Oligo-metastasis concept: A way to downstage not to under-stage a stage IV metastatic disease.

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Editorial

In Medical Oncology, there are two types of tumors. If the tumor is localized, the goal of treatment will be curative and it will consist of surgery, chemotherapy (either neo-adjuvant or adjuvant) and radiation therapy. However, if the disease is locally advanced/unresectable or disseminated, the patients are treated in a palliative, non-curative intent, with an aim of prolonging the survival in an acceptable quality of life. In the era of the targeted therapies, antibody drug conjugate, immunotherapy and with the advances in the stereotactic localized treatments, it was possible to include the entity of oligo-metastatic disease while staging the tumors. The main objective was to downstage the metastatic disease while giving the possibility to surgically/locally control certain metastatic areas in order to continue the same anti-neoplastic treatment and improve the disease control. Thus, it was possible to offer long term remissions in a pseudo-curative intent to a group of patients that were previously considered for palliation. This transition from an incurable disease towards a potentially curable – controlled disease requires the determination of certain criteria to label a disease "oligo-metastatic'': number of metastatic lesions, the evolution in space and time, as well as the way the remaining primitive lesion is treated, either via surgery or radiation therapy as done in the curative settings. This emerging approach has been applied in metastatic melanoma, non-small cell lung cancer, breast cancer, colorectal and renal cell carcinomas.

The concept of oligo-metastatic disease was elucidated for the first time in 1995, when Hellman suggested that in some patients with a limited number of clinically detectable metastases, a transitional state between localized and widespread systemic disease may better define the extent of the disease. This theory was original in the way it went against the dogma that the control of oligo-metastatic disease wouldn't be of a therapeutic benefit since it represents a clinical manifestation of a few detectable lesions in the setting of widespread occult disease. According to the literature and the different retrospective series, an oligo-metastatic disease is defined as a limited number of lesions (3-5 lesions) that are not rapidly progressing with a controlled primary disease if the primitive lesion is in place (in case of synchronous metastatic disease). It can also present as an oligo-recurrence or oligo-progression. In this perspective, if the primary site (when it is still present) is controlled, or resected, and the few metastatic sites are ablated (surgically or with radiation), there will be a trend towards a prolonged disease-free interval. This new clinical implication opened the discussion and hypothesis of a more indolent biology and progression, and it offered an improvement of certain stereotactic ablative techniques, either surgical or via radiation oncology. Nevertheless, patients must be adequately selected. Not only is there a relationship between increased number of metastases and a decreased efficacy of local therapy, there is also a certain challenge in defining the oligo-metastatic state. According to the literature and the previous series, it still remains undefined when to consider the disease as "limited in number and location". Some published studies have used specific criteria related to the number of the distant lesions, as a solitary lesion v/s less than 3 lesions v/s less than 5 lesions, in order to establish the study eligibilities. Controversially, other studies associated some factors that are probably also important, such as the volume, histology, genetics and location of tumor. It was found that among the patients who were defined as having a limited/oligo-metastatic disease, only 10-15% were able to benefit from a more prolonged disease free survival interval, as it was planned.

In conclusion, the oligo-metastatic concept had downstaged many stage IV diseases. Medical oncologist and oncologic surgeons must be aware who to include in this transitional zone between localized and widespread systemic disease. They should "*downstage*" towards longer disease free survival interval rather than "*under-stage*" with a resulting under treatment and a fulminant disease progression. It remains a challenge in the daily practice and depends mainly on the clinical judgement and expertise. Prospective randomized data are lacking to clearly ascertain who may benefit from the oligo-metastasis directed local therapy.

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