Keytruda Is Comparable or Superior to Chemotherapy for Some Stomach Cancers

The immunotherapy led to an improvement in survival for people with gastric or gastroesophageal junction cancers with a high PD-L1 level.

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Treating advanced gastric or gastroesophageal junction cancer with Keytruda (pembrolizumab) is associated with similar overall survival time compared with chemotherapy in people with PD-L1–positive tumors. Among those whose tumors had high levels of PD-L1 expression, Keytruda treatment yielded superior survival time, according to recent research. However, other measures appeared to favor chemotherapy.

Gastric cancers are stomach cancers while gastroesophageal junction cancers occur at the site where the esophagus meets the stomach.

Keytruda is a PD-1 checkpoint inhibitor, which is a form of immunotherapy that helps the immune system combat cancer. PD-1 is a receptor on the surface of T cells that plays a role in regulating immune function. Some tumors can hijack PD-1 to turn off the very immune responses that would otherwise attack them. Drugs that block PD-1 or its binding partner, known as PD-L1, can essentially release the brakes and restore T-cell activity. People with higher PD-L1 levels in their tumors tend to have a better response to checkpoint inhibitors, but this is not a reliable predictor of individual response.

Keytruda received accelerated approval from the Food and Drug Administration in September 2017 for individuals with recurrent, locally advanced or metastatic gastric or gastroesophageal junction cancer whose tumors express PD-L1 with a combined positive score (CPS) of 1 or greater. Calculating the CPS involves comparing the number of PD-L1–positive cells drawn from biopsied tissue with the number of viable tumor cells.

Josep Tabernero, MD, PhD, head of the medical oncology department at the Vall D'Hebron Barcelona Hospital University Hospital and Institute of Oncology in Barcelona, presented findings from the randomized Phase III KEYNOTE-062 trial at the American Society of Clinical Oncology annual meeting last week in Chicago.

The trial enrolled 763 people who were starting treatment for the first time. They had a median age of 62 years old, and about 75% were men. Over two thirds (69%) had gastric cancer, and 30% had gastroesophageal junction cancer; 26% had previously undergone surgery to remove a tumor.

All of the participants in this study had a PD-L1 CPS of 1 or greater and 281 (37%) had a score of 10 or greater. Previous research has indicated that people with gastric or gastroesophageal junction cancer who have a PD-L1 score of 1 or higher may benefit to a greater extent from Keytruda than those with a lower PD-L1 score. Those with a PD-L1 score of 10 or higher likely stand to benefit to an even greater extent. Their tumors tested negative for human epidermal growth factor receptor 2, meaning they were not susceptible to HER2–targeted therapies like Herceptin (trastuzumab).

The study participants were evenly randomized to receive one of three different regimens:

- 200 milligrams of Keytruda every three weeks for up to 35 cycles (256 people, 253 of whom were treated)
- 200 mg of Keytruda under the same protocol plus fluorouracil or capecitabine chemotherapy (257 people, 251 treated)
- a placebo under the Keytruda protocol plus chemotherapy (257 people, 251 treated)

Treatment continued until the participants experienced unacceptable toxicity or disease progression or they or their physicians decided to discontinue the treatment. The participants were followed for a median of 11.3 months.

The overall survival rate was comparable between those who received Keytruda alone and those who received chemotherapy alone. The two groups had respective median overall survival times of 10.6 months and 11.6 months, a difference that was not statistically significant, meaning it could have been driven by chance.

Those with a PD-L1 score of 10 or greater had a clinically meaningful improvement in overall survival rate when treated with Keytruda rather than chemotherapy, Tabernero reported. The two groups had respective median overall survival times of 17.4 months and 10.8 months. This meant that Keytruda reduced the risk of death by 31% during the follow-up period. Two years into the study, 39% of those receiving Keytruda and 22% of those receiving chemotherapy were still living.

However, overall response rates, meaning complete or partial tumor shrinkage, appeared to favor chemotherapy. Response rates were numerically lower with Keytruda compared with chemotherapy, both for those with a PD-L1 score of 1 or greater (14.8% versus 37.2%) and for those with scores of 10 or greater (25.0% versus 37.8%, respectively).

Combining Keytruda and chemotherapy did not lead to an improvement in overall survival for those with PD-L1 scores of 1 or greater (12.5 months with Keytruda plus chemotherapy versus 11.1 months with chemotherapy alone) or 10 or greater (12.3 months versus 10.8 months, respectively). However, overall response rates favored the combination.

Keytruda was better tolerated than chemotherapy: 16% of those receiving Keytruda alone experienced severe (grade 3) or higher treatment-related adverse events, compared with 68% of those receiving just chemotherapy and 71% of those receiving the combination. Rates of discontinuation because of side effects were 4%, 18% and 27%, respectively. The most common side effects were nausea, fatigue and decreased appetite. Keytruda's safety profile proved consistent with previous studies of the treatment.

The study authors are currently further parsing their data to better understand who benefitted most from Keytruda. Tabernero told ASCO attendees that the field needs better biomarkers than PD-L1 to more precisely identify who might respond best to the treatment, whether given alone or in combination with chemotherapy.

Commenting on the study, ASCO senior vice president and chief medical officer Richard L. Schilsky, MD, said, "Chemotherapy has been our only option for many years. These results introduce a potential alternative in pembrolizumab that comes with fewer side effects, and, importantly, for some it can greatly extend survival. This opens the door to helping patients live longer and better lives."

To read the conference abstract, click here.

To read an ASCO press release about the study, click here.

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