AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: No Drug
ACTIVE INGREDIENT: No Drug

Study No: NIS-PLA-XXX-2011/1
P**R**EVALENCE STUDY OF G**A**S**T**RO**I**NTESTINAL RISK FACTORS IN PATIENTS WITH **O**STEOARTHRITIS, RHEUMATOID ARTHRITIS AND A**N**KYLOSING SPONDYLITIS RECEIVING TREATMENT WITH NON-STEROIDAL **A**NTI-INF**L**AMMATORY DRUGS: **RATIONAL Study**

Developmental Phase: IV
Study Completion Date: 31-Mar-2013 (DBL)
Date of Report: 16-Apr-2014

OBJECTIVES:

Primary objective:

- To describe the prevalence of gastrointestinal (GI) risk factors in patients with OA, RA or AS receiving treatment with non-steroidal anti-inflammatory drugs (NSAIDs), at least one dose for at least 2 weeks (15 days) before the study visit.

Secondary objectives:

- To describe the demographic characteristics, clinical profile and functionality of patients with OA, RA and AS according to international classification criteria, in patients taking at least one dose of NSAID for at least 2 weeks (15 days) before the study visit.
- To describe the type of NSAIDs used in the study population.
- To assess the class of gastroprotective agents (GPAs) used as concomitant therapy with NSAIDs.
- To describe the prevalence of GI events in patients with OA, RA and AS receiving treatment with NSAIDs.
- To assess quality of life of patients in this cohort study.
- To assess the relationship between patients' satisfaction with treatment and persistence and treatment adherence.
- To describe the health care resources consumption.

Study design

This was an observational, multicenter, multinational, cross-sectional study designed to evaluate the prevalence of GI risk of factors in patients with OA, RA and AS receiving at least one dose of NSAIDs for at least 15 days before the study visit. The single study visit was part of standard practice and was conducted by GPs, Rheumatologists and/or Orthopaedic Surgeons, in countries in Latin America, Asia Pacific and in Russia.

TARGET POPULATION AND SAMPLE SIZE

The target population for study as defined in the protocol was 6216 subjects with OA, RA or AS who had received NSAID treatment during the 15 days prior to the study visit. The total population actually recruited was 5373 from 140 study centers in 10 countries. Data from all 5373 patients were included in the study analysis.

CRITERIA FOR EVALUATION

Information collected included patient demographics, medical history, disease characteristics, concomitant diseases and all treatment information. Specific information in relation to rheumatic diseases was collected regarding NSAID treatment over the year preceding the study visit and the occurrence of any of a defined range of GI events during this period. The GI events were divided into those that were classified as symptomatic (eg, heartburn or mucosal lesions) and complications (eg, bleeding or perforations). Information on the use of any gastroprotective treatments was also collected.

The prevalence of GI symptoms in the study population and use of GPAs was analysed according to the presence or absence of previously described risk factors as follows:

- Age ≥60 years.
- Concomitant use of acetylsalicylic acid (ASA), oral corticosteroids or anticoagulants.
- Previous ulcer history.
- Previous ulcer bleeding history.
- History of dyspepsia.
- Use of two NSAIDs.
- Use of high dose of one NSAID, eg, diclofenac ≥150 mg/day; meloxicam ≥15 mg/day; naproxen ≥1000 mg/day; piroxicam ≥20 mg/day; ibuprofen >1800 mg/day.

Results were also analyzed by disease type (ie, OA, RA or AS).

Use of health care resources was obtained from the medical history and focused specifically on the number of hospitalizations due to the rheumatic disorder and/or GI complications, and the requirement for endoscopy.

PATIENT REPORTED OUTCOMES

Several questionnaires were used at the assessment visit:

- Detailed information on the occurrence and severity of GI events was collected using the Gastrointestinal Symptom Rating Scale (GSRS).
- Quality of life was assessed using the EuroQol-5 Dimension (EQ-5D) questionnaire, employing both the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS).
- Functional status in relation to rheumatic disease was determined using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC OA Index, version 3.1) and the Health Assessment Questionnaire (HAQ) which was developed as a comprehensive measure of outcomes in patients with a wide variety of rheumatic diseases, including RA, OA, AS, juvenile RA, lupus, scleroderma, fibromyalgia, and psoriatic arthritis.
- Satisfaction with treatment was recorded using the Treatment Satisfaction Questionnaire for Medication for OA patients (TSQM version 1.4).
- Information on treatment adherence was collected using the Morisky-Green-Levine Medication Assessment Scale for all patients (MMAS).

The PRO questionnaires were self-administered after the patient signed the Informed Consent Form. Patients completed the questionnaires independently, so that the answers reflected their own perceptions and views. It was recommended that the questionnaires were completed prior to patient-physician interview to minimize investigator influence on the patients' answers.

STATISTICAL METHODS

The presence or absence of GI symptoms and risk factors as defined above was considered for the primary analysis. Prevalence was measured as the number of patients with the GI risk factors as the numerator and the total study population as the denominator.

Descriptive statistics were also used for the secondary objectives according to the type of distribution variability. For normally distributed variables, the arithmetic mean was used as a central tendency measure, and standard deviation and range as measures of dispersion. For variables with non-normal distributions, the median was used as a measure of central tendency and interquartile range (IQR) as a measure of dispersion.

To describe the prevalence of GI events by disease group (OA, RA and AS), patients with GI events were used as the numerator and the number of patients in each disease group as the denominator.

For the analysis of the objective "To assess the relationship between patients' satisfaction with treatment, and persistence and treatment adherence", the Wilcoxon test was used to compare the scores of the TSQM for adherent and non-adherent patients.

RESULTS

Patient demography and social characteristics

A total of 5373 patients participated in the study, 2469 (45.95%) from Latin America, 2127 (39.59%) from Asia, and 777 (14.46%) from Europe.

In the overall study population 81.6% (4384) patients were female. There were significant variations in gender distribution between regions; the percentage of females from Latin America was 82.79% while the corresponding figures for Asia and Europe were 82.32% and 75.80%, respectively ($\chi^2 = 20.431$, $p < 0.001$).

The average age of the patients was 58.885 years (± 13.301 years, range 19.93 - 94.24 years), with 48.9% of subjects aged 60 and over. Average age was significantly higher in patients from Asia (60.895 ± 11.625 years), than in those from Latin America (58.490 ± 14.295 years) and Europe (54.632 ± 13.225 years) (ANOVA $F = 66.671$, $p < 0.001$). Consequently, the proportion of subjects aged 60 years and over, was also significantly higher in Asia (53.8%) than in the other regions ($\chi^2 = 67.314$, $p < 0.001$).

The distribution of ethnic groups in the total population was: oriental 38.6%, caucasian 23.0%, mestizo 22.3%, white 14.6%, others 1.5%. As expected, ethnicity was related to the areas of origin of the subjects, and 98.1% of patients from Europe were caucasian, 96.8% from Asia were oriental and 48.5% from Latin American were mestizo.

Most (61.3%) of the study population had only primary or secondary education. The level of education also showed significant differences by region, with 94.8% of patients from Europe having had high school or college education. The corresponding proportions for Asia and Latin America were 39.0% and 46.3%, respectively ($\chi^2 = 963.237$; $p < 0.001$). Approximately one third (34.8%) of patients in the study were employed, 33.7% were retired, and 30.0% unemployed. There was an association between employment status and age, with 52.7% of those aged <60 years employed and 52.1% of those ≥60 years retired ($\chi^2 = 1041.387$, $p < 0.001$).

Evaluation of health insurance status showed that 72.5% of patients had social health insurance. In Europe, 99.5% of patients had social health insurance, while 15.4% in Asia and 22.4% in Latin America had no health insurance ($\chi^2 = 541.13$, $p < 0.001$).

Patient disease characteristics

The distribution of rheumatic disorders in the total population of 5373 was OA 2996 (55.8%), RA 1882 (35.0%), AS 283 (5.3%), OA + RA 185 (3.4%), AS + OA 19 (0.4%), and AS + RA 7 (0.1%); 1 patient (0.02%) had no recorded diagnosis of disease.
The proportions of rheumatic diseases varied between regions. The most common disease was RA in patients from Latin America (48.6%) and Europe (53.3%), while 82.0% of patients from Asia had OA. These differences were significant ($\chi^2 = 1172.326$, $p < 0.001$).

The median time since diagnosis of OA was 2 years (IQR 0-5 years, range 0 - 45 years) and 69.3% of patients had 1 or more years of diagnosis. In the 16.8% of patients with OA where the location of the disease was recorded, 84.6% had the disease in the knees and 13.0% in the hips.

The median time since diagnosis of RA was 6 years (IQR 2-12 years, range 0 - 66 years) and 80.6% of patients had 1 or more years of diagnosis. A positive test for rheumatoid factor was recorded in 80.3% of patients with RA.

The median time since diagnosis of AS was 4 years (IQR 1-9 years, range 0 - 42 years) and 84.3% of patients had 1 or more years of diagnosis.
The differences in the times since diagnosis between the three conditions were statistically significant (Kruskal-Wallis = 709.596, p <0.001).

Frequency of previously defined GI risk factors in the study population (primary objective)

Analysis of the frequency distribution of risk factors in the study population showed that the highest frequencies were observed for patients with one (34.2%) or two (32.0%) of the defined risk factors. Only 12.3% of patients in the study had none of the defined risk factors.

The prevalence of known risk factors in the study population is shown in the Table 1. The most commonly occurring risk factors were 'age ≥60 years' (48.89%), 'taking a high dose of NSAID' (22.45%), and 'taking concomitant corticosteroids' (22.37

Table 1 Prevalence of GI risk factors in the study population

Risk factor	Risk factor present				Total
	Yes		No		
	n	%	n	%	
Any risk factor	4711	87.70	662	12.30	5373
Age ≥60 years	2627	48.89	2746	51.11	5373
Concomitant ASA	564	10.50	4809	89.50	5373
Concomitant corticosteroids	1202	22.37	4171	77.63	5373
Concomitant anticoagulants	87	1.62	5286	98.38	5373
History of gastric/duodenal ulcer, complicated	38	0.70	5335	99.30	5373
History of GI complications	405	7.50	4960	92.30	5365
History of dyspepsia	569	10.59	4804	89.41	5373
High dose NSAID	1206	22.45	4165	77.55	5371
More than one NSAID	21	0.39	5350	99.61	5371

Stratification of patients by rheumatic disease showed that the majority of patients with OA (63.6%) were aged 60 or over, compared with 32.3% of patients with RA and 6.7% of patients with AS. Patients with OA were more likely to be taking concomitant ASA (12.6% of OA patients) and anticoagulants (2.1%) than those with RA and AS. In contrast, patients with RA were more likely to be receiving concomitant corticosteroids

(49.0%) than those with AS (19.1%) or OA (4.5%). The proportions of patients taking a high dose of a NSAID was similar across all disease groups.

Secondary objectives

Multivariate analysis

In a multivariate analysis involving all patients with complete data sets, the factors with the highest odds ratios and that were significantly associated with the occurrence of GI symptoms were, 'being a patient from South Korea' (OR = 12.978, 95% CI 6.426 to 26.211, p <0.001), and 'not using gastroprotective therapies' (OR = 5.369, 95% CI 4.672 to 6.170, p <0.001). Other factors that were associated with a significantly increased odds ratio for experiencing GI symptoms were, 'being from Asia', 'having a diagnosis of OA or RA', male gender, and not using corticosteroids. Factors that were not associated with a significantly increased risk of GI events included age ≥60 years, use of NSAIDs, and use of ASA, anticoagulants or SSRIs. The scope and power of the multivariate analysis was limited by the availability of complete data sets.

When this analysis was repeated using data only from patients not receiving a GPA, the only factors with statistically significant odds ratios for developing GI events were, 'being a patient from South Korea' (OR = 20.407, 95% CI 2.323 to 179.235, p =0.007), 'not using DMARDs' (OR = 12.436, 95% CI 1.266 to 125.000, p =0.031), and 'not using corticosteroids' (OR = 1.387, 95% CI 1.031 to 1.886, p =0.032). The scope of this analysis was further limited by the availability of complete data sets and because omission of patients receiving a GPA also removed many of the patients with defined risk factors.

Clinical profile and functionality

The WOMAC questionnaire was completed by 2274 of the 2600 patients with OA in Latin America, Thailand, South Korea, and Russia (n = 2467). Of these patients, 88.4% had localized pain in the knees and 11.6% in the hips. The highest median rating scores for the various measures relating to pain, stiffness and difficulty were associated with pain when going up or down stairs (49, IQR 14-72), followed by difficulty when doing heavy housework (47, IQR 11-73) and difficulty when climbing stairs (44.5, IQR 12-69).

The HAQ was applied to the 3824 patients who did not have a diagnosis of OA and was fully completed by 2165 patients. Of these, the majority of responders fell into the no difficulty/some difficulty categories for all activities assessed. The categories with the highest scores for being unable to complete an activity were 'reach/retrieve a 2 kg object' (10.0%), 'take a bath' (9.7%), 'do housework/light gardening' (8.4%), and 'go to bank/shopping' (6.6%).

When asked to record how much pain had been felt in the previous 7 days, the median score was 52 (IQR 37-67) (scale 0-99).

The second part of the HAQ documented the use of special equipment and the need for assistance to complete functional activities more than 50% of the time. Fewer than 12%

of patients needed to use one or more of the items listed more than 50% of the time and a walking stick (11.1%) was the most commonly used piece of equipment. However, almost a quarter of patients required functional assistance in carrying out daily activities: the most common forms of assistance were with ‘gripping and opening things (23.5%) and ‘going to the bank and shopping: (18.9%).

NSAID use

At the time of evaluation 97% of the total study population was receiving a NSAID other than ASA. The most frequently used NSAIDs among these patients were diclofenac (25.2%) (92.7% orally), meloxicam (20.5%) (98.4% orally), acetaminophen (18.8%) (98.7% orally), celecoxib (16.1%) (99.9% orally) and naproxen (10.8%) (100% orally). Other individual NSAIDs had a usage frequency of <10%.
NSAID use differed significantly according to disease pathology. In general, more patients with OA (98.0%) were using NSAIDs than patients with RA (96.2%) or AS (95.4%) ($\chi^2 = 16.858$, $p < 0.001$). Diclofenac (34.40%) and ibuprofen (10.15%) were used by a significantly higher proportion of patients with RA ($p < 0.05$) than patients with OA or AS. In contrast, meloxicam (25.30%), acetaminophen (22.70%), celecoxib (18.92%), naproxen (11.67%), etoricoxib (8.57%), tramadol (9.81%), and piroxicam (2.29%) were significantly more often used by patients with OA ($p < 0.05$) than those with RA or AS. Indomethacin (18.71%) and acemetacin (5.04%) were significantly used in a higher proportion of patients with AS ($p < 0.001$) than in patients with RA or OA.

The general use of NSAIDs was not significantly higher in patients aged 60 years and over than in patients aged <60 years, even after stratifying by type of rheumatic disease ($p > 0.05$).
Similarly, the general use of NSAIDs was not significantly higher in patients who were concomitantly using ASA, oral corticosteroids or anticoagulants ($p > 0.05$). However, when stratified by type of rheumatic disease, it was observed that patients with AS who were not concomitantly using ASA, oral corticosteroids or anticoagulants had a higher use of NSAIDs (96.2%) than those who were using these agents (82.4%) ($\chi^2 = 7.032$, $p = 0.008$).

There was no significant difference in current NSAID use between patients with a previous history of ulcers/erosions and those who had not experienced these GI effects. All patients (100%) with a history of NSAID-related ulcers/erosions were currently taking NSAIDs compared with 97.0% with no history of ulcers/erosions ($\chi^2 = 1.268$, $p = 0.260$). This pattern did not change when patients were stratified by rheumatic disease.

In the total population, the proportion (97.8%) of patients with a documented history of NSAID-related GI complications who were currently using NSAIDs was not significantly different from those with no previous history of GI side effects (97.1%) ($\chi^2 = 0.657$, $p = 0.418$), even when stratified by type of rheumatic disease ($p > 0.05$).

High doses of NSAIDs

Another potential risk factor for GI symptoms is the use of high doses of NSAIDs. Within the total study population, documented high NSAID doses were diclofenac ≥150 mg/day in 251 (4.9%) patients, meloxicam ≥15 mg/day in 760 (14.7%) patients, naproxen

≥1000 mg/day in 83 (1.6%) patients, piroxicam ≥20 mg/day in 84 (1.6%) patients, and ibuprofen >1800 mg/day in 6 (0.1%) patients.

This pattern differed significantly by type of rheumatic disease only for diclofenac and naproxen. For patients receiving diclofenac, 38.03% of those with AS were taking ≥150 mg/day) compared with 24.36% patients with RA and 11.62% of patients with OA ($p < 0.001$). For naproxen, 40.00% of patients with AS who received this drug were taking ≥1000 mg/day, while consumption of high doses in patients with RA was 24.23% and in those with OA was 8.67% ($p < 0.001$).

Use of GI protective agents

Treatment with GPAs was received by 57.9% of the patients in the study; 34.5% had a history of GI risk, 21.7% had other GI symptoms, and 4.6% had reflux disease. There was a strong preference for using PPIs as the class of GPA. Other classes of GI protection used to a lesser extent were histamine (H_2) receptor antagonists, 5-hydroxytryptamine (type 4) receptor agonists/(type 3) receptor antagonists, and simple antacids. The most commonly used individual treatments were omeprazole (36.35%) (100% oral), ranitidine (6.51%) (99.7% oral), and pantoprazole (3.83%) (99.5% oral).

Analysis of provision of a GPA according to the presence or absence of individual defined risk factors showed that GPA use in patients aged ≥60 years or concomitant use of anticoagulants was close to the study average (57.9%). A modest numerical increase from this mean value was observed in patients taking concomitant ASA (63.8%) and those taking high doses of a NSAID (64.1%). A greater numerical increase in this percentage was seen for all of the other risk factors with values of 96.6% and 93.3% for those with histories of GI complications and GI ulcer, respectively.

Use of GPAs varied significantly by region. General use was significantly higher (71.71%) in Europe than in the other two regions ($p < 0.001$). While omeprazole was the most widely used GPA in all regions, there was significantly higher use in Europe (95.12%) ($p < 0.001$) than in Latin America (66.18%) or Asia (42.89%). In Latin America, ranitidine, pantoprazole, aluminum hydroxide, magnesium hydroxide and cinitapride, drugs were used significantly more than in other regions ($p < 0.05$). In Asia, esomeprazole, lansoprazole, rabeprazole and mosapride were used significantly more often than in the other regions ($p < 0.05$). There were no significant differences in use of cimetidine by region but overall use of this drug was low (0.51%).

Analysis of which NSAIDs were most likely to be accompanied by concomitant GPA therapy revealed significant associations between the two types of drugs. In patients who were taking any NSAID, the use of GPAs was significantly higher than in those not using NSAIDs (OR = 1.692, 95% CI 1.218 to 2.349). Comparison of individual NSAIDs with the rest of the total population taking NSAIDs showed a significant correlation ($p < 0.05$) of greater use of GPAs when the NSAID was tramadol, acetaminophen, ketoprofen or naproxen (OR >1.200). However, when the NSAID was acemetacine, etoricoxib and celecoxib, significantly less use of GPAs was found (OR <1.000). No significant association with the use of GPAs for indomethacin, diclofenac, ibuprofen and piroxicam ($p > 0.05$) was detected.

Prevalence of GI symptoms

Since commencing treatment with NSAIDs, 39.8% of patients in the study reported experiencing GI symptoms. In these patients the symptoms most frequently reported were heartburn (48.78%), abdominal pain (34.38%), gastritis (25.54%), and regurgitation (25.34%).
Analysis of the historical prevalence of GI symptoms by pathology showed that these were significantly more frequent in AS (52.3%), than in RA (49.7%) and OA (32.4%) ($\chi^2 = 164.849$, $p < 0.001$).
Heartburn was reported in 54.1% of patients with AS who had GI symptoms. This percentage was significantly higher than that in patients with RA (50.8%) or OA (46.0%) ($\chi^2 = 6.116$, $p = 0.047$). Gastritis, diarrhea, duodenitis, and esophageal ulcer were also significantly more frequent in AS than in RA or OA. Abdominal pain was the only symptom that was reported significantly more frequently in patients with OA than in AS or RA, while nausea and ulcers/erosions were the only symptoms significantly more frequently reported in patients with RA.

Results of the analysis of symptom severity reported using the GSRS scale by 2469 patients from Latin America showed that across all 15 items ≥40.5% of patients reported scores of 0, suggesting that ≤59.5% of patients experienced GI side effects that caused mild discomfort or worse.

Analysis of the percentage of patients (including those receiving a GPA) who reported GI symptoms during the previous year in relation to the presence or absence of defined risk factors showed that age ≥60 years, concomitant use of anticoagulants, and the use of high dose NSAIDs were associated with values close to the study average (40.3%). In contrast, a higher percentage of patients with any of the other risk factors reported experiencing GI symptoms in the previous 12 months; the highest values being associated with a history of ulcer (100%), dyspepsia (99.8%) or GI complications (93.1%), whether or not the condition was still present.

GI symptoms according to NSAID use

The presence of GI events at the time of evaluation was assessed in relation to whether or not the patient was currently taking a NSAID. Of the 5213 currently taking NSAIDs, GI events were present in 40.21%. Of the 150 patients not currently taking NSAIDs, the GI symptom prevalence rate was 40.00% ($p = 0.959$). Assessment of each associated GI event type showed no significant differences in occurrence according to current NSAID use ($p > 0.05$). However, the incidence of GI events was generally numerically higher in patients who were taking NSAIDs.
When stratified by rheumatic disease, it was found that there was greater reporting of abdominal pain (51.4%) in patients with RA who were not currently taking NSAIDs compared with those who were taking them (32.1%) ($\chi^2 = 5.942$, $p = 0.015$). In contrast, patients with AS who were taking NSAIDs had significantly more heartburn (55.9%) than those who were not taking NSAIDs (0%) ($\chi^2 = 6.088$, $p = 0.014$).

GI complications

Complications related to GI symptoms were documented for 7.2% of patients. The most common events were 'gastric bleeding' (5.84%), 'bleeding of hiatal hernia' (2.92%), and 'bleeding of the large intestine (excluding hemorrhoids)' (2.92%).

Overall, GI complications were significantly more frequently observed in patients with AS (16.0%) ($p < 0.001$) compared with those with RA (10.9%) and OA (4.0%). However, specific complications did not differ significantly by rheumatic disease pathology ($p > 0.05$).

Quality of life

Results collated from 5329 responses to the EQ-5D questionnaire suggested that the majority of patients had some trouble walking and with carrying out day-to-day activities. The highest individual category score (73.0%) was for the number of patients reporting mild-to-moderate pain or discomfort.

Results by dimension are summarized below:

- *Mobility:* 32.7% of patients had no trouble walking, 66.1% had some trouble walking, and 0.9% were confined to bed.
- *Self-care:* 62.6% of patients had no problems with self-care, 35.6% had some trouble bathing or dressing, and 1.4% were unable to bathe or dress themselves.
- *Usual activities (e.g. work, study, housework, family or leisure activities):* 39.3% had no problems with their usual activities, 56.7% had some problems, and 3.6% were unable to perform their usual activities.
- *Pain/discomfort:* 15.7% had no pain or discomfort, 73.0% had some pain, and 11.0% had extreme pain.
- *Anxiety/depression:* 54.2% were not anxious or depressed, 39.7% were moderately anxious or depressed and 5.8% were extremely anxious or depressed.

Self-classification of overall state of health using a visual analog scale yielded a median value of 70.0 (IQR 50-80) (min 0 - max 100).

Satisfaction with NSAID treatment and treatment adherence

Analysis of responses to the TSQM by 5064 patients showed that 67% of patients were 'satisfied' to 'extremely satisfied' with the ability of their NSAID to prevent or treat pain, with the way that the drug relieved symptoms, with its speed of onset, and with the drug in general. In addition 72.2% of patients indicated that they experienced no side effects (27.8% experienced side effects). Patients who experienced side effects (n=1379) reported the degree of bother caused by these (Question 5) as, extremely 3.7%, very 14.8%, somewhat 39.2%, some 35.0%, and not bothersome at all 7.4%.

The 1379 patients who were eligible to respond to the questions related to the impact of side effects on their physical health and functional capacity reported that at least 47.6% (ie, approximately half of the eligible responders to these questions), experienced no, or minimal impact of side effects.

More than 87% of patients reported that NSAIDs were easy/extremely easy to use and to schedule, and convenient to take. Approximately 90% of patients had some degree of confidence in the suitability of their prescribed NSAID and treatment schedule.

Approximately 87% of patients considered that the benefits of NSAID treatment outweighed the risk of side effects.

According to the TSQM, patients who stated that they were very satisfied or extremely satisfied with their NSAID treatment were significantly more likely to remain treatment adherent (using various measures of treatment adherence, $p < 0.001$ for each category) than those who were less convinced about the benefits of treatment.

Morisky Adherence Scale

Responses to the Morisky Scale questionnaire were obtained from 94% of patients in the study. While 57.89% of patients stated that they never forgot to take their medication, 38.93% stated that they stopped taking it because they felt better and 23.08% stopped because they felt worse.

Use of healthcare resources

Records of endoscopic investigation and/or hospitalization due to GI complications of NSAID treatment were available for 445 patients in the study, corresponding to 8.6% of the total patients with OA, RA or AS. Of these, 87.6% (7.6% of total study population) had undergone endoscopy. Patients with AS (91.7%) were significantly more likely to have had endoscopies performed than those with RA (90.9%) or OA (81.2%) ($\chi^2 = 9.125$, $p = 0.010$).

Within this group, 10.6% had been hospitalized for GI complications related to NSAID use (0.9% of the total study population). When stratified by disease, a significantly higher percentage of patients with OA were hospitalized (15.6%) than those with AS (8.3%) or RA (7.8%) ($\chi^2 = 6.300$, $p = 0.043$).

Differences between regions

Future analysis will address variations in patient management practices regarding the provision of GPA treatment in patients with OA, RA and AS in the different geographic regions in which the RATIONAL study was conducted.

Safety

Safety reporting in a non-interventional study was at the discretion of the treating physician. No reports of adverse drug reactions other than those that were the subject of the study or any other safety concerns were communicated to AstraZeneca during the conduct of this study.