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# ADVANCED LUNG CANCER AND AGE: IS IT STILL IMPORTANT TO TAKE IT INTO ACCOUNT IN THE ALGORITHM OF DECISION-THERAPY?

A. BEARZ, U. TIRELLI

Department of Medical Oncology, CRO Aviano, National Cancer Institute of Aviano, Aviano (PD), Italy

## INTRODUCTION

Lung cancer is the leading cause for cancer death worldwide: most lung cancers are Non-Small Cell Lung Cancer (NSCLC) and about 70% are diagnosed at an advanced stage[1]. Until 1995, no treatment had been demonstrated to be active for advanced or metastatic lung cancer; since the BMJ metanalysis published in 1995[2] a platinum-based doublet chemotherapy had been used as first-line treatment, with modest but significative improvements in overall survival (OS) and progression-free survival[3], confirmed when platin was combined with third generation chemotherapy[4]. Although cisplatin is considered more active than carboplatin[5] in the treatment of lung cancer, it has been always considered potentially harmful due to its toxicity profile for elderly patients, whose renal clearance could be physiologically impaired. In fact, creatinine clearance decreases by 1% per year from a peak in early adulthood, with elderly individuals having substantially lower renal function than younger populations[6]. The milestones clinical trials ELVIS and MILES from the Naples group have demonstrated that a single agent treatment has better results than the best supportive care according to progression free survival and quality of life, therefore a mono-chemotherapy, gemcitabine or vinorelbine, has less toxicity than their combination, obtaining similar activity[7,8]. Back then, when a diagnosis of advanced or metastatic lung cancer was made, it was important to take into account in the algorithm of treatment, the difference between Small- and Non-Small Lung Cancer. The second most important information was the age of the patient, elderly versus young, to consequently tailoring a systemic therapy according to the age. Later on, the importance of the histology within NSCLC was demonstrated[9,10], and the molecular profiling was shown to be a milestone for EGFR mutant and ALK-translocated tumors[11,12] with a tailored choice of therapy. Meanwhile, many suggestions about tolerability of doublets in fit elderly patients have been reported[13,14], so that, although elderly age is still considered to be a negative prognostic factor[15], the recent ASCO guidelines for treatment of lung cancer do not take age into account for the appropriate treatment choice[16]. The algorithm of decision making nowadays includes the differentiation accoding to histology and molecular profiling of EGFR and ALK, while Performance Status remains the milestone to define the choice of antiblastic treatment. For unfit patients, single-agent chemotherapy represents a valuable option, especially in the elderly. On this basis it is interesting the analysis of the quality of life of elderly patients with NSCLC treated with oral vinorelbine made by Pumo et collegues[17]. The paper suggests an advantage of the oral versus the intravenous chemotherapy. However, there are several issues to remind thinking of oral treatments in the elderly population and warning for caution: 1) adherence to treatment could be an issue; 2) discussions regarding the goals and duration of chemotherapy administration for patients with metastatic NSCLC could be inappropriate especially when oral agents are prescribed[18]; 3) equivalence of activity remains to be demonstrated, with concerns about pharmacokinetics[19]. Moreover, performance status more than age is to be take into account in the treatment decision choice.

*Corresponding Author:* Alessandra Bearz, MD; e-mail: abearz@cro.it

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