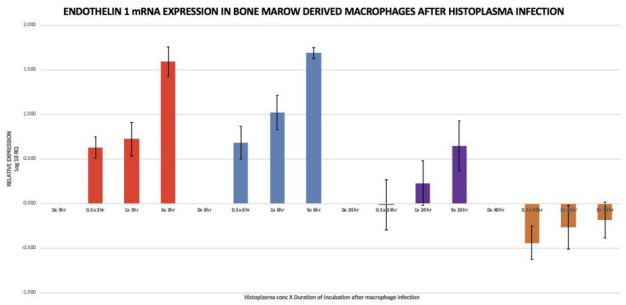
in the pathogenesis of sepsis caused by bacteria, viruses and even parasites. However, there are no published studies that have explored the role of ET-1 in *Histoplasma capsulatum* infection. Studying the role of ET-1 in histoplasmosis is important because understanding its role in the host defense mechanism may serve as the foundation for future discovery of novel therapeutic options.

Methods. Bone marrow cells were isolated from mice and set up for tissue culture. Bone marrow derived macrophages (BMDM) were harvested after 5-7 days of incubation, and infected with varying ratios (0.5,1 and 5) of yeasts to macrophages. RNA was extracted from the BMDM after 3, 6, 24 and 48 hours of infection. For comparison, RNA was also extracted from uninfected BMDM at the same time points. Real-time PCR (polymerase chain reaction) was performed on complementary DNA. ET-1 (*Edn1*) messenger RNA (mRNA) gene expression was quantified relative to the expression of the house keeping /endogenous control gene that encodes for beta-2 microglobulin (*B2m*).

Results. In BMDM infected with *H. capsulatum* there was upregulation of *Edn1* after 3, 6 and 24 hours of infection. During this same time points, the expression of ET-1 mRNA in the uninfected BMDM remained constant. Expression of *Edn1* was highest in the BMDM infected with 5x *H. capsulatum* after 3 and 6 hours of infection. After 24 hours, the expression of ET-1 mRNA decreased markedly in all concentrations of *H. capsulatum*. At 48 hours post-infection the *Edn1* was downregulated in the 0.5,1 and 5-fold quantities of *H. capsulatum* across all time the time intervals.

Figure 1



Conclusion. Results from this study indicate that *H. capsulatum* infection induced an upregulation of the *Edn-1* in BMDM. This may correlate with an increase in levels of ET-1 production by the BMDM in the face of *H. capsulatum* infection. These results provide a platform in which to examine the influence of ET-1 on the host response to this fungus.

Disclosures. **All Authors**: No reported disclosures

1196. Influence of antibiotic use on the effectiveness and safety of immune checkpoint inhibitors in Japan.

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Session: P-53. Microbial Pathogenesis

Background. It has been reported that antibiotic use changes the gut microbiome and alters the outcome of treatment with immune checkpoint inhibitors (ICIs). However, in Asia, this has not been well studied, and there is insufficient evidence to support these reports.

Methods. In this study, we investigated the concurrent use of antibiotics and the administration of PD-1 inhibitors in Japanese patients, and examined the relationship between antibiotics and the clinical benefit or safety of PD-1 inhibitors.

Results. In total, 152 patients were analyzed: 62 patients received systemic antibiotics within 2 months before or 1 month after the first dose of PD-1 inhibitors (the antibiotic group); the remaining patients comprised the non-antibiotic group. There was a significantly higher proportion of patients under 65 years of age in the antibiotic group. Overall survival (OS) was not reached in the antibiotic and non-antibiotic groups, and there was no statistically significant difference between the two groups (HR = 1.48) (Figure 1). Progression-free survival (PFS) was 3.29 months in the antibiotic group and was significantly shorter than that in the non-antibiotic group (5.99 months, HR = 1.75) (Figure 2). Multivariate analysis by Cox regression analysis also showed that PFS was shorter in the antibiotic group (HR=1.63). As age may be a confounding factor, we performed a stratified analysis, a common method used to adjust for bias. The results of the stratified log-rank test after adjustment for age showed that the PFS was significantly shorter in the antibiotic group. There were no statistically significant differences between the two groups in the response rate, incidence of adverse events of Grade 3 or above, and laboratory data (Table 1).

Figure 1

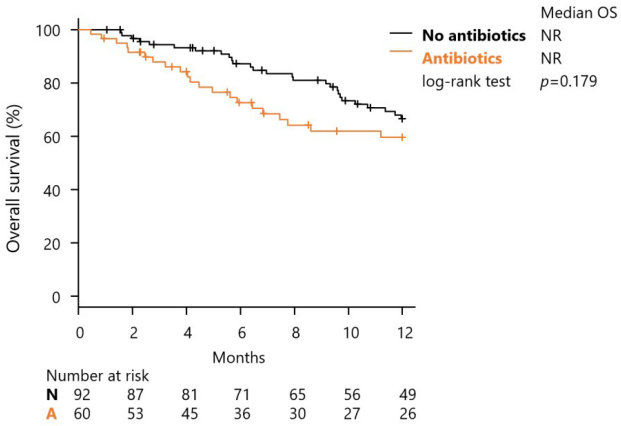

Figure 2

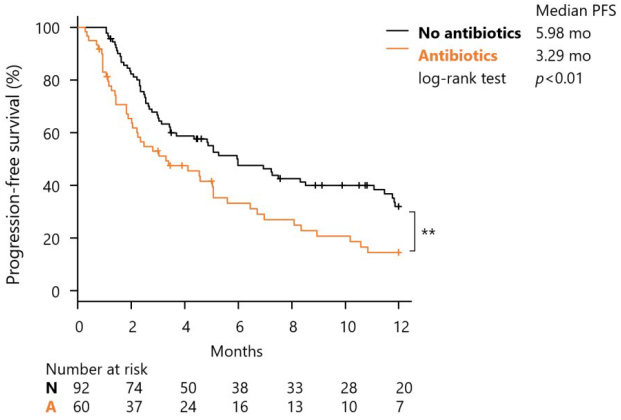

Table 1

	No antibiotics n=92		Antibiotics n=60		*p* value	
	All Grade	Grade 3	All Grade	Grade 3	All Grade	Grade 3
Any adverse event	75	11	50	9	0.831	0.629
Infusion reaction	0	0	2	0	0.154	
Fatigue	26	0	17	0	1.000	
Itching	25	1	13	1	0.566	
Rash	27	3	11	0	0.179	
Diarrhea	9	0	5	0	1.000	
Nausea	7	0	3	0	0.741	
Decreased appetite	14	0	10	0	0.823	
Joint pain	6	0	4	0	1.000	
Muscle pain	6	0	2	0	0.480	
Fever	10	0	13	0	0.104	
Anemia	10	3	8	1	0.798	
Pneumonitis	9	1	10	3	0.221	
Hyperthyroidism	10	1	3	0	0.248	
Hypothyroidism	17	0	9	0	0.663	
Hypophysitis	4	3	2	0	1.000	
Type 1 DM	1	1	0	0	1.000	
Myocarditis	0	0	1	1	0.395	
Joint inflammation	0	0	2	0	0.154	
Increase in AST level	12	0	14	4	0.124	
Increase in ALT level	12	0	13	2	0.183	
Increase in γ-GTP level	17	1	16	1	0.236	
Increase in T-Bil level	2	0	2	0	0.648	
Increase in SCr level	7	0	5	0	1.000	
Otherwise	5	0	7	0	0.220	

CTCAE v4.0, Fisher's exact test

Conclusion. Our results suggest that the use of antibiotics may affect the anticancer treatment outcomes of Japanese patients who are administered PD-1.

Disclosures. **All Authors**: No reported disclosures