

Bispecific immune checkpoint inhibitor improves survival in gastric cancer patients regardless of PD-L1 status

April 8 2024



Credit: Tima Miroshnichenko from Pexels

The PD-1/CTLA-4 bispecific antibody cadonilimab plus chemotherapy improved progression-free survival and overall survival in patients with untreated, HER2-negative, locally advanced or metastatic gastric or gastroesophageal junction (GEJ) cancer, including those with PD-L1-low tumors, compared with chemotherapy alone, according to results from the phase III [COMPASSION-15](#) trial presented at the [American Association for Cancer Research \(AACR\) Annual Meeting 2024](#), held April 5–10.

Immune checkpoint inhibitors (ICIs), including those that target the PD-1/PD-L1 checkpoint pathway, are approved by the U.S. Food and Drug Administration (FDA) for the first-line treatment of gastric and GEJ cancers that do not express HER2. However, ICIs are typically most effective in patients whose tumors express high levels of PD-L1.

For patients whose tumors have low PD-L1 expression, treatment options are limited, explained Jiafu Ji, MD, Ph.D., DrPh, a professor at the State Key Laboratory of Holistic Integrative Management of Gastrointestinal Cancers, the Beijing Key Laboratory of Carcinogenesis and Translational Research, and the Gastrointestinal Cancer Center at Peking University Cancer Hospital & Institute in Beijing.

"In many countries, chemotherapy is still the optimal treatment option for these patients, who have an overall survival of less than a year," Ji said. "There is a great unmet medical need to explore new treatment options for patients with PD-L1-low, HER2-negative gastric and GEJ cancer."

Cadonilimab is a bispecific antibody that inhibits both PD-1 and another immune checkpoint protein, CTLA-4. It is approved for use in China to treat patients with relapsed or metastatic cervical cancer following

treatment with [platinum-based chemotherapy](#). "We anticipated that by blocking both PD-1 and CTLA-4, cadonilimab plus chemotherapy could yield longer survival than a PD-1 inhibitor plus chemotherapy," Ji said.

Ji and colleagues launched the COMPASSION-15 trial, which enrolled 610 patients with untreated, unresectable, HER2-negative, locally advanced or metastatic gastric/GEJ cancer. Patients were randomly assigned (1:1) to receive cadonilimab plus capecitabine/oxaliplatin chemotherapy or placebo plus chemotherapy.

Overall, patients in the cadonilimab arm had a median [progression-free survival](#) of 7 months and a [median overall survival](#) of 15 months.

Patients in the placebo arm had a median progression-free survival of 5.3 months and a median overall survival of 10.8 months. The overall response rate was 65.2% with a median response duration of 8.8 months in the cadonilimab arm and 48.9% with a median response duration of 4.4 months in the placebo arm.

A survival benefit was also observed in the subgroup of patients with low PD-L1 (defined as a visualized combined positive score of less than 5%). Those in the cadonilimab arm had a progression-free survival of 6.9 months and an overall survival of 14.8 months, compared with 4.6 months and 11.1 months, respectively, in the placebo arm.

Ji explained that tumors with low expression of PD-L1 may rely on other immune checkpoints, such as CTLA-4, and may therefore respond to CTLA-4 inhibition. "Dual blockade of PD-1 and CTLA-4 may improve the sensitivity of patients with PD-L1 low tumors to immunotherapy," Ji said. "Moreover, there may be synergistic effects between the targets of the two bispecific antibodies, and further mechanistic studies are needed."

These data represent an interim analysis of COMPASSION-15, and the

researchers will continue monitoring the enrolled patients to assess long-term outcomes. In the meantime, they have submitted cadonilimab plus chemotherapy to the China National Medical Products Administration for approval in this patient population.

"These findings may change the current practice of gastric cancer treatment," Ji said. "Cadonilimab combined with chemotherapy could become a new standard of care in first-line treatment of gastric cancer, even for patients with low PD-L1 expression."

Limitations of this study include the inclusion of only Chinese patients, which may limit the applicability of the results to other regions.

Provided by American Association for Cancer Research

Citation: Bispecific immune checkpoint inhibitor improves survival in gastric cancer patients regardless of PD-L1 status (2024, April 8) retrieved 2 May 2024 from <https://medicalxpress.com/news/2024-04-bispecific-immune-checkpoint-inhibitor-survival.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.