CLINICAL ROUNDUP

Botensilimab + balstilimab showed no CRC recurrences in resectable colon cancer, phase II NEST trial shows

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The phase II NEST trial evaluating neoadjuvant botensilimab, a multifunctional, Fc-enhanced anti-CTLA-4 antibody, and balstilimab, an anti-PD-1 antibody, showed no colorectal cancer recurrences in patients with resectable colon cancer.

The results of the clinical trial were published in *Clinical Cancer Research.*

Botensilimab and balstilimab are sponsored by Agenus.

Earlier findings from NEST were presented at the 2025 ASCO Gastrointestinal Cancers Symposium. The publication provides longer follow-up and a fuller peer-reviewed analysis of tumor responses, circulating tumor DNA dynamics, disease-free follow-up and immune changes in the tumor microenvironment.

At the March 31 data cutoff, no colorectal cancer recurrences had been observed, with median follow-up of 32.2 months in NEST-1 and 23.5 months in NEST-2.

Among 22 mismatch repair proficient/microsatellite stable tumors, 59% achieved a pathologic response, including 41% with a major pathologic response and 32% with a pathologic complete response.

MSS/pMMR tumors represent approximately 85% of early-stage colorectal cancers and have historically derived limited benefit from conventional immunotherapy treatment, particularly in metastatic disease.i,ii In localized colon cancer, treatment remains centered on surgery and chemotherapy, creating a need for approaches that may deepen response and reduce recurrence risk.

Administering immunotherapy before surgery offers a distinct biological opportunity to activate the immune system while the primary tumor, tumor-draining lymph nodes and surrounding immune microenvironment remain intact.

The publication adds peer-reviewed clinical and biological support for Agenus' previously announced decision to prioritize BOT+BAL in earlier-stage, curative-intent MSS colon cancer.

Agenus is advancing ROBBIN, a planned global randomized phase III trial evaluating neoadjuvant BOT+BAL followed by standard of care versus standard of care alone in previously untreated patients with high-risk stage II or stage III MSS colon cancer, with event-free survival as the primary endpoint.

NEST's deep tumor regression, pre-surgical ctDNA clearance, preserved surgical timing and no observed recurrences at longer follow-up supports the clinical hypothesis ROBBIN is designed to test.

"NEST provides important context for Agenus' strategic focus on neoadjuvant BOT+BAL in MSS colon cancer," Steven O'Day, chief medical officer of Agenus, said in a statement. "With longer follow-up now extending beyond two years across both NEST cohorts, the findings show BOT+BAL can generate deep tumor responses and immune activation before surgery, without delaying surgery. These results strengthen the rationale for our phase 3 ROBBIN trial and for evaluating BOT+BAL in a curative-intent setting, where the goal is to reduce the risk of recurrence and improve long-term outcomes."

NEST was a single-center, open-label, single-arm phase II study that enrolled 24 eligible patients with 26 resectable colorectal tumors, including 22 pMMR/MSS tumors and four dMMR/MSI-H tumors. The study evaluated two pre-surgical treatment intervals; approximately four weeks in NEST-1 and approximately eight weeks in NEST-2. Patients in both cohorts proceeded to planned surgical resection without treatment-related delays.