Mesothelioma: No Benefit for Added Radiation to Chest Wall

BY ED SUSMAN

MADRID—The addition of radiation to the chest wall following extensive surgery to remove malignant pleural mesothelioma does not appear to benefit patients when compared with the results for patients who do not receive radiotherapy aimed at preventing disease relapse, according to data reported here at the European Society for Medical Oncology Congress.

"Our study demonstrates that, like in other solid tumors, when two modalities are not sufficient it's very rare that the third modality added would have a benefit," said Rolf Stahel, MD, Professor of Medicine at University Hospital Zurich in Switzerland, who is also this year's President of ESMO.

For the primary endpoint of the study, patients who were randomized to receive radiation therapy following surgery had a median relapse-free survival of 12.2 months compared with 11.0 months for patients who did not receive radiation, he reported at a news briefing at the meeting.

Similarly, median overall survival times were 20.8 months and 19.3 months, respectively. Neither of the differences in relapse-free survival or overall survival achieved statistical significance, he said.

"We aimed for a one-year delay in local recurrence, which would be meaningful, because it's an aggressive treatment for patients," but the addition of radiation failed to show that benefit.

He explained that the standard surgery for mesothelioma is extrapleural pneumonectomy. "This is very radical surgery: Surgeons take away the lung and the tumor around it; they take away the lining of the chest wall and they take away part of the pericardium.

"Surgery in cancer means trying to take all the cancer, but this cannot be done with cancer on the chest wall. This is the reason why even after such a surgery there are relapses in this area."

Study Details

Hence, Stahel and his colleagues in the SAKK 17/04 study recruited 151 patients diagnosed with Stages 1-3, N0-3, M0 mesothelioma. "The question we posed in this study is: would surgery and thoracic radiosurgery prevent those relapses that we see; could we delay these relapses?"

All the patients were in Performance Status 0-1 when they began the treatment regimen. They first underwent three cycles of chemotherapy: cisplatin at 75 mg/m^2 and pemetrexed at 500 mg/m^2 every three weeks. Following the chemotherapy regimen, patients were then restaged. No surgery was performed on 26 patients, and a limited surgery was performed in 12 patients. Of the 113 patients who underwent the grueling surgery, 96 achieved an R0/R1resection; 17 patients had R2 resection.

Of the 125 patients who underwent some form of surgery in the study, the 30-day mortality rate was four percent and 60-day was eight percent. Overall, 10 of the surgery patients died within two months of the procedure.

Of the 96 patients who achieved the R0/R1 resection after chemotherapy, 54 agreed to be randomized into the radiation study. The other patients either refused or were excluded due to protocol violations.

A total of 27 patients underwent radiation; the other 27 patients acted as controls. The patients who received radiation were treated with a dose of 46 Gy to the hemithorax and mediastinal nodes, and they also received a boost of 10 Gy, for a total dose of 56 Gy.

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"We have to conclude that radical surgery and radiation are not successful in controlling this disease. So what are the next steps?" Stahel said. "Currently, instead of doing radical surgery we have seen that lung-sparing surgery is nearly as good as radical surgery, and there are investigations of providing chemotherapy after surgery.

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Chemotherapy, surgery, radiation, and recovery amounts to six months' time, Stahel said, and "survival is just 20 months, so this is a very heavy treatment burden."

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Mesothelioma remains a difficult disease to find better treatment options."

High Morbidity

Commenting on the results of the study, Paul Baas, MD, PhD, Professor of Thoracic Oncology at the Netherlands Cancer Institute, said that although 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, it is 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," he said, noting, though, that the results did not lead him to conclude that there was no role for adjuvant radiation in this setting. Since SAKK 17/04 was a Phase II trial, it is not necessarily the final conclusion. He also suggested that selection of patients with differing pathology, stage, and performance could have influenced the outcome.

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

The SAKK 17/04 researchers noted that originally 37 patients were sought for each arm of the radiation study, but because of slow accrual the trial was stopped in 2013. The limited number of patients may have impacted the ability of the study to show differences, they suggested.