



Treatment of Elderly Patients With Non—Small-Cell Lung Cancer: Results of an International Expert Panel Meeting of the Italian Association of Thoracic Oncology

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Abstract

Most patients with non—small-cell lung cancer (NSCLC) are elderly, and age has important implications for their management and treatment. In May 2014, the Italian Association of Thoracic Oncology organized an International Experts Panel Meeting with the intent to review the available evidence regarding the treatment of elderly patients with NSCLC and to discuss the implications for clinical practice and future research in this field; this article summarizes the panelists' conclusions. All patients aged more than 70 years should receive an assessment of physiologic age, including mortality and toxicity prediction. Age itself does not contraindicate adjuvant chemotherapy after resection. Elderly patients with locally advanced NSCLC should be considered for combined chemo-radiotherapy. In the advanced setting, the combination of carboplatin/paclitaxel results in prolonged survival compared with single-agent gemcitabine or vinorelbine, albeit with increased toxicity. In fit selected patients, other carboplatin-based or cisplatin-based regimens are feasible, but randomized trials specifically showing survival prolongation in elderly patients are lacking. The survival benefit for bevacizumab added to chemotherapy seems limited to patients aged less than 75 years. In unfit elderly patients, single agents are recommended. Regardless of age, patients with advanced non-squamous NSCLC, and those who have never smoked independently of their histologic subtype, should be tested for epidermal growth factor receptor (EGFR) mutation and anaplastic lymphoma kinase (ALK) rearrangement. In patients with NSCLC harboring EGFR mutation or ALK rearrangement, targeted drugs are feasible and well tolerated.

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Treatment of NSCLC in Elderly Patients

Introduction

Lung cancer is the most common cancer worldwide and the leading cause of cancer-related deaths.^{1,2} In an analysis by the Surveillance Epidemiology End Results database, approximately half of lung cancer cases are diagnosed in people aged more than 70 years, and approximately 15% of cases are diagnosed in patients aged more than 80 years.³

Aging may be associated with decreased physiologic reserve, polymorbidity and polypharmacy, functional dependence, and inadequate social support, which lead to limited life expectancy and reduced tolerance of stress, such as cancer chemotherapy.⁴ The benefits of cancer treatment may be reduced and the risks increased in the older person. Undertreatment is an additional risk for older individuals. Practitioners may assume that age itself is a contraindication to treatment even when the physiologic reserve is adequate and there are no other serious medical conditions.⁵ Furthermore, elderly patients are underrepresented in clinical trials,^{6,7} and treatment decisions are based on results of trials conducted in younger individuals.

In May 2014, the Italian Association of Thoracic Oncology (Associazione Italiana di Oncologia Toracica) organized an International Experts Panel Meeting, with the intent to review the available evidence regarding the treatment of elderly patients with non-small-cell lung cancer (NSCLC) and to discuss the implications for clinical practice and future research in this field. The consensus results are presented in this article.

Materials and Methods

The International Experts Panel Meeting on the treatment of elderly patients with NSCLC was held in Sperlonga, Italy, on May 9, 2014. Nine medical oncologists (4 from Italy, 3 from the United States, and 1 each from Spain and The Netherlands) formed the scientific panel.

Published data useful for panel discussion were identified by a PubMed search, performed with combinations of the following search terms: “carcinoma, non-small-cell lung” [Majr] AND “elderly.” Only articles written in English were considered. For the discussion, each panelist selected the references that were considered relevant to the assigned topic. Abstracts presented between 2009 and 2013 at the main international meetings also were searched. The search has been updated for this article with the proceedings of 2014 American Society of Clinical Oncology meeting. Relevant references from selected articles also were included, and other articles were selected from the personal collections of the panelists.

Clinical Assessment of Aging and Role of Geriatric Assessment in Clinical Practice

Elderly patients with NSCLC represent a diverse population; thus, accurate evaluation of prognosis, prediction of treatment tolerability, and selection of the most appropriate management for each patient are crucial issues in clinical practice. Comprehensive geriatric assessment (CGA) is a multidimensional, interdisciplinary patient evaluation that leads to the identification of patients’ problems⁸ (Table 1). CGA complements history and physical examinations. Although this can be time-consuming, it is considered the most appropriate clinical method to obtain a global view on the health status of elderly patients,⁹ providing information on the

Table 1 Main Elements of a Comprehensive Geriatric Assessment

Parameter	Elements
Functional status	Performance status
	Activities of Daily Living
	Instrumental Activities of Daily Living
Comorbidity	No. of comorbidities
	Severity of comorbidities
	Comorbidity index or scale
Socioeconomic status	Living conditions
	Presence and adequacy of caregivers
	Income
Cognitive status	Access to transportation
	Folstein’s Mini Mental Status
	Other tests
Emotional status	Geriatric Depression Scale
Poly-pharmacotherapy	No. of drugs assumed
	Appropriateness of medications
	Risk of drug interactions
Nutritional status	Mini-Nutritional Assessment
Presence of geriatric syndromes	Dementia, delirium, depression, falls, neglect and abuse, spontaneous bone fractures, failure to thrive

risk of mortality¹⁰ and treatment toxicity.^{11,12} In particular, given the narrow therapeutic index of treatments for NSCLC, instruments allowing the estimate of individual risk of severe toxicity are particularly useful for elderly patients. The Chemotherapy Risk Assessment Scale for High-Age Patients score, developed through a prospective, multicenter study of patients aged more than 70 years who were starting chemotherapy, is an example of how both hematologic and nonhematologic toxicity may be predicted on the basis of the CGA (Table 2).¹¹

In patients with NSCLC, the role of CGA for therapeutic decision-making remains undefined. A randomized trial conducted in patients aged more than 70 years with stage IV NSCLC compared a “classic” strategy of treatment allocation based on age and performance status versus an experimental strategy based on geriatric assessment.¹³ In the control arm, patients aged less than 75 years and with performance status 0 to 1 received a platinum-based doublet, whereas patients aged more than 75 years or with performance status 2 received single-agent docetaxel. In the experimental arm, patients were classified as fit, pre-frail, or frail according to a geriatric evaluation: Fit patients received platinum-based doublet regardless of age, pre-frail patients received single-agent docetaxel, and frail patients received best supportive care (BSC) only. The primary end point was treatment failure-free survival. In the control arm, 66% of patients received single-agent docetaxel, whereas in the experimental arm only 32% received single-agent, and 21% were considered frail and received BSC only. There was no difference observed between the 2 arms in treatment failure-free survival or overall survival. However, this study has not been published, thus limiting panelists’ discussion of its full results. In a randomized trial dedicated to elderly patients, comparing carboplatin plus paclitaxel with single-agent gemcitabine or vinorelbine, Activities of Daily

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