EU Clinical Trials Register

Clinical trial results:

A randomised, controlled, open-label phase III clinical trial in patients with recurrent Clostridioides difficile (CD) infection, to evaluate the efficacy and safety of capsules of lyophilised faecal microbiota vs fidaxomicin

Summary

EudraCT number	2020-004591-17
Trial protocol	ES
Global end of trial date	15 November 2023

Results information

Result version number	v1 (current)
This version publication date	12 February 2025
First version publication date	12 February 2025

Trial information

Trial identification

Sponsor protocol code	ICD-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05201079
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mikrobiomik Healthcare Company S.L.
Sponsor organisation address	Astondo Bidea, building 612, Derio, Spain, 48160
Public contact	Clinical trials, Mikrobiomik Healthcare Company S.L., ensayosclinicos@mikrobiomik.net
Scientific contact	Clinical trials, Mikrobiomik Healthcare Company S.L., ensayosclinicos@mikrobiomik.net

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 November 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of the study is to evaluate the efficacy of the investigational medicinal product (MBK-01) compared to the control medication (fidaxomicin), 8 weeks after the treatment completion.

Protection of trial subjects:

Regarding the lack of efficacy, patients with a new recurrence of Clostridioides difficile infection were withdrawn from the study and treated with rescue medication (vancomycin or fidaxomicin).

All patients who dropped out of the study and/or were discontinued before the end of the planned follow-up had an end-of-study visit ≥ 30 days after initiation of treatment, in which at least the relevant information for safety assessment (adverse events and concomitant treatments) was collected.

Background therapy:

Therapeutic support measures were allowed as deemed most appropriate (e.g., hydration-control of the patient's electrolytes and antipyretics in case of fever (>38°C) and as deemed appropriate by the treating medical team).

Evidence for comparator:

Fidaxomicin is the treatment of choice for primary episodes of Clostridioides difficile infection (CDI), first recurrences, high risk of recurrence and multiple recurrences of CDI by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). The Infectious Diseases Society of America (IDSA) recommends both vancomycin and fidaxomicin as the initial treatment for CDI, and fidaxomicin as the treatment of choice for patients with CDI with a high risk of recurrences. European and Spanish expert groups recommend fidaxomicin for critically ill patients, for immunosuppressed patients, and for patients with chronic kidney failure, undergoing transplantation or cancer.

Actual start date of recruitment	29 October 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 92
Worldwide total number of subjects	92
EEA total number of subjects	92

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	42
From 65 to 84 years	39
85 years and over	11

Subject disposition

Recruitment

Recruitment details:

The inclusion of the first patient was on 29 October 2021. The inclusion of the last patient was on 6 October 2023 (end of recruitment). All patients were recruited in sites in Spain.

Pre-assignment

Screening details:

Screening period: within 24h after informed consent, patients were evaluated for study eligibility. Participants were tested to determine if they met all the inclusion criteria and none of the exclusion criteria.

93 patients were screened in the study. 1 of them was a screening failure and only 92 were finally included in the study.

Pre-assignment period milestones

Number of subjects started	93[1]
Number of subjects completed	92

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screening failure: 1

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same. Justification: 93 patients were intially included in the study. 1 of these patients was a selection failure and there is no available data for this patient. Therefore, 92 patients completed the screening period and were randomised to any of the two treatment groups.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

There are no bliding techniques in this study, as it is an open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	MBK-01

Arm description:

Patients randomized to MBK-01 received a single dose of 4 oral capsules of MBK-01.

Arm type	Experimental
Investigational medicinal product name	MBK-01
Investigational medicinal product code	
Other name	Heterologous gut microbiota from healthy donors
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received 4 capsules of MBK-01 in a single dose (≥2.1-2.5 x 10^11 microorganisms) after being randomized. If patients had been treated with antibiotic they had to undergo a 24 hours washout period before randomization.

Arm title	Fidaxomicin

Arm description:

Patients randomized to fidaxomicin received treatment with oral fidaxomicin 200mg/12h for 10 days

Arm type	Active comparator
Investigational medicinal product name	Fidaxomicin
Investigational medicinal product code	
Other name	Dificlir
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received an oral dose of 200 mg (one tablet) of fidaxomicin twice a day (every 12 hours) for 10 days since randomization. If patients had been treated with antibiotic they had to undergo a 24 hours washout period before randomization.

Number of subjects in period 1	MBK-01	Fidaxomicin
Started	45	47
Completed	23	25
Not completed	22	22
Physician decision	1	1
Consent withdrawn by subject	1	-
Transfer to other hospital	-	1
Death	1	1
Clinical conditions	1	-
Forbidden medication	9	5
Adverse event	7	11
Serious adverse event and sepsis	1	-
Lost to follow-up	-	1
Ineffective treatment	-	2
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	MBK-01
Reporting group description:	
Patients randomized to MBK-01 received a single dose of 4 oral capsules of MBK-01.	
Reporting group title	Fidaxomicin
Reporting group description:	
Patients randomized to fidaxomicin received treatment with oral fidaxomicin 200mg/12h for 10 days	

Reporting group values	MBK-01	Fidaxomicin	Total
Number of subjects	45	47	92
Age categorical			
Age was calculated as the difference in years between the date of signing the informed consent form and the date of birth.			
Units: Subjects			
Adults (18-64 years)	18	24	42
From 65-84 years	21	18	39
85 years and over	6	5	11
Age continuous			
Age was calculated as the difference in years between the date of signing the informed consent form and the date of birth.			
Units: years			
arithmetic mean	65.22	65.26	
standard deviation	± 17.24	± 14.65	-
Gender categorical			
Units: Subjects			
Female	30	30	60
Male	15	17	32
Type of Clostridioides difficile infection episode			
A primary episode would be the first episode of Clostridiodes difficile (CD) infection confirmed by laboratory tests. A patient with a recurrent episode would be one with previous episodes.			
Units: Subjects			
Primary	25	28	53
Recurrent	20	19	39
Previous antibiotic			
The number of patients that received antibiotic treatment previous to receiving MBK-01/fidaxomicin.			
Units: Subjects			
Yes	23	29	52
No	22	18	40

End points

End points reporting groups

Reporting group title	MBK-01
Reporting group description:	
Patients randomized to MBK-01 received a single dose of 4 oral capsules of MBK-01.	
Reporting group title	Fidaxomicin
Reporting group description:	
Patients randomized to fidaxomicin received treatment with oral fidaxomicin 200mg/12h for 10 days	
Subject analysis set title	Patients with a primary episode of CDI assigned to MBK-01
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in MBK-01 group that presented a primary episode of CDI	
Subject analysis set title	Patients with a primary episode of CDI assigned to fidaxomicin
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in fidaxomicin group that presented a primary episode of CDI	
Subject analysis set title	Patients with a recurrence of CDI assigned to MBK-01
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in MBK-01 group that presented a recurrent episode of CDI	
Subject analysis set title	Patients with a recurrence of CDI assigned to fidaxomicin
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in fidaxomicin group that presented a recurrent episode of CDI	
Subject analysis set title	Patients with no previous antibiotic assigned to MBK-01
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in MBK-01 group that did not receive antibiotic pre-treatment before the treatment with MBK-01	
Subject analysis set title	Patients with no previous antibiotic assigned to fidaxomicin
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Patients in MBK-01 group that did not receive antibiotic pre-treatment before the treatment with fidaxomicin	
Subject analysis set title	Baseline visit, MBK-01 group
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients from the MBK-01 group in whom the quality of life measured by the SF-36 questionnaire was reported and analysed at the baseline visit (V1).	
Subject analysis set title	Baseline visit, fidaxomicin group
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients from the fidaxomicin group in whom the quality of life measured by the SF-36 questionnaire was reported and analysed at the baseline visit (V1).	
Subject analysis set title	Visit 4, MBK-01 group
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Patients from the MBK-01 group in whom the quality of life measured by the SF-36 questionnaire was reported and analysed at visit 4 (V4, 8 weeks).	
Subject analysis set title	Visit 4, fidaxomicin group
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients from the fidaxomicin group in whom the quality of life measured by the SF-36 questionnaire was reported and analysed at visit 4 (V4, 8 weeks).

Subject analysis set title	Visit 6, MBK-01 group
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients from the MBK-01 group in whom the quality of life measured by the SF-36 questionnaire was reported and analysed at visit 6 (V6, 6 months).

Subject analysis set title	Visit 6, fidaxomicin group
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Patients from the fidaxomicin group in whom the quality of life measured by the SF-36 questionnaire was reported and analysed at visit 6 (V6, 6 months).

Primary: Absence of diarrhoea from Clostridioides difficile

End point title	Absence of diarrhoea from Clostridioides difficile

End point description:

Absence of recurrence (a new episode of Clostridioides difficile infection within 8 weeks after the onset of the previous episode).

End point type	Primary

End point timeframe:

8 weeks after the onset of the previous episode of Clostridiodes difficile infection (8 weeks after the start of the treatment with MBK-01/fidaxomicin).

End point values	MBK-01	Fidaxomicin	Patients with a primary episode of CDI assigned to MBK-01	Patients with a primary episode of CDI assigned to fidaxomicin
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	37	40	21	27
Units: patients				
Recurrence	4	9	1	1
No recurrence	33	31	20	26

End point values	Patients with a recurrence of CDI assigned to MBK-01	Patients with a recurrence of CDI assigned to fidaxomicin	Patients with no previous antibiotic assigned to MBK-01	Patients with no previous antibiotic assigned to fidaxomicin
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	13	17	15
Units: patients				
Recurrence	3	8	0	3
No recurrence	13	5	17	12

Statistical analyses

Statistical analysis title	Non-inferiority analysis of recurrence probability

Statistical analysis description:

The compared efficacy of the two treatments was assessed as a difference of proportions between MBK-01 (P1) and fidaxomicin group (P2). The proportions indicate the probability of no recurrence among the total patients in each group.

There are 77 evaluable for recurrence (37 in MBK-01 group and 40 in Fidaxomicin group). Reasons for non-evaluable are: death, forbidden medication, investigator decision, adverse event, informed consent withdrawal and transfer to another hospital.

Comparison groups	Fidaxomicin v MBK-01
Number of subjects included in analysis	77
Analysis specification	Post-hoc
Analysis type	non-inferiority[1]
P-value	= 0.013 [2]
Method	Miettinen-Nurminen
Parameter estimate	Difference of proportions
Point estimate	2.228
Confidence interval	
level	Other: 97.06 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[1] - Non inferiority margin: -0.10.
Null hypothesis: P1-P2 ≤-0.10
Alternative hypothesis: P1-P2 > -0.10
α=0.0221
[2] - Confidence interval for the point estimate was not calculated. It is inputed as 0 and 100.

Statistical analysis title	Superiority analysis of recurrence probability

Statistical analysis description:

The compared efficacy of the two treatments was assessed as an Odds Ratio of the probability of no recurrence in each group, using the MBK-01 group as a reference.

There are 77 evaluable for recurrence (37 in MBK-01 group and 40 in Fidaxomicin group). Reasons for non-evlauable are: death, forbidden medication, investigator decision, adverse event, informed consent withdrawal and transfer to another hospital.

Comparison groups	MBK-01 v Fidaxomicin
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.228
Method	Wald method
Parameter estimate	Odds ratio (OR)
Point estimate	2.395
Confidence interval	
level	Other: 97.79 %
sides	2-sided
lower limit	0.54
upper limit	10.624

Notes:

[3] - α=0.0221

Statistical analysis title	Non-inferiority analysis of primary CDI subgroup

Statistical analysis description:

The compared efficacy of the two treatments was assessed as a difference of proportions between MBK-01 (P1) and fidaxomicin group (P2). The proportions indicate the probability of no recurrence among the total patients in each group.

There are 48 evaluable for recurrence (21 in MBK-01 group and 27 in Fidaxomicin group). Reasons for non-evaluable are: adverse event, forbidden medication and death.

Comparison groups	Patients with a primary episode of CDI assigned to MBK-01 v Patients with a primary episode of CDI assigned to fidaxomicin
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority[4]
P-value	= 0.013 [5]
Method	Miettinen-Nurminen
Parameter estimate	Difference of proportions
Point estimate	2.228
Confidence interval	
level	Other: 97.06 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[4] - Non inferiority margin: -0.10.
Null hypothesis: P1-P2 ≤-0.10
Alternative hypothesis: P1-P2 > -0.10
α=0.0294
[5] - Confidence interval for the point estimate was not calculated. It is inputed as 0 and 100.

Statistical analysis title	Superiority analysis of primary CDI subgroup

Statistical analysis description:

The compared efficacy of the two treatments was assessed as an Odds Ratio of the probability of no recurrence in each group, using the MBK-01 group as a reference.

There are 48 evaluable for recurrence (21 in MBK-01 group and 27 in Fidaxomicin group). Reasons for non-evaluable are: adverse event, forbidden medication and death.

Comparison groups	Patients with a primary episode of CDI assigned to MBK-01 v Patients with a primary episode of CDI assigned to fidaxomicin
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 1
Method	Wald method
Parameter estimate	Odds ratio (OR)
Point estimate	0.769
Confidence interval	
level	Other: 97.79 %
sides	2-sided
lower limit	0.019
upper limit	31.82

Notes:

[6] - α=0.0294

Statistical analysis title	Non-inferiority analysis of recurrent CDI subgroup

Statistical analysis description:

The compared efficacy of the two treatments was assessed as a difference of proportions between MBK01 (P1) and fidaxomicin group (P2). The proportions indicate the probability of no recurrence among the total patients in each group.

There are 29 evaluable for recurrence (16 in MBK-01 group and 13 in Fidaxomicin group). Reasons for non-evaluable are: investigator decision, forbidden medication, transfer to another hospital, death and adverse event.

Comparison groups	Patients with a recurrence of CDI assigned to MBK-01 v Patients with a recurrence of CDI assigned to fidaxomicin
Number of subjects included in analysis	29
Analysis specification	Post-hoc
Analysis type	non-inferiority[7]
P-value	= 0.003 [8]
Method	Miettinen-Nurminen
Parameter estimate	Difference of proportions
Point estimate	2.744
Confidence interval	
level	Other: 97.06 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[7] - Non inferiority margin: -0.10.
Null hypothesis: P1-P2 ≤-0.10
Alternative hypothesis: P1-P2 > -0.10
α=0.0294
[8] - Confidence interval for the point estimate was not calculated. It is inputed as 0 and 100.

Statistical analysis title	Superiority analysis of recurrent CDI subgroup

Statistical analysis description:

The compared efficacy of the two treatments was assessed as an Odds Ratio of the probability of no recurrence in each group, using the MBK-01 group as a reference.

There are 29 evaluable for recurrence (16 in MBK-01 group and 13 in Fidaxomicin group). Reasons for non-evaluable are: investigator decision, forbidden medication, transfer to another hospital, death and adverse event.

Comparison groups	Patients with a recurrence of CDI assigned to fidaxomicin v Patients with a recurrence of CDI assigned to MBK-01
Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.027
Method	Wald method
Parameter estimate	Odds ratio (OR)
Point estimate	6.933
Confidence interval	
level	Other: 97.79 %
sides	2-sided
lower limit	0.762
upper limit	63.12

Notes:

[9] - α=0.0294

Statistical analysis title	Non-inferiority analysis of no pretreated subgroup

Statistical analysis description:

The compared efficacy of the two treatments was assessed as a difference of proportions between MBK-01 (P1) and fidaxomicin group (P2). The proportions indicate the probability of no recurrence among the total patients in each group.

There are 32 evaluable for recurrence (17 in MBK-01 group and 15 in Fidaxomicin group). Reasons for non-evaluable are: forbidden medication, adverse event, transfer to another hospital and investigator decision.

Comparison groups	Patients with no previous antibiotic assigned to MBK-01 v Patients with no previous antibiotic assigned to fidaxomicin
Number of subjects included in analysis	32
Analysis specification	Post-hoc
Analysis type	non-inferiority[10]
P-value	= 0.008 [11]
Method	Miettinen-Nurminen
Parameter estimate	Difference of proportion
Point estimate	2.396
Confidence interval	
level	Other: 97.06 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[10] - Non inferiority margin: -0.10.
Null hypothesis: P1-P2 ≤-0.10
Alternative hypothesis: P1-P2 > -0.10
α=0.0294
[11] - Confidence interval for the point estimate was not calculated. It is inputed as 0 and 100.

Secondary: Favourable/unfavourable outcome

End point title	Favourable/unfavourable outcome

End point description:

An unfavourable outcome is defined as the detection within 48-72 hours from the start of treatment of a worsening of the episode of diarrhoea (defined as at least one stool more than at baseline, with baseline being considered as the time of initiation of study treatment) and, additionally, at least one of the following criteria:
1. Increase of the C-reactive protein (CRP) value (>5% of the value at baseline).
2. Increase of the absolute value of leukocytes (>5% of the value at baseline).
3. Progression to sepsis: hypotension or organ failure with no other apparent cause.

End point type	Secondary

End point timeframe:

48-72 hours from the start of study treatment.

End point values	MBK-01	Fidaxomicin	Patients with a primary episode of CDI assigned to MBK-01	Patients with a primary episode of CDI assigned to fidaxomicin
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	43	45	25	27
Units: patients				
Favourable	43	44	25	26
Unfavourable	0	1	0	1

End point values	Patients with a recurrence of CDI assigned to MBK-01	Patients with a recurrence of CDI assigned to fidaxomicin	Patients with no previous antibiotic assigned to MBK-01	Patients with no previous antibiotic assigned to fidaxomicin
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19	18	20	17
Units: patients				
Favourable	19	18	20	16
Unfavourable	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Time to recurrence

End point title	Time to recurrence

End point description:

The baseline visit is taken as the start date. The end date will depend on whether the patient has had a recurrence at visit 4 (8 weeks after the start of study treatment):
- If the patient has had a recurrence, the end date is the date on which the recurrence occurred.
- If the patient has not had a recurrence, the end date is either the end of study date or the last available date.
- If the patient has not had a recurrence and is ongoing, the last available date is imputed as the end date.

End point type	Secondary

End point timeframe:

Up to 6 months after the start of study treatment.

End point values	MBK-01	Fidaxomicin	Patients with a primary episode of CDI assigned to MBK-01	Patients with a primary episode of CDI assigned to fidaxomicin
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	37	40	21	27
Units: weeks				
arithmetic mean (standard deviation)	24.70 (± 1.34)	22.40 (± 1.53)	26.30 (± 1.268)	26.70 (± 0.872)

End point values	Patients with a recurrence of CDI assigned to MBK-01	Patients with a recurrence of CDI assigned to fidaxomicin	Patients with no previous antibiotic assigned to MBK-01	Patients with no previous antibiotic assigned to fidaxomicin

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16	13	17	15
Units: weeks				
arithmetic mean (standard deviation)	22.40 (± 2.240)	13.10 (± 3.01)	0 (± 0)	22.40 (± 2.31)

Statistical analyses

Statistical analysis title	Time to recurrence analysis
Comparison groups	Fidaxomicin v MBK-01
Number of subjects included in analysis	77
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3 [12]
Method	Regression, Cox
Parameter estimate	Likelihood Ratio Test
Point estimate	1.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[12] - The Likelihood Ratio Test does not provide a confidence interval. It is inputed as 0 and 100.

Statistical analysis title	Time to recurrence of primary CDI subgroup
Comparison groups	Patients with a primary episode of CDI assigned to MBK-01 v Patients with a primary episode of CDI assigned to fidaxomicin
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8 [13]
Method	Regression, Cox
Parameter estimate	Likelihood Ratio Test
Point estimate	0.07
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[13] - The Likelihood Ratio Test does not provide a confidence interval. It is inputed as 0 and 100.

Statistical analysis title	Time to recurrence of recurrent CDI subgroup
Comparison groups	Patients with a recurrence of CDI assigned to MBK-01 v Patients with a recurrence of CDI assigned to fidaxomicin

Number of subjects included in analysis	29
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02 [14]
Method	Regression, Cox
Parameter estimate	Likelihood Ratio Test
Point estimate	5.35
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[14] - The Likelihood Ratio Test does not provide a confidence interval. It is inputed as 0 and 100.

Statistical analysis title	Time to recurrence of no pretreated subgroup

Statistical analysis description:

Arithmetic mean and standard deviation of time to recurrence in MBK-01 group are inputed as 0 because there were no recurrences in this group.

Comparison groups	Patients with no previous antibiotic assigned to MBK-01 v Patients with no previous antibiotic assigned to fidaxomicin
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04 [15]
Method	Regression, Cox
Parameter estimate	Likelihood Ratio Test
Point estimate	4.09
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[15] - The Likelihood Ratio Test does not provide a confidence interval. It is inputed as 0 and 100.

Secondary: Overall survival: patients	
End point title	Overall survival: patients

End point description:

Deaths indicated as number of events.

End point type	Secondary

End point timeframe:

Up to 6 months after the start of the treatment.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: patients				
Events	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival: time

End point title	Overall survival: time
End point description:	
End point type	Secondary
End point timeframe:	
Up to 6 months after the start of the treatment	

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: weeks				
arithmetic mean (standard error)	26.80 (± 0.712)	27 (± 0.581)		

Statistical analyses

Statistical analysis title	Overall survival analysis
Comparison groups	MBK-01 v Fidaxomicin
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9 [16]
Method	Regression, Cox
Parameter estimate	Likelihood Ratio Test
Point estimate	0.02
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[16] - The Likelihood Ratio Test does not provide a confidence interval. It is inputed as 0 and 100.

Secondary: Quality of life

End point title	Quality of life

End point description:

Quality of life is measured by the Short Form-36 Health Survey (SF-36), which consists of 36 questions (items) that assess both positive and negative states of quality of life. These 36 items cover the following areas: physical function, physical role, bodily pain, general health, vitality, social role, emotional role and mental health. For each area, the scale ranges from 0 (the worst health status for that dimension) to 100 (the best health status).

End point type	Secondary

End point timeframe:

Up to 6 months after the start of study treatment. It was assesed at baseline visit (V1), visit 4 (V4, 8 weeks) and visit 6 (V6, 6 months).

End point values	Baseline visit, MBK-01 group	Baseline visit, fidaxomicin group	Visit 4, MBK-01 group	Visit 4, fidaxomicin group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	42	46	30	31
Units: punctuation				
arithmetic mean (standard deviation)				
Physical function	56.9 (± 35.9)	57.07 (± 33.71)	68.5 (± 30.6)	62.58 (± 30.44)
Bodily pain	52.91 (± 29.84)	57.25 (± 29.07)	35.19 (± 29.19)	40.5 (± 28.33)
General health	55.13 (± 17.07)	54.85 (± 20.62)	47.18 (± 18.04)	49.13 (± 17.5)
Vitality	38.1 (± 11.52)	35.69 (± 18.56)	36.39 (± 17.02)	40.86 (± 11.85)
Social role	65.08 (± 15.53)	63.77 (± 19.02)	63.33 (± 14.78)	63.44 (± 11.72)
Emotional role	59.13 (± 39.04)	68.3 (± 32.18)	82.78 (± 25.7)	70.43 (± 28.04)
Mental health	55.27 (± 16.92)	56.06 (± 17.17)	60 (± 16.42)	57.83 (± 13.84)
Physical role	33.48 (± 33.44)	36.55 (± 32.81)	69.17 (± 35.84)	57.46 (± 30.64)

End point values	Visit 6, MBK-01 group	Visit 6, fidaxomicin group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	11		
Units: punctuation				
arithmetic mean (standard deviation)				
Physical function	77.5 (± 27.01)	77.73 (± 27.14)		
Bodily pain	35.19 (± 33.78)	27.27 (± 28.27)		

General health	41.03 (± 15.5)	38.46 (± 16.14)	
Vitality	35.42 (± 7.22)	36.36 (± 8.56)	
Social role	59.72 (± 11.14)	69.7 (± 10.05)	
Emotional role	86.11 (± 22.29)	84.09 (± 20.57)	
Mental health	63.69 (± 11.97)	62.34 (± 12.81)	
Physical role	72.92 (± 29.95)	74.43 (± 34.51)	

Statistical analyses

Statistical analysis title	Analysis of the group and physical function

Statistical analysis description:

The relationship between the treatment group and the changes in physical function was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.749
Method	ANOVA

Notes:

[17] - $α=0.0221$. F (contrast statistic) = 0.104. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the time and physical function

Statistical analysis description:

The relationship between the passing of time and the changes in physical function was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.62
Method	ANOVA

Notes:

[18] - $α=0.0221$. F (contrast statistic) = 0.249. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of group-time and physical function

Statistical analysis description:

The relationship between the interaction treatment group-passing of time and the changes in physical function was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	= 0.16
Method	ANOVA

Notes:

[19] - α=0.0221. F (contrast statistic) = 2.024. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the group and bodily pain

Statistical analysis description:

Therelationship between the treatment group and the changes in bodily pain was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	= 0.614
Method	ANOVA

Notes:

[20] - α=0.0221. F (contrast statistic) = 0.257. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the time and bodily pain

Statistical analysis description:

The relationship between the passing of time and the changes in bodily pain was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	= 0.007 [22]
Method	ANOVA

Notes:

[21] - α=0.0221. F (contrast statistic) = 7.705. Degrees of freedom: 1, 56

[22] - Effect size = 0.046

Statistical analysis title	Analysis of group-time and bodily pain

Statistical analysis description:

The relationship between the interaction treatment group-passing of time and the changes in bodily pain was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group

	v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.718
Method	ANOVA

Notes:

[23] - α=0.0221. F (contrast statistic) = 0.132. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the group and general health

Statistical analysis description:

The relationship between the treatment group and the changes in general health was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	= 0.494
Method	ANOVA

Notes:

[24] - α=0.0221. F (contrast statistic) = 0.474. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the time and general health

Statistical analysis description:

The relationship between the passing of time and the changes in general health was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	= 0.339
Method	ANOVA

Notes:

[25] - α=0.0221. F (contrast statistic) = 0.932. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of group-time and general health

Statistical analysis description:

The relationship between the interaction treatment group-passing of time and the changes in general health was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	= 0.38
Method	ANOVA

Notes:

[26] - α=0.0221. F (contrast statistic) = 0.783. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the group and vitality

Statistical analysis description:

The relationship between the treatment group and the changes in vitality was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.79
Method	ANOVA

Notes:

[27] - α=0.0221. F (contrast statistic) = 0.072. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the time and vitality

Statistical analysis description:

The relationship between the passing of time and the changes in vitality was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[28]
P-value	= 0.498
Method	ANOVA

Notes:

[28] - α=0.0221. F (contrast statistic) = 0.465. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of group-time and vitality

Statistical analysis description:

The effect of the interaction between the treatment group and the passing of time in the changes in vitality was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.023
Method	ANOVA

Notes:

[29] - α=0.0221. F (contrast statistic) = 5.490. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the group and social role

Statistical analysis description:

The relationship between the treatment group and the changes in social role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[30]
P-value	= 0.553
Method	ANOVA

Notes:

[30] - α=0.0221. F (contrast statistic) = 0.356. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the time and social role

Statistical analysis description:

The relationship between the passing of time and the changes in social role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.718
Method	ANOVA

Notes:

[31] - α=0.0221. F (contrast statistic) = 0.132. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of group-time and social role

Statistical analysis description:

The relationship between the interaction treatment group-passing of time and the changes in social role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.574
Method	ANOVA

Notes:

[32] - α=0.0221. F (contrast statistic) = 0.319. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the group and emotional role

Statistical analysis description:

The relationship between the treatment group and the changes in emotional role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	= 0.49
Method	ANOVA

Notes:

[33] - α=0.0221. F (contrast statistic) = 0.482. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the time in emotional role

Statistical analysis description:

The relationship between the passing of time and the changes in emotional role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[34]
P-value	= 0.032
Method	ANOVA

Notes:

[34] - α=0.0221. F (contrast statistic) = 4.850. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of group-time and emotional role

Statistical analysis description:

The relationship between the interaction treatment group-passing of time and the changes in emotional role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	= 0.145
Method	ANOVA

Notes:

[35] - α=0.0221. F (contrast statistic) = 2.181. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the group and mental health

Statistical analysis description:

The relationship between the treatment group and the changes in mental health was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[36]
P-value	= 0.467
Method	ANOVA

Notes:

[36] - α=0.0221. F (contrast statistic) = 0.535. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the time and mental health

Statistical analysis description:

The relationship between the passing of time and the changes in mental health was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	= 0.1
Method	ANOVA

Notes:

[37] - α=0.0221. F (contrast statistic) = 2.795. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of group-time and mental health

Statistical analysis description:

The relationship between the interaction treatment group-passing of time and the changes in mental health was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[38]
P-value	= 0.89
Method	ANOVA

Notes:

[38] - α=0.0221. F (contrast statistic) = 0.019. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the group and physical role

Statistical analysis description:

The relationship between the treatment group and the changes in physical role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[39]
P-value	= 0.742
Method	ANOVA

Notes:

[39] - α=0.0221. F (contrast statistic) = 0.109. Degrees of freedom: 1, 56

Statistical analysis title	Analysis of the time and physical role

Statistical analysis description:

The relationship between the passing of time and the changes in physical role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[40]
P-value	< 0.001 [41]
Method	ANOVA

Notes:

[40] - α=0.0221. F (contrast statistic) = 21.912. Degrees of freedom: 1, 56

[41] - Effect size = 0.109

Statistical analysis title	Analysis of group-time and physical role

Statistical analysis description:

The relationship between the interaction treatment group-passing of time and the changes in physical role was analysed with ANOVA. The total number of subjects in this analysis (172) is calculated as the addition of the number of patients in all the visits, and does not reflect the actual number of patients analysed.

Comparison groups	Baseline visit, MBK-01 group v Baseline visit, fidaxomicin group v Visit 4, MBK-01 group v Visit 4, fidaxomicin group v Visit 6, MBK-01 group v Visit 6, fidaxomicin group

Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	superiority[42]
P-value	= 0.089
Method	ANOVA

Notes:

[42] - α=0.0221. F (contrast statistic) = 2.986. Degrees of freedom: 1, 56

Secondary: Number of Adverse Events

End point title	Number of Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Adverse events were assessed continuously during the study for up to 6 months after treatment, until the end-of-study visit.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Adverse events	89	103		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients who have had Adverse Events

End point title	Number of patients who have had Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Adverse events were assessed continuously during the study for up to 6 months after treatment, until the end-of-study visit.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Adverse events	36	38		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Serious Adverse Events

End point title	Number of Serious Adverse Events
End point description:	

End point type	Secondary
End point timeframe:	

Serious adverse events were assessed continuously during the study for up to 6 months after treatment, until the end-of-study visit.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Serious Adverse Events	11	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients who have had Serious Adverse Events

End point title	Number of patients who have had Serious Adverse Events
End point description:	

End point type	Secondary
End point timeframe:	

Serious adverse events were assessed continuously during the study for up to 6 months after treatment, until the end-of-study visit.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Serious Adverse Events	9	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of treatment-related Adverse Events

End point title	Number of treatment-related Adverse Events
End point description:	
Adverse events classified under the categories "Likely" and "Definitely related" are considered treatment-related Adverse Events.	
End point type	Secondary
End point timeframe:	
Adverse events were assessed continuously during the study for up to 6 months after treatment, until the end-of-study visit.	

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Adverse Events				
Unrelated	93	79		
Unlikely	2	2		
Possible	5	7		
Likely	3	1		
Definitely related	0	0		

Statistical analyses

Statistical analysis title	Analysis of relation to treatment
Statistical analysis description:	
Relationship between the treatment groups and the Adverse Events related to treatment is analysed. Adverse events classified under the categories "Likely" and "Definitely related" are considered treatment-related Adverse Events.	
Comparison groups	Fidaxomicin v MBK-01
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.692 [43]
Method	Chi-squared corrected
Parameter estimate	Mean difference (final values)
Point estimate	1.459
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	100
Notes:	

[43] - The assumption according to which no more than 25% of the cells in the table should have an expected frequency is violated. Yates' continuity correction is reported.

Confidence interval was not calculated. It is inputed as 0 and 100.

Secondary: Severity of Adverse Events

End point title	Severity of Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Adverse events were assessed continuously during the study for up to 6 monthsafter treatment, until the end-of-study visit.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Adverse Events				
Mild	77	70		
Moderate	22	17		
Severe	4	1		
Life threatening	0	0		
Death	0	1		

Statistical analyses

Statistical analysis title	Analysis of severity

Statistical analysis description:

Relationship between the treatment groups and the severity of the Adverse Events is analysed.

Comparison groups	MBK-01 v Fidaxomicin
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.429 [44]
Method	Chi-squared corrected
Parameter estimate	Mean difference (final values)
Point estimate	2.768
Confidence interval	
level	90 %
sides	2-sided
lower limit	0
upper limit	100

Notes:

[44] - The assumption according to which no more than 25% of the cells in the table should have an expected frequency is violated. Yates' continuity correction is reported.

Confidence interval was not calculated. It is inputed as 0 and 100.

Secondary: Adverse Events in relation to Clostridium difficile infection

End point title	Adverse Events in relation to Clostridium difficile infection

End point description:

End point type	Secondary

End point timeframe:

Adverse events were assessed continuously during the study por up to 6 months after treatment, until the end-of-study visit.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Adverse Events				
Diarrhoea	17	28		
Clostridium diffcile colitis	0	1		
Clostridium difficile infection	3	4		
Positive Clostridium test	1	0		
Total	21	33		

Statistical analyses

No statistical analyses for this end point

Secondary: Mortality associated with CDI

End point title	Mortality associated with CDI
End point description:	
The number of deaths related to Clostridium difficile infection is assessed.	
End point type	Secondary
End point timeframe:	
Up to 6 months after the start of the treatment.	

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: patients	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: ICU admissions

End point title	ICU admissions
End point description:	
The number of Intensive Care Unit Admissions related to Clostridium difficile infection or to the treatment was assessed.	
End point type	Secondary

End point timeframe:

Up to 6 months after the start of the treatment.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: patients				
Related to CDI	0	0		
Related to the treatment	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Adverse Events of Special Interest

End point title	Number of Adverse Events of Special Interest

End point description:

AESI (Adverse Events of Special Interest) have also been considered either AEs or SAEs.

AESI defined by protocol and Statistical Analysis Plan (SAP) are as follows: abdominal cramping, bloating and pain; flatulence, nausea, vomiting, transient fever (>38ºC), increased C-reactive protein (>20 mg/L), fatigue, weight gain, headache, anorexia, constipation, diarrhea, ulcerative colitis, bacteremia, inflammatory bowel disease and enteropathogenic infections.

Some events that, in the clinician's opinion should be considered AESI despite not being isted as such in the list provided in the protocol and the SAP, are included in this analysis. In addition, some events were not considered AESI by the clinician despite being listed as such in the protocol and the SAP, hence they were not included in this analysis.

End point type	Secondary

End point timeframe:

Adverse events were assessed continuously during the study for up to 6 months afer treatment, until the end-of-study visit.

End point values	MBK-01	Fidaxomicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: Adverse events	64	63		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Regarding safety assessments, adverse events were assessed continuously during the study for up for 6 months after treatment until the end-of-study visit (End of Study date: 15 Nov 2023).

Adverse event reporting additional description:

For the adverse events, System Organ Class (SOC) and Preferred Term (PT) were reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	MBK-01

Reporting group description:

Patients randomized to MBK-01 received a single dose of 4 oral capsules of MBK-01.

Reporting group title	Fidaxomicin

Reporting group description:

Patients randomized to fidaxomicin received treatment with oral fidaxomicin 200mg/12h for 10 days.

Serious adverse events	MBK-01	Fidaxomicin	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 45 (20.00%)	4 / 47 (8.51%)	
number of deaths (all causes)	1	1	
number of deaths resulting from adverse events	1	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal cancer			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Colitis ulcerative			

subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory bowel disease			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal fluid collection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute respiratory failure			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Clostridium difficile infection			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2.13 %

Non-serious adverse events	MBK-01	Fidaxomicin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 45 (80.00%)	38 / 47 (80.85%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Hypertensive crisis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Surgical and medical procedures			

Prophylaxis		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Tooth extraction		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
General disorders and administration site conditions		
Fatigue		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Medical device site reaction		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Pain		
subjects affected / exposed	2 / 45 (4.44%)	1 / 47 (2.13%)
occurrences (all)	3	1
Polyp		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Pyrexia		
subjects affected / exposed	2 / 45 (4.44%)	2 / 47 (4.26%)
occurrences (all)	3	2
Reproductive system and breast disorders		
Prostatitis		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Respiratory, thoracic and mediastinal disorders		
Catarrh		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Psychiatric disorders		
Agitation		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Insomnia		

subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Mixed anxiety and depressive disorder			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	11 / 45 (24.44%)	6 / 47 (12.77%)	
occurrences (all)	13	7	
Cardiac murmur			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Clostridium test positive			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
International normalised ratio increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	0 / 45 (0.00%)	2 / 47 (4.26%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Spinal fracture			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Synovial rupture			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			

Cardiac failure			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	3 / 45 (6.67%)	4 / 47 (8.51%)	
occurrences (all)	3	4	
Migraine			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Leukocytosis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 45 (2.22%)	2 / 47 (4.26%)	
occurrences (all)	1	2	
Abdominal pain			
subjects affected / exposed	4 / 45 (8.89%)	3 / 47 (6.38%)	
occurrences (all)	4	3	
Abdominal pain lower			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	

Abdominal pain upper		
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)
occurrences (all)	1	1
Colitis ulcerative		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Constipation		
subjects affected / exposed	1 / 45 (2.22%)	2 / 47 (4.26%)
occurrences (all)	1	2
Dental discomfort		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Diarrhoea		
subjects affected / exposed	16 / 45 (35.56%)	22 / 47 (46.81%)
occurrences (all)	17	27
Erosive duodenitis		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Flatulence		
subjects affected / exposed	2 / 45 (4.44%)	4 / 47 (8.51%)
occurrences (all)	2	4
Gastrointestinal sounds abnormal		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Gastrooesophageal reflux disease		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Haemorroids		
subjects affected / exposed	2 / 45 (4.44%)	1 / 47 (2.13%)
occurrences (all)	2	1
Irritable bowel syndrome		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Nausea		
subjects affected / exposed	2 / 45 (4.44%)	2 / 47 (4.26%)
occurrences (all)	3	3

Odynophagia		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Reflux gastritis		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Vomiting		
subjects affected / exposed	3 / 45 (6.67%)	1 / 47 (2.13%)
occurrences (all)	4	2
Skin and subcutaneous tissue disorders		
Angioedema		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Hidradenitis		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Pruritus		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Toxic skin eruption		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Vascular purpura		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Renal and urinary disorders		
Microalbuminuria		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Oliguria		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0
Musculoskeletal and connective tissue disorders		
Back pain		
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)
occurrences (all)	1	1

Musculoskeletal chest pain		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1

Infections and infestations

Clostridium difficile colitis		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1

COVID-19		
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)
occurrences (all)	1	1

Clostridium difficile infection		
subjects affected / exposed	2 / 45 (4.44%)	3 / 47 (6.38%)
occurrences (all)	2	3

Cystitis		
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)
occurrences (all)	1	1

Escherichia urinary tract infection		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1

Gastroenteritis		
subjects affected / exposed	2 / 45 (4.44%)	0 / 47 (0.00%)
occurrences (all)	3	0

Influenza		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0

Oral candidiasis		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0

Perineal abscess		
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)
occurrences (all)	1	0

Pneumonia		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1

Respiratory tract infection

subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Urinary tract infection		
subjects affected / exposed	3 / 45 (6.67%)	2 / 47 (4.26%)
occurrences (all)	3	2
Metabolism and nutrition disorders		
Folate deficiency		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Hypokalaemia		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Hyponatraemia		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Vitamin B12 deficiency		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1
Vitamin D deficiency		
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2021	Changes in the exclusion criteria were made, which directly impact on the recruitment capacity of the study. The modification of the exclusion criteria was motivated by the following causes: 1. The modification or elimination of some of the initially proposed exclusion criteria significantly favours the recruitment capacity of the centres involved in the study. 2. The proposed modifications of the exclusion criteria do not affect the fulfilment of the objectives (primary and secondary) of the study. The increase in the study's recruitment capacity favours the fulfilment of the study's objectives within the established timeframe. 3. The population of patients treated in the clinical trial is more heterogeneous than the previous one, and therefore more representative of the population intended to be treated with MBK-01.
15 December 2021	Four new sites were added to the clinical trial.
07 February 2022	Changes in the inclusion and exclusion criteria were made, by allowing the use of antibiotic pre-treatment for patients included in the study, making necessary to consider a washout period prior to the administration of the study treatment. The modification of the inclusion and exclusion criteria was motivated by the following reasons: 1. Due to the low recruitment rate and the fact that the modification of inclusion and exclusion criteria directly impacts on recruitment capacity, the aim is to improve the recruitment capacity of the sites involved. 2. The proposed modifications do not affect the fulfilment of the objetives of the study. Increased recruitment capactiy woul help meet the objectives within the stablished timeframe. 3. The population to be treated in the study is more representative of the population intended to be treated with MBK-01. In addition, the time for carrying out the intermediate analysis of the study was modified, so that it would be performed when half of the patients had completed treatment. In this way, the partial efficacy results of the study would be known earlier.
12 May 2022	Two new sites were added to the clinical trial.

16 September 2022	The clinical trial population was broadened and the study inclusion criteria were modified, motivated by the following reasons: 1. Due to the low recruitment rate and the fact that the modification of inclusion criteria directly impacts on recruitment capacity, the aim is to improve the recruitment capacity of the sites involved. 2. The proposed modifications do not affect the fulfilment of the objetives of the study. An increased recruitment capacitiy woul help meet the objectives within the stablished timeframe. 3. The adjustments that were made allow an additional group of patients with Clostridioides difficile infection to have access to a potentially effective treatment, while still using the same patient population as before and without compromising the data already collected in the study. 4. The extension of the deadline for detection of Clostridioides difficile toxin within the 7 days prior to enrolment of the patient in the trial was made to take into account the duration of vancomycin treatment and the washout period that may be required by some participants. The statistical analysis was adapted to include the assessment of an additional secondary safety variable, which would provide more information on the safety of the investigational medicinal product. The sample size was adapted without affecting the achievement of the study objectives. Some aspects of the study design were modified, allowing the inclusion in the trial of patients previously treated with fidaxomicin if the duration of treatment was not therapeutic. In addition, it was included that the interim analysis of the study could lead to early discontinuation of the study, with the aim of early termination of the study, in order to maintain the safety of the participants.
21 July 2023	The measures taken in October 2022 were included in the protocol, following the recommendations of the guidance document 'Safety Alert Regarding Use of Fecal Microbiota for Transplantation and Additional Safety Protections Pertaining to Monkeypox Virus', issued by the FDA in 2022, and which were notified to the AEMPS by Urgent Safety Notification on 21/10/2022. The donor inclusion criteria were modified in line with these measures. The sample size was adapted from 66 to 82 patients, in order to adjust the expected number of patients recruited to the actual observed drop-out rate of the study, without affecting the achievement of the study objectives. A new planned study schedule was established, taking into account the changes in the number of patients to be recruited.

09 October 2023	The definition of the study variables were revised to add the odds ratio and logistic regression in the analysis of the main efficacy variable, thus allowing the study of the probability of recurrence in addition to the number of episodes of diarrhea. The variable "Duration of hospitalisation" was deleted as many patients were treated as outpatients or the reason of admission was not CDI. The variable "Duration of the treatment" was also deleted.
	Complementary ITT subpopulations were added for the analysis of probability of recurrence and time to recurrence. The analysis of covariates was eliminated.
	In addition, a revision of the definition of recurrence of CDI was added.
	The reformulation of the primary variable resulted in the revision of the statiscal calculation of the sample size, which would be based on a confidence level of 97.06%, Odds Ratio of 2.5, stastical power of 80% and loss rate of 50%, generating a sample size of 104 subjects. The dropout rate was maintained at 50%.
	Criteria were defined to allow the early termination of the clinical trial. The possibility of early termination could provide advantages such as minimisation of risks to subjects, greater efficiency in the management of research resources, and/or, where appropriate, acceleration of product development and market access.
	The possibility of early termination of the trial makes it necessary to plan for a second, intermediate statistical analysis to assess trends in efficacy and safety outcomes.
	The high rate of loss to follow-up, as well as the possibility of premature trial termination, made it necessary to define a strategy for the follow-up of patients withdrawn before completing the scheduled follow-up. Thus, it was defined that all patients withdrawn before the end of the planned follow-up should have an end-of-study visit ≥ 30 days after initiation of treatment, in which, as a minimum, relevant safety information should be collected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The statistical power of the study was limited due to the small sample size, which may have prevented finding statistically significant differences between MBK-01 and fidaxomicin in some analyses.

Notes: