CONTEMPORARY REAL-WORLD EVIDENCE ON ALK+ NSCLC PATIENTS IN ITALY

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INTRODUCTION

Primary lung cancer is one of the most common malignancies and cause of death worldwide[1]. In Italy, lung cancer represents the third most frequently diagnosed cancer (11% of all cancers), with a risk of developing markedly related to gender and age and an overall incidence progressively increasing over time.[2] Similarly, mortality rates show gender differences, with higher rates in men and a steady increase over time.[3]

There are two major types of lung cancer, non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). In patients with advanced/metastatic stages of NSCLC, several genetic alterations have been identified as driver mutations underlying the development of NSCLC, including EGFR, KRAS, MET, ALK, and ROS-1. For patients with ALK rearrangements, various target therapies have been developed or are being developed and in most cases, the treatment aims at increase life expectancy of patients with a highly advanced and severe forms of NSCLC.[4,5]

The aim of this research was to provide an estimation of the actual incidence of patients affected by ALK+ NSCLC in Italy and to describe demographics and tumor-related characteristics.

METHODS

A desk research was conducted to gather information on national epidemiological data on ALK+ NSCLC patients; incidence data were collected from the most recent AIRTUM (Italian Association of Cancer Registries) reports (i.e. 2017).

Epidemiological evidence was then enriched with real-world data from 116 medical records of advanced/metastatic ALK+ NSCLC patients (monitoring period: June – December 2017) collected through the Oncoview database. Oncoview is a continuative study relying on a panel of 480 specialists (including 250 Oncologists), which provides data from oncologic patient records. Real world data included information about age, gender, smoking status and tumor-related characteristics.

RESULTS

In 2017, AIRTUM estimated approximately 41,800 lung cancer new cases.1 At the time of the present analysis, NSCLC represented approximately 88% of all lung cancers and included different subtypes such as adenocarcinoma, squamous carcinoma, large cell carcinoma and other forms/not tested.

Different genetic abnormalities had been associated to NSCLC: most common biomarkers were EGRF, KRAS, ALK and ROS-1. Among these, ALK gene rearrangement showed a frequency ranging from 3 to 7% (i.e.1,100-2,500 incident cases) (Table 1).1

The analysis on real world data profiled patients with advanced/metastatic ALK+ NSCLC based on demographic characteristics and tumor-related parameters.

ALK rearrangement showed a higher frequency in patients aged 51-60 years, the majority of them were ex-smokers or non-smokers/light smokers, with no gender differences (Figure 2).

The most frequent tumor histotype was adenocarcinoma (≈95% of patients). For a small percentage, ALK mutation was associated to adeno-squamous (3.5%) and undifferentiated (1.8%) cell carcinoma.

Around 90% of patients showed a malignant neoplasm within the G2-G4 grades (measure of cell anaplasia), which were linked to the most aggressive tumor forms. Furthermore, due to the high severity of their disease, these patients showed a pluri-metastatic tumor. Liver, lungs, kidneys, bones and brain were the most commonly affected organs.

Around 80% of patients received ALK+ NSCLC diagnosis in the last 2 years (2016 -2017), while less than 20% of patients had been diagnosed more than 3 years ago, maybe due to the increased adoption of ALK testing, subsequent to the introduction of the first ALK inhibitor.

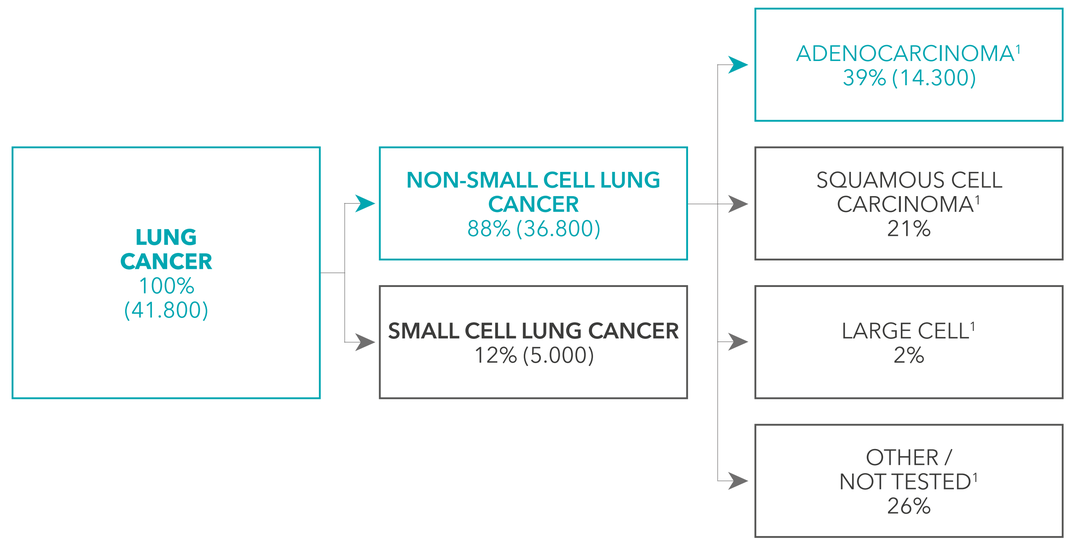
Beside ALK testing, in these patients, genetic characterization included simultaneous assessment of multiple mutations, such as EGFR (≈90% of cases) and KRAS (≈ 21% of cases): among ALK+ NSCLC patients tested for EGFR, a small percentage (3.5%) resulted also EGFR positive. The variability related to the type of additional mutations tested depended on physician's choice and availability of diagnostic equipment (Table 2).

CONCLUSION

As treatment scenario for non-small-cell lung cancer is evolving from the use of cytotoxic chemotherapy to personalized treatment based on molecular alterations, identification of target population becomes crucial, in order to optimize treatment outcome and improve patients survival.

This study provided contemporary real-world evidence on Italian patients with ALK+ NSCLC, which showed a more advanced and severe disease. These data provided useful information for screening ALK+ cases in clinical practice and might be beneficial for informing future decisions about individualized therapeutic patterns and research on specific treatments.

FIGURE 1
Lung cancer incidence (2017)[1]



1. Of total NSCLC
2. The percentage of the population subject to ALK mutation varies according to the population study

TABLE 1
Genetic alterations most frequently associated to NSCLC adenocarcinoma (2017)[1,3]

MOLECULAR ALTERATION	TYPE	RANGE FREQUENCY*[1]	OVERLAP WITH OTHER NSCLC ALTERATIONS
EGFR	Activating mutation	10% - 15 % of NSCLC	Rare
KRAS	Activating mutation	20% - 30% of NSCLC	Rare
ALK	**Chromosomal translocation**	**3% - 7% of NSCLC (1,100-2,500 patients)**	**Rare**
ROS-1	Chromosomal translocation	1% - 2% of NSCLC	No

FIGURE 2
ALK+ NSCLC patient demographics and risk factors

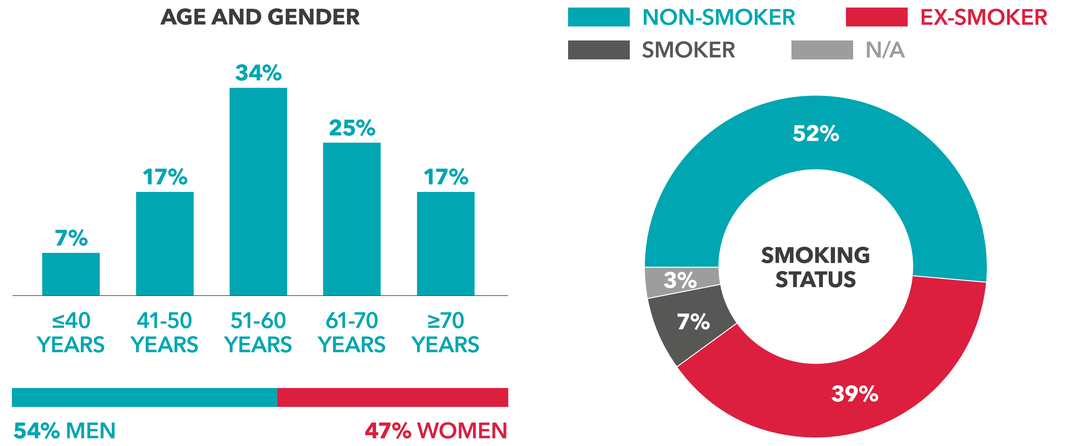


TABLE 2
ALK+ NSCLC patient tumor-related characteristics

PARAMETER	RECORD	PATIENT (%)
CLINICAL		
YEAR OF DIAGNOSIS	≤2013 2014 2015 2016 **2017**	9.8% 2.7% 7.1% 17.9% **62.5%**
ECOG PS: score from 0 (fully active) to 4 (completely disabled)	0 1 2	36.6% **51.8%** 11.6%
HISTOTYPE	**Adenocarcinoma** Adeno-squamous cell carcinoma Undifferentiated carcinoma	**94.7%** 3.5% 1.8%
GRADING Grading score from G1 to G4 according to the level of tumor differentiation	G1 **G2** **G3-G4**	9.3% **45.8%** **44.9%**
NUMBER OF METASTASES	[1-2] **[3-4]** >4	30.4% **47.9%** 21.7%
GENETICS		
EGFR TESTING	**TESTED** NOT TESTED	**89.4%** 10.6%
K-RAS TESTING	**TESTED** NOT TESTED	**20.7%** 79.3%

Source: IQVIA Oncoview

1. ESMO Guidelines for Lung Cancer, 2017
2. AIRTUM Report "I numeri del cancro", 2017
3. ISTAT - I.Stat – "Causa iniziale di morte - di cui tumori maligni della trachea, dei bronchi e dei polmoni; Data extracted on 31/01/2018
4. Korpanty, Grzegorz J., Donna M. Graham, Mark D. Vincent, e Natasha B. Leighl. "Biomarkers That Currently Affect Clinical Practice in Lung Cancer: EGFR, ALK, MET, ROS-1, and KRAS". Frontiers in Oncology 4 (2014)
5. Shaw AT, Engelman J. "ALK in lung cancer: past, present, and future." J Clin Oncol. 2013 Mar 10; 31(8):1105-11

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