Name of Sponsor/Company: Astellas Pharma Europe Ltd		
Name of Finished Product: Fidaxomicin		
Name of Active Ingredient: Fidaxomicin		

SYNOPSIS

Title of Study: A Phase IIIb/IV Randomized, Controlled, Double-blind, Double-dummy, Parallel Group Study to Compare the Efficacy of Fidaxomicin to Vancomycin in the Sustained Clinical Cure of *Clostridium Difficile* Infection in Adults Receiving Immunosuppressive Therapy (FID-EC-0001)

Investigators/Coordinating Investigator: [redacted], MD, FACP, FIDSA, [redacted].

Study Center(s): This study was planned to be conducted at 50 centers in 14 European countries: Austria (5 centers), Belgium (3), Denmark (1), Finland (2), France (4), Germany (4), Greece (4), Hungary (4), Italy (6), Poland (3), Russia (6), Spain (4), Sweden (2), and the United Kingdom (2). Eight centers in 6 countries randomized patients to the study: Austria (1 center), Denmark (1), France (2), Germany (2), Greece (1), and Spain (1).

Publication Based on the Study: None

Study Period: 4.5 months

Study Initiation Date (Date of First Enrollment): 29 November 2012

Study Completion Date (Date of Last Evaluation): 15 April 2013 (study was terminated early)

This study was terminated by the Sponsor due to slow recruitment. Patients who had already entered the study were allowed to continue and the study was stopped once all recruited patients had completed the study.

Phase of Development: Phase IIIb/IV

Objectives: The primary objective of the study was to demonstrate superiority of fidaxomicin versus vancomycin for the sustained clinical cure of *Clostridium difficile* infection (CDI) in adult patients receiving immunosuppressive therapy. Sustained clinical cure was defined as clinical cure without recurrence within 14 days from Test of Cure (TOC).

The key secondary objective of this study was to demonstrate superiority of fidaxomicin versus vancomycin for clinical cure of CDI at TOC on Day 12.

Further secondary objectives were:

- to compare the rate of sustained clinical cure of CDI at Day 40 after treatment with fidaxomicin or vancomycin
- to compare the recurrence rate of CDI after treatment with fidaxomicin or vancomycin
- to compare the time to resolution of diarrhea on treatment with fidaxomicin or vancomycin.

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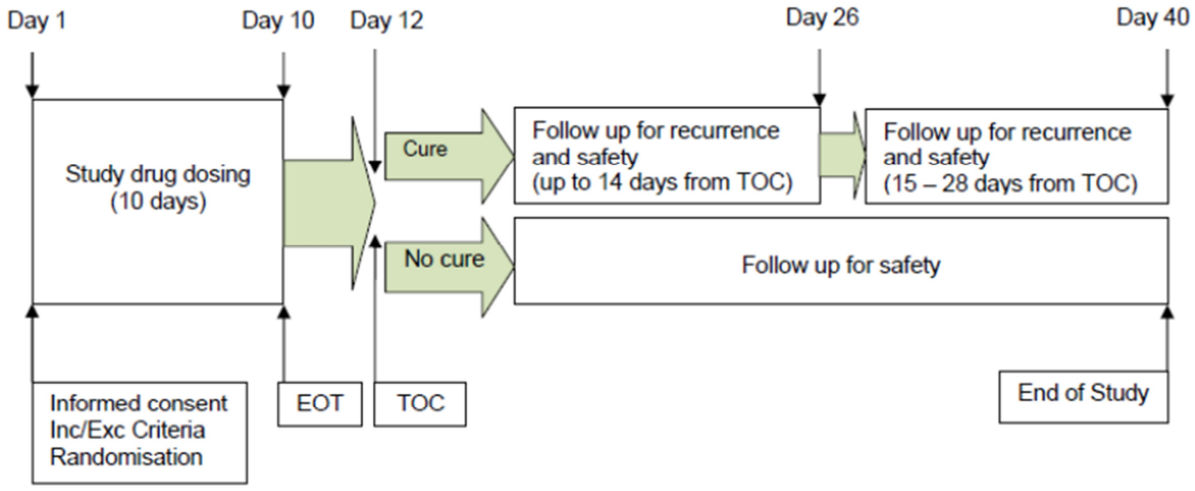
Note: A patient was considered clinically cured at the TOC if the patient required no further CDI therapy following the completion of study medication and the patient had one of the following:

- ≤ 3 unformed bowel movements (UBM) for 2 consecutive days and sustained to TOC, or
- marked reduction (≥ 50%) in the number of UBM at the end of treatment (EOT) compared with baseline, or
- 75% reduction in the volume of liquid stool collected or was no longer passing liquid stools (for patients having a rectal collection device).

Patients achieving ≤ 3 UBM for 2 consecutive days before the time of study medication discontinuation and who remained well until TOC were also to be considered clinically cured. Patients not meeting the definition of clinical cure at TOC were defined as treatment failures.

Recurrence of CDI after TOC was defined as the re-establishment of diarrhea to an extent (judged by the frequency of passed UBM) that was greater than the frequency recorded on the last day of study medication (confirmed by a positive rapid CDI test) and that required re-treatment with CDI anti-infective therapy.

Methodology: This was a multi-centre, randomized, double-blind, double-dummy, parallel-group study comparing the efficacy of fidaxomicin and vancomycin in patients with CDI who were receiving immunosuppressive therapy. A study flow chart is included below.



EOT: End of treatment; Exc: Exclusion; Inc: Inclusion; TOC: Test of Cure.

On Day 1 (baseline), patients receiving immunosuppressive therapy who had diarrhea (> 3 UBM or ≥ 200 mL of unformed stool [for patients having rectal collection devices] within 24 hours) and CDI (confirmed by a rapid CDI test being positive for both toxins A and B, and glutamate dehydrogenase) were randomized to receive

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fidaxomicin or vancomycin (1:1 randomization). Randomization was stratified by centre and reason for immunosuppression.

Patients were treated with study medication from Day 1 to Day 10. The TOC took place 48 to 72 hours after the EOT. A stool sample for evaluation of microbial cure was taken at TOC on Day 12. Patients meeting the criteria for clinical cure at TOC were monitored for recurrence until 28 days after TOC (Day 40). Patients not meeting the definition of clinical cure at TOC on Day 12 were defined as treatment failures and were followed only for safety until Day 40. Further CDI treatment for patients not meeting the criteria for clinical cure at TOC or with recurrence of CDI was at the discretion of the Investigator.

Stool samples that tested positive by rapid CDI test at baseline, all samples at TOC (Day 12), and samples taken to confirm recurrence were sent to a central laboratory for secondary analysis. The strain of *Clostridium difficile* was determined in all samples.

Number of Patients (Planned, Enrolled and Analyzed): A total of 696 patients (348 per arm) were planned to be recruited and randomized. A total of 12 patients (4 in the fidaxomicin arm and 8 in the vancomycin arm) were randomized prior to early termination of the study. All 12 patients received at least 1 dose of study medication and were analyzed for efficacy and safety.

Diagnosis and Main Criteria for Inclusion: Male and female patients aged ≥ 18 years who were receiving immunosuppressive therapy due to undergoing a stem cell transplant procedure or for the treatment of a hematological malignancy, for a solid tumor malignancy or following solid organ transplantation, or for an autoimmune disease or related illness, and who had been diagnosed with CDI (confirmed by clinical symptoms and a rapid CDI test) were eligible. Patients must not have been treated with medication or other therapy for CDI within the preceding 10 days. Patients who had more than 1 previous episode of CDI within the 3 months prior to study inclusion, were taking or needed to be treated with prohibited medications (oral vancomycin, metronidazole, oral bacitracin, fusidic acid, rifaximin, nitazoxanide, tigecycline, anti-diarrheal medications) or were receiving prohibited concomitant non-medication therapy (fecal transplant), had a history of ulcerative colitis or Crohn's disease, or a history or diagnosis of toxic megacolon or pseudomembranous colitis were not eligible for the study.

Test Product, Dose and Mode of Administration, Batch Numbers: Patients randomized to the fidaxomicin arm took alternate oral doses of fidaxomicin 200 mg (over-encapsulated to maintain the blind) and matching placebo capsules each day throughout the 10-day treatment period, resulting in 1 dose of fidaxomicin 200 mg every 12 hours (2 doses each day) and 1 dose of placebo every 12 hours (2 doses each day).

Batch numbers (fidaxomicin): Bulk batch: [redacted] ([redacted] = parent "original" batch); final product: [redacted] and [redacted].

Batch number (placebo): [redacted]

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Duration of Treatment (or Duration of Study, if applicable): The duration of the study was 40 days, with a 10-day treatment period.

Reference Product, Dose and Mode of Administration, Batch Numbers: Patients randomized to the vancomycin arm received 4 doses (1 dose every 6 hours) of oral vancomycin hydrochloride 125 mg capsules (over-encapsulated to maintain the blind) each day for the duration of the 10-day treatment period. Vancomycin was chosen as the comparator as it is the current gold standard for the treatment of CDI for the treatment of severe as well as recurrent CDI.

Batch numbers (vancomycin): Bulk batch: [redacted] ([redacted] = parent batch) and [redacted] ([redacted] = parent batch); final product: [redacted], [redacted] and [redacted].

Criteria for Evaluation:

Efficacy

Primary

- Sustained clinical cure of CDI at Day 26, defined as clinical cure at TOC and no recurrence of CDI from TOC until Day 26

Key secondary efficacy variable:

- Clinical cure of CDI at TOC on Day 12

Other secondary efficacy variables:

- Sustained clinical cure of CDI at Day 40, defined as clinical cure at TOC with no recurrence within 28 days after TOC
- Microbial eradication at TOC, for the population with a positive culture at baseline
- Time to resolution of diarrhea, as measured from the first dose of study medication
- Use of further CDI therapy required between EOT and TOC
- Number of unformed stools between EOT and TOC
- Marked reduction (≥ 50%) in the number of unformed stools at TOC compared with baseline
- Recurrence of CDI after TOC (for patients with clinical cure at TOC)
- Time to recurrence of CDI (for patients with clinical cure at TOC)

Safety

- Incidence and severity of adverse events (AEs)

Other

- [redacted]
- Health Related Quality of Life: EuroQoL 5-Dimension Questionnaire 5 Level descriptive assessment and visual analogue scale

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Statistical Methods: Due to the early termination of the study, the 12 patients randomized versus the 696 patients planned to be recruited and randomized was insufficient to allow meaningful statistical comparisons of the 2 treatments. Only key study data have been summarized descriptively. The originally defined analysis sets (Safety Analysis Set, Modified Full Analysis Set, Per Protocol Set, Microbiologically Evaluable Analysis Set) have not been used and all data summaries and data listings have been provided for the Intent-to-Treat (ITT) population, which comprised all patients who were randomized.

For continuous variables, descriptive statistics included the number of patients (n), mean, standard deviation, median, minimum, and maximum. Frequencies and percentages were displayed for categorical data. Percentages by categories were based on the number of patients with no missing data. Summary tables were stratified by treatment arm.

Study population

Summary tables were produced for: patient disposition; demographics and baseline characteristics, baseline CDI status (severity of disease, number of UBM, use of antibiotics for conditions other than CDI in the preceding 10 days, result of the rapid CDI test, and incidence of prior episodes of CDI); and medical history.

Efficacy

Summary tables were produced for:

- Clinical cure at TOC on Day 12
- Recurrence of CDI after TOC (for patients with clinical cure at TOC)
- Sustained clinical cure 14 days after TOC (at Day 26)
- Sustained clinical cure of CDI over 28 days after TOC (at Day 40)
- Use of further CDI therapy required between EOT and TOC
- Marked reduction (at least 50%) in the number of UBM at TOC compared with baseline
- Time to resolution of diarrhea
- Time to recurrence of CDI (for patients with clinical cure at TOC).

Safety

Summary tables were produced for: an overview of treatment-emergent AEs (TEAEs); TEAEs; and serious TEAEs. All available data have been listed.

Other

All available data for [redacted] and health related quality of life have been listed.

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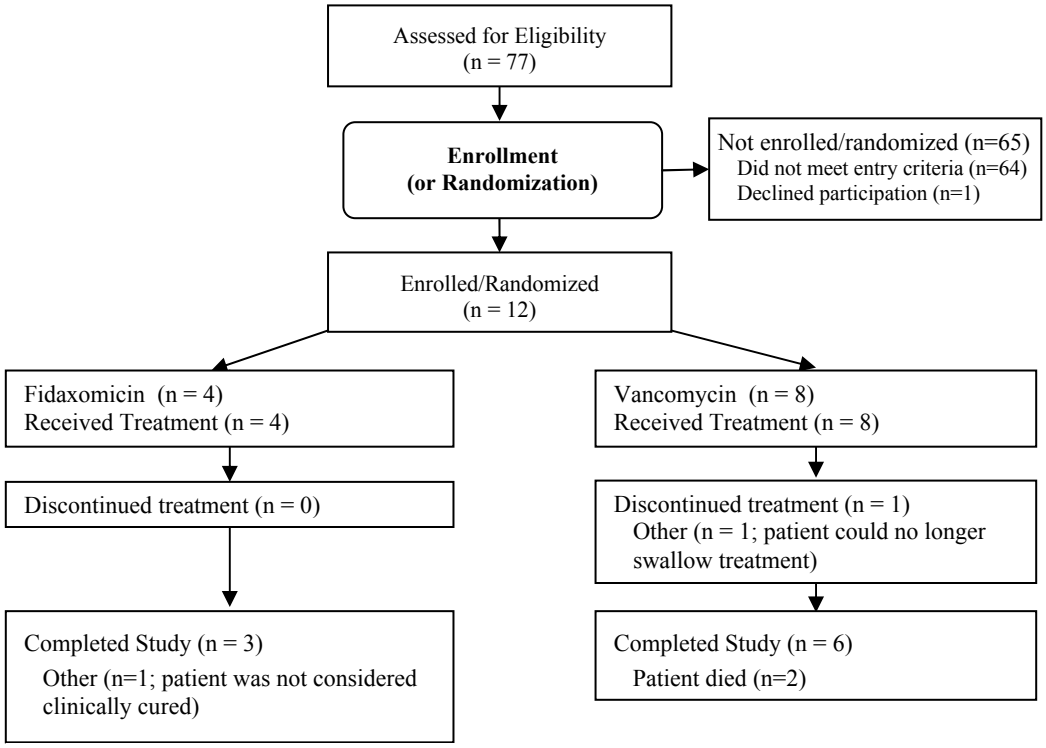
Summary of Results/Conclusions:

Study Population: A total of 12 patients were randomized to the study (Figure 1). All 12 patients received study medication and were included in the ITT population.

Figure 1 Disposition of Patients



Source: Table 12.1.1.1, 12.1.1.2 and Appendix 13.2.1.3.

Eleven (91.7%) patients completed the 10-day treatment period and 9 (75.0%) patients completed all study assessments. One patient (vancomycin arm [redacted]) did not complete the 10-day treatment period as the patient could no longer swallow the study medication; the last dose was received on Day 7. The patient died on Day 9 due to progression of metastatic bladder cancer and thus did not complete the study. A second patient in the vancomycin arm [redacted] died and thus did not complete the study. One patient in the fidaxomicin arm did not complete the study after the EOT (patient was not considered by the investigator to be clinically cured [redacted]).

The mean age of patients randomized in the study was 57.8 years (range 37 to 73 years) (Table 1). All patients were White and 7 (58.3%) patients in the study were male. Hematological malignancy and solid tumor malignancy/solid organ transplant were the reasons for immunosuppression in 7 (58.3%) patients and 5 (41.7%) patients, respectively.

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Table 1 Patient Characteristics

Characteristic	**Fidaxomicin N=4**	**Vancomycin N=8**	**Total N=12**
Sex, n (%)			
Male	2 (50.0)	5 (62.5)	7 (58.3)
Female	2 (50.0)	3 (37.5)	5 (41.7)
Race, n (%)			
White	4 (100)	8 (100)	12 (100)
Age, years			
Mean (standard deviation)	57.8 (9.8)	57.8 (11.2)	57.8 (10.3)
Median	60.0	60.0	60.0
Minimum-Maximum	45-66	37-73	37-73
Reason for immunosuppression, n (%)			
Hematological malignancy	3 (75.0)	4 (50.0)	7 (58.3)
Solid tumor malignancy/solid organ transplant	1 (25.0)	4 (50.0)	5 (41.7)

Patient Base: Intent-to-Treat analysis set.
Source: Table 12.1.2.1.

Overall, 6 (50%) patients had severe CDI at baseline; 3 (75%) patients in the fidaxomicin arm and 3 (37.5%) patients in the vancomycin arm (Table 2). None of the patients had had previous CDI episodes. In total, 75% of patients in each arm had used antibiotics for conditions other than CDI. The number of UBM in the 24 hours prior to baseline ranged from 4 to 10 in the fidaxomicin arm (median: 7.5) and 3 to 16 in the vancomycin arm (median: 6.0). Mean ATLAS score was similar between the treatment arms. All 12 patients were positive for glutamate dehydrogenase in the rapid CDI test and 11 patients were also positive for CDI toxins A/B. The single patient not positive for CDI toxins A/B was considered a protocol violator and is discussed below.

Table 2 Baseline CDI Status

Baseline CDI status	**Fidaxomicin n=4**	**Vancomycin n=8**	**Total N=12**
CDI status, n (%)[a]			
Severe	3 (75.0)	3 (37.5)	6 (50.0)
Non-severe	1 (25.0)	5 (62.5)	6 (50.0)
Prior CDI episodes, n (%)			
Yes	0	0	0
No	4 (100)	8 (100)	12 (100)
Use of antibiotics for conditions other than CDI, n (%)			
Yes	3 (75.0)	6 (75.0)	9 (75.0)
No	1 (25.0)	2 (25.0)	3 (25.0)

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Baseline CDI status	**Fidaxomicin n=4**	**Vancomycin n=8**	**Total N=12**
Number of UBM[b]			
Mean (standard deviation)	7.3 (3.2)	7.6 (4.6)	7.5 (4.1)
Median	7.5	6.0	6.0
Minimum-Maximum	4-10	3-16	3-16
≤3	0	1 (12.5)	1 (8.3)
4-5	2 (50.0)	3 (37.5)	5 (41.7)
6-10	2 (50.0)	2 (25.0)	4 (33.3)
≥11	0	2 (25.0)	2 (16.7)
ATLAS score (based on age, temperature, leukocytes, albumin, and systemic antibiotics)			
n	3	8	11
Missing	1	0	1
Mean (standard deviation)	3.3 (1.2)	3.8 (1.5)	3.6 (1.4)
Median	4.0	3.5	4.0
Minimum-Maximum	2-4	2-6	2-6
Result of the rapid CDI test, n (%)			
Glutamate dehydrogenase			
Positive	4 (100)	8 (100)	12 (100)
Negative	0	0	0
Toxins A/B			
Positive	3 (75.0)	8 (100)	11 (91.7)
Negative	1 (25.0)	0	1 (8.3)

Patient Base: Intent-to-Treat analysis set.
ATLAS: Age, temperature, leukocytes, albumin, and systemic antibiotics; CDI: *Clostridium difficile* infection; TOC: Test of Cure; UBM: unformed bowel movements.
[a] CDI severity classified using European Society of Clinical Microbiology and Infectious Diseases criteria.
[b] Number of UBM over the previous 24 hours prior to baseline.

Source: Table 12.1.2.2.

All but 1 patient had a medical history reported. Ten (83.3%) patients had an infection within the previous 3 months; 1 of which had been gastrointestinal in nature leading to diarrhea (1 patient).

One patient in each arm did not meet an inclusion criterion.

- Patient [redacted] (fidaxomicin arm): CDI was not confirmed by clinical symptoms and a rapid CDI test.
- Patient [redacted] (vancomycin arm): At the time of enrolment, the patient was not receiving immunosuppressive therapy (or undergoing a stem cell transplant procedure) for the treatment of a hematological malignancy, a solid tumor malignancy or following solid organ transplantation. However, a review of the data shows the patient was being treated with an immunosuppressant for graft versus host disease (GVHD; autoimmune disease) at the time of enrolment. Thus, while the patient was initially reported to have violated the protocol, the patient had in fact met all the inclusion and exclusion criteria as GVHD is a severe complication of hematopoietic stem cell transplantation and results in significant immune suppression.

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Efficacy Results: Overall, for 11 patients (4 [100%] patients in the fidaxomicin arm and 7 [87.5%] patients in the vancomycin arm) resolution of diarrhea was observed under treatment, while 2 (50.0%) patients in the fidaxomicin arm and 5 (62.5%) patients in the vancomycin arm achieved clinical cure at TOC (secondary efficacy endpoint) (Table 3). Of the 5 patients who did not achieve clinical cure at TOC, 1 patient in the fidaxomicin arm had resolution of diarrhea but did not remain well until TOC ([redacted] [the patient had SAEs of diarrhea and malnutrition reported]), 1 patient in the vancomycin arm died ([redacted]), and 3 patients (1 patient in the fidaxomicin arm and 2 patients in the vancomycin arm) had resolution of diarrhea but were not considered clinically cured as they did not have a marked reduction (≥ 50%) in the number of UBM at the EOT compared with baseline. None of the 12 patients randomized required CDI therapy between EOT and TOC. None of the 7 patients achieving clinical cure of CDI had a recurrence of CDI after TOC. For the 2 (50.0%) patients in the fidaxomicin arm who achieved clinical cure at TOC, clinical cure was sustained on Day 26 (primary efficacy endpoint) and Day 40 (secondary efficacy endpoint). For the 5 (62.5%) patients in the vancomycin arm who achieved clinical cure at TOC, clinical cure was sustained for 4 (50.0%) patients on Day 26 and Day 40. The remaining patient in the vancomycin arm ([redacted]) achieved clinical cure at TOC but died due to septic shock on Day 25.

Table 3 Efficacy Results

Parameter	**Fidaxomicin n=4**	**Vancomycin n=8**
Clinical cure at TOC, n (%)		
Yes	2 (50.0)	5 (62.5)
No	2 (50.0)	3 (37.5)
Sustained clinical cure 14 days after TOC (Day 26), n (%)		
Yes	2 (50.0)	4 (50.0)
No	2 (50.0)	4 (50.0)
Sustained clinical cure 28 days after TOC (Day 40), n (%)		
Yes	2 (50.0)	4 (50.0)
No	2 (50.0)	4 (50.0)
Time to resolution of diarrhea (statistics), hours		
N	4	7
Mean (standard deviation)	111.8 (109.7)	153.0 (98.7)
Median (minimum, maximum)	119.0 (1-208)	207.0 (6-246)
Time to resolution of diarrhea (number of patients), n (%)	4	7
≤ 24	1 (25.0)	1 (14.3)
25-48	1 (25.0)	0
49-72	0	1 (14.3)
72-96	0	1 (14.3)
≥ 97	2 (50.0)	4 (57.1)
Use of further CDI therapy between EOT and TOC, n (%)		
Yes	0	0
No	4 (100)	8 (100)

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Parameter	**Fidaxomicin n=4**	**Vancomycin n=8**
≤ 3 UBM for 2 consecutive days and sustained to TOC, n(%)[a]		
N	4	7
Yes	4 (100)	7 (100)
No	0	0
Marked reduction in UBM[b]		
N	4	6
Yes	3 (75.0)	4 (66.7)
No	1 (25.0)	2 (33.3)
Recurrence of CDI after TOC, n (%)[c]		
Yes	0	0
No	2 (100)	5 (100)

Patient Base: Intent-to-Treat analysis set.
CDI: *Clostridium difficile* infection; EOT: End of Treatment; TOC: Test of Cure; UBM: unformed bowel movements.
[a] Two patients in each arm had resolution of diarrhea but were not considered clinically cured.
[b] Marked reduction (≤ 50%) in the number of UBM compared with baseline.
[c] Percentage based on the number of patients with clinical cure at TOC.
Source: Table 12.3.1.1 and Table 12.3.1.2.

Safety Results: Four (100%) patients in the fidaxomicin arm had a total of 41 TEAEs and 7 (87.5%) patients in the vancomycin arm had 26 TEAEs (Table 4). The number of TEAEs reported was highest in the gastrointestinal disorders system organ class (SOC) for the fidaxomicin arm and in the infections and infestations SOC for the vancomycin arm. Preferred terms (PTs) reported for more than 1 patient in the fidaxomicin arm were: anal infection, blood uric acid increased, diarrhea, hypokalemia, neutropenia, and tachycardia (2 [50.0%] patients each). The only PT reported for more than 1 patient in the vancomycin arm was pyrexia (2 [25.0%] patients).

The majority of TEAEs in both treatment arms were mild and moderate in intensity. Eight severe TEAEs were reported in 3 patients in the fidaxomicin arm: acute renal failure and neutropenia (1 patient [redacted]), diarrhea, febrile neutropenia, pyrexia, and thrombocytopenia (1 patient [redacted]), and abdominal pain upper and nausea (1 patient [redacted]). Three severe TEAEs were reported in 2 patients in the vancomycin arm: metastatic carcinoma of the bladder (1 patient [redacted]) and bacterial infection and septic shock (1 patient [redacted]). Most of the patients in both treatment arms received treatment for the severe TEAE. The severe TEAE (SAE) of neutropenia in the fidaxomicin arm (Patient [redacted]) was the only TEAE considered by the reporting investigator to be possibly related to study medication.

The majority of TEAEs in both treatment arms resolved or were resolving at the time of the last visit. Exceptions in the fidaxomicin arm were depression (1 patient [redacted]), hypokalemia (1 patient [redacted]) and thrombocytopenia (1 patient [redacted]) and in the vancomycin arm were metastatic carcinoma of the bladder (1 patient; fatal [redacted]), abdominal pain upper, blood folate decreased, hypovitaminosis, and blood uric acid

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increased (all 4 terms in 1 patient [redacted]), pyrexia (1 patient [redacted]), and bacterial infection and septic shock (1 patient [redacted]; the event of septic shock was fatal).

Table 4 Summary of TEAEs in Either Treatment Arm

MedDRA (v. 14.1) **System Organ Class** **Preferred Term**	**Number (%)of Patients [Events]** **Fidaxomicin n=4**	 **Vancomycin n=8**
All Systems, Any TEAE	**4 (100) [41]**	**7 (87.5) [26]**
Gastrointestinal Disorders	**3 (75.0) [8]**	**1 (12.5) [1]**
Diarrhea	2 (50.0) [2]	0
Abdominal pain upper	1 (25.0) [1]	1 (12.5) [1]
Flatulence	1 (25.0) [1]	0
Hematochezia	1 (25.0) [1]	0
Mouth hemorrhage	1 (25.0) [1]	0
Palatal disorder	1 (25.0) [1]	0
Vomiting	1 (25.0) [1]	0
Investigations	**3 (75.0) [7]**	**1 (12.5) [2]**
Blood uric acid increased	2 (50.0) [3]	1 (12.5) [1]
Blood bilirubin increased	1 (25.0) [2]	0
Blood potassium decreased	1 (25.0) [1]	0
Hemoglobin decreased	1 (25.0) [1]	0
Blood folate decreased	0	1 (12.5) [1]
Blood and lymphatic system disorders	**3 (75.0) [4]**	**1 (12.5) [1]**
Neutropenia	2 (50.0) [2]	1 (12.5) [1]
Febrile neutropenia	1 (25.0) [1]	0
Thrombocytopenia	1 (25.0) [1]	0
Metabolism and nutrition disorders	**3 (75.0) [3]**	**2 (25.0) [2]**
Hypokalemia	2 (50.0) [2]	1 (12.5) [1]
Malnutrition	1 (25.0) [1]	0
Hypovitaminosis	0	1 (12.5) [1]
Infections and infestations	**2 (50.0) [6]**	**4 (50.0) [8]**
Anal infection	2 (50.0) [2]	0
Cystitis	1 (25.0) [1]	0
Device-related infection	1 (25.0) [1]	1 (12.5) [1]
Fungal infection	1 (25.0) [1]	0
Sepsis	1 (25.0) [1]	0
Bacteremia	0	1 (12.5) [1]
Bacterial infection	0	1 (12.5) [1]
Cytomegalovirus infection	0	1 (12.5) [1]
Enterococcal bacteremia	0	1 (12.5) [1]
Epstein-Barr virus infection	0	1 (12.5) [1]
Respiratory tract infection bacterial	0	1 (12.5) [1]
Septic shock	0	1 (12.5) [1]

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MedDRA (v. 14.1) **System Organ Class** **Preferred Term**	**Number (%)of Patients [Events]** **Fidaxomicin n=4**	**Vancomycin n=8**
General disorders and administration site conditions	**2 (50.0) [5]**	**3 (37.5) [4]**
Catheter site pruritus	1 (25.0) [1]	0
Fatigue	1 (25.0) [1]	1 (12.5) [1]
Mucosal inflammation	1 (25.0) [1]	0
Edema	1 (25.0) [1]	0
Pyrexia	1 (25.0) [1]	2 (25.0) [2]
Edema peripheral	0	1 (12.5) [1]
Respiratory, thoracic, and mediastinal disorders	**2 (50.0) [2]**	**1 (12.5) [1]**
Cough	1 (25.0) [1]	0
Dyspnea	1 (25.0) [1]	0
Dyspnea exertional	0	1 (12.5) [1]
Cardiac disorders	**2 (50.0) [2]**	**0**
Tachycardia	2 (50.0) [2]	0
Ear and labyrinth disorders	**1 (25.0) [1]**	**1 (12.5) [1]**
Vertigo	1 (25.0) [1]	1 (12.5) [1]
Nervous system disorders	**1 (25.0) [1]**	**1 (12.5) [1]**
Dizziness	1 (25.0) [1]	0
Headache	0	1 (12.5) [1]
Psychiatric disorders	**1 (25.0) [1]**	**1 (12.5) [2]**
Depression	1 (25.0) [1]	0
Anxiety	0	1 (12.5) [1]
Insomnia	0	1 (12.5) [1]
Renal and urinary disorders	**1 (25.0) [1]**	**0**
Renal failure acute	1 (25.0) [1]	0
Musculoskeletal and connective tissue disorders	**0**	**1 (12.5) [1]**
Bone pain	0	1 (12.5) [1]
Neoplasms benign, malignant and unspecified (including cysts and polyps)	**0**	**1 (12.5) [1]**
Metastatic carcinoma of the bladder	0	1 (12.5) [1]
Skin and subcutaneous tissue disorders	**0**	**1 (12.5) [1]**
Night sweats	0	1 (12.5) [1]

Patient Base: Intent-to-Treat analysis set.
MedDRA: Medical Dictionary for Regulatory Activities; TEAE: Treatment-emergent AEs.
Source: Table 12.6.1.2.

Two (50.0%) patients in the fidaxomicin arm had a total of 4 SAEs and 2 (25.0%) patients in the vancomycin arm had a total of 3 SAEs (Table 5). No SAE PT was reported for ≥1 patient in either treatment arm. In the fidaxomicin arm diarrhea and malnutrition were reported in 1 patient ([redacted]), and neutropenia and renal failure acute were reported in 1 patient ([redacted]). In the vancomycin arm bacterial infection and septic shock were reported in the 1 patient ([redacted]). Two of the 3 SAEs in the vancomycin arm resulted in death; one due to progression of metastatic bladder cancer ([redacted]) and the other due to septic shock ([redacted]). Neither was considered by the reporting investigator to be related to study medication.

Name of Sponsor/Company: Astellas Pharma Europe Ltd		
Name of Finished Product: Fidaxomicin		
Name of Active Ingredient: Fidaxomicin		

In addition, Patient [redacted] (fidaxomicin arm) had SAEs of sepsis and acute myocardial infarction, which had a fatal outcome (events not reported in Table 5). These events occurred 51 days after the last dose of study medication but within 30 days of the last study visit; neither event was considered by the reporting investigator to be related to study medication (Safety line listings).

No TEAEs led to discontinuation from study medication or the study.

Table 5 Summary of Serious TEAEs in Either Treatment Arm

MedDRA (v. 14.1) System Organ Class Preferred Term	**Number (%)of Patients [Events]**	
	Fidaxomicin n=4	**Vancomycin n=8**
All Systems, Any TEAE	**2 (50.0) [4]**	**2 (25.0) [3]**
Blood and lymphatic disorders	**1 (25.0) [1]**	**0**
Neutropenia	1 (25.0) [1]	0
Gastrointestinal disorders	**1 (25.0) [1]**	**0**
Diarrhea	1 (25.0) [1]	0
Metabolism and nutrition disorders	**1 (25.0) [1]**	**0**
Malnutrition	1 (25.0) [1]	0
Renal and urinary disorders	**1 (25.0) [1]**	**0**
Renal failure acute	1 (25.0) [1]	0
Infections and infestations	**0**	**1 (12.5) [2]**
Bacterial infection	0	1 (12.5) [1]
Septic shock	0	1 (12.5) [1]
Neoplasms benign, malignant and unspecified (including cysts and polyps)	**0**	**1 (12.5) [1]**
Metastatic carcinoma of the bladder	0	1 (12.5) [1]

Patient Base: Intent-to-Treat analysis set.
MedDRA: Medical Dictionary for Regulatory Activities; TEAE: Treatment-emergent AEs.
Source: Table 12.6.1.3.

Results for [redacted] and Quality of Life data: Due to the low number of patients randomized to this study, no summary tables were produced for [redacted] and quality of life data. Data are listed.

CONCLUSIONS:

The study was terminated early due to slow recruitment. The low number of patients randomized to this study does not allow a formal statistical analysis to be performed on the data collected. The objectives were not met and no conclusions on efficacy could be drawn from the study. No new safety concerns were identified.

Date of Report: 16 December 2013