JOURNAL OF GERIATRIC ONCOLOGY 6 (2015) 111–118

Available online at www.sciencedirect.com

ScienceDirect

# Do elderly patients with non-small cell lung cancer get the best out of recent advances in first-line treatment? A comparative study in two tertiary cancer centers in Greece

*Marios Bakogeorgos*[a,b], *Giannis Mountzios*[a,b,*], *Evangelos Bournakis*[b], *Panagiota Economopoulou*[a], *Giannis Kotsantis*[a], *Nikolaos Fytrakis*[a], *Georgios Kouvatseas*[c], *Meletios-Athanassios Dimopoulos*[b], *Nikolaos Kentepozidis*[a]

[a]*251 Airforce General Hospital, Department of Medical Oncology, Athens, Greece*
[b]*"Alexandra" University Hospital, Department of Clinical Therapeutics, University of Athens School of Medicine, Athens, Greece*
[c]*Health Data Specialists Office, Athens, Greece*

ARTICLE INFO

*Article history:*
Received 5 May 2014
Received in revised form 6 September 2014
Accepted 7 November 2014
Available online 4 December 2014

*Keywords:*
NSCLC
Elderly patients
Chemotherapy
Adherence
Tolerance
Efficacy

ABSTRACT

*Background:* Elderly patients with advanced non-small cell lung cancer (NSCLC) are thought to receive suboptimal treatment mainly due to concerns for poor compliance and/or excessive toxicity.

*Patients and Methods:* Using the age of 70 years as the pre-defined cut-off, we compared elderly patients with advanced NSCLC suitable for first line chemotherapy with their younger counterparts in terms of: i) diagnosis and disease characteristics ii) adherence to treatment schedule, including dose intensity (DI), and relative dose intensity (RDI), iii) toxicity, tolerance, and efficacy outcomes.

*Results:* Among 292 eligible patients, data were available for 245, of whom 107 (43.7%) belonged to the elderly group. This group was more likely to present with co-morbidities, non-smoking current status and diagnosis based on cytology alone. As compared to the non-elderly, elderly patients were more likely to receive single-agent therapy (8.0% vs. 29.2% respectively, $p < 0.001$) and less likely to receive platinum-based chemotherapy (80.3% vs. 57.9%, $p < 0.001$). Elderly patients also received docetaxel (24.3% vs. 40.4%), and bevacizumab (7.5% vs. 21.3%) significantly less often and received oral vinorelbine (24.3% vs. 11.8%) more frequently. Non-elderly patients were more likely to receive any of the cytotoxic drugs with RDI > 0.8 (49.6% vs. 33.0%, $p = 0.012$) and RDI > 0.9 (29.6% vs. 16%, $p = 0.015$). Substantial toxicity, as well as median overall survival did not differ significantly between the two groups.

*Conclusions:* Only one third of the elderly patients received at least 80% of the scheduled treatment intensity. Nearly half received diagnosis based on cytology alone, which may deprive them from new, histology-driven, therapeutic approaches.



* *Corresponding author at: "Alexandra" University Hospital, Department of Clinical Therapeutics, University of Athens School of Medicine, Athens, Greece.*
E-mail address: gmountzios@gmail.com (G. Mountzios).

http://dx.doi.org/10.1016/j.jgo.2014.11.001
1879-4068/

## 1. Introduction

Cancer prevails among older patients[1–3] and age is considered to be the most important risk factor for carcinogenesis, including non-small cell lung cancer (NSCLC).[1] The threshold that separates elderly from non-elderly patients is controversial,[4,5] but most of the published trials in NSCLC use the cut-off of 65 or 70 years for this purpose.[1,6] Recent evidence suggests that the biological rather than the chronological age should guide therapeutic decisions in patients with cancer.[4,6] However, a trend has been recorded for less aggressive anti-cancer treatment in elderly patients.[6] Possible explanations with respect to elderly patients include the presence of substantial co-morbidities, polypharmacy, decreased physiologic hepatic and/or renal reserves, poor compliance, and barriers in the elderly person's access to medical care. Physician's reluctance due to concerns regarding excessive toxicity has been also reported.[7]

The median age at diagnosis of NSCLC in Western countries is approximately 67-68 years and approximately 40% of new cases occur in patients >70 years.[8] Accumulating data suggest that a platinum-based doublet therapy might be an appropriate option for "fit" elderly patients.[9–11] Nevertheless, many elderly patients receive monotherapy as first-line treatment in clinical practice and are under-represented – and often per-protocol excluded – from clinical trials.[12] In order to assess if elderly patients with advanced NSCLC are treated differently compared to their younger counterparts in routine clinical practice, and whether this discordance is translated into differences in toxicity and efficacy outcomes, we undertook a retrospective analysis of all patients who received first line chemotherapy for NSCLC in two tertiary cancer centers in Greece and compared treatment delivery, tolerance, and efficacy between the two age groups.

## 2. Patients and Methods

### 2.1. Patients

Adult patients with a histological or cytological diagnosis of non-small cell lung cancer, who were deemed suitable to receive first line chemotherapy by their treating physician between January 2007 and April 2012, in two tertiary cancer centers in Greece (University Hospital "Alexandra", Oncology Department and 251 Airforce General Hospital, Oncology Department, both in Athens and both categorized as "tertiary cancer centers" in the Hellenic Oncology Services registry of the Ministry of Health and Social Insurance of Greece) were eligible for the analysis. Patients were excluded if histological diagnosis included a small-cell lung cancer element, if they had a history of a second malignancy (excluding squamous and basal-cell carcinoma of the skin), and if they had a life expectancy of less than three months at diagnosis.

For all eligible patients, we collected clinicopathological data, treatment-related characteristics [chemotherapy regimen, duration, dose intensity (DI), and related dose intensity (RDI) for all administrated agents], and information on treatment efficacy and toxicity. Routine re-evaluation, including diagnostic imaging with computed tomography of the brain, thorax, and abdomen, was performed every three months during chemotherapy unless clinically indicated. Dose intensity (DI) was calculated as the dose delivered per square meter and per week for each chemotherapeutic agent (expressed as mg/m$^2$/week) and relative dose intensity (RDI) was calculated as the ratio of administered to the planned dose intensity (ranging from zero to 1) for each pharmacological agent. (Hryniuk method).[13] For combination regimens, RDI was calculated as the mean of the single drugs' RDI. Toxicities were defined by the Common Terminology Criteria Adverse Events (CTCAE), Version 4.03.[14] The study was approved by the institutional review boards (IRB) of both study centers.

## 3. Statistical Considerations

The age of 70 years at diagnosis was used as the threshold for assignment to the elderly and non-elderly patient group, on the basis of the median age at diagnosis of advanced NSCLC (67–68 years) and literature data favoring 70 years as the preferred cut-off for comparative studies in advanced NSCLC.[5]

Overall survival (OS) was measured from the time of treatment initiation until death from any cause or date of last contact. Time-to-event distributions were estimated using Kaplan–Meier curves. Associations between basic patient and tumor characteristics with elderly and non-elderly patient groups were examined using the Fisher's exact test or chi-square test. Toxicity profiles between elderly and non-elderly patient groups were examined either as 0 vs. 1–4 or 0–2 vs. 3–4 with the Fisher's exact test or as continuous variables with the Jonckheere–Terpstra test. The log-rank test was used for evaluating progression free survival (PFS) and OS.

Cox proportional hazards regression was used for multivariate analysis. The multivariate model contained every significant variable and interaction from univariate analyses. A backward selection procedure with 10% removal cut-off was used. The SAS software was used for statistical analysis (SAS for Windows, version 9.2, SAS Institute Inc., Cary, NC, USA), all tests were two-sided while no adjustment for multiple comparisons is reported.

## 4. Results

### 4.1. Patients

The main clinical features of the patients and pathological features of their tumors are summarized in Tables 1A and 1B, respectively. Among 292 patients who fulfilled the inclusion criteria, complete data were available for 245 patients (83.9%). Using the cut-off of 70 years, 107 (43.7%) patients were assigned to the elderly and 138 (56.3%) to the non-elderly group of patients. 81.6% of patients were males in the whole study cohort. As depicted in Table 1A, 59.8% of the elderly and 76.1% of the non-elderly patients had good Performance Status at diagnosis (PS = 0–1) and this difference was statistically significant ($p = 0.012$). Of note, the prominent histological type in the non-elderly patients was adenocarcinoma