Novel Antibody Helps Patients With Advanced Gastric Cancer Live Longer

Summary includes updated data not in the abstract
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ASCO Perspective

“It’s exciting to see immunotherapy improving survival in gastric cancer. Claudin18.2 is commonly expressed in multiple cancers, and this treatment may apply to half of all patients with gastric cancer,” said Smitha Krishnamurthi, MD, ASCO Expert in gastric cancer and moderator of today’s press briefing.

CHICAGO – Findings from a European phase II study showed that the novel, first-in-class antibody IMAB362 can significantly extend median survival when added to standard chemotherapy (13.2 months vs. 8.4 months) for patients with advanced gastric cancer. This therapy targets a protein called claudin18.2, and patients in the study with the highest levels of claudin18.2 had an even longer median overall survival (16.7 months).

The study will be featured in a press briefing today and presented at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting.

“As claudin18.2 is abundant in gastric tumors, we estimate that half of all patients with advanced gastric cancer may be candidates for this new treatment,” said lead study author Salah-Eddin Al-Batran, MD, a medical oncologist and director at the Institute of Clinical Cancer Research, Nordwest Hospital in Frankfurt am Main, Germany. “In addition, this unique target is not present in any healthy tissues except the lining of the stomach, thereby minimizing treatment side effects.”

Claudin18.2: A Novel Cancer Target

Besides gastric cancer, claudin18.2 is found in a variety of other tumors, including pancreatic, lung, esophageal, and ovarian. Claudin18.2 belongs to a family of proteins that make tight junctions, which control the flow of molecules between cells in a layer. In tumors, however, tight
junctons become disrupted and claudin proteins lose their primary role.

IMAB362 is the first antibody to target claudin18.2. When the antibodies attach to claudin18.2 on the surface of cancer cells, various types of cellular and soluble immune effectors respond by killing the cancer cells that are coated with antibodies. These processes are known as antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).

**About the Study**

Gastric cancer is the fifth most common cancer in the world, with nearly one million new patients diagnosed with this disease in 2012. The standard initial (first-line) treatment for advanced or recurrent gastric cancer is chemotherapy. The addition of trastuzumab to chemotherapy provides some benefit to the group of patients with HER2-positive tumors, but only 15% all gastric cancers are HER2-positive.

The study included 161 patients with advanced or recurrent gastric or gastroesophageal junction cancer with a specific minimal level of claudin18.2 in the tumor (assessed from analysis of tumor biopsy specimen with a validated CE-marked diagnostic assay). The patients had not received prior therapy for metastatic cancer and were not eligible to receive HER2 therapy trastuzumab. The patients were randomly assigned to receive standard chemotherapy (epirubicin, oxaliplatin, and capecitabine) alone or with IMAB362.

**Key Findings**

Compared to chemotherapy alone, IMAB362 extended the median time to disease progression from 4.8 to 7.9 months and the median overall survival from 8.4 to 13.2 months. Among the patients with the highest levels of claudin18.2, the median overall survival was 16.7 months with IMAB362 and 9 months with chemotherapy alone.

According to the authors, the treatment was well tolerated. Vomiting (34.5% of patients with grade 1/2 and 3.6% with grade 3/4 in control arm vs. 55.8% of patients with grade 1/2 and in 10.4% with grade 3/4 in IMAB362 arm) and low blood counts or neutropenia (21.4 % of patients with grade 1/2 and 21.4 % with grade 3/4 in control arm vs. 23.4% of patients with grade 1/2 and in 32.5% with grade 3/4 in IMAB362 arm) were slightly more common in the IMAB362 group. The rates of severe adverse effects were not increased with IMAB362 compared to chemotherapy alone.

**Next Steps**
A phase III study is planned for launch in early 2017. The researchers are also planning a phase II study of IMAB362 in patients with pancreatic cancer.

This study received funding from Ganymed Pharmaceuticals AG.


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