Imfinzi Extends Lives of People with Early-Stage Small Cell Lung Cancer

People treated with the checkpoint inhibitor durvalumab stayed in remission longer and lived longer than those who received a placebo.

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The immunotherapy drug durvalumab (Imfinzi) helped people with early-stage small cell lung cancer live longer, according to initial results from a large clinical trial. Durvalumab is a type of immunotherapy called an immune checkpoint inhibitor.

The standard initial treatment for early-stage (also called limited-stage) small cell lung cancer—cancer that is confined to one lung or one side of the chest—is chemotherapy and radiation given at the same time. Although this treatment tends to work well at first, the cancer often comes back quickly, at which point it has typically spread throughout the body.

“There really have not been any major advances in the treatment of limited-stage small cell lung cancer for several decades,” said the study’s leader, David Spigel, M.D., of Sarah Cannon Research Institute in Nashville, Tennessee.

In the new trial, dubbed ADRIATIC, more than 500 people with limited-stage small cell lung cancer who had finished chemotherapy and radiation were randomly assigned to receive durvalumab or a placebo for up to 2 years.

People who received durvalumab stayed in remission longer and lived substantially longer than those treated with placebo. Three years after starting the treatment, 57% of people in the durvalumab group were still alive, compared with 48% in the placebo group, Dr. Spigel reported at the annual meeting of the American Society of Clinical Oncology on June 2.

“The ADRIATIC trial is a landmark study and provides a new standard of care for patients with early-stage small cell lung cancer,” said Lauren Byers, M.D., professor of thoracic head and neck medical oncology at the University of Texas MD Anderson Cancer Center, at a press briefing where the study was discussed. Dr. Byers was not involved in the trial.

The findings are “definitely practice changing,” said Anish Thomas, M.D., of NCI’s Center for Cancer Research, who studies small cell lung cancer but wasn’t involved in the new trial.

“This is really encouraging for patients as well as people who are working on this cancer,” Dr.

Thomas said.

Durvalumab extends overall survival and progression-free survival

Small cell lung cancer grows quickly and often spreads beyond the lungs before it is even diagnosed. While targeted therapies have had less success for small cell than for non-small cell lung cancer, immunotherapy is a somewhat different story.

Over the past 5 years, durvalumab and two other immunotherapies—atezolizumab (Tecentriq) and tarlatamab (Imdelltra)—have been approved for the treatment of people with advanced, or extensive-stage, small cell lung cancer.

Spurred by the improvements seen with durvalumab for extensive-stage small cell lung cancer and non-small cell lung cancer, Dr. Spigel and his colleagues launched the ADRIATIC trial to see if durvalumab could improve outcomes of people with limited-stage small cell lung cancer.

All participants in the trial had cancer that had responded to standard chemotherapy and radiation.

Durvalumab was given after the standard treatment to help kill any leftover cancer cells—a strategy known as consolidation therapy. The trial was funded by AstraZeneca, the company that makes durvalumab.

Participants in the durvalumab group lived longer without their cancer growing back. Two years after the start of the trial, 46% of those in the durvalumab group and 34% in the placebo group didn't have any sign of the cancer returning.

Durvalumab also extended the median overall survival by nearly 2 years, Dr. Spigel noted, from 33 months with placebo to 56 months with durvalumab.

That is in stark contrast to the magnitude of benefit seen in extensive-stage small cell lung cancer, Dr. Thomas emphasized. In that setting, atezolizumab and durvalumab each extended median overall survival by only 2 or 3 months, he explained.

"ADRIATIC is the first phase 3 study to establish the role of immunotherapy in [treating] limited-stage small cell lung cancer," Dr. Spigel concluded.

However, the findings haven't yet been peer-reviewed—meaning, evaluated for scientific quality and accuracy by other experts in the field.

Side effects of durvalumab consolidation therapy

Durvalumab, which is given every 4 weeks as an infusion, didn't cause any unexpected side effects, Dr. Spigel noted. The side effects were typical of those seen with durvalumab and other immunotherapies, which rev up the immune system.

In particular, those in the durvalumab group experienced inflammatory conditions in the lungs, skin, and thyroid. Serious immune-related side effects occurred in 5% of people in the durvalumab group and 2% of those in the placebo group.

Durvalumab can also cause a serious and sometimes fatal lung inflammation called pneumonitis. This condition also develops frequently in people who have just received chest radiation, like the patients in this study.

In the ADRIATIC trial, 38% of people in the durvalumab group and 30% of those in the placebo group developed pneumonitis, including one participant in the durvalumab group who died of pneumonitis.

About a quarter of participants in both groups experienced a serious side effect of any kind. Side effects led 16% of patients in the durvalumab group and 11% of those in the placebo group to stop the treatment.

Next steps for small cell lung cancer research

The ADRIATIC trial is ongoing and more will be learned about durvalumab treatment, Dr. Spigel said.

In addition, another arm of the trial is evaluating the combination of durvalumab and another immunotherapy drug, tremelimumab (Imjudo). Results from that group of 200 patients are still being collected.

In the meantime, small cell lung cancer researchers are already thinking about what questions to investigate next.

“One important next step will be to understand who is benefitting the most from the addition of durvalumab and how we can start thinking about personalizing treatment for the different subtypes of small cell lung cancer,” Dr. Byers said.

Like many other kinds of cancer, small cell lung cancer can be separated into subtypes based on the molecular characteristics of the cancer cells, she explained. Some subtypes are more easily recognized by cancer-killing immune cells and may have better responses to immunotherapy, she added.

As for Dr. Thomas, his mind is on earlier detection because most small cell lung cancers are found when the disease is already widespread. If more of these cancers could be found when the disease is at an early stage, he said, patients could potentially get more benefit from durvalumab treatment.

The challenge is that low-dose CT scans, which are used to screen people at risk for lung cancer, don’t pick up small cell lung cancers early enough.

“Can we come up with methods to identify small cell [lung cancer] earlier than CT scans [can]?”

Dr. Thomas asked. Given the recent progress with blood tests for early cancer detection, he said he’s hopeful that such a test will someday be developed for small cell lung cancer.

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