Clinical trial results:
A Multicenter Randomized Parallel Group Phase III Study Comparing the Bowel Cleansing Efficacy, Safety and Tolerability of NER1006 (a Low Volume Bowel Cleansing Solution) versus MOVIPREP® using a 2-Day Split-Dosing and 1-Day Morning Split-Dosing Regimens in Adults

Summary

EudraCT number	2014-002185-78
Trial protocol	GB BE IT ES FR
Global end of trial date	19 August 2015

Results information

Result version number	v1 (current)
This version publication date	04 September 2016
First version publication date	04 September 2016

Trial information

Trial identification

Sponsor protocol code	NER1006-02/2014

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02273167
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Norgine Limited
Sponsor organisation address	Norgine House, Widewater Place, Moorhall Road, Harefield, United Kingdom, UB9 6NS
Public contact	Director Clinical Operations, Clinical Development, Norgine Limited, 0044 01895826603, ClinicalTrials@norgine.com
Scientific contact	Director Clinical Operations, Clinical Development, Norgine Limited, 0044 01895826603, ClinicalTrials@norgine.com

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	22 April 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 August 2015
Global end of trial reached?	Yes
Global end of trial date	19 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the overall bowel cleansing efficacy and the 'Excellent plus Good' cleansing rate in the colon ascendens of 2-day split-dosing and 1-day morning of colonoscopy split-dosing regimens with NER1006 compared to a 2-day split-dosing regimen with MOVIPREP®, graded according to the Harefield Cleansing Scale (HCS) in patients undergoing screening, surveillance or diagnostic colonoscopy.

Protection of trial subjects:

Screening/Randomisation visit and on the day of colonoscopy prior to the procedure:

- Medical history at the time of screening visit.
- Informed consent.
- Full physical examination, including height and body weight.
- Inclusion/exclusion.
- Orthostatic blood pressure, pulse rate and body temperature measurements.
- 12-lead ECG.
- Blood sample collection: hematology, coagulation profile and biochemistry analyses.
- Urinalysis.
- Pregnancy test (urine) for all female patients of child bearing potential.
- Concomitant medication documentation/review.
- Eligibility check.

After the colonoscopy procedure and recovery period:

- Arterial blood pressure and pulse rate measurements 1 to 2 hours (± 30 minutes) after colonoscopy.
- Physical examination, including body weight.
- Concomitant medication documentation to include medication or IV fluids during colonoscopy.
- Recording and review of adverse events.

Each patient discharged from the colonoscopy unit with an appointment for a follow-up visit. There are two follow up visits. The following assessments performed at each of those two follow up visits:

- Physical examination.
- Blood sample collection: Biochemistry and hematology analyses.
- Review of any outstanding adverse events.
- Concomitant medication review.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 October 2014
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	Poland: 311
Country: Number of subjects enrolled	Spain: 192
Country: Number of subjects enrolled	United Kingdom: 36
Country: Number of subjects enrolled	Belgium: 110
Country: Number of subjects enrolled	France: 32
Country: Number of subjects enrolled	Germany: 119
Country: Number of subjects enrolled	Italy: 49
Worldwide total number of subjects	849
EEA total number of subjects	849

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
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)	641
From 65 to 84 years	208
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 28 OCT 2014 (first patient first visit) to 19 AUG 2015 (last patient last visit).
Territories : Belgium, France, Germany, Italy, Poland, Spain and United Kingdom.

Pre-assignment

Screening details:

Male or female outpatients and inpatients aged ≥18 to ≤85 years undergoing a screening, surveillance, or diagnostic colonoscopy were eligible for inclusion.

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Data analyst, Assessor[2]

Arms

Are arms mutually exclusive?	Yes
Arm title	NER1006 : 2-Day Split-Dosing

Arm description:

Experimental : NER1006 Powder for Oral Solution (2-Day Split-Dosing)

Arm type	Experimental
Investigational medicinal product name	NER1006
Investigational medicinal product code	NER1006
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

NER1006 Powder for Oral Solution consisting of one sachet of Dose 1 and two sachets (A & B) for Dose 2.
Dosing regimen : 2-Day Split-Dosing. Self administered. Dose 1 in the evening prior to colonoscopy (Day 1) and Dose 2 in the morning of colonoscopy (Day 2).

Arm title	NER1006 : 1-Day Morning Split-Dosing

Arm description:

Experimental : NER1006 Powder for Oral Solution (1-Day Morning Split-Dosing)

Arm type	Experimental
Investigational medicinal product name	NER1006
Investigational medicinal product code	NER1006
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

NER1006 Powder for Oral Solution consisting of one sachet of Dose 1 and two sachets (A & B) for Dose 2.
Dosing regimen : 1-Day Morning Split-Dosing. Self administered. Both doses (Dose 1 and Dose 2) of study drug in the morning of the clinical procedure. Doses within a 1 to 2 hour interval.

Arm title	MOVIPREP

Arm description:

Comparator

Arm type	Active comparator

Investigational medicinal product name	MOVIPREP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

MOVIPREP Powder for Oral Solution
Dosing regimen : Patients allocated to the MOVIPREP treatment group at randomization self-administered Dose 1 in the evening of Day 1 and the Dose 2 in the morning of Day 2 (day of colonoscopy).

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: Assessor : Colonoscopist

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: Data analyst : Central reader

Number of subjects in period 1	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP
Started	283	283	283
Completed	260	262	259
Not completed	23	21	24
Consent withdrawn by subject	12	11	10
Non Compliant	1	1	2
Required surgery	1	-	-
Adverse event, non-fatal	1	-	1
Other	2	5	3
Screen failure	-	-	1
Lost to follow-up	1	1	-
Met exclusion criteria	5	3	5
Non compliance with study drug	-	-	1
No colonoscopist available	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	NER1006 : 2-Day Split-Dosing
Reporting group description:	
Experimental : NER1006 Powder for Oral Solution (2-Day Split-Dosing)	
Reporting group title	NER1006 : 1-Day Morning Split-Dosing
Reporting group description:	
Experimental : NER1006 Powder for Oral Solution (1-Day Morning Split-Dosing)	
Reporting group title	MOVIPREP
Reporting group description:	
Comparator	

Reporting group values	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP
Number of subjects	283	283	283
Age categorical			
Units: Subjects			
Adults (18-64 years)	203	209	228
From 65-84 years	80	74	55
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	56.3	54.9	54.3
standard deviation	± 12.03	± 13.21	± 12.48
Gender categorical			
Units: Subjects			
Female	163	152	139
Male	120	131	144

Reporting group values	Total		
Number of subjects	849		
Age categorical			
Units: Subjects			
Adults (18-64 years)	640		
From 65-84 years	209		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	454		
Male	395		

Subject analysis sets

Subject analysis set title	NER1006 : 2-Day Split-Dosing
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mFAS included all randomized patients with the exception of any patient who
(i) was randomized but subsequently failed to meet entry criteria and
(ii) in whom it was confirmed (from their patient diary) that the same patient did not receive any study drug.

The mFAS was used as the primary population for all efficacy analyses. Patients in this analysis set were summarized according to the treatment to which they were randomly assigned.

Patients who did not have their eligibility confirmed based on the entry criteria were included in the mFAS, regardless of whether they received any study drug.

Subject analysis set title	NER1006 : 1-Day Morning Split-Dosing
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mFAS included all randomized patients with the exception of any patient who
(i) was randomized but subsequently failed to meet entry criteria and
(ii) in whom it was confirmed (from their patient diary) that the same patient did not receive any study drug.

The mFAS was used as the primary population for all efficacy analyses. Patients in this analysis set were summarized according to the treatment to which they were randomly assigned.

Patients who did not have their eligibility confirmed based on the entry criteria were included in the mFAS, regardless of whether they received any study drug.

Subject analysis set title	MOVIPREP
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mFAS included all randomized patients with the exception of any patient who
(i) was randomized but subsequently failed to meet entry criteria and
(ii) in whom it was confirmed (from their patient diary) that the same patient did not receive any study drug.

The mFAS was used as the primary population for all efficacy analyses. Patients in this analysis set were summarized according to the treatment to which they were randomly assigned.

Patients who did not have their eligibility confirmed based on the entry criteria were included in the mFAS, regardless of whether they received any study drug.

Reporting group values	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP
Number of subjects	275	275	272
Age categorical Units: Subjects			
Adults (18-64 years)	197	205	219
From 65-84 years	78	70	53
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	56.5	54.8	54.2
standard deviation	± 11.91	± 13.19	± 12.6
Gender categorical Units: Subjects			
Female	161	148	132
Male	114	127	140

End points

End points reporting groups

Reporting group title	NER1006 : 2-Day Split-Dosing
Reporting group description:	
Experimental : NER1006 Powder for Oral Solution (2-Day Split-Dosing)	
Reporting group title	NER1006 : 1-Day Morning Split-Dosing
Reporting group description:	
Experimental : NER1006 Powder for Oral Solution (1-Day Morning Split-Dosing)	
Reporting group title	MOVIPREP
Reporting group description:	
Comparator	
Subject analysis set title	NER1006 : 2-Day Split-Dosing
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mFAS included all randomized patients with the exception of any patient who
(i) was randomized but subsequently failed to meet entry criteria and
(ii) in whom it was confirmed (from their patient diary) that the same patient did not receive any study drug.

The mFAS was used as the primary population for all efficacy analyses. Patients in this analysis set were summarized according to the treatment to which they were randomly assigned.

Patients who did not have their eligibility confirmed based on the entry criteria were included in the mFAS, regardless of whether they received any study drug.

Subject analysis set title	NER1006 : 1-Day Morning Split-Dosing
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mFAS included all randomized patients with the exception of any patient who
(i) was randomized but subsequently failed to meet entry criteria and
(ii) in whom it was confirmed (from their patient diary) that the same patient did not receive any study drug.

The mFAS was used as the primary population for all efficacy analyses. Patients in this analysis set were summarized according to the treatment to which they were randomly assigned.

Patients who did not have their eligibility confirmed based on the entry criteria were included in the mFAS, regardless of whether they received any study drug.

Subject analysis set title	MOVIPREP
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mFAS included all randomized patients with the exception of any patient who
(i) was randomized but subsequently failed to meet entry criteria and
(ii) in whom it was confirmed (from their patient diary) that the same patient did not receive any study drug.

The mFAS was used as the primary population for all efficacy analyses. Patients in this analysis set were summarized according to the treatment to which they were randomly assigned.

Patients who did not have their eligibility confirmed based on the entry criteria were included in the mFAS, regardless of whether they received any study drug.

Primary: To evaluate the overall bowel cleansing efficacy of a 2-day and 1-day dosing regimen with NER1006 compared to a 2-day dosing regimen with MOVIPREP, graded according to the HCS in patients undergoing colonoscopy

End point title	To evaluate the overall bowel cleansing efficacy of a 2-day and 1-day dosing regimen with NER1006 compared to a 2-day dosing regimen with MOVIPREP, graded according to the HCS in patients undergoing colonoscopy

End point description:

The hypothesis for this endpoint was to demonstrate non-inferiority of each NER1006 regimen in turn to MOVIPREP (10% margin).

End point type	Primary

End point timeframe:

Visit 2, Day of colonoscopy

End point values	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	275	275	272	
Units: Harefield Cleansing Scale	253	245	238	

Statistical analyses

Statistical analysis title	Fisher's exact test

Statistical analysis description:

The success rate was the number of patients with successful overall bowel cleansing as a proportion of the number of patients in each group. Missing data were imputed as failures. The treatment effect was the NER1006 success rate minus the MOVIPREP success rate. A Hochberg procedure was used to control Type I error. A closed testing procedure was used to evaluate superiority. Heirarchically, NER1006 2-Day was tested first against MOVIPREP and NER1006 1-Day tested second.

Comparison groups	MOVIPREP v NER1006 : 2-Day Split-Dosing v NER1006 : 1-Day Morning Split-Dosing
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.025
Method	Fisher exact

Notes:

[1] - The 97.5% 1-sided lower confidence interval (CI) for the difference between bowel preparation cleansing rates was determined using exact Clopper-Pearson confidence limits.

Primary: To evaluate the "Excellent plus Good" cleansing rate in the colon ascendens of a 2-day and 1-day dosing regimen with NER1006 compared to a 2-day dosing regimen with MOVIPREP, graded according to the HCS in patients undergoing colonoscopy

End point title	To evaluate the "Excellent plus Good" cleansing rate in the colon ascendens of a 2-day and 1-day dosing regimen with NER1006 compared to a 2-day dosing regimen with MOVIPREP, graded according to the HCS in patients undergoing colonoscopy

End point description:

The hypothesis for this endpoint was to demonstrate non-inferiority of each NER1006 regimen in turn to MOVIPREP (10% margin).

End point type	Primary

End point timeframe:

Visit 2, Day of colonoscopy

End point values	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	275	275	272	
Units: Harefield Cleansing Scale	87	93	41	

Statistical analyses

Statistical analysis title	Fisher's exact test

Statistical analysis description:

The success rate was the number of patients with successful colon ascendens cleansing as a proportion of the number of patients in each group. Missing data were imputed as failures. The treatment effect was the NER1006 success rate minus the MOVIPREP success rate. A Hochberg procedure was used to control Type I error. A closed testing procedure was used to evaluate superiority. Heirarchically, NER1006 2-Day was tested first against MOVIPREP and NER1006 1-Day tested second.

Comparison groups	NER1006 : 2-Day Split-Dosing v NER1006 : 1-Day Morning Split-Dosing v MOVIPREP
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.025
Method	Fisher exact

Notes:

[2] - The 97.5% 1-sided lower confidence interval (CI) for the difference between bowel preparation cleansing rates was determined using exact Clopper-Pearson confidence limits.

Secondary: To assess NER1006 compared to MOVIPREP: 1) the adenoma detection rate (ADR) for the colon ascendens

End point title	To assess NER1006 compared to MOVIPREP: 1) the adenoma detection rate (ADR) for the colon ascendens

End point description:

If at least one of the alternative primary endpoints were met, then key secondary endpoints were evaluated hierarchichally in a pre-specified order. Non-inferiority was concluded if the 1-sided 97.5% CL for difference in proportion of events between 2 groups excluded a 10% or greater difference in favor of MOVIPREP. Formal testing was to proceed in the hierarchy if preceding key secondary endpoint had at least met non-inferiority.

End point type	Secondary

End point timeframe:

Day of colonoscopy, Visit 2

End point values	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	275	275	272	
Units: Adenoma detection rate (ADR)	12	12	8	

Statistical analyses

Statistical analysis title	Fisher's exact test

Statistical analysis description:

ADR was defined as the number of patients with at least one adenoma in the colon ascendens divided by the number of patients in the modified full analysis set.
Difference was calculated as NER1006 rate – MOVIPREP rate.
1-sided P value was obtained from Fisher's exact test. The comparison was with the difference in rate between NER1006 and MOVIPREP versus a hypothesized difference of zero.

Comparison groups	MOVIPREP v NER1006 : 1-Day Morning Split-Dosing v NER1006 : 2-Day Split-Dosing
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.025
Method	Fisher exact

Notes:

[3] - 10% Non-inferiority margin

Secondary: To assess NER1006 compared to MOVIPREP: 2) the overall adenoma detection rate (ADR)

End point title	To assess NER1006 compared to MOVIPREP: 2) the overall adenoma detection rate (ADR)

End point description:

If at least one of the alternative primary endpoints were met, then key secondary endpoints were evaluated hierarchichally in a pre-specified order. Non-inferiority was concluded if the 1-sided 97.5% CL for difference in proportion of events between 2 groups excluded a 10% or greater difference in favour of MOVIPREP. Formal testing was to proceed in the hierarchy if preceding key secondary endpoint had at least met non-inferiority.

End point type	Secondary

End point timeframe:

Day of colonoscopy, Visit 2

End point values	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	275	275	272	
Units: Adenoma detection rate (ADR)	27	28	27	

Statistical analyses

Statistical analysis title	Fisher's exact test

Statistical analysis description:

ADR was defined as the number of patients with at least one adenoma in the overall colon divided by the number of patients in the modified full analysis set.
Difference was calculated as NER1006 rate – MOVIPREP rate.
1-sided P value was obtained from Fisher's exact test. The comparison was with the difference in rate between NER1006 and MOVIPREP versus a hypothesized difference of zero.

Comparison groups	NER1006 : 2-Day Split-Dosing v MOVIPREP v NER1006 : 1-Day Morning Split-Dosing
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	< 0.025
Method	Fisher exact

Notes:

[4] - 10% Non-inferiority margin

Secondary: To assess NER1006 compared to MOVIPREP: 3) the polyp detection rate (PDR) for the colon ascendens

End point title	To assess NER1006 compared to MOVIPREP: 3) the polyp detection rate (PDR) for the colon ascendens

End point description:

If at least one of the alternative primary endpoints were met, then key secondary endpoints were evaluated hierarchichally in a pre-specified order. Non-inferiority was concluded if the 1-sided 97.5% CL for difference in proportion of events between 2 groups excluded a 10% or greater difference in favor of MOVIPREP. Formal testing was to proceed in the hierarchy if preceding key secondary endpoint had at least met non-inferiority.

End point type	Secondary

End point timeframe:

Day of colonoscopy, Visit 2

End point values	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	275	275	272	
Units: Polyp detection rate (PDR)	23	19	16	

Statistical analyses

Statistical analysis title	Fisher's exact test

Statistical analysis description:

PDR was defined as the number of patients with at least one polyp in the colon ascendens divided by the number of patients in the modified full analysis set.
Difference was calculated as NER1006 rate – MOVIPREP rate.
1-sided P value was obtained from Fisher's exact test. The comparison was with the difference in rate between NER1006 and MOVIPREP versus a hypothesized difference of zero.

Comparison groups	MOVIPREP v NER1006 : 1-Day Morning Split-Dosing v NER1006

	: 2-Day Split-Dosing
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.025
Method	Fisher exact

Notes:

[5] - 10% Non-inferiority margin

Secondary: To assess NER1006 compared to MOVIPREP: 4) To assess the overall polyp detection rate (PDR)

End point title	To assess NER1006 compared to MOVIPREP: 4) To assess the overall polyp detection rate (PDR)

End point description:

If at least one of the alternative primary endpoints were met, then key secondary endpoints were evaluated hierarchichally in a pre-specified order. Non-inferiority was concluded if the 1-sided 97.5% CL for difference in proportion of events between 2 groups excluded a 10% or greater difference in favor of MOVIPREP. Formal testing was to proceed in the hierarchy if preceding key secondary endpoint had at least met non-inferiority.

End point type	Secondary

End point timeframe:

Day of colonoscopy, Visit 2

End point values	NER1006 : 2-Day Split-Dosing	NER1006 : 1-Day Morning Split-Dosing	MOVIPREP	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	275	275	272	
Units: Polyp detection rate (PDR)	44	45	44	

Statistical analyses

Statistical analysis title	Fisher's exact test

Statistical analysis description:

PDR was defined as the number of patients with at least one polyp in the overall colon divided by the number of patients in the modified full analysis set.
Difference was calculated as NER1006 rate – MOVIPREP rate.
1-sided P value was obtained from Fisher’s exact test. The comparison was with the difference in rate between NER1006 and MOVIPREP versus a hypothesized difference of zero.

Comparison groups	MOVIPREP v NER1006 : 1-Day Morning Split-Dosing v NER1006 : 2-Day Split-Dosing
Number of subjects included in analysis	822
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
P-value	< 0.025
Method	Fisher exact

Notes:
[6] - 10% Non-inferiority margin

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were monitored continuously and were reported to the Investigator by the patient for the duration of the study (This definition includes events occurring from the time of informed consent until 28 days after last patient last visit.)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	NER1006 2-Day Split-Dosing
Reporting group description:	
Experimental	
Reporting group title	NER1006 1-Day Morning Split Dosing
Reporting group description:	
Experimental	
Reporting group title	MOVIPREP
Reporting group description:	
Active Comparator	

Serious adverse events	NER1006 2-Day Split-Dosing	NER1006 1-Day Morning Split Dosing	MOVIPREP
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 262 (0.76%)	0 / 269 (0.00%)	0 / 263 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Procedural intestinal perforation			
subjects affected / exposed	1 / 262 (0.38%)	0 / 269 (0.00%)	0 / 263 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 262 (0.38%)	0 / 269 (0.00%)	0 / 263 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	NER1006 2-Day Split-Dosing	NER1006 1-Day Morning Split Dosing	MOVIPREP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 262 (17.18%)	49 / 269 (18.22%)	31 / 263 (11.79%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 262 (0.76%)	3 / 269 (1.12%)	0 / 263 (0.00%)
occurrences (all)	2	3	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 262 (1.53%)	2 / 269 (0.74%)	4 / 263 (1.52%)
occurrences (all)	4	3	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 262 (0.00%)	0 / 269 (0.00%)	5 / 263 (1.90%)
occurrences (all)	0	0	5
Feeling cold			
subjects affected / exposed	0 / 262 (0.00%)	1 / 269 (0.37%)	4 / 263 (1.52%)
occurrences (all)	0	1	4
Thirst			
subjects affected / exposed	2 / 262 (0.76%)	5 / 269 (1.86%)	2 / 263 (0.76%)
occurrences (all)	2	5	2
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 262 (1.15%)	1 / 269 (0.37%)	6 / 263 (2.28%)
occurrences (all)	3	1	6
Abdominal pain lower			
subjects affected / exposed	0 / 262 (0.00%)	3 / 269 (1.12%)	1 / 263 (0.38%)
occurrences (all)	0	3	1
Dry mouth			
subjects affected / exposed	3 / 262 (1.15%)	3 / 269 (1.12%)	0 / 263 (0.00%)
occurrences (all)	3	3	0
Nausea			
subjects affected / exposed	15 / 262 (5.73%)	14 / 269 (5.20%)	9 / 263 (3.42%)
occurrences (all)	16	14	9
Vomiting			

subjects affected / exposed occurrences (all)	11 / 262 (4.20%) 11	18 / 269 (6.69%) 18	3 / 263 (1.14%) 3
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all)	1 / 262 (0.38%) 1	4 / 269 (1.49%) 4	1 / 263 (0.38%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 December 2014	Protocol amendment: -Implementation of paper rather than electronic diaries and Patient Reported Outcome measures. -Changes to Visit 3 and Visit 4 for monitoring patients for any potential kidney injury. -Exclusion criterion "Regular use of laxatives or colon motility altering drugs in the last month (i.e. more than 2-3 times per week)" changed to "last 28 days" prior to Screening Visit instead"last month". -For clarification, word "known" added to Exclusion Criteria "Patients with known liver disease of grades B and C according to the Child Pugh classification". -More precise definition for 'post-menopausal and surgically sterile' included in Inclusion Criterion. -Advice given for contraception amended. -To reflect clinical practice and enable flexibility, the sites will be allowed to schedule the IMP / MOVIPREP® intake +/- 2 hrs before or after the suggested approx. time in the protocol. -Clarification regarding capturing the site colonoscopist's experience and personal Adenoma Detection Rate. -Clarification regarding the conduct of the colonoscopy and scoring. -'Thrombin Time' has been removed from the 'Coagulation' profile. -Genitourinary system deleted as not a requirement under "Physical Examination" for purpose of conducting colonoscopy. -Clarification added to ensure patients have recovered sufficiently from the colonoscopy procedure prior to discharge from clinic. -Clarification to Exclusion Criteria "known hypersensitivity to PEG, ascorbic acid and sulfates or any other component of IMP or comparator" does not include those with sulfa/sulpha drug allergy/intolerance. -Clarifications in Biochemistry panel: "Urea" is same as "Blood Urea Nitrogen". -In line with the Sponsor Company's policy "Management of Product Quality Complaints relating to IMP", a reporting requirement included. -Change of company/contact details for "Statistical Expertise". -Confidence limit relating to key secondary endpoints amended.
30 March 2015	Protocol amendment to update the study location to include the United States, ensuring all the applicable conditions to allow this are included in the protocol. The amendment is also to document a planned increase in the number of patients to be evaluated to account for a 15% drop out as opposed to 10% stated in protocol. These changes are substantial. Further amendments have been made to incorporate additional information for site logistical purposes, alignment with the Statistical Analysis Plan and general clarification. These changes are non-substantial.
25 June 2015	Protocol amendment following statistical input recommending three distinct population analyses on the data, namely the Full Analysis Set (FAS), the modified Full Analysis Set (mFAS), and the Per Protocol (PP) set. In addition, one administrative amendment made relating to a change to the Sponsor's Project Manager.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported