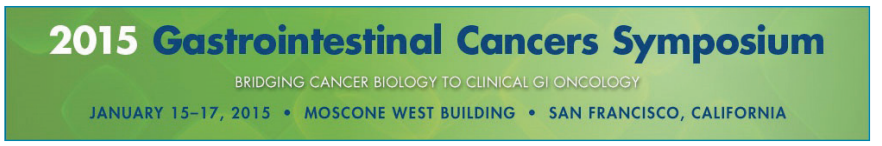
Vitamin D Levels Linked to Colorectal Cancer Progression and Survival

BY ED SUSMAN

SAN FRANCISCO—Patients with advanced colorectal cancer who present with higher levels of vitamin D in their plasma appear to have a greater likelihood of living longer and having a longer interval before their disease progresses, according to data reported here at the Gastrointestinal Cancers Symposium (***Abstract 507***).

When those patients with the highest levels of 25-hydroxy vitamin D were compared with patients whose blood work showed the lowest levels, there was a 12-month longer overall survival, said Kimmie Ng, MD, MPH, Assistant Professor of Medicine at Dana-Farber Cancer Institute/Harvard Medical School, speaking in a teleconference for reporters in advance of the meeting.



The meeting is sponsored by the American Gastroenterological Association Institute, American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology.

Ng said patients in the highest quintile of vitamin D levels had a median overall survival of 32.6 months compared with 24.5 months for patients with the lowest levels.

"We divided the 25-hydroxy vitamin D levels into quintiles for the purposes of our analysis," she said. Patients in the lowest quintile had median 25-hydroxy vitamin D levels of 8 ng/mL compared with those in the highest quintile who had a median level of 27.5 ng/mL, she said.

The research team subjected their findings to multivariate analysis to test whether known prognosis factors and diet and lifestyle factors could have played a role in the findings. "Our base model adjusted for age and season of blood draw and the hazard ratio for survival when the highest quintile was compared with the lowest was 0.64 (p=0.0003), she said.

"After adjusting for additional known prognostic factors as well as potential confounders the significant association between higher vitamin D levels and better survival persisted with a hazard ratio of 0.65 when comparing extreme quintiles—P=0.001," she said.

"We took great pains to try to control for lifestyle factors and other indicators for health that may potentially explain what we found. But even adjustment for obesity or lack of activity or markers of poor health did not change our results that higher vitamin D levels seem to be associated with better survival.

"We also tried to address this issue by excluding patients who died very quickly after their blood levels were measured. These tend to be the patients with most aggressive disease and tend to do more poorly. But even after excluding that group of patients, the persistence of the significant relationship between higher levels of vitamin D and survival was still seen."

ASCO/Todd Buchanan

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Same for PFS

The story was similar when the researchers scrutinized the secondary endpoint of the study of progression-free survival. Patients with levels in the highest quintile had a median progression-free survival of 12.2 months compared with 10.1 months for those in the lowest quintile, Ng said.

In multivariable analysis, the base model adjusted for age and season of blood draw had a hazard ratio of 0.80 comparing extreme quintiles. Again, after adjusting for multiple known prognostic factors as well as potential confounders, the significant relationship between higher vitamin D levels and improved progression-free survival persisted, she said.

Another analysis showed that all the adjusted hazard ratios favored higher vitamin D levels when the patients and outcomes were stratified by various demographic and disease factors.

'Adds to the Literature'

Commenting on the results, the moderator of the news conference, Smitha Krishnamurthi, MD, Associate Professor of Hematology and Oncology at Case Western Reserve University School of Medicine, said: "This study will be of great interest to patients with colorectal cancer who frequently want to know if there is anything they can do besides chemotherapy to improve their outcomes. This study adds to the literature that suggests that vitamin D may have protective effects on colorectal polyps and could help patients with colorectal cancer live longer.

"Of note is that patients in this study with the highest levels of vitamin D have the longest survival and also that progression-free survival was improved, suggesting that in highest levels there are slower-growing tumors and the higher level of vitamin D may enhance the effects of chemotherapy."

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iPad Extra!

Listen to Dr. Ng elaborate on her findings in a podcast report on the iPad edition of this issue with *OT* reporters Sarah Maxwell and Peter Goodman in an interview at the symposium.

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VITAMIN D

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Too Early for a Recommendation

Ng said the ultimate goal is to translate the research into an effective intervention for patients by conducting randomized trials of vitamin D supplementation for treatment of colorectal cancer. "It is too early to recommend vitamin D as a treatment for colon cancer, but we do know that maintaining adequate vitamin D levels has other health benefits, such as for bone health."

Krishnamurthi agreed that it is premature to suggest the study would call for a recommendation for supplementation: "We really need a randomized controlled trial of vitamin D supplementation versus placebo to know if vitamin D really has anti-cancer effects. "Until then, patients should have their vitamin D levels checked and undergo supplementation if needed because we know vitamin D is necessary for bone health.

Built on Team's Earlier Investigations

Ng and colleagues have been studying the effects of vitamin D in cancer for several years and this trial was built on previous investigations. "Vitamin D is known to inhibit cell proliferation and angiogenesis; it induces cell differentiation and apoptosis and has anti-inflammatory effects. Obviously many of these processes are dysregulated in cancer, which led to the hypothesis that perhaps vitamin D has anti-cancer activity," she explained.

> "The results suggest that in the highest levels of vitamin D there are slower-growing tumors and the higher level of vitamin D may enhance the effects of chemotherapy."

She noted that laboratory data supported the hypothesis, with experiments demonstrating that the administration of vitamin D to mouse models of intestinal cancer results in decreased tumor burden. "Epidemiologic studies also support this hypothesis, with multiple prospective observational studies reporting that higher levels of vitamin D in the blood are significantly associated with decreased risk of colorectal cancer as well as increased survival of patients already diagnosed with colorectal cancer.

"Our previous work has also demonstrated that metastatic colorectal cancer patients are commonly deficient in vitamin D," she said. "This is concerning because we believe that higher levels of vitamin D may be beneficial."

Study Details

For the Phase III, prospective observational study, which was supported by the National Cancer Institute, the researchers enrolled 1,043 metastatic colorectal cancer patients, who were a subgroup of a Phase III randomized Intergroup trial of first-line chemotherapy plus biologics. Vitamin D levels in blood samples were measured that had been collected prior to treatment, and patients also completed diet and lifestyle questionnaires.

The median 25-hydroxy vitamin D level in plasma—the best indicator of vitamin D status—in the overall study cohort was 17.2 ng/mL, Ng said. "This falls into the deficient range, which is typically defined as a 25-hydroxy vitamin D level of less than 20 ng/mL."

"For now, patients should have their vitamin D levels checked and undergo supplementation if needed because we know vitamin D is necessary for bone health."