Clinical Study Report Synopsis	
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LuCaReAl : Lung Cancer Registry in Algeria

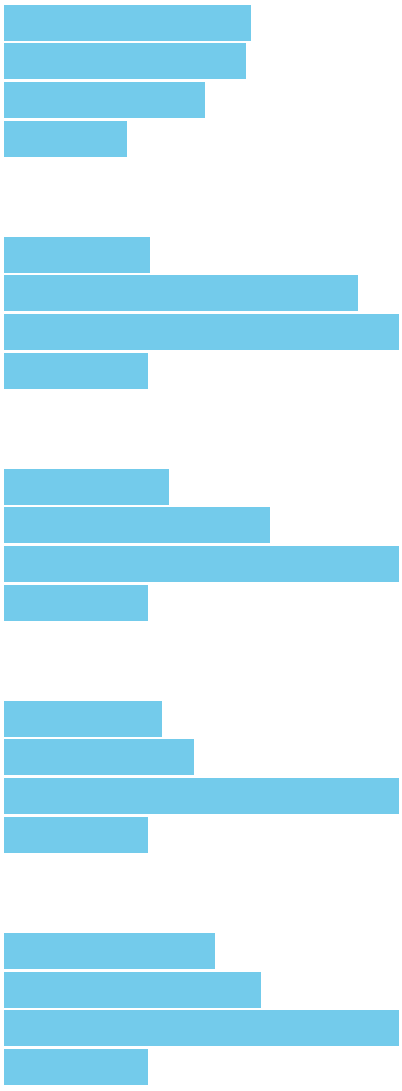
National Lung Cancer Registry in Men and Women based on Diagnosis in Algeria

Incidence and survival of lung cancer in men and women treated in Algeria

Study dates: First subject enrolled: 13/07/2016
Last subject last visit: 29/09/2020

Phase of development: Non-interventional study

International Co-ordinating Investigator: [redacted]

Sponsor's Responsible Medical Officer: 

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

This submission /document contains trade secrets and confidential commercial information, disclosure of which is prohibited without providing advance notice to AstraZeneca and opportunity to object.

Study centre(s)

24 centers from public sector in Algeria: 17 (70.8%) centers were oncology departments, and 7 (29.2%) centers were pneumology departments.

Publications

Bounedjar.A et al, Cancer Epidemiol. 2020 Dec;69:101799.

Objectives and criteria for evaluation

Table S1 Objectives and outcome variables

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Primary		To determine the incidence of lung cancer, all types, stages and ages combined, in men and women diagnosed with lung cancer in Algeria over 12 months of recruitment period.	Number of new diagnosed cases of lung cancer, all genders, types and stages combined, in men and women, reporting to the general population in Algeria during the 12 months of recruitment period.
Secondary		To characterize the incidence of newly diagnosed lung cancer in Algeria in a 12-month period according to patient and disease characteristics (Wilaya, sex, age, lung cancer type, stage disease and smoking status).	Number of new cases diagnosed with lung cancer, in men and women, to the general male and female population respectively in Algeria by Wilaya, sex, age, type of lung cancer smokers, non-smokers status and stage disease.
Secondary		To evaluate the mortality among men and women diagnosed with lung cancer in Algeria, overall and by stage, age, Wilaya, sex, smoking status, carcinogen exposure (e.g., asbestos, oil gas), lung cancer type.	Number of recorded deaths of men and women diagnosed with lung cancer, all lung cancer types, stages, genders and ages combined, to the general population in Algeria at 3, 6, 12, 24 and, 36 months, then respectively, by Wilaya, sex, age, smoking status, lung cancer type and stage disease at 3, 6, 12, 24 and 36 months.

Objective			Outcome Variable
Priority	**Type**	**Description**	**Description**
Secondary		To document patients' clinical characteristics, treatment patterns and evaluate the frequency of the different anatomopathological types of lung cancer diagnosed by the investigators in Algeria by Wilaya, sex, age and smoking status.	Patients' profiles and characteristics (demographics, smoking history, clinical information, status, performance status at diagnosis, cancer family history, occupational disease, molecular testing, etc…) and frequency of the different anatomopathological type of patients with lung carcinomas pattern (histology subtype, TNM classification, tumor grade and differentiation grade, patients' eligibility for molecular testing and biomarker status if available).
Secondary		To evaluate the survival status at 12, 24 and 36 months of follow-up.	Survival status (1-year overall survival (OS), 2-year OS and 3-year OS, and cause of death).
Secondary		To evaluate the quality of life of patients diagnosed with lung cancer in Algeria according to EORTC QLQ-C30 and EORTIC QLQ– LC13.	Quality of life questionnaires.

Study design

National, prospective, multicentric, non-interventional registry-based study, conducted among oncologists and pulmonologists in community and university hospitals, from the public sector in Algeria.

The study collected information on the characteristics, and lung carcinomas patterns of patients whose lung cancer diagnosis was confirmed by a pathologist during the study period.

Patients underwent clinical assessments and received the standard medical care as determined by the treating physician. Patients did not receive experimental intervention or experimental treatment as a consequence of their participation in this observational study. In addition, the study intended to collect data on patients diagnosed with lung cancer under conditions of routine clinical care.

The study consisted of:

- Four in-hospital visits (Inclusion visit, visit at 3, 6 and 12 months). All patients presenting to their oncologists/pulmonologists during a routine visit were sequentially asked to participate to the study.

- In addition to the 4 visits, a phone contact with the patients every 6 months at 2 and 3 years was performed by the investigator or during a routine visit to the investigator, to check the patient's survival status.

The data for this observational study were collected with electronic case report forms (eCRF). It was anticipated that patient recruitment would last 12 months (expected from March 2016 to end of January 2017) and each patient would be followed for 36 months.

Target subject population and sample size

Adults patients diagnosed with lung cancer.

Inclusion criteria:

1. Men or women diagnosed with lung cancer all types and stages confirmed over 12 months of recruitment period by a pathologist;

2. Aged at least 18 years at diagnosis;

3. Patients who provide their informed consent form.

Exclusion criteria:

1. Patients who did not provide the informed consent form;

2. Patients with a mental or psychological disorder according to their treating clinicians.

As the study was representative and national, patient recruitment was open. Hence, no formal sample size calculation was performed, and the sample was not powered a priori for specific comparisons. All patients diagnosed with lung cancer during the study period and who gave their informed consent were included in the study.
The patients who did not consent were only reported as new case of lung cancer for the incidence study.

Statistical methods

Statistical analysis was performed using SAS software SAS 9.4 and SAS/STAT 14.3 or later for Microsoft Windows.

Standard descriptive statistics were used:

- Continuous quantitative variables were summarized by the number of data, number of missing data, mean, standard deviation (SD), median, quartile Q1, Q3, minimum and maximum.

- Categorical variables were summarized as frequency of missing data, frequencies and percentages of each documented modality.

No statistical test was performed for descriptive statistics.

All statistical tests were two-sided and the statistically significant threshold was set at 5%.

No adjustment of risk alpha was done as this was an observational study where all analyses were exploratory analyses.

Normality of distributions were visually checked for continue parameters, if normality of distributions was rejected the quantitative variables were categorized using quartiles.

Bilateral 95% confidence interval (CI) for overall survival analysis was estimated following the asymptotic Wald method.

Frequency and percentage of each major protocol deviations were displayed.

All dates after inclusion visit were analyzed in this final analysis according to follow-up.

Otherwise specified, all follow-up data were summarized on the included population according to follow-up period.

Subject population

24 centers included 877 patients in the study: 17 (70.8%) centers were oncology departments, and 7 (29.2%) centers were pneumology departments. Their specialty was oncology for 16 (66.7%), pneumology for 7 (29.2%) or radiotherapy for 1 (4.2%). 858 (97.8%) patients constituted the population of analysis with 736 (85.8%) males.

Summary of efficacy results

Overall incidence of lung cancer, estimated over the recruitment period, was 5.4 [95%CI: 5.2; 5.7] per 100,000 inhabitants. Incidence according to the sex was 9.3 [95%CI: 8.8; 9.8] for males and 1.6 [95%CI: 1.3; 1.8] for females.

Median overall survival was 44 [95%CI: 40; 48] weeks. Survival rate was 43%, 20%, 12.7%, at 1, 2 and 3 years respectively.

Median survival was 54 [95%IC: 47; 60] weeks in patients aged [25-52] years, 49 [95%IC: 41; 60] weeks in patients aged [53-61] years, 44 [95%IC: 34; 54] weeks in patients aged [62; 66] years, 41 [95%IC: 34; 51] weeks in patients aged [67; 74] years and 27 [95%IC: 21; 37] weeks in patients aged [75-91] years.

Median survival was 60 [95%IC: 50; 72] weeks in females and 41 [95%IC: 37; 47] weeks in males.

Median survival was 78 [95%IC: 51; 94] weeks in patients diagnosed with a stage IIIa, 46 [95%IC: 38; 54] weeks in patients diagnosed with a stage IIIb, 58 [95%IC: 10; 86] weeks in patients diagnosed with a stage IIIc and 37 [95%IC: 33; 43] weeks in patients diagnosed with a stage IV.

Median survival was 46 [95%IC: 40; 50] weeks in patients diagnosed with an adenocarcinoma, 43 [95%IC: 36; 53] weeks in patients diagnosed with a squamous cell carcinoma and 43 [95%IC: 22; 55] weeks in patients diagnosed with a small cell carcinoma.

Median survival was 62 [95%IC: 45; 108] weeks in patients living in the Center, 39 [95%IC: 34; 44] weeks in patients living in the North Center, 65 [95%IC: 56; 83] weeks in patients living in the North East and 37 [95%IC: 29; 48] weeks in patients living in the North West.

Median survival was 48 [95%IC: 41; 54] weeks in former smokers, 35 [95%IC: 29; 40] weeks in smokers and 55 [95%IC: 48; 66] weeks in non-smokers.

Summary of safety results

Overall, 689 (80.3%) patients had at least one serious adverse event (SAE); 632 (92%) patients had only 1 SAE. SAE was death in 672 (71%) patients. SAE were coded using the MedRA dictionary version 23.1. The most frequent SAE by SOC was neoplasms benign, malignant and unspecified (including cysts and polyps) in 516 (77%) patients. Only 3 (1.2%) SAEs were related to an AZ product.

Conclusion(s)

LuCaReAl is the first study to report overall incidence in lung cancer in Algeria. Incidence had been previously estimated in two studies [1, 2]. In LuCaReAl, the overall incidence was estimated to be 5.4 cases per 100,000 inhabitants, which was much higher than the published Globocan 2018 estimated incidence of 1.31 cases per 100,000 in Algeria [2]. The overall incidence estimated in LuCaReAl was also higher than the Globocan incidence in Northern Africa of 1.23 cases per 100,000 inhabitants and the incidence of 4.27 and 4.25 cases per 100,000 inhabitants in Northern America and Western Europe, respectively.

It is interesting to point out that almost all patients had no family history of lung cancer but most males in the study were either active or former smokers. Incidence of lung cancer in males was higher than the WHO estimated global incidence (9.3 vs 3.8 cases per 100,000) [2] contrary to the incidence in females that was very similar (1.6 vs 1.8 cases per 100,000) [2].

In the LuCaReAl study, adenocarcinoma was the major type of lung cancer and squamous cell carcinoma rate was more than 3-times higher in males than in females.

Clinical classification of the tumor with the international TNM nomenclature showed that most patients in the study were diagnosed at an advanced stage of the disease (Stage IV).

Prognosis for patients diagnosed in Stage IV of the disease is was poor with a 5-year survival estimate of only 13% as opposed to 73% for patients diagnosed in Stage Ia [3]. In LuCaReAl, survival rate was 43%, 20%, 12.7% at 1, 2 and 3 years respectively. Survival was not different depending on the histological cancer type. However, non-smokers did have an increased survival compared to smokers (current and former).

Preventive measures in particular non-smoking awareness campaigns, and early screening, so as estimations of available treatment capacities and specialized staffs, are required. Further studies are required to better understand the etiology of lung cancer in Algeria, with a special focus on passive smoking.

References:

1. Hamdi Cherif M, Bidoli E, Birri S, Mahnane A, Zaidi Z, Boukharouba H, et al. Cancer estimation of incidence and survival in Algeria 2014. J Cancer Res Ther. 2015;3:100–4.

2. WHO, Globocan 2018, Lung fact sheet. https://gco.iarc.fr/today/data/factsheets/cancers/15-Lung-fact-sheet.pdf. Accessed 4 Jun 2020.

3. Woodard GA, Jones KD, Jablons DM. Lung Cancer Staging and Prognosis. Cancer Treat Res. 2016;170:47–75.