A novel first-in-class antibody can significantly extend median survival when added to standard chemotherapy for patients with advanced gastric cancer.
Salah-Eddin Al-Batran, MD, discussing the results at a press conference

CHICAGO—A novel first-in-class antibody can significantly extend median survival when added to standard chemotherapy for patients with advanced gastric cancer, according to the results of a new study presented at a press briefing at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting, held June 3–7 (abstract LBA4001).

The antibody IMAB362 targets the protein claudin18.2. “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 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 belongs to a family of proteins that make tight junctions, which control the flow of molecules between cells in a layer. In tumors, tight junctions become disrupted, and claudin proteins lose their primary role. Claudin18.2 is also found in a variety of other tumors, including pancreatic, lung, esophageal, and ovarian.

When the IMAB362 antibody attaches 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. It induces antibody-dependent cell-mediated cytotoxicity and complement-dependent cytotoxicity, said Al-Batran.

Chemotherapy is the standard first-line treatment for advanced or recurrent gastric cancer. The addition of trastuzumab to chemotherapy provides some benefit to the group of patients with human epidermal growth factor receptor 2 (HER2)-positive tumors, but only 15% of all gastric cancers are HER2-positive, he noted.

The international, multicenter, randomized, phase II trial included 161 patients with advanced or recurrent gastric or gastroesophageal junction cancer with a specific minimal level of claudin18.2 in the tumor. The patients had not received prior therapy for metastatic cancer and were not eligible to receive HER2 therapy with trastuzumab.

The patients were randomly assigned to receive standard chemotherapy with epirubicin, oxaliplatin, and capecitabine alone or with IMAB362.

Results show that IMAB362 extended the median time to disease progression (7.9 months) as compared with chemotherapy alone (4.8 months). Median overall survival also improved with IMAB362 (13.2 months) vs chemotherapy alone (8.4 months).

Among the patients with the highest levels of claudin18.2, survival advantage was even more pronounced. The median progression-free survival improved from 5.6 months with chemotherapy alone to 7.2 months with IMAB362, and overall survival improved from 9 months with chemotherapy alone to 16.7 months with IMAB362.

The overall response rate was also higher with IMAB362 (39%) vs chemotherapy alone (25%).
The treatment was well tolerated. Neutropenia and vomiting were slightly more common in the IMAB362 group. The rates of severe adverse effects were not increased with IMAB362 compared with chemotherapy alone.

“The trial met its primary endpoint. IMAB362 plus chemotherapy was feasible and well tolerated,” said Al-Batran.

The results provide “a strong rationale for a confirmatory phase III trial,” he said, which is planned to be launched in early 2017. Researchers are also planning a phase II study of IMAB362 in patients with pancreatic cancer.

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