AstraZeneca

NIS-ARO-HCH-2006/1

SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: ARIMIDEX™

ACTIVE INGREDIENT: Anastrozole

Trial title (number): ARIMIDEX Study (Non-interventional study to evaluate Arimidex in adjuvant therapy in partial or complete response or stabilized disease after first line chemotherapy in postmenopausal women with advanced breast cancer).

Developmental phase: N/A
First subject recruited: 15 December 2006
Last subject recruited: 31 December 2006
Approval date: 01 December 2006

OBJECTIVES

Primary objective
Evaluation of anastrozol as an adjuvant treatment in postmenopausal patients with advanced breast cancer in whom a partial or complete response or stabilized disease were obtained with first line chemotherapy, by tumoral response assessment.

Secondary objective
Anastrozol potential to re-stage the disease (from stabilized disease to partial response or from partial to complete response).

Safety and tolerability of anastrozol therapy by recording all side effects.

METHODS

The programme included all patients that the doctors have already decided to start to treat with Arimidex (anastrazole) for at least one month. The patients followed current practice during all 6 visits specified in the protocol.

The programme included all patients that the doctors already decided to start to treat with anastrozol for at least 1 month. The patients will followed current practice (demographic data, breast cancer history and actual tumor status, previous medical and surgical treatments, menopausal and receptor status and response to previous therapies, physical examination, weight and ECOG status, bone scintigraphy, chest X-ray, hepatic ultrasound, concomitant medication), adverse events, concurrent therapy (including anticholinergic medication) during all 6 visits specified in the protocol. The bone scintigraphy, chest x-ray, hepatic ultrasound will be collected for patients only in the case that they have been part of routine practice and they are not obligatory ones (to be performed every month). The treatment consisted of administration of 1 tablet/day, 6 months period.

The total number of patients to participate to the program was minimum 160 and maximum 200.

Programme Assessments

	Visit #1	Visit #2	Visit #3	Visit #4	Visit #5	Visit #6
Patient registration	X					
Informed consent	X					
Physical examination, status ECOG	X	X	X	X	X	X
Concomitant medication	X	X	X	X	X	X
Metastasis evaluation/disease stage TNM (*scintigraphy, Rx pulmonary, echography**)	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X

* This data were collected for patients where they have been part of routine practice and they are not obligatory ones; this diagnostic tests not have been repeated every month, unless will be performed through routine practice.

Assessment
Treatment efficiency was multiply assessed during the trial.

Tumours were initially classified by the investigators as measurable or not measurable according to the following criteria:

Measurable lesions: lesion with at least one measurable dimension (the highest will be recorded) greater than 20 mm, using conventional techniques. Clinically assessed lesions will be considered measurable when superficially positioned (for example palpable lymph nodes).

Not measurable lesions: lesion that's any dimension is less than 20 mm with conventional techniques.

Tumoral response assessment:

- complete response (CR): no tumour remnants;
- partial response (PR): ≥ 30% regression of tumoral dimensions from the greatest dimensions sum, related to initial dimension sum;
- progressive disease (PD): ≥ 20% expansion of tumoral dimension relative to smallest dimensions sum or appearance of a new tumor;
- stabilized disease (SD): no modification of tumour dimensions.

Reporting Adverse Drug Reactions
All participating physicians have been responsible to comply with local law on ADR reporting MoH Ordinance 406/2005 Adverse Events.

Recording of Adverse Events
All AEs must recorded on standard forms (AstraZeneca post-marketing adverse event report form attached).

For the purpose of this programme, any detrimental change in a patient's condition subsequent to them entering the programme and during the 7-day follow-up period after the final treatment should be considered to be an AE. All SAEs occurring during the programme period, or within 30 days after the last dose of study medication, must be reported to AstraZeneca within one day of doctor becoming aware of the event. Any fatal or life threatening AEs must be reported to AstraZeneca immediately and AstraZeneca will report the event, if causally related to study drug, in accordance with the required regulatory reporting guidelines. A causality assessment must be provided for all SAEs. Follow-up

information on SAEs must be provided as soon as it is available, on the same day as the investigator becoming aware of the information. All SAEs, including those that are ongoing at the end of any follow-up period, will be followed to resolution or until assessed by the doctor that the condition is stabilised and unlikely to change.

Data Processing
Simple descriptive statistical analysis have been performed.
Data were statistical analyzed using SPSS v13 Windows XP Professional, Stata v9 and Epi Info program. Descriptive statistical tests, parametric t-Student test, correlation and regression tests were used.

RESULTS

A total of 200 patients were included from 20 centres in Romania. 26 patients had early breast cancer and were excluded from this statistical analyze.
174 patients eligible from 200 included in NIS: complete response19 (10.9%); partial response 43 (24.7%), stabile disease 61 (35.1%), not measurable lesions 39 (22.4%), progressive disease 6 (3.4%), missing data 2 (1.1%). 0% adverse events reported.
Median time from advanced breast cancer diagnosis was 2 years.

N	Valid	168
	Missing	6
Mean		3.2738
Median		2.0000
Std. Deviation		3.67986
Minimum		.00
Maximum		22.00

15 patients (8.6%) have been diagnosed in the last year with advanced breast cancer

Time from diagnosis (years)					
		Number of patients	Percent	Valid Percent	Cumulative Percent
Valid	.00	15	8.6	8.9	8.9
	1.00	46	26.4	27.4	36.3
	2.00	31	17.8	18.5	54.8
	3.00	22	12.6	13.1	67.9
	4.00	18	10.3	10.7	78.6
	5.00	13	7.5	7.7	86.3
	6.00	6	3.4	3.6	89.9
	7.00	4	2.3	2.4	92.3
	8.00	3	1.7	1.8	94.0
	9.00	1	0.6	0.6	94.6
	10.00	1	0.6	0.6	95.2
	11.00	2	1.1	1.2	96.4
	14.00	1	0.6	0.6	97.0
	17.00	1	0.6	0.6	97.6
	18.00	1	0.6	0.6	98.2
	19.00	1	0.6	0.6	98.8
	20.00	1	0.6	0.6	99.4
	22.00	1	0.6	0.6	100.0
	Total	168	96.6	100.0	
Missing	System	6	3.4		
Total		174	100.0		

19 (10.9%) patients obtained complete response, 43(24.7%) patients obtained partial response and 61(35.1%) patients had stabile disease.
22.41% patients had not measurable lesions.

PD = progressive disease; SD = stabile disease; UN = not measurable lesions; SUR = surgery; RC = complete response; RP = partial response

STATUS	Number of patients	%	Cumulative Percent
PD	6	3.4	3.4
SD	61	35.1	38.5
Not measurable lesions	39	22.4	60.9
Missing data	2	1.1	62.1
Surgery	4	2.3	64.4
RC	19	10.9	75.3
RP	43	24.7	100.0
Total	174	100.0	

BS+RC+RP= 70.7%

96% from patients received previous chemotherapy.

	Previous chemotherapy		Previous surgery		Concomitant therapy	
	NR	%	NR	%	NR	%
Yes	167	96.0	139	79.9	131	75.3
No	7	4.0	35	20.1	43	24.7
Total	174	100.0	174	100.0	174	100.0

Concomitant pathology
16.7 % from patients have had concomitant cardiovascular pathology.

	Nr	%	% cum
No concomitant pathology	117	67.2	67.2
Neuro-psychiatry	2	1.1	68.4
Ophthalmology	3	1.7	70.1
Otolaryngology	1	0.6	70.7
Cardiovascular	29	16.7	87.4
Respirator	1	0.6	87.9
Gastrointestinal	2	1.1	89.1
Liver disease	3	1.7	90.8
Genitourinary	4	2.3	93.1
Renal	1	0.6	93.7
Musculoskeletal	2	1.1	94.8
Endocrinology	5	2.9	97.7
Allergies	1	0.6	98.3
Liver and respirator diseases	1	0.6	98.9
Neurology and cardiovascular disease	1	0.6	99.4
Neurology, renal and musculoskeletal	1	0.6	100.0
Total	174	100.0	

Concomitant medication	V1	V2	V3	V4	V5	V6
Yes	77 (44.3%)	55 (31.6%)	53 (31.2%)	51 (30.5%)	50 (30.5%)	47 (28.7%)
No	97 (55.7%)	119 (68.4%)	117 (68.8%)	116 (69.5%)	114 (69.5%)	117 (71.3%)
Total	174	174	170	167	164	164

48 (28.6%) patients have had bone metastasis and 18 patients (10.3%) have had lung metastasis at visit 1.

Bone metastasis	V1	V2	V3	V4	V5	V6
Yes	48(28.6%)	46(26.4%)	42(24.7%)	42(25.1%)	42(25.6%)	39(23.9%)
No	120(69%)	122(70.1%)	123(72.4%)	121(72.5%)	119(72.6%)	120(73.6%)
Abnormal bone non metastasis	6(3.4%)	6(3.4%)	5(2.9%)	4(2.4%)	3(1.8%)	4(2.5%)
Total	174	174	170	167	164	163
Lung metastasis	V1	V2	V3	V4	V5	V6
Yes	18(10.3%)	19(10.9%)	19(11.2%)	16(9.6%)	16(9.8%)	17(10.4%)
No	149 (85.6%)	147 (84.5%)	146 (85.9%)	145 (86.8%)	142 (86.6%)	140 (85.9%)
Abnormal lung non metastasis	7(4%)	7(4%)	5(2.9%)	6(3.6%)	6(3.7%)	6(3.7%)
Total	174	173	170	167	164	163
Stage	V1	V2	V3	V4	V5	V6
III	14(8.1%)	15(8.6%)	16(9.5%)	15(9%)	16(9.8%)	15(9.2%)
III A	38(22%)	38(21.8%)	37(21.9%)	38(22.9%)	38(23.3%)	37(22.7%)
III B	52(30.1%)	52(29.9%)	50(29.6%)	48(28.9%)	46(28.2%)	46(28.2%)
IV	69(39.9%)	69(39.7%)	66(39.1%)	65(39.2%)	63(38.7%)	65(39.9%)
TOTAL patients	173	174	169	166	163	163

39.9% from patients included have been with stage IV breast cancer.

ECOG status

ECOG	V1	V2	V3	V4	V5	V6
0	39(24.8%)	38(24.2%)	39(25.5%)	41(27.5%)	44(29.9%)	48(32.7%)
1	82	38(52.2%)	77(51.7%)	74(50.3%)	74(50.3%)	75(51%)
2	39(24.8%)	36(22.9%)	29(19.5%)	29(19.5%)	28(19%)	23(15.6%)
3	1(0.6%)	1(0.6%)	2(1.3%)		1(0.7%)	1(0.7%)
4				2(1.3%)		
TOTAL patients	157	157	153	149	147	147

No of patients who finalized the study	Number	%
Yes	164	94.3
No	10	5.7
Total	174	100.0

10 patients withdrawal from the study.

		Causes that led to the withdrawal				Total
		Violation of protocol	Missing from control visits	Others	Death	
Finalized the study	No	2	4	1	3	10
Total patients		2	4	1	3	10

Final status for the patients with bone or liver metastasis

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	PD	3	4.9	4.9	4.9
	SD	25	41.0	41.0	45.9
	UN	14	23.0	23.0	68.9
	SUR	4	6.6	6.6	75.4
	RP	15	24.6	24.6	100.0
	Total	61	100.0	100.0	

BS+RP=65.6%

Safety results
There were no adverse events reported.

REFERENCE: None