Editorial

Lung-sparing intensity-modulated radiotherapy in malignant pleural mesothelioma: palliative or potentially radical?

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Malignant pleural mesothelioma (MPM) is a rare and aggressive tumour and its prognosis is dismal. The ASCO and the ESMO guidelines both place a platinum-pemetrexed (or raltitrexed)-based chemotherapy for 4 to 6 cycles as standard of care in fit patients (1,2). However, the median overall survival (OS) is only approximately 12 months, with hardly any 5-year survivors (2).

In recent years, the role of surgery and the role of radiotherapy have been both redefined. New surgical techniques (less invasive compared to the extrapleural pneumonectomy-EPP), such as the lung-sparing pleurectomy/decortication (P/D), have been increasingly used, mainly due to the high post-operative mortality and morbidity of EPP, even in specialized centres (3).

Recent advances in radiotherapy planning and delivery have enabled dose escalation while maintaining acceptable dose constraints to normal tissues, even after a lung-sparing surgery, thus in patients with two intact lungs. The MSKCC group has been the leader in optimizing lung-sparing intensity-modulated radiotherapy (IMRT) (4-6), with encouraging results (median OS from the end of radiotherapy of 20.2 months (6). The median delivered dose was 46.8 Gy and 90% of patient received chemotherapy. Toxicity was acceptable, with a grade ≥3 radiation pneumonitis rate between 13.6% and 20% (5,7). However, up to now, few groups confirmed the MSKCC data on lung-sparing IMRT (8,9).

The report of Parisi and colleagues is therefore of great interest. They reported the results of a retrospective study in biopsy-proven MPM patients, in which 25 Gy in 5 fractions (or 37.5 Gy in 5 fractions, if residual disease after P/D) were delivered to the hemi-pleura. This palliative lung-sparing IMRT was preceded by chemotherapy and/or lung-sparing surgery (P/D).

The main objective was to investigate the feasibility of such a regimen in a cohort of patients with intact lungs (after biopsy or P/D). Thirty-six patients were retrospectively included: 19/36 (52.8%) underwent P/D, 80% received chemotherapy and 14/36 (39%) were stage III (N2 mediastinal lymph nodes).

The median OS was 21.6 months. The proposed treatment was well tolerated, with 8% of patients who experienced grade ≥3 radiation pneumonitis, 17% grade 2 cough and 14% grade 2 dyspnea.

There are several limitations to this study. First of all, this is not a clinical trial but a retrospective analysis of a group of patients treated with a nonstandard of care protocol. This raises serious concerns as to whether the patients truly gave informed consent to be entered in this protocol and what alternative options were offered to them. The latter is particularly relevant for the 41% of patients who presented with stage I–II disease and received chemotherapy and a palliative radiotherapy). One of the main limitations of MPM literature is the lack of high-quality data, and we

strongly believe that, whenever possible, those patients should be included in prospective clinical trials.

Second, the objective of this analysis is to evaluate the feasibility of a palliative regimen in MPM patients after biopsy or P/D in terms of toxicity. However, little is said about the palliation of the symptoms (dyspnoea or thoracic), i.e., did this palliative IMRT reduce symptoms?

Nevertheless, the reported OS is nearly 22 months, which compares favourably with published prospective studies in patients who received higher doses of radiotherapy.

The results may therefore raise the hypothesis that lung-sparing IMRT may lead to a promising OS in selected patients, but that high doses may not be necessary for achieving this.

It is hoped that the authors and centers will continue to pursue this strategy in a prospective study, and integrate this with chemotherapy and new drugs such as immune therapy (10).

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Footnote

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