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Oral diindolylmethane (DIM): pilot evaluation of a nonsurgical treatment for cervical dysplasia.

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Abstract

OBJECTIVE: Standard surgical treatment for CIN may impair fertility generating a need for alternative treatment options. We tested the efficacy and toxicity of oral DIM in the treatment of CIN 2 or 3 lesions.

METHODS: Patients with biopsy-proven cervical intraepithelial neoplasia (CIN) 2 or 3 scheduled for loop electrosurgical excision procedure (LEEP) were randomized 2:1 to receive diindolylmethane (DIM) (BioResponse-DIM, BioResponse, Boulder, CO) orally at approximately 2 mg/kg/day for 12 weeks or placebo (defatted rice bran, BioResponse). Subjects were evaluated every 3-4 months for 1 year. Analysis of data up to 1 year was assessed including Pap smear, HPV, colposcopy, biopsy and physical examination were performed at follow-up. Central pathology review confirmed all histology diagnoses.

RESULTS: To date, 64 subjects (mean age 28 years, range 18-61) have been enrolled (45 in the DIM arm, 19 in the placebo arm), with 60 available for analysis. Average follow-up was 6 months. At enrollment, 58% were diagnosed with CIN 2 and 42% with CIN 3, 57% of subjects were Caucasian, 15% African American, 12% Hispanic and 17% Asian. During treatment 2 subjects (3%) complained of nausea (grade 2) at the 3- to 4-month visit. No systemic toxicities were observed (normal CBC, LFTs, comprehensive metabolic). Forty-six subjects had biopsies at first follow-up (77%). Twenty-one subjects (47%) in the DIM group had improved CIN with a decrease by 1-2 grades or a normal result. Median time to improvement was 5 months. Improved Pap smear was seen in 49% (22/45) with either a less severe abnormality or normal result. Colposcopy improved in twenty-five subjects in the DIM group (56%). Of these 25 subjects, 21 (84%) had improved colposcopic impression, 13 (52%) had a decrease in involved quadrants and 18 (72%) had a decrease in lesion number. Complete colposcopic response was observed in 4 subjects (9%). Stratifying by level of dysplasia, age, race, HPV status, tobacco use, contraceptive used did not alter the results. At median follow-up of 6 months, 85% of subjects have not required LEEP based on routine clinical triage of improving global assessment. There was no statistically significant difference in any outcome between the DIM and placebo group.

CONCLUSION: Oral DIM at 2 mg/kg/day is well tolerated with no significant toxicity. We observed a high rate of clinically significant improvement in confirmed CIN 2 or 3 lesions among both treatment groups in this randomized clinical trial.

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