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# A Prospective Randomized Controlled Trial of Morphine versus Oxycodone for Cancer Pain: Genetic Determinants of Response to Opioids

**Submission date**
18/03/2005

**Recruitment status**
No longer recruiting

**Registration date**
29/03/2005

**Overall study status**
Completed

**Last Edited**
14/08/2015

**Condition category**
Cancer

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

## Plain English summary of protocol

Background and study aims
Cancer related-pain continues to be a major problem for eight out of ten cancer patients. For many years the main treatment for cancer-related pain has been morphine. Morphine is a strong painkiller which belongs to a family of drugs called opioids. About one in four people do not respond well to morphine either because of severe side effects or not enough pain relief. If this happens, switching to another strong opioid painkiller, such as oxycodone, appears to be helpful. The main aim of the study was to find out which strong opioid is best to use first-line in the treatment of moderate to severe cancer-related pain, morphine or oxycodone. Another aim was to find out whether switching from one strong opioid to another when the first is not working does indeed improve pain relief. The study also investigated whether there was anything that could predict which strong painkiller would be best for a particular person. Part of this was done by looking for differences in DNA, the genetic code that is unique to each person, which could be linked to certain responses.

Who can participate?
The study included patients who were over 18 years of age, had a diagnosis of cancer and had pain that was not controlled on a weak opioid painkiller such as codeine.

What did the study involve?
Two hundred participants with cancer-related pain were recruited to the study. Participants were randomised to receive either morphine or oxycodone by mouth. Neither the participant nor the doctor could choose which strong opioid they would be given. Participants were monitored daily until good pain control was achieved. If the participants did not experience good pain relief despite increasing the dose or reported bad side effects they were switched to the alternative strong opioid painkiller. Questionnaires on pain and side effects were collected together with information about other medications, and blood and urine samples at the different time points. The study lasted one year in total. The time-points were: at the beginning, when a good response was achieved, when a switch to the other opioid painkiller was necessary, if the dose required for good pain control trebled in follow-up period and at the end of the study.

What were the possible benefits and risks of participating?
This study was designed to find out which painkiller is best to use first-line for cancer-related pain in order to get symptoms under control as safely and as quickly as possible. Ultimately we would like to be able to predict a person's response to each painkiller before they start in order to tailor care to the individual.
The two opioid painkillers used in the study are commonly used in the treatment of cancer-related pain, so doctors and nurses are very familiar with their use. The study participants were closely followed-up and side effects were reported. Common side effects include constipation, nausea, vomiting and drowsiness. The number of times the participants were asked to come to the hospital was kept to a minimum.

Where was the study run from?
The Royal Marsden Hospital (UK).

When is the study starting and how long is it expected to run for?
The study started in 2006 and finished recruiting in 2011.

Who is funding the study?
Palliative Care Research Fund, Royal Marsden Hospital and St Joseph's Hospital. The study also received an unrestricted educational grant from NAPP Pharmaceutical Group.

Who is the main contact?
Dr Julia Riley
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# Contact information

### Type(s)
Scientific

### Contact name
Dr Julia Riley

### Contact details
The Royal Marsden Hospital
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# Additional identifiers

### Protocol serial number
N0258161811

# Study information

### Scientific Title
A Prospective Randomized Controlled Trial of Morphine versus Oxycodone for Cancer Pain: Genetic Determinants of Response to Opioids

## Study objectives
1. To compare the response rates of morphine and oxycodone when used as first line strong opioids in moderate to severe cancer pain.
2.1 To compare the toxicity profiles of morphine and oxycodone and identify which factors predict that need to switch from one opioid to the other.
2.2 To compare clinical, laboratory, genomic, proteomic and metabonomic parameters of the study populations in order to design a model that predicts response and non-response to morphine and oxycodone.

On 23/06/2011 various updates were made to this trial record. These can be found under this date of update in the relevant fields below.
1. The overall trial start date has been updated from 01/05/2005 to 01/05/2006.
2. The overall trial end date has been extended from 01/11/2007 to 31/08/2011.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
London-Surrey Borders Research Ethics Committee, 07/07/2005, ref: 05/Q0806/58

## Study design
Randomised controlled trial

## Primary study design
Interventional

## Study type(s)
Quality of life

## Health condition(s) or problem(s) studied
Moderate to severe cancer pain

## Interventions
Randomisation to receive oral morphine or oral oxycodone as first line Step 3 analgesics in moderate to severe cancer pain, and switch to alternative arm of study if lack of response to drug of initial study treatment arm.

## Intervention Type
Drug

## Phase
Not Applicable

## Drug/device/biological/vaccine name(s)
Morphine, oxycodone

## Primary outcome(s)
Difference in response rate to morphine versus oxycodone.

## Key secondary outcome(s))

Differences in levels of toxicity and differences in pre-specified clinical, laboratory, genetic, immunological and proteomic determinants between the two study groups.

### Completion date
31/08/2011

## Eligibility

### Key inclusion criteria
1. Patients must have a clinical or histological diagnosis of cancer
2. Patients whose pain is not controlled on Step 2 (weak opioid) analgesics (as defined by the WHO analgesic ladder) who clinically require a strong opioid
3. Patients must be over 18 years of age
4. Patients must be able to give written informed consent
5. Patients must be willing to undergo genetic screening

### 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 23/06/2011:
1. Patients with renal failure (1.5x ULN). These patients should be treated with alfentanil as per Palliative Care Clinical Guidelines
2. Patients must not currently be taking regular strong opioids
3. Patients requiring parenteral administration of opioids
4. Patients with predominantly incident pain
5. Patients with a clearly defined history of intolerance to morphine or oxycodone
6. Patients who are pregnant

Previous exclusion criteria:
1. Patients with renal failure (1.5 x upper limit of normal [ULN]). These patients should be treated with alfentanil as per palliative care guidelines.
2. Patients must not have been taking regular Step 3 analgesics in the last month
3. Patients requiring parenteral administration of opioids
4. Patients with predominantly neuropathic pain
5. Patients with predominantly incident pain
6. Patients with a clearly defined history of intolerance to morphine or oxycodone

**Date of first enrolment**
01/05/2005

**Date of final enrolment**
31/08/2011

# Locations

**Countries of recruitment**
United Kingdom

England

**Study participating centre**
**The Royal Marsden Hospital**
London
United Kingdom
SW3 6JJ

# Sponsor information

**Organisation**
The Royal Marsden NHS Foundation Trust (UK)

**ROR**
https://ror.org/0008wzh48

# Funder(s)

**Funder type**
Research organisation

**Funder Name**
The Palliative Care Research Fund

**Funder Name**
Royal Marsden Hospital and

**Funder Name**
St Josephs Hospital.

**Funder Name**
NAPP Pharmaceutical Group (unrestricted educational grant)

# 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 | 01/02/2015 | | Yes | No |