SUNSHINE: Randomized double-blind phase II trial of vitamin D supplementation in patients with previously untreated metastatic colorectal cancer.

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Abstract Disclosures

Abstract:

Background: In prospective observational studies of mCRC patients, higher plasma levels of 25-hydroxyvitamin D have been associated with improved progression-free (PFS) and overall survival (OS), but the role of vitamin D supplementation in the treatment of mCRC is unknown. 

Methods: SUNSHINE was a multi-center double-blind phase II randomized controlled trial in previously untreated mCRC patients. Patients were eligible if they had histologically confirmed mCRC, no prior therapy for metastatic disease, ECOG PS 0-1, and were not taking vitamin D >2,000 IU/day x 1 year. All subjects received standard treatment with mFOLFOX6 + bevacizumab with 1:1 randomization to concurrent: HiVitD (vitamin D3 po 8,000 IU/d x 2 wks as loading dose followed by 4,000 IU/d) or LowVitD (standard vitamin D3 400 IU/d) until disease progression, intolerable toxicity, or withdrawal of consent. The primary endpoint was PFS, with the sample size designed to provide 80% power to detect a HR of 0.66 for PFS at a 1-sided alpha=0.2. 

Results: From April 2012 to November 2016, 139 patients were randomized. Median age was 54 yrs (range 24-82), 57% were male, 77% were white, and 7% had received prior adjuvant chemo. Baseline characteristics were balanced between arms except ECOG PS = 0 was 42% vs. 60% in HiVitD vs. LowVitD. Median follow-up was 16.1 mos (range 0-45.9) and median compliance with VitD capsules was 98%. Patients randomized to HiVitD experienced longer PFS than those receiving LowVitD (median PFS, 12.4 vs. 10.7 mos, respectively; log rank P=0.03). After multivariate adjustment for prognostic variables, HR was 0.66 (95% CI, 0.45-0.99, 2-sided P=0.04). Comparing HiVitD vs LowVitD, RR was 58% vs. 63% (P=0.54) and disease control rate was 100% vs. 94% (P=0.05). The most common grade 3-4 toxicities were as expected for FOLFOX-bevacizumab, and none were related to vitamin D. Currently, 14 patients are still actively receiving treatment, and OS data are not yet mature. 

Conclusion: SUNSHINE met its prespecified primary endpoint, with patients randomized to HiVitD experiencing longer PFS compared to those randomized to LowVitD. A larger confirmatory phase III randomized trial appears warranted. Clinical trial information: NCT01516216