Clinical trial tests combination antibody therapy in adults with advanced cancer

February 26 2024

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In an early-phase clinical trial, a combination of antibody-based medications targeting the immune system generated promising safety data and anti-tumor activity in individuals with various types of

advanced cancer. The findings are published in *Cancer*.

Both medications tested in the trial support immune responses against tumor cells. CS1002 increases the activation and proliferation of T immune cells by binding to a T cell receptor called CTLA-4. CS1003, also called nofazinlimab, blocks the programmed cell death protein 1 that is expressed on various types of immune cells and plays a role in suppressing the immune system.

In this first-in-human multicenter, open-label study conducted from April 26, 2018, to January 18, 2022, at 9 study sites in Australia and China, phase Ia involved monotherapy dose-escalation (Part 1), which was followed by phase Ib combination therapy dose escalation (Part 2) and expansion (Part 3). Various dosing schedules of CS1002 (0.3, 1, or 3 mg/kg once every 3 weeks, or 3 mg/kg once every 9 weeks) were evaluated with 200 mg CS1003 once every 3 weeks.

Parts 1, 2, and 3 of the trial included 13, 18, and 61 patients, respectively, who had advanced/metastatic solid, relapsed, or refractory tumors. During treatment, investigators did not observe any dose-limiting toxicities or a maximum tolerated dose.

Treatment-related side effects such as diarrhea, fatigue, and rash were reported in 30.8%, 83.3%, and 75.0% of patients in Parts 1, 2, and 3, respectively. Serious side effects such as intestinal inflammation and severe skin reactions were experienced by 15.4%, 50.0%, and 18.3% of patients in each part.

Of 61 patients evaluable for treatment efficacy, 23 (37.7%) with different types of tumors experienced a positive response. Higher response rates occurred with conventional and high-dose CS1002 regimens (1 mg/kg once every 3 weeks or 3 mg/kg once every 9 weeks) compared with low-dose CS1002 (0.3 mg/kg once every 3 weeks) in

certain cancers such as melanoma and skin cancer.

"CS1002 in combination with CS1003 had manageable safety profile across a broad dosing range and showed promising anti-tumor activities across CS1002 dose levels when combined with CS1003," the investigators wrote. "This supports further assessment of CS1002 in combination with CS1003 for the treatment of solid tumors."

More information: Dual CTLA-4 and PD-1 checkpoint blockade using CS1002 and CS1003 (nofazinlimab) in patients with advanced solid tumors: A first-in-human, dose-escalation, and dose-expansion study, *Cancer* (2024). DOI: 10.1002/cncr.35226 doi.wiley.com/10.1002/cncr.35226

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