

Treatment Response and Disease Characteristics in Non-Small Cell Lung Cancer (NSCLC) Patients Receiving Pemetrexed-Based Therapy

Qusay Jassam Shandookh, FICMS* Ahmed Hamza Al-Shammari, FICMS** Ali Muneam Kamil Hussein, MSc*** Mohaimen Majid Albasri, MSc*** Hayder M. Abdulhamza, MSc**** Amjad I. ORAIBI, PhD***** Haidar A Abdulamir, PhD*****

ABSTRACT

Non-small cell lung cancer (NSCLC) is the primary lung cancer. In this condition, the initiation of cancerous cells within the tissues of the lungs involves. NSCLC exhibits a comparatively slow growth rate in comparison to small cell lung cancer (SCLC). However, it frequently spreads to other regions of the body by the time it is detected. Therefore, timely identification and therapy are crucial. Moreover, at the metastatic stage of the NSCLC, a combination of drugs was administered as treatment. Pemetrexed was often used in combination with atezolizumab or carboplatin. Consequently, in the present study, pemetrexed uptake in the 19 individuals was analyzed. Here, 13 males and 6 females were analyzed on the basis of type of cancer, grade of disease, gender, molecular factor, and risk factors. Adenocarcinoma was discovered to be the most common type of cancer among the 12 patients who participated in our study, with 10 of those patients having a Grade 2 disease. Our study showed that the EGFR molecular marker was the most prevalent among the 5 cases. In the context of the patient's condition, eleven individuals were classified as having an ECOG1 status, and the RECIST criteria indicated a favorable response rate of sixty-three percent for both partial and complete responses to pemetrexed treatment. In older adults, specifically those aged 60 and older, a disturbing pattern was observed: they displayed an increased incidence of metastases in various areas. Moreover, smoking impacted individuals within this age group, particularly those diagnosed with adenocarcinoma and squamous cell carcinoma. Overall, the study signifies the role of age and lifestyle factors, including smoking, in NSCLC progression and in response to treatment, as well as the efficacy of pemetrexed in combination with other drugs, primarily for particular patient demographics and disease grades, providing guidance for customized therapy strategies..

Keywords: Carcinoma; Non-Small-Cell Lung; Lung Neoplasms; Pemetrexed; Carboplatin.

INTRODUCTION

Cancer is the leading cause of death around the world^{1,2}, and lung cancer is a common type of cancer globally. There are several types of lung cancer. One of them is non-small-cell lung cancer (NSCLC). This type has the highest incidence rates all over the world^{3,4}. An estimated 2,206,771 cases, which account for 11.4% of all cancers, were diagnosed in the year 2020, with a mortality rate of 1,796,144. This information was derived from data collected from 185 countries (18.0%)⁵⁻⁷. In addition, non-small-cell lung cancer is considered one of the most common types of lung cancer, as we mentioned previously, as its percentage is about 85% of all types of lung cancer. In addition to that, non-small-cell lung cancer itself is divided into three types. In addition, there are many reasons that may cause this disease, including, for example, smoking, which is associated with frequent coughing and shortness of breath⁸⁻¹⁰.

Diagnosis of this disease depends mainly on the use of computed tomography (CT) scans, and there are also many other devices to diagnose it, such as, magnetic resonance imaging (MRI) scans, chest x-rays, and positron emission tomography (PET) scans. In addition, this disease, its severity, and its stages depend on the patient's health condition in general. Treatment also depends on the health condition. If the patient has Stage 1, it can be treated using radiation or surgery. As for Stages 2 and 3, it must be treated with chemotherapy. As for Stage 4, this must be treated only with chemotherapy medications associated with several side effects for the patient. However, there are many factors that control the extent of the disease's development or recovery, including genetic factors, in addition to smoking, inhaling dust, and polluted air, as well as if the person has dealt with asbestos for a long time and other causes. However, in recent periods, many medications have been approved by the FDA for immunotherapy, such as nivolumab, pembrolizumab, and atezolizumab.

* Department of Pharmacy, Al-Yarmouk University College
Baqubah, Diyala, Iraq.

Email: qusayjassam@gmail.com

** Department of Anesthesia Techniques
College of Health and Medical Techniques
University of Kut, Wasit, Kut, 52001, Iraq.

*** Department of Pharmaceutics, College of Pharmacy
University of Kut, Wasit, Kut, 52001, Iraq.

**** Department of Pharmaceutical chemistry, College of Pharmacy
University of Kut, Wasit, Kut, 52001, Iraq.

***** Al-Manara College For Medical Sciences
University of Manara, Maisaan, Iraq.

***** College of Pharmacy, University of Hilla
Babylon, Iraq.

Moreover, several studies show that combination therapy involves combining one or more drugs, maybe even one and two, to produce better results^{11,12}. Initially, in 2018, the combination of pembrolizumab pemetrexed and carboplatin was approved as the first defense treatment for the metastatic stage of the NSCLC¹³, and it was also performed in a real-life study in 2023¹⁴. Similarly, atezolizumab with pemetrexed and carboplatin/cisplatin found similar inferences to treat the metastatic stage of the NSCLC¹⁵. Overall, it was observed that pemetrexed was used to treat the metastatic stage of the NSCLC in combination with the other drugs. Pemetrexed is a multitargeted antifolate chemotherapeutic agent that functions as a third-generation antitumor agent and has demonstrated activity against NSCLC¹⁶. Furthermore, the enzymes thymidylate synthase, dihydrofolate reductase, and glycinamide ribonucleotide formyl transferase, which are involved in the synthesis of DNA, are inhibited by pemetrexed. Pemetrexed disrupts the synthesis of DNA and RNA, which inhibit the growth and proliferation of the tumor cell¹⁷.

Moreover, the drugs are frequently used in combination with other chemotherapy medications, including cisplatin, to enhance their effectiveness in treating NSCLC. Nevertheless, the prolonged use of pemetrexed contributes to the development of resistance mechanisms in NSCLC, limiting its potential efficacy in treatment^{17,18}. Furthermore, the study by Dediu et al. (2014) showed that pemetrexed is a highly suggested single agent for the second-line defense of the NSCLC. Notably, it is the sole chemotherapeutic agent that has received approval for both persistence and switch maintenance therapy, and it showed better efficacy in the non-squamous cell type¹⁹. The study by Zhao (2023) assessed the clinical importance of pemetrexed while combined with cisplatin in the treatment of the NSCLC²⁰. Other study conducted in China showed that giving cisplatin co administrated with pemetrexed result in improving the anticancer effect in patients with None- Small cell lung cancer with low level of side effect comparative to other antineoplastic therapy for that reason its important to analyze the potency in different stages and types of cancer²¹.

MATERIAL AND METHODS

Study Design: This research was carried out in Baghdad on a group of patients suffering from adenocarcinoma, small cell carcinoma, and large cell undifferentiated carcinoma in the period between January and March 2023. Moreover, the age range of the patients who were selected for this study ranged from less than forty years to more than sixty years, and the measurable tumors were evaluated using the Response Evaluation Criteria for Solid Tumors (RECIST) specifications^{22,23}. Other eligibility criteria included the Eastern Cooperative Oncology Group (ECOG), which evaluates the performance status of cancer progression and how it affects the daily activity of the patients to regulate the appropriate treatment for them²⁴⁻²⁶.

Data analysis: The data was analyzed between the age and grade, age, grade and type, age, gender and grade, molecular result, grade and age, molecular result and type of cancer, age, type and smoking, metastasis, type and age, type, gender, and progression-free survival^{27,28}. Gender, grade, performance status, type of carcinoma, and molecular factors^{29,30}.

RESULTS AND DISCUSSION

Here, Table 1 presents demographic data, including the total number of patients (n=19), their age distribution (40-60 years, <40 years, >60 years), gender distribution (male, female), and the incidence of different types of cancer (Adenocarcinoma, Large cell undifferentiated carcinoma, Squamous cell carcinoma, small cell carcinoma) among males and females. Approximately 47.37 percent of the population is comprised of males who are over the age of 60. (68.42%). Additionally,

it categorized the incidence of various types of carcinomas according to the gender of the patient³¹.

Table 2 categorizes patients based on molecular markers (EGFR, EGFR_ALK, PDL1, None) and the grade of their disease (Grades 1 to 4). It provides information on the number of patients in each category and the molecular traits linked to various disease grades. Moreover, most of the cases showed no molecular markers ('None of them' category). This indicated that the molecular factors and grades of the disease show no correlation. Overall, the total number of patients is 19. Grade 1 has the least number of patients (n=1). Grade 2 is the most prevalent, n=10. Grade 3 has n=5, and Grade 4 has n=3. Patients without any of these specific molecular markers (none of them) predominantly fall in the Grade 2 category. Higher disease grades (Grades 2, 3, and 4) are related to EGFR mutations, suggesting that these patients may have more advanced disease. Patients with combined EGFR and ALK mutations, as well as those with PDL1,

Table 1. Demographics and Cancer Type Distribution among Patients.

Demographic data	Number of patients
Total	19(100%)
Age	
40-60 years	7(36.84%)
< 40 years	3(15.79%)
> 60 years	9(47.37%)
Gender	
Male	13(68.42%)
Female	6 (31.58)
Adenocarcinoma	
Male	7(36.84%)
Female	5 (26.31)
Large cell undifferentiated carcinoma	
Male	3(15.79%)
Female	1(5.26%)
Squamous cell carcinoma	
Male	2(10.5)
Female	0
Small cell carcinoma	
Male	1(5.26)
Female	0
Uptake of Pemetrexed	
Male	13(68.84)
Female	6 (31.58)

Table 2. Molecular characterization of tumours.

Molecular result	Grade 1	Grade 2	Grade 3	Grade 4
EGFR	0	1	2	2
EGFR_ALK	0	1	0	0
PDL1	0	1	0	0
PDL1 None of them	1	0	1	0
None of them	0	7	2	1
Grand Total	1	10	5	3

Table 3. Patient distribution by Eastern Cooperative Oncology Group (ECOG) performance status.

ECOG Status	Total Patients
ECOG (0)	4 (21%)
ECOG 1	11(57%)
ECOG 2	4 (21%)

are only present in Grade 2, suggesting a possible correlation between these molecular markers and the Grade 2 severity of the disease. The presence of PDL1, either alone or in combination with none of them, is associated with a spread across Grades 1–3, but not Grade 4. The data indicated that the uptake of pemetrexed treatment and its efficacy differ depending on the molecular characteristics of the cancer. The increased proportion of Grade 2 disease patients in all molecular results suggests that pemetrexed may be more widely prescribed or more beneficial at this stage of the disease. Higher disease grades and specific molecular markers (like EGFR) may indicate that these patients require more aggressive or alternative treatment approaches³².

Table 3 provides a comprehensive breakdown of the ECOG (Eastern Cooperative Oncology Group) performance status of patients. Clinicians and researchers use the ECOG performance status to assess patients' conditions and how disease impacts a patient's quality of life. Here, it displays the distribution of patients, both in terms of total numbers and percentages, across the ECOG statuses 0, 1, and 2. Most patients in the study had an ECOG score of 1, comprising up to 57% of the sample. The ECOG1 categorizes a performance status that signifies physical restrictions in activities demanding strength, although the person can still walk and participate in light or sedentary duties like light housekeeping or office work. The substantial intake of pemetrexed in the ECOG 1 category may suggest that it's suitable or efficient in individuals who are moderately active but have certain restrictions. The use in ECOG 0 and 2 patients suggests a wide range of applications of pemetrexed across different levels of patient functionality. The data help clinicians in their decision-making about pemetrexed uptake, considering the patient's general health and capacity for day-to-day functioning³³.

Table 4. illustrates the follow-up radiological findings of patients categorized by RECIST (Response Evaluation Criteria in Solid Tumours) criteria: Stable, Progression, Partial response, and complete response. It also indicates the age groups of these patients.

As per the RECIST criteria, it was observed that among the total number of patients, 10.5% exhibited a stable response, 26.3% demonstrated progression, 15.7% achieved a complete response, and 47.3% had a partial response. Based on these results, it is evident that the majority of patients (63%, combining Complete and Partial Responses) exhibited a favorable response to the treatment, resulting in either decrease or total removal of the target tumours. However, a significant portion (26.3%) experienced progression of the disease, and a smaller fraction (10.5%) showed no change in tumour size.

Table 5 presents a patient according to age cohorts and the severity of their disease. Predominantly, Patients are grouped into two age groups: those over 60 and those between 40 and 60. Within these cohorts, a wide range of disease grades have been found.

As a result, it was observed that the majority of the patients are in the Grade 2 category, which signifies that pemetrexed is possibly more effective in patients with this disease severity. Individuals over 60 years old have the highest patient number is 9, suggesting a higher use of pemetrexed or a higher occurrence of the disease in this age bracket. In the 40-60 years age group, there is a spread across Grades 2 to 4, but no cases were identified in Grade 1, that indicated pemetrexed is being used for moderately severe to severe cases in this age bracket. The age group less than 40 years old, despite having the smallest total number

Table 4. Patient outcomes by radiological findings using RECIST criteria across different age groups

Follow up radiological finding by RECIST criteria	Patients	Age
Stable	2(10.5%)	40-60
Progression	5 (26.3 %)	40-60, less than 40 yr, more than 60 yr
Partial response	9 (47.3%)	40-60, less than 40 yr, more than 60 yr
Complete response	3 (15.7 %)	40-60, more than 60 yr

Table 5. Distribution of disease grades across different age groups

Age	Count of Grades of the disease				Total
	Grade 1	Grade 2	Grade 3	Grade 4	
40- 60 years	0	4	2	1	7
Less than 40 years	0	1	1	1	3
More than 60 years	1	5	2	1	9
Total	1	10	5	3	19

Table 6. Distribution of age and type of tumors across the various grades of the disease.

Age and Type of Tumours	Grades				Total
	Grade 1	Grade 2	Grade 3	Grade 4	
40-60 years	0	4	2	1	7
Adenocarcinoma	0	2	2	1	5
Large cell undifferentiated carcinoma	0	1			1
Squamous cell carcinoma	0	1			1
less than 40 years		1	1	1	3
Adenocarcinoma	0	1	1	1	3
more than 60 years		5	2	1	9
Adenocarcinoma	0	3		1	4
Large cell undifferentiated carcinoma	0	1	2		3
Small cell carcinoma	0	1			1
Squamous cell carcinoma	0	0			
Grand Total		10	5	3	19

3, shows a spread across Grades 2 to 4, indicating its use in relatively severe cases in younger patients.

This distribution indicates that pemetrexed is prescribed for various disease severities, although it is most frequently used in Grade 2 cases. The increased presence of seniors (over 60 years old) taking pemetrexed may suggest a higher occurrence or detection rate of the disease in this age category, or it might indicate a particular efficacy or inclination towards utilizing pemetrexed in older individuals³⁴. The lack of Grade 1 in younger age groups could suggest a delayed diagnosis or a tendency to use pemetrexed in more progressed stages of the disease in these patients.

Table 6 combines the factors of patient age, cancer type, and disease grade, presenting a detailed breakdown of how different types of cancer (Adenocarcinoma, Large cell undifferentiated carcinoma, Squamous cell carcinoma) are distributed among various grades and age groups. As an outcome, it was observed that a major number of patients underwent grade 2 diseases. This suggested uptake of pemetrexed decreases the progression of cancer(re-arrangement). Moreover, adenocarcinoma is the most frequent type of tumor in each age group, with variable grades. The age group of 40-60 years shows a higher diversity in tumor types (adenocarcinoma, large cell undifferentiated carcinoma, squamous cell carcinoma)³⁵. Patients over 60 years have the highest incidence of Grade 1 tumours, suggesting that pemetrexed may be effective in less advanced stages of cancer in this age group. Pemetrexed shows usage across a range of tumour types and disease severities. Pemetrexed's efficacy can be influenced by the patient's age and the cancer form. The increased occurrence of adenocarcinoma in patients treated with pemetrexed indicates that it may be a more frequently used or more effective therapy for this type of tumour.

Table 7 categorizes data by gender (male and female) within each age group and disease grade to analyze how disease grades change among different age groups and genders. Overall, the total number of patients treated with pemetrexed across all age groups is 19. The most common grade of disease across all patients is Grade 2, with 10 cases. Grades 1, 3, and 4 are less prevalent, with 1, 5, and 3 cases, respectively. Moreover, males in the age group over 60 years show a higher prevalence and a wider range of disease grades (1 to 4). Both genders show a similar pattern in the 40-60 years age group, but with fewer cases in total compared to the over 60 years group. In the group under 40 years old, the distribution is relatively even between genders, although there is a low number of cases. This indicates that the older age groups have a higher proportion of patients and are likely to have more severe disease grades, which could be important for treatment planning and analysing outcomes.

The correlation between molecular results (EGFR, EGFR ALK, PDL1, None), disease grade, and age groups is shown in Table 8. The analysis between these two variables showed across all age groups, and Grade 2 is the most common disease grade among all age groups, with 10 instances, followed by Grades 3, 4, and 1, with 5, 3, and 1 case(s) correspondingly, as shown in the analysis. Among patients who had pemetrexed treatment, Grade 2 is the most prevalent, impacting 10 people. In addition, the most common grade for patients treated with pemetrexed is Grade 2, with 10 patients. Patients with no identified molecular markers (None of Them) are present across all age groups and are most prevalent in the age group of more than 60 years, suggesting pemetrexed is widely used regardless of specific molecular markers. EGFR mutations have been associated to various disease grades; however, no Grade 1 occurrences suggest the potential use of pemetrexed in later stages for these patients. Patients over 60 years,

Table 7. Analysis of disease grades by gender and age group.

Gender and Age	Grades				Grand Total
	Grade 1	Grade 2	Grade 3	Grade 4	
40- 60 years		4	2	1	7
Female		2	1		3
Male		2	1	1	4
Less than 40 years		1	1	1	3
Female			1		1
Male		1		1	2
More than 60 years	1	5	2	1	9
Female		2			2
Male	1	3	2	1	7
Grand Total	1	10	5	3	19

Table 8. Correlation of age and molecular markers with disease grades among patients.

Age and Molecular Result	Grades				Grand Total
	Grade 1	Grade 2	Grade 3	Grade 4	
40- 60 years		4	2	1	7
EGFR		1	1	1	3
EGFR, ALK		1			1
None of them		2	1		3
Less than 40 years		1	1	1	3
EGFR			1	1	2
None of them		1			1
More than 60 years	1	5	2	1	9
None of them		4	1	1	6
PDL1		1	1		1
PDL1, none of them	1				2
Grand Total	1	10	5	3	19

particularly those without any of the specific molecular markers or with PDL1, show a higher incidence of Grade 1 disease, suggesting pemetrexed might be effective in less advanced stages in this age group. Moreover, pemetrexed shows usage across various molecular profiles and disease severities. Its effectiveness might vary depending on the molecular characteristics of the tumour, especially in relation to EGFR and PDL1 markers. Understanding the relationship between molecular markers, age, and disease severity could be crucial for personalizing pemetrexed treatment in cancer patients³⁶.

Here, Table 9 shows the relationship between molecular results (EGFR, EGFR ALK, PDL1, None) and specific types of cancer (adenocarcinoma, large-cell undifferentiated carcinoma, small-cell carcinoma, and squamous-cell carcinoma). The majority of patients who take pemetrexed have adenocarcinoma, indicating that pemetrexed might be more commonly used or more effective for this carcinoma type³⁷.

Patients with EGFR mutations mainly have adenocarcinoma, suggesting a possible correlation between EGFR mutations and adenocarcinoma in the context of pemetrexed treatment.

Pemetrexed is used in cases of adenocarcinoma and large cell undifferentiated carcinoma where certain molecular indicators are absent, as indicated by a considerable number of individuals lacking these variables³⁸. The study suggests that the efficacy of pemetrexed may be influenced by the molecular profile of the cancer. The high occurrence of adenocarcinoma in the patients suggests a possible inclination or effectiveness of pemetrexed in treating this specific type of cancer. Understanding the correlation between molecular markers and various tumour types is crucial for tailoring pemetrexed treatment approaches.

Table 10 shows the correlation among age, smoking status (smoker, ex-smoker, non-smoker), and several forms of cancer. This analysis is essential for comprehending the correlation between smoking

status and various forms of cancer among different age groups. Adenocarcinoma is the predominant cancer type in patients of all age groups receiving pemetrexed treatment. Individuals aged 40-60 who do not smoke mostly develop adenocarcinoma, whereas smokers tend to have a combination of adenocarcinoma and squamous cell carcinoma. All patients under 40 years old are diagnosed with adenocarcinoma, regardless of whether they smoke or not. Individuals over 60 years old who smoke tend to have a greater range of cancer kinds, such as big cell undifferentiated carcinoma, small cell carcinoma, and squamous cell carcinoma, while non-smokers typically get adenocarcinoma.

The distribution of metastasis sites (bone, liver, brain, etc.) across various age groups and cancer types is indicated in Table 11. This enunciates the significance of knowing the pattern of metastasis concerning age and type of cancer. Overall, adenocarcinoma belongs to the group of the most common cancer types in this cohort and is associated with a multiple metastasis site. It is evident that brain metastasis in this group of young age (age less than 40 years) predominates over other sites. Furthermore, older patients (aged more than 60 years) are the ones seen with a maximal range of metastasis sites. Data shows the uptake of pemetrexed across diverse profiles of metastasis, indicating its use in cancer in advanced stages with metastasis. It indicates data that highlights the profile of pemetrexed treatment for various types of carcinomas with differing metastasis profiles. It may be important to customize treatment in relation to age and cancer type. This may be relevant to the use of pemetrexed in oncologists' decisions, especially with respect to its use within a complex metastatic spread³⁹.

According to the data presented in Table 12, adenocarcinoma is the most common form of cancer among patients who were treated with pemetrexed. This kind of cancer was found in patients with all grades of the disease. According to the findings, there is a significant number of patients who have Grade 2 disease, which suggests that pemetrexed may be very helpful or successful for individuals who are at this point of the severity of their cancer. It's probable that pemetrexed is used

Table 9. Distribution across molecular results and type of cancer.

Molecular Factors	Adenocarcinoma	Large cell undifferentiated Carcinoma	Small cell Carcinoma	Squamous cell Carcinoma	Grand Total
EGFR	4			1	5
EGFR, ALK	1				1
None of them	7	2	1		9
PDL1				1	1
PDL1, none of them		2			2
Grand Total	12	4	1	1	19

Table 10. Influence of age and smoking status on types of carcinomas.

Age and smoking	Adenocarcinoma	Large cell undifferentiated Carcinoma	Small cell Carcinoma	Squamous cell Carcinoma	Grand Total
40-60 years	5	1		1	7
No	4	1			5
Yes	1			1	2
Less than 40 years	3				3
No	2				2
Yes	1				1
More than 60 years	4	3	1	1	9
Ex-Smoker	1				1
No	3				3
Yes		3	1	1	5
Grand Total	12	4	1	2	19

Table 11. Comparison of carcinoma types by age group and metastasis Site

Age and Metastasis site	Adenocarcinoma	Large cell undifferentiated Carcinoma	Small cell Carcinoma	Squamous cell Carcinoma	Grand Total
40-60 year	5	1		1	7
Bone	1	1			2
Liver, Brain, Bone, Others site	1				1
Liver, Others site	1				1
Others site	2			1	3
Less than 40 years	3				3
Brain, Bone	2				2
Brain, Others site	1				1
More than 60 years	4	3	1	1	9
Bone				1	1
Bone, other site		1			1
Brain			1		1
Brain, Bone	2				2
Liver, Bone		1			1
Liver, Bone, Others site		1			1
Liver, Other site	1				1
Others site	1				1
Grand Total	12	4	1	2	19

Table 12. Distribution of cancer grades among different types of carcinoma patients.

Grades	Types of Cancer				
	Adenocarcinoma	Large cell undifferentiated carcinoma	Small Cell Carcinoma	Squamous Cell Carcinoma	Grand Total
Grade 1	0	1			1
Grade 2	6	1	1	2	10
Grade 3	3	2			5
Grade 4	3				3
Grand Total	12	4	1	2	19

Table 13. Progression-Free Survival Among Patients Treated with Pemetrexed

Progression free survival	Count of Does the patient take pemetrexed
2-4 months	6
4-8 months	6
Less than 2 months	2
More than 8 months	5
Grand Total	19

Table 14. Variability in Overall Survival Among Patients Treated with Pemetrexed

Overall Survival	Count of Does the patient take pemetrexed
2-4 months	4
4-8 months	6
Less than 2 months	1
More than 8 months	8
Grand Total	19

more frequently in these stages of the disease or that adenocarcinoma and large-cell undifferentiated carcinoma are more preventable as a result of the spread of Grades 2 and 3. Pemetrexed has been used wisely in the treatment of adenocarcinoma in the array of grades, which is an indication of its potential efficacy in treating this type of lung cancer. Moreover, pemetrexed has limited usage and efficacy in the most advanced stages of other cancer types, as it was observed that it is absent in the patients of Grade 4 in other cancer types, with the exception of adenocarcinoma. Oncologists can use the data to inform their judgments on pemetrexed treatment, especially when considering the treatment's likely efficacy given the kind of cancer and the severity of the disease⁴⁰.

Table 13 shows an array of pemetrexed's effectiveness in the patient group, with progression-free survival (PFS) times that vary from less than two months to more than eight months. The treatment exhibited an intermediate-term efficacy for the majority of patients, as indicated by 12 out of 19 patients experiencing a PFS duration ranging between 2 and 8 months. Patients demonstrating a PFS exceeding 8 months highlight the substantial benefits of pemetrexed in delaying disease progression. The overall distribution underscores the variable effectiveness of pemetrexed in impeding disease advancement among patients, with diverse responses observed across individuals. The hypothesis posits that all patients exhibit a uniform condition and undergo treatment in comparable settings⁴¹.

Table 14 shows the pemetrexed uptake in patients with the overall progression. The data in Table 14 indicated that only one patient survived less than 2 months after the intake of pemetrexed, this suggests the disease progressed rapidly, leading to a short survival period. Four individuals had an average overall survival ranging from 2 to 4 months. These findings suggest that the treatment slightly prolonged the lifespan of these patients. A total of six patients exhibited an overall survival period ranging from 4 to 8 months, indicating a moderate advantage of the treatment in terms of prolonging life. There was a significant increase in the overall survival rate of 8 patients over a period of 8 months when pemetrexed medication was administered. This was the most significant improvement among the groups. In general, data showed that a very small number of patients had a very restricted survival duration of less than two months, which gives rise to the possibility that the treatment may have been inefficient or that the patients' condition was overly advanced at the time that treatment was initiated. The diverse range of survival rates showed the efficacy of the broad spectrum of drugs, with a significant number of patients experiencing improvements ranging from moderate to exceptional³⁵.

CONCLUSION

The findings of the current study indicate that the efficacy of pemetrexed changes based on patient demographics, specific forms of cancer, and molecular marker analysis associated with uptake. The drug demonstrates potential, particularly in the treatment of adenocarcinoma and in individuals with specific molecular profiles, including those with EGFR mutations. Although its efficacy varies substantially, its implementation requires a customised approach. The correlation between treatment response and individual attributes, including age, smoking status, and molecular markers, demonstrates the importance of adapting treatment strategies to each individual. Furthermore, based on the likelihood of disease severity and the ECOG performance level of the patients, pemetrexed is frequently administered to individuals with mild to severe conditions who are not completely immobile. Moreover, the study of progression-free survival and overall survival data in patients taking pemetrexed shows effectiveness in variable form. Most of the patients suffer from long periods without disease advancement, which improves overall survival, while a subgroup has a modestly limited effect on disease progression or life extension. Pemetrexed remains a beneficial treatment choice for specific patient groups. This data helps oncologists in their clinical practice to make decisions, particularly when choosing pemetrexed for patients with distinct profiles and illness stages. The study emphasizes the importance of considering a large set of patient factors when designing cancer treatment.

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