AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: NOT APPLICABLE
ACTIVE INGREDIENT: NOT APPLICABLE

Study No: NIS-OEU-DUM-2008/1 **NCT:** NCT00831909
TITLE: Epidemiological study to describe NSCLC clinical management patterns in Europe. Lung-EPICLIN

Developmental Phase: NOT APPLICABLE
Study Completion Date: 07/31/2010 (Last Subject Last Visit)
Date of Report: 07/04/2011. Updated 27/Jan/2014

This study summary is updated in March 2014, following publication of two manuscripts about the study:

- Carrato A *et al*. Clinical management patterns and treatment outcomes in patients with non-small cell lung cancer (NSCLC) across Europe: EPICLIN-Lung study. Curr Med Res Opin. 2014 Mar;30(3):447-61.
- Vergnenègre A *et al*. Real-world healthcare resource utilization in a European non-small cell lung cancer population: the EPICLIN-Lung study. Curr Med Res Opin. 2014 Mar;30(3):463-70.

OBJECTIVES:

Primary Objectives:

- To provide accurate, reliable information on NSCLC clinical management across European countries in order to detect unmet medical needs of this disease

Secondary Objectives:

- To assess the differences in patient characteristics, disease stage (differentiating between non-advanced disease, locally advanced disease, metastatic disease), and in clinical management across European countries.
- To detect differences in clinical outcomes and related factors among countries.

- To identify factors associated with clinical outcomes (patient, disease stage and clinical management related factors): predictive modelling for improved patient outcome.
- To identify factors associated with the different levels of functional status and quality of life.
- To compare the use of health care resources among countries.

METHODS:

This was a multinational, multicentre, non-interventional, prospective cohort study carried out in a representative selection of hospitals to assess lung cancer management in 8 countries throughout Europe. To ensure that the disease management of patients in this study was not modified with respect to that of normal clinical practice, no extra visits or extra procedures were performed for study purposes.

The study comprised a 3-month inclusion period, and a 1-year follow up period. All patients were followed for at least a year.

All NSCLC patients attending the department responsible for treating these patients at the selected sites for the first time during the inclusion period were included. Information was taken from the medical records regarding patient and disease characteristics, management approaches regarding the visit plan, diagnostic tests performed and therapies received by the patient. A sample of patients (approximately 25%) was selected to complete Quality of Life (QoL) questionnaires (FACT and EUROQoL/EQ-5D).

A descriptive analysis approach was used to analyse the NSCLC population, clinical management, clinical outcomes and health care resources.

Logistic and general linear models (GLM) were used to assess the association of patient characteristics (including stage of disease, histology, PS, etc) and clinical management (independent variable) with clinical outcome variables (clinical evolution, treatment related events, mortality). Model-based point estimates of odds ratios and corresponding 95% confidence intervals were reported (when applicable). P-values were reported for comparisons between different treatments.

A descriptive analysis approach was used to assess factors related to the use of health care resources, and a comparison of the level of use of health care resources was carried out.

Changes in FACT-L total score and in EQ-5D total score from first visit to the visit prior to a specific treatment response, and from the first visit to each assessment were analysed using an ANCOVA model.

RESULTS:

3508 patients were included in the overall analysis; mean (S.D.) age 64.5 years (10.5); males:females ratio 3.5:1; 11% never-smokers. 308 (8.8%) patients were tested for biomarkers; 122 (3.2%) for EGFR mutations. 2645 patients received chemotherapy (CT) at any point, managed as follows: 259 (9.8%) had Stage I/II disease, of which 146 (56.4%) also had surgery; 862 (32.6%) had Stage III disease (319 (12.1%) IIIa and 543 (20.5%) IIIb), of which 192 (22.3%) had surgery, plus adjuvant CT in 46.6% of cases; 1398 (52.8%) had Stage IV disease, of which 533 (38.13%) also received radiotherapy. Median (med) survival was analysed by systemic treatment regimen, tumour histology and Stage at diagnosis. Effect of treatment regimen on med survival: 10.8 months (Platinum regimens); 8.5 (Non-platinum regimens); 12.9 months (regimens with Bevacizumab); 10.8 months (Investigational regimens); and 6.6 months (Basic supportive care). Effect of tumour histology: 14.4 months (adenocarcinoma); > 15 months (squamous cell carcinoma); 11.9 months (large cell carcinoma); 12.7 months (Carcinoma); > 15 months (other). Effect of Stage: > 15 months (Stage I); > 15 months (II), > 15 months (IIIa), 14.3 months (IIIb) and 10.8 months (IV)..

Spontaneously mentioned Adverse Event (AE) data were available for 2446 patients (Table 1). AEs were reported in all treatment regimens. The most frequently reported severe (CTCAE ≥3) AEs were classified as blood (16.0%, mostly treatment-related), and pulmonary/upper respiratory (7.8%, mostly disease-related). Investigational regimens and regimens with bevacizumab had the highest AE frequencies. AEs requiring treatment were most frequent in patients receiving regimens with bevacizumab (CTCAE ≤2) and in patients receiving investigational regimens (CTCAE >2). Overall, 6.9% and

6.0% of patients receiving first-line chemotherapy required dose reductions and discontinuations, respectively.

Table 1

	No pts treated	**No (%) pts with CTCAE ≤ 2**	**No (%) pts with CTCAE > 2**
Platinum regimens	1985	1203 (60.6)	703 (35.4)
Non-platinum regimens	287	156 (54.5)	85 (29.6)
Regimens with Bevacizumab	100	67 (67.0)	39 (39.0)
Best supportive care	6	0 (0.0)	0 (0.0)
Investigational regimens	68	52 (76.5)	41 (60.3)
Total	**2446**	**1478 (60.4)**	**868 (35.5)**

Baseline (visit 1; V1) QoL data were available for 1626 patients; of these, 734 provided QoL data at visit 2 (V2). At V1, mean EQ-5D scores were 63.97 ± 20.02 for patients <70 years old and 62.42 ± 19.03 for patients ≥70 years old; p=0.179. Mean EQ-5D scores by disease stage at V1 were: 64.51 ± 20.51 (Stage I); 68.24 ± 18.72 (Stage II); 67.06 ± 18.49 (Stage IIIa); 64.21 ± 18.82 (Stage IIIb); 61.15 ± 20.33 (Stage IV). An adjusted analyses was performed on the EQ-5D scores with imputation of missing data at V2 as '0' for patients who had died and '70' for patients who had progressed. This was to account for potential bias as more favourable outcomes may have been more likely to complete the QoL self-assessment form at 2nd study visit, compared with those with poorer outcomes, and those who had died. In the analysis, variables associated with increased risk of worsening QoL (V1-V2) were Stage at diagnosis IIb (p=0.045), IIIa (p=0.010), IIIb (p=0.022), and IV (p=0.010); performance status (PS) 3 or 4 (p=0.049); and presence of CTCAE>2 (p=0.006). Variables associated with a lower risk of

worsening QoL were CTCAE≤2 (p=0.001); being treated in Greece (p=0.027), France (p=0.002), Spain (p≤0.0001), Italy (p≤0.0001); or being treated in a university hospital (p=0.006).

In terms of use of healthcare resources, the overall mean (S.D.) number of hospitalization days was 16.4 (18.4). Most patients (96.0%) underwent imaging procedures, most commonly scanning (93.9%). Surgery was associated with a mean of 12.5 (9.3) hospitalization days, with lobectomy and extended procedures (20.3%) being the most common surgery types. Radiotherapy resulted in a mean of 11.6 (14.1) hospitalization days. The majority of radiotherapy was palliative (56.0%), which resulted in fewer (mean 9.5 [11.1]) hospitalization days. Administration of systemic treatment resulted in a mean of 6.5 (8.0) hospitalization days, 1.7 (3.6) visits for disease-related events, 2.3 (1.8) adverse events and 5.4 (5.9) blood-specific resources.