

The Comparison of Efficacy between Paclitaxel and Carboplatin Regimen Versus Gemcitabine and Carboplatin Regimen as Palliative Chemotherapy for Advanced Non-Small Cell Lung Cancer

Sarwar SMR¹, Sarkar GC², Elahi MQ³, Sarker F⁴, Hasan T⁵

¹Dr. S M Rahid Sarwar, Classified Specialist in Department of Medicine and Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh

²Dr. Gopal Chandra Sarkar, Medical officer in Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

³Dr. MD Quadrate-Elahi, Advisor Specialist in Department of Medicine and Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh

⁴Dr. Fatema Sarker, Classified Specialist in Department of Medicine and Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh

⁵Dr. Tariq Hasan, Classified Specialist in Department of Medicine and Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh

Corresponding Author: Dr. S M Rahid Sarwar, Classified Specialist in Department of Medicine and Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh

Abstract

Introduction: Advanced Non-Small Cell Lung Cancer (NSCLC) is a serious and often fatal condition that is characterized by the spread of cancer beyond the lungs. The most common forms of NSCLC are adenocarcinoma and squamous cell carcinoma. Palliative chemotherapy is often used to manage advanced NSCLC, which aims to relieve symptoms and improve quality of life, rather than cure the disease. Paclitaxel-Carboplatin and Gemcitabine-Carboplatin are both commonly used regimens for palliative chemotherapy in advanced NSCLC. Comparing the efficacy of these two regimens is important to determine if any one of them is more effective and has fewer side effects for patients compared to the other.

Aim of the study: The aim of the study was to compare the clinical efficacy of Paclitaxel-Carboplatin and Gemcitabine -Carboplatin as palliative chemotherapy for Advanced Non-Small Cell Lung Cancer

Methods: This Quasi-Experimental study was conducted at the Department of Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh, the National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka, Bangladesh, and the Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka, Bangladesh. The study duration was 10 months, from January 2022 to October 2022. During this period, a total of 74 participants were divided into two equal groups, Arm-A receiving the Paclitaxel-Carboplatin treatment regimen, and Arm-B receiving the Gemcitabine-Carboplatin treatment regimen.

Result: The mean age of participants was 58.35 years in Arm-A and 57.54 years in Arm-B, with the majority of participants being from the age group of 51-60 years (40.54% in Arm-A, 43.24% in Arm-B). An overall male prevalence was observed, with 78.38% of participants in Arm-A and 70.27% in Arm-B being male. The majority of participants had an ECOG status of 1 (45.95% in Arm-A, 59.46% in Arm-B). Risk factors such as smoking and various lung diseases were present among participants, but there was no significant difference between the two arms. After 3 cycles of chemotherapy, partial response was observed in 48.64% of Arm-A and 43.24% of Arm-B, and stable disease was observed in 45.95% of Arm-A and 56.76% of Arm-B. No statistically significant difference was found between the response rate of both arms. After 6 weeks of follow-up, 62.16% of Arm-A and 56.76% of Arm-B had a partial response, with a slightly higher prevalence of progressive disease in Arm-B (10.81%). However, this difference was not statistically significant.

Conclusion: The study found that both Paclitaxel-Carboplatin and Gemcitabine-Carboplatin regimens were suitable options for palliative chemotherapy for advanced Non-Small Cell Lung Cancer (NSCLC) with similar response rates, and both treatments can be considered equally responsive and effective.

Keywords: Cancer, Advanced, Chemotherapy, Paclitaxel, Gemcitabine, Carboplatin

I. Introduction

Cancer is a group of diseases involving abnormal cell growth that can spread to other parts of the body. Lung cancer is one of the most frequently diagnosed cancers and is the leading cause of death worldwide.(1,2) According to GLOBOCAN 2020, lung cancer is the top most frequent cancer with an incidence of 22,06,771 (11.4%) and mortality of 17,96,144 (18%).(3) Lung cancer is the 4th most prevalent cancer in both men and women in Bangladesh, with an incidence of 12,999 (8.3%) and the 2nd most common cause of cancer-related mortality.(3–5) There are two main subtypes of lung cancer; small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). NSCLC accounts for 80-85% of lung cancers.(6,7) Several environmental and lifestyle factors have been linked to the development of lung cancer, with cigarette smoking being the most common cause.(8)The diagnostic evaluation includes a biopsy or cytology of the primary or the metastatic site in a patient with suspected NSCLC which can be done by image guidance or by bronchoscopy.(9,10) The staging workup includes history, physical examination, imaging studies, and other tests as per the guidelines.(8) The treatment options for NSCLC are determined by the stage, histology, and performance status of the patient.(7) Surgery, radiation therapy, chemotherapy, targeted therapy, and immunotherapy are the different modalities of treatment used for NSCLC.(11,12) In advanced-stage NSCLC, the mainstay of treatment is chemotherapy. Paclitaxel-Carboplatin and Gemcitabine-Carboplatin are two commonly used chemotherapy regimens for the treatment of advanced NSCLC.(13,14) The comparison of efficacy through clinical response between these two regimens will help to determine which regimen is more effective in treating advanced NSCLC. Clinical response is an important measure of the efficacy of a treatment, which is used to determine the effectiveness of a specific chemotherapy regimen in treating advanced NSCLC.(15,16)Paclitaxel-Carboplatin is a chemotherapy regimen that is commonly used to treat advanced non-small cell lung cancer (NSCLC). Paclitaxel is a chemotherapy drug that works by inhibiting the growth of cancer cells. Carboplatin is a chemotherapy drug that is used to treat various types of cancer, including lung cancer. The combination of these two drugs is effective in treating advanced NSCLC.(6,17,18)Gemcitabine-Carboplatin is another chemotherapy regimen that is commonly used to treat advanced non-small cell lung cancer. Gemcitabine is a chemotherapy drug that is used to treat various types of cancer, including lung cancer. Carboplatin is also a chemotherapy drug that is used to treat various types of cancer, including lung cancer. The combination of these two drugs is also effective in treating advanced NSCLC.(19,20)There have been several studies that have compared the efficacy of Paclitaxel-Carboplatin with Gemcitabine-Carboplatin as palliative chemotherapy for advanced NSCLC. These studies have shown that both regimens are effective in treating advanced NSCLC, but Paclitaxel-Carboplatin has been found to be more cost-effective in terms of overall response rate and progression-free survival.(21) However, Gemcitabine-Carboplatin has been found to be better tolerated with fewer side effects.The present study was conducted to observe the efficacy of both treatment methods via clinical response among participants, and to see if there are any significant differences between the two.

II. OBJECTIVE

General Objective

- To observe the clinical efficacy of Paclitaxel-Carboplatin as a palliative chemotherapy for Advanced Non-Small Cell Lung Cancer
- To observe the clinical efficacy of Gemcitabine -Carboplatin as a palliative chemotherapy for Advanced Non-Small Cell Lung Cancer

Specific Objectives

- To compare the clinical efficacy of Paclitaxel-Carboplatin and Gemcitabine -Carboplatin as palliative chemotherapy for Advanced Non-Small Cell Lung Cancer

III. METHODS

This Quasi-Experimental study was conducted at the Department of Medical Oncology, Combined Military Hospital, Dhaka, Bangladesh, the National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka, Bangladesh, and the Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka, Bangladesh. The study duration was 10 months, from January 2022 to October 2022. During this period, a total of 74 participants were selected through purposive sampling from the patients with clinically and histologically proven advanced-stage, inoperable non-squamous non-small cell lung cancer following the inclusion and exclusion criteria. The patients were divided into two equal groups or Arms, Arm-A having 37 patients being treated with infusional Paclitaxel–Carboplatin (PC) regimen, and Arm-B having 37 patients being

treated with an infusional Gemcitabine-Carboplatin (GC) regimen. The patients were informed about treatment costs, expected response rate, and toxicity of both arms. Informed consent was obtained from the patients prior to data collection. All patients had a baseline complete blood count, biochemical evaluation, creatinine clearance rate (CCR), and cardiac evaluation, inclusive of an ECG and 2D ECHO before the start of treatment. CT scan 6 weeks post-treatment was done as and when required. Patients were assessed for acute toxicities during the treatment through weekly investigations and clinical examination by using National Cancer Institute Common Terminology Criteria for Adverse Events (NTC-CTCAE) v 5.0 criteria. T, N, and M staging of the patients was done according to the AJCC 8th edition.(22) Treatment response evaluation was done using RECIST criteria during chemotherapy as a mid-cycle evaluation and then at 6 weeks of completion of chemotherapy. A semi-structured Data collection form was used as the research instrument. Data collection methods included interviews, oral histories, observations, and investigation records. Statistical analysis of the collected data was performed using SPSS Software.

Inclusion Criteria

- Clinically diagnosed and histopathologically or cytologically proven previously untreated non-squamous non-small cell carcinoma of the lung.
- Advanced stage disease, AJCC stage IIIB to IV diseases (TNM- T1-2N3, T3-4N2, Any T, Any N, M1a or M1b).
- Patients who had given consent to participate in the study.

Exclusion Criteria

- Those who are not willing to take part in this study.
- Patients with a history of prior chemotherapy or radiotherapy.
- Initial surgery (excluding diagnostic biopsy) of the primary site.
- Patients with double primaries or previous primaries.
- Pregnant or lactating woman.
- Patients with ECOG performance status of more than two.
- Patients aged less than 18 years & more than 70 years.
- Very serious co-morbidity like clinically significant CVD.
- Who cannot afford the cost of treatment

IV. RESULTS

Table 1: Baseline characteristics of the study population

Variables	Arm-A (n=37)	Arm-B (n=37)
Age (Years)	58.35 ±9.62	57.54 ±8.61
Weight (kg)	52.56±10.17	53.86±7.64
Height (cm)	165.53±3.60	163.81±4.78

Among the participants of the present study, the mean age was 58.35 years in Arm-A and 57.54 years in Arm-B. The mean weight was 52.56 kg among Arm-A and 53.86 kg among Arm-B participants. The mean height was slightly higher among Arm-A participants at 165.53 cm, and among Arm-B it was 163.81 cm.

Table 2: Sociodemographic characteristics of the study participants

Variables	Arm-A		Arm-B	
	n	%	n	%
Age				
30-40	0	0.00%	1	2.70%
41-50	10	27.03%	8	21.62%
51-60	15	40.54%	16	43.24%

61-70	12	32.43%	12	32.43%
Mean Age	58.35 ±9.62		57.54 ±8.61	
Gender				
Male	29	78.38%	26	70.27%
Female	8	21.62%	11	29.73%
Educational Status				
Illiterate	3	8.11%	2	5.41%
Literate	34	91.89%	35	94.59%

In terms of age, the majority of the participants from both groups had been from the age group of 51-60 years (40.54% in Arm-A, 43.24% in Arm-B). An overall male prevalence was observed among the participants, with 78.38% male in Arm-A and 70.27% male in Arm-B. In terms of educational status, 8.11% of Arm-A and 5.41% of Arm-B had been illiterate, while 91.89% of Arm-A and 94.59% of Arm-B had been literate.

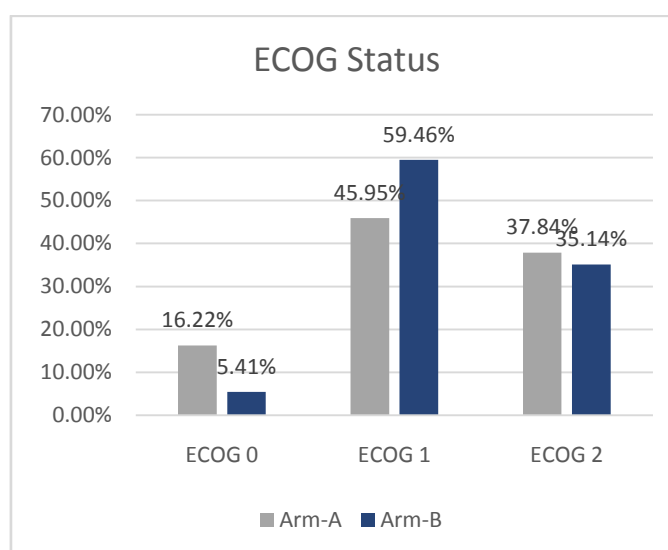


Figure 1: Distribution of participants by ECOG status

At baseline, the ECOG status of a majority of the participants was ECOG 1. 45.95% of Arm-A and 59.46% of Arm-B had ECOG status 1, while 37.84% of Arm-A and 35.14% of Arm-B had ECOG status 2. 16.22% of Arm-A, but only 5.41% of Arm-B had ECOG status 0

Table 3: Distribution of patients according to the risk factors

Risk factors		Arm A	Arm B	P – value
		(n = 37)	(n = 37)	
Tobacco related	Smoking	28 (75.67%)	26 (70.27%)	0.87
	Jarda	19 (51.35%)	21 (56.75%)	
	Betel Leaf	25 (67.56%)	27 (72.97%)	
Lung disease	COPD	8 (21.62%)	12 (32.43%)	0.63
	Asthma	4 (10.81%)	5 (13.51%)	
	Tuberculosis	6 (16.21%)	4 (10.81%)	

Others Comorbidities	Hypertension or Diabetes Mellitus	14 (37.83%)	16 (43.24%)	0.46
Occupation	Factory Worker	5 (13.51%)	7 (8.91%)	0.14
	Firewood user	12 (32.43%)	8 (21.62%)	

In terms of risk factors, various risk factors were identified among both Arms. 28 (75.67%) patients in Arm A and 26 (70.27%) patients in Arm B were smokers. A good number of patients were also associated with various lung diseases such as COPD, Asthma, TB, etc., in both arms. The findings were statistically insignificant ($p > 0.05$).

Table 4: Distribution of participants by clinical presentations

Symptoms	Arm A (n = 37)	Arm B (n = 37)	P – value
Cough	32 (86.48%)	31 (83.78%)	0.49
Dyspnea	11 (29.73%)	17 (45.94%)	0.31
Hemoptysis	10 (27.03%)	06 (16.22%)	0.36
Chest Pain	03 (08.11%)	08 (21.62%)	0.12
Infection	10 (27.02%)	15 (40.54%)	0.21
Hoarseness	03 (08.11%)	02 (05.40%)	0.16
SVCO	05 (13.51%)	07 (18.92%)	0.55
Others (weight loss, loss of appetite, weakness, etc.)	09 (24.32%)	13 (35.14%)	0.6

In terms of clinical symptoms, it was observed that the majority of the patients in Arm A presented with cough (32 out of 37, 86.48%) followed by dyspnea (11 out of 37, 29.73%), whereas patients in Arm B presented with cough (31 out of 37, 83.78%) followed by dyspnea (17 out of 37, 45.94%). The findings were statistically insignificant ($p > 0.05$).

Table 5: Distribution of patients according to the T, N, and M stage

Variable	Arm A (n = 37)	Arm B (n = 37)	P- value
T stage			
T1	03 (08.11%)	05 (13.51%)	0.27
T2	06 (16.22%)	07 (18.92%)	
T3	16 (43.24%)	18 (48.65%)	
T4	12 (32.43%)	07 (18.92%)	
N stage			
N2	12 (32.43%)	13 (35.14%)	0.86
N3	14 (37.84%)	14 (37.84%)	
M stage			
M0	10 (27.03%)	09 (24.32%)	0.96
M1a	13 (35.13%)	14 (37.84%)	
M1b	06 (16.21%)	05 (13.51%)	
M1c	08 (21.62%)	09 (24.32%)	

The table indicates the TNM staging of the patient in both Arms. The finding was statistically insignificant, with a p-value of >0.05 , which indicated a homogenous distribution of the study population in both Arms.

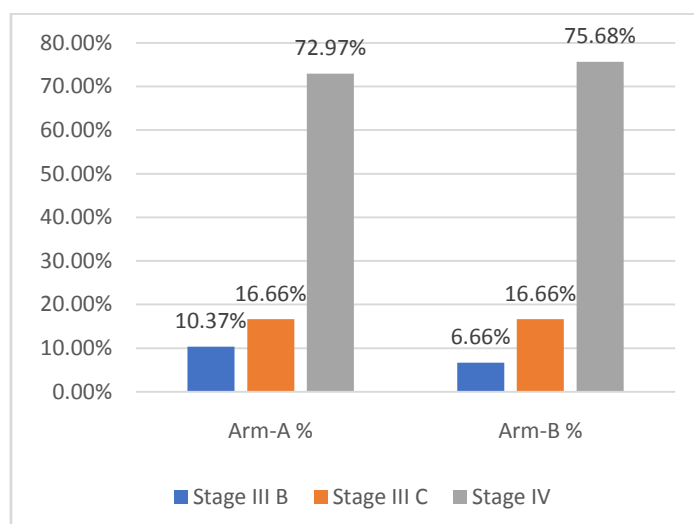


Figure 2: Distribution of participants by stage of the tumor

Among the participants of the present study, the majority of the patient presented with Stage IV disease in both Arms. In Arm A, 10 (27.03%) and 27 (72.97%) patients were in Stage III and IV, whereas 09 (24.32%) and 28 (75.68%) patients were in Stage III and IV respectively in Arm B. The finding was statistically insignificant ($p > 0.05$) which shows that there was a uniform distribution of the cases.

Table 6: Distribution of patients by histopathological type of tumor in percentage

Histopathological Type	Arm A (n=37)	Arm B (n=37)	Overall (n=74)	P value
Adenocarcinoma	32 (86.48%)	33 (89.19%)	65 (87.84%)	0.55
Large cell carcinoma	05 (13.51%)	04 (10.81%)	09 (12.16%)	1

Adenocarcinoma was the most commonly observed histopathological type in both arms, with 86.48% prevalence in Arm-A and 89.19% prevalence in Arm-B. overall, the prevalence of adenocarcinoma was 87.84% and for large cell carcinoma, it was 12.16%.

Table 7: Mid-term evaluation after completion of 3rd cycle of chemotherapy

Response	Arm A (n = 37)	Arm B (n = 37)	P-value
Complete response (CR)	0 (0%)	0 (0%)	0.75
Partial response (PR)	18 (48.64%)	16 (43.24%)	
Stable disease (SD)	19 (45.95%)	21 (56.76%)	

After 3 cycles of chemotherapy had been completed for all participants, an evaluation of disease response was observed. None of the patients had any complete response in either Arm. 48.64% of Arm-A and 43.24% of Arm-B had a partial response, while 45.95% of Arm-A and 56.76% of Arm-B participants had stable disease. There was no statistically significant difference between the response rate of both arms.

Table 8: Clinical response at 6weeks of follow-up after completion of chemotherapy

Clinical Response	Arm A (n = 37)	Arm B (n = 37)	P-Value
Complete response (CR)	0 (0%)	0 (0%)	0.6
Partial response (PR)	23 (62.16%)	21 (56.76%)	
Stable disease (SD)	13 (35.14%)	12 (32.43%)	
Progressive disease (PD)	01 (02.70%)	04 (10.81%)	

After 6 weeks following the completion of treatment, none of the patients had a complete response, but the partial response rate had increased compared to before. Among Arm-A participants, 62.16% had a partial response, 35.14% had stable disease, and 2.70% had progressive disease. On the other hand, among Arm-B participants, 56.76% had a partial response, 32.43% had stable disease and 10.81% had progressive disease. Although the prevalence of progressive disease was higher among Arm-B participants, this difference was not statistically significant.

V. Discussion

The present study aimed to compare the efficacy of the Paclitaxel-Carboplatin regimen (Arm-A) and Gemcitabine-Carboplatin regimen (Arm-B) as palliative chemotherapy for advanced Non-Small Cell Lung Cancer (NSCLC). The baseline characteristics of the study population were similar between the two arms. The mean age of the participants was 58.35 years in Arm-A and 57.54 years in Arm-B, with a majority of the participants being from the age group of 51-60 years. These findings correlated with other studies as well, with a majority of participants belonging to the 5th or 6th decade of life. (23,24) Among 74 patients, 55 (74.32%) patients were male and only 19 (25.68%) patients were female. The male and female ratio was 2.89 to 1. This observation also correlates with other studies that observed a higher male prevalence. (25,26) At presentation, most of the patients in both arms had an ECOG performance score of 1 (47 % in Arm A and 59% in Arm B), followed by ECOG 2 (37% in Arm A and 35% in Arm B). Multiple risk factors were analyzed among the participants. Smoking is globally recognized as the leading cause of lung cancer (27,28). In this study, 28 (75.67%) patients in Arm A and 26 (70.27%) patients in Arm B were smokers. So, in the total study population, 54 (72.97%) patients were smokers. Many of the study populations also used tobacco in different forms, such as jarda, gul, and tobacco leaf. However, there were no significant differences in the distribution of risk factors among both arms. Overall, the most common clinical presentation was cough, observed in 86.48% of Arm-A and 83.78% of Arm-B participants, with a combined prevalence of 85.14%. Tumor stage distribution of the participants among both arms was uniform and showed no significant difference. Adenocarcinoma was the most commonly observed histopathological type in both Arm A and Arm B. These presentations were similar to the study findings of a phase III study. (29) After starting with the treatment, all the participants had been given at least 95% of their initially determined dosage. At the mid-term evaluation of patients after 3-cycles of chemotherapy were done, partial response was seen in the majority of the patient, 18 (48.64%) in Arm A and 16 (43.24%) in Arm B. Stable disease was observed in 45.95% of Arm-A and 56.76% of Arm-B participants. There was no statistically significant difference between the response rate of both arms. This suggests that after 3 cycles of chemotherapy, both regimens were similarly effective in controlling the disease. The study also observed that at the clinical response at 6-weeks of follow-up after completion of chemotherapy, none of the patients had a complete response, but the partial response rate had increased compared to before. Among Arm-A participants, 62.16% had partial response, 35.14% had stable disease, and 2.70% had progressive disease. On the other hand, among Arm-B participants, 56.76% had partial response, 32.43% had stable disease and 10.81% had progressive disease. Although the prevalence of progressive disease was higher among Arm-B participants, this difference was not statistically significant. This suggests that both regimens were similarly effective in controlling the disease at 6-weeks of follow-up. These findings were also supported by multiple other studies and clinical trials. (13,30–34) In conclusion, the study found that both Paclitaxel-Carboplatin and Gemcitabine-Carboplatin regimens were suitable options for palliative chemotherapy for advanced NSCLC, with similar response rates at 3-cycle and 6-weeks follow-up. As such, both treatments can be considered equally responsive and effective.

Limitations of The Study

The study was conducted with a small sample size. So, the results may not represent the whole community. It was a non-randomized quasi-experimental study, so selection bias is present. Due to the short study period, the overall survival of the patients in the longterm was not possible.

VI. CONCLUSION

The study found that the baseline characteristics of the study population were similar between the two arms, with a majority of the participants being from the age group of 51-60 years and a higher male prevalence. The study also found that multiple risk factors, such as smoking and tobacco use, were present among the participants, but there was no significant difference in the distribution of risk factors between the two arms. The study also evaluated the disease response after the completion of 3rd cycle of chemotherapy and 6-weeks of follow-up after the completion of chemotherapy and found that both regimens were similarly effective in controlling the disease. These findings support the idea that both Paclitaxel-Carboplatin and Gemcitabine-Carboplatin regimens can be considered suitable options for palliative chemotherapy for advanced NSCLC and both treatments can be considered equally responsive and effective.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

RECOMMENDATION

- Further long-term randomized studies need to be done with multicenter trials to see survival benefits and late toxicities.
- Studies with larger sample size could help establish the significant benefit in terms of response.

REFERENCES

- [1]. Cancer [Internet]. [cited 2022 Dec 5]. Available from: <https://www.who.int/health-topics/cancer>
- [2]. Cooper GM. The Development and Causes of Cancer. The Cell: A Molecular Approach 2nd edition [Internet]. 2000 [cited 2023 Jan 22]; Available from: <https://www.ncbi.nlm.nih.gov/books/NBK9963/>
- [3]. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021 May;71(3):209–49.
- [4]. Hussain SMA. Comprehensive update on cancer scenario of Bangladesh. *South Asian J Cancer* [Internet]. 2013 [cited 2023 Jan 22];2(4):279–84. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3889062/>
- [5]. Islam MR, Hasan ATMK, Khatun N, Ridi IN, Rasheed MdMO, Islam SMA, et al. Demographic differentials of lung cancer survival in Bangladeshi patients. *PLoS One* [Internet]. 2021 Dec 10 [cited 2023 Jan 22];16(12):e0261238. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8664208/>
- [6]. 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*. 2006 Dec 14;355(24):2542–50.
- [7]. DeVita VT, Lawrence TS, Rosenberg SA. DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology. Lippincott Williams & Wilkins; 2008. 1748 p.
- [8]. Alberg AJ, Brock MV, Ford JG, Samet JM, Spivack SD. Epidemiology of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013 May;143(5 Suppl):e1S–e29S.
- [9]. Zhu J, Tang F, Gu Y. A prospective study on the diagnosis of peripheral lung cancer using endobronchial ultrasonography with a guide sheath and computed tomography-guided transthoracic needle aspiration. *Ther Adv Med Oncol* [Internet]. 2018 Jan 22 [cited 2023 Jan 23];10:1758834017752269. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5784539/>
- [10]. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger K, Yatabe Y, et al. Diagnosis of Lung Cancer in Small Biopsies and Cytology. *Arch Pathol Lab Med* [Internet]. 2013 May [cited 2023 Jan 23];137(5):668–84. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4509741/>
- [11]. Treating Non-Small Cell Lung Cancer | Lung Cancer Treatment Options [Internet]. [cited 2023 Jan 23]. Available from: <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell.html>
- [12]. Non-small Cell Lung Cancer Treatment by Stage [Internet]. [cited 2023 Jan 23]. Available from: <https://www.cancer.org/cancer/lung-cancer/treating-non-small-cell/by-stage.html>
- [13]. Schiller JH, Harrington D, Belani CP, Langer C, Sandler A, Krook J, et al. Comparison of Four Chemotherapy Regimens for Advanced Non-Small-Cell Lung Cancer. *New England Journal of Medicine* [Internet]. 2002 Jan 10 [cited 2023 Jan 23];346(2):92–8. Available from: <https://doi.org/10.1056/NEJMoa011954>
- [14]. Zhang B, Zhu W, Tao J, Li Y, Du C, Chen Y, et al. Short- Term Efficacy of Different First- Line Chemotherapy Regimens for Advanced Non- Small Cell Lung Cancer: A Network Meta- Analysis. *Clin Transl Sci* [Internet]. 2020 May [cited 2023 Jan 23];13(3):589–98. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7214664/>
- [15]. Gerber DE, Schiller JH. Maintenance Chemotherapy for Advanced Non-Small-Cell Lung Cancer: New Life for an Old Idea. *J Clin Oncol* [Internet]. 2013 Mar 10 [cited 2023 Jan 23];31(8):1009–20. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3589699/>
- [16]. Hwang KE, Kim HR. Response Evaluation of Chemotherapy for Lung Cancer. *Tuberc Respir Dis (Seoul)* [Internet]. 2017 Apr [cited 2023 Jan 23];80(2):136–42. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5392484/>
- [17]. Belani CP. Paclitaxel/carboplatin in the treatment of non-small-cell lung cancer. *Oncology (Williston Park)*. 1998 Jan;12(1 Suppl 2):74–9.
- [18]. Ramalingam S, Belani CP. Paclitaxel for non-small cell lung cancer. *Expert Opin Pharmacother*. 2004 Aug;5(8):1771–80.
- [19]. Yuh YJ, Lee HR, Kim SR. Gemcitabine and Carboplatin Combination Chemotherapy for Elderly Patients with Advanced Non-small Cell Lung Cancer: A Feasibility Study. *Cancer Res Treat* [Internet]. 2008 Sep [cited 2023 Jan 23];40(3):116–20. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2697464/>

- [20]. National Cancer Institute (NCI). A Phase II Trial of Gemcitabine, Carboplatin and PS-341 (NSC-681239) in the First-Line Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC) [Internet]. clinicaltrials.gov; 2013 Feb [cited 2023 Jan 19]. Report No.: NCT00075751. Available from: <https://clinicaltrials.gov/ct2/show/NCT00075751>
- [21]. Chen YM, Perng RP, Lee YC, Shih JF, Lee CS, Tsai CM, et al. Paclitaxel plus carboplatin, compared with paclitaxel plus gemcitabine, shows similar efficacy while more cost-effective: a randomized phase II study of combination chemotherapy against inoperable non-small-cell lung cancer previously untreated. *Ann Oncol*. 2002 Jan;13(1):108–15.
- [22]. Mb A, Fl G, Sb E, Cc C, Je G, Rk B, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more “personalized” approach to cancer staging. *CA: a cancer journal for clinicians* [Internet]. 2017 Mar [cited 2023 Jan 23];67(2). Available from: <https://pubmed.ncbi.nlm.nih.gov/28094848/>
- [23]. Khodadad K, Khosravi A, Esfahani-Monfared Z, Karimi S, Seifi S. Comparing Docetaxel Plus Cisplatin with Paclitaxel Plus Carboplatin in Chemotherapy-Naïve Patients with Advanced Non-Small-Cell Lung Cancer: a Single Institute Study. *Iran J Pharm Res* [Internet]. 2014 [cited 2023 Jan 23];13(2):575–81. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4157033/>
- [24]. Abratt RP, Lee JS, Han JY, Tsai CM, Boyer M, Mok T, et al. Phase II Trial of Gemcitabine-Carboplatin-Paclitaxel as Neoadjuvant Chemotherapy for Operable Non-small Cell Lung Cancer. *Journal of Thoracic Oncology* [Internet]. 2006 Feb 1 [cited 2023 Jan 23];1(2):135–40. Available from: <https://www.sciencedirect.com/science/article/pii/S1556086415315288>
- [25]. Effect of sex on the efficacy of patients receiving immune checkpoint inhibitors in advanced non-small cell lung cancer - Wang - 2019 - *Cancer Medicine* - Wiley Online Library [Internet]. [cited 2023 Jan 24]. Available from: <https://onlinelibrary.wiley.com/doi/full/10.1002/cam4.2280>
- [26]. de Perrot M, Licker M, Bouchardy C, Usel M, Robert J, Spiliopoulos A. Sex differences in presentation, management, and prognosis of patients with non-small cell lung carcinoma. *The Journal of Thoracic and Cardiovascular Surgery* [Internet]. 2000 Jan 1 [cited 2023 Jan 24];119(1):21–6. Available from: <https://www.sciencedirect.com/science/article/pii/S0022522300702133>
- [27]. Koike T, Koike T, Yoshiya K, Tsuchida M, Toyabe S ichi. Risk factor analysis of locoregional recurrence after sublobar resection in patients with clinical stage IA non-small cell lung cancer. *The Journal of Thoracic and Cardiovascular Surgery* [Internet]. 2013 Aug 1 [cited 2023 Jan 24];146(2):372–8. Available from: <https://www.sciencedirect.com/science/article/pii/S0022522313002559>
- [28]. Walsler T, Cui X, Yanagawa J, Lee JM, Heinrich E, Lee G, et al. Smoking and Lung Cancer. *Proc Am Thorac Soc* [Internet]. 2008 Dec 1 [cited 2023 Jan 24];5(8):811–5. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4080902/>
- [29]. Grønberg BH, Bremnes RM, Fløtten O, Amundsen T, Brunsvig PF, Hjelde HH, et al. Phase III study by the Norwegian lung cancer study group: pemetrexed plus carboplatin compared with gemcitabine plus carboplatin as first-line chemotherapy in advanced non-small-cell lung cancer. *J Clin Oncol*. 2009 Jul 1;27(19):3217–24.
- [30]. Helbekkmo N, Sundstrøm SH, Aasebø U, Fr Brunsvig P, von Plessen C, Hjelde HH, et al. Vinorelbine/carboplatin vs gemcitabine/carboplatin in advanced NSCLC shows similar efficacy, but different impact of toxicity. *Br J Cancer* [Internet]. 2007 Aug 6 [cited 2023 Jan 24];97(3):283–9. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2360329/>
- [31]. Huebner G, Link H, Kohne CH, Stahl M, Kretzschmar A, Steinbach S, et al. Paclitaxel and carboplatin vs gemcitabine and vinorelbine in patients with adeno- or undifferentiated carcinoma of unknown primary: a randomised prospective phase II trial. *Br J Cancer* [Internet]. 2009 Jan 13 [cited 2023 Jan 24];100(1):44–9. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2634671/>
- [32]. Langer C, Li S, Schiller J, Tester W, Rapoport BL, Johnson DH. Randomized Phase II Trial of Paclitaxel Plus Carboplatin or Gemcitabine Plus Cisplatin in Eastern Cooperative Oncology Group Performance Status 2 Non-Small-Cell Lung Cancer Patients: ECOG 1599. *JCO* [Internet]. 2007 Feb [cited 2023 Jan 24];25(4):418–23. Available from: <https://ascopubs.org/doi/10.1200/JCO.2005.04.9452>
- [33]. Novello S, Kielhorn A, Stynes G, Selvaggi G, De Marinis F, Maestri A, et al. Cost-minimisation analysis comparing gemcitabine/cisplatin, paclitaxel/carboplatin and vinorelbine/cisplatin in the treatment of advanced non-small cell lung cancer in Italy. *Lung Cancer* [Internet]. 2005 Jun 1 [cited 2023 Jan 24];48(3):379–87. Available from: <https://www.sciencedirect.com/science/article/pii/S0169500204006063>
- [34]. Treat JA, Gonin R, Socinski MA, Edelman MJ, Catalano RB, Marinucci DM, et al. A randomized, phase III multicenter trial of gemcitabine in combination with carboplatin or paclitaxel versus paclitaxel plus carboplatin in patients with advanced or metastatic non-small-cell lung cancer. *Annals of Oncology* [Internet]. 2010 Mar 1 [cited 2023 Jan 24];21(3):540–7. Available from: <https://www.sciencedirect.com/science/article/pii/S0923753419383115>

Dr. S M Rahid Sarwar, et al. “The Comparison of Efficacy between Paclitaxel and Carboplatin Regimen Versus Gemcitabine and Carboplatin Regimen as Palliative Chemotherapy for Advanced Non-Small Cell Lung Cancer.” *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 22(2), 2023, pp. 01-09.