

## Higher Vitamin D Levels and 'Markedly' Improved CRC Survival

Roxanne Nelson | January 13, 2015

Higher levels of vitamin D were associated with "markedly" improved survival in patients with advanced colorectal cancer in a prospective study of more than 1000 patients.

Median overall survival was significantly better in patients with the highest vitamin D levels than in those with the lowest levels (32.6 vs 24.5 months; hazard ratio [HR], 0.67; *P* trend < .002).

Higher levels were also associated with better progression-free survival (10.1 vs 12.2 months; *P* = .02).

The results were consistent across subgroups, such as *KRAS* mutation status, after adjustment for various prognostic factors.

This was an observational study, not a randomized study, emphasized lead author Kimmie Ng, MD, MPH, assistant professor of medicine at the Dana-Farber Cancer Institute, Harvard Medical School, in Boston.

"But it still adds to the growing evidence that suggests that maintaining higher levels of vitamin D may be beneficial in colorectal cancer," she told *Medscape Medical News*. "It is the largest study to date of metastatic colorectal cancer patients and vitamin D."

Dr Ng spoke at a press briefing held in advance of the 2015 Gastrointestinal Cancers Symposium in San Francisco, where the study will be presented.

Despite these results, it is too early to recommend vitamin D as a treatment for colorectal cancer. "We need to do a randomized controlled trial," said Dr Ng. "Even though vitamin D is pretty benign, we really don't know the effect on cancer patients until we put it to a rigorous test."

However, maintaining adequate vitamin D levels has other benefits, such as improving bone health, and it would be beneficial for a cancer patient whose levels are low to bring them up to what is considered optimal ranges, she explained.

Current practice guidelines from the Endocrine Society define vitamin D deficiency as levels below 20 ng/mL.

Even though many people do get their vitamin D levels checked, it is usually in the primary care setting or by a nutritionist; it is not the standard of care to check levels in oncology.

"I discuss the data with my patients, and if they are interested, we check their levels. If they're low, they are supplemented to bring them up to sufficient levels," Dr Ng said.

Presscast moderator Smitha S. Krishnamurthi, MD, from the Case Western Reserve University School of Medicine in Cleveland, said she agrees that a randomized trial is needed to see if vitamin D really has anticancer effects. Until then, "cancer patients should have their vitamin D levels checked and undergo supplementation if needed."

She noted that these data will be of great interest to colorectal cancer patients who frequently want to know if there is anything they can do, other than chemotherapy, to improve their outcomes.

"This study adds to the literature that suggests that vitamin D may have protective effects in preventing colorectal polyps and can help cancer patients live longer," said Dr Krishnamurthi.

### Data Support Previous Research

A number of studies have examined the relation between cancer risk and vitamin D levels, and some data have suggested that higher blood levels of vitamin D are linked to a reduced risk for colorectal cancer.

One study published last year found that higher vitamin D levels were linked to better survival in colorectal cancer patients, and another found the same effect for lymphoma and breast cancer.

Dr Ng was involved in a previous study of about 300 patients with colorectal cancer (*J Clin Oncol.* 2008;26:2984-2991). "We found that patients who had higher vitamin D levels prior to diagnosis seemed to live longer," she said. "But that was a small study, it included patients with all stages of disease, and the levels were measured before their cancer diagnosis."

However, she noted, in that study, preliminary findings showed that the benefit of vitamin D seemed to be greatest in patients with more advanced disease.

Even though there is biologic plausibility, and multiple studies have shown a positive trend toward improvements in outcomes, there are insufficient prospective randomized trials. It is difficult to show a causal link between vitamin D levels and survival without definitive evidence.

### Wide Range of Levels

In their study, Dr Ng and colleagues prospectively assessed the association between plasma 25-hydroxyvitamin D (25[OH]D) and overall survival in 1043 untreated patients with metastatic colorectal cancer who were enrolled in CALGB 80405, a randomized phase 3 trial of chemotherapy plus bevacizumab, cetuximab, or both.

Overall survival was the primary end point and progression-free survival was a secondary end point.

Blood levels of 25(OH)D were measured at the time of enrollment in the CALGB 80405 study, and information about diet and lifestyle was obtained from self-administered questionnaires.

To address the possibility of reverse causation, patients who died within 6 months of the blood draw were excluded from sensitivity analyses.

The median plasma level of 25(OH)D in the cohort was 17.2 ng/mL (range, 2.2 to 72.7 ng/mL). The recommended range is 20 to 30 ng/mL.

On multivariate analysis, the data were adjusted for age, sex, race, Eastern Cooperative Oncology Group (ECOG) performance status, chemotherapy backbone, previous adjuvant chemotherapy, assigned biologic, Ras mutation status, body mass index, physical activity, season of blood draw, and geographic region.

Levels of 25(OH)D were significantly lower in patients who were older, black, had a low dietary and supplemental vitamin D intake, had an ECOG performance status of 1 (as opposed to 0), had a higher body mass index, were less physically active, and had blood draws taken during the winter and spring. Levels were also lower for those living in the Northern and Northeastern parts of the United States.

On average, patients in the quintile with the highest vitamin D level survived 33% longer than those in the lowest quintile.

### Future Steps

The next step is a randomized double-blind phase 2 trial of patients receiving standard chemotherapy and bevacizumab. The 120 patients will be randomized to one of two groups. One group will receive the standard dose

of 400 IU of vitamin D — an amount that "really doesn't significantly raise blood levels," according to Dr Ng. "The other group will receive 8000 IU a day for 2 weeks as a loading dose and then 4000 IU a day as a maintenance dose. We will see if progression-free survival is improved with the higher doses," she explained.

To date, about 80 patients have been enrolled at multiple centers around the country, Dr Ng reported.

*This study received funding from the National Cancer Institute at the National Institutes of Health. Dr Ng reports serving as a consultant or in an advisory role for Genentech/Roche, McCann Regan Campbell Ward, Havas Life Metro, and CBPartners; receiving travel, accommodations, and expenses from Gilead Sciences; and receiving research funding (institutional) from Genentech/Roche and Pharmavite LLC. Several coauthors report financial relationships with industry, as noted in the abstract.*

2015 Gastrointestinal Cancers Symposium (GICS): Abstract 507. Presented January 17, 2015.

Medscape Medical News © 2015 WebMD, LLC

Send comments and news tips to [news@medscape.net](mailto:news@medscape.net).

Cite this article: Higher Vitamin D Levels and 'Markedly' Improved CRC Survival. *Medscape*. Jan 13, 2015.