A Randomised Controlled Trial to investigate the effectiveness of ThOracic Epidural and Paravertebral Blockade In reducing Chronic Post- Thoracotomy Pain: 2

TRIAL SUMMARY

Primary Objective: to test the hypothesis that in adult patients undergoing elective open thoracotomy, the use of paravertebral blockade (PVB) for peri-operative pain relief reduces the presence of chronic pain at six months post randomisation by at least 10% compared with thoracic epidural blockade (TEB).

Secondary objectives:

- To compare the effectiveness of PVB versus TEB in terms of quality of life, neuropathic pain symptoms, symptoms of anxiety/depression and patients satisfaction up to 12 months following surgery.
- To compare the effectiveness of PVB versus TEB in terms of acute pain control up to 72 hours following surgery, incidence of post-operative major and minor complications and length of post-operative hospital stay.
- To analyse the costs and effectiveness of PVB compared with TEB.

Trial Design: **TOPIC 2** is a multi-centre, open label, parallel group, superiority randomised controlled trial, with an internal pilot, of 1026 adult (≥18 years old) thoracotomy patients in a 1:1 ratio.

Participant Population and Sample Size: 1026 Consenting adults undergoing elective open thoracotomy, in the UK.

Setting: At least twenty large adult UK thoracic centres with a track record of successful recruitment to clinical trials and typical patient case mix.

Duration: 54 months

Eligibility Criteria

Inclusion:

- Aged ≥18 years
- Elective open thoracotomy
- Able to provide written informed consent
- Willingness to complete trial questionnaires up until 12 months post randomisation

Exclusion:

- Contraindication to TEB or PVB e.g. known allergy to local anaesthetics; infection near the proposed puncture site; coagulation disorders, thoracic spine disorders
- Rib/chest wall resection or planned pleurectomy
- Previous thoracotomy on the same side
- Median sternotomy within 90 days

Interventions

Two existing peri-operative analgesic techniques: i) PVB: three pre-incision injections followed by placement of catheter; ii) TEB placed pre-incision: usual practice

Outcome Measures

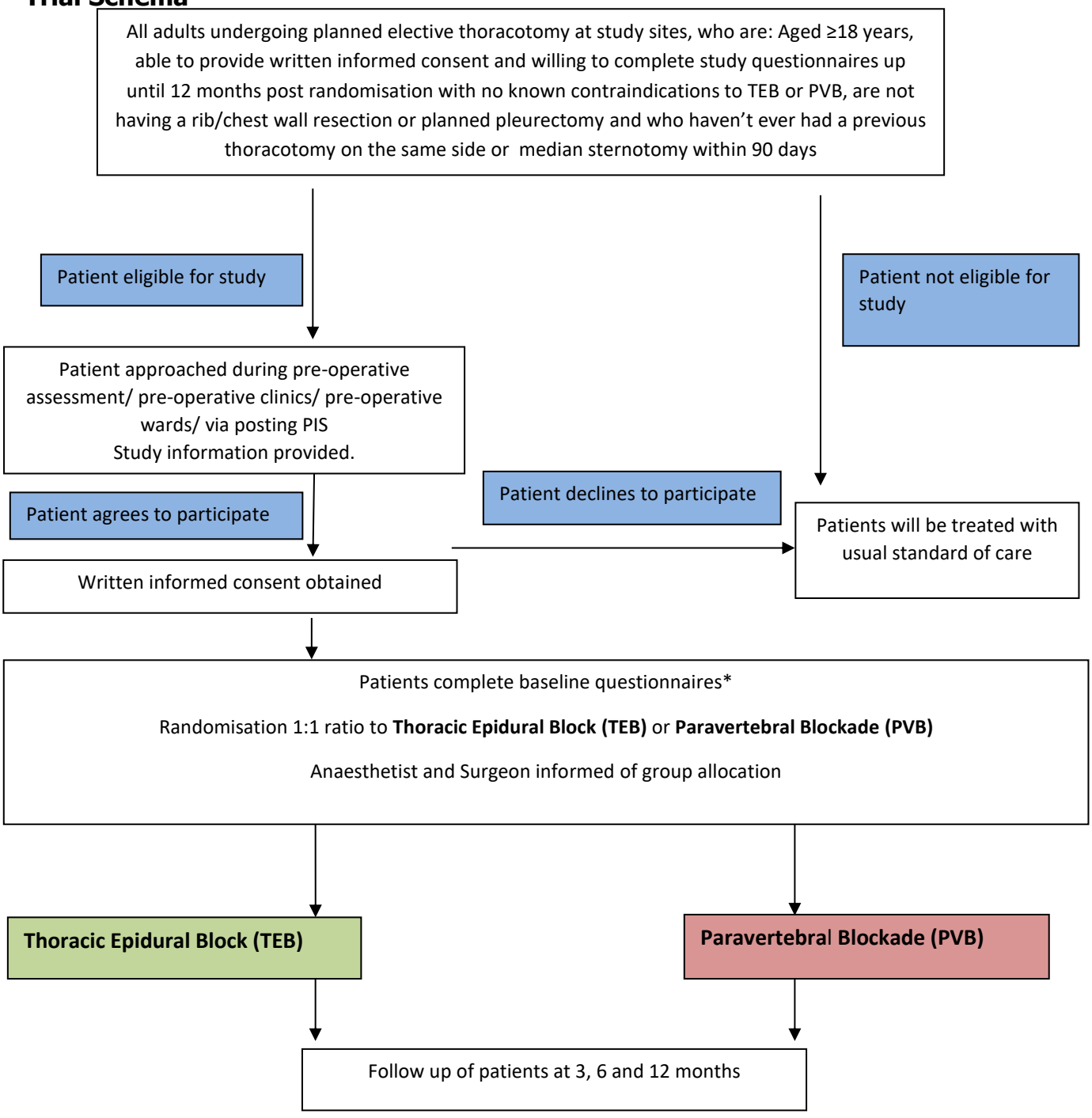
Primary outcome: Presence of CPTP at 6 months post-randomisation. Participants will be asked to indicate their 'worst chest pain over the last week' on a visual analogue scale (VAS; 0-100). Presence of CPTP will be taken to be a score greater or equal to 40 indicating at least a moderate level of pain.

Secondary outcomes measured at, 3, 6 and 12 months post randomisation:

There are a number of secondary outcome measures from the time of randomisation. The following is a non-exhaustive list. For a full list please refer to the TOPIC 2 protocol, section 8.2.

- Complications of regional analgesia
- Occurrence and severity of surgical complications until discharge from hospital
- post-operative pulmonary complications (PPCs) until discharge from hospital
- critical care admission (levels 2 and 3)
- mortality (reported for all deaths due to all causes)
- analgesic use
- acute pain (during initial trial admission), pain at discharge from hospital and chronic pain at 3, 6 and 12 months post randomisation
- resource use and cost data (resource use intraoperatively, during and following hospital admission, and at 3, 6 and 12 months post randomisation)
- general health-related quality of life (by EQ-5D-5L, completed by the participant at discharge and at 3, 6 and 12 months)
- mental health state (measured by HADS, completed by the participant at discharge and at 3,6 and 12 months).
- Patient satisfaction (by Likert scale, completed by the participant at discharge and at 3,6 and 12 months)
- Serious Adverse Events

Trial Schema



*Visual Analogue Score (VAS), Brief Pain Inventory interference score (BPI), Short Form McGill Pain Score (SF-MPQ2), Generic health related quality of life (EQ-5D-5L), Hospital Anxiety and Depression Scale (HADS)

Schedule of Assessments

All timings are taken from date of intervention during the acute phase (up to hospital discharge) then from randomisation

			Acute Phase				Chronic Phase			
Visit	Screening	Baseline	Day 0 (day of intervention)	Day 1 *	Day 2 *	Day 3 *	Hospital Discharge	Month 3	Month 6	Month 12
Eligibility check	x									
Medical History		x								
Baseline Clinical Assessments[1]		x								
Valid informed consent		x								
Randomisation[2]			x							
Lung function tests (FEV1, FVC, DLCO/TLCO)[3]		x								
Trial Intervention			x							
Resource use (analgesics use etc.)			x	x	x	x	x	x	x	x
Mortality Check			x	x	x	x	x	x	x	x
Post-operative surgical complications[4]			x	x	x	x	x			
Post-operative pulmonary complications[5]			x	x	x	x	x			
Complications of regional anaesthesia[6]			x	x	x	x	x			
SAE check			x	x	x	x	x	x	x	x
Out of pocket costs incurred by participants								x	x	x
Societal cost (productivity loss etc.)								x	x	x
Pain questionnaires (VAS, BPI)		x		x	x	x	x	x	x	x
Pain questionnaire (SF-MPQ-2)		x					x	x	x	x
Quality of life questionnaires (EQ-5D-5L and HADS)		x					x	x	x	x
Patient Satisfaction (patient questionnaire)							x	x	x	x

Notes

* Day 1 is first full calendar day (from 12 midnight) post-surgery, day 2 is second full calendar day, day 3 is third full calendar day. Please note that if patient is discharged prior to day 3 then on the day of discharge they should complete only the hospital discharge patient booklet.

[1]To include: ASA grade, Height & Weight, ECOG, Shortness of Breath Category, Smoking Status, Alcohol Consumption. These should be assessed within 28 days of the intervention.

[2]Randomisation should ideally be performed on day of surgery or working day prior to surgery.

[3]Lung function data can be taken from assessment within past 6 months prior to the intervention.

[4]Post-operative surgical complications are defined in Appendix C.

[5]Post-operative pulmonary complications are defined in Appendix E.

[6]To include the following: Failure of blockade, hypotension (systolic blood pressure (<90mmHg)), inadequate pain relief, low respiratory rate (<10/minute), drowsiness, nausea and vomiting, urinary retention, itching, high block, post-dural puncture headache, vascular puncture, pleural puncture).