



ORIGINAL RESEARCH PAPER

Oncology

RETROSPECTIVE VISION OF LUNG CANCER IN ECUADOR

KEY WORDS:

lung, cancer, chemotherapy, Ecuador.

Leonardo David Villacrés*	MD. Medical Oncology Fellow, "Universidad Central del Ecuador" Corresponding Author
Gabriela Claudio	Medical Resident at "Hospital Carlos Andrade Marín", Quito-Ecuador
Paola Claudio Pombosa	Medical Resident at "Hospital Carlos Andrade Marín", Quito-Ecuador
Juan José Navarrete	General Practitioner
Daysi León	Medical Resident at "Hospital de especialidades de las Fuerzas Armadas N°1", Quito- Ecuador
Marco León Montenegro	Medical Resident at "Hospital de especialidades de las Fuerzas Armadas N°1", Quito- Ecuador
Tannia Soria	MD. Clinical Oncology Attending Physician at "Hospital Oncologico Solon Espinosa Ayala" Quito-Ecuador

ABSTRACT	OBJECTIVE.- Retrospective analysis of patients survival with non-small cell lung cancer who received Paclitaxel / Carboplatin chemotherapy.
	METHODS.- Patients older than 18 years old with a diagnosis of non-small cell lung adenocarcinoma, clinical stage IV or early clinical in progression; without knowledge in relation to mutation of EGFR and reordering of ALK, during the years 2010-2016.
	RESULTS.- there is no stadistic difference in patients younger than 60 years old and older than 60 years old with p = 0.54. There is no statistical difference in survival in patients who consumed tobacco with p = 0.2. Patients who received Paclitaxel / Carboplatin chemotherapy have an average survival of 11.10 months, HR: 1.26 IC95% (8.67-13.62)
	CONCLUSION.- In Ecuador, in 2018, we continued using Paclitaxel / Carboplatin chemotherapy as a first line of treatment in metastatic lung adenocarcinoma +/- Bevacizumab; state policies should be changed and ways to improve this problem should be sought even more with the medical advances in lung cancer with specific drivers as the use of tyrosine kinase inhibitors and immunotherapy and thus improve the average survival of this population group.

INTRODUCTION

The incidence of lung cancer is low in Ecuador, according to the National Registry of Tumors it has been established that it ranks eighth in incidence in men (7.7 x100.000 inhabitants) and the ninth in women; (6.7 x100.000 inhabitants) (1)

There are 2 main types of lung cancer; about 80% - 85% of these correspond to non-small cell lung cancer (NSCLC "Non Small Cell Lung Cancer") while 10% to 15% are small cell lung cancer (SCLC "Small Cell Lung Cancer") (2,3,3-5)

The recognition of a subgroup of patients with NSCLC harboring mutations of the epidermal growth factor receptor (EGFR) gene exhibits a good response to treatment with tyrosine kinase inhibitors (TKI), which denotes the personalized therapeutic approach. (6-20)

Previous studies have shown a variation of the EGFR genotype according to ethnic origin; with data that vary between continents, and in America variations between countries have been observed, as reported by Arrieta et al. (13,21,22)

In Ecuador we have reported in our first studies an incidence of mutation of EGFR of 48.6% and a rearrangement of ALK of 3%, these data determined in patients who reside at a height higher than 2000 meters above sea level (23). The objective of the present investigation is to determine the survival of patients with lung cancer receiving chemotherapy and a descriptive analysis of lung cancer in Ecuador in a retrospective manner.

MATERIALS AND METHODS

Data from electronic medical records were collected from 2000 to 2016 of those patients with confirmed diagnosis of lung cancer stage IV treated at the Oncology Hospital Solon Espinosa Ayala (SOLCA) Quito core and registered in the Department of National Registry of tumors of the Institution

POPULATION

Patients older than 18 years with a confirmed diagnosis of non-small cell lung adenocarcinoma, clinical stage IV or early clinical stage that progresses later; without knowledge in relation to EGFR mutation and ALK rearrangement.

STATISTIC ANALYSIS

A descriptive analysis was made with the variables collected and a statistical analysis with the SPSS and EXCEL program, the statistical analysis was performed by 2 and the survival by means of Kaplan Meier curves until 01/15/2016.

RESULTS

There is not much research in Ecuador that talks about lung cancer, through this study we can retrospectively determine the first analysis of patients with lung adenocarcinoma in various scenarios, as shown in Table 1.

From these analyzes it was possible to appreciate that the patients older than 60 years old live more than 12 months (17.3% / 13) while they live less than 12 months (82.7% / 62) whereas the people under 60 years old, live less than 12 months (59.5% / 22) and more than 12 months (40.5% / 15) with p = 0.008.

It was also observed that there is no statistically significant difference in survival between the major groups and those under 60 years old with a $p = 0.54$; in the same way in relation to survival less than 12 months and more than 12 months of patients who consumed tobacco did not present a statistically significant difference with a $p = 0.2$.

Regarding the age range, it can be seen that people under 60 years old have an average survival of 11.10 months, while people over 60 years old live an average of 7.4 months with an HR 0.9 IC 95% (6,883 - 10,420) as shown in figure 1.

Finally, a survival analysis was performed with respect to the Paclitaxel / Carboplatin chemotherapy since it was the most used scheme, with an average survival of 11.15 months, as shown in Figure 2.

DISCUSSION

Kosmidis et al, described in the year 1997 on the basis of the high activity of single agent paclitaxel and the higher survival rates in one year of patients with non-small cell lung cancer (SCLC) treated with carboplatin, started a phase II trial with both agents in patients with inoperable disease in stages III and IV to investigate the efficacy and toxicity of the combination, reporting an average survival of 8.95 months. (2)

Sandler et al, showed that bevacizumab, a monoclonal antibody against vascular endothelial growth factor, increased mean survival from 10.3 months to 12.3 months. (24)

In our investigation we can appreciate that when using Paclitaxel / Carboplatin only a survival of 11.10 months is appreciated, that is to say that it is within the ranges reported by Sandler.

CONCLUSION

Ecuador is a developing country, economic measures and state problems affect vulnerable points in health issues, although the weaknesses of this study is that it is a retrospective analysis until 2016, In 2018 this treatment scheme continues to be used for patients with lung cancer clinical stage IV plus the addition of Bevacizumab, this due to the lack of economic access of patients and state health services to purchase drug-directed, such as tyrosine kinase inhibitors and even less to enter the field of Immunotherapy.

It is also pharmaceutical companies that investigate the mutation of EGFR and reordering of ALK, exams that should be handled by the state in the future, to finalize this is an example of the social problems of developing countries in Latin America and the world.

ANNEXES

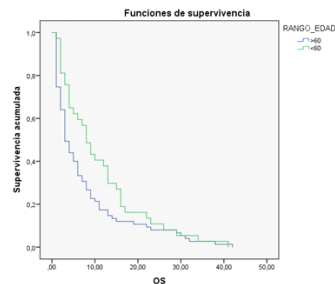
Table 1.- Descriptive analysis of lung cancer

Variable		Number	Percentage
SEX	MEN	80	50
	WOMEN	80	50
		160	100
AGE	>60	110	68,8
	<60	50	31,3
		160	100
SURVIVAL*	<12 MONTHS	84	75
	>12 MONTHS	28	25
		112	100
TNM	I	2	1,8
	II	5	4,5
	III	14	12,5
	IV	91	81,3
		112	100
TOBACCO	SI	62	55,4
	NO	50	44,6
		112	100

Chemotherapy	Gemcitabina	1	2,2
	Gemcitabina/Cisplatino	1	2,2
	Paclitaxel/carboplatino	40	88,9
	Paclitaxel/Carboplatino/Bevacizumab	1	2,2
	Pemetrexed/Carboplatino	1	2,2
	Pemetrexed/Cisplatino	45	100
	Total		

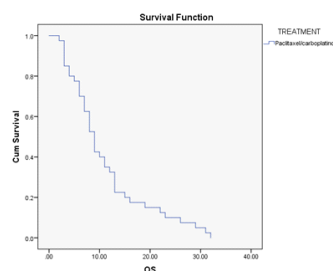
* 48 patients are excluded due to lack of information

FIGURE 1. - Global survival in relation to age



HR 0,9 IC95% (6,883 – 10,420)

FIGURE 2.- Overall survival in relation to the Paclitaxel / Carboplatin chemotherapy scheme.



HR: 1.26 IC95% (8,67-13,62)

REFERENCE

- SOLCA. EPIDEMIOLOGÍA DEL CÁNCER EN QUITO 2006-2010 [Internet]. 15th ed. Cueva P, editor. Quito; 2014. Available from: <http://www.estadisticas.med.ec/Publicaciones/PUBLICACION-QU-2006-2010.pdf>
- Kosmidis PA, Mylonakis N, Fountzilias G, Samantas E, Athanasiadis A, Andreopoulou E, et al. Short report Paclitaxel and carboplatin in inoperable non-small-cell lung cancer: A phase II study [Internet]. Annals of Oncology. 1997. Available from: <https://academic.oup.com/annonc/article-abstract/8/7/697/235196>
- Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin [Internet]. 2017; 65(1): 5–29. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25559415>
- Herbst RS, Heymach J V., Lippman SM. Lung Cancer. N Engl J Med [Internet]. 2008 Sep 25; 359(13): 1367–80. Available from: <http://www.nejm.org/doi/abs/10.1056/NEJMra0802714>
- Couraud S, Zalzman G, Milleron B, Morin F, Souquet P-J. Lung cancer in never smokers – A review. Eur J Cancer [Internet]. 2012 Jun;48(9):1299–311. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0959804912002523>
- Yatabe Y, Mitsudomi T. EGFR mutation in lung cancers. Biotherapy. 2006;
- Shin D-Y, Na I Il, Kim CH, Park S, Baek H, Yang SH. EGFR Mutation and Brain Metastasis in Pulmonary Adenocarcinomas. J Thorac Oncol [Internet]. 2014 Feb; 9(2): 195–9. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1556086415301891>
- Rossi A, Di Maio M. LUX-Lung: determining the best EGFR inhibitor in NSCLC? Lancet Oncol [Internet]. 2015 Feb;16(2):118–9. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1470204514711969>
- Toyooka S, Kiura K, Mitsudomi T. EGFR mutation and response of lung cancer to gefitinib. N Engl J Med. 2005;
- Wu Y-L, Sequist L V, Hu C-P, Feng J, Lu S, Huang Y, et al. EGFR mutation detection in circulating cell-free DNA of lung adenocarcinoma patients: analysis of LUX-Lung 3 and 6. Br J Cancer [Internet]. 2017 Jan 22;116(2):175–85. Available from: <http://www.nature.com/articles/bjc2016420>
- Wu Y-L, Sequist LV, Hu C-P, Feng J, Lu S, Huang Y, et al. EGFR mutation detection in circulating cell-free DNA of lung adenocarcinoma patients: Analysis of LUX-Lung 3 and 6. Br J Cancer. 2017;
- Wu Y-L, Sequist L V, Hu C-P, Feng J, Lu S, Huang Y, et al. EGFR mutation detection in circulating cell-free DNA of lung adenocarcinoma patients: analysis of LUX-Lung 3 and 6. Br J Cancer. 2017;
- Arrieta O, Cardona AF, Martín C, Más-López L, Corrales-Rodríguez L, Bramuglia G,

et al. Updated Frequency of EGFR and KRAS Mutations in NonSmall-Cell Lung Cancer in Latin America: The Latin-American Consortium for the Investigation of Lung Cancer (CLICaP). *J Thorac Oncol* [Internet]. 2015 May;10(5):838–43. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1556086415323984>

14. Köhler J, Schuler M. LUX-Lung 3: redundancy, toxicity or a major step forward? Afatinib as front-line therapy for patients with metastatic EGFR-mutated lung cancer. *Futur Oncol* [Internet]. 2014 Mar;10(4):533–40. Available from: <https://www.futuremedicine.com/doi/10.2217/fon.14.9>
15. Vinet L, Zhedanov A. A 'missing' family of classical orthogonal polynomials. *J Phys A Math Theor* [Internet]. 2011 Feb 25;44(8):085201. Available from: <http://arxiv.org/abs/1011.1669>
16. Addeo A. What is the clinical impact of the LUX-Lung 5 trial? *Ann Oncol* [Internet]. 2016 Jun;27(6):1171–2–1172. Available from: <https://academic.oup.com/annonc/article-lookup/doi/10.1093/annonc/mdw102>
17. Metro G, Crinà L. The LUX-Lung clinical trial program of afatinib for non-small-cell lung cancer. *Expert Rev Anticancer Ther* [Internet]. 2011 May 10;11(5):673–82. Available from: <http://www.tandfonline.com/doi/full/10.1586/era.11.34>
18. Tseng C-H, Chen K-C, Hsu K-H, Tseng J-S, Ho C-C, Hsia T-C, et al. EGFR mutation and lobar location of lung adenocarcinoma. *Carcinogenesis* [Internet]. 2016 Feb;37(2):157–62. Available from: <https://academic.oup.com/carcin/article-lookup/doi/10.1093/carcin/bgv168>
19. Yang JC-H, Wu Y-L, Schuler M, Sebastian M, Popat S, Yamamoto N, et al. Afatinib versus cisplatin-based chemotherapy for EGFR mutation-positive lung adenocarcinoma (LUX-Lung 3 and LUX-Lung 6): analysis of overall survival data from two randomised, phase 3 trials. *Lancet Oncol* [Internet]. 2015 Feb;16(2):141–51. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1470204514711738>
20. Caliez J, Monnet I, Pujals A, Rousseau-Bussac G, Jabot L, Boudjema A, et al. Adénocarcinome bronchique avec mutation de l' EGFR et réarrangement ALK concomitants. *Rev Mal Respir* [Internet]. 2017 May;34(5):576–80. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S076184251630167X>
21. Arrieta O, Cardona AF, Federico Bramuglia G, Gallo A, Campos-Parra AD, Serrano S, et al. Genotyping Non-small Cell Lung Cancer (NSCLC) in Latin America. *J Thorac Oncol* [Internet]. 2011 Nov;6(11):1955–9. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1556086415322620>
22. G Lopes. EGFR mutation prevalence in an access program in Brazil [Internet]. *Journal of Thoracic Oncology*. 2014. Available from: https://www.researchgate.net/journal/1556-0864_Journal_of_Thoracic_Oncology
23. Villacrés LD, Villarreal N, Moreno P, Carrasco EA, Castillo J, Muñoz MJ, et al. Lung cancer: EGFR-ALK mutation in the high lands. *J Clin Oncol* [Internet]. 2018 May 20;36(15_suppl):e24248–e24248. Available from: http://ascopubs.org/doi/10.1200/JCO.2018.36.15_suppl.e24248
24. Sandler A, Gray R, Perry MC, Brahmer J, Schiller JH, Dowlati A, et al. Paclitaxel–Carboplatin Alone or with Bevacizumab for Non-Small-Cell Lung Cancer. *N Engl J Med* [Internet]. 2006 Dec 14;355(24):2542–50. Available from: <http://www.nejm.org/doi/abs/10.1056/NEJMoa061884>