AstraZeneca

DRUG PRODUCT	Naropin	**Synopsis**	(FOR NATIONAL AUTHORITY USE ONLY)
DRUG SUBSTANCE(S)	Ropivacaine	REFERRING TO PART	
DOCUMENT NO.	802-550-LC-0495-01	OF THE DOSSIER	
VERSION NO.	01		
STUDY CODE	SP-ROA-0025		
DATE	November 27, 2000		

Intrathecal administration of ropivacaine 5 mg/ml and bupivacaine 5 mg/ml to patients undergoing total hip arthroplasty. A double-blind efficacy study

STUDY CENTRE(S)

This was a single center study.

PUBLICATION (REFERENCE)

Not applicable.

STUDY PERIOD

- **DATE OF FIRST PATIENT ENROLLED** February 2000
- **DATE OF LAST PATIENT COMPLETED** June 2000

PHASE OF DEVELOPMENT

Phase III (therapeutic use)

OBJECTIVES

The primary objective of this study was to compare the efficacy, duration of motor block until return of normal function in the non-operated leg after the start of injection, of ropivacaine 5 mg/ml and bupivacaine 5 mg/ml when used for spinal anesthesia in patients undergoing primary unilateral total hip arthroplasty (cemented prosthesis). The secondary objective was to evaluate the tolerability (safety).

STUDY DESIGN

Double-blind, randomized, single center study. Patients received either 3.5 ml of ropivacaine 5 mg/ml (17.5 mg) or bupivacaine 5 mg/ml (17.5 mg) for spinal anesthesia for primary unilateral total hip arthroplasty surgery.

DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION/EXCLUSION

Patients in the age range 18-80 years scheduled for primary unilateral total hip arthroplasty performed under spinal anesthesia were included. ASA risk category I, II or III. No known history of allergy, sensitivity or other form of reaction to local anesthetics of the amide type. Written informed consent was obtained.

TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Ropivacaine 5 mg/ml [batch no. 1403(471-44-7), expiry date 2001-11-01] in a 5-ml ampoule. Single administration of 3.5 ml intrathecally.

COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION

Bupivacaine 5 mg/ml [batch no. 1203(417-70-8), expiry date 2001-11-01] in a 5-ml ampoule. Single administration of 3.5 ml intrathecally.

DURATION OF TREATMENT

Single injection.

MAIN VARIABLE(S):

- **EFFICACY**

Primary variable:

1. Duration of motor block (Bromage score ≥1) until return of normal motor function (Bromage score 0) after the start of injection in the non-operated leg

Secondary variables:

2. Time to onset of sensory block at T10
3. Duration of sensory block at T10
4. Maximum upper and lower spread of sensory block
5. Time to onset of sensory block at other dermatome levels than T10
6. Duration of sensory block at other dermatome levels than T10
7. Sensory block development over time
8. Time to onset of motor block at Bromage degrees 1,2,3
9. Duration of motor block at Bromage degrees 2,3
10. Frequency of patients with motor block at Bromage degrees 1,2,3
11. Motor block development over time
12. Quality of muscle relaxation and anesthesia judged by the surgeon and anesthesiologist
13. Patient pain during surgery
14. Total morphine consumption in the first 24 hours after injection of investigational product
15. Time to first request of analgesia

- **SAFETY**

16. Adverse events
17. Blood pressure
18. Pulse rate
19. Blood loss

STATISTICAL METHODS

The data analyzed 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. Wilcoxon (mid)rank sum test, Fischer's exact test and survival analysis, e.g., the log rank test, were used for comparisons between the two treatment groups. All p-values were two-tailed and a p-value less than 0.05 was considered to show statistical significance.

PATIENTS

	Ropivacaine 5 mg/ml	**Bupivacaine 5 mg/ml**	**Total**
No. planned	30	30	60
No. randomized	34	34	68
No. analyzed for safety	32	34	66
No. analyzed for efficacy (ITT)	32	34	66
Males/Females (ITT)	21/11	22/12	43/23
Mean age (range) (ITT)	65 (33-79)	64 (33-78)	65 (33-79)
No. completed (PP)	32	34	66

SUMMARY

- EFFICACY RESULTS

An equal dose (17.5 mg) of ropivacaine (5 mg/ml) and bupivacaine (5 mg/ml) for intrathecal anesthesia produced a statistically significantly shorter duration of motor block at all Bromage scores 1, 2 and 3 for ropivacaine compared to bupivacaine. Onset was rapid and equal for motor as well as for sensory block in both groups. The duration of sensory block at dermatome T10 was statistically significantly shorter in the ropivacaine group than in the bupivacaine group. Maximum upper and lower spread of sensory block for analgesia was similar in the two groups. Time to first request of analgesia occurred earlier for the patients administered ropivacaine than for the patients administered bupivacaine. Ropivacaine 5 mg/ml provided excellent anesthetic condition for 97% of the patients, the corresponding figure for bupivacaine 5 mg/ml was 100%. In all patients, but one in each group, the muscle relaxation during surgery was found to be excellent. All patients reported no pain during surgery.

- SAFETY RESULTS

The changes in vital signs seen in this study reflect the expected physiological effects of intrathecal administration of a local anesthetic. There were no differences in the profile of cardiovascular parameters between the two drugs. The most commonly reported adverse events are frequently seen in connection with major surgery and intrathecal anesthesia. Safety data from this study do not suggest any difference in the safety profile of the two drugs.