Multicenter observational program HDQ

Protocol N° IC4-05682-063-RUS

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The Russian multicenter observational study «Evaluation of the HDQ for the diagnosis of hemorrhoidal disease».

28/06/2021

Protocol of the Observational Clinical Study

Title of the study: The Russian multicenter observational study “Evaluation of the HDQ for the diagnosis of hemorrhoidal disease.”

Sponsor: JSC “Servier”

Protocol number: IC4-05682-063-RUS

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Non-disclosure agreement

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1 Contents

2 List of abbreviations

ADR	Adverse drug reaction
AE	Adverse event
CI	Confidence interval
FAS	Full Analysis Set
HDQ	Hemorrhoid Disease Questionnaire
ICH E9	ICH E9 guideline “Statistical principles for clinical trials”
ICH	International Conference on Harmonization
LEC	Local ethics committee
MCID	Minimal Clinically Important Difference
MedDRA	Medical Dictionary for Regulatory Activities
OR	Odds Ratio
PT	Preferred Term
SAE	Serious adverse event
SOC	System Organ Classes (classification)

3 Introduction

A long-term painful condition associated with severe physical discomfort, including haemorrhoids, is a powerful stress factor affecting psychological and physiological components of human health.

Nowadays, more than 10% of the adult population of the planet suffer from haemorrhoids, and haemorrhoids account for more than 40% of all cases of the coloproctological diseases (1,2,3). The prevalence of haemorrhoids is 130 to 145 cases per 1000 adult population, and in the group of people of mature and old age it reaches 210 to 240 cases per 1000 population (2,4). Haemorrhoids represent an especially urgent health care concern in terms of impact on the quality of life of the patient (5,6,7).

At the same time, haemorrhoids remains underdiagnosed, which is partly due to the specificity and delicacy of this problem. As a result, the patient often prefers not to see a doctor, but to look for a solution to the problem on the Internet. Patients often underestimate the importance of the symptoms or misinterpret them (bleeding, prolapse, pain).

The HDQ (Hemorrhoid Disease Questionnaire) study was aimed at evaluating a specific diagnostic questionnaire for patients.

4 Aim and goals of the study

Primary goal:

Currently in Russia there is no available self-evaluating tools with appropriate diagnostic accuracy for screening of patients with haemorrhoids. Therefore, the primary objective of this study is to evaluate a new patient specific questionnaire (HDQ) with appropriate sensitivity and specificity to use for screening of patients with haemorrhoids in Russia. Once evaluated, the HDQ will be used in clinical practice for wider screening of haemorrhoids in population and for increasing patients' awareness of the disease and prompting them to seek professional advice.

Secondary goals:

Secondary objectives of the study are

- to describe a prevalence of haemorrhoids among patients in the study

- to describe a prevalence of the symptoms of haemorrhoids among patients in the study

4.1 Main and additional parameters evaluated in the study

Main parameters (primary outcomes) to be evaluated in the study are:

- sensitivity of the HDQ for screening of patients with haemorrhoids;

- specificity of the HDQ for screening of patients with haemorrhoids;

Objective examination by physicians will be made that is required to determine the sensitivity and specificity of the patient's HDQ (for more information on evaluation methodology see Chapter 8).

Additional parameters (secondary outcomes) in the study are:

- Prevalence rate of haemorrhoids among study population established by physicians basing on the results of the objective examination;
- Prevalence of the symptoms of haemorrhoids among patients in the study

4.2 Description of the study design, flowchart, procedures and stages of the study

4.2.1 Description of the study design

The HDQ study is a Russian observational cross-sectional multicenter study. The patients eligible according to the inclusion/non-inclusion criteria will be included in the study only after providing a signed informed consent form.

The study is scheduled for 2021-2022. It is expected that up to 83 proctologists in 60 cities of the Russian Federation will participate in the study. The planned number of patients is 415. Each participating coloproctologist will include approximatively 5 consecutive patients seeking help from a coloproctologist.

All diagnostic procedures, if any, will be carried out as part of routine practice therefore independently from this protocol and at discretion of the investigator.

One visit is scheduled during the study: inclusion visit (V0). The study is cross-sectional study.

4.2.2 Study flowchart

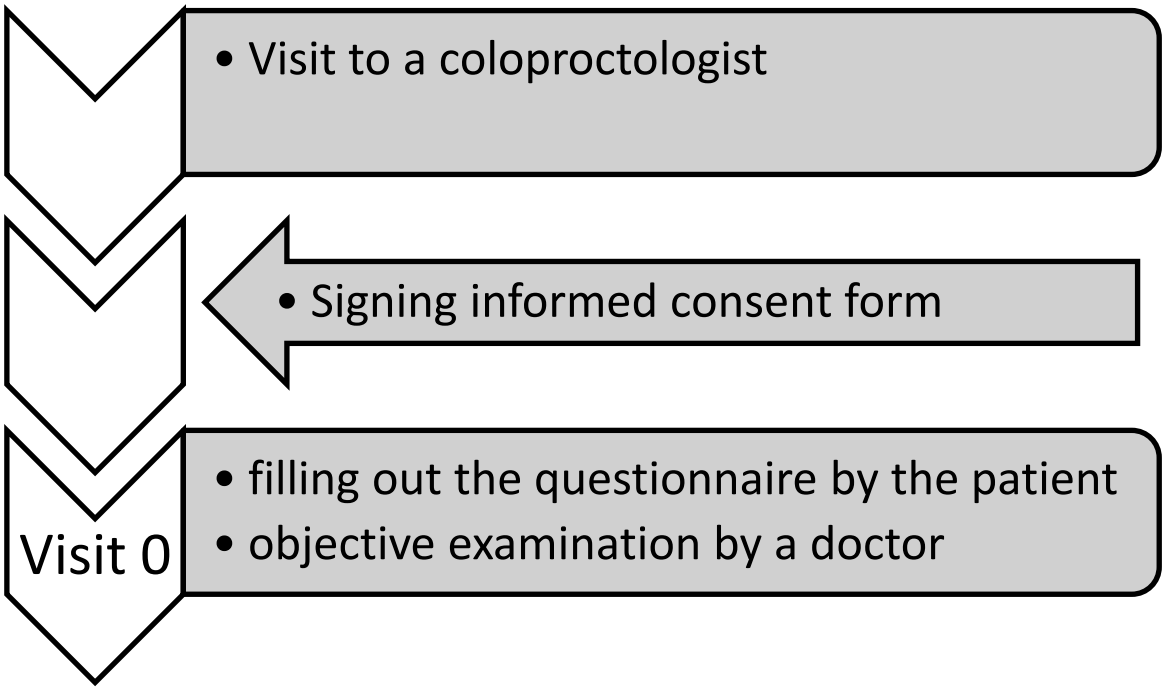

Figure 1 – Study flowchart

4.2.3 Description of the study procedures

The procedures are carried out according to the methods adopted in routine clinical practice. The timing of the procedures is approximate and remains at the discretion of the doctor.

Table 1 – Procedures during the study

Procedures	Visit 0
	Day 0
Eligibility according to inclusion criteria	+
Eligibility according to non-inclusion criteria	+
Informed consent	+
AE collection	+
Filling out the HDQ by the patient	+
Collection of demographic and anthropometric data	+
Collection of medical history (duration of haemorrhoids)	+
Assessment of the clinical symptoms of haemorrhoids (by the investigator) [1]	+

[1] Assessment of the presence of hemorrhoidal prolapse and its severity, the presence of rectal bleeding and its intensity, the presence of anal pain and itching/discomfort

Procedures	Visit 0
	Day 0
Objective examination" (by the investigator)[2]	+

[2] Assessment of the external component of hemorrhoids (the presence of hemorrhoids, thrombosed hemorrhoids, sphincter tone) and the internal component of hemorrhoids (anoscopy, if deemed necessary, to determine a grade of hemorrhoids according to the Goligher's classification, assessment on the Wexner Faecal Continence Grading Scale).

4.2.3.1 Patient HDQ

At Visits 0, all patients will be advised to complete the HDQ prior to examination (see Section 13.2). The HDQ will be used to assess symptoms that prompted the patient to seek help from a coloproctologist:

- prolapse of haemorrhoids after a bowel movement;
- swelling of external haemorrhoids;
- bleeding during bowel movements;
- color of blood when bleeding;
- the presence of pain in the anus;
- the presence of itching/discomfort in the anus;
- frequency of occurrence of the above symptoms.

The data from the HDQ will be the main substrate to achieve the main goal of the study which is to develop a patient questionnaire for the screening of haemorrhoids with appropriate level of sensitivity and specificity.

4.2.3.2 Collection of demographic and anthropometric data, and medical history

At Visit 0, the following data will be collected from all patients:

- gender,
- age (years),
- height (cm),
- body mass (kg),
- duration of haemorrhoids (years).

4.2.3.3 Assessment of the clinical symptoms of haemorrhoids

At Visits 0, the following clinical symptoms of haemorrhoids will be evaluated:

- prolapse of haemorrhoids and its severity;
- rectal bleeding and its intensity;
- anal pain;
- anal itching/discomfort;

4.2.3.4 Objective examination

An objective examination is performed at the discretion of the doctor at Visits 0. It will include:

- assessment of the external component of haemorrhoids:
  - the presence of haemorrhoids;
  - the presence of thrombosed haemorrhoids;
  - assessment of the anal sphincter tone;
- assessment of the internal component of haemorrhoids:

- anoscopy, if necessary, with the determination of the grade of haemorrhoids according to Goligher's classification (see Section 11.2),
- assessment on the Wexner Faecal Continence Grading Scale (see Section 4).

4.2.4 Description of study periods and visits

During the study, the doctor will independently determine the volume of examinations, based on his/her own experience and practice in the clinical center.

4.2.4.1 Inclusion visit (Visit 0) (Day 0)

At Visit 0, the following will be executed:

- Obtaining informed consent. All subsequent procedures will be completed only after obtaining informed consent;
- Eligibility assessment according to inclusion and non-inclusion criteria;
- Filling out the HDQ by the patient (strictly before the examination);
- Collection of demographic and anthropometric data;
- Collection of medical history;
- Assessment of the clinical symptoms of haemorrhoids;
- Objective examination;

Measures to minimize breaching of a non-interventional nature of the study

Due to the observational nature of the study, the allocation of patients to treatment groups is not prespecified by the Study protocol, but is determined by the current practice depending on the clinical situation. The prescription of medicinal products is strictly separated from the decision to include a patient in the study and will be made by a Investigator based on current treatment standards, guidelines.

4.3 Expected duration of a participation of subjects in the study

The study is cross-sectional and involves one visit

4.4 Enrolment and inclusion of the study participants

4.4 Inclusion criteria

The patient's eligibility according to inclusion criteria will be assessed by the following parameters:

1) The patient has symptoms of coloproctological disease;
2) Male or female aged over 18 years;
3) Signed informed consent form to participate in the study has been obtained;

4) Absence of conditions requiring emergency medical care.
5) The patient is not taking VAD for at least 1 month before the date on inclusion to the study

4.5 Non-inclusion criteria:

1) Confirmed or suspected malignant tumor;
2) Diagnosed coloproctological disease at the time of inclusion
3) Severe somatic disorders (of heart and blood vessels, lungs, kidneys, pancreas, or liver), associated with decompensation of organ functions;
4) Mental disorders;
5) Presence of contraindications for examination;

5 Safety considerations

5.1 Definitions

5.1.1 Pharmacovigilance information

Pharmacovigilance data include any unintended or adverse event associated with the use of a medicinal product in humans, whether or not considered drug related, including the following **special situations** (situations where no adverse event occurred but information needs to be collected):

- exposure during pregnancy or breastfeeding;
- overdose, abuse, misuse, off-label uses, medication error, occupational exposure (including professional one), suspected transmission via a medicinal product of an infectious agent, or unexpected beneficial therapeutic effect;
- lack of efficacy of drug.

5.1.2 Adverse Event (AE)

Adverse event is any untoward medical occurrence in a patient or a clinical-trial subject who received the medicinal product, which does not necessarily have a causal relationship with the use of this medicinal product.

An adverse event can therefore be any unfavourable and unintended sign (e.g. an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

5.1.3 Adverse (drug) reaction (ADR)

Adverse reaction (synonyms: Adverse drug reaction, Suspected adverse (drug) reaction, Adverse effect, Undesirable effect) is a response to a medicinal product which is noxious and unintended.

“Response” in this context means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility.

Adverse reactions may arise from use of the product within or outside the terms of the marketing authorization or from occupational exposure. Conditions of use outside the marketing authorization include off-label use, overdose, misuse, abuse and medication errors.

5.1.4 Serious adverse (drug) reaction (SADR)

Serious adverse reaction is an adverse reaction, which results in death, is life-threatening, requires in-patient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly/birth defect.

“Life threatening” in this context refers to a reaction in which the patient was at risk of death at the time of the reaction; it does not refer to a reaction that hypothetically might have caused death if more severe.

Medical and scientific judgement should be exercised in deciding whether other situations should be considered serious reactions, such as important medical events that might not be immediately life threatening or result in death or hospitalisation but might jeopardise the patient or might require intervention to prevent one of the other outcomes listed above.

Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation or development of dependency or abuse.

Any suspected transmission via a medicinal product of an infectious agent is also considered a serious adverse reaction.

5.2 Responsibilities

5.2.1 Events to be reported

Not applicable

5.2.2 Responsibilities of the Investigator

Not applicable

5.2.3 Responsibilities of the Sponsor/Marketing Authorisation Holder

Independently of the regulatory obligations of treating physician, the Sponsor/Marketing Authorisation Holder must report the pharmacovigilance data to the appropriate authorities in accordance with the Good Vigilance Practice and local regulations.

Cases are closed when an adverse event has recovered, or patient's condition was stabilised and the report is deemed sufficiently detailed for adequate medical analysis of the case.

6 Statistical analysis

6.1 Description of statistical methods

Statistical analysis will be performed in accordance with ICH (International Conference on Harmonization) E9 Guidelines "Statistical Principles For Clinical Trials". To perform statistical analysis, specialized software will be used, the selection of which will be carried out at the stage of preparing the statistical analysis plan.

Errors and inconsistencies in the data will be identified and corrected at the stage of medical data analysis by the Data Manager, before the preparation of the statistical analysis plan.

This section briefly describes the planned analysis. A complete analysis will be described in the statistical analysis plan, which will be finalized before the database closure. Differences were considered statistically significant at P value <0.05. The P values will be presented in the report with an accuracy of hundredths if P ≥0.05 and with an accuracy of thousandths if P <0.05.

Quantitative parameters will be described using the number of cases, mean, standard deviation, 95% confidence interval (CI) for the mean, median, interquartile range (IQR) in the form of two figures (25% -75%), and the minimum and maximum values.

Qualitative parameters will be described using the absolute number of cases, proportion (in percentage), and two-sided 95% CI for proportions.

Methodology to calculate the HDQ Sensitivity (Se) and Specificity (Spe) will be elaborated in the statistical analysis plan that will be developed later during the study conduction. However, it is worth noting that a cross tabulation method followed by calculations of Se and Spe with utilization of the following formulas will be used:

Questionnaire result	Subjects with the disease	Subjects without the disease
Positive	Yes (True positives – TP)	No (False positives – FP)
Negative	Yes (False negatives – FN)	No (True negatives – TN)
Total	TP + FN	FP + TN

$$Se = \frac{True\ positives\ (TP)}{True\ positives + False\ negatives\ (TP + FN)}$$

$$Spe = \frac{True\ negatives\ (TN)}{False\ positives + True\ negatives\ (FP + TN)}$$

The choice of statistical tests for comparisons between groups will be made based on the type of parameter. For quantitative parameters, the choice of test will be based on the results of checking the normality of distribution using the Shapiro-Wilk test. For qualitative parameters, the choice of test will depend on the size of the cross table.

Adverse events will be encoded using the Medical Dictionary for Regulatory Activities (MedDRA), version 23.0 or higher, in Russian, with aggregation of preferred terms (PT) by System Organ Classes (SOC).

According to ICH E9 guidelines, safety data will be presented only in descriptive form, and no testing of statistical hypotheses is planned.

6.1.1 Demographic, baseline characteristics

Demographic, baseline, and characteristics will be described in the Full Analysis Set (FAS). The list of descriptive statistics will depend on the type of variable.

Quantitative parameters will be described using the number of cases, mean, standard deviation, 95% CI for the mean, median, interquartile range in the form of two figures (25% -75%), and the minimum and maximum values.

Qualitative parameters will be described using the absolute number of cases, proportion (in percentage), and two-sided 95% CI for proportions.

The choice of statistical tests for comparisons between groups will be made based on the type of parameter. For quantitative parameters, the choice of test will be based on the results of checking the normality of distribution using the Shapiro-Wilk test. For qualitative parameters, the choice of test will depend on the size of the cross table.

6.1.2 Safety analysis

Not applicable

6.1.3 Analysis of the correlation between the parameters of the HDQ and the presence of haemorrhoids in the patient

To develop the HDQ for patients, a search will be made for linear and non-linear correlations between the parameters of the HDQ and the evidence of haemorrhoids confirmed or excluded by the objective examination in patients included in the study.

This analysis will include patients of the FAS. The patients with a diagnosis of haemorrhoids with or without concomitant coloproctological diseases will be considered as “positive” (outcome: 1),

while patients with other coloproctological diseases without the diagnosis of haemorrhoids will be considered as “negative” (outcome: 0).

The search for correlations between the evidence of haemorrhoids and following parameters of the HDQ will be carried out:

- status (present/ not present) of prolapsed haemorrhoids after a bowel movement;
- characteristics of the haemorrhoids reduction (spontaneous reduction, manual reduction, non-reducible haemorrhoids);
- status of swelling of the external haemorrhoids;
- status of bleeding during bowel movement;
- the intensity of bleeding during bowel movements (mild, moderate, severe);
- color of blood during bleeding (bright red, dark red);
- status of anal pain;
- status of itching/discomfort pain;
- the incidence of haemorrhoid symptoms at the time of assessment (prolapsed and enlarged haemorrhoids, bleeding, anal pain/itching/discomfort).

To search for correlations between the mentioned above parameters of the HDQ and the evidence of haemorrhoids, a test sample will be formed from the FAS. The possibility of forming the test sample will be determined before the statistical analysis plan development.

6.1.3.1 Search for linear relationships

The search for linear relationships will be performed by construction of linear regression models. The results of search will be provided for each parameter in the form of:

- the number of completed cases used to build the model;
- correlation coefficient with indication of the correlation test;
- F-test values for the model;
- P value for the model;
- P value for the intercept term;
- P value for the covariate;
- the proportion of variance of the dependent parameter attributable to the covariate (η^2, %);
- the linear regression graph.

Additionally, each statistically significant linear relationship will be described with a linear regression equation:

$y = ax + b$,

where *y* is the fact of haemorrhoids, *x* is the HDQ parameter, *a* is the coefficient of the HDQ parameter, *b* is the intercept term of the equation.

6.1.3.2 Search for nonlinear relationships

The search for nonlinear relationships will be performed by the creation of logistic regression models. The results of search will be provided for each parameter of the HDQ in the form of:

- values of the χ2 test for the model;
- P value for the model;
- P value for the independent variable (predictor) in the model;
- the logistic regression graph;
- odds ratio (OR) the independent variable (predictor);
- sensitivity of the model;
- specificity of the model;
- ROC-curve graph;
- cut-off threshold for model evaluation;
- area under the ROC-curve (AUC).

Additionally, each statistically significant nonlinear relationship will be described by a logistic regression equation of the form of:

$$y = \frac{exp^{logit}}{(1+exp^{logit})},$$

where *y* is the fact of haemorrhoids, *exp* is the exponent, the base of the natural logarithm, *logit* is an equation of the form *ax* + *b*, where *x* is the HDQ index, *a* is the coefficient of the HDQ index in the equation, and *b* is the intercept term of the equation.

6.1.3.3 Development of the diagnostic questionnaire and its evaluation

Based on the results of linear and non-linear relationships, all parameters of the HDQ that showed statistically significant relationships with the confirmed presence of haemorrhoids will be selected. These parameters and the corresponding questions of the HDQ will be finally included in the diagnostic HDQ.

Scores to assess answers to the HDQ questions will be obtained by discretization, a process of conversion of the coefficients of corresponding HDQ parameters from linear/logistic regression equations into a discrete form.

The discretization method will be defined and described in the statistical and final reports. To obtain scores, either linear or non-linear models will be used. The choice between the type of

models for this purpose will also be made while performing a statistical analysis and described in statistical and final reports.

As a next step, a *post hoc* analysis of answers to HDQ questions obtained at Visit 0 will be performed for each patient in the FAS. In this analysis scores derived from the previous step of the statistical analysis will be used to, eventually, obtain a total score of the questionnaire for each patient.

To determine a threshold value of the total score an excess of which will indicate a presence of haemorrhoids in a particular patient, the relationship between the total score and the fact of haemorrhoids will be carried out using logistic regression.

A total score corresponding to the threshold value produced in the logistic regression model will be used then as a threshold score in the HDQ.

Conclusion on a diagnostic accuracy of the developed HDQ will be made based on sensitivity and specificity assessments during the analysis of the ROC curve of the resulting model.

Evaluation of the obtained HDQ will be carried out at least on the initial (training) data. If it is possible to create a “training” sample, evaluation will also be carried out on the “training” sample data.

6.1.4 Interim analysis

An interim analysis is not planned.

6.2 Planned number of subjects

This study is observational by nature, therefore, there is no formal statistical hypothesis for testing. Nevertheless, the study should be sufficiently powered to obtain results as close as possible to the general population.

To create a questionnaire for the diagnosis of haemorrhoids, a sample is required containing both patients suffering from haemorrhoids and patients who do not have this nosology. Therefore, the calculation of the sample size was based on data on the prevalence of haemorrhoids in the population.

The prevalence of haemorrhoids in the population of coloproctological patients who came to the coloproctologist is from 35% to 41% (8); and the average prevalence is 38%.

The calculation of the sample size was carried out on the basis of the following assumptions:

- estimated prevalence of haemorrhoids in the population of coloproctological patients who came to the coloproctologist (p_0) is 38%;
- error margin (ε, half the width of the CI) is 5% (0.05);
- type I error rate (α) = 5% (0,05);
- confidence level (1-α) = 95% (0,95);

- expected withdrawal during the study is 10%.

Therefore, the purpose of the calculation was to find a sample size at which, with a type I error of 5% and an estimated prevalence of haemorrhoids of 38%, the confidence interval for the actual prevalence of haemorrhoids in a population of coloproctologic patients contacting a coloproctologist would be within 33% to 43%.

The calculations were made using the Agresti-Coull equation in accordance with Walter W. Piegorsch, 2004 (9):

$$n = \frac{Z_{\alpha/2}^2 \times p_0 \times (1-p_0)}{\varepsilon^2} - Z_{\alpha/2}^2 ,$$

where n is sample size;

α – type I error rate,

$Z_{\alpha/2}$ – value of the normal distribution function for the set α;

p_0 – estimated proportion of haemorrhoids in the population;

ε – error margin (half the width of the CI).

The calculations were performed using the programming language R version 3.6.1 and the package "binomSamSize" version 0.1-5.

Based on the above assumptions, with the α level set at 5%, an estimated prevalence of haemorrhoids at 38%, and an error margin of 5%, the minimum sample size at which 95% CI for the actual prevalence of haemorrhoids in the study population will be within 33% to 43%, will be 373 people. Taking into account the premature withdrawal from the study of up to 10% of patients, a total of 415 persons should be included in the study.

6.3 Level of significance used

In all statistical tests, a significance level of 5% will be used. In all cases, two-sided statistical tests will be used.

6.4 Criteria for termination of the study

not applicable

6.5 Procedures for handling missing, inaccessible and doubtful data

Details of work with missing data will be described in the data management plan, which will be finalized before the start of the clinical phase of the study. Methods of working with missing data at the stage of statistical analysis will be described in the statistical analysis plan, and the refinement of methods can be carried out at the stage of data analysis by biostatistics during the development of a statistical analysis plan.

6.6 Procedures for reporting any deviations from the original statistical analysis plan

The decision to modify the statistical plan presented in this protocol can be made by the Sponsor.

All changes in the initial statistical plan with their justification will be described in the final report of the clinical trial.

6.7 Selection of study participants for the analysis

6.7.1 Full Analysis Set (FAS)

Full Analysis Set (FAS) will consist of all patients included in the study.

6.7.2 Safety population

Not applicable

7 Ethical considerations (The Independent Interdisciplinary EC of Russian Academy of Medicine Science)

The study will be conducted in accordance with the principles set forth in the Helsinki Declaration (version adopted in Fortaleza, Brazil, in 2013).

Patients will be fully informed of the study, and written consent will be obtained from them to participate in the study. Investigator must confirm in the CRF that the patient's information consent has been obtained. "Informed consent" also means conducting an individual interview with the patient about the content of the interview and examination that are planned to be conducted.

Confidentiality of patient data will be ensured by using identification code (ID) numbers made up of an individual three-digit investigator's code and a two-digit patient serial number in the center, separated by a hyphen (for example, doctor ID is "001", patient serial number in the center is "03", and the patient ID is "001-03").

The relation between the ID and the identity of the patient will be known only to Investigator ensure the anonymity of patients.

8 Data collection

Please inform patients of their participation in this survey using the Patient Information Sheet attached to this file. All CRFs filled out will be sent to Servier. Data anonymity is guaranteed.

9 Results

The data obtained will be used to generate a study report under the supervision of independent scientific experts.

10 Publication of results

Any manuscript containing the results of this study must be submitted to Servier for review before being submitter to print. Servier reserves the right to ask for modifications, if necessary.

11 References

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11.1 Appendix 1.

Patient questionnaire for completion at Visit 0

Date of completion: ____/____/_____ (DD.MM.YYYY)

№	Symptoms		Patient's answers
I	Do you have a prolapsed (dropping out) haemorrhoid after a bowel movement? If «Yes», please indicate one of the following options:		Yes ☐2 No ☐1
1.	Does the prolapsed (dropping out) haemorrhoid reduce spontaneously after a bowel movement?		☐2
2.	Does the prolapsed (dropping out) haemorrhoid require manual reduction after a bowel movement?		☐4
3.	Are the prolapsed (dropping out) haemorrhoids not reducible after a bowel movement?		☐6
II	Is there a swelling of the external haemorrhoids?		Yes ☐2 No ☐1
III	Do you have bleeding during bowel movements? If «Yes», please indicate one of the following options:		Yes ☐2 No ☐1
1.	Mild (blood on the toilet paper)		☐2
2.	Moderate (small amounts of blood visible in the toilet bowl)		☐4
3.	Severe (big amounts of blood visible in the toilet bowl)		☐6
IV	What color is the blood when bleeding?	Bright red	☐4
		Dark red	☐2
V	Do you notice pain in the anus?		Yes ☐1 No ☐2
VI	Do you notice itching/discomfort in the anus?		Yes ☐2 No ☐1
VII	How often the following symptoms occur now (prolapse and swelling of the haemorrhoids, bleeding, pain/itching/discomfort in the anus)? Please choose one of the following options:		
1.	Never ☐0 Rarely ☐1 Sometimes ☐2 Regularly ☐3 Always ☐4		

11.2 Appendix 2

Classification of Chronic Haemorrhoids According to Goligher

Grade	Symptoms and signs
1	Bleeding, no prolapse
2	Internal haemorrhoids prolapse, but reduce spontaneously, with or without bleeding
3	Internal haemorrhoids requiring digital reduction, with or without bleeding
4	Prolapse, cannot be reduced, with or without bleeding

11.3 Appendix 3

Wexner Faecal Continence Grading Scale

Type of incontinence	**Frequency**				
	Never	Rarely	Sometimes	Usually	Always
Solid	___0	___1	___2	___3	___4
Liquid	___0	___1	___2	___3	___4
Gas	___0	___1	___2	___3	___4
Wears pad	___0	___1	___2	___3	___4
Lifestyle alteration	___0	___1	___2	___3	___4
Total (summary score):					

Scores: Never, 0; Rarely, <1/month; Sometimes, <1/week, 1/month; Usually, <1/day, 1/week; Always, 1/day.