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Overview of Non-Squamous Cell Subtypes of Iraqi Lung Cancer Patients and Their Progression Free Survival

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Abstract: Lung cancer is most common malignancy and is the first cause of death in Iraq. To assess the progression free survival (PFS), and to describe the role of maintaining pemetrexed drug. Retrospective study conducted in Oncology Teaching Hospital /Medical city complex. The period from January 2014 to June 2017. A total of forty seven patients with non-small cell lung cancer, treated by chemotherapy enrolled. Patients assessed for age, gender, histopathological subtypes, first line chemotherapy protocol and progression free survival. The progression free survival was 18.6 months with (95% Confidence Interval (CI)). The progression free survival for adenocarcinoma and squamous cell carcinoma were 19.6, 9.8(months). The maintenance pemetrexed showed a better Progression free survival than other patients. Patients with adenocarcinoma histology have better Progression free survival than other subtypes.

Keywords: Lung cancer, non-small cell cancer, Pemetrexed.

INTRODUCTION

Throughout the world, lung cancer accounts for 13% (1.6 million) of the total cases and 18% (1.4 million) related deaths based on 2008 estimate [1]. The American Cancer Society estimate 156,940 people in the United States died of lung cancer in 2011 [2]. The 5-year survival rate for lung cancer is approximately 16% [3]. Although the lung cancer numbers in the general population are startling, the main risk based on exposures to carcinogens. Voluntary or involuntary cigarette exposure accounts for 80% to 90% of all cases of lung cancer [4].

The Surveillance Epidemiology and End Results (SEER) analyzed that, 15% localized to the primary site; 22% had regional lymph node spread, and 56% distant metastasis; and the remaining 7% were stage unknown [5]. In patients with adenocarcinoma, pemetrexed has demonstrated activity and garnered U.S. Food and Drug Administration (FDA) approval in the first-line, second- line, and maintenance therapy settings and has tested in phase II trials in combination with carboplatin and Bevacizumab in non-squamous histology, generating a median PFS of 7.8 months and median survival of 14.1 months [6, 7]. Pemetrexed maintenance therapy improved PFS and OS following a non-pemetrexed–containing platinum doublet [8].

METHODS

Study Design

Retrospective study of NSCLC patients treated from January 2014 to June 2017.

Data collection

The sample size calculated based on histopathology subtype and treatment protocol.

Eligibility criteria

On justification of strict inclusion and exclusion criterias after informed consent.

Inclusion criteria

Patients proven NSCLC and by investigations appear they stage IV.

Exclusion criteria

Other histopathology subtype excluded and in stage I-III of NSCLC.

Data analysis

Microsoft excels sheet file used, and statistical analysis by SPSS v22. Kaplan – Meier used to get progression free survival. Level of significance was set at P value of 0.05.

RESULTS

The mean±SD of age participated in this study was 60.7±10.4 years with median 61.5 years, which ranged from 33-86 years. The number of male patients in this study was 34 (72.3%) while the number of

female patients was 13 (27.7%). About chemotherapy (first line protocol) options, commonly used pemetrexed/platinume based as 19(42.2%), others protocol taxanes/platinume based 10(22.2%), vinorelbine/platinum based 7(15.6%), single agent chemotherapy 6(13.3%) and gemcitabine/ platinume based 3(6.7%), Table-1. Twenty three patients continued on pemetrexed as maintenance chemotherapy after first line. Two different subtypes of NSCLC recorded in this study; the most common observed subtype was adenocarcinoma 28(68.2%) followed by SCC 13(31.8%), as in Table-2. The period for PFS was 18.6 months with and the median period of PFS is 18 months, Fig-1. The Kaplan-Meier survival curve for PFS according to adenocarcinoma and SSC subtypes as shown in Fig-2. The results showed, male patients 22(46.8%) were adenocarcinoma while 12(25.5%) were SCC. Furthermore female 12(25.5%) were adenocarcinoma and the rest 1(2.2%) were SCC, Table-3. Among gender of patients, male (mean=19.87) (95% CI 11.60-28.14) and female (mean =16.2) (95% CI 11.73-20.66), Table-4. Regarding Kaplan-Meier curve of PFS, estimate significant results, Fig-3. PFS mean for adenocarcinoma and squamous cell carcinoma were 19.6, 9.8(months). 95% Confidence Interval (CI) was (12.09-27.13) for adenocarcinoma and (7.06-12.68) for SCC, Table-5.

Table-1: Frequancy of chemotherapy (first line protocol)

Chemotherapy protocols	**Frequency (%)**
pemetrexed/cisplatin or carboplatin	19(42.2)
gemcitabine / cisplatin or carboplatin	3(6.7)
vinorelbine / cisplatin or carboplatin	7(15.6)
Taxanes / cisplatin or carboplatin	10(22.2)
single agent chemotherapy	6(13.3)
Total	45

Table-2: Distribution of NSCLC according to their histopathology subtype (n=41)

NSCLC subtype	Total N	N of Events	Censored	
			N	Percent
Adenocarcinoma	28	8	20	71.4%
SCC	13	2	11	84.6%
Total	41	10	31	75.6%

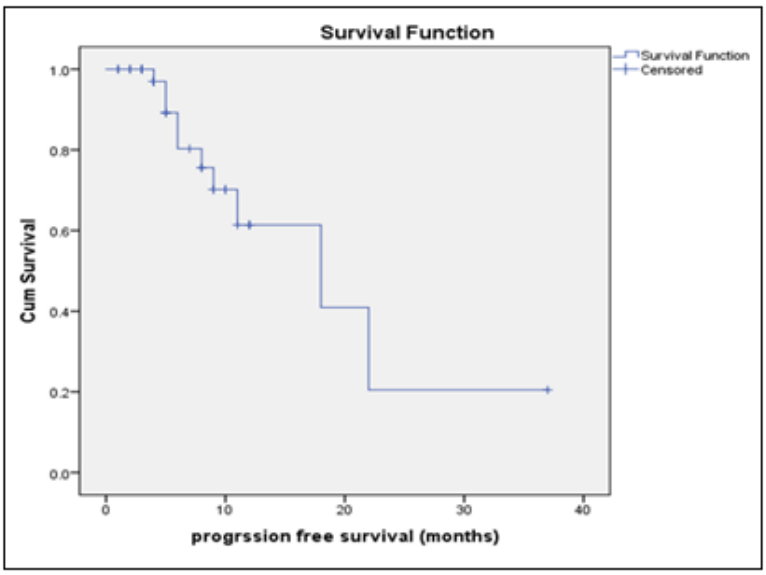

Fig-1: Kaplan-Meier curve of (PFS): for lung cancer patients

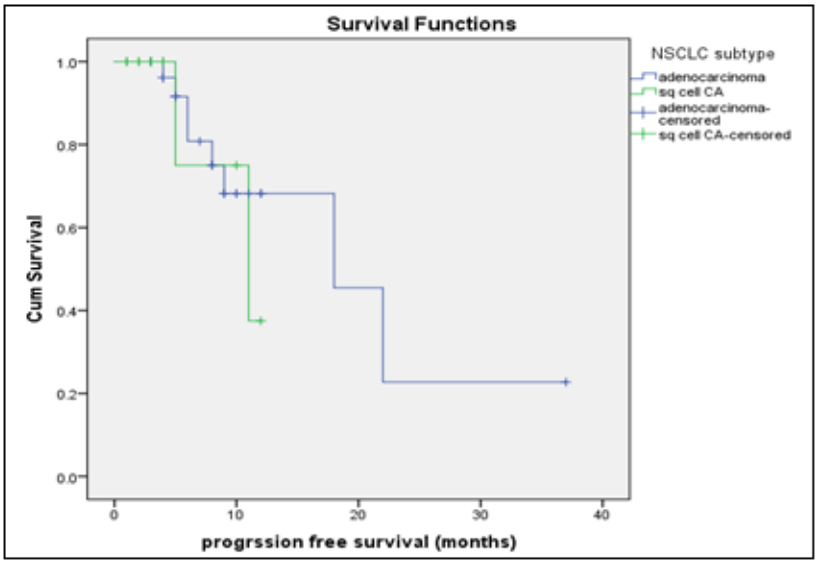

Fig-2: Kaplan-Meier curve of (PFS): for adenocarcinoma and squamous cell carcinoma

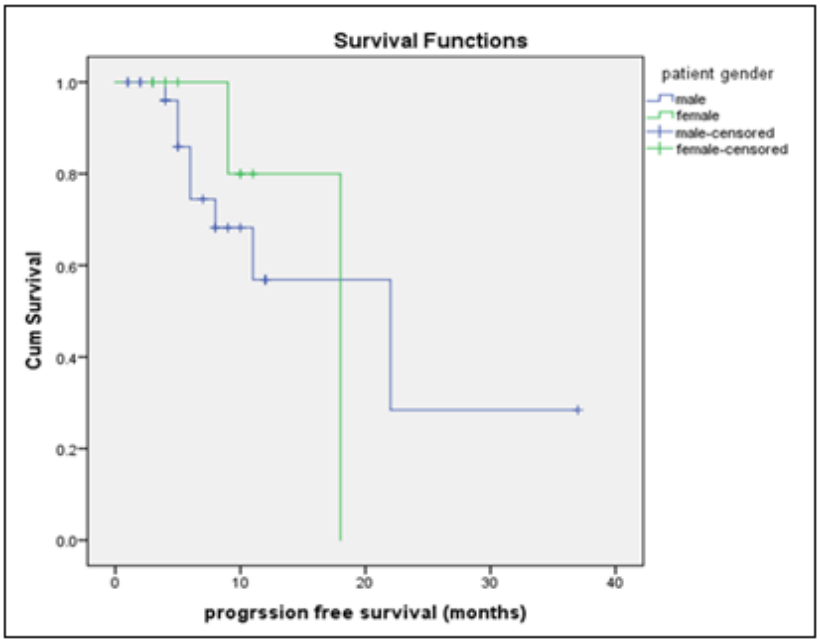

Fig-3: Kaplan-Meier curve of (PFS): for gender (N: 41)

Table-3 Cross percentage among NSCLC subtype and gender

Gender	NSCLC subtype		Total
	Adenocarcinoma (%)	Sq cell CA (%)	
Male	22(46.8)	12(25.5)	34(72.3)
Female	12(25.5)	1(2.2)	13(27.7)
Total	34	13	47
Pearson Chi-sequare= 3.581, Fisher's exact test= 0.076, P = 0/058			

Table-4: Mean and median of lung cancer PFS according to gender. (n=47)

	Mean	95% CI		Median	95% CI	
		Lower	Upper		Lower	Upper
Male	19.87	11.60	28.14	22.00	5.88	38.12
Female	16.20	11.73	20.66	18.00		
Overall	18.62	11.65	25.60	18.00	5.61	30.38

Table-5: Mean and median of PFS for adenocarcinoma and SCC

NSCLC subtype	Mean			Median		
	PFS	95% CI		PFS	95% CI	
		Lower	Upper		Lower	Upper
Adenocarcinoma	19.6	12.09	27.12	18	6.80	29.19
sq cell CA	9.8	7.06	12.68	11	2.01	19.98
Overall	18.6	11.65	25.60	18	5.61	30.38

DISCUSSION

This is a retrospective study of 47 patients diagnosed with NSCLC, their age range from 33 to 86 with a mean age of 60 years, which was concordant with other Iraqi studies [9, 10], besides to another study from India 2013 [11]. While in western countries the mean of age at time of diagnosis was 70 years [12]. This attributed to many factors one of them the higher life expectancy in the western word than in our community. The association between cancer incidence and age explained by the prolonged exposure to different carcinogens like tobacco smoke, asbestos, air pollutions and other types of chemicals or radiations [13]. The study showed that male more affected than female (72.3%) (27.7%) respectively, the results resemble other Iraqi studies in which male represent 83.3% of the total number, while females represent 16.7% [14]. Approximately 40% of diagnosed lung cancers patients are stage IV. The goal for treating is to improve survival and reduce disease-related adverse events [15]. For stage IV, cytotoxic combination chemotherapy is the first-line therapy, which might influence by histology, age vs. comorbidity, and performance status (PS) [16, 17]. The most used first line chemotherapy that takes part pemetrexed with either cisplatin or carboplatin. And these depend on a large randomized clinical trial conducted by the Eastern Cooperative Oncology Group (ECOG) [18, 19]. All patient take part in which they treated with alimta (pemetrexed) and either cisplatine or carpoplatine protocol of chemotherapy often maintain treatment on alimta (pemetrexed) after 4-6 cycle, and that depend on another phase 3 study with a different design, in which patients with non-progressive disease after 4 cycles of platinum-based combination therapy randomized to therapy with pemetrexed or placebo [18] of median progression-free survival was superior with pemetrexed therapy. The association between pemetrexed and non-SCC histology in term of clinical benefit was also observed in maintenance setting. In our study adenocarcinoma appear to be the most common subtype with 68.2%. Similar Iraqi previous studies show also the increase adenocarcinoma incidence than SCC [19]. A study in the kingdom of Saudi Arabia also show higher incidence of adenocarcinoma [18, 19]. However, disagree with the findings recorded by Hussam H. Ali et al 2006 [17-19] who reported that the common type of lung cancer was squamous cell carcinoma. The PFS was 18.6 months and the median was 18 months and adenocarcinoma lung cancer seem to have the longer time of PFS, with mean of 16.9 months and the median of PFS are 18 months which explained by the fact that because the use of first line chemotherapy which pemetrexed + platinum based chemotherapy. Emerging data have suggested that histology could be an important factor in selecting certain chemotherapy drugs [19]. Based on results of this trial, pemetrexed approved for use with platinum as first-line therapy in patients with non-squamous NSCLC. While other study results show no significant difference in PFS among the four platin-based doublet regimens in patients with squamous as well as non-squamous carcinomas.

CONCLUSIONS

The mean age of NSCLC were 60.7 years while the median of 61.5 year. Male to female ratio was 2.6:1. The most used 1st line chemotherapy is pemetrexed with either cisplatin or carboplatin. Maintenance pemetrexed showed a better PFS than others. Adenocarcinoma subtypes have better PFS than other subtypes. Male using 1st line combinations of chemotherapy have better PFS than female.

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