

## STUDY REPORT SUMMARY

### ASTRAZENECA PHARMACEUTICALS

**FINISHED PRODUCT:** NA

**ACTIVE INGREDIENT:** NA non drug study

<b>Study No:</b> D2285M00029
Investigation of Biomarkers in an Exploratory Study in Patients with Osteoarthritis (OA) of the Knee Undergoing Total Knee Replacement Surgery

**Developmental Phase:** NA Non drug study

**Study Completion Date:** June 2012

**Date of Report:** June 2013

#### OBJECTIVES:

The primary objective of the study:

To provide an estimate of the proportion of patients with upregulation of IL-6 or the IL-6 signalling pathway in the target joint.

The secondary objectives:

To identify one or several biomarkers in blood, urine or by MRI that correlate with upregulation of IL-6 or the IL-6 signalling pathway in synovial fluid, synovial membrane or cartilage.

Mandatory genetic sample to genotype patients for polymorphisms in a range of candidate genes to evaluate whether these genes are associated with measures of pain or inflammation, in patients with osteoarthritis of the knee.

**METHODS:**

This was a 3 to 20 day (depending on the half-lives of NSAID, COX-2s and scheduling of the MRI investigation) multi-centre exploratory biomarker study, performed in Canada and Sweden with no investigational product, in patients with osteoarthritis (OA) of the knee undergoing a total knee replacement surgery.

Biomarker samples were collected from each patient as follows: a mandatory specific genetic sample, an optional genetic sample, plasma/serum, blood (mRNA) and urine. Synovial fluid, synovial membrane and cartilage were collected during surgery. Two different pain questionnaires were used, the WOMAC® Osteoarthritis index version VA3.1 and the Neuropathic Pain Questionnaire (NPQ).

An MRI examination of the knee, which included the administration of a gadolinium-based contrast medium, was performed before surgery.

**RESULTS:**

105 subjects were recruited into the study from 6 participating sites.

A subset of subjects showed elevated IL-6 pathway induced gene expression signatures in target joint tissue.

No SNPs or peripheral biomarkers were found to be strong predictors of IL-6 pathway activation in the target joint.