

# Does oral colistin (antibiotic) eradicate extensively drug-resistant bacteria (Klebsiella) from the gastrointestinal tract?

<b>Submission date</b> 11/01/2023	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 12/01/2023	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 25/09/2023	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Infections caused by carbapenem-resistant *Klebsiella pneumoniae* (CRKP) bacteria are common, difficult to treat with extremely limited antimicrobial options, and are associated with high death rates. These infections present an everyday clinical challenge to patients and their families, physicians, and health systems alike.

Decolonization therapy (DT) using oral non-absorbable colistin (an antibiotic) might be useful as a tool for preventing invasive bloodstream infections by CRKP in high-risk situations such as in intensive care, high dependency, and hematology units. The exact benefits and potential risks of oral colistin use are largely unknown.

This study aims to examine the impact of short-term use of oral colistin on the eradication of CRKP and the prevention of invasive bloodstream infection by this organism. The purpose is to investigate whether oral colistin eradicates *Klebsiella* from the gastrointestinal tract and whether this impacts the risk of invasive bloodstream infection by this organism.

### Who can participate?

Patients aged 18 years and over admitted to intensive care, high dependency, and hematology wards at Sultan Qaboos University Hospital (Oman) during the study period who are colonised with CRKP (colistin susceptible)

### What does the study involve?

This study will be conducted during the participants' hospitalization. The participants' discharge from the hospital shall not be affected by the study.

The treatment approach being investigated in this study differs from the standard treatment offered in this institution which is a "no decolonization strategy". Participants will be given oral colistin or placebo four times per day for 7 days. Rectal swabs will be performed on day 7 after the end of treatment or placebo.

### What are the possible benefits and risks of participating?

This study aims to further medical knowledge and may improve future strategies to prevent invasive disease by this difficult-to-treat bacterium. This research intervention may also directly

benefit the participants but it is not known for certain at this point. Potential risks include hypersensitivity to colistin and possibly gastrointestinal side effects such as nausea, vomiting, diarrhea, and abdominal pain, and the development of colistin resistance.

Where is the study run from?

Sultan Qaboos University Hospital (Oman)

When is the study starting and how long is it expected to run for?

July 2022 to September 2024

Who is funding the study?

Sultan Qaboos University (Oman)

Who is the main contact?

Dr Abdullah Balkhair, balkhair2020@gmail.com

## Contact information

### Type(s)

Principal investigator

### Contact name

Dr Abdullah A Balkhair

### ORCID ID

<https://orcid.org/0000-0001-6911-5568>

### Contact details

Mazoun Street Al hail South

Muscat

Oman

111

+968 (0)243404

balkhair2020@gmail.com

## Additional identifiers

### Clinical Trials Information System (CTIS)

Nil known

### Protocol serial number

IG/MED/MEDE/23/03

## Study information

### Scientific Title

Eradication of carbapenem-resistant *Klebsiella pneumoniae* gastrointestinal colonization and prevention of secondary bloodstream infections with oral colistin

### Acronym

CRKP-CoIDT

### **Study objectives**

This study aims to examine the impact of decolonization therapy (DT) using oral colistin on the eradication of CRKP (carbapenem-resistant *Klebsiella pneumoniae*) and the prevention of invasive bloodstream infection by this organism. It is hypothesized that oral colistin will result in a reduction in carriage, attributable and all-cause mortality, and incidence of invasive infection caused by CRKP.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 08/11/2022, Medical Research Ethics Committee (MREC) College of Medicine & Health Science, Sultan Qaboos University (PO Box 35, Al Khodh, 123, Oman; +968 (0)24143427; mrec@squ.edu.om), ref: SQU-EC/232/2022, MREC #2918

### **Study design**

Double-blind placebo-controlled trial with balanced (1:1) randomization

### **Primary study design**

Interventional

### **Study type(s)**

Treatment

### **Health condition(s) or problem(s) studied**

Eradication of carbapenem-resistant *Klebsiella pneumoniae* gastrointestinal colonization and prevention of invasive bloodstream infection by this organism

### **Interventions**

Current intervention as of 09/05/2023:

Active screening of eligible patients for gastrointestinal colonization with CRKP will be performed by way of rectal swabs according to the hospital's standard operation procedures.

Eligible patients with a positive screening rectal swab for CRKP (colistin susceptible) and who are able to provide informed consent will be randomized by single sequence simple randomization to one of two arms:

Intervention arm:

Selective gastrointestinal decolonization with oral colistin [dose: 2 million units QID for 7 days].

Placebo [control] arm:

5 ml of sterile water for injection preparation QID for 7 days

Patients in both arms will be assessed at baseline and on day 7 after the end of treatment. At each time point, rectal swabs will be performed. The pre-defined primary outcome of the study was the detection of gastrointestinal CRKP carriage by a rectal swab at day 7 post-treatment (rate of eradication of CRKP at day 7 post-treatment). CRKP bacteremia, CRKP attributable death, and change in colistin MICs between baseline and day 7 after end of treatment will be assessed.

---

Previous intervention:

Active screening of eligible patients for gastrointestinal colonization with CRKP will be performed by way of rectal swabs according to the hospital's standard operation procedures.

Eligible patients with a positive screening rectal swab for CRKP (colistin susceptible) and who are able to provide informed consent will be randomized by single sequence simple randomization to one of two arms:

Intervention arm:

Selective gastrointestinal decolonization with oral colistin [dose: 2 million units QID for 7 days].

Standard of care [control] arm:

No interventions ("watch and wait" strategy).

Patients in both arms will be assessed at baseline, on the last day of treatment (day 7), on days 14 and 28 after the end of treatment, and subsequent admissions within 6 months (when applicable). At each time point, rectal swabs will be performed. The pre-defined primary outcome of the study was the detection of gastrointestinal CRKP carriage by a rectal swab during day 28 post-treatment (rate of eradication of CRKP at day 28 post-treatment). CRKP bacteremia, CRKP-attributable death, and change in colistin minimal inhibitory concentrations (MICs) between baseline and day 28 after the end of treatment will be assessed.

### **Intervention Type**

Drug

### **Phase**

Not Applicable

### **Drug/device/biological/vaccine name(s)**

Colistin (colistin sulphate) for oral use

### **Primary outcome(s)**

Current primary outcome measure as of 09/05/2023:

CRKP eradication: Eradication [clearance] rate of CS-CRKP assessed by culture positivity of rectal swabs for CRKP at day 14 [day 7 post Rx]

---

Previous primary outcome measures:

1. Eradication of CRKP assessed by culture positivity of rectal swabs for CRKP at day 28 post-intervention
2. CRKP bloodstream infection (bacteremia) assessed by blood culture for 28 days post-intervention
3. CRKP-related death will be captured by active follow-up of patients in both groups during hospitalization and for 28 days, whichever is longer

### **Key secondary outcome(s)**

Current secondary outcome measure as of 09/05/2023:

1. Incidence of CS-CRKP bacteremia during the same hospitalization
2. In-hospital all-cause mortality during the same hospitalization

3. Incidence of colistin resistance in positive rectal swabs at day 14 [day 7 post Rx]

---

Previous secondary outcome measures:

Development of resistance to colistin evaluated by performing susceptibility testing of colistin for all post-intervention CRKP isolates from any site for 28 days

**Completion date**

30/09/2024

## Eligibility

**Key inclusion criteria**

Current inclusion criteria as of 09/05/2023:

1. Adult: Aged >18 years
  2. Location: ICU, HD, Hematology
  3. Able to provide informed consent
  4. Expected to stay for 14 days in hospital
  5. Undergone a screening rectal swab for CRKP within 72 h of admission
- 

Previous inclusion criteria:

1. Aged  $\geq$ 18 years
2. Admitted to intensive care, high dependency, and hematology wards at SQUH, Oman during the study period
3. Positive screening rectal swab for CRKP [colistin susceptible]
4. Able to provide informed consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

Current exclusion criteria as of 09/05/2023:

1. Not meeting inclusion criteria
2. Rectal swab is negative for CRKP
3. CRKP is colistin-resistant [MIC >2 mg/L]
4. Pregnant or nursing women
5. Known hypersensitivity to colistin/placebo

6. NPO [nil by mouth]

7. On colistin OR ceftazidime-avibactam/aztreonam at time of enrollment or up to 7 days before enrollment

---

Previous exclusion criteria:

1. Age <18 years
2. Pregnant or nursing women
3. Known hypersensitivity
4. Gastrointestinal colonization with colistin-resistant *Klebsiella pneumoniae*
5. Enrollment in the present study for a previous episode

**Date of first enrolment**

15/10/2023

**Date of final enrolment**

30/04/2024

## Locations

**Countries of recruitment**

Oman

**Study participating centre**

**Sultan Qaboos University Hospital**

PO Box 35, PC 123, Al Khod

Muscat

Oman

123

## Sponsor information

**Organisation**

Sultan Qaboos University

**ROR**

<https://ror.org/04wq8zb47>

## Funder(s)

**Funder type**

University/education

## Funder Name

Sultan Qaboos University Project Code: IG/MED/MEDE/23/03

## Alternative Name(s)

SQU

## Funding Body Type

Government organisation

## Funding Body Subtype

Local government

## Location

Oman

# Results and Publications

## Individual participant data (IPD) sharing plan

The dataset will be made available upon request from the principal investigator Dr Abdullah Balkhair (balkhair2020@gmail.com).

The type of data that will be shared: Report of the board of data monitoring and any other essential data requested.

Dates of availability: Recruitment end date.

Whether consent from participants was required and obtained: Yes, a written consent is required and shall be obtained.

Comments on data anonymization: All data is anonymous

Any ethical or legal restrictions: None to the best of my knowledge

Any additional comments: None

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Other files</a>	Consent form		12/01/2023	No	No
<a href="#">Other files</a>	Withdrawal of consent form		12/01/2023	No	No
<a href="#">Other files</a>	Consent form version 3		03/04/2023	No	No
<a href="#">Participant information sheet</a>			12/01/2023	No	Yes
<a href="#">Participant information sheet</a>	version 2		03/04/2023	No	Yes