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Survival of patients with advanced lung cancer treated with CIMAvax-EGF®

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Abstract: Introduction: The national biotechnology industry has developed therapies targeting the epidermal growth factor receptor, and one of them is the CIMAvax-EGF vaccine as an active immunotherapy that is directly related to increased overall survival. Objective: To estimate the survival of patients with advanced lung cancer treated with CIMAvax-EGF. Methods: A retrospective cohort study was conducted at the María Curie Provincial Teaching Oncology Hospital in Camagüey Province between 2016 and 2018. The study population consisted of 32 patients who had received chemotherapy with unsatisfactory outcomes and were subsequently treated with Cimavax-EGF and followed up in the oncology clinic. The primary source of information was each patient's individual medical record. Data were processed using the Statistical Package for the Social Sciences (SPSS) version 26.0. Results: The majority of patients were male, aged 70 to 79 years, with the squamous cell carcinoma histological subtype and clinical stages IIIB and IVA. Overall and progression-free survival were 12.4 and 6.7 months, respectively. The predominant response to first-line treatment was partial remission, and the most frequent adverse reaction reported in immunized patients was pain at the injection site. Conclusions: In patients who had a complete response to the first line of treatment, the probability of survival improved when receiving maintenance treatment with the CiMAvax-EGF vaccine.

Key words: lung cancer; CIMAvax-EGF; survival

1 Introduction

Lung cancer has been a major global health problem due to its high incidence, increasing mortality, and difficult management [1]. It is one of the most common solid tumors worldwide, with 2.1 million new cases and 1.8 million deaths in 2019 [2]. In the Americas, it is the third most frequent malignant neoplasm and the leading cause of cancer-related death on the continent.

In Cuba, it represents the third leading cause of death, preceded by skin cancer for both sexes, prostate cancer for men, and breast cancer for women [3].

According to data published in the 2021 Statistical Yearbook, 3,821 new cases were reported in males, for a rate adjusted to the world population of 37.2 per 100,000 inhabitants, and 2,426 in females, for a rate adjusted to the world population of 21.6 per 100,000 inhabitants [4].

Currently, alterations in the epidermal growth factor receptor superfamily, which is overexpressed in malignant diseases, is considered among the etiologies of lung cancer. This receptor regulates vital cellular processes and is an indicator of negative prognosis [5,6].

Epidermal growth factor (EGF) is a peptide capable of stimulating epithelial and mesenchymal cell proliferation in vitro and in vivo through a membrane receptor. Therefore, EGF-R expression is important for regulating growth in some types of epithelial tumors. Overexpression of the EGF receptor is implicated in the malignant transformation process and promotes cell proliferation, survival, and migration. In lung cancer, this overexpression is correlated with greater progression, increased cell proliferation, and poor differentiation [7].

Recent advances in understanding cell signaling in tumor genesis have led to the development of new therapies that offer renewed hope. Among these is the therapeutic vaccine CIMAvax-EGF®, composed of human epidermal growth factor (EGF) conjugated to the P64K protein. When a patient is treated with this vaccine, there is an increase in the titers of neutralizing antibodies against EGF and a proportional reduction in circulating EGF in the serum [8].

This research was carried out with the aim of obtaining data related to the survival of patients with advanced lung cancer, who did not respond to previous chemotherapy, in whom CIMAvax-EGF was applied in the Oncology Medicine Clinic.

2 Methods

A retrospective cohort study was conducted at the María Curie Provincial Teaching Oncology Hospital in Camagüey Province, Cuba, between January 2016 and December 2018.

The study population consisted of 32 patients diagnosed with advanced lung cancer of various histological types who were treated with CIMAvax-EGF.

The medical records containing all the necessary information for the study were available at the Oncology Clinic.

Patients over 18 years of age with histological confirmation of the tumor after first-line chemotherapy with unfavorable results were included and received the vaccine.

Patients with incomplete medical records were excluded from the study.

The following data were collected from the medical records: age, sex, comorbidities, histological type, functional status according to the Eastern Cooperative Group of Oncology (ECOG) scale, clinical stage, response to treatment, and adverse reactions. All data were processed using the Statistical Package for the Social Sciences (SPSS) version 26.0.

3 Results

The demographic characteristics of the patients studied are shown, where the average age was estimated to be 64.91 years with a standard deviation of 8.938 years, with a predominance of the 70-79 age group, followed by the 60-69 age group. Regarding sex, a greater predominance was observed in the male sex (Table 1).

Table 1. Distribution of patients according to age and sex

Age group	Sex				Total	
	Female		Male			
	No	%	No	%	No	%
40-49 years	1	3.1	0	0.0	1	3.1
50-59 years	3	9.4	6	18.8	9	28.1
60-69 years	2	6.3	8	25.0	10	31.3
70-79 years	4	12.5	7	21.9	11	34.4
≥80 years	0	0.0	1	3.1	1	3.1
Total	10	31.3	22	68.8	32	100.0

$\bar{x}$

= 64,91; DE: 8,938.

Regarding functional status, the predominance of patients with an ECOG 2 is reflected, followed by those with an ECOG 1 and ECOG 0 (Fig. 1).

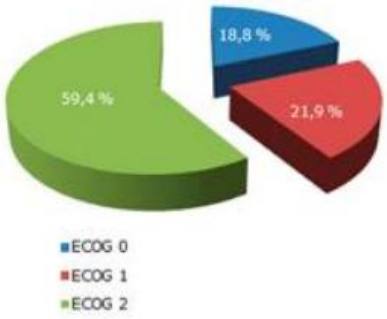


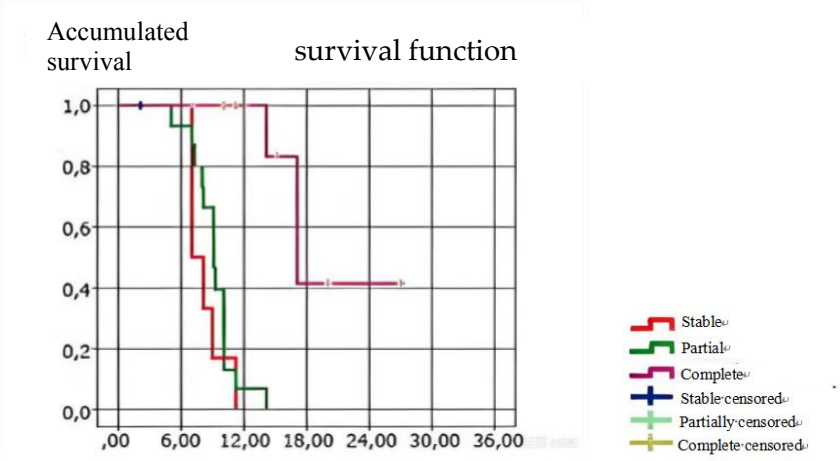
Figure. 1 Distribution of patients according to functional status (ECOG classification).

Regarding the histopathological characteristics of the tumors in the patients studied, it was evident that the predominant histology was squamous cell carcinoma, followed by non-small cell lung cancer; while stages IIIB and IVA grouped the highest percentage of cases (table 2).

Table 2. Distribution in patients according to histopathological characteristics and clinical stage

	Histopathological characteristics	No	%
Histological type	Adenocarcinoma	7	21.9
	Squamous cell carcinoma	14	43.8
	Non-small cell lung cancer	11	34.4
Clinical stage	IIIB	8	25.0
	IIIC	2	6.3
	IVA	16	50.0
	IVB	8	18.8
	Total	32	100.0

The cumulative survival at two years for complete response reached almost half of the sample, followed very closely by partial response, while patients with stable and partial response died before the year (Fig. 2).



Survival time (months)

Response to first line of treatment

Figure. 2 Distribution according to the survival and response curves to first line of treatment

It is shown that most patients did not suffer adverse events, among the main adverse events related to the use of CIMAvax-EGF was pain at the injection site, followed by chills and to a lesser extent other events such as tremors and headache occurred (table 3).

Table 3. Patients according to adverse events secondary to the use of Cimavax-EGF

Adverse events	No	%
Tremors	2	6.3
Headache	2	6.3
Pain at the injection site	6	18.8
Chills	3	9.4
No events reported	19	59.4
Total	32	100.0

4 Discussion

Age remains the most important risk factor for carcinogenesis; undoubtedly, the passage of time leads to the accumulation of damage from free radicals, viruses, carcinogens, or other agents that can cause mutations and favor the development of oncoproliferative processes [9].

In Cuba, lung cancer remains the leading cause of death in both sexes, although it is more frequent in men, where 65% has been reported, followed by women with 35%, as in other studies [10,11].

In this investigation, when the most frequent ages were identified, it was found that the average was 65 years, which is generally consistent with other investigations on the subject [10,12].

In the present investigation, the reflex functional state predominated in patients with an ECOG 2, which differs from other studies, such as Rodríguez et al. [13] who reported that 90.8% (n = 374) of the patients had a functional state according to the ECOG index equal to 0 or 1 and only 7.5% presented ECOG of 2 or more. However, it should also be noted that there is a difference in the sample size of both studies, which may explain this discrepancy.

On the other hand, Camacho et al. [14] found, unlike this study, that 85.71% of the patients studied had an ECOG-1 at the beginning of immunotherapy treatment; the rest reached two on the scale, with minimal restrictions in their daily life.

Villanueva-Bueno et al.[15] report on the clinical evolution of the patients studied. When functional status was assessed using the ECOG scale at the beginning of therapy, eight patients (61.5%) were fully active (scale score 0), while 38.5% had difficulty with strenuous physical activity. After six months, a deterioration in functional status was observed, with only 15.4% remaining fully active, 23.1% having difficulty with strenuous physical activity, and 30.8% progressing to stages of greater functional difficulty. Only two patients could partially care for themselves, and two were completely dependent.

Analysis of the histopathological diagnosis revealed that the most frequent tumor was squamous cell carcinoma, while stages IIIB and IVA accounted for 75.0% of cases, which is partly consistent with what has been observed in other studies [16,17].

The research carried out by Tabio and others [18] at the National Institute of Oncology and Radiobiology known as "Overall survival of patients with non-small cell lung carcinoma" unlike what was found in this study, adenocarcinoma predominated as the most frequent histological variety, followed by squamous cell carcinoma, even though it was not possible to establish the histological variety in 282 patients.

According to the results found by Carballo and others [19], they asserted in their study that the CIMAvax-EGF vaccine is positioned as the therapeutic possibility with the greatest survival and provides a better quality of life to patients with advanced stages of malignant lung cancer.

This research found that in patients studied who received immunotherapy after chemotherapy as first-line treatment,

the results were unfavorable. However, the response was very favorable regardless of the histological type, improving the likelihood of longer survival. This was evidenced by the predominance of 15 patients with a partial response, followed by 10 with a complete response and 7 patients with a stable response.

The median survival time was 20,753 days for complete response; 9,181 days for partial response and 8,268 days for stable response; demonstrating the favorable response to the use of CIMAvaxEGF in patients with advanced lung cancer (regardless of histology) with poor response to the use of polychemotherapy.

This is consistent with the study by Columbié et al. [10] who, when performing an intention-to-treat analysis with CIMAvax-EGF®, also found a significant increase in overall survival.

In another study comparing the use of the CIMAvax-EGF vaccine with the monoclonal antibody nimotuzumab carried out by Carballo et al [19], they found a median overall survival of CIMAvax-EGF of 18.0 months, higher than the use of the monoclonal antibody nimotuzumab, which was statistically significant (p= 0.021).

It can be stated that immunotherapy, because it can be administered for a prolonged period in cancer treatment, may increase the probability of recurrent events [20].

This investigation reported adverse events in only 13 patients, all of low intensity, and more than 59% were free of these effects, unlike those found by Carballo et al. [19], who reported among the most frequent events: pain at the injection site in 77.4% of the cases studied, and fever and headache with 32.3 and 32.0% respectively.

However, this study coincided with Columbié et al. [10], where adverse events were recorded in less than 25% of vaccinated patients.

It is important to consider the toxicity profile of immunotherapies, especially in cancer patients in advanced stages of their disease; however, they have not altered the safety and efficacy profile in controlled clinical studies in medical practice.

This research concludes that a high overall progression-free survival was found after the use of the CIMAvax-EGF vaccine, with a very positive response to treatment, independent of the histological type, which improved the probability of survival with adverse events of mild intensity and the most frequent being pain at the injection site.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

[1] Bradley SH, Kennedy MPT, Neal RD. Recognising Lung Cancer in Primary Care. AdvTher. 2019 [acceso 08/07/2023];36(1):9-30. Disponible en: https://pubmed.ncbi.nlm.nih.gov/30499068/

[2] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019 [acceso 08/07/2023];69(1):7-34. Disponible en: https://acsjournals.onlinelibrary.wiley.com/journal/15424863

[3] Abreu Ruíz G, Bermejo Bencomo W, Romero Pérez T, Monzón Fernández AN. Programa Integral para el Control del Cáncer en Cuba. Diagnóstico y tratamiento del cáncer de pulmón. La Habana: Editorial Ciencias Médicas; 2020. [Links]

[4] Cuba. Ministerio de Salud Pública. Anuario Estadístico de Salud 2021. La Habana: MINSAP. 2022 [acceso 08/07/2023]. Disponible en: https://temas.sld.cu/estadisticassalud/

[5] Gatalica Z, Xiu J, Swensen J. Molecular characterization of cancers with NTRK gene fusions. Mod Pathol 2019 [acceso 08/07/2023];32(1):147-53. Disponible en: https://pubmed.ncbi.nlm.nih.gov/30171197/

[6] Palanca Ballester C. Identificación de GRHL2 como biomarcador epigenético en la resistencia a terapias anti-EGFR en el cáncer de pulmón no microcítico. [Tesis]; Universidad de Valencia. España. 2023. Disponible en: https://roderic.uv.es/handle/10550/86028

[7] Oliu-Bosch SB, Acosta-Brooks SC, Romero-García I, Bosch-Nuñez AI. Asociación plaquetas-factor de

crecimiento epidérmico en pacientes con cáncer pulmonar de células no pequeñas tratados con quimioterapia. Revista de Ciencias Médicas de Pinar del Río. 2022 [acceso 08/07/2023];26(3). Disponible en: http://scielo.sld.cu/scielo.php?pid=S1561-31942022000300018&script=sci_arttext

[8] Ortiz Carrodeguas RA, Monteagudo GL, Alemán SA, Abreu Ruiz G, Fernández Torres N, Álvarez-Guerra Gonzáles L. Methodology to prepare a comprehensive treatment guideline for lung cancer in Villa Clara.
Medicentro Electrónica. 2022 [acceso 08/07/2023];26(2):364-85.
Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30432022000200364&lng=es

[9] Saavedra Hernández D, García Verdecia B, González Morera A, Lorenzo Luaces Álvarez P, Lage Dávila A. Marcadores de inmunosenescencia y su relación con el cáncer de pulmón. Anales de la ACC. 2021 [acceso 08/07/2023];11(1):9. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S2304-01062021000100027&lng=es&tlng=es9. [Links]

[10] Columbié Regüeiferos JC, Rosales Calas M, Torres Puentes S, Veranes García M, Quintero Salcedo S. Uso de la vacuna CIMAvax-EGF(r) como práctica médica habitual. MEDISAN. 2019 [acceso 08/07/2023];23(2):219-31. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1029-30192019000200219&lng=es

[11] Quispe Rodriguez GH. Cáncer de pulmón: características clínico epidemiológicas y sociodemográficas en el hospital Antonio Lorena del Cusco, 2015-2021. [Tesis]; Universidad Nacional San Antonio Abad del Cusco. Perú. 2022 [acceso 08/07/2023]. Disponible en: http://repositorio.unsaac.edu.pe/handle/20.500.12918/6703

[12] Prado RA, Ortiz-Barboza A. Comportamiento epidemiológico del cáncer de pulmón en Costa Rica: incidencia y mortalidad. Horizonte Sanitario. 2023 [acceso 08/07/2023];22(2):279-87.
Disponible en: https://revistahorizonte.ujat.mx/index.php/horizonte/article/view/5207

[13] Rodríguez Abreu D. Resultados en el manejo del cáncer de pulmón avanzado en el Hospital Insular de Las Palmas de Gran Canaria entre los años 2009-2015. [Tesis]. Palmas de Canarias, España: Universidad de Palmas de Canarias. España. 2021 [acceso 08/07/2023].
Disponible en: https://accedacris.ulpgc.es/bitstream/10553/106586/1/Resultados_manejo_cancer.pdf

[14] Camacho Sosa K, Martí Coruña MC, Ferreira Moreno VG, García Soto J, Lemus Alonso L. Efficacy of computed tomography in the follow-up to lung cancer treated with Cuban immunotherapy. Rev Med Electrón. 2022 [acceso 08/07/2023];44(2):278-87. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1684-18242022000200278&lng=es

[15] Villanueva-Bueno C, Collado-Borrell R, Revuelta-Herrero JL, Fernández-Román AB, Casado-Abad G, Escudero-Vilaplana V. Implantación de una metodología para evaluar patient-reported outcomes en pacientes con cáncer de pulmón: protocolo del estudio PeOpLe (Patient-reported Outcomes in Lung cancer). Farm Hosp. 2022 [acceso 08/07/2023];46(4):265-69.
Disponible en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1130-63432022000400010&lng=es

[16] Viada González C, Lorenzo Monteagudo G, Ramos Suzarte M, Álvarez Cardona M, Frías Blanco A, Neninger Vinagera E, et al. Evaluación de la calidad de vida de pacientes con cáncer de pulmón de células no pequeñas tratados con la vacuna CIMAvaxEGF(r). Vaccimonitor. 2021 [acceso 08/07/2023];30(2):69-80.
Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1025-028X2021000200069&lng=es

[17] Howlader N, Noone AM, Krapcho M, Miller D, Bishop K, Altekkruse SF, et al. SEER Cancer Statistics Review, 1975-2013. Bethesda, MD: National Cancer Institute. 2021 [acceso 08/07/2023].
Disponible en: https://seer.cancer.gov/csr/1975_2018

[18] Tabio Lage A, Collado Otero JC, Gómez Trueba G, Ropero Toirac RD. Supervivencia global de pacientes con carcinoma del pulmón de células no pequeñas. Rev Cub Oncol. 2021 [acceso 08/07/2023];19(2):25. Disponible en: http://revoncologia.sld.cu/index.php/onc/article/view/96

[19] Carballo Torres D, Menínger Vinageras E, Soriano García JL. Supervivencia en pacientes con cáncer pulmonar no microcítico avanzado en mantenimiento con CIMAvax-EGF o Nimotuzumab. Rev Cuban de Oncol. 2021 [acceso 08/07/2023];19(1):1-23.
Disponible en: http://www.revoncologia.sld.cu/index.php/onc/article/download/112/55

[20] Saumell Nápoles Y, Sánchez Valdés L, Suárez Pérez Y, Batista Romagoza M. Nueva metodología para la vigilancia de la seguridad durante el desarrollo prerregistro de productos inmunoterapéuticos. Revista Cuban Farmacia. 2020 [acceso 08/07/2023];53(2):1-21.
Disponible en: http://www.revfarmacia.sld.cu/index.php/far/article/viewFile/406/312

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