DESIGN OF CLINICAL TRIALS INTEGRATING LOCAL TREATMENTS WITH SYSTEMIC THERAPY FOR M1 DISEASE

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Palliative radiotherapy plays a major role in the management of metastatic patients, it is effective in controlling pain, maintaining patient quality of life and / or stabilizing tumor progression. Delivery of an ablative radiotherapeutic dose with technologies such as image-guided stereotactic body radiotherapy (SBRT) may allow a higher biologically effective dose to be delivered for better pain relief and potential local tumor control. Integration of SBRT into oligometastatic patients care may yield future benefits, with improved disease-free and overall survival. It has been recently proposed that during the evolution of some tumors, a clinical state of oligometastasis may exist when metastases are limited in number and/or in destination organs. Gain in accuracy and sensitivity of imaging techniques has in parallel induced a relative increase in the "early onset" metastatic cases. Phase I/II studies have shown potentially improved local control over conventional techniques in both primary tumors and metastasis. The translation of these technological improvements into changes in clinical practice need to be established by a robust demonstration that radiotherapy for M1 stage patients can provide clinical usefulness. At the same time we are at a turning point where novel anti-cancer agents have yielded unprecedented survival gains in metastatic patients. The challenges will be to integrate novel radiotherapy capabilities with optimal systemic therapies, while the positioning of stereotactic radiotherapy for brain mets appears to be univocal, the precise impact of SBRT for limited stage M1 patients is still a matter of debate. Biological identification parameters will be key to define the optimal patient population. The clinical setting also requires to be defined, should radiotherapy be used as a salvage alternative for tumors refractory to systemic therapies or do we have to consider SBRT as a debunking strategy independently of chemosensitivity parameters? Emerging concepts such as immune cell death and selection of refractory cells under therapeutic pressure are pleading for an early use of radiotherapy.

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