ISRCTN77829558 https://doi.org/10.1186/ISRCTN77829558

Using taurolidine to attenuate the surgically-induced endotoxaemia and the subsequent inflammatory response in patients with primary non-metastatic colon cancer

Submission date
10/08/2007

Recruitment status
No longer recruiting

Registration date
06/11/2007

Overall study status
Completed

Last Edited
08/08/2018

Condition category
Cancer

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Henry Paul Redmond

Contact details
Department of Surgery
Cork University Hospital
Wilton
Cork
Ireland
-
-
henry.redmond@hse.ie

Additional identifiers

Clinical Trials Information System (CTIS)
2008-005570-12

Protocol serial number
RCSI SR&D 09/08/07-1

Study information

Scientific Title
Using taurolidine to attenuate the surgically-induced endotoxaemia and the subsequent inflammatory response in patients with primary non-metastatic colon cancer

Study objectives
Amended as of 25/11/2008:
To examine the role of taurolidine in attenuating the surgically-induced systemic endotoxaemia and subsequent inflammatory response thereby assessing its anti-neoplastic effects in patients undergoing surgery for non-metastatic colon cancer and prevention of (micro) metastases.

Initial information at time of registration:
To assess the role of taurolidine in the following:
1. The attenuation of the pro-inflammatory cytokine response in the perioperative period in patients with colon cancer
2. The reduction of post-operative infectious complications
3. The reduction of post-operative respiratory complications
4. The return of Gastro-Intestinal (GI) function post-operatively
5. Post-operative recovery and length of hospital stay
6. Preventing tumour recurrence

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of University College Cork (Ireland) granted provisional approval on the 11th September 2007 pending authorisation from the Irish Medicines Board (IMB). The IMB gave their approval on the 8th September 2008 (added 25/11/2008).

Study design
Open prospective multi-centre randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Colon cancer

Interventions
Amended as of 25/11/2008:
From induction of anaesthesia, patients will be administered 250 ml of 2% taurolidine or normal saline four times daily intravenously for four days.

Initial information at time of registration:
From induction of anaesthesia, patients will be administered 250 ml of 2% taurolidine or the same volume of normal saline intravenously three times a day for three days.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Taurolidine

Primary outcome(s)
Amended as of 25/11/2008:
1. Percent change in taurolidine as compared to control group in mean day 1 IL-6 relative to mean baseline IL-6. Mean day-1 lL-6 defined as mean of available values from (+3, +6, +24 hours post-induction). Mean baseline defined as mean of available pre-op IL-6 levels.

Initial information at time of registration:
The following will be measured twice pre-operatively and at 4 hours, 24 hours, 48 hours, 3 days and 5 days post-operatively:
1. Pro-inflammatory cytokine levels (Interleukin-6 [IL-6], Interleukin-1-beta [IL-1beta], Tumour Necrosis Factor-alpha [TNF-alpha], Vascular Endothelial Growth Factor [VEGF])
2. Anti-inflammatory cytokine levels (Interleukin-1-Receptor Antagonist [IL-1RA], Interleukin-10 [IL-10])
3. C-Reactive Protein (CRP)
4. Endotoxin/Lipopolysaccharides (LPS) level

The following will be measured twice pre-operatively and at 24 hours and 5 days post-operatively:
5. Natural Killer (NK) Cell and Cytotoxic T-Lymphocyte (CTL) cytotoxic activity
6. Neutrophil/monocyte receptor expression (CD11b, CD14, Toll-Like Receptor-4 [TLR4])

Key secondary outcome(s))
Amended as of 25/11/2008:
1. Laboratory endpoints:
1.1. Percent change in taurolidine as compared to control group in mean day 2 and day 3 IL-6 relative to mean baseline Il-6. Mean day 2/day 3 defined as available IL-6 from 48 and 72 hours post-induction.
1.2. Percent change in taurolidine as compared to control group in mean available day 1 to day 3 versus mean baseline IL-10, endotoxin level, and C-reactive protein (CRP)
2. Clinical endpoints:
2.1. Comparison of Taurolidine with control group with regard to occurrence and severity of post-operative infections over 10 days post-operatively or until hospital discharge
2.2. Time to bowel functional recovery defined as time to first flatus or return of bowel sounds
2.3. Comparison of taurolidine with control group with regard to analgesic requirements (using ordinal ranking scale) and self assessed pain control using visual analogue scale at 24 and 72 hours post-induction
2.4. Percent tumour recurrence at 12 months following operation in taurolidine as compared to control group

Tertiary outcomes:
Percent change in taurolidine compared to control group in mean available day 1 - day 3 versus

mean baseline:
1. Inflammatory cytokine levels (tumour necrosis factor alpha [TNF-a], vascular endothelial growth factor [VEGF], interleukin-1 receptor antagonist [IL-1ra], IL-1beta)
2. Natural Killer (NK) cell and cytotoxic T-lymphocyte (CTL) cytotoxic activity
3. Neutrophil/monocyte receptor expression (cluster of differentiation-14 [CD14], cluster of differentiation-11b [CD11b], toll-like receptor-4 [TLR4])

Safety endpoints:
Comparison of routine haematological and biochemical data at day 1, 2, 3, 5, hospital discharge, and 1 month. Clinical status at hospital discharge, 1, 6 and 12 months.

Initial information at time of registration:
1. Post-operative pain scores (Visual Analogue Scales [VAS])
2. Post-operative GI function (time to first flatus and to bowel sounds)
3. Post-operative respiratory function/infections (clinical)
4. Clinical wound infection rate
5. Length of hospital stay
6. Survival at 1 and 2 years
7. Time to tumour recurrence (radiological)

Completion date
01/06/2009

Eligibility

Key inclusion criteria
Initial information at time of registration:
1. Patients of both genders who are 18 to 75 years of age
2. Patients with a solitary, non-metastatic extraperitoneal colonic tumour that already has been histologically confirmed
3. Patient has given full written informed consent
4. Elective setting

Added as of 25/11/2008:
5. Negative pregnancy test in women of childbearing age

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria

Amended as of 25/11/2008:
1. Rectal tumours (within 15 cm of the anal orifice)
2. Known allergy to taurolidine/taurine
3. Pregnant and lactating women
4. Liver disease:
4.1. Abnormal liver function tests (LFTs) greater than 2 times upper limit of normal (ULN)
4.2. International normalised ratio (INR) greater than 1.5
5. Renal disease:
5.1. Creatinine greater than 180 (women), greater than 150 (men)
5.2. Serum sodium less than 132 or greater than 145
6. Blood dyscrasia:
6.1. Neutropenia less than 1500 cells/cm^3
6.2. Thrombocytopenia less than 100,000 cells/cm^3
7. Intestinal obstruction
8. Infiltration of adjacent organs
9. Tumour diameter greater than 8 cm on computed tomography (CT) scan
10. Severe obesity (body mass index greater than 32 kg/m^2)
11. Operative risk greater than American Society of Anaesthesiologists (ASA) - III
12. Another cancer/malignant disease other than non melanoma skin cancer
13. Coexisting active inflammatory disorder (including active Rheumatoid Arthritis [RA], Inflammatory Bowel Disease [IBD], Systemic Lupus Erythematosus [SLE])
14. Immunocompromised:
14.1. Corticosteroids
14.2. Immunosuppressive drugs
14.3. Patients with human immunodeficiency virus (HIV), chronic active hepatitis B or C virus
15. Active infection

Initial information at time of registration:
1. Known allergy to taurolidine/taurine
2. Pregnancy and lactation
3. Liver disease (abnormal Liver Function Test [LFT's] results or International Normalised Ratio [INR] greater than 1.5)
4. Renal disease
5. History of electrolyte imbalance
6. Blood dyscrasia (neutropenia less than 1500 cells/cm^3, thrombocytopenia less than 100,000 cells/cm^3)
7. Intestinal obstruction
8. Infiltration of adjacent organs
9. Tumour diameter greater than 8 cm on Computerised Tomography (CT) scan
10. Severe obesity (body mass index greater than 32 kg/m^2)
11. Operative risk greater than American Society of Anaesthesiologists (ASA) grade III
12. Another cancer/malignant disease
13. Another chronic inflammatory disorder (e.g. Rheumatoid Arthritis [RA], Inflammatory Bowel Disease [IBD], Systemic Lupus Erythematosus [SLE])
14. Immunocompromised
15. Active infection

Date of first enrolment

01/11/2008

Date of final enrolment
01/06/2009

Locations

Countries of recruitment
Ireland

Study participating centre
Cork University Hospital
Cork
Ireland
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Sponsor information

Organisation
Geistlich Pharma AG (Switzerland)

ROR
https://ror.org/055f9sm34

Funder(s)

Funder type
Industry

Funder Name
Geistlich Pharma AG (Switzerland)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Results article	results	06/08/2018	Yes	No