

# How aggressive one need to be in treatment of patients with oligometastasis from non-small cell lung cancer?

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The concept of “oligometastases” was first proposed by Hellman and Weichselbaum in 1995 and defined as metastases limited in number and location (1,2). Though being in blood-borne nature, eradication of oligometastatic lesions, by aggressive local therapy (surgery and/or radiation therapy), has been shown to provide additional chance for cure to many patients in a few clinical settings. A few important favorable factors were documented in the patients with oligometastases from non-small cell lung cancer (NSCLC): controlled primary; long disease-free interval; and initially low N-stages (3). However, the general advice has been to employ aggressive local therapy mainly to those with favorable factors in order to optimize the risk of morbidity.

A recently published article by Johnson *et al.* evaluated the clinical outcomes of NSCLC patients with synchronous oligometastasis (4). According to the institutional policy, invasive mediastinal staging procedure was mandatory for all oligometastatic NSCLC patients at the time of diagnosis, and curative intent local therapy both to the primary and metastatic lesions, with or without systemic chemotherapy, was applied to those with no mediastinal lymph node metastasis (N2). Authors, though all their patients had synchronous metastasis, could achieve very favorable and promising 5-year survival rate of 58% in 22 N2-negative patients following curative therapy, which was dramatically contrasted to the dismal survival figure of 0% in 13 N2-positive patients following palliative therapy only. Based on

this observation, authors advocate aggressive local therapy effort to those without mediastinal lymph node metastasis following invasive staging procedures.

This article has a strong point of adopting invasive mediastinal staging policy, however, could not be free from a few criticisms. First, the vast majority of patients had brain metastasis (29 patients, 82.9%). An aggressive therapy approach has been already accepted as a standard recommendation for the patients in favorable performance status having limited brain metastasis, regardless of the timing of detecting brain metastasis (5,6). Local therapy options for brain metastasis usually include stereotactic radiosurgery or open surgical resection, both with or without whole brain radiation therapy, based on the presence of neurologic symptom. This study included 16 patients with brain metastasis among 22 N2-negative patients, and all 16 were treated with either radiosurgery or open surgery. Expectancy of high rate of local control following radiosurgery and surgical resection for brain metastasis, coupled with the accuracy of mediastinal staging effort, could be the explanations to the favorable survival outcome in this patients' group. Second, only palliative intent treatment was offered to the N2-positive patients. It was previously shown that long-term survival could be achieved in those having oligometastasis, either synchronous or metachronous, from NSCLC and N1 or N2 disease on the condition that the patients could tolerate and receive aggressive therapy approach (3,7-9).

Though the long-term survival outcome was not very high, it is assumed that a small subset of patients having lymphatic spread could have been benefitted by more aggressive therapy approach. However, authors seemed to have pursued palliative intent consistently to all of 13 synchronous N2-positive patients. This could mean, as the authors stated, that they prevented the N2-positive patients from the chance for long-term survival and cure, though not high enough. We have witnessed a remarkable progress in diagnosing small metastatic foci through the improved quality of diagnostic imaging studies including CT and PET and minimally invasive procedure like endobronchial ultrasonography guided needle aspiration for cytopathologic evaluation. Moreover, most of the oncologists treating the NSCLC patients, through the intimate collaboration among several different specialties, are currently equipped with highly effective local therapy modalities, such as stereotactic radiation therapy, either in a single fraction radiosurgery or within a few fractions, as well as systemic therapy regimens. Therefore, the effort that could lead to the chance for local cure as well as systemic control needs not be abandoned for improving survival outcome. Naturally, the issue of aggressiveness that has the potential for cure should be carefully weighed against the subsequent risk of life quality deterioration. Third, this study enrolled rather small population size (total 35 patients). As the oligometastatic state is being rather frequently encountered at our routine clinics, we could validate and optimize the aggressiveness of a certain treatment approach by accruing more patients to the prospective clinical trials. There are several prospective clinical trials on the way to evaluate the benefit of adding local therapy to the “standard” systemic therapy in oligometastatic NSCLC setting, whose results are awaited (10-12).

In summary, an enthusiastic treatment attitude toward the NSCLC patients having oligometastatic state seems highly worthwhile and the accumulation of more clinical trial data are awaited, based on which one could wisely determine the level of treatment aggressiveness.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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