AstraZeneca

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|---|---|---|---|
| DRUG PRODUCT | Ropivacaine | **Synopsis** | (FOR NATIONAL AUTHORITY USE ONLY) |
| DRUG SUBSTANCE(S) | Ropivacaine | REFERRING TO PART | |
| DOCUMENT NO. | 802-550-LC-0460-01 | OF THE DOSSIER | |
| VERSION NO. | 01 | | |
| STUDY CODE | SP-ROA-0022 | | |
| DATE | 19 June, 2000 | | |

# A double-blind placebo controlled study comparing efficacy and tolerability of intra-articular saline, 7.5 mg/ml or 10 mg/ml ropivacaine following arthroscopic knee surgery.

**STUDY CENTRE**

This was a single center study.

**PUBLICATION**

Not applicable

**STUDY PERIOD**

- **DATE OF FIRST PATIENT ENROLLED** May 1999
- **DATE OF LAST PATIENT COMPLETED** February 2000

**PHASE OF DEVELOPMENT**

Phase III (Therapeutic use)

**OBJECTIVES**

The primary objective of this study was to investigate the postoperative analgesia (by assessment of pain at rest) of two doses of intra-articular ropivacaine compared to placebo in patients subjected to arthroscopic knee surgery. The secondary objective was to evaluate the tolerability (safety).

## STUDY DESIGN

Double-blind, randomised, placebo-controlled, single center study. Patients received either 20 ml of saline 9 mg/ml, ropivacaine 7.5 mg/ml or ropivacaine 10 mg/ml for postoperative pain management after arthroscopic knee surgery.

## STUDY DESIGN

Double-blind, randomised, placebo-controlled, single center study. Patients received either 20 ml of saline 9 mg/ml, ropivacaine 7.5 mg/ml or ropivacaine 10 mg/ml for postoperative pain management after arthroscopic knee surgery.

## DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION/EXCLUSION

Patients in the age range 18-75 years scheduled for ambulatory arthroscopic knee surgery, diagnosed for meniscal resection were included. ASA risk category I, II or III. No known history of allergy, sensitivity, or any other form of reaction to local anesthetics, of the amide type, paracetamol, codeine or morphine was allowed. Written informed consent was obtained.

## TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Ropivacaine 7.5 mg/ml [batch no. 472-64-8 (AA132), expiry date 2002-01-17] and 10 mg/ml [batch no. 465-42-3 (AA182), expiry date 2002-01-17] in 20-ml ampoules. Single dose at end of surgery into the knee joint.

## COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Saline 9 mg/ml [batch no. 400-92-6 (11), expiry date 2002-01-18] in 20-ml ampoules. Single dose at end of surgery into the knee joint.

## DURATION OF TREATMENT

Single injection.

## MAIN VARIABLE(S):

- EFFICACY

Primary efficacy variable:

- VAS score at rest (AUCM0-24)

Secondary efficacy variables:

- VAS score on movement (AUCM0-24)
- AUCM score for pain at rest before discharge from hospital
- AUCM score for pain at rest after discharge from hospital
- AUCM score for pain on movement before discharge from hospital
- AUCM score for pain on movement after discharge from hospital
- Time to first request of supplementary analgesics
- Total dose of supplementary analgesics

- **SAFETY**

- Systolic blood pressure over time
- Diastolic blood pressure over time
- Pulse rate over time
- Adverse event questioning

## STATISTICAL METHODS

The data analysed were based on different populations of patients according to evaluability. These sets of patients are referred to as the per protocol (PP) and the intention to treat (ITT) datasets.

The statistical analysis for all variables consists of descriptive statistics and graphs. Stratified Wilcoxon (mid) rank sum test and survival analysis, e.g. the log rank test were used for pairwise comparisons between the three groups. The improved Bonnferroni-Holm method was used to correct for multiplicity and reach an overall alpha-level of 0.05.

## PATIENTS

| | **Saline** | **Ropi 7.5 mg/ml** | **Ropi 10 mg/ml** | **Total** |
| --- | --- | --- | --- | --- |
| No. planned (PP) | 35 | 35 | 35 | 105 |
| No. randomised | 49 | 50 | 48 | 147 |
| No. analysed for safety | 40 | 40 | 34 | 114 |
| No. analysed for efficacy (ITT) | 40 | 39 | 33 | 112 |
| Males/Females (ITT) | 34/6 | 36/3 | 26/7 | 96/16 |
| Mean age (range) (ITT) | 36 (21-59) | 32 (18-56) | 35 (18-53) | 34 (18-59) |
| No. completed (PP) | 38 | 38 | 33 | 109 |

## SUMMARY

- **EFFICACY RESULTS**

The majority of patients in all three treatment groups received adequate postoperative pain management after arthroscopic meniscal resection. No statistically significant differences in pain scores both at rest and on movement were found between the two ropivacaine groups (7.5 mg/ml and 10 mg/ml) and in comparison to placebo (saline 9 mg/ml). No statistically significant difference in paracetamol and codeine intake was seen. There were more patients who required morphine in the saline group (30%) than in the ropivacaine 7.5 mg/ml group (8%) and the ropivacaine 10 mg/ml group (15%), and the dose of morphine administered was statistically significantly higher in the placebo group than in the ropivacaine 7.5 mg/ml group.

- **SAFETY RESULTS**

Vital signs were stable during the stay in hospital. No safety problems and no clinical evidence of local anesthetic toxicity were seen. Three patients in the saline group stayed over night (unplanned admissions), two of them possibly related to morphine.