

STUDY SUMMARY: NER1006-03/2014 (DAYB)

Short Title

A study comparing a new bowel cleansing agent, NER1006, with another bowel cleansing agent, Sodium Picosulfate and Magnesium Salt (SP+MS), using day-before dosing.

Full Scientific Title

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 a Sodium Picosulfate and Magnesium Salt (SP+MS) Solution Using a Day Before-Only Dosing Regimen in Adults

General Information

Study Dates

The first person entered this study on 12th November 2014, and the last person completed the study on 19th August 2015.

Background

Polyps in the human bowel are an early sign of cancer, but if polyps are detected at an early stage and removed, it can stop cancer developing. Polyps can be seen and removed using a procedure called colonoscopy, which involves putting a narrow, flexible telescopic camera into the bowel through the rectum.

When a colonoscopy is performed the person's bowel must be as empty as possible, so that the doctor can see the bowel wall clearly. To empty the bowel, strong laxatives are taken before the procedure, which are called "bowel preparations". Sodium Picosulfate and Magnesium Salt (SP+MS) is a commonly used bowel preparation. SP+MS is a powder, which is made into solution with water by the person having the colonoscopy. In our study, SP+MS was taken in two doses on the day before the colonoscopy. Each dose consists of SP+MS mixed up in 1 cup of water (about 150 mL). The person also has to drink 250 mL of water or other clear fluid every hour until the bowel is empty. This means that the person has to drink several litres of fluid in total. This is a lot of fluid to drink, and it often makes the person feel sick. Because of this, some people do not drink all of the SP+MS solution, or do not finish drinking the extra fluid. This means that the bowel is not properly emptied and the doctor cannot see the bowel wall properly.

As it is difficult for people to drink such large amounts of fluid, we have developed a new bowel preparation, which requires a smaller quantity of additional fluid. This should mean that more people will drink all of the solutions, and have a properly cleaned bowel.

Reason for Conducting the Study

This study was conducted to test whether our new bowel preparation, NER1006, cleans the bowel as well as SP+MS, when given in the same way – in two doses on the day before the colonoscopy. In addition to looking at whether NER1006 cleans the bowel as well as SP+MS, the study was designed to check that it did not have unforeseen side effects.

Study Methods

1) People Included in the Study

Men and women aged between 18 and 85 years old were allowed to take part in this study. They were all going to have a colonoscopy regardless of the study, either as part of a cancer screening programme, because they had had previous signs of cancer, or because they had a bowel problem that their doctor wanted to understand more about.

2) Where the Study was Conducted

A total of 19 hospitals took part in the study. These were in six European countries: Germany, Italy, Netherlands, Poland, Spain and the United Kingdom.

3) Bowel Preparations Used

- a) NER1006 taken as two doses, 1 to 2 hours apart on the evening before the colonoscopy
- b) SP+MS taken as two doses, 6 to 8 hours apart on the day before the colonoscopy

4) Measurements Made

The main aim of this study was to find out whether overall, NER1006 was able to clean the bowel as well as SP+MS. In order to do this the different parts of the bowel were rated for cleanliness using a scale called the Harefield Cleansing Scale.

The Harefield Scale

Using the Harefield Scale, the inside of bowel is assessed in five different places. Each of the five places is given a score as follows:

Score	Doctor's finding
0	Heavy, hard stools are still in the bowel that the doctor is unable to move
1	Stools are still in the bowel but these are only part solid, and some can be removed using the colonoscope
2	There is brown liquid in the bowel, or part solid stools, but it can all be removed with the colonoscope
3	There is clear liquid in the bowel
4	The bowel is empty and clean

A score of 2 in the above table is classed as “adequate”, a score of 3 is classed as “good” and a score of 4 is classed as “excellent”.

When all five parts of the bowel have been given a score of 0 to 4, a final grade of A, B, C or D is given, as shown below. Grades A and B are called “successful cleansings”, because most of the bowel is very clean.

Grade	Description
A	All 5 parts of the bowel were given a score of 3 or 4
B	One or more parts of the bowel were given scores of 2 or higher, and the others got 3 or 4
C	One or more parts of the bowel got a score of 1
D	One or more parts of the bowel scored 0

When all of the colonoscopies had been graded, the number of successful cleansings following the use of NER1006 was compared with the number of cleansings following SP+MS.

As well as testing whether NER1006 works as well as SP+MS, the study looked at how safe the bowel preparation is. In order to do this, the doctors collected information on any side effects that were seen, and recorded whether they were serious or not. They checked on people regularly after they had taken the bowel preparation, measuring their heart rate and blood pressure and doing ECGs. Finally, they took samples to make sure that the bowel preparation had no effect on their blood or urine.

Study Results

1) Number of People Studied

A total of 515 people entered the study, and these were put into one of two groups at random, so that 258 were assigned to NER1006 and 257 were assigned to SP+MS.

2) Bowel Cleansing Success

The number of successful cleansings was almost the same in the two groups. Statistical testing showed that the new bowel preparation NER1006 cleans the bowel equally well as the tried and tested SP+MS. The number of successful cleansings in each group is shown in the table below.

	Number of Successful Cleansings: Harefield Scale
NER1006	155 (62.0%)
SP+MS	135 (53.8%)

In addition, the number of excellent plus the number of good results in one place inside the bowel (the ascending colon) was compared between the two groups. NER1006 had more excellent plus good cleansings in this part of the bowel than SP+MS but the numbers were very low in both groups.

	Number of Excellent plus Good Cleansings in the ascending colon
NER1006	11 (4.4%)
SP+MS	3 (1.2%)

3) Safety Findings

One person had an abscess of the ovary. This person had taken NER1006, and while the abscess was considered serious, it was believed to have been nothing to do with taking the bowel preparation. One person who had taken NER1006 stopped taking the bowel preparation due to vomiting.

A number of people said they felt unwell or had something wrong with them after they had taken the bowel preparation. The things that were complained about most often, that were believed to be caused by the bowel preparation, are shown in the table below.

	Number of People Saying Something was Wrong	Most Commonly Reported
NER1006	28 (11.9%)	Vomiting and nausea
SP+MS	10 (4.1%)	Headache

Blood and urine samples taken at the end of the study were not different from the ones taken before use of the bowel preparations.

Conclusions

This study showed that the new bowel preparation, NER1006, is as good at cleaning the bowel as SP+MS, when taken in the same way as SP+MS (two doses on the day before colonoscopy). Although some people felt a little unwell after taking NER1006, the same can be said of SP+MS. These are direct and obvious effects of drinking a preparation that is intended to empty the bowel.

Further Information

This study is registered on the European Clinical Trials Register (<https://www.clinicaltrialsregister.eu>), EudraCT Number 2014-002186-30 and on the US Clinical Trials Registry (www.clinicaltrials.gov), ID Number NCT02273141.