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# Role of dietary polyamines in a phase III clinical trial of DFMO and sulindac for prevention of metachronous colorectal adenomas.

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## Abstract

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**Background:** Our group has previously demonstrated that polyamine-inhibitory regimen difluoromethylornithine (DFMO) plus sulindac vs. placebo has marked efficacy in preventing metachronous colorectal adenomas in a phase-III trial. Polyamines are synthesized endogenously but also obtained from diet. Here we investigate the role of dietary polyamines in the phase III placebo controlled colorectal adenoma prevention trial with DMFO + sulindac.

**Methods:** Dietary polyamine data were available for 222 of 375 baseline study patients, and for 188 of 267 patients completing the study. A dietary questionnaire completed by each patient was collected at the initiation of the study. Total dietary polyamine content was derived by the sum of dietary putrescine, spermine and spermidine values and further categorized into highest (75%-100%) quartile group vs. a group with lower three quartiles (0-25, 25-50 and 50%-75%). Baseline tissue polyamine concentration was determined using HPLC methodology. Linear and logistic regression analyses were used for risk estimation.

**Results:** A significant direct association was observed between dietary polyamine intake and tissue spermidine ( $p = 0.02$ ) and spermine concentrations ( $p = 0.04$ ) at baseline. Higher dietary polyamine group at baseline was associated with adenomas  $> 1$  cm (43.6 % vs. 26.4 %;  $p = 0.01$ ), high grade adenomas (32.7% vs. 20.4 %;  $p = 0.06$ ) and advanced adenomas (52.7% vs. 35.9 %;  $p = 0.02$ ). Among all patients, a significant interaction was observed between treatment, dietary polyamines and the risk of metachronous adenomas ( $p = 0.01$ ). Therefore we stratified the final analyses ( $n = 188$ ) by polyamine intake groups. We observed a significant risk reduction of metachronous adenomas from treatment with DFMO+sulindac in the lower dietary polyamine group (RR = 0.19 [0.09-0.40]  $p < 0.0001$ ) and no benefit in the higher dietary polyamine group (RR = 1.04 [0.32-3.36]  $p = 0.94$ ).

**Conclusions:** Controlling dietary polyamines may be an effective strategy for preventing the occurrence of colorectal adenomas and colorectal cancer.

Author Disclosure

Employment or Leadership Position	Consultant or Advisory Role	Stock Ownership	Honoraria	Research Funding	Expert Testimony	Other Remuneration
	Cancer Prevention Pharmaceuticals	Cancer Prevention Pharmaceuticals				