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Detection of Gastrointestinal Pathogens in Oncology Patients by Highly Multiplexed Molecular Panels

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Abstract

We compared the frequency of gastrointestinal (GI) pathogen detection in an oncology patient population by two multiplexed molecular assays, the Luminex xTAG® GI Pathogen Panel (GPP, which identifies 14 GI pathogens) and the BioFire GI pathogen panel (BFGP, which identifies 22 GI pathogens). We additionally reviewed the clinical characteristics of patients tested with both panels. A total of 200 prospectively collected and 81 archived stool samples were tested by both panels. In the prospective cohort, the GPP and BFGP identified a pathogen in 33.5% (95% CI: 27.3–40.35%) and 39.6% (95% CI: 33.0%–46.6%) of samples respectively (p=0.25). The BFGP detected significantly more pathogens than the GPP (p=0.038) with 21.3% of samples positive for targets only detected by the BFGP. The concordance between the assays was very good at 91.1% (κ=0.8, 95% CI=0.7–0.9) when considering only pathogens detected by both assays. The most frequent pathogens detected were *Clostridium difficile*, Norovirus, *Campylobacter* and *Salmonella* species. On the archived samples, the BFGP was positive in 92.6% of samples but detected more pathogens than the GPP (86 vs 97, p=0.033), including both targets unique to the BFGP and targets common to both panels. A pathogen was more frequently detected in patients with hematological malignancies than solid tumors and in ambulatory patients compared to hospitalized patients but these differences were not statistically significant. Overall, the detection rates were similar for both the GPP and the BFGP and the latter detected more than one pathogen in additional patients. The impact of increased detection of GI pathogens by multiplexed panels on the clinical care of oncology patients will require further investigation.

Keywords

Syndromic panels; oncology patients; gastroenteritis; molecular diagnostics

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INTRODUCTION

Infectious gastroenteritis is a major cause of morbidity and mortality worldwide with an estimated 2 billion annual cases. Approximately 179 million annual cases of acute gastroenteritis are estimated to occur in the United States resulting in 474,000 hospitalizations and 5,000 deaths [1]. Chemotherapy treatment for oncology patients is well known to be associated with various side effects, in particular toxicity to the gastrointestinal (GI) tract. GI toxicity can manifest as mucositis, a painful inflammatory condition that affects all parts of the GI tract [2]. Mucositis causes breaches in the integrity of the bowel and subsequently increases the risk of secondary infections and provides a nidus for systemic infections [2, 3]. In addition, these patients have compromised immune systems and are, therefore, at a higher risk of serious complications from gastroenteritis [4, 5]. To further confound oncology patient management, frequent side effects of chemotherapy include nausea and vomiting, making it difficult to clinically distinguish between infectious and non-infectious sources of symptoms [6].

In recent years, large, syndromic panels for the detection of GI pathogens have received clearance by the U.S. Food and Drug Administration (FDA) for use in the diagnosis of infectious diarrhea. Two of these assays are the Luminex xTAG® GI Pathogen Panel (GPP; Luminex Corporation, Toronto, Canada) and the BioFire GI pathogen panel (BFGP; BioFire, Inc., Salt Lake City, Utah). The Luminex GPP is FDA-cleared for 14 targets (8 bacterial, 3 viruses, and 3 parasites) while the BFGP includes 22 FDA-cleared targets (13 bacteria, 5 viruses, and 4 parasites). A few studies have evaluated the performance of these assays in a variety of patient populations such as immunocompetent hosts, hospitalized patients, outpatients settings, pediatric oncology patients, and kidney transplant recipients [7–11]. Fewer studies have performed head-to-head comparison of these multiplexed panels [9, 10] and to date, no studies have focused on their performance in a primarily adult, oncology and hematopoietic stem cell transplant (HSCT) recipient patient population.

We performed a study at Memorial Sloan Kettering Cancer Center (MSKCC), a 465-bed tertiary cancer care center in New York City. The objectives of this study were to compare the frequency of GI pathogen detection in diarrheal illness in an oncology (solid tumors and hematologic malignancies) patient population by two multiplexed molecular assays and to determine the characteristics of patients with GI pathogens detected by either panel.

MATERIAL AND METHODS

Study Design

A total of 200 consecutive stool samples from hospitalized and ambulatory adult and pediatric patients were collected over 4 weeks (September to October 2014) and tested by the GPP as part of the routine clinical testing. The samples were stored at 4°C and tested by the BFGP within 7 days. An additional 81 archived samples, initially identified as positive for a GI pathogen by the GPP, were selected for testing by the BFGP. Samples were selected to cover all available GPP viral, bacterial and parasite targets and included samples for every week since use of the GPP test was implemented for routine clinical care (March 2014).

Archived specimens were stored at −80°C following routine clinical testing by the GPP for up to six months prior to testing by the BFGP.

Multiplexed Gastrointestinal Panels

The GPP panel includes the following targets: *C. difficile, Shigella*, *E. coli* O157:H7, *Salmonella*, *Campylobacter*, shiga toxin-producing *E. coli* (STEC), enterotoxigenic *E. coli* (ETEC), *Vibrio cholerae,* Norovirus GI/GII, Rotavirus A, Adenovirus F40/41, *Cryptosporidium* spp., *Giardia,* and *Entamoeba histolytica.* The BFGP includes all targets listed above for the GPP plus *Plesiomonas shigelloides*, Vibrio species (*parahaemolyticus, vulnificus),* enteroaggregative *E. coli* (EAEC), Shigella/enteroinvasive *E. coli* (EIEC), enteropathogenic *E. coli* (EPEC), *Yersinia enterolitica,* Astrovirus, Sapovirus, and *Cyclospora cayetanensis.*

Testing by the GPP assay was performed per manufacturers' instructions on raw, unpreserved stool specimens. For BFGP, the following modifications to the manufacturers' instructions were made: 1) samples were tested after storage for up to 7 days at 4°C or after storage at −80°C for up to six months 2) samples were not collected in Cary-Blair media, the FDA-cleared specimen type. To best approximate the volume and dilution that occurs when stool samples are collected in Cary-Blair media (1 g or 1–5 mL into 9–15 mL media depending on manufacturers), raw stools were first thawed (if frozen) and diluted (1:4, stool: water) into PCR-grade water. Testing was then performed per manufacturer's instructions, using 200 μL of stool sample.

Discordant result analysis

Additional testing was performed to investigate targets with greater than 5 samples with discordant results between the two panels. Discordant analysis was performed for C. *difficile* with the Cepheid GeneXpert *C. difficile* assay and for Noroviruses with a lab-developed qRT-PCR assay [12, 13].

Demographic and Clinical data

Medical records were reviewed to determine the clinical characteristics of patients enrolled in the prospective study. The following information was extracted directly from the medical records: age, sex, underlying malignancy, hospital length of stay (LOS), GI symptoms, white blood cell count, mortality, recent antibiotics and chemotherapy treatment (within 30 days of testing) and transplant status.

Statistics and data analysis

Assay concordance and 95% confidence intervals were calculated using GraphPad Prism (version 7.01). Analysis was performed with a chi-square test or Fisher's exact probability test for comparisons of proportion between two groups. A p value of <0.05 was considered significant.

RESULTS

A total of 200 consecutive samples were tested by both multiplex molecular panels. Three samples collected during the study period were from hospital employees and, therefore, excluded from further analysis. Overall, 197 samples from 170 patients were included in the final analysis with 24 samples from 20 pediatric patients (Table 1). The GPP identified 66 positive samples for a detection rate of 33.5% (95% CI: 27.3–40.35%) while the BFGP identified 78 positive samples for a detection rate of 39.6% (95% CI: 33.0%–46.6%). Four patients with samples positive for more than one pathogen were identified by both the GPP and the BFGP. The BFGP detected more than one pathogen in an additional 13 patients that were previously unrecognized, primarily due to the additional detection of EPEC and EAEC. There were no statistically significant differences in the overall detection rates between the two panels (p=0.25). However, the BFGP detected significantly more pathogens than the GPP (100 vs 72, p=0.038) with 21.3% (n=22) of the increased detection due to targets that are not included on the GPP (Table 1).

There were 32 discordant specimens: 20 specimens had completely discordant results (i.e. negative by one panel but positive by the other panel; e.g. negative by GPP but positive for *C. difficile* by BFGP) and 12 specimens had partially discordant results (i.e. both panels were positive for different or additional pathogens; e.g. positive for STEC by GPP and positive for Astrovirus by BFGP) (Table 1). 14 samples overall were completely (n=11) or partially (n=3) discordant for pathogens common to both panels. The concordance between the assays was very good at 91.1% (κ=0.8, 95% CI=0.7–0.9) when considering only pathogens detected by both assays with the most frequently identified pathogens being *Clostridium difficile*, Norovirus, *Campylobacter* and *Salmonella* species (Table 1).

The performance of the two assays was further compared by testing archived positive samples initially tested by the GPP assay as part of routine clinical care. This analysis was performed primarily to estimate the frequency of the additional BFGP targets in these samples. Of the 81 samples tested, the BFGP was positive in 75 samples (92.6%) but detected 97 pathogens compared to 86 pathogens by the GPP (Table 2). The BFGP detected 10 additional pathogens not included on the GPP panel and 9 pathogens common to both panels while the GPP detected 8 pathogens not detected by the BFGP (Table 2). Two or more pathogens were detected in 4 samples by both methods. The BFGP detected more than one pathogen in an additional 16 samples with 50% of those samples positive for EPEC/EAEC (Table 2).

Overall, Norovirus and *C. difficile* were more frequently found individually whereas ETEC, EAEC, and EPEC were more frequently found along with another pathogen (data not shown). In particular, EAEC was frequently associated with *Shigella*, STEC, and ETEC while EPEC was most frequently associated with *Shigella*, *Campylobacter*, ETEC, and EAEC (data not shown). These associations, however, were not statically significant (p>0.05).

A high number of samples with discordant results (n >5) between the two panels was noted for *C. difficile* and Norovirus (p <0.001). The Xpert *C. difficile* assay (Cepheid Inc.,

Sunnyvale, CA) was used to arbitrate the discordant *C. difficile* results for both the prospective and archived samples. All 12 discordant samples were positive by the Xpert PCR assay, confirming the positive BFGP results (Table 3). The Xpert *C. difficile* real-time PCR cycle threshold (C_t) values (a surrogate of *C. difficile* bacterial loads) was further reviewed for all positive samples (concordant and discordant samples). There was a significant difference ($p<0.05$) in the mean Ct value between samples positive for *C. difficile* by both panel (Ct 26.2) compared to the mean Ct value for sample positive by the BFGP only (Ct value=28.6), suggesting that differences observed could be due to a higher detection rate of the BFGP at low bacterial loads (data not shown). There were 7 discordant Norovirus results between the BFGP and GPP. Five samples were positive by GPP only and two positive by BFGP only. The third PCR assay confirmed 5 of the 7 GPP results (2 negative, 3 positive) and 2 of the 7 BFPG results (2 negative) (Table 3).

Demographic and clinical characteristics of 170 patients prospectively enrolled and tested by both panels were reviewed. Results are summarized in Table 4. The median patient age was 54.5 years (range 3–86 year) with 11.8% of patients under the age of 18, 54.7% female, 51.2% with a diagnosis of hematologic malignancy (e.g. leukemia or lymphoma) or receipt of a HSCT and 51.5% with recent chemotherapy treatment (within 30 days prior to GI panel testing). A total of 120 patients (70.6%) were hospitalized at the time of testing with 17.5% in the ICU and 50% having received antibiotics within 30 days of GPP testing. Diarrhea was recorded in 78.5% of all patients and 43% of patients with diarrhea had a positive GPP or BFGP result. A pathogen was detected in more than 50% of patients with gastrointestinal graft versus host disease (54.5%) or colitis on imaging (62.5%). The median hospital LOS was 11.5 days (95% CI: 8–17 days) with an all cause mortality rate of 5.9%. The median LOS was shorter for patients positive for a GI pathogen (6 days, 95% CI: 4–14 days) compared to patients with no GI pathogens detected (16 days, 95% CI: 10–24 days) ($p<0.0001$).

There were no significant differences between frequency of positive results of patients with hematologic malignancies or HSCT recipients or patients with solid tumors (47.1% vs 37.3%, $p=0.21$). The distribution of pathogens common to both panels was similar in both groups of oncology patients with *C. difficile* as the most frequently identified pathogen. Unique to the BFGP, EPEC was the second most frequent pathogen (Table 5). More *Salmonella* and *Campylobacter* infections were detected in patients with hematologic malignancies or HSCT recipients but the differences were not statistically significant ($p=0.06$). A small percentage (11.8%) of patients was under the age of 18 and, as with the adult patients, *C. difficile* was the most frequently identified pathogen. The second most frequently identified pathogen by the BFGP was EPEC in 4 pediatric patients. Detection rates by both panels were similar for all common targets in all patient groups (Table 5).

Review of clinical characteristics of patients positive for more than one pathogen showed that these infections were not associated with more severe disease as measured by LOS, ICU admission, 30-day mortality, antibiotics use, or GI symptoms including nausea, vomiting, diarrhea, fever, or abdominal pain (data not shown).

DISCUSSION

To the best of our knowledge, our study is the first to compare the frequency of GI pathogens detection by the Luminex® xTAG® GI Pathogen Panel (GPP) and the BioFire GI pathogen panel (BFGP) in both adult and pediatric oncology patients exclusively. Our data show that the two assays had similar detection rates with an overall concordance of greater than 90% for targets common to both assays, similar to other studies performed in different patient populations [9, 14]. The most frequent GI pathogens in our oncology patient population were *C. difficile*, Norovirus, *Campylobacter,* and *Salmonella* species. The high rate of *C. difficile* detection was expected in this population of patients who are at increased risk for both *C. difficile* infection and asymptomatic *C. difficile* carriage, given their frequent and prolonged exposure to healthcare environments and antibiotics usage. Unlike other studies where Sapovirus and Astrovirus were detected in several patients, only one patient in our cohort was positive for Astrovirus [9, 14]. This difference may reflect differences in patients tested, as both viruses are more frequently detected in pediatric patients, which only represented ~12% of our patient cohort. A larger study over an extended timeframe could provide a different pathogen epidemiology.

There were some notable differences between the two panels. The Luminex GPP assay showed lower detection rate for *C. difficile*. On average, the corresponding Xpert *C. difficile* Ct values of the negative GPP samples were higher than those of the samples positive by both panels, suggesting that the negative samples likely had a lower bacterial load. This result is in contrast with the study by Gu et al conducted in pediatric oncology patients showing higher detection rate for *C. difficile* by the Luminex assay [14]. Additional discordant samples were observed for Norovirus results. One previous report noted poor specificity of the Luminex GPP assay for Norovirus [9]. In that study, discrepant Norovirus results were attributed to lot-specific problems and corrected upon retesting with a new lot of reagents [9]. In our data set, a third Norovirus specific RT-PCR was used to confirm the presence of Norovirus identified by the GPP and the BFGP. Resolution of discordant results showed that the overall performance of both assays for Norovirus was equivalent.

Diarrhea is a frequent symptom in cancer patients and differentiating between infectious or non-infectious causes requires laboratory testing. Similar to our study, Mhaissen et al reviewed the clinical characteristics of pediatric oncology patients positive by the GPP and BFGP [10]. In our study, 78.5% of patients had diarrhea and 43% of these patients had a pathogen identified by the multiplexed GI panels. In contrast, Mhaissen et al [10] showed that 95% of patients in the pediatric oncology population had diarrhea and 60–65% of patients were positive for a GI pathogen, which is similar to data from our small pediatric cohort. Although the presence of a pathogen alone does not imply symptoms causation, the results provided by these GI panels along with other clinical data may help inform clinical decisions.

A pathogen was more frequently detected in patients with hematological malignancies than solid tumors and more frequently in ambulatory patients than in hospitalized patients, although the differences were not statistically significant. Of interest, both *Salmonella* and *Campylobacter* species were detected more frequently in adult patients with hematologic

malignancies but the overall numbers were too small to draw significant conclusions. There was no significant correlation between a positive multiplex panel and ICU stay, 30 day mortality, or number of symptoms, but there was a significant correlation between a negative GI panel and a longer LOS. However, given the complex presentation of these more critically ill cancer patients who are often admitted for extended period of time, the observed differences in LOS could be a result of multiple factors not measured in this study.

More than one pathogen was more frequently detected by BFGP, largely due to the detection of EPEC or EAEC, which are not detected by the GPP assay. The increased detection of diarrheogenic *E. coli* and their recovery in mixed infections are consistent with previous reports and unlikely to represent false positive results or contamination although these possibilities were not investigated further in our study [7, 9]. Further review of the clinical characteristics of patients with multiple pathogens detected did not reveal more severe disease than in patients with monomicrobial infections. The increased detection of more than one pathogen with BFGP indicates that the presence of multiple pathogens in diarrheal stool samples may be underestimated. While these diarrheogenic *E. coli* are known to be associated with GI symptoms in patients [15], their role in causing polymicrobial infections in oncology patients remains unclear. However, our study is limited by the small number of patients positive for more than one pathogen and larger studies may reveal a stronger association with disease severity.

Our study has some limitations. First, this is a single-center study in an oncology patient population and as such our results may not be applicable to other centers or patient populations. However, as the number of immunocompromised cancer patients continues to increase and treatment options improve, these patients tend to survive longer and remain a significant part of our healthcare system [16]. Therefore, the data presented here should be of interest to a wider audience. Second, discordant analysis was only performed for *C. difficile* and Norovirus as these were the most frequently identified targets. While assays specificity or possible contamination may explain the few differences observed, the sensitivity and specificity of these two panels have been previously evaluated and although comparable, is not expected to be identical [9, 14]. Finally, the off-label testing and the testing of samples frozen for a few months may have negatively impacted detection of pathogens by BFGP although the overall detection rate remained higher than GPP.

CONCLUSION

In conclusion, multiplexed, molecular panels are new technologies that are changing the frequency and distribution of gastrointestinal pathogens in immunocompromised oncology patients. Further outcome studies on the impact of tests results in various patient populations, including cancer patients, are needed to determine the value of these panels on patient care, antimicrobial stewardship, and infection control programs.

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Table 1

Comparison of the Luminex to the BioFire Panels on prospective stool samples (n=197)*

Pathogens	GPP N	BFGP N	P value
Negative specimens	**131 (66.5%)**	**119 (60.4%)**	**0.25**
Positive specimens	**66 (33.5%)**	**78 (39.6%)**	
C. difficile	33	39	
Shigella	3	3	
E. coli O157:H7	0	0	
Salmonella species	5	5	
Campylobacter species	9	9	
STEC	2	2	
ETEC	3	4	
EAEC	n/a	5	
EIEC	n/a	0	
EPEC	n/a	16	
Plesiomonas shigelloides	n/a	0	
Yersinia enterolitica	n/a	0	
Vibrio cholerae /Vibrio species	0	0	
Norovirus GI/GII	11	12	
Rotavirus A	0	1	
Adenovirus F40/41	1	0	
Astrovirus	n/a	1	
Sapovirus	n/a	0	
Cryptosporidium species	1	1	
Giardia lamblia	2	2	
Entamoeba histolytica	2	0	
Cyclospora cayetanensis	n/a	0	
Total pathogens detected	**72**	**100**	0.038
Positive for >1 pathogen	4	17	
Discordant specimens			
No pathogen detected	16	4	
Different pathogens detected	1		
Additional pathogens detected	0	11	

* 24 samples from pediatric patients. STEC: Shiga-toxin producing *E. coli*; ETEC: Enterotoxigenic *E. coli*; EAEC: Enteroaggregative *E. coli*; EIEC: Enteroinvasive *E. coli*; EPEC: Enteropathogenic *E. coli*. N/A: Not applicable (target not included on panel)

Table 2

Comparison of the Luminex to the BioFire Panels on archived stool samples (n=81)*

Pathogens	GPP N	BFGP N	P value
Positive specimens	**81**	**75**	**0.028**
Negative specimens	**0***	**6**	
C. difficile	3	9	
Shigella	0	0	
E. coli O157:H7	1	0	
Salmonella species	5	4	
Campylobacter species	9	10	
STEC	3	3	
ETEC	4	4	
EAEC	n/a	2	
EIEC	n/a	0	
EPEC	n/a	8	
Plesiomonas shigelloides	n/a	0	
Yersinia enterolitica	n/a	0	
Vibrio cholerae /Vibrio species	0	0	
Norovirus GI/GII	36	32	
Rotavirus A	16	18	
Adenovirus	2	2	
Astrovirus	n/a	0	
Sapovirus	n/a	0	
Cryptosporidium species	0	0	
Giardia lamblia	6	5	
Entamoeba histolytica	1	0	
Cyclospora cayetanensis	n/a	0	
Total pathogens detected	**86**	**97**	0.033
Positive for >1 pathogen	**4**	**20**	
Discordant specimens			
No pathogen detected	**0***	**6**	
Different pathogens detected	**1**		
Additional pathogens detected	**0**	**16**	

* Positive samples originally tested by the Luminex GI panel. STEC: Shiga-toxin producing *E. coli*; ETEC: Enterotoxigenic *E. coli*; EAEC: Enteroaggregative *E. coli*; EIEC: Enteroinvasive *E. coli*; EPEC: Enteropathogenic *E. coli*. N/A: Not applicable (target not included on panel)

Table 3

Summary of *C. difficile* and Norovirus Discordant Resolution

	GPP	BFGP	Xpert C. difficile	Norovirus RT PCR
Sample 1	Norovirus GI/GII	Norovirus GI/GII, *C. difficile*	*C. difficile*	ND
Sample 2	Norovirus GI/GII	Norovirus GI/GII, *C. difficile*	*C. difficile*	ND
Sample 3	Norovirus GI/GII	*C. difficile*	*C. difficile*	Negative
Sample 4	Rotavirus	Rotavirus, *C. difficile*	*C. difficile*	ND
Sample 5	Rotavirus	Rotavirus, *C. difficile*	*C. difficile*	ND
Sample 6	Norovirus GI/GII	Norovirus GI/GII, *C. difficile*	*C. difficile*	ND
Sample 7	Negative	*C. difficile*	*C. difficile*	ND
Sample 8	Negative	*C. difficile*	*C. difficile*	ND
Sample 9	Negative	*C. difficile*	*C. difficile*	ND
Sample 10	Negative	*C. difficile*, EAEC	*C. difficile*	ND
Sample 11	Negative	*C. difficile*, STEC	*C. difficile*	ND
Sample 12	Negative	*C. difficile*, Norovirus GI/GII	*C. difficile*	Negative
Sample 13	Norovirus GI/GII	Negative	ND	Norovirus GI/GII
Sample 14	Norovirus GI/GII	Negative	ND	Negative
Sample 15	Norovirus GI/GII	Negative	ND	Norovirus GI/GII
Sample 16	Norovirus GI/GII	Negative	ND	Norovirus GI/GII
Sample 17	ETEC	ETEC, Norovirus GI/GII	ND	Negative

*ND: Not done

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Table 4

Demographic and clinical characteristics of patients in the prospective study (n=170)

Clinical Data	N (%)	Positive by either GI Panel N (%)
Median age (range)	54.5 (3–86)	n/a
Pediatric patients (<18 years)	20 (11.8)	16 (80.0)
Sex, female	93 (54.7)	36 (34.6)
Hematologic malignancies/HSCT	87 (51.2)	41 (47.1)
Solid tumor (e.g. Lung cancer)	83 (48.8)	31 (37.3)
Outpatient	50 (29.4)	25 (50)
Inpatient	120 (70.6)	47(39.1)
Intensive care unit	21 (17.5)	3 (9.5)
Mortality (30 days)	10 (5.9)	2 (20.0)
Length of stay (days), median (95%CI)	11.5 (8–17)	6 (4–14)
Diarrhea	133 (78.5)	57 (43)
WBC count (10^9/L), mean ± SD	6.8 ± 7.1	n/a
Colitis on imaging	8 (4.7)	5 (62.5)
GI GVHD	11 (6.5)	6 (54.5)
Antibiotics within 30 days	85 (50)	39 (39.0)
Chemotherapy within 30 days	87 (51.5)	33 (37.9)

*GI: Gastrointestinal; HSCT: Hematopoietic Stem Cell Transplant; GVHD: Graft versus Host Disease; WBC: White Blood Cells

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Table 5

Distribution of pathogens in different oncology populations[a]

Pathogens	Hematologic/HSCT N (%)		Solid tumor N (%)		Pediatric[b] N (%)	
	GPP	BFGP	GPP	BFGP	GPP	BFGP
Any pathogen	33 (37.9%)	38 (43.6%)	23 (27.7%)	30 (36.1%)	12 (60%)	13 (65%)
Multiple pathogens	3 (3.4%)	8 (9.2%)	1 (1.2%)	9 (10.8%)	2 (10%)	5 (25%)
C. difficile	18	20	12	16	7	7
Shigella	1	1	1	1	1	1
E. coli O157:H7	0	0	0	0	0	0
Salmonella species	4	4	1	1	0	0
Campylobacter species	4	3	2	2	1	2
STEC	1	1	1	1	1	0
ETEC	2	2	1	2	1	0
EAEC	n/a	1	n/a	4	n/a	1
EIEC	n/a	0	n/a	0	n/a	0
EPEC	n/a	8	n/a	8	n/a	4
Plesiomonas shigelloides	n/a	0	n/a	0	n/a	0
Yersinia enterolitica	n/a	0	n/a	0	n/a	0
Vibrio cholerae /species	0	0	0	0	0	0
Norovirus GI/GII	5	5	4	5	2	2
Rotavirus A	0	0	0	0	0	0
Adenovirus	1	0	0	0	0	0
Astrovirus	n/a	0	n/a	1	n/a	0
Sapovirus	n/a	0	n/a	0	n/a	0
Cryptosporidium spp.	1	1	0	0	1	1
Giardia lamblia	0	0	2	2	1	1
Entamoeba histolytica	1	0	0	0	0	0
Cyclospora cayetanensis	n/a	0	n/a	0	n/a	0

[a]HSCT: Hematopoietic Stem Cell Transplant;

[b] Pediatric patients (included in the total hematologic (n=11)/solid tumors numbers (n=5)). STEC: Shiga-toxin producing *E. coli*; ETEC: Enterotoxigenic *E. coli*; EAEC: Enteroaggregative *E. coli*; EIEC: Enteroinvasive *E. coli*; EPEC: Enteropathogenic *E. coli*. N/A: Not applicable (target not included on panel)