Efficacy, safety and tolerability of a bowel cleansing preparation (Eziclen®/Izinova®) in paediatric subjects undergoing colonoscopy: a Phase III, multicentre, randomised, comparative study versus Klean-Prep® (PEG-Electrolytes), administered on the day before colonoscopy, Investigator-blinded, non-inferiority in adolescents of 12 to 17 years of age (inclusive) > 40 kg.

Published: 11-05-2017
Last updated: 31-12-2024

Primary objective:To demonstrate that Eziclen, given on the day before colonoscopy has non-inferior efficacy to Klean-Prep on colon cleansing in adolescents aged 12 to 17 years (inclusive) with a body weight > 40 kg, scheduled to undergo a...

Ethical review	Approved WMO
Status	Completed
Health condition type	Gastrointestinal therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON49151

Source
ToetsingOnline

Brief title
EASYKID

Condition

- Gastrointestinal therapeutic procedures

Synonym
Colonoscopy, examination of intestine

Research involving
Human

Sponsors and support

Primary sponsor: Ipsen Pharmaceuticals
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Bowel cleansing, Colonoscopy, Eziclen, Klean-Prep

Outcome measures

Primary outcome

Primary Endpoints and Evaluations concerning efficacy:

Non-inferiority of Eziclen versus Klean-Prep in the cleansing of the colon.

This is determined by the blinded colonoscopist upon finalization of the scopy,

by completion of a questionnaire (Cleansing Score) that is based on a 4-point

scale (Poor, Fair, Good, Excellent cleaning).

Only perfect bowel cleansing (graded as 4 or 3), which allow full, reliable

examination of the mucosa, will be considered as successful.

Primary efficacy will be assessed on the basis of preparation success or

failure.

Secondary outcome

Secondary endpoints and evaluations concerning efficacy:

* Need to place a nasogastric tube to complete preparation;

* Time to clear effluent (from first intake of preparation), as reported by the subject;

* Need for rescue treatment (saline enema) because of inadequate preparation;

* Cleansing Scores assessed by the 4-point scale (poor, fair, good, excellent);

* Overall and segmental Cleansing Scores assessed by Boston Bowel Preparation Scale (BBPS);

* Duration of intubation (from colonoscope introduction to caecal intubation);

* Duration of examination, measured by colonoscope withdrawal time from caecum;

* Procedures documented as completed (procedures that reached the caecum);

* Treatment compliance: volumes ingested as measured by research staff;

* Treatment acceptability, assessed by questionnaire completed by research staff or subject at the time of intake (unacceptable; badly but accepted; neither good nor bad; well accepted; very well accepted).

Secondary endpoints and evaluations concerning safety and tolerability:

* Collection of adverse events for up to 30 days following the day of colonoscopy:

- Diagnosis or diagnostic findings made at colonoscopy will be reported as such and will not be reported as AEs unless the investigator observes mucosal lesions that he/she suspects to be related or possibly

related to the colonic lavage. Such lesions will be biopsied. In this situation only, description of the colonoscopy findings and histological examination results will be reported as AEs.

* Tolerability by a Symptom Scale after each dose of treatment. Subjects will rate their preparation related symptoms after intake (stomach cramping, stomach bloating and nausea) on a 5-point scale (ranging from no symptoms to severely distressing symptoms);

* Description and histological examination of any colonic biopsy specimens of mucosal lesions suspected to have been caused by colonic lavage;

* Vital signs including body weight and physical examination;

* Laboratory data (serum and urinary biochemistry) collected at visit 1, day 2 (colonoscopy) and visit 4.

Study description

Background summary

A wide variety of bowel cleansing preparations prior to a colonoscopy are used in children. These preparations are often poorly accepted due to their unpleasant salty taste and the large volume to be ingested over a relatively short period. As a consequence the preparation may not be taken completely. This affects the quality of the colonoscopy. If the intestine is not completely cleaned, the examination may be incomplete or may last longer because the doctor additionally needs to clean during the examination. It might even that the procedure needs to be repeated. A good preparation is particularly important in children as the examination is conducted under general anaesthesia. Eziclen, the treatment under investigation in this study, is approved in adult patients and on the market in Europe since 2014. It is not yet approved in children. The study is conducted at the request of the European Health Authorities in order to allow prescription of Eziclen to children.

Study objective

Primary objective:
To demonstrate that Eziclen, given on the day before colonoscopy has non-inferior efficacy to Klean-Prep on colon cleansing in adolescents aged 12 to 17 years (inclusive) with a body weight > 40 kg, scheduled to undergo a colonoscopy for a routinely accepted diagnostic indication.

Secondary objectives:
* To compare efficacy of Eziclen versus Klean-Prep on overall and segmental cleansing and colonoscopy quality indicators;
* To assess compliance with preparation administration in both study arms;
* To compare safety, acceptability and tolerability of Eziclen versus Klean-Prep.

Study design

This is a multicentre, phase III, randomized, comparative study between Eziclen and Klean-prep, administered as bowel preparation to adolescents on the day prior to colonoscopy. The investigator will be blinded.

Patients (both male and female and > 40 kg) will be randomized to Eziclen or Klean-prep in a 1:1 ratio.

Patients will be hospitaliozed from (Visit 1, day 1) to completion of colonoscopy (Visit 2, day 2). The duration of the study for each subject will be maximal 47 days:
* Baseline (Visit 1) and treatment administration;
* Colonoscopy (Visit 2) on day 2;
* Phone contact (Visit 3) at Day 4 ±1 day;
* End of Treatment visit (Visit 4) on day 32 (-5/+15 days).

Intervention

In this study, half of the children (i.e. around 125) will receive the study drug (Eziclen) and the other half will receive the comparator treatment (Klean-Prep).

Eziclen is administered as a one-day treatment on the evening before the colonoscopy is performed. The total ingested volume of the Eziclen solution is 750 mL plus 1500 mL water (2250 mL in total). This is 3/4 of the dosis that is used in adults.
Klean-Prep is also administered as a one-day treatment on the evening prior to the colonoscopy takes place in a dose of 70 mL/kg body weight. Depending on his/her weight, the patient will need to drink a volume between 2800 to 4000 mL.

At study visit 1,2 and 4, about 5.5 mL of blood will be collected for safety

testing.

Study burden and risks

Eziclen is, in contrast to Klean-prep, not yet authorized to use for bowel preparation in children. This study is conducted as part of the pediatric investigation plan (PIP) to get this marketing authorisation. The dose of Eziclen used in this study will be 3/4 of the dose that is used in adults. Klean-prep is used as bowel preparation for children in the Netherlands.

Klean-prep and Eziclen have a comparable safety profile. The expected outcome after ingestion is watery diarrhoea.
In adult patients, the most frequently reported adverse reactions for Eziclen (in at least 1 out of 10 patients) are gastrointestinal symptoms such as feeling sick (nausea), being sick (vomiting), abdominal discomfort, cramping or pain, abdominal bloating or distension.
The most common side effects for Klean-prep include gastrointestinal symptoms such as nausea, vomiting, abdominal pain, anal discomfort, abdominal swelling and flatulence.

Recently, a study with Eziclen has been conducted in 29 adolescent patients. The adverse reactions observed were similar in nature to what has been observed in adult patients. Adolescent patients experienced slightly more nausea and vomiting. Reports of preparation related symptoms were generally low with both preparations. More than 75% of subjects reported their symptoms as *none* or *mild*.

During the study, three blood samples are collected (about 16.5 mL in total). Blood sampling may cause pain, discomfort, swelling, bruising (hematoma), fainting or extremely rarely, infection from the needle puncture site. The use of an anaesthetic patch will limit or avoid discomfort and pain. But also may be associated with transient local reactions such as swelling, redness or burning sensation.
The colonoscopy is conducted by using general anaesthesia and if necessary a nasogastric tube can be placed. It might also necessary to administer a clyster. These procedures are standard procedures for a colonoscopy.

Contacts

Public
Ipsen Pharmaceuticals

quai Georges Gorse 65
Boulogne-Billancourt 92100

FR
Scientific
Ipsen Pharmaceuticals

quai Georges Gorse 65
Boulogne-Billancourt 92100
FR

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

Subject MUST satisfy all of the following entry criteria before being allowed to participate in the study:
(1) Provision of signed informed consent form (ICF) to participate in the study obtained from the adolescent's parent(s)/ legal representative and a signed assent form from the adolescent according to local law
(2) Male or female subjects between 12 to 17 years of age (inclusive)
(3) Body weight more than 40 kg
(4) Female of childbearing potential must have a negative pregnancy test
(5) If female, and of child-bearing potential, subject must use an acceptable form of birth control (hormonal birth control, intrauterine device (IUD), double-barrier method, or depot contraceptive)
(6) Routinely accepted indication for undergoing colonoscopy, including but not limited to polyposis coli diagnosis or surveillance, gastrointestinal bleeding, unexplained diarrhoea or constipation, surveillance of inflammatory bowel disease or confirmation of mucosal healing, abdominal pain, abnormal endosonography or manometry, anaemia of unknown aetiology, cancer surveillance
(7) In the investigator*s judgment, the parent(s)/legal representative are/is mentally competent to provide informed consent for the subject to participate in the study
(8) In the investigator*s judgement, subject is able and willing to follow

study procedures including drug administration and response to questionnaires

Exclusion criteria

If any of the following apply, the subject MUST NOT enter/continue in the study:
(1) Subject with known or suspected ileus, gastrointestinal obstruction, gastric retention (gastroparesis), rectal impaction, toxic colitis, severe ulcerative colitis or toxic megacolon, advanced carcinoma, swallowing disorders
(2) Subject with known or suspected inflammatory bowel disease (Crohn*s disease, ulcerative colitis) in moderate to severe active phase defined by PCDAI >30 (Crohn*s disease) or PUCAI >34 (ulcerative colitis)
(3) Subject with bowel perforation or increased risk of bowel perforation, including connective tissue disorders or recent bowel surgery
(4) Subject with previous significant gastrointestinal surgery (e.g. colostomy, colectomy, gastric bypass, stomach stapling)
(5) Subject with uncontrolled pre-existing electrolyte abnormalities, or with electrolyte abnormalities based on Visit 1 laboratory results such as hypernatremia, hyponatremia, hyperphosphatemia, hypokalaemia, hypocalcaemia, uncorrected dehydration, or secondary to the use of medications such as diuretics or angiotensin converting enzyme (ACE) inhibitors judged clinically significant by the investigator
(6) Subject with a prior history or current condition of severe renal (estimated glomerular filtration rate (eGFR) less than 30 mL/min/1.73 m2 as calculated by using the Schwartz bedside equation* [Schwartz et al, 2009]**), liver (ascites, Child-Pugh C), cardiac insufficiency (including congestive heart failure all grades) or hyperuricemia
*The estimated GFR will be calculated in patients with elevated creatinine at baseline.
** Schwartz GJ and Work DF. Measurement and Estimation of GFR in Children and Adolescents. Clin J Am Soc Nephrol. 2009; 4: 1832*1843
(7) Female subject who is pregnant or lactating
(8) Subject who has participated in another investigational drug treatment within the last 90 days before the first study visit
(9) Subject with phenylketonuria
(10) Subject with history of asthma or hypersensitivity to any ingredient of either drug product
(11) Subject for whom intake of substances likely to affect gastrointestinal motility or urinary flow rate is required
(12) Subject with requirement to take any other oral medication within 3 hours of starting the bowel preparation, as this may impact medication absorption
(13) Subject with tendency for nausea and/or vomiting
(14) Subject with impaired consciousness that predisposes them to pulmonary aspiration or who have known swallowing disorders
(15) Subject with history of major medical/psychiatric conditions that, in the judgment of the investigator, would compromise safety in the study

(16) Subject with mental or psychiatric condition rendering the subject unable to understand the nature, scope and possible consequences of the study, and/or evidence of an uncooperative attitude
(17) Subject with a condition that, in the opinion of the investigator, might increase the risk to the subject or decrease the chance of obtaining satisfactory data needed to achieve the objectives of the study
(18) Subject who has previous enrolment in this study or concomitant enrolment in other clinical studies

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-11-2017
Enrollment:	65
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Eziclen/Izinova
Generic name:	Magnesium sulphate heptahydrate, Potassium sulphate, Sodium sulphate anhydrous
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Klean-Prep

Generic name:	Polyethylene Glycol and Electrolytes
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	11-05-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-10-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-11-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-12-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-04-2018
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-08-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2020
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2016-002265-60-NL
CCMO	NL59332.018.17

Study results

Date completed:	29-06-2020
Results posted:	28-01-2021

First publication
23-12-2020