



ESOGIA: a “first step” for comprehensive geriatric assessment-guided treatment in non-small cell lung cancer

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We thank Dr. Leduc and Pr. Quoix (1) for their interest in and valuable comments about the role of the comprehensive geriatric assessment (CGA) in metastatic non-small cell lung cancer (NSCLC).

We share their comments about the difficulties to manage elderly with advanced NSCLC. Today's guidelines recommend carboplatin-based doublet as first-line treatment for fit elderly NSCLC patients, whereas single-agent treatment (gemcitabine, vinorelbine, taxanes) represents a valid option for less fit patients (2). But as a matter of fact, no consensual definition of fit elderly patients exists.

The main goals of a CGA are to provide a comprehensive health appraisal to guide appropriate cancer treatment selection and to target geriatric interventions.

ESOGIA trial objective was to evaluate prospectively the first part of this definition: the relevance of CGA to guide the treatment selection for elderly patients with stage IV NSCLC. We compared in first line setting a standard strategy of treatment allocation (carboplatin-based doublet or single agent on the basis of PS and age) with experimental CGA-based allocation of the same chemotherapies or BSC (3). Carboplatin-based doublets were allocated according to histology, squamous and non-squamous histologies were well-balanced between the two arms. The association carboplatin-weekly paclitaxel was successfully tested in the IFCT 05-01 trial (4) and conducted to modifications of international recommendations. Consequently, ESMO guidelines recommend a carboplatin based-doublet as first-line treatment for fit elderly NSCLC patients but without naming the second drug. Carboplatin-pemetrexed doublet has also been successfully tested in

a phase II trial (5) and in a large phase III trial dedicated to PS2 (36% of the patients were ≥ 70 years old) (6). Carboplatin-gemcitabine doublet was compared to carboplatin-paclitaxel in a large phase III trial published by Treat *et al.* in 2010 with no difference in terms of overall survival, the median age of the patients enrolled was 64 years old (7). According to ESMO recommendations, a single-agent treatment represents a valid option for less fit patients: gemcitabine, vinorelbine and taxanes are the most evaluated. Every three weeks administration schedule of docetaxel has been more evaluated than weekly schedule.

Even if ESO GIA trial provides interesting data concerning efficacy and safety of carboplatin-pemetrexed and carboplatine-gemcitabine in non-squamous and squamous histologies respectively, it is important to note that this trial compared two strategies of allocation of treatment and not chemotherapy regimen. So it was crucial to have the same chemotherapy regimen in the two arms, to answer correctly to the primary objective of the study.

CGA-based treatment allocation failed to improve the TFFS or OS. Can we conclude that CGA is useless in advanced NSCLC?

We consider that CGA can be relevant because, in our study, CGA-based treatment allocation allowed to reduce all grade toxicities and toxicity-related treatment failures. Moreover the CGA identified a sub-group of patients with a very poor prognosis (median OS BSC was 2.8 months), even if further studies are needed to determine how to treat the best these frail patients. Moreover, as mentioned by Dr. Leduc, several geriatric indexes have been shown as independent prognostic factors in lung cancer, such as

ADL in the IFCT-0501 study, IADL or BMI (1). We can add that in ESOgia trial a BMI ≤ 20 kg/m², a Charlson comorbidity index ≥ 2 , and the existence of a geriatric syndrome were associated to a worse TFFS in multivariate analysis. Published studies that included various types of cancer and among them NSCLC demonstrated that the ADL score and malnutrition were independently associated with changes in cancer treatment (8), and that in advanced solid cancers, a low MNA score (≤ 23.5) and a poor mobility predicted early death (<6 months) after initiation of chemotherapy treatment (9).

Moreover, it's important to remember that ESOgia trial did not evaluate the second part of CGA's definition: its ability to guide appropriate targeted geriatric interventions. CGA reveals deficits that are not routinely captured in standard history and physical examination. Geriatric interventions adapted to these deficits can be planned. The impact on outcomes of such interventions has not been prospectively evaluated in the elderly with advanced NSCLC. But in a study comparing the impact of early palliative cares to standard care in patients with metastatic NSCLC, the early palliative interventions improved quality of life and also overall survival (10). Early palliative cares consisted on specific attention to assessing physical and psychosocial symptoms, establishing goals of care, assisting with decision making regarding treatment, and coordinating care on the basis of the individual needs of the patient. This management is probably not so far from what are the geriatric interventions proposed to an elderly population. The precise impact remains nevertheless to evaluate.

Does simplified and less time consuming geriatric assessment adding to other few scales (PS, ADL, BMI...) would be of more interest? Probably not because it appears difficult to summarize a complex status like frailty through very few questions. The strategy that consists to select the patients that could justify a CGA through a previous shorter geriatric screening tool seems to be more relevant.

A lot of progress remains to do in geriatric oncology, we move forward together slowly but surely.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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