International Surgery Journal
Kumari N et al. Int Surg J. 2025 Feb;12(2):191-197
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20250144

Original Research Article

Effect of ramucirumab on progression free survival and quality of life in conventional drug resistant or metastatic non-squamous variant of non-small cell lung cancers: a pilot study

Neelam Kumari[1], Rambit Chandra Dwivedi[1], Krishna Kant Singh[1]*, Shailendra Kumar Yadav[1], Dharmendra Kumar[2], Dhirendra Pratap Singh[1]

[1]Department of General Surgery, KGMU, Lucknow, UP, India
[2]Department of Anaesthesia and Critical Care, S. N. Medical College, Agra, UP, India

Received: 23 October 2024
Revised: 26 December 2024
Accepted: 10 January 2025

***Correspondence:**
Dr. Krishna Kant Singh,
E-mail: drkksinghkgmu@gmail.com

ABSTRACT

Background: Lung cancer is the leading cause of cancer-related death in India overall with the lowest five-year survival rate. Early detection of lung cancer is challenging due to the absence of usual clinical signs.
Methods: This non-randomised, single-arm, retrospective and prospective, pilot observational study enrolled 20 adult patients who have histologically or cytologically confirmed metastatic/drug-resistant/relapsed non-squamous NSCLC, having measurable disease at the time of study entry as defined by the response evaluation criteria in solid tumours (RECIST) with an Eastern cooperative oncology group (ECOG) performance status score of 0 to 2 and adequate organ function are eligible to participate in the study.
Results: The survival rate is exceedingly poor in the case of metastatic non-small cell lung cancer. The primary mass shrunk in size as the sum of the largest diameters (SLD) fell by a modest 12.22% up to the third chemotherapy cycle and a further 9.78% up to the sixth chemotherapy cycle. The progression-free survival duration was found 250.82 days, or roughly 8.33 months, and the overall survival (OS) period was 459 days, or approximately 15.3 months. Overall, the mean trial outcome index increased by 9.31% with additional chemotherapy cycles, while FACT-L increased by a comparable 24.25 percent.
Conclusions: Angiogenesis inhibitors, due to their novel mechanism of action, provide new therapeutic options for metastatic NSCLC. Despite our inability to draw statistically significant conclusions from these encouraging data, our experience with ramucirumab has been truly pleasant thus far.

Keywords: NSCLC, Ramucirumab, Lung cancer

INTRODUCTION

Lung cancer is the major cause of cancer-related death globally, with an approximate 15% five-year survival rate; roughly 85 percent of all cases are non-small cell lung cancers (NSCLC).[1] It is classified histologically as small cell lung cancer (SCLC) or NSCLC, with the latter accounting for around 80-85 percent of cases. The lifetime chance of dying from lung cancer is 82% larger in women than in males (the second leading cause of death from cancer in women).[2] Lung cancer has the lowest five-year survival rate of the four most common malignancies, including prostate cancer (95%), breast cancer (89%), and colorectal cancer (65%).[3] Early detection of lung cancer is challenging, however, due to the absence of usual clinical signs. The majority of them received a diagnosis at an advanced stage and were unable to undergo surgery. The prognosis for patients is often dismal. Although recent improvements have improved clinical outcomes for individuals with

targetable driver mutations, the majority of NSCLC tumors lack these alterations, emphasizing the importance of innovative therapeutic intervention. The most recent contribution to the therapy of NSCLC is the use of molecular targeting against angiogenesis factors.[4]

Ramucirumab (IMC-1121B; LY3009806) is a human immunoglobulin G monoclonal antibody that has a high affinity for the extracellular domain of VEGFR2. Ramucirumab inhibits the interaction of VEGFR2 and VEGF ligands, as well as the proliferation and migration of endothelial cells driven by VEGF. Ramucirumab in combination with docetaxel has been approved for the treatment of metastatic NSCLC that has progressed during or following platinum-based chemotherapy.[5] Among the several questionnaires available for assessing lung cancer patients' quality of life (QOL), FACT-L is one of the most straightforward questions to administer and has a high degree of relevance and specificity. The FACT-L includes a 21-question subsegment known as the Trial outcome index, which is one of the most effective indicators of patient-reported QOL.

Worldwide, lung cancer is the most prevalent type of cancer, accounting for more than half of all cancer-related fatalities.[6] It strikes men three times more commonly than prostate cancer and females twice as frequently as breast carcinoma. Lung cancer is the main cause of cancer-related death in India, ranking second in males behind lip and oral cavity carcinoma and fifth in females behind breast, cervical, ovarian, lip, and oral cavity carcinoma, in that order.[7] Lung cancer patients have few systemic first-line treatment options, with a median OS of 8 to 13 months and a 5-year survival rate of only 4%. The use of molecular targets directed against angiogenesis factors is the most recent addition to the therapy of NSCLC.

METHODS

Study design and participants

We performed non-randomized, single-arm, prospective, pilot observational study between 2018 and 2022 at the department of general surgery, King Georges medical university, Lucknow, India which is a high-volume, tertiary care and ultimate referral center of the state. The study was approved by the ethics committee, research cell, King George's medical university, Lucknow

Data collection and outcome measures

To comply with RECIST, all measurements were reported in the form of metric measurements. To characterize each lesion, the same method and technique were employed at both the beginning and end of the study. We have conducted an imaging-based evaluation rather than a clinical exam. Lesions selected for response assessment were measured by CT, which is the most accurate and reproducible approach available today. A CT slice thickness of 5 mm or less has been assumed in this guideline to specify the measurement of lesions on CT scans. The total baseline diameters are derived by adding all of the target lesions' diameters (shortest axis for nodal lesions, longest axis for non-nodal lesions) together. Including lymph nodes merely adds the short axis to the aggregate. The baseline total diameters were utilized as a baseline to further quantify any objective tumor regression in the quantifiable dimension of disease.

The SLD=the largest dimension of target mass+the largest short axis diameter of the lymph node.

In our study tumor is re-evaluated every third cycle of chemotherapy.

For the assessment of QOL the FACT-L (version 4) questionnaire is used having 36-item self-reporting questions. It is a five-point Likert-type scale with a seven-day memory span. Data was recorded on paper before the administration of chemotherapy. Using this, FACT-L trial outcome index (TOI), FACT-G total score and FACT-L total score were derived.

Statistical analysis

Statistical analysis was done in SPSS IBM Statistics 26th edition. The descriptive statistics done for consecutive 10 cycles of chemotherapy and PFT and FACT-L instrument values are logged and means compared in trend.[8,9] Survival analysis is done with the Kaplan-Meier method.

The date of progression is taken on the day of detecting radiological evidence of progression by CECT thorax for determining progression-free survival. Progression-free survival is calculated by taking into account all those patients who died and advanced during the trial, while the remainder of the patients are censored.[10]

For determining OS, death is taken as terminal event all other outcomes are censored. The last day of follow-up in the trial was used to calculate survival duration for individuals who opted out and were lost to follow-up. 31st of October 2021 was chosen as the last day of follow-up for patients who were still receiving chemotherapy.

RESULTS

In the study population, majority of patients were between 60-70 years [n=9 (45%] of range followed by between 40-50 years [n=5 (25%)] of range and 70-80 years [n=4 (20%)] of range, respectively. Majority of patients were males [n=13 (65%] followed by females [n=7 (35%)], respectively. Majority of patients had ECOG 1 [n=8 (40%] as well as ECOG 2 [n=8 (40%)] followed by ECOG-0 [n=4 (20)], respectively. Majority of patients had no proper risk factor [n=7 (35%] followed by smoking [n=6 (30%)] and TB [n=4 (20%)], respectively. Majority of patients had hypertension [n=9 (45%] followed by previous history of TB [n=6 (30%)] and type 2 diabetes mellitus [n=3 (15%)], respectively.

Most of patients had previous history of chemotherapy with paclitaxel and carboplatin chemo drugs [n=8 (40%] and pemetrexed and cisplatin [n=8 (40%)] and docetaxel [n=2 (10%)] of range, respectively. Majority of patients were in stage IV A T4N3M1A [n=21 (55%] followed by stage IV B T4N3M1B [n=7 (35%)] and stage IV C T4N3M1C [n=2 (10%)], respectively. Majority of patients had metastasis in bone [n=8 (40%] followed by in visceral [n=7(35%)] and in opposite lungs [n=3 (15%)], and CNS in 10% respectively.

The following table shows the status of patient's post-trial in the study population, majority of patients were analysed [n=13 (65%] followed by expired [n=6 (30%)] and lost to FU [n=1 (5%)], respectively (Table 1).

Mean of trend of sum of largest diameter upon chemo in study population at baseline, after 3rd cycle and after 6th cycle chemotherapy that were 69.84±7.14 with 100%, 61.86±5.76 with 11.4% decrease and 56.85±4.21 with 8.1% decrease, respectively (Table 2).

Following table shows the mean of trial outcome index (TOI) scale, majority of patients had pre chemo TOI [n=20] scale with mean of 41.5±8.80 followed by1st FACTG [n=20] with mean of 41.5±9.7 and FACTG-2nd (19) with mean of 39±9.9, respectively (Table 4).

The following table shows the mean of assessment of QOL (FACT-L instrument) (59) in study population, majority of patients had FACT-L pre chemo stage (n=20) with mean of 64.4±13.9 followed by1st FACT-L [n=20] with mean of 66.7±15.0 and FACT-L-2nd (19) with mean of 65.54±15.87, respectively (Table 3).

Table 1: Tabular presentation of status of patient's post-trial in study population.

Variables	N	Percent (%)
Expired	6	30
Lost to f/u	1	5
Patients analyse	13	65
Opted out	0	0
Total	20	100

Table 2: Tabular presentation of trend of sum of largest diameter upon chemo in study population.

SLD	Value (cm)	Change (%)
Baseline SLD mean	69.84±7.14	100
SLD after 3rd cycle mean	61.86±5.76	11.4 decrease
SLD after 6th cycle mean	56.85±4.21	8.1 decrease

Table 3: Tabular presentation of assessment of quality of life (FACT-L instrument) (59) in study population.

Descriptive statistics	N	Minimum	Maximum	Mean	SD
FACT-L pre-chemo stage	20	46	85	64.4	13.9
FACT-L 1st	20	47	89	66.7	15.0
FACT-L 2nd	19	37	85	65.54	15.87
FACT-L 3rd	16	62	80	68.32	7.9
FACT-L 4th	16	57	76	68.00	8.4
FACT-L 5th	16	44	82	67.54	14.67
FACT-L 6th	16	49	83	69.87	15.69
FACT-L 7th	16	39	83	65.83	19.3
FACT-L 8th	14	67	88	75.67	8.9
FACT-L 9th	14	61	87	73.56	14.09
FACT-L 10th	13	83	89	84.76	4.55
Valid (listwise)	13				

Table 4: Tabular presentation of TOI in study population.

Variables	N	Minimum	Maximum	Mean	SD
TOI pre-chemo	20	29	64	41.5	8.80
TOI 1st	20	30	63	41.5	9.7
TOI 2nd	19	27	61	39	9.9
TOI 3rd	15	32	62	42	9.6
TOI 4th	16	34	53	38.5	7.7
TOI 5th	15	31	60	40.5	10.8
TOI 6th	16	26	59	37.5	12.1
TOI 7th	15	22	56	34	13.6
TOI 8th	14	29	49	34	8.98
TOI 9th	14	32	57	39.5	9.87
TOI 10th	13	33	55	39	11.5
Valid (listwise)	13				

Mean of fact G scale, majority of patients had pre chemo fact G [n=20] scale with mean of 46.8±11.7 followed by1st fact G [n=20] with mean of 46.8±11.7 and fact G-2nd (19) with mean of 50.6±12.8, respectively (Table 5).

Kaplan Meier analysis provided a mean estimated OS duration of 459 days which is 15.3 months (Table 7).

The following table shows the assessment of FEV1 at different cycles of chemotherapy in the study population at PRECHEM, after 3rd, 6th and 9th post chemo cycles of FEV1 that were 1.59±0.39 with change of 100%, 1.73±0.49 with change of +8.8%,2.01±0.42 with mean change of +16.2% and 2.31±0.57 with mean change of +14.9%, respectively (Table 10).

Table 5: Tabular presentation of assessment of FACT-G in study population.

Descriptive statistics	N	Minimum	Maximum	Mean	SD
Fact G pre-chemo	20	32	61	46.8	11.7
Fact G 1st	20	34	65	51.6	11.9
Fact G 2nd	19	33	68	50.6	12.8
Fact G 3rd	16	37	66	54.4	10.6
Fact G 4th	16	35	62	49.8	9.7
Fact G 5th	15	31	63	47.7	9.9
Fact G 6th	16	25	67	46.8	13.2
Fact G 7th	15	36	68	44.9	13.7
Fact G 8th	14	33	68	52.4	9.8
Fact G 9th	14	58	59	47.3	10.3
Fact G 10th	13	61	69	61.7	6.7
Valid	13				

Table 6: Tabular presentation of mean of progression free survival time in study population.

Drug	Mean			
	Estimate	Std. error	95% confidence interval	
			Lower bound	Upper bound
Ramucirumab with docetaxel	250.82	45.65	165.89	338.79
Overall	250.82	45.65	165.89	338.79

Table 7: Tabular presentation of estimation of OS in study population.

Mean for OS time				
Drug	**Estimate**	**Std. error**	**95% confidence interval**	
			Lower bound	**Upper bound**
Ramucirumab and docetaxel	459	44.02	260	658
Overall	459	44.02	260	658

Table 8: Tabular presentation of cox-regression analysis case summary in study population.

Cox regression-case processing summary		N	Percentage (%)
Cases available in analysis	Events	7	35
	Censored	13	65
	Total	20	100
Cases dropped	Cases with missing value	0	0
	Cases with negative time	0	0
	Censored cases before earliest event in a stratum	0	0
	Total	0	0
Total		20	100

*Dependent variable: duration of follow-up.

Table-9: Tabular presentation of omnibus tests of model coefficients in study population.

2 log likelihood	Overall (score)			Change from previous step		
	Chi-square	Df	Sig.	Chi-square	Df	Sig.
15.929	1.86	1	0.26	2.21	1	0.21

*Beginning block number 1. Method=enter.

Table 10: Tabular presentation of assessment of FEV1 upon chemotherapy in study population.

Trend of fev_1 upon chemotherapy	Pre-chemo Fev_1	Fev_1 3rd cycle post chemo	Fev_1 6th cycle post chemo	Fev_1 9th post chemo
N	19	18	14	13
Minimum	1.09	1.19	1.29	2.86
Maximum	2.32	2.65	2.54	2.87
Mean	1.59	1.73	2.01	2.31
Change	100%	+8.8%	+16.2%	+14.9%
SD	0.39	0.49	0.42	0.57

DISCUSSION

Worldwide, lung cancer is the most prevalent type of cancer, accounting for more than half of all cancer-related fatalities. It strikes men three times more commonly than prostate cancer and females twice as frequently as breast carcinoma. Lung cancer is the main cause of cancer-related death in India, ranking second in males behind lip and oral cavity carcinoma and fifth in females behind breast, cervical, ovarian, lip, and oral cavity carcinoma, in that order.[7] Lung cancer patients have few systemic first-line treatment options, with a median OS of 8 to 13 months and a 5-year survival rate of only 4%. The use of molecular targets directed against angiogenesis factors is the most recent addition to the therapy of NSCLC.

In our study, ramucirumab gave promising result having progression free survival of roughly 8.33 months, overall survival period was 15.3 months and increase in quality of life by 24.25% that compared favourably with the previous studies.[14,17,18]

Demographics

Twenty patients were enrolled, ranging in age from 46 to 75 years, with a median of 65 years.

The 45% of patients were between the ages of 60 and 70, and 65 percent were male. We enrolled subjects with an ECOG of up to 2, and 40% had an ECOG of 2 at the time of admission. The 49.3% of the population was classified as ECOGI relatively healthy, whereas 61.1 percent was classified as ECOG I severely and terminally ill.[11]

Risk factors

Tobacco use is a well-documented risk factor for the development of NSCLC. Similarly, 45% of patients were found to be addicted to tobacco, the most prevalent method being smoking.

Comorbidities

In total, 45% of patients in the study group had pre-existing hypertension, followed by 30% with pulmonary tuberculosis and 15% with a history of type 2 diabetes mellitus.

Previous chemotherapy

According to standard NSCLC treatment regimens, nineteen (95%) patients had previously received chemotherapy. A total of 40% of the population received a paclitaxel carboplatin combination as first-line therapy, while another 40% received a pemetrexed cisplatin combination followed by pemetrexed maintenance therapy. One patient tested positive for the EGFR receptor and was treated with a combination of gefitinib and erlotinib.

Clinical features

Shortness of breath was the most frequently reported symptom in the research population, with 100% of patients suffering some degree of shortness of breath during admission. With 65% of participants reporting chest pain, it was the second most often reported symptom. The 25% of patients reported experiencing voice changes and had recurrent laryngeal nerve palsy on one side, while haemoptysis was the least often occurring symptom in our study group.[12,13]

Staging and metastasis

At admission, 55% of patients were diagnosed with stage IVA T4N3MIA disease, 35% with stage IVB T4N3MlB disease, and 10% with severe stage IVC T4N3MlC disease. Bony metastasis was the most frequently encountered type of metastasis in the study (33%), with the lower dorsal and upper lumbar spine being the most frequently encountered sites, while one person had metastasis to the adrenal gland but did not present clinical indications of crisis. Indeed, adrenal metastases associated with NSCLC are uncommon.[14]

Receptor status

All patients had a histological diagnosis of non-small cell variant adenocarcinoma and a receptor status report at the time of enrolment. Two (16%) patients tested positive for EGFR, and one of them progressed on RECIST despite treatment with TKI-Gefitinib and Erlotinib. None of the research patients possessed an ALKI or ROS1 mutation. By the time the experiment concluded on august 31, 2022, 30% (6) of patients had died, 1 patient had been

lost to follow up after receiving one round of chemotherapy.

Tumour assessment

Recist ver. 1.1 criteria were used to evaluate the tumour. Upon admission, all patients had detectable illness, and each patient had one target lesion evaluated in their target organs.[15] Measuring is done using the diameter of the lymph nodes with the largest short axis. The total of the largest diameters, which comprises the largest diameter of the target lesion and the short axis diameter of the target lymph node mass, is taken into account. SLD was estimated following third-round chemotherapy and demonstrated a modest 12.22 percent decrease and an extra 9.78% reduction in the total diameter of the largest diameter following the sixth cycle of treatment. Despite the positive findings, their statistical significance could not be determined due to a deficient sample size.

Assessment of QOL

The FACT-L tool was used to assess the respondents' quality of life. It contains items measuring physical wellbeing (PWB), emotional wellbeing (EWB), social wellbeing (SWB), functional wellbeing (FWB), and the lung cancer subscale (LCS).[16] The trial outcome index (TOI) is a 21-item subsegment of the FACT-L comprised of PWB+FWB+LCS. TOI is likely the most meaningful and precise measure of patient-reported quality of life available for lung cancer patients who complete the FACT-L while engaged in a clinical trial for oncology. The mean TOI increased 10%, from 32 to 42. FACT-L values were reported to have increased by 20.36 percent, from 64.4 to 84.76. Increased TOI suggests a more favourable outcome, which is corroborated by comparable increases in FACT-L. To achieve a proportionate outcome with the FACT-L score as a TOI, the treatment strategy must increase or maintain SWB and EWB. Additionally, the FACT-G increased by 16.8% from 44.9 to 61.7, correlating with the upward trend in TOI.

Survival analysis

To conduct the survival analysis, the Kaplan-Meier method was utilised. The progression-free survival rate is calculated using all patients who died or advanced during the duration of the trial, while the remaining patients are censored. The progression-free survival rate was determined to be 250.82 days, or 8.33 months, and the OS rate to be 459 days, about 15.3 months

Assessment of pulmonary function test

PFT values provide information on the lungs' functional state, and they were monitored meticulously throughout the trial. The mean forced vital capacity FVC increased by 5.51% from a baseline value of 2.025 to the third cycle, 10.85% between the sixth and third post-chemotherapy cycles, and a commendable 9.08 percent between the ninth and sixth post-chemotherapy cycles. Additionally, successive treatment enhanced the forced expiratory volume in the first second, or FEV1.

Assessment of chemotherapy related adverse effects

To identify adverse drug events, the CTCAE v5.0 [Common terminology criteria for adverse events] was used. The most often reported adverse event was nausea, which happened in 90% of patients, followed by anorexia, which occurred in 75% of patients. The most often occurring grade 3 adverse event was hypertension, which was identified in one patient who had to continue using a combination of three antihypertensive drugs. The remaining three hypertensive patients were managed successfully with a single drug regimen. Two patients' nails exhibited grade 1 changes, including ridging and blackening. A one-year-old male developed a corneal perforation in his left eye and was suddenly paralysed. Although acute transverse myelitis was initially identified, the likelihood of a complicated vertebral fracture from an underlying vertebral metastasis could not be ruled out due to the patient's death prior to adequate study.

Limitations

Because our study was a pilot, it lacked an appropriate sample size. As a result, despite a number of positive findings regarding enhanced quality of life, functional lung measures, and RECIST staging, statistical analysts were unable to corroborate them.

Another notable constraint was the absence of PET-CT at this tertiary care hospital, as well as the individuals' inability to pay for PET-CT at an outpatient facility. Secondary tumour deposits could not be analysed accurately or methodically due to a lack of PET-CT secondary tumour deposits. To accurately measure the response of this novel medication, its influence on metastatic disease must be thoroughly researched.

Further research

The favourable results of this investigation indicate that a multi center randomised control trial aimed at improving OS in patients with metastatic drug-resistant NSCLC will be conducted in the future. Prior studies did not include measurements of pulmonary function. The diffusion capacities of DL-CO in the lung may be investigated in depth, offering insight into the novel chemotherapy's effect on oxygenation. PET-CT imaging can be utilised to assess the chemotherapy's influence on later metastatic deposits with extreme precision.

CONCLUSION

The progression-free survival duration was found 250.82 days, or roughly 8.33 months, and the OS period was 459

days, or approximately 15.3 months. Overall, the mean trial outcome index increased by 9.31% with additional chemotherapy cycles, while FACT-L increased by a comparable 24.25%.

Despite our inability to draw statistically significant conclusions from these encouraging data, our experience with ramucirumab has been truly pleasant thus far.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Molina JR, Yang P, Cassivi SD, Schild SE, Adjei AA. Non-small cell lung cancer: epidemiology, risk factors, treatment, and survivorship. In Mayo clinic proceedings 2008;83(5):584-94.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA: a cancer journal for clinicians. 2019;69(1):7-34.
3. Spiro SG, Silvestri GA. One hundred years of lung cancer. Am J Respiratory Crit Care Med. 2005;172(5):523-9.
4. Lee SH. Chemotherapy for lung cancer in the era of personalized medicine. Tuberculosis and respiratory diseases. 2019;82(3):179-89.
5. Doebele RC, Spigel D, Tehfe M, Thomas S, Reck M, Verma S, et al. Phase 2, randomized, open-label study of ramucirumab in combination with first-line pemetrexed and platinum chemotherapy in patients with nonsquamous, advanced/metastatic non-small cell lung cancer. Cancer. 2015;121(6):883-92.
6. Jemal A, Siegel R, Ward E, Yongping H, Jiaquan X, Taylor M, et al. Cancer statistics, 2008. CA Cancer J Clin. 2008;58:71-96.
7. Iuliis FD, Vendittozzi S, Taglieri L, Salerno G, Lanza R, Scarpa S. Metronomic chemotherapy preserves quality of life ensuring efficacy in elderly advanced non small cell lung cancer patients. Int J Cancer Clin Res. 2016;3:46
8. Gandara DR, Chansky K, Albain KS, Leigh BR, Gaspar LE, Lara Jr PN, et al. Consolidation docetaxel after concurrent chemoradiotherapy in stage IIIB non-small-cell lung cancer: Phase II Southwest Oncology Group Study S9504. J Clin Oncol. 2003;21(10):2004-10.
9. Yoon HH, Bendell JC, Braiteh FS, Firdaus I, Philip PA, Cohn AL, et al. Ramucirumab (RAM) plus FOLFOX as front-line therapy (Rx) for advanced gastric or esophageal adenocarcinoma (GE-AC): Randomized, double-blind multicenter phase 2 trial. J Clin Oncol. 2014:32(15):4004.
10. Hong S, Tan M, Wang S, Luo S, Chen Y, Zhang L. Efficacy and safety of angiogenesis inhibitors in advanced non-small cell lung cancer: a systematic review and meta-analysis. J Cancer Res Clin Oncol. 2015;141(5):909-21.
11. Buccheri G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. Europ J Cancer. 1996;32(7):1135-41.
12. Greer JA, Pirl WF, Jackson VA, Muzikansky A, Lennes IT, Gallagher ER, et al. Perceptions of health status and survival in patients with metastatic lung cancer. J Pain Symptom Management. 2014;48(4):548-57
13. Beckles MA, Spiro SG, Colice GL, Rudd RM. Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes. Chest. 2003;123(1):97S-104S.
14. Das M, Wakelee H. Angiogenesis and lung cancer: ramucirumab prolongs survival in 2nd-line metastatic NSCLC. Translational Lung Cancer Res. 2014;3(6):397.
15. Camidge DR, Berge EM, Doebele RC, Ballas MS, Jahan T, Haigentz Jr M, et al. A phase II, open-label study of ramucirumab in combination with paclitaxel and carboplatin as first-line therapy in patients with stage IIIB/IV non-small-cell lung cancer. J Thoracic Oncol. 2014;9(10):1532-9.
16. Eser S, Göksel T, Erbaycu AE, Baydur H, Başarık B, Yanık AÖ, et al. Comparison of generic and lung er-specific quality of life instruments for predictive ability of survival in cancer-patients with advanced lung cancer. SpringerPlus. 2016;5(1):1-1.
17. Camidge DR, Berge EM, Doebele RC, Ballas MS, Jahan T, Haigentz Jr M, et al. Phase II, open- label study of ramucirumab in combination with paclitaxel and carboplatin as first-line therapy in patients with stage IIIb/IV non-smaller lung cancer. J Thoracic Oncol. 2014:9(10):1532-9.
18. Perol M, Ciuleanu TE, Arrieta O, Prabhas K, Syrigos KN, Goksel T, et al. Quality of life results from the phase 3 REVEL randomized clinical trial of ramucirumab -plus-docetaxel versus placebo-plus-docetaxel in advanced/metastatic non-small cell lung cancer patients with progression after platinum based chemo therapy. Lung Cancer. 2016;93:95-103.

Cite this article as: Kumari N, Dwivedi RC, Singh KK, Yadav SK, Kumar D, Singh DP. Effect of ramucirumab on progression free survival and quality of life in conventional drug resistant or metastatic non-squamous variant of non-small cell lung cancers: a pilot study. Int Surg J 2025;12:191-7.