Article published online: 2020-11-09

Original Article

Importance of dose intensity in treatment of advanced non-small cell lung cancer in the elderly

Narayanan Prasad, Ashish Bakshi[1], Chetan Deshmukh[2], Sachin Hingmire[2], AA Ranade[3], Purvish Parikh[4]

Abstract

Maintaining appropriate dose intensity is important not only in the curative setting but also in treatment with palliative intent. We evaluated the outcome of advanced non small cell lung cancer treated with doublet platinum based chemotherapy. Outcome was compared between patients treated by medical oncologists at a tertiary cancer center and those treated by non medical oncologists in the community. The dose intensity, overall response rate and overall survival was significantly better when patients were treated by trained qualified and experienced medical oncologists. Hence, even in the palliative setting, cancer directed systemic therapy will yield maximum benefit for the patients when treated by medical oncologists.

Key words: chemotherapy, prolonged infusion, medical oncologist, response rate

Introduction

Appropriate treatment at the right time is a crucial factor for optimizing outcome in oncology. This is true even for patients with an advanced disease where palliation is the aim of the treatment. For instance, outcome is better when a qualified, trained gyneco-oncologist operates on a patient with an ovarian cancer in a high volume center as opposed to being treated by a gynecologist or a general oncologist. So also patients with locally-advanced head neck cancer patients treated with 3D conformal RT using linear accelerators have better quality of life as compared to those receiving radiation using 2-field cobalt teletherapy. Similarly, cancer-directed systemic therapy is optimally given by qualified and trained medical oncologists. However, patients continue to be treated thus by non-medical oncologists and organ specialists with the "assumed belief" that such "palliative treatment" can be given equally well by non-medical oncologists without compromising patient outcome. Hence, we decided to compare the differences and outcome for patients receiving cancer-directed systemic therapy under medical oncologists at our institution vs. similar patients treated by non-medical oncologists.

Lung cancer is one of the most common cancers globally. In India, Lung cancer forms 11 to 13% of all cancers.[1] Less than 10 % are operable at an initial presentation. This is because usually such patients present in an advanced stage, requiring cancer-directed systemic therapy whose objective is to offer palliation. Hence, this became the obvious disease to ask our question. Globally, more than 50% of all patients with non-small cell lung cancer (NSCLC) are older than 65 years and about 1/3rd of all patients are older than 70 years old at diagnosis.[2] The 2001 Tata Memorial Hospital (TMH) cancer registry showed that the median age for lung cancer was 56 years and by 2004, as many as 35% (91/262) of these patients were above the age of 60 years.

We, therefore, retrospectively analyzed the prospectively-collected data from our center among the patients above the age of 60 year with NSCLC treated with a uniform protocol of prolonged infusion Gemcitabine and Carboplatin chemotherapy. The objective was to identify whether there was any difference in the outcome between those treated by medical oncologists at TMH (Group 1) and those treated by other oncologists/ physicians outside TMH (Group 2).

Department of Medical Oncology, Kiran Majumdar Shah Cancer Center, Bangalore, Karnataka, [1]Jupiter Hospital, Thane, [2]Deenanath Mangeshkar Hospital, Pune, [3]Joshi Hospital, Pune, [4]Director of Clinical Research, BSES GH Hospital, Mumbai, Maharashtra, India

Correspondence to: Dr. Purvish Parikh,
E-mail: Purvish1@gmail.com

Access this article online

Quick Response Code:

Website: www.sajc.org

DOI: 10.4103/2278-330X.96494

Materials and Methods

Prospectively collected data on patients with advanced (stage IIIB and IV) NSCLC of age 60 or above was retrospectively analyzed to evaluate variables, dose intensity, response rate, and overall survival. This included all consecutive treatment-naïve patients presenting at TMH, Mumbai, with good performance status (ECOG 0, 1 or 2) at initiation of therapy, histologically-confirmed diagnosis of NSCLC, adequate renal function (serum creatinine < 1.25 times the upper limit of normal), and adequate hepatic function (AST and ALT < 3.0 x upper limit of normal) who were willing for treatment.

The cancer-directed systemic therapy protocol consisted of Inj Gemcitabine 350 mg/m2 as 4 hour infusion on days 1 and 8, q 3 weeks along with Inj Carboplatin AUC 5 as a 60 minute infusion on day 1 only q 3 weeks. Cycles were to be repeated every 3 weeks for a total of 6 cycles. Patients were evaluated for response at end of 3 cycles and end of treatment (6 cycles). Thereafter, they were followed up every 12 – 16 weeks for survival.

All patients were recommended treatment at our center for the entire course of the chemotherapy. However, when they were unable to do so (for financial, geographic, family or social reasons) and chose to take treatment elsewhere, they were provided detailed instructions and a treatment recommendation reference letter for their local doctor. The letter included specific recommendations for protocol modifications based on hematological toxicity. Day 1 of starting a new cycle was to be delayed only in the event of neutropenia [ANC < 1500 /mm^3] or thrombocytopenia [platelets < 100,000/ mm^3], CBC repeated twice-weekly until recovery [ANC > 1500/mm^3 and platelet count > 1, 00,000 /mm3]) and then the cycle commenced. Dose modifications within a cycle, i.e. for day 8 of chemotherapy, was also specified [Table 1].

The TNM staging for lung cancer was used for staging an evaluation and diagnosis of stage IIIB and IV disease. Response evaluation was based on the modified WHO criteria. For overall survival, time to death was defined as the interval from day of diagnosis to day of death. SPSS software version 14 was used for analysis of data. Kaplan – Meier curves were used to display the survival data. The log – rank test was used to compare survival curves.

Results

A total of 75 consecutive patients aged 60 years and above were the subjects of this study. This included 60 males and 15 females. Their features at diagnosis are mentioned in Table 2.

The majority of the patients were less than 65 years of age. About 1/5th were above the age of 70 years [Table 3].

Of the 75 patients in this study, 45 had no other illness. Among the remaining 30 patients, the commonest co-morbidities were diabetes mellitus, hypertension, and coronary artery disease. A total of 7 had multiple additional co-morbidities [Table 4].

Of the 75 patients, 43 (57.3%) chose to take their chemotherapy under the direct supervision of the medical

Table 1: Recommendations for dose modifications for day 8 of chemotherapy

For hematological toxicity (based on that day's blood counts)		
ANC/ml	**Platelets / ml**	**% Dose on day 8**
> 1500	> 1,00,000	100
1000 - 1500 and / or	75,000 – 1,00,000	75
500 – 999 and / or	50,000 – 74,999	50
< 500 and / or	<50,000	Omit day 8 chemotherapy
For non-hematological toxicity		
No dose modification - for any WHO grade of nausea, vomiting, and alopecia or for any other WHO grade 0 – 2 toxicities. Dose modification at the discretion of the treating physician - for other Grade 3 – 4 non-hematological toxicities.		

Table 2: Demographic features of patients at diagnosis

Characteristics	Number of patients	Percentage
Total Number of patients	75	
Age in years		
Median	65	
Range	60 to 79	
Gender		
Male	60	80
Female	15	20
Stage		
IIIB	35	46.7
IV	40	53.3
ECOG PS	54	72
0,1	21	28
2		
Histology		
Adenocarconima	46	61.33
Squamous Cell Carcinoma	14	18.67
NSCLC – NOS	15	20

Table 3: Age-wise distribution of patients

Age group (years)	Number of patients	Percentage
60 – 65	43	57.33
66 – 70	18	24
> 70	14	18.66

oncology department of our hospital (Group 1). The remaining 32 patients (42.7%), chose to take the treatment nearer home, were given detailed written instructions along with the chemotherapy protocol, and were treated by physicians other than medical oncologists (Group 2). This included radiation oncologists, chest physicians and other specialists.

6 cycles of chemotherapy were completed in 46 out of total 75 patients (61.3%), whereas 29 patients (38.7%) received less than 6 cycles of chemotherapy. The median number of cycles was 6, with a range of 2 to 6. Dose reduction was necessary in 27 patients (36%). This dose reduction was spread across 34 out of the total 371 cycles administered (9.16%). Details of chemotherapy administered to the 2 groups are shown in Table 5.

The overall response rate was compared between the 2 groups [Table 6]. It was 41.8% for patients treated by medical oncologists at TMH (Group 1), whereas the patients treated by other doctors treated outside TMH had an ORR of 25% (Group 2).

Table 4: distribution of co-morbidities in the patients

Other co- morbidities	Number of patients	Percentage
Nil	45	60.0
Diabetes Mellitus	5	6.7
Hypertension	8	10.7
CAD	5	6.7
Others	5	6.7
More than one	7	9.3
Total	75	100.0

CAD: Coronary artery diseases

There was no treatment-related death. Grade III and IV toxicities were seen in 28 (37%) of patients. The hematological and non - hematological toxicities are shown in Table 7. The non - hematological toxicities were renal dysfunction, hepatotoxicity, and cardiac dysfunction in 1 patient each. Hematological toxicities were thrombocytopenia in 11 and neutropenia in 14 patients. Febrile neutropenia occurred in only 2 patients, and there were no deaths due to hematologic toxicity. There was no difference in the toxicity between the 2 groups.

The overall survival (OS) for the entire group of 75

Table 6: Overall response rate – comparison between patients treated by medical oncologists at TMH vs. other doctors treating outside TMH

CT administration	Medical oncologists at TMH (N = 43) (%)	Physicians of others specialties outside TMH (N = 32) (%)
CR	0	0
PR	18 (41.8)	8 (25)
ORR	18 (41.8)	8 (25)
SD	16 (37.2)	16 (50)
PD	9 (20.9)	8 (25)

CR: Complete response; PR: Partial response, SD: Stable disease, PD: Progressive disease, ORR: Overall response rate

Table 7: Grade III and IV toxicities in the study population

Type of toxicity	Total N (%)	Grade III	Grade IV
Hematological	25 (33.3)	15	10
Non - hematological	3	3	None

Table 5: Details of chemotherapy administration between the two groups

Chemotherapy administration	By medical oncologists at TMH (N = 43)	By physicians of others specialties outside TMH (N = 32)	Total
Number of patients (Max cycles possible)	43 (258 cycles)	32 (192 cycles)	75 (450)
PD identified at the end of 3 cycles (actual cycles given)	9 (27 cycles)	8 (24 cycles)	17 (51)
Remaining Patients (Max cycles possible)	34 (204 cycles)	24 (144 cycles)	58 (348)
6 cycles completed 46/75 (61.33 %) [actual cycles given]	31 patients (71.9%) [186 cycles]	15 patients (46.88%) [90 cycles]	46 [276]
Remaining patients not receiving all 6 cycles for reasons other than PD (maximum cycles possible)	3 (18 cycles)	9 (54 cycles)	12 (72)
Actual cycles received in these patients [cycles omitted]	15 cycles (each received 5 cycles x 3 patients) [3 cycles omitted]	32 cycles (6 pts received 3 cycles, 1 received 4 cycles and 2 received 5 cycles) [22 cycles omitted]	47 [25]
Total cycles received (rows 2+4+6)	228	146	
Number of cycles in which dose reduced 29/374 (9.89%)	9/228 (3.94%)	20/146 (13.70%)	29/374
Number of cycles in which dose intensity not maintained (other than for PD)	12/ 231 (5.19%)	42/168 (25%)	54/399

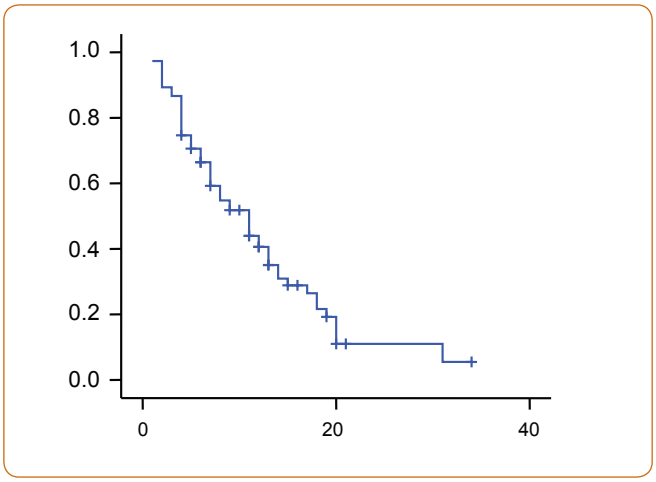

Figure 1: Overall Survival (OS) of the all the 75 patients (Median OS of 11 months and range of 1 to 34 months)

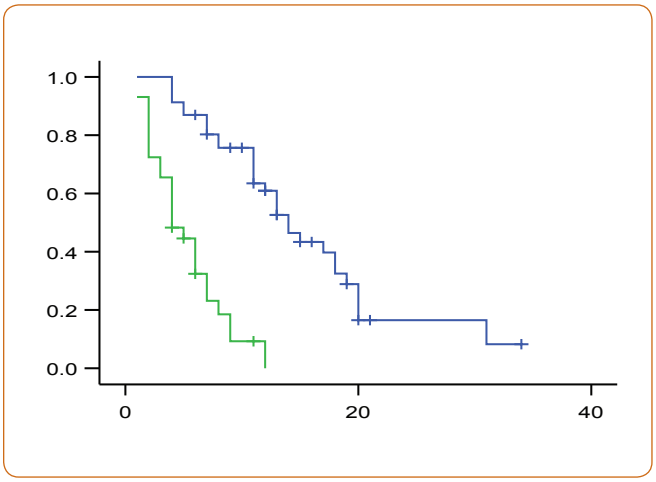

Figure 2: Comparison of overall survival: 6 cycles vs. < 6 cycles of chemotherapy (Median OS 14 vs. 4 months; *P* value 0.000)

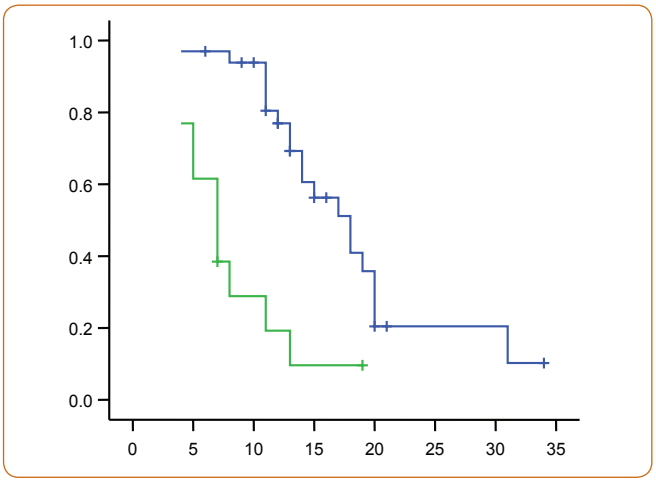

Figure 3: Comparison of overall survival in patients with or without dose reduction (Median OS 18 vs. 7 months; *P* value = 0.000)

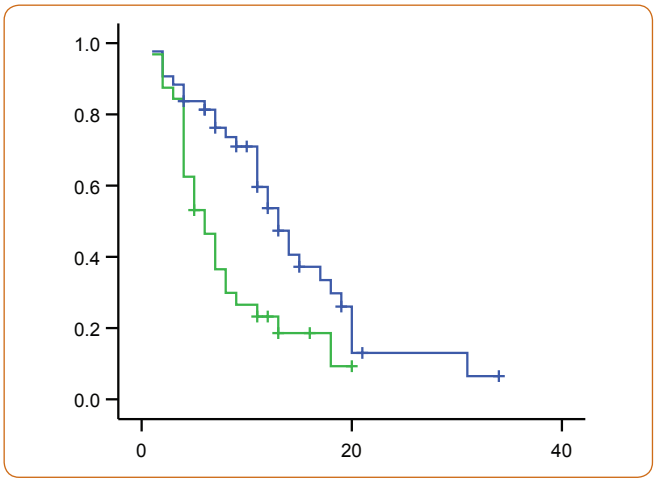

Figure 4: Comparison of survival between the two groups Treatment given by medical oncologists at TMH vs. treatment given by other doctors outside TMH Median Overall Survival 13 vs. 6 months (*P* value 0.004)

Table 8: Prognostic factors affecting survival

Variable	Comparison	Median overall survival (months)	*P* value
Chemotherapy completion	6 cycles vs. < 6 cycles	14 vs. 4	0.000
Dose reduction	Dose reduction vs. no reduction	18 vs. 7	0.000
Best response to treatment	PR + SD vs. PD	15 vs. 5	0.000
Chemotherapy administration	Medical Oncologists at TMH vs. other doctors outside TMH	13 vs. 6	0.004

PR: Partial response, SD: Stable disease, PD: Progressive disease

patients was a median of 11 months [Figure 1].

OS was also compared between those receiving the full intended protocol (6 cycles) vs. those who received less than 6 cycles of chemotherapy [Figure 2]. The median OS for the former group was 14 months as compared to the 4 months for the later (*P* value = 0.000)

The impact of dose intensity on OS is shown in Figure 3. For patients given the full dose, the medial OS was 18 months as compared to 7 months for patients requiring dose reduction (*P* value = 0.000).

The OS was also compared among the 2 groups of patients [Figure 4]. The median OS was 13 months for those treated at TMH (Group 1) as compared to 6 months for those treated elsewhere (Group 2; *P* value = 0.004).

Table 8 summarizes the factors that influences outcome in patients with advanced NSCLC treated with combination chemotherapy.

Discussion

A number of randomized trials and meta-analyzes have demonstrated that chemotherapy can improve the survival of patients with an advanced disease as compared to best supportive care. Modern cisplatin-based doublet chemotherapy has become the standard of care in the treatment of advanced NSCLC.

Elderly patients with NSCLC seem to have a poorer prognosis compared to younger ones. This has been shown recently by the data on 5-year relative survival of lung cancer patients, registered in 8 Italian cancer registries collected within the Itacare project.[3] The ratio between 5-year relative survival of patients aged 65 or more and that of patients aged 55 – 64 is 0.55, indicating that prognosis for elderly patients with lung cancer is notably worse than for the younger ones. Brown and colleagues reported data collected by a lung cancer registry and age alone appeared to be a major factor in influencing treatment choices. There was an increase of inappropriate treatment with increasing age, in particular decreasing use of chemotherapy.[4] This could be due to existence of co-morbidities, compromised body reserve, lack of tolerance chemotherapy toxicity or due to the treatment being given in an incorrect manner or by an inexperienced physician.[5]

About 1/3rd of all NSCLC patients are elderly. Unfortunately, they are under-represented in clinical trials evaluating new treatments for an advanced disease.[6] New agents for the treatment of advanced NSCLC, such as gemcitabine, vinorelbine, taxanes and camptothecin, have been introduced over the last 10 years. Their good activity (20% response rates in monotherapy) and favorable toxicity profiles have increased the possibility of treatment applications and patient eligibility, especially for the elderly patients.[7]

A number of phase II studies have shown that single-agent gemcitabine therapy leads to an overall response rate of approximately 20%, with little hematological (potentially dangerous in elderly patients) and non-hematological toxicity (nausea, alopecia, hepatic and renal toxicity).[8,9] This stimulated its use in phase III trials that focused on the elderly population.

In the present study, we have used Gemcitabine at a dose of 350 mg/m2 as a 4 hour infusion on day 1 and day 8 along with Carboplatin AUC 5 as 60 minute infusion on day 1 only. The phosphorylation of gemcitabine into the active gemcitabine – triphosphate (dFdCTP) is catalyzed by deoxycytidine kinase. This enzyme is saturated at 30 minutes by the plasma concentrations achieved following its infusion (30 minutes). Accumulation of higher intracellular dFdCTP concentrations is required for an enhanced antineoplastic activity. However, due to the rate limiting step of converting the prodrug into the active metabolite, this cannot be achieved simply by a higher dosage. Prolonging the infusion time, on the other hand, has a sound scientific basis to achieve this objective.

In a pharmacokinetic evaluation of gemcitabine and 2', 2'-difluorodeoxycytidine-5'-triphosphate after prolonged infusion, gemcitabine 300 mg/m2 was administered during 1 h, 2 h, or 3 h and as a conventional dose of 1000 mg/m2 during 30 min infusion. Administration was on days 1, 8, and 15 every 4 weeks. 300 mg/m2 gemcitabine during 3 h infusion produced the highest accumulation of gemcitabine triphosphate. Thus, to achieve the highest possible gemcitabine triphosphate level, prolonged infusion time would appear to be more important than a high dose administered as a short infusion. However, there was no substantial difference in toxicity or anti-tumoral activity in the all different patient groups.[10]

Prolonged infusion of gemcitabine has also been tried in clinical situations. In an Italian trial, patients who had stable disease post 30 minutes infusion of gemcitabine were treated with prolonged infusion of the same drug. It was noted that 13% of the patients who had SD to 30 minutes infusion had a partial response on prolonged infusion.[11] Prolonged infusion of gemcitabine in combination with carboplatin has been tried in a phase II trial in NSCLC with response rates 41%, median overall survival of 11.5 months, and 1 year survival of 42%.[12] In a Slovenian trial of 61 patients, gemcitabine was used at a dose of 250 mg/m2 over 6 hours. 1 patient had complete response and 27 had partial responses, for a 28 of 61 (46%) response rate. Median progression-free survival, median survival, and 1-year survival were 6 months, 9.5 months, and 40%, respectively.[13] Preliminary data on the TMH experience in using prolonged infusion gemcitabine in combination with carboplatin has been presented at ASCO 2005.[14]

In a review of 48 published trials on advanced NSCLC in the elderly, it was noted that none of the trials had considered the economic aspects of treatment.[15] This is an important aspect of treatment in the elderly population considering the fact that most of them are dependant and also the fact that insurance agencies will be reluctant to support advanced age patients. The low dose gemcitabine protocol will save the cost of chemotherapy by decreasing gemcitabine cost by 66%. This is of utmost importance when considering treatment options in advanced stage disease in elderly population – particularly in developing countries.

In a recent review of prognostic factors in NSCLC, the NCCTG have pooled data of 1053 patients of advanced stage NSCLC. In their analysis, age, gender, eastern cooperative oncology group performance status (PS), tumor stage (stage IIIB vs. stage IV), body mass index (BMI), creatinine level, hemoglobin level, white blood cell count, and platelet count were evaluated for their prognostic significance in both univariate and multivariate analyzes by using a Cox proportional-hazards model. Patients who had high WBC counts, low hemoglobin levels, PS > 0, BMI < 18.5 kg/m2, and TNM stage IV disease had significantly worse TTP and OS. Patients who had stage IV disease with a high WBC count had a particularly poor prognosis.[16]

There was also a predominance of ECOG PS 0, 1 among patients in our study; this observation also has been seen internationally in all studies of elderly NSCLC which suggests that patients of poor PS are not taken in most of the trials in elderly patients. Our results also showed a detrimental effect in survival of PS 2 as compared to PS 0, 1 (median OS 13 months vs. 7 months *P* value 0.001). Performance status is a known prognostic factor affecting survival in lung cancer. The impact of PS in survival has been shown in elderly NSCLC population[17] as well as NSCLC in general in all age groups.[18]

The response rates and survival outcome in the present trial is comparable to published literature. Toxicity data is very important in treatment of advanced stage disease patients. In the present study, grade III and IV toxicities were noted in 28 patients (37.3%). Majority of the toxicities were hematological (n = 25 33.3%) while non-hematological toxicities constituted 4% (n = 3 patients). The grading of toxicities showed that there were 18 grade III and 10 grade IV toxicities. All non-hematological toxicities were grade III. The hematological toxicities were thrombocytopenia in 11 patients (14.66%) and neutropenia in 14 patients (18.66%). 1 patient each had renal, hepatic, and cardiac toxicities. There was no death due to toxicity.

One of most important observations in the study was the significant impact of dose intensity on the outcome of the patients.

Survival was significantly better among the patients who completed the full planned 6 cycles of chemotherapy as compared to those who had < 6 cycles. The median survival was 14 months vs. 4 months, favoring the patients who received 6 cycles. This carries significance because the study population constituted elderly patients with advanced NSCLC. Among the uninitiated, there is a general tendency to compromise on dose intensity in such patients with the "assumption" that they don't tolerate chemotherapy as well as the young. The significant difference in survival in fully-treated vs. incompletely-treated patients underscores the importance of adhering to protocol and completing planned treatment.

In the group that completed 6 cycles (n = 46 patients), it was analyzed whether dose reduction had any impact on survival. It was noted that the median OS was 18 months vs. 7 months, favoring the group without any dose reduction.

We also evaluated whether receiving the cancer-directed systemic therapy under the direct supervision of medical oncologists influenced the outcome. As mentioned earlier, the venue of chemotherapy was TMH in 57.3% (n = 43) patients (Group 1) and outside TMH in 42.7% (n = 32) patients (Group 2). Overall survival comparison of these 2 groups showed a significant difference, median overall survival being 13 months in Group 1 and 6 months in the Group 2. This difference was due to more patients in TMH completing full-planned treatment (full dose intensity) as compared to outside TMH (74.4% vs. 43.8% patients completing 6 cycles respectively).

Conclusions

Maintaining dose intensity is important for optimizing an outcome in patients with advanced NSCLC requiring cancer-directed systemic therapy. This dose intensity is best maintained (and hence survival is best) when qualified and trained medical oncologists are imparting the treatment. Even when written protocol, instructions, and guidelines are given, community doctors did not maintain dose intensity, compromising outcome and survival. Among the elderly patients, who have influencing factors like comorbidities, this conclusion is especially important. This should be implemented for all patients, requiring cancer-directed systemic therapy to provide them with maximum benefit.

In addition, the chemotherapy protocol of low dose prolonged infusion of Gemcitabine (350 mg/m2 intravenous infusion over 4 hours) and Carboplatin (AUC – 5 over 1 hour) was well-tolerated in this group of elderly patient. The response rate and overall survival for these patients is comparable to the published literature for elderly NSCLC patients with advanced stage disease. Thus, prolonged infusion Gemcitabine protocol allows saving of 66% of the cost of this drug while maintaining response, an important health economics benefit.

References

1. Cohen HJ. Oncology and aging. In: Hazzard WR, Blass JP, Ettinger WH, editors. Principles of Geriatric Medicine and Gerontology. 4th ed. New York: McGraw–Hill; 1998.
2. Yancik R, Ries LA. Aging and cancer in America. Demographic and epidemiologic perspectives. Hematol Oncol Clin North Am 2000;14:17-23.
3. Vercelli M, Quaglia A, Casella C, Mangone L. Cancer patient survival

in the elderly in Italy. Tumor 1997;83:490-6.
4. Brown JS, Eraut D, Trask C, Davison AJ. Age and treatment of lung cancer. Thorax 1996;51:564-8.
5. Non Small Cell Lung Cancer Cooperative Group. Chemotherapy in non small cell lung cancer: A meta-analysis using update data on individual patients from 52 randomized clinical Trials. Br Med J 1995;311:899-909.
6. Hutchins LF, Unger JM, Crowley JJ, Coltman CA Jr, Albain KS. Under representation of patients of 65 years of age or older in cancer treatment trials. N Engl J Med 1999;341:2061-7.
7. Stinchcombe TE, Socinski MA. Drug development in patients with advanced non small cell lung cancer and poor performance status. Semin Oncol 2004;31 Suppl 11:S21-6.
8. Abratt RP, Bezwoda WR, Falkson G, Goedhals L, Hacking D, Rugg TA. Efficacy and safety profile of gemcitabine in non small cell lung cancer: A phase II study. J Clin Oncol 1994;12:1535-40.
9. Gatzemeier U, Shepherd FA, Le Chevalier T, Weynants P, Cottier B, Groen HJ, *et al*. Activity of gemcitabine on patients with non-small cell lung cancer: A multicenter extended phase II study. Eur J Cancer 1996;32:243-8.
10. Cattel L, Airoldi M, Delprino L. Pharmacokinetic evaluation of gemcitabine and 2',2'-Difluorodeoxycytidine-5'-triphosphate after prolonged infusion in patients affected by different solid tumors. Ann Oncol 2006;17 Suppl 5:v142-7.
11. Tibaldi C, Bernardini I, Chella A. Prolonged gemcitabine infusion in advanced non-small-cell lung cancer with stable disease after gemcitabine 30-min infusion. Lung Cancer 2006;51:217-23.
12. Xu N, Shen P, Zhang XC, Yu LF, Bao HY, Shi GM, *et al*. Phase II trial of a 2-h infusion of gemcitabine plus carboplatin as first-line chemotherapy for advanced non-small-cell lung cancer. Cancer Chemother Pharmacol 2007;59:1-7.
13. Zwitter M, Kovac V, Smrdel U, Kocijancic I, Segedin B, Vrankar M. Phase I-II trial of low-dose gemcitabine in prolonged infusion and cisplatin for advanced non-small cell lung cancer. Anticancer Drugs 2005;16:1129-34.
14. Parikh PM, Narayanan P, Mistry RC, Agarwal JP, Pai VR, Nair R, *et al*. Treatment of advanced NSCLC with low dose gemcitabine and carboplatin. ASCO Abstract Book; 2005.
15. Hotta K, Ueoka H, Kiura K, Tabata M, Tanimoto M. An overview of 48 elderly-specific clinical trials of systemic chemotherapy for advanced non-small cell lung cancer. Lung Cancer 2004;46:61-76.
16. Mandrekar SJ, Schild SE, Hillman SL, Allen KL, Marks RS, Mailliard JA, *et al*. A prognostic model for advanced stage nonsmall cell lung cancer: Pooled analysis of North Central Cancer Treatment Group trials. Cancer 2006;107:781-92.
17. Stanley KE. Prognostic factors for survival in patients with inoperable lung cancer. J Natl Cancer Inst 1980;65:25-32.
18. Hespanhol V, Queiroga H, Magalhaes A. Survival predictors in advanced non-small cell lung cancer. Lung Cancer 1995;13:253-67.

How to site this article: Prasad N, Bakshi A, Deshmukh C, Hingmire S, Ranade AA, Parikh P. Importance of dose intensity in treatment of advanced non-small cell lung cancer in the elderly. South Asian J Cancer 2012;1:9-15.
Source of Support: Nill **Conflict of Interest:** None declared.

News

The 17th Annual Symposium of the Hong Kong Cancer Institute

Clinical Application of Biomarkers in Cancer Therapy

Date: Saturday 24th November, Sunday 25th November 2012

Venue: Postgraduate Education Centre, Prince of Wales Hospital, Shatin, Hong Kong, China

Organized by: Hong Kong Cancer Institute & Department of Clinical Oncology

In conjunction with the State Key Laboratory in Oncology in South China, The Chinese University of Hong Kong

For further information:

Dr. Brigette Ma, Email: brigette@clo.cuhk.edu.hk