**FULL PROTOCOL TITLE**

# LICPIC: A Double-Blind Randomised Placebo-Controlled Trial Assessing the Effect of Peri-Operative Intravenous Lignocaine and Post-Operative Lignocaine Neurovascular Plane Infusion on Natural Killer Cell Function in Laparoscopic Colorectal Neoplasia Surgery

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**LINK TO STUDY**

https://gicancer.org.au/clinical-trial/licpic/

**TRIAL IDENTIFIER**

ACTRN12618000754246

**COORDINATING CENTRE**

John Hunter Hospital

**FUNDING SOURCES**

Internal departmental grants from John Hunter Hospital

CSSANZ Research Grant

## STUDY CHAIR

### Prof Stephen Smith

John Hunter Hospital

**FINANCIAL DISCLOSURE**
None to declare.

## AIM/S

### PRIMARY

To compare the perioperative NK cell number and function of patients receiving either intraoperative lignocaine infusion or placebo in patients undergoing laparoscopic colon surgery for colonic neoplasia.

### SECONDARY

To compare plasma lignocaine, cortisol, CRP, Interleukin-6, Interleukin-2 and Interferon gamma levels, opiate consumption, return of gut function, surgical complications and mortality between the 2 study arms.

## BACKGROUND

Surgery is the most effective method for treating colorectal cancer but 25% of patients develop recurrent disease within 5 years of surgery.

Natural Killer (NK) cells play an important role in reducing metastatic burden but their function is suppressed over the perioperative period due to stress, pain, opioid consumption, the types of anaesthesia used during surgery and the surgery itself.

Lignocaine is an inexpensive and well-known local anaesthetic which can be effective when administered intravenously during the perioperative period. Lignocaine has known opiate sparing effects and suspected anti-inflammatory effects. In vitro studies of therapeutically relevant concentrations of lignocaine have been shown to improve NK cell function.

## STUDY DESIGN

The primary aim of this study is to measure the effect of IV lignocaine infusion with subsequent TAP lignocaine infusion versus placebo on NK cell number and function in people with colorectal neoplasia (cancer or polyp) undergoing surgical resection.

This will be assessed by incubation with established tumour cell lines to measure cytotoxic function and measurement of interferon gamma to assess secretory function alongside measurement of interleukin-2 which is known to influence NK cell function.

This study will be a two-armed prospective, double-blind, randomised, placebo-controlled trial in patients with colorectal neoplasia undergoing elective laparoscopic resection without the expectation of a stoma, to compare the use of peri-operative intravenous lignocaine and post-operative wound infusion lignocaine with placebo.

## ELIGIBILITY CRITERIA

### INCLUSION CRITERIA

All patients undergoing elective or semi-urgent booked laparoscopic colon resection for colorectal neoplasia (cancer or polyp) at the John Hunter and Calvary Mater Hospitals and Newcastle Private Hospital.

### EXCLUSION CRITERIA

a. are under 18 years of age, or
b. refuse or are unable to give written informed consent to participate in the study, or
c. have had previous abdominal surgery where there is a significant chance of the procedure not being able to be completed in a laparoscopic manner, based in the clinical judgement of the operating surgeon, or
d. have severe renal impairment or
e. receive an epidural, spinal or other neuroaxial anaesthetic as determined by the Anaesthetist on day of surgery, or
f. have a planned stoma formation or
a. have received neoadjuvant chemo-radiotherapy or have been on immunosuppressive agents in the preceding 8 weeks including glucocorticoids (not including inhaled steroids), antimetabolites, cytostatics (e.g. platinum compounds), antimetabolites (e.g. methotrexate, mercaptopurine, azathioprine, 5FU, anthracyclines, cytotoxic antibiotics e.g. bleomycin) , TNF binding proteins (e.g. infliximab), drugs acting on immunophilins or
b. have known stage 4 colorectal cancer disease
c. have known immunological disease including leukaemia or
d. have known allergy or adverse reaction to lignocaine or opioid drugs or
e. are pregnant or lactating or
f. have a history of arrhythmia or long QT syndrome associated with the drugs used in this trial, or
g. are taking regular opiate narcotics pre-operatively.

## STUDY UPDATE

- Sample analysis is underway for NKC and lignocaine levels.
- Ongoing data cleaning

### PARTICIPATING SITES

- John Hunter Hospital
- Newcastle Private Hospital
- Calvary Mater Newcastle

### PROTOCOL AMENDMENTS

Most recent to increase accrual target by 10.

## RECRUITMENT

Completed September 2022.

- Barriers to recruitment were largely due to pandemic with reduction in surgery and face to face perioperative appointments.
- Strategies employed to increase equity: eConsent

## PUBLICATIONS

Nil to date.

## TRANSLATIONAL RESEARCH

Research bloods from various timepoints of the procedure and admission have been collected.

## STUDY SCHEMA