Institutional Experience and Survival Analysis of ALK Positive Non-Small Cell Lung Cancer

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Introduction

EML4-ALK, an aberrant fusion gene, has been identified in approximately 4%-7% in non-small cell lung cancer. It encodes a cytoplasmic chimeric protein with constitutive kinase activity. Crizotinib, an oral inhibitor of the *EML4-ALK* kinase activity was de first molecule that showed and important anti tumoral activity in ALK positive non-small cell lung cancer and showed an improvement in overall survival compared to standard chemotherapy [1]. Alectinib, another potent inhibitor of the *EML4-ALK* kinase, with Central Nervous System (CNS) penetration was also superior to standard chemotherapy as second line and showed superior efficacy compared with crizotinib in the first line setting becoming the standard of care in this scenario. Ceritnib, brigatinib and lorlatinib are also effective molecules for the treatment of patients with ALK positive non-small cell lung cancer. We present the characteristics and treatment outcomes of ALK positive patients treated in the Guatemalan Social Security Institute (IGSS) [2,3].

Description

Of the universe of patients of the medical oncology department of our institution, from January 2013 to December 2020, 269 patients with thoracic tumors were treated [4,5]. 240 were diagnosed with non-small cell lung cancer, identifying 10 patients with *EML4-ALK* gene fusion and its protein, corresponding to an incidence of 4.16%. Patients characteristics are shown in Table 1.

Table 1. Characteristics of patients.

Characteristics	No. (%)
Age (Years)	
Median	54
Range	(28-62)
Gender	
Male	7 (70)
Female	3 (30)
Smoking exposure	
Never exposed	8 (80)
Exposed	2 (20)
Histologic type	
Adenocarcinoma	8 (80)
Bronchioloalveolar	1 (10)
Adenosquamous	1 (10)
Diagnostic method	
FISH	6 (60)
IHC	4 (40)
SNC metastases	

At diagnosis	3 (30)
At progression	1 (10)
Treatment	
Hole brain radiotherapy	4 (100)
Previous chemotherapy	
Platinum based duplet	8 (80)
Monotherapy	1 (10)
No chemotherapy	1 (10)
Cycles average	5
Range	(2-12)
Chemotherapy response	
No response	6 (66.7)
At least 30%	3 (33.3)
Anti-ALK treatment	
1st line	
Crizotinib	10 (100)
2nd line	
Alectinib	2 (20)
Ceritinib	2 (20)
3rd line	
Alectinib	1 (10)

All 10 patients received *EML4-ALK* protein inhibitors at the moment when de alteration was determined (anti-ALK treatment). 6 patients progressed with a progression free survival of 20.0 months (6.80-52.34). 4 patients received a second line with anti-ALK treatment and 1 patient developed a second progression starting anti-ALK treatment as third line [6,7]. At the time of the analysis 3 patients had died. Median overall survival of the group is 32.27 months (9.7-80.28) (Figures 1 and 2).

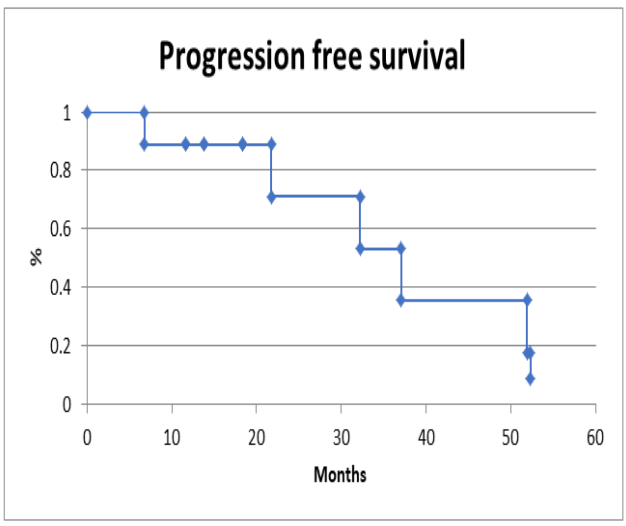

Figure 1. Progression free survival.

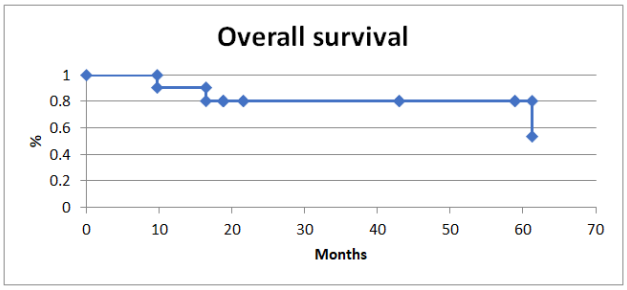

Figure 2. Shows overall survival months.

Lung cancer continues to be the leading cause of cancer deaths worldwide. Since the identification of oncogenic alterations like mutations in the gene encoding Epidermal Growth Factor Receptor (EGFR), translocations in Rat Osteosarcoma (ROS1), expression of Programmed Death Ligand 1 (PD-L1) and *EML4-ALK* fusion gene, survival has been improved with different therapies targeting these alterations [8,9]. *EML4-ALK*, an aberrant fusion gene, has been identified in approximately 4%-7% in non-small cell lung cancer. Crizotinib was the first anti-ALK treatment that showed an important activity in patients with ALK positive non-small cell lung cancer with response rates of 57%, and had a superior efficacy in previously treated patients compared with chemotherapy and also in previously untreated patients with a median progression free survival of 10.9 months versus 7.0 months compared with chemotherapy [10,11]. Second generation ALK inhibitors like alectinib showed a benefit after crizotinib failure and penetration to CNS with a brain metastases response rate of

33% to 57%. In a randomized trial (ALEX trial) alectinib showed superior efficacy as compared with crizotinib and a lower toxicity rates in the first line treatment of ALK-positive non-small cell lung cancer, becoming de standard of care in this scenario. Our ALK positive patients had the characteristics of the patients described in the literature (mostly younger men, non smokers and a high incidence of brain metastases). Although alectinib is the treatment of choice in the first line setting in ALK positive lung cancer all of our patients use crizotinib as a first line treatment. However, they achieved an important progression free survival of 20 months [12,13].

Conclusion

EML4-ALK rearrangement is a rare alteration that define a distinctive clinical and molecular subtype of lung cancer that is more prevalent in younger patients without a smoking exposure, high incidence of CNS metastases and poor prognosis. However, with the development of inhibitors of its kinase activity these kind of patients should receive an anti ALK treatment for an improvement of their clinical outcomes and survival as we have seen in our patients.

References

1. Soda, M., et al. "Identification of the transforming *EML4-ALK fusion gene in non-small-cell lung cancer*." *Nature*. 448.7153 (2007): 561-566.
2. Kwak, EL., et al. "Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer." *N Engl J Med*. 363.18 (2010): 1693-1703.
3. Shaw AT., et al. "Crizotinib versus chemotherapy in advanced ALK-positive lung cancer." *N Engl J Med*. 368.25 (2013): 2385-2394.
4. Novello, S., et al. "Alectinib versus chemotherapy in crizotinib-pretreated Anaplastic Lymphoma Kinase (ALK)-positive non-small-cell lung cancer: Results from the phase III ALUR study." *Ann Oncol*. 29. 6 (2018): 1409-1416.
5. Peters, S., et al. "Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer." *N Engl J Med*. 77.9 (2017): 829-838.
6. Shaw, AT., et al. "Ceritinib versus chemotherapy in patients with ALK-rearranged and crizotinib (ASCEND-5): A randomised controlled, open-label, phase 3 trial." *Lancet Oncol*. 18.7 (2017): 874-886.
7. Goldstraw, P., et al. "Non-small-cell lung cancer." *The Lancet*. 378.9804 (2011):1727-1740.
8. Ferlay, JM., et al. "Cancer statistics for the year 2020: An overview." *Int Cancer*. 149.4 (2021): 778-789.
9. Reck M., et al. "Precision diagnosis and treatment for advanced non-small-cell lung Cancer." *N Engl J Med*. 377.9 (2017): 849-861.
10. Halliday, PR., et al. "Emerging targeted therapies for the treatment of non-small cell lung cancer." *Curr Oncol Rep*. 21 (2019): 1-12.
11. Dempke WC., and Suto T., "Targeted therapies for non-small cell lung cancer." *Lung cancer*. 67.3 (2010): 257-274.
12. Pirker, R., "Conquering lung cancer: Current status and prospects for the future." *Pulmonology*. 26.5 (2020): 283-290.
13. Cheng, Y., et al. "Therapeutic advances in non-small cell lung cancer: Focus on clinical development of targeted therapy and immunotherapy." *MedComm*. 2.4 (2021): 692-729.

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