Informed Consent Form to Participate in the Clinical Study

Study Title:

Single center, Open Label, controlled Study to assess the safety & efficacy of Oral Ciprodiazole ® tablets (Ciprofloxacin/Metronidazole) versus currently used Ciprofloxacin tablets & Metronidazole tablets in pelvi-abdominal infections and following IV antibiotics in post-operative period, for pelvi-abdominal surgeries or acute conditions

Researchers:

Dr.: Ahmed Farag El kased
Dr.: Fatma Ibrahim Youssef

Study Objectives:

Primary Objectives:

1- Primary safety:

- To compare safety of oral Ciprodiazole ® tablets (Ciprofloxacin/Metronidazole) versus currently used Ciprofloxacin tablets & Metronidazole tablets for pelvi-abdominal infections, either non-operative or post-operative following IV antibiotics.

2- Primary efficacy:

- To compare efficacy of oral Ciprodiazole ® tablets (Ciprofloxacin/Metronidazole) versus currently used Ciprofloxacin tablets & Metronidazole tablets for pelvi-abdominal infections, either non-operative or post-operative following IV antibiotics.

Secondary Objectives:

1- Secondary safety:

- Presence of any signs/symptoms of post-operative wound infection such as redness, fever or wound discharge.
- Presence of undesirable effects on total leukocyte count and liver enzymes (SGOT & SGPT)

2- Secondary efficacy:

- To compare the complete resolution or improvement of pelvi-abdominal infection between ciprodiazole® versus combined treatment, based on pelvi-abdominal ultrasound and others and/or clinical response.
- To compare the days for complete healing of post-operative wounds between ciprodiazole® versus combined treatment

Study Procedures to be performed on the patient:

Your health status will be examined, and if found eligible in accordance with the inclusion/exclusion criteria of the protocol and you are willing to participate in the study; the Sponsor will be responsible for providing the medicinal drugs; either Ciprodiazole® tablets or Ciprofloxacin tablets & Metronidazole tablets to the patient in a quantity enough to be used till the end of the study in addition to sponsoring all the required study procedures (Lab tests, pelvi-abdominal Ultrasound and others).

Blood samples will be collected and tested, pelvi-abdominal Ultrasound and other examinations (if required) will be done in addition to be sure that prescribing the study medications will be beneficial to the patient and will not worsen the patient's status.

Study Visits:

This study consists of: Screening & treatment initiation visit (Visit 1 - Day 0), Follow-up V1: Day 8 (+/-) 3 days , and Follow-up V2 (End of Study Visit): Day 15 (+/-) 3 days for all patients

Visit 1 (Screening & treatment initiation visit - Day 0):

During this visit: you will be informed about the study. If you are willing to participate in the study, you will sign the written Informed Consent or finger print and a witness will sign that you are willing to participate in the study. You will be evaluated for study eligibility according to the inclusion and exclusion criteria.

- Screening Assessments will include: physical examination, vital signs, medical history, current disease status, concomitant medications and demographic data (age & gender)
- Presence of any signs/symptoms of post-operative wound infection such as redness, fever or wound discharge will be recorded (in case of post- operative subjects)
- Lab results to be checked for: Hematology (Total leukocyte count), Blood Chemistry (FBS, ALT, AST, Total Bilirubin, and serum creatinine), and Serum β-HCG for females of child bearing potential only.
- Pelvi - Abdominal Ultrasound and other examinations (if required) will be performed.
- Child-Pugh Score will be calculated for liver impairment patients
- You will be instructed how to contact your Investigator immediately if any medical problem or emergency occurred. All concomitant medications and any AEs whether serious or non-serious and whether it is related to the study drug or not will be recorded.

The study population consists of 312 patients with pelvi-abdominal infection will be randomized by computer system into 2 groups:

1. Group A will receive Ciprodiazole ® (156 patients)
2. Group B will receive Ciprofloxacin tablets & Metronidazole tablets (156 patients)

- You will be administered either Ciprodiazole ® tablets (Ciprofloxacin & Metronidazole) or Ciprofloxacin tablets & Metronidazole tablets. Ciprodiazole ® tablets and Ciprofloxacin tablets will be taken 1 tablet every 12 hours, while Metronidazole tablets will be taken 7 .5 mg/kg every 6 hours (approx. 500 mg for a 70-kg adult every 6 hours), for a duration not exceeding 15 days, according to the investigator's decision. Sufficient medications will be given to you for the next 8 days and it could be kept in room temperature (max 30˚C).
- You will be asked to come after 8 days and bring empty blisters of all medicinal products received, with window of 3 days. You will be asked to contact the investigator and inform him/her about any SAE that may occur during the next 8 days, whether it is related to the study drug or not

Follow Up 1 Visit (Day 8):

The following procedures will be done during this visit:

- You will undergo through general physical examination, and vital signs.
- Complete resolution, improvement, failure or, relapse of pelvi- abdominal infection will be recorded.
- Presence of any signs/symptoms of post-operative wound infection such as redness, fever or wound discharge will be recorded (in case of post- operative subjects)
- Number of days for complete healing will be recorded.
- Checking if any AE or SAEs happened and recording them in their separate forms. Any changes in concomitant medication, illness and treatment will be recorded.

- A new lab request will be provided to you, with the required lab tests for the next visit
- Empty blisters for the past 8 days will be collected and recorded in the accountability form.
- Improved patients will finish their participation in study and Study Completion Form will be completed
- Non-improved patients will be administered either Ciprodiazole ® tablets or Ciprofloxacin capsules & Metronidazole tablets. Ciprodiazole ® tablets and Ciprofloxacin tablets will be taken 1 tablet every 12 hours, while Metronidazole tablets will be taken 7 .5 mg/kg every 6 hours (approx. 500 mg for a 70-kg adult every 6 hours), according to the investigator's decision. Sufficient medications will be given to you for the next 8 days and it could be kept in room temperature (max 30˚C).
- You will be asked to come after 8 days (Day 15) for follow up, and bring empty blisters of all medicinal products received, with window of 3 days. You will be asked to contact the investigator and inform him/her about any SAE that may occur during the next 8 days, whether it is related to the study drug or not
- It could be the end of treatment for some subjects; In case of complete resolution, end of the study lab testing will be asked and recorded and End of the study form will be completed.

Follow Up 2 Visit (End of Study visit – Day 15):

It is the end of study visit for all patients.

The following procedures will be done during this visit:

- You will undergo thorough general physical examination and vital signs.
- Complete resolution, improvement, failure or, relapse of pelvi- abdominal infection will be recorded
- Presence of any signs/symptoms of post-operative wound infection such as redness, fever or wound discharge will be recorded (in case of post- operative subjects)
- Number of days for complete healing will be recorded
- Checking if any AE or SAEs happened and recording them in their separate forms. Any changes in concomitant medication, illness and treatment will be recorded.

  Pelvi-abdominal Ultrasound and other examinations (if required) will be done.
- Lab results to be checked for: Hematology (Total leukocytes count), Blood Chemistry (ALT, AST, Total Bilirubin, and serum creatinine).
- Empty blisters for the past 8 days will be collected and recorded in the accountability form, for the non-improved patients.
- The study completion form will be completed.

Requested from the Patient:

1- To understand and agree to comply with the prescribed dosing regimens and procedures, report for regularly scheduled study visits, and reliably communicate.
2- To store the study drugs at room temperature up to 30 degrees C, to keep them in the original containers and to store away from heat, moisture, light and children.
3- You should come to the site every 8 days till end of the study; with a window of 3 days before/after the date of visit and should bring all the empty and/or partially used blisters that were taken in the previous visit.

4- You should inform the investigator about any untoward or unusual event that occurred since last visit, whether you believe it is related to the study drug or not
5- You should inform the investigator if he/she had taken any concomitant medications between the visits

Study Duration: 12 months

- The screening and treatment period is planned to be 12 months including the screening visit.
- Follow up will be 15 days from enrolment till End of treatment.

Study Population:

312 Egyptian Patients with pelvi-abdominal infection or started IV antibiotics in post-operative period, for pelvi - abdominal surgeries or acute conditions will be enrolled from the surgical department in Menoufia University Hospital and some patients might be referred from other departments in Menoufia University Hospital such as and not limited to; the department of Gynecology and Obstetrics

Expected Risks and side effects:

The most frequently reported side effects of ciprofloxacin are nausea, diarrhea, liver function tests abnormality, vomiting, and rash.

The most common side effects of Metronidazole are allergic reactions such as skin rash, swelling of the face, lips, tongue or throat, fever or difficulty in breathing.

Benefits of participating in the study:

Ciprodiazole® (Ciprofloxacin & Metronidazole) is active against a broad spectrum of aerobic/anaerobic bacteria. So, it is indicated in pelvi-abdominal infections and/or following IV antibiotics in post-operative period, for pelvi-abdominal surgeries or acute conditions and so follow up for the drugs available in the market to assess its safety and efficacy after long duration in the market.

Personal Benefit for the participant:

The patient's status will be examined, and if found eligible to the study in accordance with the inclusion and exclusion criteria; the Sponsor will be responsible for providing the medicinal drugs to the patient in a quantity enough to be used till the end of the study, in addition to sponsoring all the required study procedures (Lab tests, Pelvi-abdominal Ultrasound and other examinations if required).

Privacy of the Participant and data confidentiality: Yes

Voluntary Participation:

This Informed Consent Form is to be signed and dated by all patients. In case the patient can't read or write, he/she will finger print in the presence of a witness who'll also sign prior undertaking any study related procedures.

The patient should sign/agree to participate without any pressure or unduly influence from the treating doctor or the witness.

In case the patient refused to participate, there will not be any penalty, and he/she will have the right to complete your treatment as you used to.

Compensation:

There is no financial reward or compensation for your participation in the study. In case of trial related injuries or harms, patients will be supported by insurance certificate provided to all patients.

The right of withdrawal:

The patient has the right to withdraw from the study at any time.

In Case the patient refused to participate:

Patient shall have the right to receive his/her treatment as planned and will be followed up

Signing this document will not prevent you to get any of your legal rights, and also it doesn't give the right to the sponsor or the participating physicians to leave their responsibilities

- **For more information regarding the study you can contact:**

  Dr.: Ahmed Farag **Tel:** 01006639418

- **In case you had any health problems as a result of participating in the study, you can contact:**

  Dr.: Fatma Ibrahim Youssef **Tel:** 01091400575

  Or, you can go directly go to Menoufia University Hospital

- **In case you have any other complain, please contact the Ethics Committee office:**

  Tel:

If you are willing to participate in this study, please make a sign in the appropriate place below:

___ All information in this agreement has been explained.

___ I have read and understood all the information mentioned in this agreement.

Name of the Participant_____

Participant's signature:_____

Date:_____

Witness for the agreement procedures:_____

Witness Signature:_____

Investigator's Signature:_____

Date:_____

This document will not be approved unless it has the stamp of the Ethics Committee.

Valid from: -/-/201- till -/-/201-

A copy of the informed consent to be given to the participant and the original to be kept with the Principal investigator.