Revlimid Reduces Risk That Smoldering Disease Will Progress to Multiple Myeloma

Around 90% of people treated with the immunomodulator did not develop cancer.

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An immune-based therapy that blocks blood vessel formation can help prevent a low-grade precancerous condition known as smoldering myeloma from progressing to malignant multiple myeloma, according to study results presented Sunday at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago.

Among people with smoldering disease who were treated with Revlimid (lenalidomide), around 90% did not to progress to cancer within three years, compared with two thirds of those who did not receive the drug—a 72% risk reduction.

Multiple myeloma is a blood cancer that affects the bone marrow, where blood cells are produced. Abnormal plasma cells (mature B cells) multiply too rapidly and make ineffective antibody fragments known as M proteins. Excess myeloma cells can interfere with cells that repair bone and can crowd out normal blood-forming cells in the bone marrow, leading to bone fractures, low blood cell counts and increased risk of infection. The abnormal proteins can build up and damage the kidneys and other organs.

Some people first develop smoldering myeloma, an asymptomatic precursor condition characterized by elevated M protein levels and a higher than normal percentage of plasma cells in the bone marrow. About half of people with smoldering disease go on to develop cancer within five years.

Treatment for multiple myeloma may involve chemotherapy; immunomodulators related to thalidomide that boost immune function, slow the growth of abnormal cells and block blood vessel formation; and various targeted therapies. Watchful waiting with frequent lab tests and scans is often recommended for people with smoldering myeloma, which can lead to anxiety about whether the condition will progress.

“We typically see two types of patients—those who are anxious and want to do something to prevent cancer from developing and those who are more cautious and are willing to watch and

wait," said Sagar Lonial, MD, of Winship Cancer Institute at Emory University in Atlanta. "It's gratifying to know that especially for the first group of patients there may now be a viable treatment option."

Lonial's team conducted the E3A06 trial (sponsored by the National Cancer Institute) to evaluate whether Revlimid, a newer immunomodulator that is better tolerated than thalidomide, would reduce the risk of progression to multiple myeloma in people with intermediate or high-risk smoldering myeloma. In the non-randomized Phase II portion of the study, 44 people received Revlimid as a daily pill for three weeks, followed by a week off. In the Phase III portion, 182 people were randomly assigned to take Revlimid or undergo observation without treatment.

In both portions of the trial, Revlimid led to improved outcomes, Lonial reported. After three years, the progression-free survival rate—meaning participants were still alive and had not developed multiple myeloma—was 86% in the Phase II portion; by five years, 78% had not yet progressed to cancer. In the Phase III portion, 98% of those treated with Revlimid had not developed multiple myeloma after one year, compared with 89% in the observation group. By three years, the corresponding rates were 91% and 66%, respectively.

Many people taking Revlimid experienced side effects, however. A majority of people in both the Phase II portion (80%) and in the Phase III portion (51%) stopped treatment, mostly because of adverse events, according to Lonial. The most common side effects included fatigue and loss of blood cells. About 5% of those taking Revlimid developed serious neutropenia, or white blood cell deficiency. Nonetheless, people in the Revlimid group and the observation group reported similar quality of life.

Given that around half of people with intermediate or high-risk smoldering disease would be expected to have progressed to multiple myeloma without therapy, early treatment with Revlimid can prevent the development of symptomatic disease and possible irreversible organ damage in a large proportion of patients, Lonial noted.

"Living with the uncertainty of whether cancer will develop is very difficult, so it's exciting to be able to tell patients at high risk of multiple myeloma that they can take a pill to prevent or delay cancer," commented ASCO president Monica Bertagnolli, MD, of Dana-Farber Cancer Institute in Boston.

"This approach is not for everyone, however, because it comes with potentially heavy side effects and costs, so watching and waiting still has clear advantages that every patient should discuss with their doctor," she added.

Click here to read the study abstract.

Click here to read an ASCO press release about the study.

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