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

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 age 64.5 years (±10.5); males:females ratio 3.4; 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 155 (59.8%) also had surgery; 862 (32.6%) had Stage III disease (319 (12.1%) IIIa and 543 (20.5%) IIIb), of which 238 (27.61%) had surgery, plus adjuvant CT in 30.1% 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: 0.69 years (cisplatin [Cis]-based doublets); 0.55 years (carboplatin [Car]-based doublets); 0.80 years (bevacizumab-containing triplets); 0.36 (monotherapy with gemcitabine [Gem] or vinorelbine [Vin]); 0.27 years (erlotinib [Erl]); 0.44 years (investigational products), 0.55 years (other). Effect of tumour histology: 0.58 years (adenocarcinoma); 0.64 years (squamous cell carcinoma); 0.4 years (large cell carcinoma); 0.62 years (NOS); 0.56 years (other). Effect of Stage: 1.05 years (Stage II), 1.07 years (IIIa), 0.7 years (IIIb) and 0.47 years (IV). Med survival was not reached for Stage I patients (> 1.25 years). Variables associated with a lower risk of death/clinical progression were age ($p \leq 0.0001$), 1% increased risk per year; female sex ($p=0.011$); CTCAE$\leq$2 ($p=0.008$). Variables associated with a higher risk were Stage at diagnosis (IIIb, $p=0.035$; IV $p \leq 0.0001$); performance status (PS)>0, CTCAE>2, attending a regional hospital, receiving, Erl, Gem, Vin, or best supportive care (all $p \leq 0.0001$); or receiving Car + Gem ($p=0.009$).

Spontaneously mentioned Adverse Event (AE) data were available for 2243 patients (Table 1). CTCAE ≤2 were reported in all treatment regimens. Patients receiving cisplatin (Cis)-based regimens experienced the highest incidence of severe (CTCAE >2) events (19.7%). The most frequently-reported AEs >grade 2 were blood (16.0%) and pulmonary (7.8%). Dose reductions and treatment interruptions were most frequently required with Car + paclitaxel + investigational (30.0%) and Car + vinblastine (Vib) (15.2%), respectively. Patients receiving Cis + docetaxel experienced the highest mean number of therapy-related events (2.8 ± 6.3) resulting in a hospital visit, following initial treatment. Patients receiving Car + pemetrexed or Cis + Vib required the highest mean number of blood-specific resources (0.4; transfusion, EPO or G-CSF).

Table 1

	No pts treated	No (%) pts with CTCAE ≤ 2	No (%) pts with CTCAE > 2
Cis-based doublets	960	363 (37.81)	189 (19.69)
Car-based doublets	689	268 (38.90)	125 (18.14)
Bevacizumab-containing triplets	25	7 (28.00)	3 (12.00)
Gemcitabine or vinorelbine	114	37 (32.46)	17 (14.91)
Erlotinib	84	23 (27.38)	12 (14.29)
Investigational regimens	87	30 (34.480	14 (16.09)
Best supportive care	6	1 (16.67)	0 (0.00)
Other	278	122 (43.88)	73 (26.26)
Total	**2243**	**851 (37.94)**	**433 (19.30)**

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).

Use of resources for management of NSCLC patients was generally high, driven by diagnostic tests, need for surgery, follow-up visits and hospitalizations. Prior to the final diagnosis, almost all patients underwent imaging as a diagnostic test (scanner and x-ray were the most commonly used) laboratory tests and bronchoscopy. Following diagnosis, management of NSCLC required considerable resource use, including need for surgery, standard laboratory tests, resources for chemotherapy treatment in almost all treatment regimens, radiation therapy and imaging techniques (most frequently scans).