PRC

TVT Study

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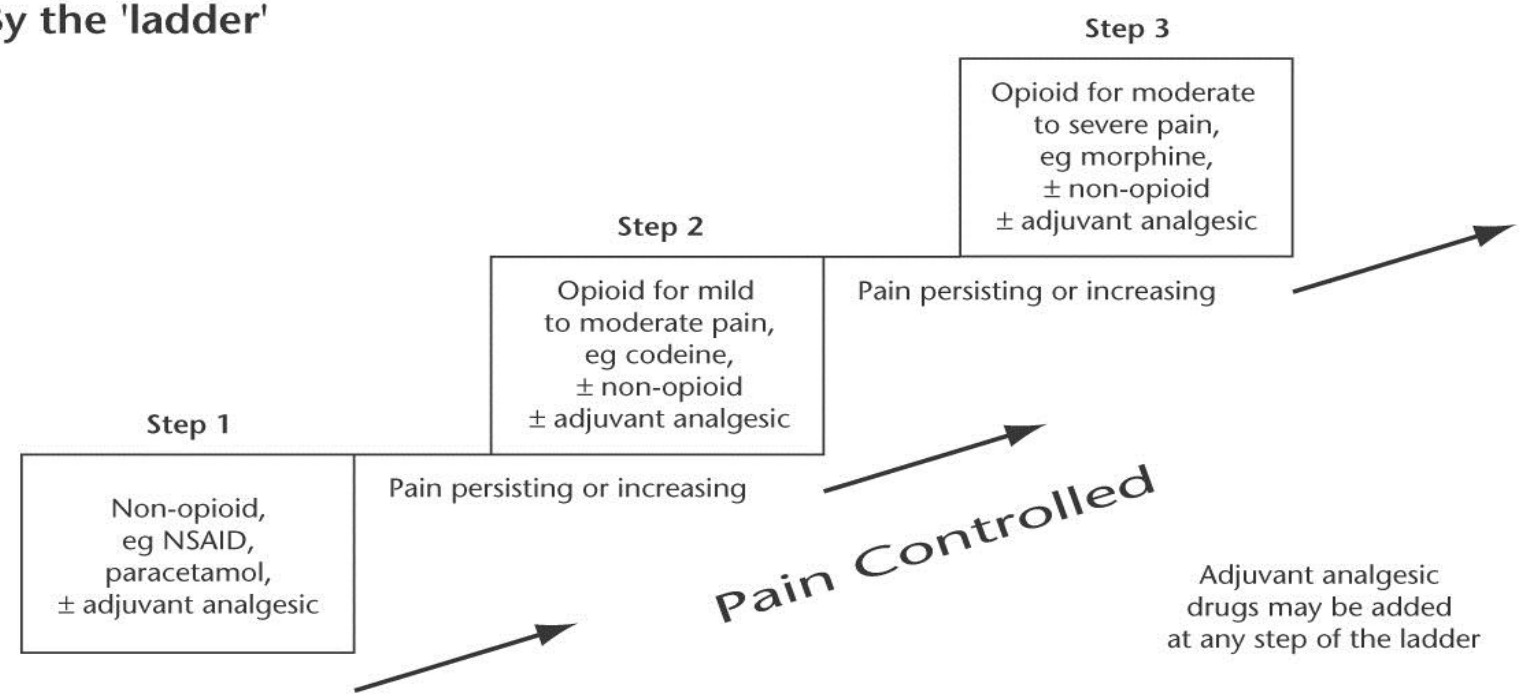
TVT Study: An international, multicentre, open randomised parallel group trial comparing a two step approach for cancer pain relief with the standard three step approach of the WHO analgesic ladder in patients with cancer pain requiring step 2 analgesia

1. **By the clock**
   Cancer pain is continuous - use regular dose intervals (**not** prn)

2. **By the 'ladder'**



The ladder has no "top rung" as there is no maximum dose for strong opioids. If pain is still a problem with high doses of morphine (eg >300mg/24 hours), or severe side effects, reconsider the cause of pain, eg bone pain may be better helped by NSAIDs, and/or seek specialist advice.

3. **By the mouth**
   The oral route is preferred for all steps of the analgesic 'ladder'.

The second step.....

- In many countries (for a variety of reasons) step two is still used routinely
- Particularly outside specialist palliative care

- 50% of patients needed to move from step 2 to step 3 after 2weeks due to lack of analgesic efficacy (De Conno et al. JPSM 1991)
- Use of strong opioids supported in opioid-naïve patients (Vielvoye-Kerkmeer et al JPSM 2000 Mercadante S et al JPSM 2006)

Edinburgh Pain Assessment Tool (EPAT) (Fallon et al)

- CRUK funded cluster randomised controlled trial
- 19 centres, n=1930. Completed

- Early result:

Step 2 is still used routinely

Patients were 5 times more likely to have poor pain control if on step 2 at initial assessment (compared to step 3)

THE NEED FOR TVT STUDY IS ALIVE AND WELL!

Trial Question

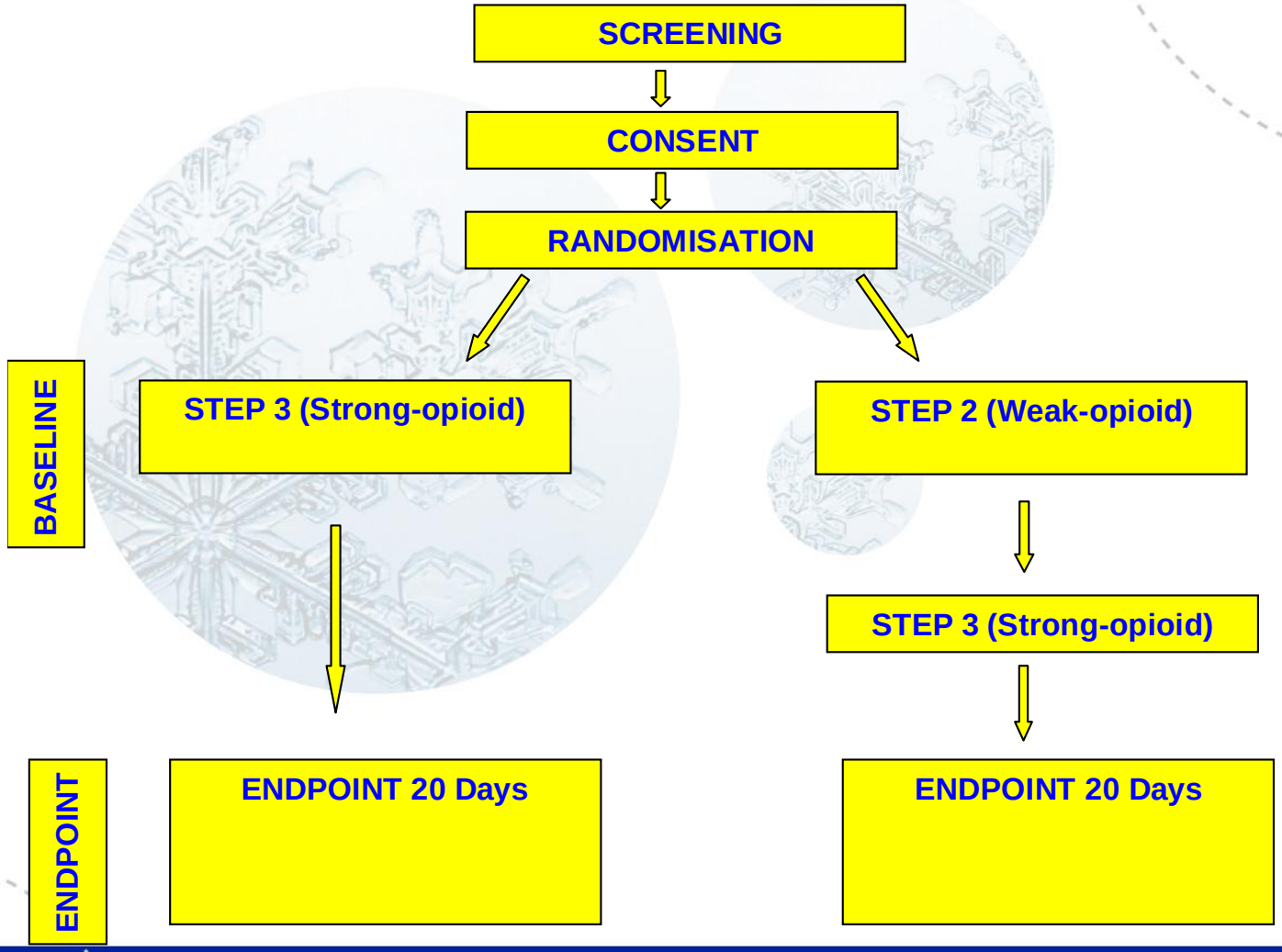
- Is a two step approach more efficient?
- Does it acheive pain control quicker (efficacy) without increased side effects?

Pilot Study

Pilot Study (Reid&Hanks)

- 2 step vs 3 step WHO (Oxycodone)
- “worst pain” and “average pain” lower in 2 step approach ($p<0.05$)
- Pain control achieved faster in 2 step approach (Mean 7.1 days vs 10.8 days)

Trial Design



Trial Arms

- **Two step arm**: Participants will commence an approved strong opioid and this will be titrated as per local practice.

- **Three step arm**: Participants will commence an approved weak opioid. If pain control is not achieved on this (average pain≥ 4) participants will commence a strong opioid.

Inclusion Criteria

- ≥18 years of age.
- Patient has a cancer diagnosis (based on radiological, histological, cytological, or operative evidence). Those with haematological malignancies are eligible.
- Cancer related pain – which in the opinion of the clinician is caused by the presence of tumour or metastases.
- Average pain score ≥ 4, on a numerical rating scale from 0-10, requiring step 2 analgesia (weak opioid).
- Patient is able to comply with trial procedures.

Exclusion Criteria

- Received chemotherapy or radiotherapy in the preceding six weeks that is likely to affect pain during the trial.
- Expected to have a change in anti-cancer therapy during the period of the trial that is likely to alter pain during the trial.
- Pain due to surgery in the preceding 4 weeks.
- Life expectancy less than two months (based on clinical impression)
- Patients with psychotic disorders or cognitive impairment.
- Patients who have received regular doses (scheduled doses – NOT as required dosing) of weak or strong opioids in the preceding two weeks.
- Patients using immediate release opioids > 2 doses/24 hours, in the previous 24 hours.

Choice of opioids (oral only)

Weak Opioids

Codeine 240mg

Tramadol 400mg

Strong Opioids

Morphine

Oxycodone

Baseline/Endpoint Assessments

- Worst/Average pain in last 24 hours
- Brief Pain Inventory
- NCCN Distress Thermometer
- Analgesic Use (previous, current)
- Non-analgesic Medication (previous, current)
- Opioid Toxicity and Side-effects Questionnaire
- EQ-5D

During the trial....

Every day

Average pain, worst pain, analgesic use

Every 2nd Day

Non-analgesic medication, side-effects

Day 10, 20

NCCN, EQ-5D, BPI

Measures of Efficacy

Primary:

Time to achieving stable pain control: defined as the first day of three consecutive days with average pain score ≤ 3

Secondary:

Mean of daily average and worst pain scores

% of days with AP and WP≥ 6

BPI and NCCN baseline, day 10 and day 20.

Measuring Side-effects

Primary

A score of 1 or more for each symptom (occurrence)

Secondary

Frequency of reporting a symptom score of 1 or more

Worst of alternate daily symptom scores

Economic Analysis

- KEY COMPONENT!!

- Endpoints will include resource use and cost (NHS perspective)
- Assessed using EQ-5D

Progress

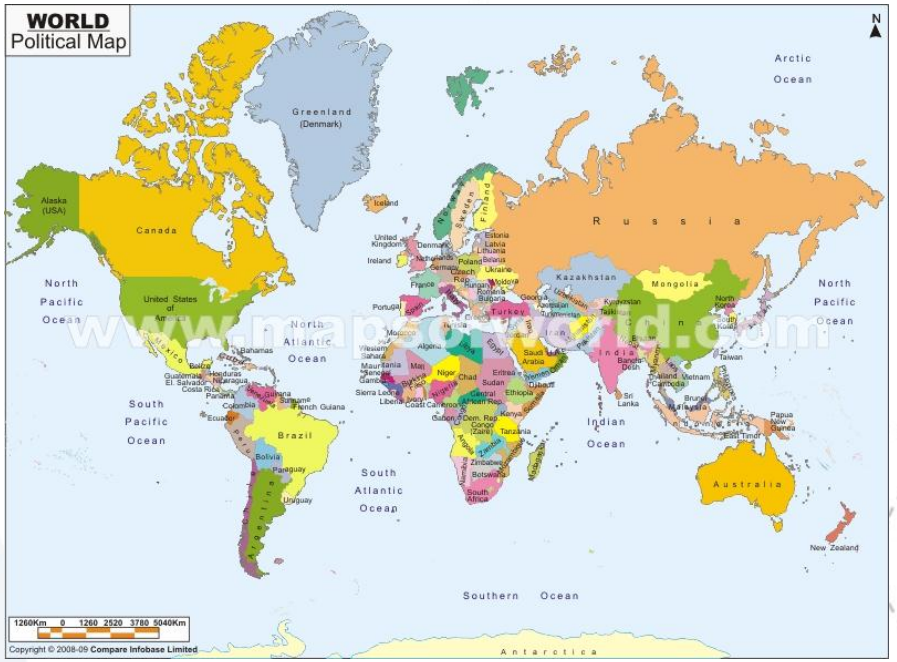
- Piloted a web based CRF and database which will allow the study to run smoothly internationally

- UK (Glasgow*, Edinburgh*, Royal Marsden**, Newcastle**)

- *open for recruitment **ethical approval

Countries

- Spain (Seville)**
- Italy (Milan)
- Germany (Cologne)
- Norway (Trondheim)
- Uganda**
- Australia (Flinders)



- **ethical approval

Summary

Key study in PRC portfolio

Now open for recruitment

Other centres are welcome to participate.

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