AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: NA
ACTIVE INGREDIENT: NA

Study No:
NIS-OAR-XXX-2011/1

Developmental Phase: NA

Study Completion Date: 30-04-2014

Date of Report: 20-11-2014

OBJECTIVES:

Primary objective

- To compare the proportion of disease free survival of lung cancer in patients with or without EGFR mutation test as part of the diagnosis and treatment strategy after 12 months of treatment.

Main secondary objective

- To describe the demographic and clinical characteristics of patients in the study cohort with mutation in the EGFR.
- To describe the EGFR mutations present in the studied population.
- To compare the survival in patients with lung cancer with or without the EGFR mutation test as part of the diagnosis and treatment strategy after 12 months of treatment.
- To compare the number of hospitalizations, and treatment suspensions and interruptions between the cases and controls.

METHODS:

Target subject population

The study target population is lung cancer patients under first line treatment being followed up by specialists. Patients who were or were not requested the mutation study will be identified, being it possible to use historical controls.
According to previous data, 50% of the patients with lung cancer will need a second line of treatment due to their disease, and 25% a third.

A multicenter, observational, longitudinal, retrospective phase IV study is proposed, which could be defined as of cases and controls according to Almeida Filho's classification. As the response variable is less frequent (appearance of mutation in EGFR), the use of the design of cases and controls was decided. Two controls are proposed for each case, paired by sex, age and site of oncologic treatment received.
Cases: persons diagnosed with lung adenocarcinoma under first line treatment, who were requested the test to detect EGFR mutations as part of the diagnosis and treatment strategy.
Controls: persons diagnosed with lung adenocarcinoma under first line treatment, who were not requested the test to detect EGFR mutations as part of the diagnosis and treatment strategy.
Historical controls will be used to compare with the cases. Even though this design could add bias, it also reduces the variability about the kind of patient follow-up as the controls would come from patients monitored by the same physicians when the test was not available.
Between 80 and 100 sites will be participating in the study. It is planned to include 450 patients, between cases and control (two controls per each case).
It is a national study, with only one participating country.
There is no assignment to any study treatment. This is a retrospective study, evaluating patients having performed or not the EGFR test, irrespectively the treatment they have received.
Patient information will be collected from the time of being diagnosed of IIIb/IV stage of NSCLC (*Lung. En: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 253–70*) to 12 month after.

RESULTS:

The planned analysis could not be performed due to the number of patients included at each group did not correlate with the original plan to have 2 controls for each case, so that, the proposed characteristics for the matching cases and controls have not been included in the analysis.
Following this, descriptive statistic has been performed and it has also been performed the association analysis though the use of OR.

Table 1. Baseline characteristics and treatment of patients with diagnose of IIIb/IV stage lung adenocarcinoma with (cases) or without (historic controls) EGFR test as part of a diagnosis and treatment strategy.

		Cases n=106	Controls n=168	*p*
Males % (n/n)		38.7(41/106)	42.8(71/166)	0.55
Smokers/past-smokers		67.6 (71/105)	74.1 (123/166)	0.24
Oriental race% (n/n)		1.9 (2/106)	0.6 (1/161)	0.56
Media age (SD)		63.3 (10.61)	63.96 (10.6)	0.54
ECOG % (n/n)	0	29.2(31/106)	31.5(53/168)	0.68
	1	55.6(59/106)	46.4(78/168)	0.13
	2	14.1(15/106)	18.4(31/168)	0.35
	3	0.9(1/106)	2.4(4/168)	0.65
	4	0(0/106)	1.2(2/168)	-------
Stage % (n/n)	III B	22.1(23/104)	24.5(41/167)	0.38
	IV	77.9 77.8(81/104)	75.4(126/167)	
Gefitinib% (n/n)		15.0%(16/106)	-------	
Carboplatin% (n/n)		43.4%(46/106)	53.3%(89/167)	
Paclitaxel% (n/n)		36.8%(39/106)	41.9%(70/167)	
Pemetrexed% (n/n)		19.8%(21/106)	8.4%(14/167)	
Gemcitabine% (n/n)		9.4%(10/106)	23.3%(39/167)	
Vinorelbine% (n/n)		11.3%(12/106)	14.3%(24/167)	
Docetaxel% (n/n)		0.9%(1/106)	1.8%(3/167)	
Cisplatin% (n/n)		11.3%(12/106)	29.9%(50/167)	

Primary Objective:

The primary objective of this NIS was to compare the proportion of disease free survival (DFS) of lung cancer.
It has not been observed a significant association between the strategy with or without EGFR testing regarding the clinical evolution up to 12 months, evaluated trough DFS (CR, SD, PR, PD) and hospitalization.
However, it has been detected a significant association between the inclusion of EGFR testing as part of a diagnostic and treatment strategy and a decrease of mortality rate.

It should also be highlighted that patients receiving gefitinib during their treatment have lower mortality rate tan the control group mortality rate and that other treatment options within the cases group.

Table 2. Clinical progression of control and cases after one year diagnosed of IIIb/IV stage lung adenocarcinoma

	Cases	Controls	OR (IC95%)	*p*
Mortality rate % (n/n)	40.4 (42/104)	53.1 (76/143)	0.59 (0.35-0.98)	0.044
Mortality Rate M+ [Number of gefitinib/TKI treated]	37.5 (6/16)	NA		
Mortality Rate M-/M Unknown		NA		
Lost to follow up % (n/n)	1.9 (2/106)	14.9 (25/168)	8.9 (2.0-38.4)	0.0002
Disease progression % (n/n)	69.3(70/101)	66.6(106/159)	1,13 (0,66- 1,93)	0.65
Complete response % (n/n)	1.2 (1/80)	3.9 (5/129)	3,18 (0,36-27,7)	0.26
Partial response % (n/n)	13.7(11/80)	13.9 (18/129)	0,98 (0,43-2,2)	0.96
Stable disease % (n/n)	21.2(17/80)	20.1(26/129)	1,06 (0,53- 2,12)	0.84

Secondary Objectives:

- To describe the demographic and clinical characteristics of patients in the study cohort with mutation in the EGFR.

EGFR mutations have been detected in 54 patients, most of them were females with a median age of 64.8 years (range: 42-81).
3.7% were oriental race (2/54), 58.5% have antecedents of tobacco use (current or past smokers) (31/53), 78% (42/54) were measured as performance status ECOG 0 or 1 and most of them have been diagnosed as stage IV disease (79.6%, 43/54).
Regarding diagnostic strategies, the highly reported test was histology (77.8%, 42/54), while Fine Needle Aspiration has been performed in 16.7% (9/54), and citology in 14.8% (8/54).
40.7% of patients in this population have been hospitalized at least one time and of those, 90.9% (20/22) has been related with disease progression, while 22.7% (5/22) has been related with side effects of pharmacologic treatment.
Mortality rate up to 12 months was 42.59% (23/54). Of those patients, 6 have received gefitinib.

- To describe the EGFR mutations present in the studied population.

The mutation most commonly detected was in exon 20, alone in 26 patients (48.2%), associated to exon 19 mutation in 10 patients (18.5%), associated to exon 21 in 6 patients (11.1%) and to exon 18 in 1 patient (1.9%).
Mutation of exon 21 was observed in 6 patients (11.1%) and associated to mutation in exón 19 in 1 patient (1.9%).
Muration of exon 19 has been observed in 3 patients (5.6%) and associated to exón 18 in 1 patient (1.9%).

- To compare the survival in patients with lung cancer with or without the EGFR mutation test as part of the diagnosis and treatment strategy after 12 months of treatment.

This study shows, in patients with IIIb/IV stage lung adenocarcinoma, the testing practice to detect EGFR mutations as part of the diagnosis and treatment strategy has an impact on the mortality rate at one year follow up when compared with patients of similar characteristics to whom the test had not been performed: cases 40.4 (42/104) vs controls 53.1 (76/143). OR (IC95%): 0.59 (0.35-0.98). p: 0.044

- To compare the number of hospitalizations, and treatment suspensions and interruptions between the cases and controls.

	Cases	Controls	OR (IC95%)	*p*
Hospitalization % (n/n)	45.3(48/106)	39.9(65/163)	0,80 (0,48- 1,31)	0.38
Hospitalization due to oncologic medication % (n/n)	11.4(9/79)	12.9(14/108)	1,15 (0,47-2,82)	0.74
Hospitalization due to baseline disease % (n/n)	56.9(45/79)	52.3(57/109)	0,82(0,46-1,48)	0.52
Number of hospitalizations median (IQR)	1 (0-2)	1 (0-3.4)	_____	0.47