MedicalXpress

First 'targeted' treatment for small cell lung cancer shows promise

September 28 2015

Small cell lung cancer (SCLC) is an aggressive disease that is difficult to treat and is frequently only diagnosed when it has spread to other parts of the body (metastasised). Five-year survival rates in SCLC, which accounts for about 14% of all lung cancers, are very low, at only six percent. But today US researchers will present two novel findings with important implications for treatment at the 2015 European Cancer Congress.

Dr M. Catherine Pietanza, MD, an Assistant Attending Physician at the Memorial Sloan Kettering Cancer Center, New York, USA, will report on results from a phase I trial of a novel agent, rovalpituzumab tesirine (Rova-T, or S16LD6.5), in 79 patients with SCLC who had progressed after first line (given when the disease is newly diagnosed) or second line therapy (given when the disease progresses or recurs).

"While other cancers have multiple treatment options, there is only one agent approved in SCLC, and none available in the third line setting; the outlook for these patients is dismal," she will say. Third line therapy is given after first and second line treatments have failed to halt the progression of disease.

The patients ranged in age from 44-81, with a median age of 62 years. As is normal in phase I trials, they received escalating doses of Rova-T once every three weeks until toxicity reached a point at which the increase in dose needed to be stopped. The drug was designed to bind to DLL3 (delta like protein 3), a protein that is highly expressed in

approximately 70% of SCLCs.

"Of the 48 tumour samples we were able to analyse, 33 were positive for DLL3. Among the 29 DLL3+ patients we could treat at the maximum tolerated dose of Rova-T, ten (34%) had a partial response and nine (31%) had disease stabilisation. The duration of response among these patients was more than 178 days, with no cases of disease progression," Dr Pietanza will say.

Rova-T is an antibody drug conjugate (ADC) consisting of three components - an antibody, a linker and the active chemotherapy, or cytotoxic payload. The antibody portion of an ADC can recognise cell surface receptors specific to and that are over-expressed in cancer cells, allowing the delivery of the chemotherapy directly to the tumour. This means the treatment is more effective, and also minimises its exposure to normal cells, with a consequent reduction in toxicity.

"The high response rate is exciting in itself, and above that we have been able to identify a biomarker for SCLC in DLL3+, thus enabling us to 'target' treatment in SCLC. The activity of the drug that we have seen is remarkable, and importantly, the durable, long-term responses are notable in such an aggressive disease where progression is normally very rapid," says Dr Pietanza.

Whereas the most common treatment for early stage NSCLC is surgery, SCLC is not usually diagnosed in time for this to be a viable possibility, and chemotherapy is the standard of care. It remains a worldwide public health problem, since it is associated with exposure to tobacco smoke, and it is a major cause of death from cancer. Currently, standard first line therapy is the chemotherapy combination etoposide/platinum, which is combined with radiation therapy to the chest in limited stage disease, and second line chemotherapy consists of topotecan. Because SCLC can spread quickly to the brain, cranial radiation therapy may also be given.

"The first line therapy has not changed for four decades, and there is no third line treatment at present, so it is clear that Rova-T is likely to fulfil an unmet need for these patients. I would like to see additional, larger trials to develop it further in settings where there is a clear need in this disease. We are looking forward to further assisting in its development and to gaining a better understanding of its value in all cases of SCLC," Dr Pietanza will conclude.

Professor Peter Naredi, the ECCO scientific co-chair of the Congress, who was not involved in the research, commented: "Dr Pietanza's presentation underlines once again how exciting this Congress is. Not only have we had reports of the large-scale efficiency of checkpoint inhibitors in many tumour types, but Dr Pietanza reports remarkable early results of rovalpituzumab tesirine, a drug designed to bind to DLL3, a protein that is highly expressed in approximately two-thirds of SCLCs, a disease where we have seen no novel treatment options for many years.

"I was pleased to see that in patients who were DLL3 positive a majority had long lasting stable disease or partial response. It will be exciting to follow further phase II and III trials of this treatment."

Provided by ECCO-the European CanCer Organisation