ISRCTN61139514 https://doi.org/10.1186/ISRCTN61139514

# The effect of supplementation with an amino acid that helps the body build protein (L-arginine) on change in the immune system of colorectal cancer patients

**Submission date**
31/03/2021

**Recruitment status**
No longer recruiting

**Registration date**
19/04/2021

**Overall study status**
Completed

**Last Edited**
26/09/2022

**Condition category**
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
Colorectal cancer is cancer that occurs in the colon or rectum. Sometimes it is called colon cancer, for short. As the drawing shows, the colon is the large intestine or large bowel. The rectum is the passageway that connects the colon to the anus.
L-arginine (L-arg) is an amino acid that helps the body build protein. Your body usually makes all the L-arginine it needs. L-arginine is also found in most protein-rich foods, including fish, red meat, poultry, soy, whole grains, beans and dairy products.
L-arg supplementation may improve treatment outcomes from tumours by altering the activity of the immune system.

Who can participate?
Adult patients with diagnosed colorectal cancer qualified to undergo radical surgical treatment

What does the study involve?
Participants will be randomly allocated to receive either L-arg or placebo for 9 days prior to surgery.

What are the possible benefits and risks of participating?
Benefits: Currently, there is insufficient evidence and long-term follow-up to conclusively conclude that L-arginine supplementation improves the outcome treatment in colorectal cancer patients. The aim of our study is to explore this possibility. Thus, an improvement in their health cannot be guaranteed. However, the participation of patients in the study and its results may in the future contribute to improving the results of oncological treatment of other colorectal cancer patients.
Risks: Very rarely, abdominal pain, nausea or diarrhoea may occur after high doses of L-arginine exceeding 30 g per day. These symptoms disappear after withdrawal L-arginine or reducing its doses. We plan to supplement with 10 g of L-arginine daily.

Where is the study run from?
Medical University of Gdańsk, MUG (Poland)

When is the study starting and how long is it expected to run for?
October 2017 to June 2020

Who is funding the study?
Medical University of Gdańsk, MUG (Poland)

Who is the main contact?
Dr Jarosław Szefel, jaszefel@mp.pl
Prof Wiesław Kruszewski, wieslaw.kruszewski@gumed.edu.pl

# Contact information

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Scientific

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### Type(s)
Public

### Contact name
Prof Wiesław Kruszewski

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# Additional identifiers

### Protocol serial number
NKBBN/405/2017

# Study information

### Scientific Title
The effect of L-arginine supplementation and surgical trauma on the frequency myeloid-derived suppressor cells and T lymphocytes in tumour and blood of colorectal cancer patients.

### Acronym
L-ArgRectCanc

### Study objectives
L-arginine (L-arg) supplementation improves treatment outcomes for non-auxotrophic tumours by altering the activity of the immune system.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 09/10/2017, Independent Bioethics Committee for Scientific Research at Medical University of Gdańsk (Dębinki 7, 80-211, Gdańsk, Poland; +48 58 349 10 11; irmez@gumed.edu.pl), ref: NKBBN/405/2017

### Primary study design
Interventional

### Study design
Single-centre prospective interventional randomized double-blind study

### Study type(s)
Treatment

### Health condition(s) or problem(s) studied
The effect of L-arg supplementation in patients undergoing surgery for colorectal cancer

### Interventions
L-arginine and placebo kits are prepared and labelled with numbers randomly assigned by LLC Ethifarm (Poznan, Poland). Each kit contains 180 capsules of 0.5 g of substance. Patients are instructed to take 20 capsules (5 capsules 4 times a day) for 9 days immediately prior to surgery. Researchers and patients does not know what is inside the capsules, and this information is disclosed by LLC Ethifarm after the end of the study.

Randomisation: L-arginine and placebo kits were prepared and labelled with numbers randomly assigned by LLC Ethifarm (Poznan, Poland). Information on the content of the kits was disclosed by LLC Ethifarm to our research team at the end of the trial.

### Intervention Type
Supplement

### Primary outcome(s)
Measured :
1. L-arg and ASS1 concentration, and ASS1 mRNA expression in tumour, intestinal mucosa, and blood measured using flow cytometry, quantitive PCR and ELISA
2. The frequency of M-MDSC and PMN-MDSC in tumour, intestinal mucosa (A2, B2), and blood measured using flow cytometry

### Key secondary outcome(s)
Blood parameters measured using flow cytometry and ELISA before supplementation; one day after the end of supplementation - immediately before the surgery; and one day after the surgery:
1. ASS1 concentration
2. The frequency of Th1 cells
3. The frequency of Th2 cells
4. The Th1/Th2 ratio
5. The frequency of Treg cells
6. The frequency of Th17
7. Th17/Treg ratio
8. CRP concentrations and its relation to the frequency of PMN-MDSC, M-MDSC and Th1, Th2
9. The frequency of PMN-MDSC in blood
10. The frequency of M-MDSC in blood

### Completion date
21/06/2020

## Eligibility

### Key inclusion criteria
Adult patients with diagnosed colorectal cancer qualified to undergo radical surgical treatment

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

### Sex
All

### Total final enrolment
65

### Key exclusion criteria
1. Chemotherapy and/or radiotherapy in the last 5 years
2. Autoimmune diseases

3. Liver or kidney failure
4. Uncontrolled diabetes
5. Acute and chronic inflammatory diseases

### Date of first enrolment
30/04/2018

### Date of final enrolment
30/04/2020

## Locations

### Countries of recruitment
Poland

### Study participating centre
**Maritime Polish Red Cross Memorial Hospital**
Department of Surgical Oncology
Gdynia Oncology Centre
1 Powstania Styczniowego Street
Gdynia
Poland
81-519

### Study participating centre
**Medical University of Gdansk**
Division of Oncological Propedeutics
Faculty of Health Sciences
9b Powstania Styczniowego Street
Gdynia
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### Study participating centre
**Medical University of Gdansk**
Department of Clinical Nutrition
Gdansk
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80-211

### Study participating centre
**Medical University of Gdansk**
Department of Histology

7 Debinki Street
Gdansk
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**Study participating centre**
**WSB University in Gdansk**
Faculty of Finance and Management
238A Aleja Grunwaldzka
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# Sponsor information

**Organisation**
Gdańsk Medical University

**ROR**
https://ror.org/019sbgd69

# Funder(s)

**Funder type**
University/education

**Funder Name**
Gdański Uniwersytet Medyczny

**Alternative Name(s)**
Medical University of Gdańsk, MUG

**Funding Body Type**
Government organisation

**Funding Body Subtype**
Local government

**Location**
Poland

# Results and Publications

## Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication.

## IPD sharing plan summary

Other

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | | 04/01/2022 | 12/01/2022 | Yes | No |
| Participant information sheet | | | 04/05/2021 | No | Yes |