

Studies report new findings on treatment options for mesothelioma

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Treating patients with high-dose radiotherapy after chemotherapy and surgery for malignant pleural mesothelioma does not achieve improvements in local relapse and overall survival, according to data from a prospective randomized phase II trial presented at ESMO 2014 Congress in Madrid.

"Mesothelioma remains a difficult disease to find better treatment options for, so we asked whether high-dose hemithoracic radiotherapy would decrease the rate or delay the time of local recurrence after chemotherapy and radical surgery," says lead author Prof Rolf A. Stahel, from the Clinic and Policlinic for Oncology, at the University Hospital Zurich, Switzerland, and current President of the European Society for Medical Oncology.

The multicentre trial included 153 [patients](#) with surgically-treatable [malignant pleural mesothelioma](#), who were first treated with three chemotherapy cycles of cisplatin and pemetrexed, followed by surgical removal of affected lung tissue, with the goal of complete removal of the cancerous areas of lung.

In a second part of the study, researchers randomly assigned 54 patients to receive either radiotherapy or no further treatment, with the primary endpoint being the duration of relapse-free survival.

While there had been preliminary evidence suggesting that the addition of radiotherapy might improve outcomes, the study failed to find any

differences in relapse-free survival between patients treated with the additional radiotherapy, and those who were not.

Stahel says researchers were hoping for a more positive signal from the study. "We aimed for a six month delay in local recurrence, which would be meaningful because it's an aggressive treatment for patients."

In summary, Stahel says, "It demonstrates that, like in other solid tumours, when two modalities are not sufficient it's very rare that the third modality added would make a benefit."

Commenting on the results, Dr Paul Baas, from the Department of Thoracic Oncology, The Netherlands Cancer Institute, Amsterdam, says the combined modality of chemotherapy followed by major surgery and irradiation of high volumes of the chest is one of the accepted treatments in very fit patients, however it is a combination associated with high morbidity.

"The study by Stahel et al. indicates that the contribution of radiation does not improve time to recurrence of the disease," says Baas.

However he also stressed that the results did not lead him to conclude that there was no role for adjuvant radiation in this setting, pointing out that this was a phase II trial, and therefore not necessarily the final conclusion, and that selection of patients with differing pathology, stage and performance could influence outcome.

"Times are changing and this is also true for the way that radiation therapy can be administered to the patient, so new approaches (intensity modulated radiation) can improve the local control and reduce toxicity."

Is PD-L1 a possible immunotherapy target in

mesothelioma?

In a second study presented at the ESMO 2014 Congress, researchers report that about 20% of patients with malignant pleural mesothelioma have cancer cells that express a protein called programmed cell-death ligand 1 (PD-L1) that is associated with poorer outcomes.

The results suggest this population of patients could be treated with targeted therapies to PD-L1, researchers say.

The PD-L1 protein—which is part of the PD-1/PD-L1 immune pathway—is active in many different human cancers, where it is involved in suppressing the anti-tumor immune response and therefore hampering the immune system's ability to attack the cancer.

Treatments that block this pathway are already showing considerable promise in other malignancies, such as melanoma and lung cancer, leading researchers to question whether this same pathway could be active in malignant pleural mesothelioma.

"We report that PD-L1 is expressed in 20% of malignant pleural mesothelioma patients and is associated with poor outcome, which suggests that this pathway could be targeted with PD-1/PD-L1 inhibitors," says study author Dr Susana Cedres, from Vall d'Hebron Institute Oncology, Barcelona, Spain.

Researchers analysed tissue samples from 119 patients with malignant pleural mesothelioma using an anti-PD-L1 stain. PD-L1 [expression](#) intensity was scored on a scale of 0 to 3—with '0' signifying no expression, '1' signifying weak expression, '2' moderate, and '3' strong—and then compared the score with survival data and outcomes from those patients.

They found that overall, 20.7% of patients were positive for PD-L1 expression: 18.7% of these showed strong expression of PD-L1, 25% showed moderate expression, while 56.2% showed only weak expression of PD-L1.

Most importantly, patients who were negative for PD-L1 expression survived around 11 months longer than patients who were positive for PD-L1 expression (median survival 4.79 vs 16.3 months).

Factors such as gender, smoking, asbestos exposure and disease stage did not have an effect on whether patient's disease was positive for PD-L1 expression, but researchers did find that expression of the protein was more common in non-epithelial tumours compared to epithelial tumours.

"The results of our study could offer new treatment to this population of patients, identifying a subset of malignant pleural mesothelioma who expressed PD-L1 and could be treated with targeted therapies to PD-L1," Cedres says.

Commenting on the two studies, Baas says that finding a good treatment for [mesothelioma](#) has been a challenge for many years and has so far led to many disappointments, so there is a need for investigation into new pathways such as the use of immune checkpoint inhibitors that target the PD-1/PD-L1 pathway.

"Cedres and colleagues' data are important because they might help in selecting the best patients for these kinds of (expensive) therapies," Baas says.

Some key issues need to be addressed, such as identifying the best antibody and platform to find tumours with increased expression of PD-L1, and deciding which treatment approach to take.

"It is clear from these two studies that we still have a long way to go, but proper selection of patients, improved techniques in radiotherapy and new immunotherapy treatments will help us to fight this terrible disease."

Provided by European Society for Medical Oncology

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