STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: This non interventional trial was NOT designed to document a specific product
ACTIVE INGREDIENT:

Study No: NIS-OAT-ARI-2007/1
Tumor Care Observational Programme

Developmental phase: marketed
Study Completion Date: 02/2010
Date of Report: 11/2010

OBJECTIVES:

About a third of postmenopausal women receiving AI treatment will develop arthralgia. Arthralgia cases may lead to early discontinuation.

To investigate the efficacy and tolerability of Arimidex in postmenopausal patients receiving upfront adjuvant therapy. Collect clinical data to evaluate incidence, time of onset and treatment of arthralgia in the clinical setting. To educate doctors on evaluation of arthralgia (specific patient questionnaire)
To identify patients who have joint-, muscle-or backbone symptoms before the start of AI treatment.

METHODS:

Postmenopausal, Hormonreceptor positive women were included which are already on upfront Arimidex Therapy (Start 1-4 weeks before) to measure the disease progression and tolerability in general [Time Frame: Baseline, every 3 month]

Secondary Outcome Measurement was, to collect data on Incidence, time of onset and treatment of arthralgia [Time Frame: Baseline, every 3 month]

RESULTS:

A total of 155 postmenopausal breast cancer patients from 28 centers with an average age of 66 (+/- 11) were enrolled in the cancer follow-up program. The first patient was enrolled on January 21, 2008 and the last one on February 26, 2010. The majority of cancer entities were grade 1 to 3 tumors with ductal and/or lobular invasive estrogene receptor-positive histology; 91 % of the patients were progesterone receptor-positive, and 81% of the patients had a negative HER2 status. 77% of the patients underwent radiotherapy, 24% received chemotherapy, with the adjuvant treatment with anastrozole beginning on average 12 days prior to enrollment into the study.

Entire patient population: the course of therapy in the post-observational period
On the basis of the physical examination on inclusion (visit 1; documenting the start of therapy and the patient history), documented follow-up visits (after 3, 6 and 9 months) and the final examination at 12 months, the following observations in regards to safety and tolerability of therapy were noted:

• **Mood swings**: At the time of the first follow-up visit, 72.3% of the patients were free of mood swings. 20.3 % of patients reported that they suffered from “mild“ mood swings. The figures remained the same in the post-observational phase. „Moderate“ to „severe“ subjectively-perceived mood swings were reported only occasionally, affecting 0 to 1.3% of the patients at the final visit.

• **Hot flushes**: Over the course of the observational period, approximately 60-65% of the patients have not experienced hot flushes; 20-25% complained of 'mild' symptoms, while up to 10% of the patients reported “moderate“ to “severe“ symptoms. There was no change in these numbers over the course of the study; only in rare instances were changes documented at any one of the follow-up visits.

• **Gastrointestinal complaints**: 87.7% of the patients reported no gastrointestinal symptoms whatsoever at the first follow-up visit at 3 months; 8.4% reported mild complaints. No significant changes were observed in the course of the rest of the observational period. “Moderate“ or “severe“ subjective gastrointestinal complaints were reported over the course of the observational period only as isolated cases.

• **Vaginal complications, anomalies of the endometrium and/or ischemic cerebrovascular events** have not been recorded in any patient during the entire observational period.

• C**ardiovascular events and thromboembolic complications** were noted in 5 patients only.

Patient history prior to the start of the study: musculoskeletal apparatus
General patient histories prior to the inclusion into the study revealed that 18.7% of the patients had already suffered a fracture. 11.6% of the patients had pre-existing joint or spinal injuries; 10.3% of the patients had already undergone joint or spinal surgery. In addition, 28.4% of patients had a history of degenerative arthritis, and 26.5% of the patients suffered from osteoporosis or osteopenia. Approximately one third of the patients

(25.8 - 34.2%) reported a history of muscle, joint or spinal complaints with onset within the past year.

- **Arthralgia**: As for arthralgia, the data of the entire population indicate no increase in incidence over time. The percentage of symptom-free patients remained constant (at approximately 60%) at every follow-up visit. Likewise, the percentage of patients who reported subjective "mild" (21%), "moderate" (7%) or "severe" (7%) pain at the time of the first follow-up visit remained constant during the post-observational period; a downward trend of labeling arthralgia as severe, with 2.6% at the last visit, was noted. Study the bar chart under Item 10.5 "Arthralgia".

Patient history prior to the start of the study: joint, muscle or spinal symptoms

The inclusion examination of the entire patient population (n=155) revealed a history of muscle, joint or spinal symptoms in 1/3 of the patients (n= 58); a subgroup of these patients recorded the onset of such complaints within the past year. 2/3 of the patients (n=97) were free of the above mentioned symptoms at the start of the study.

• Complaints in patients without preexisting joint, muscle or spinal symptoms.

- Of the symptom-free patients at the time of the inclusion examination, 16 (16.5%) reported new onset of joint and spinal complaints at the time of the first follow-up visit taking place at 3 months; 81 patients (83.5%) remained symptom-free. All further visits yielded a similar distribution of patients with new-onset complaints and the symptom-free patients. At the time of the final examination, 12.4% of the patients, who were asymptomatic at the time of the inclusion examination, reported joint and spinal symptoms, and the majority of the patients reported no new complaints at that time (as well as at the time of other visits during the study).

- Pain medication: The inclusion examination indicated that 18% of the total patient population (n=28) already occasionally or regularly took pain medications/anti-inflammatory drugs; 82% of the patients (n=127) were not taking the mentioned medications. Only an occasional patient from the group of symptom-free patients at the time of the inclusion examination received pain medication at some point during the course of the observational period; there were practically no new prescriptions.

• Complains in patients with preexisting joint, muscle or spinal symptoms

Of the 58 patients who had a history of joint, muscle or spinal symptoms at the time of he inclusion examination, 45% required pain medication at the time of the first follow-up examination taking place at 3 months. The remaining 55% denied the need for such medication. After 3 and 6 months, 16 and 18 patients, respectively, (approximately 30%) reported an increase in pain severity; 8 and 11 patients, respectively, (15-18%) reported a decrease in pain severity. From the third follow-up visit onwards (i.e. 9 months after the inclusion physical examination), fewer patients reported an increase in the severity of pain. Ultimately, there was a downward trend in pain severity in patients with preexisting

symptoms recorded over the entire study course; the majority of patients obtained a pain relief on standard NSAIDs.
There was a certain proportion of patients at each follow-up visit, i.e. about 10% of the total population (n=155, patients without/with preexisting joint, muscle and spinal symptoms), who reported their pain medication as insufficient.

Entire patient population: side effects and termination of therapy
During each visit, symptoms were recorded and reviewed for the cause-effect relationship with anastrozole. The frequency of therapy discontinuation and the reason for it was documented. It has been established that the incidence of anastrozole-associated side effects, evaluated over the entire observational period, dropped from 25.8% recorded at the first visit to 18.1% noted at the last visit. Severe side effects have been reported in 2 patients. The majority of patients, i.e. between 70 to 80%, have continued with the anastrozole therapy over the course of the entire study period. Reasons for therapy discontinuation were mainly adverse effects (such as arthralgia, muscle pain, joint problems). Two patients discontinued therapy due to cancer progression/ recurrence.