Melanoma drug shrinks brain metastases in phase I/II study

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A new drug being developed to treat potentially deadly melanoma skin cancers has shown a promising ability to shrink secondary tumors, known as metastases, in the brain in patients with advanced forms of the disease, Australian researchers report.

At the 35th Congress of the European Society for Medical Oncology (ESMO), Dr Georgina Long from Melanoma Institute Australia and Westmead Hospital, in Sydney, reported the results in a subgroup of 10 melanoma patients with previously untreated brain metastases from the international Phase I/II trial with the oral drug GSK2118436.

"Brain metastases in melanoma are a major unsolved problem," Dr Long said. "We are very excited about the robust activity seen with GSK2118436 in this Phase I/II trial so far. Until now, melanoma has been notoriously resistant to drug therapy in general, and responses in highly lethal brain metastases are particularly uncommon."

Of all solid tumors, melanoma has the greatest capacity to spread via the blood stream to the brain. Overall, 15 to 20% of patients with melanoma that has spread beyond the skin have brain metastases at initial diagnosis, and nearly 75% have them at autopsy.

Currently, there is no evidence that any therapy prolongs survival in patients with multiple melanoma brain metastases. The median overall survival time for all patients with melanoma brain metastases is 16 weeks from diagnosis of brain involvement.

Dr Long and colleagues are testing GSK2118436 as a potential treatment for melanoma patients who have a particular common mutation of the gene for a protein called BRAF, which is mutated in 50% of human melanomas. The drug binds to the activated form of the BRAF protein in the melanoma cell, causing the cell to stop proliferating, and in many cases, die.

The data being presented at ESMO comes from a sub-group of 10 trial participants with previously untreated brain metastases. All 10 patients experienced control of melanoma brain metastases, and 9 of the 10 patients had reductions in the overall size of their brain metastases, Dr Long reported. The overall reductions ranged from 20 to 100% of brain metastases that were 3mm or larger in diameter before treatment.

In this Phase I/II trial, this drug showed a similar effect in patients with melanoma outside the brain, Dr Long said. "We have previously reported a response rate of more than 60% which is unusually good."

"The ability to inhibit oncogenic BRAF is the most important development in the history of drug treatment of melanoma," Dr Long added. "Providing these early data are supported in larger cohorts of patients, and durable responses are confirmed, this activity in the brain may assist in addressing a large unmet need in patients with metastatic melanoma."

The Australian researchers expect to present an update of activity and safety in all subjects of the Phase I/II trial in November 2010 at the meeting of the Society for Melanoma Research in Sydney. They are also planning a Phase II study of the drug in melanoma patients with V600 BRAF mutant metastatic melanoma involving the brain. They hope to open that second trial in November or December 2010.

Provided by European Society for Medical Oncology